

**EUROPEAN ORGANISATION FOR RESEARCH  
AND TREATMENT OF CANCER**

**2001-2002**



**EORTC**

**ORGANISATION, ACTIVITIES AND CURRENT RESEARCH**



# FOREWORD

It is with great sadness that we report the EORTC founder, Prof. Henri Tagnon, passed away at the age of 89 in December 2000. He was not only a great advocate of pan-European controlled clinical studies to improve cancer treatment, but also believed in close co-operation between the different disciplines and thereby introduced a multi-disciplinary approach in Europe. He was EORTC President from 1975-1978 and was very instrumental in the creation of the EORTC Foundation in 1976. Since Prof. Tagnon's initiative to create the "Groupe Européen de Chimiothérapie Anticancéreuse" in 1962, the EORTC has grown tremendously, and it is currently a unique network to establish state-of-the-art-treatment for patients with cancer.

Until last year the EORTC Foundation was chaired by Sir Ronald Grieron and it is now chaired by Sir Christopher Mallaby.

Her Majesty the Queen of Sweden is the Honorary President of the EORTC Foundation. Her Majesty attended the Board and Council of the EORTC Foundation held at the EORTC headquarters on 8<sup>th</sup> March 2001. Thanks to the EORTC Foundation and to the various European cancer leagues supporting EORTC activities, the EORTC shall enter the new Millennium with a stronger position and an increased number of dedicated staff. The Brussels' headquarters has increased from 79 employees in 2000 to 107 in 2001 and now represents 16 different nationalities, which truly reflects the international character of this unique network. The EORTC Data Center Fellowship Program remains very successful – in 2000, 13 fellows have been trained at the EORTC Data Center.

Undoubtedly, over the past decades, cancer research and cancer care have shown significant progress. Recent achievements on novel targets and treatment concepts have been developed and show encouraging signs for today's patients with cancer and for generations to come.

Major changes at the EORTC Headquarters in 2000 include:

- The initiation of the EORTC's virtual tumor bank project which will be carried out over a period of three years. The aim of this project, conducted by the EORTC Pathology Group, in co-operation with the EORTC Data Center, and some disease-oriented groups is to standardise histopathological review methods for EORTC trials and to promote translational research in clinical trials.
- An Intergroup Office has also been set up at the EORTC Data Center to enhance international co-operation in clinical research, by providing expertise and support for large-scale intergroup studies. Intergroup studies are more and more essential to speed up the development of anti-cancer treatments; an increasing number of collaborations are taking place within Europe, and also with US and Australian groups.

Large clinical trials face organisational and procedural difficulties, financial problems relating to international co-operation and complications stemming from different national regulations. The EORTC Intergroup Office will try to overcome this lack of harmonization and the related logistical challenges.

As of December 2000, about 50 "large clinical trials" (defined as those involving more than 900 patients) were open to patient entry and conducted by EORTC Groups alone or with other

international research groups.

- The New Drug Development Program (NDDP) now coordinates more than 20 clinical trials on 13 new agents which have included more than 300 patients. It is providing support to the Early Clinical Studies Group and Biological Therapeutic development Group as well as to laboratory research groups and other disease oriented groups involved in joint studies with the Early Clinical Studies Group.

Because of the increasing number of important developments in the oncology field, the NCI-EORTC meetings will be organised yearly, rotating venues between Europe and the USA in cooperation with AACR. The next European meeting is scheduled in Frankfurt in 2002, whereas, the 12<sup>th</sup> AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics will be organised in Miami in 2001.

2001 sees the existence of the 1<sup>st</sup> EORTC Translational Research Meeting scheduled in June in Brussels, recognising the importance of Translational Research in contemporary clinical trials and the responsibility for the implementation of Translational Research in EORTC trials.

The EORTC has also established a permanent Independent Data Monitoring Committee. The inaugural meeting of the EORTC Independent Data Monitoring Committee was held in February 2001.

The EORTC will celebrate, its 40<sup>th</sup> Anniversary in 2002 and on that occasion, the EORTC Scientific Strategy Meeting (ESSM) will be organised on 26-28 March 2002 in Brussels. This occasion will allow the EORTC to review its past research and achievements and mainly to discuss its strategies for the future.

Last but not least, I would like to take this opportunity to congratulate Professor Jean-Claude Horiot, past President of the EORTC, Professor of Radiotherapy and Director of the Regional Cancer Institute of Dijon, on receiving the Distinguished Alumnus Award from M.D. Anderson. Prof. Horiot is the first European former trainee awarded this honour.

Finally, I wish to express my acknowledgement to all EORTC officers, investigators, members and staff for their contribution, enthusiasm and dedication to our EORTC's mission. I am confident that with a strong EORTC and with continuous efforts and perseverance, we will improve the standard of cancer treatment which will benefit all patients in Europe.

March, 2001

A. T. van Oosterom  
EORTC President

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All EORTC officers are listed in the Directory, page 28



# STRUCTURE AND ORGANISATION

## WHAT IS THE EORTC?

### AIMS

The aims of the European Organisation for Research and Treatment of Cancer (EORTC) are to conduct, develop, coordinate, and stimulate laboratory and clinical research in Europe to improve the management of cancer and related problems by increasing survival but also patients' quality of life. Extensive and comprehensive research in this wide field is often beyond the means of individual European laboratories and hospitals, and can best be accomplished through the multidisciplinary, multinational efforts of basic research scientists and clinicians from the European continent.

The ultimate goal of the EORTC is to improve the standard of cancer treatment in Europe, through the development of new drugs and other innovative approaches, and to test more effective therapeutic strategies, using drugs which are already commercially available, or surgery and radiotherapy. During the last few years, numerous innovative agents have been discovered as a result of tremendous development in the understanding of the molecular basis of cancer. Further clinical progress in cancer treatment will be accomplished mainly through the conduct of translational research projects, efficient new drug development and the execution of large, prospective, randomized, multicenter cancer clinical trials. In this way the EORTC facilitates the passage of experimental discoveries into state-of-the-art treatment and minimizes the delay between the discovery of new anti-cancer drugs and their therapeutic benefit for patients with cancer.

### HISTORY

The organisation was founded as an international organisation under Belgian law in 1962 by eminent oncologists working in the main cancer research institutes of the EU countries and Switzerland. It was named "Groupe Européen de Chimiothérapie Anticancéreuse" (GECA), and became the "European Organisation for Research and Treatment of Cancer" (EORTC) in 1968.

### EORTC PRESIDENTS

Georges Mathé (Villejuif, France)	1962-1965
Silvio Garattini (Milan, Italy)	1965-1968
Dirk Willem Van Bakkum (Rijswijk, The Netherlands)	1969-1975
Henri J. Tagnon (Brussels, Belgium)	1975-1978
Laszlo George Lajtha (Manchester, United Kingdom)	1979-1981
Carl Gottfried Schmidt (Essen, Germany)	1981-1984
Umberto Veronesi (Milan, Italy)	1985-1988
Louis Denis (Antwerp, Belgium)	1988-1991
Emmanuel van der Schueren (Leuven, Belgium)	1991-1994
J.Gordon McVie (London, United Kingdom)	1994-1997
Jean-Claude Horiot (Dijon, France)	1997-2000
Allan T. van Oosterom, (Leuven, Belgium)	2000-

## OVERVIEW OF THE EORTC STRUCTURE (SEE TABLE I)

The **General Assembly** is the legislative body of the EORTC. Policies, proposals, and strategies are discussed and approved by the General Assembly. The General Assembly delegates specific functions to the Board, Committees or appointed persons.

The EORTC is organized into groups of scientists and/or clinicians, each with a specific area of interest in cancer research. These groups conduct, on a voluntary basis, laboratory research and/or clinical trials on all types of cancers using a multidisciplinary approach. All groups have a voting representative (the Chairman) within the General Assembly.

The General Assembly meets once a year. The General Assembly elects the EORTC Board on a three-year basis.

The **Board** consists of 21 elected (voting) members and several ex-officio members. The voting members select among themselves the President, the Vice-President, the Treasurer and the Secretary General.

The EORTC Board is the steering and executive body, which advises the General Assembly on new activities and formulates proposals to be ratified by the General Assembly. The Board meets at least twice a year.

The **Executive Committee** was created by Emmanuel van der Schueren in 1991. This initiative was meant to help and support the President and to involve several key Board members instead of leaving the daily decisions process and strategies to the President alone.

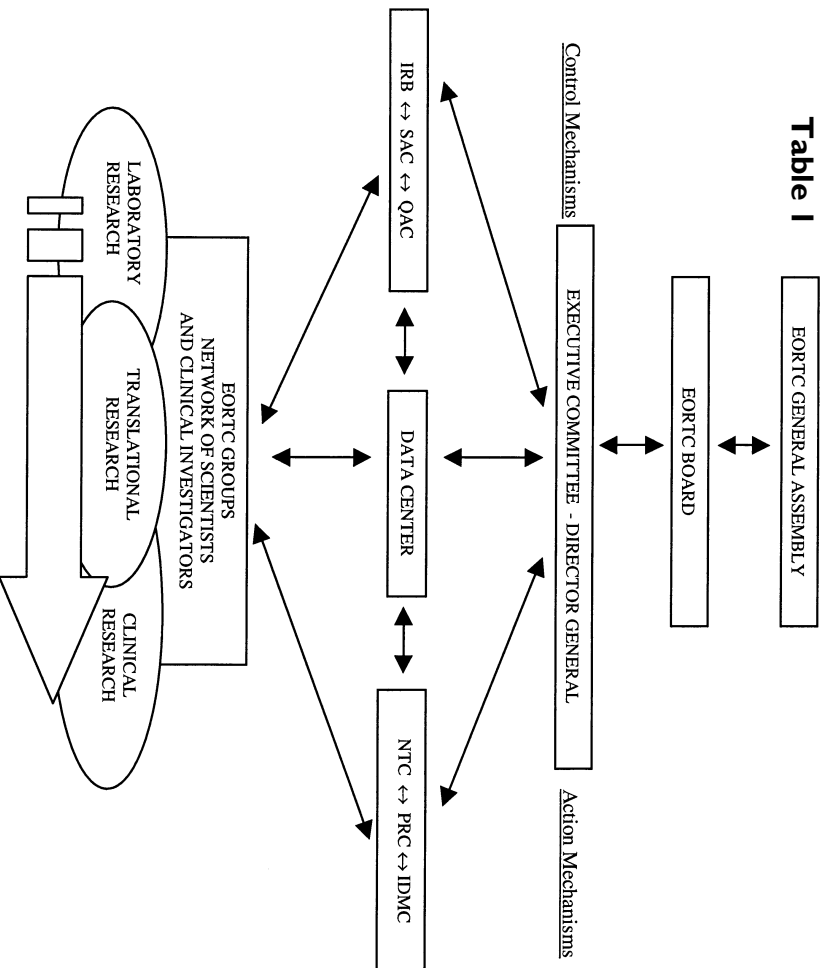
The executive Committee consists of seven voting members of the Board (the President, the Past-President, the Vice-President, the Secretary General, the Treasurer, the Chairman of Laboratory Research and the Chairman of Clinical Research) plus the Director General who is an ex-officio (non-voting) member of the Executive Committee.

The Executive Committee meets as often as needed (once every two months on average), and communicates by phone and e-mail on a weekly basis. The Executive Committee reports to the Board.

The function of the **Director General** of the EORTC was created in 1995 due to the tremendous expansion of EORTC activities, in order to coordinate and implement strategies and policies as defined by the EORTC Board.

# STRUCTURE AND ORGANISATION

**Table 1**



- IRB:** Institutional Review Board
- SAC:** Scientific Audit Committee
- QAC:** Quality Assurance Committee
- PRC:** Protocol Review Committee
- NTC:** New Treatment Committee
- IDMC:** Independent Data Monitoring Committee

Several **EORTC Committees** supervise EORTC research and activities:

- The EORTC New Treatment Committee (NTC)
- The EORTC Protocol Review Committee (PRC)
- The EORTC Scientific Audit Committee (SAC)
- The EORTC Quality Assurance Committee (QAC)
- The EORTC Independent Data Monitoring Committee (IDMC)

### **THE EORTC NETWORK**

All EORTC activities (with the exception of training courses and conferences) are research activities divided into laboratory research and clinical research conducted by multidisciplinary groups. Scientists and clinicians willing to participate in EORTC research are organized in EORTC groups (or task forces) according to their area of interest and expertise. A leading oncologist in the field heads each of these sections. Recently more, emphasis has been put on translational research, following the creation of the EORTC New Treatment Committee (NTC) in 1997. The Chairman of the NTC is also the Chairman of Translational Research.

EORTC research offers an integrated approach to drug development as well as drug evaluation programs covering the entire range of studies from early drug development up to Phase III clinical studies, therapeutic strategies and special research projects including quality of life evaluation and health economics assessment.

- The EORTC laboratory research groups are focused on pre-clinical testing of new anti-cancer agents. These groups should also provide support for translational research projects conducted within the EORTC (pharmacology, receptors, functional imaging,...).
- The EORTC clinical research groups are involved in the conduct of Phase I, Phase II and Phase III trials including cancer-related problems such as quality of life, health economics and meta-analysis. These groups are either disease oriented or modalities oriented (radiotherapy, chronotherapy,...)

There are two major routes to the establishment of a new EORTC group. The EORTC may be approached by individuals who wish to start a group and in this instance they are given guidance to establish statutes on how their group may fit into the overall structure of the EORTC. They are subsequently allocated limited financial support and human resources from the EORTC Data Center as appropriate. Alternatively, a niche in the structure of the EORTC may be noted by a member of the Board or Executive Committee and an appropriate task force is then actively established by the Board.

Prior to creating a new group, a task force is created with a probationary status for two years. Any task force is able to submit project proposals to the PRC and the NTC. It is entitled to receive financial support from the EORTC Treasury to start its activities. The Chairman of the task force is then required to send a report after one year to the EORTC Board. After two years, a full evaluation is made by the SAC. It is then recommended to the Board that the task force becomes a group, with voting rights at the General Assembly.

## EORTC BOARD 2000 - 2003

**FULL MEMBERS**

President	A. T. van Oosterom, Leuven
Past President	J-C. Horiot, Dijon
Vice President	J. Verweij, Rotterdam
Secretary General	M. Aapro, G�enolier
Treasurer	J. Double, Bradford
Chairman, Clinical Research Division	A. M. M. Eggermont, Rotterdam
Chairman, Laboratory Research Division	H. Newell, Newcastle-upon-Tyne
Chairman, New Treatment Committee	W. Steward, Leicester
Chairman, Protocol Review Committee	J-P. Armand, Villejuif
Chairman, Quality Assurance Committee	C. Van de Velde, Leiden
Chairman, Scientific Audit Committee	G. McVie, London
Member	M. Bj�orkholm, Stockholm
Member	M. Bolla, Grenoble
Member	P. de Mulder, Nijmegen
Member	M. D'Incalci, Milan
Member	G. Giaccone, Amsterdam
Member	P. Hohenberger, Berlin
Member	M. Piccart, Brussels
Member	P. Price, Manchester
Member	M. J. A. Whitehouse, London
Member	H. Zwiertzina, Innsbruck

**EX-OFFICIO MEMBERS**

Chairman, EORTC Foundation	Sir Christopher Mallaby, London
Editor-in-Chief, European Journal of Cancer	J. F. Smyth, Edinburgh
Director General, EORTC	F. Meunier, Brussels
Director, EORTC Data Center	P. Therasse, Brussels
Finance Officer	M. Nichols, London
Honorary Member (EORTC Foundation)	V. Agnew, London
Honorary Member (US-NCI Liaison Office)	S. Radtke, Brussels



# EORTC GENERAL ASSEMBLY

## FULL MEMBERS

The full members of the EORTC Board, plus the following:

### CHAIRMEN OF EORTC GROUPS

Biological Therapeutics Development	H. Zwierzina, Innsbruck
Boron Neutron Capture Therapy	W. Sauerwein, Essen
Breast Cancer	J. Jassem, Gdansk
Brain Tumor	C. Vecht, Den Haag
Children's Leukemia	E. Vilmer, Paris
Chronotherapy	F. Lévi, Villejuif
Data Management	K. Fishwick, Newcastle-upon Tyne
Early Clinical Studies	P. Fumoleau, Nantes
European Osteosarcoma Group	A. Taminiau, Leiden
Functional Imaging (former PET)	P. Price, Manchester
Gastrointestinal Tract Cancer	B. Nordlinger, Boulogne-Billancourt
Genito-Urinary Tract Cancer	to be appointed
Gynecological Cancer	I. Vergote, Leuven
Head and Neck Cancer	J. Bernier, Bellinzona
International Antimicrobial Therapy	C. Viscoli, Genova
Invasive Fungal Infections	B. De Pauw, Nijmegen
Leukemia	T. De Witte, Nijmegen
Lung Cancer	C. Manegold, Heidelberg
Lymphoma	J. Raemaekers, Nijmegen
Melanoma	D. Lienard, Lausanne
Oncology Nurses	P. di Giulio, Milan
Pathology	J.W. Oosterhuis, Rotterdam
Pharmacology and Molecular Mechanisms	A. Gescher, Leicester
Quality of Life	P. Fayers, Aberdeen
Radiation Technologists	J. Berridge, Nottingham
Radiotherapy	V.G. Budach, Berlin
Receptor and Biomarker	H. Magdelénat, Paris
Screening and Pharmacology	I. Fichtner, Berlin
Soft Tissue and Bone Sarcoma	O.S. Nielsen, Aarhus

### CHAIRMEN OF EORTC TASK FORCES

Cancer in Elderly	M. Aapro, G�enolier
Cutaneous Lymphoma	R. Knobler, Vienna
Ophthalmic Oncology	J. Prause, Copenhagen
Pain and Symptoms Control	B. Van den Eynden, Mortsel

### EX-OFFICIO MEMBER

The ex-officio members of the EORTC Board, plus the following:

Chairman, EORTC Fellowship Program and NCL-EORTC Exchange Program	F. Meunier, Brussels
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### OBSERVERS (EUROPEAN COMMISSION)

Directorate-General for Research	P. Kind, Brussels, M. Hallen, Brussels, S. Baig, Brussels
Directorate-General for Health and Consumer Protection	F. Sauer, Luxembourg

### **EORTC ADMINISTRATION**

Legal and administrative support, secretarial services, financial administration as well as dissemination of information are all coordinated within the Central Office. Arrangements have also been made for the NCI Liaison Office to be adjacent to the EORTC headquarters. Moreover, the Federation of European Cancer Societies (FECS), the European Society for Therapeutic Radiology and Oncology (ESTRO), the European Oncology Nursing Society (EONS), the European Radiotherapy Technologists Education Development Group (ERTED), and the International Society for Radiation Oncology (ISRO) are located in the same building as the EORTC.

All EORTC officers (Board, General Assembly, and Committee members), scientists, clinical investigators as well as staff members must comply with the various EORTC policies (see page 50). The EORTC Conflict of Interest/Confidentiality Policy was formally put into operation in July 1995 (EORTC Standards of conduct/conflict of interest) and amended in November 1998. All EORTC "officers" must sign a conflict of interest statement. As part of the trial activation process, each trial participant must also indicate if there is a potential conflict of interest. If the Institutional Review Board cannot reach a decision in potential cases of conflict of interest, the matter is referred to the EORTC Board for action.

In parallel to the revision of the EORTC Standards of Conduct/Conflict of Interest Policy, a new Trial Misconduct and Fraud policy was implemented in January 1998.

### **THE EORTC FOUNDATION**

In 1976, the EORTC Foundation was established by Royal Decree under the laws of the Kingdom of Belgium with the specific aim of obtaining funds for the support of the EORTC. Its Council represents all supporting countries, which include the European Union, Norway, Switzerland, and Hong Kong. The Honorary President is H.M. the Queen of Sweden and the Chairman is Sir Christopher Mallaby. Sir Ronald Grierson, Past-Chairman, is now the Honorary Vice-President of the Foundation.

Since the EORTC operates through existing national institutions and hospitals, its financial needs are modest in relation to what it is able to achieve.

In 2000, the EORTC Foundation received EORTC core support from: the Associazione Italiana per la Ricerca sul Cancro, the Cancer Research Campaign (UK), the Danish Cancer Society, the Deutsche Krebshilfe E.V., the Hong Kong Cancer Fund, the Imperial Cancer Research Fund (UK), the Nederlandse Kankerbestrijding, the Ligue Nationale Contre le Cancer (France), the Liga Portuguesa Contra o Cancro, the Norwegian Cancer Society, the Schweizerische Krebsliga and the Swedish Cancer Society. In addition, the Parthenon Trust (UK) also allocates support for three EORTC Research Projects: "Central Support for Histology Review and Tissue Banking in EORTC", "Molecular Staging in Melanoma Patients" and "Outcome Research and Collaboration in Cancer Clinical Research".

### **OTHER SOURCES OF EORTC FUNDING**

Core support for the EORTC Data Center has been provided since 1972 by the US National Cancer Institute, with which a close scientific liaison is maintained. Income is also received for the EORTC Data Center as well as for fellows on an annual basis from the "Fondation Cancer" (FOCA, Belgium) and in 2001, for Translational Research projects. Support for the EORTC Data Center is also granted by the SSTC, Services of the Prime Minister for Scientific, Technical, and Cultural Affairs (Belgium), and by the Belgian National Lottery. In 1986, the Belgian government made a e 1.1 million grant available through the National Lottery; this covers part of the rental costs of the EORTC headquarters from 1992 to 2009.

Grants for EORTC research projects have also been received from several European national cancer organisations and the European Commission. Funding is also received for studies conducted in cooperation with the pharmaceutical industry, with the aim to develop new therapeutic regimens and/or for educational projects or conferences.

# EORTC FOUNDATION

Honorary President: H.M. THE QUEEN OF SWEDEN

Honorary Vice-President: Sir Ronald Grierson

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Mrs. Marianne Boel, Denmark  
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Mr. Guido Schmidt-Chiari, Austria  
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Dr Anne Thomassen, Denmark  
Madame Gaston Thorn-Petit, Grand Duchy of Luxembourg  
Ing. Jacopo Vitorelli, Italy  
Dr. Walter Weber, Switzerland  
Mr. John Whittaker, Switzerland

## FINANCIAL REPORT 2000 AND BUDGET 2001

The EORTC Treasurer maintains tight control, with the assistance of the EORTC Finance Officer. An annual audit of the EORTC and the EORTC Foundation is carried out by Price Waterhouse Coopers.

In 2000, the Treasury received an increased grant of €800,000 from the EORTC Foundation. We gratefully thank the Foundation and its supporting leagues for their continuing support.

The income from the European Journal of Cancer rose from €100,696 in 1999 to €129,587 in 2000. €816,964 was received as the first year of three from the Parthenon Trust to sponsor projects involving the Melanoma and Pathology Groups and for treatment outcome research, intergroup studies and tumor banking research at the Data Center. €33,259 was received from Schering-Plough as the first part of the Caelyx II Intergroup project. At the very end of the year, €266,411 was received from Astra Zeneca as a one-off grant, which will be used to fund Translational Research, and will be allocated by the Board, starting in 2001.

For the Central Office/Data Center/Education Office, the grant from the US National Cancer Institute increased to €441,424 from €367,120 in 1999; the budget was €414,000, so some of this gain is due to currency fluctuations.

Industry-sponsored education grants rose to approximately €2,269,000 and industry-sponsored studies also rose to about €1,513,000. The contributions of the EORTC groups to underwrite Data Center supernumerary personnel were over €490,000. The KWF (Dutch) cancer league contributed 9,983 to assist the development of the New Drug Development Program. Thanks are due again to the 'Fondation Cancer' for its continuing support in of €56,408 directly to medical fellows.

In addition to the EORTC Treasury, Data Center and Education Office figures, a total income of €5,806,989 was received and expenditure of €3,856,043 was made by the EORTC groups and task forces in 2000 (according to the reports submitted by group officers).

The combined figures for the EORTC Treasury, Data Center and Education Office, together with the EORTC groups and task forces show a total income of €13,732,247 and expenditure of €10,822,392 in 2000.

The EORTC budget for 2001 is given below and does not include the budgets of the EORTC groups and task forces. The EORTC Foundation has increased its budget for the third year in a row to €900,000.

The cost of clinical trials insurance will rise yet again, due to the need for a separate policy for Italy in 2001. The automatic €5,000 grants to most groups and task forces were abolished by the EORTC Board meeting of November 2000, and have been replaced in 2001 by competitive grants for translational research; five of these were awarded by the Board in March 2001, with four funded by Fondation Cancer (FOCA) and one by the EORTC Foundation. We would like to thank both the Fondation Cancer and the EORTC Foundation for their generous support of these projects.

For the Data Center, it should be noted that the figures for salaries and running costs include money from the Parthenon Trust projects. The core grant from the Treasury to the Data Center will be €500,000, which together with the US National Cancer Institute core grant of €475,000 and the additional core support from the Parthenon Trust amounts to a core grant of €1,095,000.

## EORTC BUDGET 2001

<b>Income</b>	<b>EUROS</b>
Treasury	
EORTC Foundation	900,000
EORTC Foundation for Translational Research Fund	40,000
Parthenon Trust 3 Research Projects (Year 2)	800,000
Parthenon Trust 3 Research Projects (Balance of Year 1)	450,000
Parthenon Trust Data Center Core Support	120,000
Astra Zeneca Translational Research Projects	266,000
Schering-Plough Caelyx Intergroup Project	210,000
Elsevier (European Journal of Cancer)	130,000
FOCA Earmarked for Translational Research Projects	160,000
Other Income	22,000
Central Office–Data Center	
EORTC Foundation for Fellowships	25,000
EORTC Foundation for NDDP	10,000
Leagues for Cancer Communications Office	15,000
Industry Sponsored Studies	1,444,000
Industry Sponsored Educational Grants	3,100,000
From EORTC Groups for Personnel	470,000
US National Cancer Institute	475,000
Belgian National Lottery	74,000
EC Boron Neutron Capture Therapy Project	16,000
Education Office	50,000
Sundry Income (Small Donations, SSTC)	13,000
Current Projects (Brought Forward from 2000)	557,000
<b>Total</b>	<b>9,347,000</b>
<b>Expenditure</b>	<b>EUROS</b>
Treasury	
Parthenon Trust Research Projects (Years 1,2 non-Data Center)	865,000
Astra Zeneca Translational Research Projects	266,000
Schering-Plough Caelyx Intergroup Project	210,000
Board and Committees	143,000
Grants to EORTC Research Groups - Translational Research	200,000
Grants to EORTC Research Groups - General	25,000
EORTC Clinical and Laboratory Research Divisions	20,000
Clinical Trials Insurance	100,000
Finance Officer and Secretarial Support to Officers	86,000
Other Costs	100,000
HQ Building Charges	45,000
Audit and Lawyer's Fees	39,000
Professional Indemnity Insurance	11,000
Bank Charges	3,000
Central Office–Data Center	
Research Salaries	5,553,000
Running Costs	858,000
Fellowship Program	160,000
Upgrading and Replacing Computers	150,000
Office Rent, Charges and Taxes	150,000
Data Center Travel Expenses	160,000
HQ Building Office Alterations and Telephone Upgrade	150,000
New Software	28,000
EORTC Publications	25,000
<b>Total</b>	<b>9,347,000</b>

## **EORTC MEMBERSHIP**

All members of the General Assembly are the effective members of the EORTC. In addition, active members of EORTC groups and Committees are associate members of the organisation. Criteria for membership of an EORTC group are defined by the statutes of the group and according to guidelines provided by the EORTC Board.

In order to become a member of a group, please contact either Prof. Françoise Meunier, EORTC Director General, or the Chairman of the relevant Group.

(See instructions on the EORTC webpage at <http://www.eortc.be>)

## **GUIDELINES FOR STATUTES OF EORTC GROUPS**

In order to standardize the criteria for membership, functioning and publication of EORTC groups' scientific endeavors, each group must draw up its own statutes, covering all aspects of its activities, and including rules under the following headings. It is accepted that individual groups will vary in particular aspects of these general headings. However, all groups bearing the name of the EORTC must conduct their activities under the EORTC legal entity and therefore must comply with all EORTC policies and strategies defined by the Board and approved by the General Assembly.

### **1. Aims of the Group**

The group must define its principal aims and objectives and ensure that its activities and strategies fit into the policies and procedures of the EORTC. In defining the aims of an individual group the mission of the EORTC—laboratory research, clinical research, education and training in cancer-related topics - should be borne in mind.

### **2. Membership and Application for EORTC Groups Membership**

It is recommended that membership should be of two sorts, probationary and full or active. In some circumstances, ordinary membership may be considered for scientists (basic scientists, pathologists, and radiologists...) who bring a substantial contribution to the activities of a group without recruiting patients into ongoing clinical trials. Foreign membership may be considered for "temporary" affiliation of an institution to the group in the context of a specific clinical trial provided that EORTC rules allowing foreign membership have been followed. There must be a defined period of probationary membership (generally two years) during which time the individual investigator or institution must submit a certain number of patients to protocols with an 85% evaluability rate within a given period of time and thereby achieve ordinary or active / full membership.

It is recommended that failure to do this should result in membership of the group being withdrawn and that they must follow a period when that institution is unable to reapply. During that period the EORTC (group and/or EORTC Quality Assurance Unit) should offer to send one of its officers to evaluate the institution and to advise them on how they may most easily achieve full membership on subsequent application.

A period of two years should elapse after cessation of their probationary membership before they are allowed to apply again. There should be a clearly defined method of application for an individual center or clinician and this application, before it is even considered, should receive the written support of one active member of the group.

The criteria for active membership should include not only adequate follow-up of patients, again with an 85% evaluability score, but it should also incorporate the need to recruit new patients to studies on a regular basis. It is accepted that the demands of the group may require that, numerically, the criteria for full membership may vary (for example for very rare tumors).

For groups not directly involved in clinical trials, other criteria for membership must consider relevant contribution in the field of interest of these particular groups.

### **3. Officers of the Group**

The officers of the group must be defined, their period of office established (usually three years) and criteria for re-election accepted (usually once). Progress from one office to another should be allowed provided it is accepted by the group as a whole. It is suggested that there should not be a rigid hierarchy, for instance, Secretary to Vice-Chairman to Chairman etc. Re-election of a Chairman must have prior approval of the EORTC Board.

### **4. Committee Structure**

Permanent committees of the group should be defined, their membership established and the method of election of their Chairman or Secretary also clearly defined. It is suggested that the statutes should include provision for the formation of additional committees, depending on developments in the particular field in which the group is working.

### **5. Elections**

The method of electing the officers and the committees of the group must be clearly defined and, where necessary, ballots for individual positions must be secret and should be carried out in such a way as to ensure that the majority of the active membership supports the elected official.

### **6. Publication Policy**

Each group should establish a well-defined presentation and publication policy. This policy must ensure that there is no premature release of data from the studies, which could jeopardize recruitment to the study or in any way bias the results of that study. It is recommended that the study coordinator and the statistician of the group are the final arbiters on the timing of presentations and publications of results.

Appropriate recognition to the Data Center staff is needed and the statistician and, whenever indicated, the medical advisor or the research fellow appointed to a specific research project should be listed as co-authors. In addition to the study coordinator(s), other co-authors include in general

the Chairman of the group and any investigator having recruited at least 10% of the patients in the trial. Acknowledgment to other investigators, the data manager and sponsor representatives (if any) is also essential. Sponsorship does not only involve the pharmaceutical industry but also refers to any supporting organisation or body (NCI, Cancer Leagues, private donations...).

### **7. Protocol Design and Writing**

There should be a clearly defined procedure for the submission of research projects (protocols) within the group. This procedure must allow for any member of the group to submit an idea, to be guided in processing that idea to the writing of a protocol and helped to ensure the minimum delay between the acceptance of that protocol by the group and its submission to the New Treatment Committee to the Protocol Review Committee, as appropriate. Each protocol must be seen to fit into the research program approved by the group.

### **8. Meeting Agenda**

The statutes should contain information concerning the regular business meetings of the group. The statutes should also contain the policy of the group concerning symposia and closed or open scientific sessions. It is recommended that each group should establish communications with other cancer research groups within or outside the EORTC in the same field and that their meeting agenda should allow for consensus or other meetings with those groups.

### **9. Quality Assurance**

Each group should have defined quality assurance criteria for their research activities. All groups should have their own quality assurance committee to enforce the requirements for internal quality assurance as established by the EORTC Quality Assurance Committee and endorsed by the EORTC Board.

### **10. Organisation of Financial Support**

The EORTC Board provides a formal delegation of authority to three members (officers) of the group to handle the EORTC groups' account(s).

It is mandatory that the financial support for research projects carried out by the groups be organized jointly by the Chairman of the Group and the Director of the EORTC Data Center. Grants from the pharmaceutical industry, or other sources provided to the group, to support a research project, should be handled centrally by the Treasurer of the group and not necessarily allocated on a patient accrual basis to individual institutions. This will ensure that some support is available not just for individual institutions but for subsequent studies, perhaps less well supported. It may also provide a resource for other group activities such as supported travel of active members to a meeting and additional data manager or statistical help for the particular project or even for related projects.



The full financial status of all groups should be available for examination by the EORTC Finance Officer and Treasurer once a year and by the SAC Committee once every three to five years. The financial adviser to the group (the Treasurer) should present accounts to the group at each business meeting or at the least once a year. The groups' finances will be reviewed during the financial audit performed every year for the whole EORTC.

### **I I. Relations with the Data Center**

Close collaboration between the Chairman, Study Coordinators, and the EORTC Data Center Director is essential. All protocols to be submitted to the New Treatment Committee and/or the Protocol Review Committee must be reviewed by the EORTC Data Center staff (medical advisor, statistician, data manager, quality of life and health economics specialists when appropriate) prior to their submission.

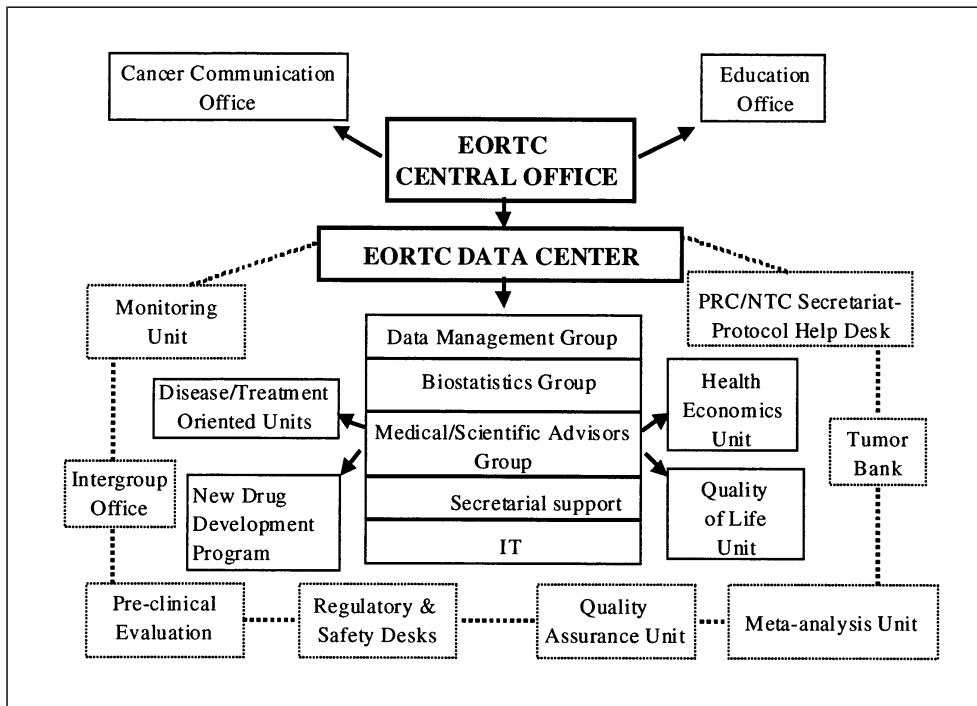
For sponsored trials, negotiations with pharmaceutical industries should be carried out jointly by the Chairman of the Group and the Director of the Data Center to guarantee financial support for the management of the study, and to assure optimal services to the pharmaceutical industries.

For all trials, sponsored or not, optimal communication between the Chairmen of the Groups and the Regulatory Affairs Manager of the EORTC is also mandatory to provide adequate insurance coverage for all studies which are conducted with the EORTC label and under EORTC legal responsibility.

**THE EORTC HEADQUARTERS**

Located in Brussels, the EORTC headquarters (see Table 2) play a coordinating role in all EORTC activities and deal with the scientific, legal and administrative issues related to the EORTC. It consists of the EORTC Central Office, the Data Center, the Education Office and the Cancer Communications Office.

Table 2



The logistic support for all EORTC groups is provided by the EORTC Data Center based in Brussels.

The EORTC Education Office provides the logistic support for the organisation of courses on methodology of cancer clinical research and EORTC conferences as well as strategic meetings.

The EORTC Cancer Communications Office was established in Brussels in 1997 to liaise with cancer leagues, patients, the media and other partners as appropriate to promote the EORTC's research activities in order to increase public awareness of the importance of cancer clinical research in Europe.



# EORTC CENTRAL OFFICE

Françoise Meunier, MD, PhD, FRCP  
Director General, EORTC

*Staff as of April 2001*

- **Administrative staff**

Executive Secretary	Dominique Eeckhoudt
Personal Assistant to the Director General	Albertine Delparte
Secretary to the Director General	Sonia Rolandi

- **Cancer Communications Office**

Cancer Communication Officer	Samantha Christey, MA
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- **Education Office**

Education Office Administrator	Danielle Zimmermann
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- **Finance Officer (London)** Martin Nichols

# EORTC Data Center

Patrick Therasse, MD, MS  
Director, EORTC Data Center

Assistant Director, Medical Affairs/NDDP  
Assistant Director, Biostatistics  
Assistant Director, Quality Manager

Denis Lacombe, MD, MS  
Richard Sylvester, PhD  
Martine Van Glabbeke, Ir., MS

## • Disease / Treatment Oriented Units

### Data Management Coordinator

Ann Marinus, RN

### Data Managers

Henriette Bartholomei  
Philip Beeldens, MS  
Marie-Laure Couvreur  
Nathalie De Beule, MS  
Muriel Debois, MS  
Claudia de Clippeleir, MS  
Linda De Prijk  
Isabelle Desaunois, MS  
Nicole Duez, MS  
Sonia Dusenne, MS  
Livia Giurgia, PhD  
Anne Kirkpatrick, MS  
Marie-Ange Lentz, MS  
Marianne Pierart, MS  
Michel Praet, PhD  
Sylvia Reuse, PhD  
Peggy Rodts  
Ingrid Roucloux, MS  
Cynthia Rozewicz, MS  
Christof Schepens  
Gabriel Solbu, MS  
Sven Vanderrijst, MS  
Irène Van Horrebeeck, MS  
Christiane Van Pottelsberghe, MS  
Christine Waterkijn, MS

### Assistant Data Managers

Anouk Allgeier, MS  
Antoine Briffaux, MS  
Michelle Brown, MS  
Sabrina Decot  
Annelore Dehoorne, MS  
Monika De Vos  
Goedele Eckhoudt, MS  
Nathalie Garzon-Vanacker, MS  
Izabella Jagiello, PhD

	Patrick Lamotte, MS Anastassia Negrouk, MS Asiru Olarunwa, MS
<b>Statisticians</b>	Benoît Baron, MS Comeel Coens, MS Laurence Collette, MS Catherine Legrand, MS Stéphane Suciu, MS Richard Sylvester, PhD Martine Van Glabekke, Ir., MS
<b>Medical Advisors</b>	Özlem Anak, MD Liliana Baila, MD Channa Debruyne, MD Eugenio Donato di Paola, MD Denis Lacombe, MD Ivana Teodorovic, MD, MS Patrick Therasse, MD, MS Alfredo Zurlo, MD

**• New Drug Development Program**

Coordinator	Denis Lacombe, MD, MS
Medical Advisor	Frédéric Lehmann, MD
Statistician	Xavier Paoletti, MS
Project Leader	Sandrine Marreaud, MD
Preclinical Project Manager	Anne-Sophie Govaerts, PhD
Monitors	Christine de Balincourt, Pharm. Marta Picciolato, MS René Selvais, MS Bart Vandael

**Data Managers**

Assistant Data Manager	Catherine Hermans
Secretary to the Senior Staff	Stéphanie Mali, MS
Assistant Secretary	Bénédicte Marchal, MS Vicky Minas Zorha Bengoudifa

**• NTC-PRC/Protocol Help Desk**

Coordinator	Martine Van Glabbeke, Ir., MS
NTC/PRC Administrator	Cécile Lardot, MS
Protocol Help Desk administrator	Françoise Peeters
Secretary	Laura Carolina Collada Ali

<p><b>• Regulatory Desk</b></p>
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Coordinator	Denis Lacombe, MD, MS
Managers	An-Joanna Baeyens, Lawyer, LL.M Eric Brabant, Lawyer
Secretary	Cristel Grimonpont

<p><b>• Safety Desk</b></p>
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Coordinator	Denis Lacombe, MD, MS
Manager	Nathalie Dubois, MS Anne-Marie Domange
Assistant	Sarah Meloen, MS
Secretary	to be appointed

<p><b>• Quality Assurance Unit</b></p>
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Coordinator	Ann Marinus, RN
Managers	Magali Klepper, MS Lesley-Ann Rea

<p><b>• Meta-Analysis Unit</b></p>
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Coordinator	Richard Sylvester, PhD
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<p><b>• Monitoring Unit</b></p>
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Coordinator	Channa Debruyne, MD
Clinical Research Associates/Monitors	Elizabeth Gray, MS Sofie Van Impe, MS

<p><b>• Health Economics Unit</b></p>
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Coordinator	Ralph Crott, PhD
Scientific Advisor	Niels Neymark, MS
Statistician	Thierry Gorlia, MS
Project Manager	Thomas Roy, MS

**• Quality of Life Unit**

Coordinator	Andrew Bottomley, PhD
Module Development Manager	Stéphanie Vachalec, MS
Data Manager	Irina Ghislain, MS
Assistant Data Manager	Sheila Sanderson-Scott
Translator	Karen West
Secretary	Tricia Morgan

**• Tumor Bank**

Coordinator	Ivana Teodorovic, MD, MS
Administrator	Martin Isabelle, MS

**• Intergroup Office**

Coordinator	Alfredo Zurlo, MD
Secretary	Paola Padovan

**• IT unit**

Coordinator	Pascal Ruyskart, MS
Computer Analysts	Eric Decossaux, MS
	Yves Dohogne, MS
	Kate Moncrieff
SAS Programmer	John Roberts, PhD
User Support Analyst	Jonathan O'Sullivan
User Support Analyst	Max Lovius

**• Fellows for special projects**

Medical fellows	Natasja Djurasinovic, MD
	Vassilios Kouloulis, MD, MS
	Marlies Landheer, MD
	Heidy Van Wijk, MD
Fellow Statistician	Gary Collins, MS



**• Human Resources Unit**

Administrator

Catherine Prévot

**• Secretaries**

Secretary to the Director, Data Center  
Assistant Secretaries  
Secretaries reception/randomization :

Zeina Tayah  
Delphine Dubois  
Sophie Hons  
Alexia Yannopoulos

Data Entry Clerks

Daniel Canneel  
Ilka Debruyne  
Francine de Vleeschouwer  
Frédéric Plasman

Volunteers

Marc Peetermans  
Eric Romain  
Amanda Thomson

# EORTC DATA CENTER Institutional Review Board

The Institutional Review Board (IRB) of the EORTC Data Center is responsible for safeguarding the rights and welfare of subjects participating in clinical trials supported by the Data Center. In particular, the IRB is responsible for protecting the privacy and confidentiality of the individuals' data. All institutions and investigators submitting data to the Data Center agree to abide by the decisions of the IRB regarding data collection, transfer, storage, release, retention, and disposition, as these pertain to individual patients' privacy and confidentiality. The IRB also reviews potential conflicts of interest reported to the Data Center.

During the last meeting on September 18, 2000, the IRB revised the review procedure for informed consent and informed consent templates for EORTC trials in order to upgrade those for patients joining translational research. Declarations of conflicts of interest were examined, but none were found to be significant. Finally, the IT Unit presented the in-built features of the evolving remote data entry system (e-forms) to ensure patient data security as well as validation of the data by investigators.

## MEMBERS

D. Lacombe (Chairman), EORTC Data Center, Brussels  
R. Sylvester, EORTC Data Center, Brussels  
J.V. De Weirt, Brussels  
F. Crawley, Leuven  
M. Peetermans, Antwerp  
P. Ruyskart, EORTC Data Center, Brussels  
S. Suci, EORTC Data Center, Brussels

## EORTC COMMITTEES

Several EORTC Committees have been created in order to ensure EORTC's independence, relevance of research efforts and scientifically sound results, thereby safeguarding the quality of science. The Chairmen of all committees are elected by the EORTC General Assembly for a three-year term.

- EORTC New Treatment Committee (NTC)
- EORTC Protocol Review Committee (PRC)
- EORTC Scientific Audit Committee (SAC)
- EORTC Quality Assurance Committee (QAC)
- EORTC Independent Data Monitoring Committee (IDMC)

## EORTC New Treatment Committee (NTC)

The EORTC NTC is responsible for reviewing protocol outlines that include the use of new, unregistered treatments of malignancy. Its aims include the prioritising of new drugs and modalities offered to the EORTC for development, the review of preclinical data and, where necessary, suggestions for additional preclinical studies. When appropriate, the NTC ensures optimal coordination and communication between EORTC groups and the Data Center whenever studies are utilising the same agent/modalities. The NTC is also responsible for stimulating translational research within the EORTC and for ensuring optimal flow of information on new drugs between the laboratory and clinical research divisions. Wherever possible, the NTC ensures appropriate communication of new agent protocols with its EORTC partners. The NTC therefore serves as a Scientific Committee for the EORTC New Drug Development Program. There are currently 45 members with expertise in all modalities of treatment involving investigational anti-cancer approaches. The specific areas of expertise are in cytotoxic/cytostatic agents, biological agents, hormones, gene therapy, radiotherapy and pathology.

### NEW TREATMENT COMMITTEE REPORT 2000

The NTC met in October 2000, jointly with the Protocol Review Committee.

The importance of rapid responses during the review process was highlighted. Currently all members are contacted via e-mail and it was agreed that a first decision should be provided within four weeks of outline submission. This includes three weeks for the expert review and one week for logistic matters including selection of reviewers and circulation of documents. The NTC-PRC Secretariat was strengthened during 2000 to provide additional support for the process and ensure that deadlines are met. The NTC review will be performed in parallel with a review by the PRC to further decrease the overall review time in the EORTC.

In 2000, the NTC reviewed 32 outlines proposals of which 28 have been jointly reviewed with the PRC. The median time of the review process was 28 days (ranging from 15 to 53 days). If a protocol involves a novel agent which is felt to be particularly important and to require a fast-track review, this should be discussed with the NTC and the PRC Chairmen through the NTC-PRC Secretariat in order to expedite the process if it is agreed that this would be of importance to the EORTC.

Outlines reviewed in 2000 by the EORTC New Treatment Committee only

PROTOCOL NUMBER	GROUP	STUDY TYPE	RESULT	OUTCOME
16001	ECSG	II	Accepted	
16005	ECSG	II	Question	Accepted
16007	ECSG	I	Accepted	
62003	Soft Tissue	II	Question	

The NTC also reviewed 28 outlines jointly with the PRC. These NTC-PRC outlines are summarized in the "PRC activity table" related to the PRC section.

## EORTC NEW TREATMENT COMMITTEE MEMBERS

### BOARD

**Chairman**, W. Steward

**Vice-Chairman**, P. Fumoleau

**Chairman**, Laboratory Research Division, H. Newell

**Chairman**, Clinical Research Division, L. Eggermont

### MEMBERS

Each NTC member has been classified according to her/his field(s) of expertise.

Cytotoxics/Cytostatic		Vaccines/Monoclonals/ Biologicals	Hormones/ Receptors
O. S. Nielsen G. Giaccone R. Baum I. Fichtner A. Ravaud J. Double A. Ardizzoni C. Twelves N. Reed E. de Vries P. Schoeffski J. Fisher A. Gesher E. van Cutsem I. Vergote S.Aamdal	I. Cree I. Judson P. Price V. Bramwell J. Wagstaff M. D'Incalci P. Fumoleau T. Roberts P. Woll S. D. Fossa P. Carde S. Giachetti C. Sternberg R. Coleman J. L. Merlin	R. Baum U. Keilholz I. Fichtner A. Ravaud C. Twelves J. Fisher H. Zwierzina I. Cree J. Wagstaff T. Roberts Y. Van Oosterhout L. Zitvogel S. Aamdal	R. Baum I. Fichtner C. Twelves N. Reed R. E. Leake E. de Vries I. Vergote C. Focan V. Bramwell T. Roberts S. Giachetti R. Coleman P. Carde C. Dittrich J. L. Merlin
Genotherapy	Radiotherapy	Pathology	
U. Keilholz I. Fichtner E. Rankin I. Cree L. Zitvogel S.Aamdal	O. S. Nielsen R. Baum N. Reed P. Price M. Robinson J. L. Merlin	A. Spatz	

### GUESTS AT NTC MEETING

F. Meunier, Director General, EORTC  
 P. Therasse, Director, EORTC Data Center  
 D. Lacombe, Assistant Director for Medical affairs, Director  
 NDDP, EORTC Data Center  
 J-P. Armand, Chairman, EORTC Protocol Review Committee  
 S. Radtke/M. Christian/E. Sausville, NCI representatives  
 S. Burtles, CRC representative  
 G. Eisenbrand or B. Keppler, AWO representatives  
 S. Marsoni, SENDO representative

## EORTC Protocol Review Committee (PRC)

The function of the EORTC PRC is to review and approve new EORTC protocols submitted by the groups with respect to their scientific value, methodology, feasibility and relevance within the EORTC framework. The PRC assists the groups whenever necessary concerning any aspect of the design and implementation of their studies from the first outline proposal to the full protocol.

The PRC comprises 24 members and external consultants chosen for their expertise in specific areas. All disciplines of oncology are represented in the review panel. About 40 % of the PRC members are non-EORTC, including a statistician external to the Data Center and representatives of the U.S NCI. The PRC additionally makes regular use of external reviewers - a minimum of three international experts are consulted and a maximum of five for each protocol.

Protocol outlines are submitted to the NTC-PRC secretariat via the Internet. The outline submission questionnaire is available from the EORTC web site <http://www.eortc.be> or see page 41 for submission procedure.

The average review time mean duration for outline concept submitted to the NTC is 31 days and 41 days for the PRC. The PRC review ranged from 21 to 71 days depending on the complexity of the outline proposal which largely depends on the type of trial (Phase I versus Phase III). During the year 2000, a total of 50 proposals have been reviewed (22 by the PRC only, 28 by both the NTC and PRC including six Phase I studies, 17 Phase II studies, 25 Phase III studies, one survey and one Quality of Life). Additionally, 17 outlines submitted in 1998-1999 received a final decision in 2000 (indicated by \*). Also, 34 full protocols have been reviewed (two Phase I studies, 12 Phase II studies, 19 Phase III studies, and one Quality of Life).

Outlines/full protocols are reviewed by e-mail. If necessary, they are reviewed at quarterly meetings. In cases of conflict, the study coordinator has the possibility to personally discuss the PRC concerns raised about their proposal during a PRC meeting or telephone conference.

Outlines/full protocols may be accepted at the time of review, but are more often only accepted after revision, and others are rejected. Most part of the protocol outlines are resubmitted after detailed comments from the PRC, and could still at that time be reviewed by external experts of the particular field.

Some protocols are run as joint protocols with non-EORTC groups (i.e. ECOG -SWOG,...). Intergroup studies are evaluated in an "ad hoc" way, depending on if the EORTC is the coordinating group or joins a protocol which will be run by another Data Center. There is often conflict between the wishes of groups to get protocols activated quickly, and the absolute necessity for the EORTC to ensure that all studies are carried out to the highest possible standards (scientific, administrative and regulatory) of clinical scientific investigation. The PRC, since implementation of the new continuous review process, has had to submit all members to a constant flow of outlines, full protocols, but also amendments to the protocols (approximately 60 per year), that has considerably increased the burden of these voluntary colleagues.

## EORTC PROTOCOL REVIEW COMMITTEE MEMBERS

J-P. Armand, Villejuif, **Chairman**  
A. F. Sobrero, Udine, **Vice-Chairman**  
J. Bernier, Bellinzona|Y. Blay, Lyon  
J. Blazeby, Bristol  
C. F. de Oliveira, Coimbra  
B. D. Cheson, Bethesda (NCI representative)  
T. de Witte, Nijmegen  
F. Guillemin, Vandoeuvre les Nancy  
E. Jäger, Frankfurt  
D. Lacombe, Brussels  
F. Meunier, Brussels  
K. Nilsson, Stockholm  
M. Parmar, London  
F. Rochard, Villejuif  
R. Rossell, Barcelona  
H. Sauer, München  
H-J. Schmoll, Halle/Saale  
R. Sylvester, Brussels  
A. Van der Meijden, 's Hertogenbosh  
M. Van Glabbeke, Brussels  
E. Van Limbergen, Leuven  
C. Williams, Oxford

**NTC / PRC REVIEW OF PROTOCOLS IN 2000**

<b>PROTOCOL NUMBER</b>	<b>REVIEWED</b>	<b>GROUP</b>	<b>STUDY TYPE</b>	<b>RESULT</b>	<b>OUTCOME</b>
05001	PRC	Chronotherapy	III	Rejected	
05991*	NTC/PRC	Chronotherapy	II	Questions	Accepted
06992*	PRC	Leukemia	III	Questions	Accepted
06993*	NTC/PRC	Leukemia	II	Questions	Accepted
08001	PRC	Lung	III	Questions	Accepted
08002	NTC/PRC	Lung	III	Questions	Accepted
10001	NTC/PRC	Breast	II-III	Rejected	Accepted
10002	PRC	Breast	survey	Resubmit	Accepted
10003	NTC/PRC	Breast	II	Questions	Accepted
10004	PRC	Breast	II	Resubmit	Withdrawn
10994*	NTC/PRC	Breast	III	Questions	Accepted
10996*	NTC/PRC	Breast	II	Questions	Accepted
10997*	PRC	Breast	III	Questions	Accepted
11001	NTC/PRC	BNCT	I	Resubmit	Accepted
13001	NTC/PRC	BTDG	I	Accepted	
13002	NTC/PRC	BTDG	I-II	Resubmit	Accepted
13993*	NTC/PRC	BTDG	I	Questions	Accepted
15001	PRC	Quality of life	other	Accepted	
16002	NTC/PRC	ECSG	I	Accepted	
16006	NTC/PRC	ECSG	II	Resubmit	Accepted
16008	NTC/PRC	ECSG	I	Accepted	
16009	NTC/PRC	ECSG	II	Questions	Withdrawn
16994G	NTC/PRC	ECSG	II	Questions	Accepted
20995*	PRC	Lymphoma	III	Questions	Accepted
22001	NTC/PRC	Radiotherapy	III	Questions	Accepted
22003	PRC	Radiotherapy	III	Accepted	
22994*	NTC/PRC	Radiotherapy	I/II	Questions	Accepted
22996*	PRC	Radiotherapy	II	Questions	Accepted
24001	PRC	Head & Neck	III	Questions	Accepted
24991*	PRC	Head & Neck	III	Questions	Rejected
26992*	PRC	Brain	III	Questions	Rejected
30001	PRC	Genito-urinary	II	Questions	Accepted
30002	NTC/PRC	Genito-urinary	III	Resubmit	Accepted
30003	NTC/PRC	Genito-urinary	III	Rejected	
30004	PRC	Genito-urinary	III	Resubmit	Accepted
30992*	NTC/PRC	Genito-urinary	II	Questions	Accepted
30994*	PRC	Genito-urinary	III	Questions	Accepted
40002	PRC	Gastrointestinal	II	Questions	Accepted
40004	NTC/PRC	Gastrointestinal	III	Resubmit	Accepted
40993*	NTC/PRC	Gastrointestinal	III	Questions	Accepted
46001	PRC	Antimicrobial	III	Resubmit	Accepted
55002	PRC	Gynecological	II	Accepted	
55005	PRC	Gynecological	III	Accepted	
55984*	PRC	Gynecological	III	Questions	Accepted
55994*	NTC/PRC	Gynecological	III	Questions	Accepted
62001	NTC/PRC	Soft Tissue	I/II	Accepted	
62002	NTC/PRC	Soft Tissue	I	Rejected	Accepted
62005	NTC/PRC	Soft Tissue	III	Accepted	
62006	NTC/PRC	Soft Tissue	II	Accepted	
88001	PRC	Ophthalmic	III	Questions	

\* outlines submitted in 1998-1999 that received a final decision in 2000.



## Submission of Outlines and Protocols to the EORTC New Treatment Committee and to the EORTC Protocol Review Committee

### PROTOCOLS ARE SUBMITTED TO THE EORTC FOR APPROVAL IN TWO STEPS:

- The concept of the study (outline), approved by one (or several) EORTC Clinical Group(s) is submitted to the NTC and/or PRC for approval.
- The full protocol, based on a NTC and/or PRC approved concept, and developed according to the EORTC standard methodology (via the Protocol Help Desk), is submitted to the PRC for final EORTC approval (EORTC label), and allocation of Data Center support

### BEFORE OUTLINE SUBMISSION

Outlines submitted to the NTC-PRC must satisfy the following conditions:

- The concept of the study must be approved by (at least) one EORTC Clinical Group; this must be documented by an official letter of approval sent by the Group chairperson to the NTC-PRC secretariat, at the time of outline submission
- If the study is intended as an "Intergroup study", the coordinating group must be clearly identified
- For single group studies one single Study Coordinator must be designated (other investigators taking part in the coordination of the study should be called co-coordinators).
- For Intergroup studies, one Study Coordinator should be designated for the coordinating group and for each EORTC participating groups.
- The participating Group(s) must demonstrate a sufficient potential recruitment to conduct the study in a reasonable time frame; for this purpose, the Study Coordinator should assemble a list of investigators (including the expected accrual of each investigator) and complete appropriately the outline section "number of centers" at the time of submission
- The EORTC Data Center must have been involved in discussions on the design of the study, and must have approved the outline; the contact person should be clearly identified in the study outline (Statistician, Medical Advisor).
- The concept of the study has to be summarized in a standard web questionnaire "Outline proposal for clinical trial protocols to be submitted to the EORTC NTC-PRC".

**OUTLINE SUBMISSION**

The concept of all trials has to be reviewed and approved by the NTC and/or the PRC, on the basis of the outline

- The outline must be electronically submitted to the NTC-PRC secretariat
- The letter of approval must be sent, preferably by e-mail, to the NTC-PRC secretariat.
- In the case of a project dealing with an investigational agent, the investigator brochure (and international publication(s) if applicable) must be sent, preferably by e-mail, to the NTC-PRC secretariat
- Outlines may be submitted at any time
- The NTC-PRC secretariat will attribute an EORTC number to each proposal. This number and a copy of the outline formatted in a "word document" will be sent by e-mail to the Study Coordinator(s), the Group chairperson(s) and the EORTC Contact person (Statistician, Medical advisor)

The first NTC-PRC decision will be notified to the Study Coordinator(s), the Group chairperson(s) and the EORTC Data Center team within one month of receipt of the outline. A copy of appropriate letters will be sent to the Chairman of all EORTC Groups involved in the study, and to the Data Center team:

- Authorize the group to develop the full protocol, with or without modifications of the original concept
- Substantially modify the outline, and submit a new version of the outline. For that purpose the Study Coordinator should address a reply to all NTC/PRC comments and modify the original outline accordingly.
- Reject the full concept
- Decide that the outline should be discussed further during a plenary meeting of the PRC (the first meeting scheduled more than six weeks after the original outline submission); the Study Coordinator will have the opportunity to participate in the PRC discussion.

In the latter case, the final PRC decision will be notified to the Study Coordinator no later than two weeks after the PRC meeting:

- Authorize the group to develop the full protocol, with or without modifications of the original concept
- Substantially modify the outline, and submit a new version
- Reject the full concept

### **FULL PROTOCOL SUBMISSION**

Full protocols are developed in a modular way with the logistical support of the Data Center Protocol Help Desk. The final version of the protocol is assembled by the Protocol Help Desk and must be approved both by the Study Coordinator and the DC team allocated to the study. The Data Center team ensures that the protocol is adequately developed in the shortest possible time. The Protocol Help Desk procedure is summarized in a working procedure "Development of EORTC full protocols" (ref: WP5103).

- The full protocols must be made available to the NTC-PRC secretariat by e-mail within three months after the outline approval.
- It should be the complete final version, including all appendices, approved by the Data Center team.
- All outline modifications requested by the NTC or the PRC have to be commented on in an accompanying letter (or e-mail) by the Study coordinator, which will refer to the appropriate chapter of the protocol.
- The conflict of interest form (sent to the Study Coordinator at the time of outline approval) must be signed by the Study Coordinator and returned to the NTC-PRC secretariat.

The final decision will be sent to the Study Coordinator by the PRC Chairman within a month of receipt by the PRC. A copy of appropriate letters will be sent to the Chairman of all EORTC Groups involved in the study, and to the Data Center team.

- Authorize the group to activate the trial, with or without modifications of the full protocol.
- Substantially modify the full protocol, and submit a new version of the full protocol together with an accompanying letter addressing all modifications requested by the NTC or the PRC.

### **INTERGROUP STUDIES**

For Intergroup studies, the EORTC has adopted the principle of a "coordinating group", responsible for protocol and CRFs development, data management and analysis. The role of the Data Center of the other participating groups is limited to randomization and circulation of information (including CRFs and queries).

If the EORTC is not the coordinating group, obtaining the EORTC label is the responsibility of the Study Coordinator of the EORTC participating group.

- The study coordinator will electronically submit an outline to the NTC- PRC secretariat.
- He/she will send to the NTC-PRC secretariat a copy of all available documentation of prior reviews (reviewers comments, letter of approval), by e-mail or mail.
- If the final version of the full protocol is already available, a copy should be sent, preferably by e-mail, to the NTC-PRC secretariat.
- If the study is already active in another group, the study coordinator should explain in the "comment section" of the outline the reasons why the EORTC is joining the trial at a late stage.

The further review process will be decided by the NTC-PRC on the basis of this information.

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### AMENDMENTS

Any modification (Immediately operational, Major, Minor) of ongoing protocols must be submitted to the NTC-PRC secretariat according to the working procedure "Implementation of amendments to protocols" (ref: WP5104) in cooperation with the Data Center team.

- All amendments to EORTC protocols should be approved by the Data Center team in charge of the study.
- Amendments should be electronically submitted to the NTC-PRC secretariat as well as a submission letter indicating the nature of the amendments. If these were suggested by an Independent Data Monitoring Committee (IDMC), the recommendations of the IDMC should be appended.
- The final decision will be sent to the Study Coordinator by the NTC-PRC Chairmen within two weeks of receipt. A copy of appropriate letters will be sent to the Chairman of all EORTC Groups involved in the study, and to the Data Center team.
- Amendments may not be implemented before NTC-PRC approval.

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### PHASE II / III STUDIES

Continuation of a randomized Phase II study as a full Phase III study will be considered as an amendment if:

- The intention to perform the Phase III trial is included in the Phase II trial.
- A decision rule is foreseen in the statistical considerations of the Phase II trial for continuation.
- If the protocol decision rule does not take into account activity and toxicity, the results of the Phase II trial must be reviewed by an Independent Data Monitoring Committee or the Protocol Review Committee which recommends to continue the trial.

## PRACTICAL INFORMATION

Outlines have to be submitted to the NTC-PRC secretariat via Internet; the submission web questionnaire is available from the EORTC Home Page. After each outline submission, an identification number and a password will be automatically be communicated.

Investigators who do not have access to Internet should contact the Data Center team to be informed of other electronic submission procedures.

Full protocols are assembled at the EORTC Data Center by the Protocol Help Desk. Submission to the NTC-PRC is done by informing the NTC- PRC secretariat (preferably by e-mail) that the final version is available at the Protocol Help Desk.

All correspondence should be addressed to (**preferably by e-mail**):

EORTC NTC-PRC Secretariat  
Avenue Mounier 83, bte 11  
B-1200 Brussels (Belgium)  
e-mail: [ntc-prc@eortc.be](mailto:ntc-prc@eortc.be)

The following information is available at the NTC-PRC secretariat and on the EORTC Home Page:

- The dates of PRC meetings.
- The web questionnaire entitled "Outline proposal for clinical trial protocols to be submitted to the EORTC New Treatment Committee and to the EORTC Protocol Review Committee" to be completed as an outline submission.

The following information is available to EORTC members, upon request to the NTC-PRC secretariat:

- The full version of the EORTC working procedure "Submission of protocols for EORTC approval" (ref: WP5101).
- The full version of the EORTC working procedure "Development of EORTC full protocols" (ref: WP5103).
- The full version of the EORTC working procedure " Implementation of amendments to protocols" (ref: WP5104).

## EORTC Scientific Audit Committee (SAC)

The EORTC Scientific Audit Committee (SAC) was created to give independent advice to the EORTC Board regarding the activities and the scientific output (as well as overall priorities and strategies) of divisions and groups of the EORTC. Recommendations also include criteria such as conformity with EORTC structure, policies, and interaction with other EORTC groups.

SAC reviews are the methods by which the EORTC is able to evaluate the effectiveness of the research programs conducted by the groups. The SAC makes suggestions about changes that would be appropriate to strengthen the groups and overall functioning of the EORTC. Each research group carrying the EORTC name is reviewed every three to five years. The SAC is comprised of about 50% of members without any EORTC involvement. Its members represent a cross-section of opinion and expertise. The choice of EORTC members or non-EORTC members is approved by the Board and revised as appropriate.

Members are committed for a three term which is renewable. The chairman of SAC reviews the composition of the SAC after his/her appointment and makes a proposal of new members to the EORTC Board. A turnover of two thirds of the members is recommended to avoid lack of continuity in SAC reviews i.e. not all members should be renewed at the time of change of chairman. SAC consists of 10 members plus two ex-officio members i.e. the EORTC Director General and the EORTC Director Data Center.

### EORTC SCIENTIFIC AUDIT COMMITTEE MEMBERS

G. Mc Vie, London, UK, **Chairman**  
 P. Alken, Mannheim, Germany  
 J-F. Doré, Lyon, France  
 G. Gahrton, Huddinge, Sweden  
 F. Meunier, Brussels, Belgium (ex-officio member)  
 J. Pater, Kingston, Canada  
 D. Raghavan, Los Angeles, USA  
 P. Schöffski, Hannover, Germany, **Secretary**  
 R. Souhami, London, UK  
 P. Symonds, Leicester, UK  
 P. Therasse, Brussels, Belgium (ex-officio member)  
 T. Tursz, Villejuif, France

**SCIENTIFIC AUDIT COMMITTEE REPORT 2000** On March 10, 2000, the Early Clinical Studies Group, the New Drug Development Program, the Cutaneous Lymphoma Group, the Brain Tumor Group, the Melanoma Group as well as the Ophthalmic Oncology Group were reviewed. Later, on November 17, 2000, the Boron Neutron Capture Therapy Group, the Functional Imaging Group (former PET), Children's Leukemia Group as well as the Leukemia Group were reviewed.

## EORTC Quality Assurance Committee (QAC)

The aim of the EORTC QAC is to improve the quality of EORTC research and data by developing guidelines for quality assurance and ensuring that adequate quality assurance mechanisms are operational in all EORTC divisions and groups. These activities include site visits with co-opted experts as appropriate. Quality assurance within the EORTC Data Center is of profound importance and problems experienced are referred to the EORTC Board. The QAC also collects detailed information on the groups' performance, i.e. return of forms, contact with Study Coordinators and other activities.

The membership of the QAC comprises a Chairman (Clinician), elected by the General Assembly three-yearly, and at least six other members. These are a Radiotherapist, a Surgeon, a Medical Oncologist, a Pathologist, a Statistician and a Data Manager.

### EORTC QUALITY ASSURANCE COMMITTEE MEMBERS

C. Van de Velde, <b>Chairman</b> , Leiden	Surgery
P. De Mulder, <b>vice-Chairman</b> , Nijmegen	Medical Oncology
A.M.M. Eggermont, Rotterdam	Chairman Clinical Research Division
J. Bernier, Bellinzona	Radiotherapy
H. van Krieken, Nijmegen	Pathology
C. Molin, Stockholm	Oncology Nursing
R. Paridaens, Leuven	Medical Oncology
F. Meunier, Brussels	Director General ( <i>ex-officio member</i> )
L. Collette, Brussels	Statistician (EORTC Data Center)
P. Therasse, Brussels	Director EORTC Data Center
A. Marinus, Brussels, <b>Secretary</b>	Data management (EORTC Quality Assurance Unit),

### QUALITY ASSURANCE COMMITTEE REPORT 2000

#### Meetings

The Quality Assurance Committee met on July 3, 2000 and October 4, 2000.

#### Discussion points

Emmanuel van der Schueren Fellowship: J. Bernier has prepared a project on Quality Assurance in radiotherapy and applications have been reviewed. Dr Vassilios Kouloulis, a fellow, has started working on the project in January 2001.

The data timeliness procedure has been running for its third year. Data still show improvement. So far only a few centers have been closed for further randomization. All problems were solved in a reasonable time.

The main emphasis during the meetings was the discussion on how to establish good surgical quality control in EORTC clinical trials. Dr Marlies Landheer, a fellow, made an inventory on the current quality procedures among the different EORTC groups performing surgical trials. Together with a literature review, she has prepared two manuscripts which will be finalized during 2001.

Projects for 2001

The committee will further focus on surgical quality control. The manuscripts prepared by Dr Marlies Landheer will be finalized and published this year. Furthermore, the committee will organise a surgical workshop, which will take place within the program of the ESSM in 2002.



## EORTC INDEPENDENT DATA MONITORING COMMITTEE (IDMC)

A permanent Independent Data Monitoring Committee (IDMC) has been established in 2001 to review the status of clinical trials and make recommendations to the groups concerning the trial's continuation, modification and/or publication.

### EORTC INDEPENDENT MONITORING COMMITTEE MEMBERS

T. Wagener, The Netherlands, **Chairman**  
B. Littbrand, Sweden  
J-P. Julien, France  
D. Machin, United Kingdom

'Ad hoc' experts will join this committee according to the specific protocols to be discussed. IDMC involvement is mandatory for Intergroup Trials and is recommended in the following situations:

- All trials requiring the randomization of more than 1 000 patients or more than four years of patient accrual.
- Trials with highly toxic regimens.
- Pivotal trials which will be used for drug registration.
- Randomized Phase II trials which may be continued as a Phase III trial.

The need for carrying out interim analyses should be precisely stated in the protocols. A general EORTC policy for IDMC and interim analysis has been established and is available on the EORTC web site at the following address:

<http://www.eortc.be/Services/Doc/policies/pol004March.pdf>

## EORTC POLICIES + LEGAL ASPECTS

Policy	NR	Last update
Conflict of interest and Confidentiality	001	Nov.1998
Human Research Subjects Protection	002	Jan. 1998
Trial Misconduct and Fraud	003	Jan. 1998
Independent Data Monitoring Committee and Interim Analyses	004	March 2001
Intergroup Trials involving non-EORTC Groups	005	Oct. 1999
Criteria and Guidelines for giving the EORTC Label to scientific meetings	006	Sept. 1999
Scientific Audit Committee	007	Dec. 2000

The full text of EORTC policies is available on EORTC web site at: <http://www.eortc.be/> in main section 'Document'/'EORTC policies'.

#### *Legal Aspects*

- The EORTC is an international association under Belgian law. All trials carried out under the auspices of the EORTC are, by definition, the responsibility of the EORTC. The registered office of the EORTC is at 83, Av. E. Mounier, B- 1200 Brussels, Belgium.
- The EORTC insurance program established in 1993 covers all patients entered in EORTC studies (except patients from the US and Canada) and for which the EORTC is the sponsor/promotor. For studies conducted in collaboration with the pharmaceutical industry, insurance coverage must be discussed on a case-by-case basis.
- In order to fulfill regulatory affairs obligations and to guarantee adequate trial insurance coverage for patients and investigators, according to their national law, the Regulatory Affairs Manager, at the EORTC Data Center must be informed and involved prior to trial activation.

#### *Ethical Aspects and Informed Consent/Insurance*

- All EORTC protocols are written and conducted in accordance with international standards for ethics: the Declaration of Helsinki, Good Clinical Practice guidelines approved by the International Conference on Harmonization. A standard chapter on Ethical Considerations is included in all EORTC protocols.
- In accordance with local, regional, and national requirements, written approval from a competent ethics committee must be obtained before an institution is given the authorization to register or randomize a patient in a study. Standard guidelines for obtaining informed consent from patients entered in EORTC protocols have been developed. Investigators must obtain a dated and signed consent form from each patient.

# EORTC NETWORK

## EORTC Groups & Task Forces

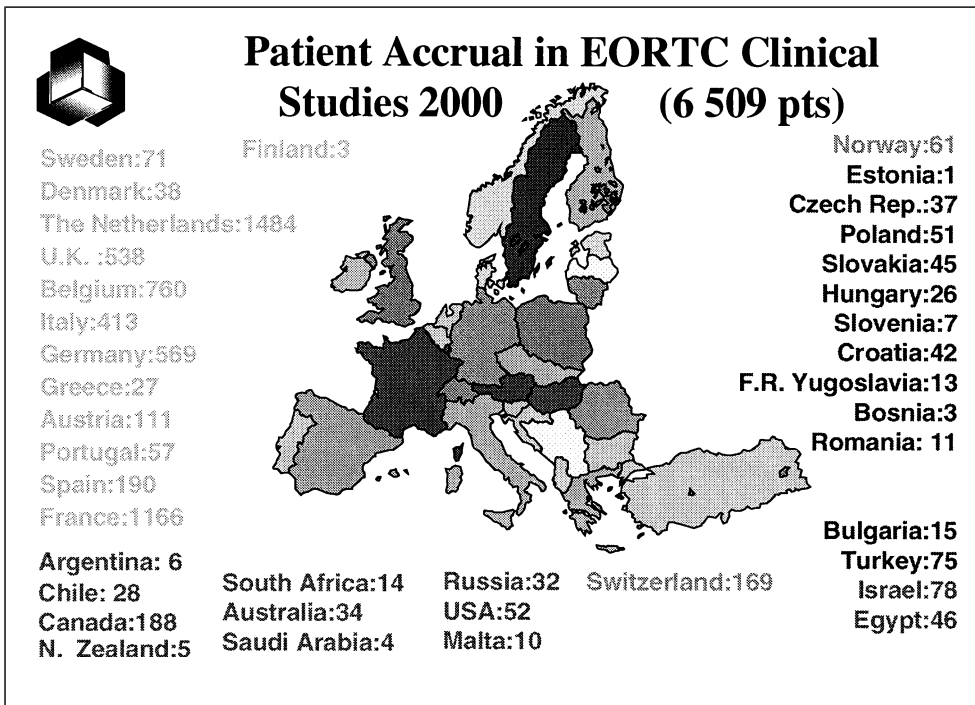
<b>Groups</b>	<b>Chairman</b>	<b>Secretary</b>
Biological Therapeutics Development	H. Zwierzina (Innsbruck)	L. Hakansson (Linköping)
Boron Neutron Capture Therapy	W. Sauerwein (Essen)	J-P. Pignol (Villejuif)
Brain Tumor	C. Vecht (Rotterdam)	M.J. van den Bent (Rotterdam)
Breast Cancer	J. Jassem (Gdansk)	E. Rutgers (Amsterdam)
Children's Leukemia	E. Vilmer (Paris)	A. Ferster (Brussels)
Chronotherapy	F. Lévi (Villejuif)	B. Coudert (Dijon)
Data Management	K. Fishwick (Newcastle/Tyne)	A. Marinus (Brussels)
Early Clinical Studies	P. Fumoleau (Nantes/St Herblain)	N. Pavlidis (Ioannina)
European Osteosarcoma Intergroup	A.H.M Taminiau (Leiden)	-
Functional Imaging (formerly PET)	P. Price (Manchester)	O. Hoekstra (Amsterdam)
Gastrointestinal Tract Cancer	B. Nordlinger (Boulogne-Billancourt)	E. Van Cutsem (Leuven)
Genito-Urinary Tract Cancer	A.V. Bono (Varese)	Z. Kirkali (Izmir)
Gynecological Cancer	I. Vergote (Leuven)	N. Reed (Glasgow)
Head and Neck Cancer	J. Bernier (Bellinzona)	J.B. Vermorken (Edegem)
International Antimicrobial Therapy	C. Viscoli (Genova)	J. Klastersky (Brussels)
Invasive Fungal Infections	B. De Pauw (Nijmegen)	C. Cordonnier (Creteil)
Leukemia	T. De Witte (Nijmegen)	J-P. Marie (Paris)

<b>Groups</b>	<b>Chairman</b>	<b>Secretary</b>
Lung Cancer	Ch. Manegold (Heidelberg)	A. Ardizzoni (Genova)
Lymphoma	J. Raemaekers (Nijmegen )	H. J. Kluin-Nelemans (Leiden)
Melanoma	D. Lienard (Lausanne)	U. Keilholz (Berlin)
Oncology Nurses	P. Di Giulio (Milan)	H. Gall (Amsterdam)
Pathology	J. W. Oosterhuis (Rotterdam)	A. Spatz (Villejuif)
Pharmacology and Molecular Mechanisms	A. Gescher (Leicester)	J. Schellens (Amsterdam)
Preclinical Therapeutic Models	J.L. Merlin (Nancy)	N. Zaffaroni (Milan)
Quality of Life	P. Fayers (Aberdeen)	T. Young (Northwood)
Radiation Technologists	J. Berridge (Nottingham)	M. A. Coffey (Dublin)
Radiotherapy	V.G. Budach (Berlin)	R. Mirimanoff (Lausanne)
Receptor and Biomarker	H. Magdelénat (Paris)	N. Brüner (Copenhagen)
Screening and Pharmacology	I. Fichtner (Berlin)	P. Lelieveld (Moerkapelle)
Soft Tissue and Bone Sarcoma	O.S. Nielsen (Aarhus)	I. Judson (London)

<b>Task Forces</b>	<b>Chairman</b>	<b>Secretary</b>
Cancer in Elderly	M. Aapro (Génolier)	-
Cutaneous Lymphoma	R. Knobler (Vienna)	S. Witthaker (London)
Ophthalmic Oncology	J. Prause (Copenhagen)	T. Kivela (Helsinki)
Pain and Symptoms Control	B. Van den Eynden (Mortsel)	A. Luebbe (Bad Lippspringe)

# EORTC CLINICAL STUDIES

In 2000, a total of 6 509 new patients were entered in EORTC trials.



## TOTAL NUMBER OF NEW PATIENTS IN EORTC CLINICAL STUDIES

<b>Country</b>	<i>1999</i>	<i>2000</i>
<i>European Union</i>		
Austria	135	111
Belgium	838	760
Denmark	22	38
Finland	4	3
France	1246	1166
Germany	364	569
Greece	50	27
Italy	512	413
The Netherlands	1619	1484
Portugal	104	57
Spain	193	219
Sweden	51	71
United Kingdom	444	538
<i>Total European Union</i>	5 582 (85,69%)	5 456 (83,82%)
<b>Other European Countries</b>		
Bulgaria	8	15
Bosnia	-	3
Croatia	29	42
Czech Republic	30	37
Estonia	2	1
F.R. Yugoslavia	35	13
Hungary	31	26
Malta	10	10
Monaco	1	-
Norway	46	61
Poland	114	51
Romania	7	11
Russia	38	32
Slovakia	45	45
Slovenia	8	7
Switzerland	191	169
Turkey	117	75
<i>Other Countries</i>		
Australia	44	34
Canada	29	188
Egypt	26	46
Israel	46	78
New Zealand	6	5
South Africa	11	14
Saudi Arabia	6	4
U.A. Emirates	2	-
USA	50	52
Argentina	-	6
Chile	-	28
<b>Total other European &amp; other countries</b>	<b>932 (14,31%)</b>	<b>1053 (16,17%)</b>
<b>Total</b>	<b>6 514</b>	<b>6 509</b>

## ACCRUAL OF NEW PATIENTS BY EORTC GROUPS

<b>EORTC Groups</b>	<b>2000</b>	<b>1998-2000</b>
	<b>Number of patients</b>	
Biological Therapeutics Development	25	80
Boron Neutron Capture Therapy	6	18
Brain Tumor	130	416
Breast	274	1 075
Children's Leukemia	250	760
Chronotherapy	199	444
Early Clinical Studies	295	851
European Osteosarcoma Intergroup	28	67
Gastrointestinal	639	1 278
Genito-Urinary	1 232	3 227
Gynecological	343	692
Head and Neck Cancer	210	501
International Antimicrobial Therapy	123	848
Invasive Fungal Infections	51	137
Leukemia	330	1 650
Lung	520	1 620
Lymphoma	329	1 207
Melanoma	218	1 213
Ophthalmic Oncology	0	5
Quality of Life	270	719
Radiotherapy	1 022	2 927
Soft Tissue and Bone Sarcoma	275	760



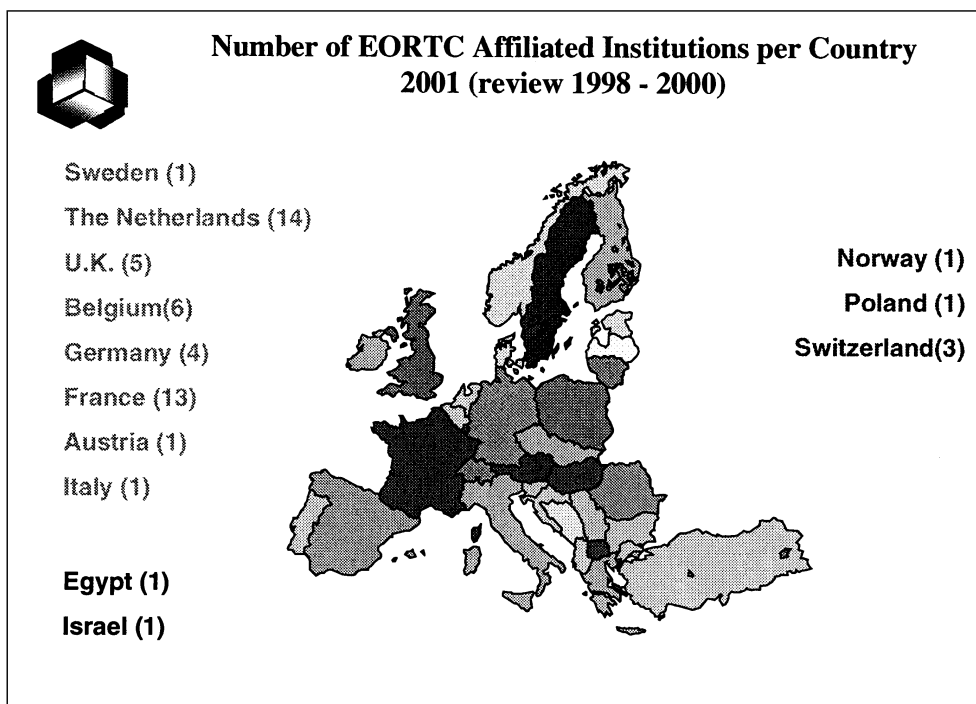
## EORTC Affiliated Institutions & Affiliated Departments 2001 (Review 1998 - 2000)

The EORTC has established a list of institutions actively participating in EORTC clinical trials that is updated on a yearly basis.

The list shows institutions which have been recognized in 2001 as EORTC affiliated institutions on account of their participation in EORTC studies over the last three years (1998-2000).

The criteria used to merit that recognition are:

1. Recruitment of 75 patients during a period of three years (1998- 2000) with a minimum of 15 patients per year.
2. Participation in more than two EORTC groups.
3. Institutions participating in less than three EORTC groups and fulfilling the other criteria are "EORTC Affiliated Departments".



## EORTC AFFILIATED INSTITUTIONS 2001 (REVIEW 1998 - 2000)

Institution	Number of groups	Accrual 2000	Accrual 1998-2000
1. UZ Gasthuisberg - Leuven, B.	16	282	778
2. UZ Rotterdam, NL	11	213	625
3. University Medical Centre Nijmegen, NL	16	158	550
4. Academisch Medisch Centrum - Amsterdam, NL	8	150	429
5. Hôpitaux Universitaires Bordet- Erasme – Brussels, B.	15	92	403
6. Cliniques Universitaires St. Luc - Brussels, B.	8	102	366
7. Leiden University Medical Center, NL	11	85	301
8. Institut Gustave Roussy - Villejuif, F.	9	100	293
9. Antoni Van Leeuwenhoekhuis – Amsterdam, NL	10	87	283
10. Dr. Bernard Verbeeten Instituut - Tilburg, NL	4	92	275
11. Academisch Ziekenhuis Der Vrije Universiteit – Amsterdam, NL	11	69	249
12. Centre Georges-François Leclerc – Dijon, F.	7	74	240
13. Newcastle General Hospital, GB	6	86	230
14. Royal Marsden Hospital - London/Sutton, GB	8	62	229
15. Maria Sklodowska-Curie Cancer Center, Warsaw, PL	8	32	229
16. Universitair Medisch Centrum- Utrecht, NL	11	71	228
17. Centre Hospitalier Universitaire Vaudois – Lausanne, CH	10	50	219
18. Hôpital Edouard Herriot - Lyon, F	4	22	204
19. Bosch Medicentrum-Groot Ziekengasthuis 'S Hertogenbosch, NL	5	70	199
20. Universitätsklinikum (Charite) - Humboldt - Universitaet -Berlin, D	4	96	186
21. Algemeen Zienkenhuis Middelheim – Antwerpen, B	12	47	164
22. Centre Hospitalier Régional - Besancon, F	8	42	147
23. Academisch Ziekenhuis Maastricht, NL	9	52	142
24. Centre Alexis Vautrin - Vandoeuvre- lez-Nancy, F	5	55	137
25. Western General Hospital - Edinburgh, GB	7	44	137
26. Western Infirmary – Glasgow, GB	7	38	132

<b>Institution</b>	<b>Number of groups</b>	<b>Accrual 2000</b>	<b>Accrual 1998-2000</b>
27. Universitair Ziekenhuis Antwerpen – Edegem, B	11	28	132
28. Norwegian Radium Hospital – Oslo, N	6	42	130
29. Centre René Gauducheau – St. Herblain, F	5	53	125
30. Institut Bergonie – Bordeaux, F	5	41	125
31. Universitätsklinik ULM - D	3	31	124
32. Academisch Ziekenhuis Groningen, NL	6	44	120
33. Center Léon Bérard – Lyon, F	7	33	119
34. Sahlgrenska Sjukhuset -Göteborg, S	3	56	118
35. Universitaetsspital – Zurich, CH	4	35	118
36. Onze Lieve Vrouw Gasthuis - Amsterdam, NL	7	34	116
37. Klinikum Grosshadern Ludwig- Maximilians Univ. München, D	4	24	113
38. Universitaair Ziekenhuis - Gent, B	5	38	111
39. Kaiser Franz Josef Spital – Vienna, A	6	37	111
40. Arnhem's Radiotherapeutisch Instituut -NL	3	39	110
41. Centre Hospitalier Régional de Grenoble -La Tronche, F	3	34	106
42. Rambam Medical Center - Haifa, IL	5	52	103
43. Hôpital Necker-Institut Curie - Paris, F	4	29	103
44. National Cancer Institute – Cairo, ET	4	46	97
45. Robert-Roessle– Klinik, Humboldt Universität – Berlin, D	4	38	95
46. St. Antonius Ziekenhuis – Nieuwegein, NL	3	27	89
47. Hôtel-Dieu – Paris, F	3	24	88
48. Centre Oscar Lambret, Lille, F	4	45	86
49. Centre Antoine Lacassagne - Nice, F	7	23	84
50. Centro di Riferimento Oncologico- Aviano, I	6	18	81
51. Inselspital - Bern, CH	6	22	77
52. Western Park Hospital - Sheffield, GB	6	30	75
<b>TOTAL number of patients</b>		<b>3 194</b>	<b>10 131</b>

## EORTC AFFILIATED DEPARTMENTS - 2001 (Review 1998-2000)

Institution	Number of groups	Accrual 2000	Accrual 1998-2000
1. Ospedale Molinette – Torino, I	2	47	156
2. Ospedale Di Circolo E Fondazione Macchi - Varese, I	2	39	143
3. Bristol Royal Infirmary - Bristol, GB	2	28	109
4. Ibnî Sina Hospital – Ankara, TR	2	17	109
5. Ospedale Sant Anna – Como, I	1	33	105
6. Hôpital Debrousse – Lyon, F	1	19	101
7. Thoraxklinik Rohrbach – Heidelberg, D	1	18	91
8. Radiotherapeutisch Instituut Stedendriekhoek En Omstreken - Deventer, NL	1	37	83
9. Clinical Hospital Rebro - Zagreb, CRO	1	34	83
10. Marmara University Hospital - Istanbul, TR	2	26	83
11. Freeman Hospital - Newcastle-upon-Tyne, GB	1	20	83
12. Centre Hospitalier Régional de Lille – Lille, F	2	21	81
<b>TOTAL number of patients</b>		<b>339</b>	<b>1 227</b>

## **EORTC FELLOWSHIP PROGRAMS**

- The EORTC Data Center Fellowship Program was established in 1991 to foster the exchange of physicians and scientists from all over the world.

The EORTC Data Center encourages the one up to three-year stay of research fellows (medical doctors, biostatisticians, health economists, computer analysts and other scientists) specifically linked to the EORTC groups, specialty units or specific research projects involving the EORTC Data Center's database.

The purpose of this fellowship program is either to provide training in the methodology of clinical research for physicians and other professionals interested in cancer clinical research or to conduct research projects and/or PhD thesis taking into account the large amount of data available within the EORTC Databases and the expertise of the EORTC Data Center staff.

Over the past nine years, more than 70 research fellowships have been awarded at the EORTC Data Center with support from various sources (EORTC Foundation, "Fondation Cancer" (Belgium), several European cancer leagues, the European Commission and pharmaceutical industries).

These fellows come from various countries within the European Union as well as from Australia, Canada, and Eastern and Central Europe and they should become excellent EORTC investigators upon their return to their own country.

Such an approach also promotes the rapid dissemination of clinical trials results; their implementation on a European-wide basis should therefore have a significant impact on clinical practice to improve cancer care for all patients.

- The EORTC Lady Grierson Research Fellowship, generously endowed by Sir Ronald Grierson, founding Chairman of the EORTC Foundation, in memory of his late wife, is dedicated to fostering research into improving the quality of life of patients with cancer. This biennial award is intended for clinical specialists or scientists who want the opportunity to conduct scientific research on quality of life evaluation in cancer clinical trials.
- The Emmanuel van der Schueren Fellowship was created in 1999 in memory of Prof. Emmanuel van der Schueren. The aim of the fellowship is to promote research on quality assurance in radiotherapy. The first Emmanuel van der Schueren Fellow (supported by the "Vlaamse Liga tegen Kanker" and the EORTC) started his/her project at the EORTC Data Center in 2001. For the following years, this program will be jointly supported by the "Vlaamse Liga tegen Kanker", the EORTC, FECS and ESTRO.
- The Sir Ronald Grierson Fellowship was established by the EORTC Board in 2000 in recognition of Sir Ronald Grierson, Chairman of the EORTC Foundation (1976–2000). The first fellow will be selected to start his/her research at the Data Center in 2001.
- Several national Cancer Leagues have agreed to support the EORTC Cancer Communications Fellowship Program at the EORTC Central Office from 1997 onwards. This program aims at providing updated information to cancer leagues supporting the EORTC Foundation on major trials conducted by the EORTC as well as on research results to be disseminated to the patients and the public. Taking into account the success of this initiative, the EORTC has allocated since 2000 a full-time staff member to the EORTC Communications Office.
- The EORTC is also actively involved in the EORTC/NCI Exchange Program (see chapter "EORTC/NCI Cooperation").

## THE EORTC DATA CENTER FELLOWSHIP PROGRAM

Pascal Piedbois, MD	France	1991
Peter Clahsen, MD	The Netherlands	1992-94
Ann Marie Ptaszynski, MD	Belgium	1992-94
Sabrina Pocceschi (lawyer)	Italy	1992-96
Patrick Therasse, MD	Belgium	1993-95
Magdalena Bielska-Lasota, MD	Poland	1993-94
Saïd Serbouti, MS	France	1993-94
Ivana Teodorovic, MD	Yugoslavia	1993
Adam Pawinski, MD	Poland	1993-95
Cristina Oliva, MD	Italy	1993-94
Anne Magotteaux, MD	Belgium	1993-94
Philomena O'Brien Computer analyst	United Kingdom	1993-94
Denis Lacombe, MD	France	1993-96
Guido Hochtin-Boes, MD,MS	Belgium	1993-95
Koen Torfs, MS	Belgium	1993
Elke Bahner, MD	Germany	1993-94
Desmond Curran, MS	Ireland	1993-97
Chrisa Tsitsa, MS	Greece	1993-94
Stephan Tomasovic, Pharm.	Belgium	1994-95
Eugenio Zabala, PhD	Spain	1994-95
Channa Debruyne, MD	Belgium	1994-97
Niels Neymark, MS	Denmark	1994-97
Thierry Gil, MD	France	1994-96
Hamdy Adham, MD	Belgium	1994-95
Jozsef Horti, MD	Hungary	1994-96
Thierry Pignon, MD	France	1995
Tracey Cooke, RN	United Kingdom	1995-96
Susan Keating, MD	United Kingdom	1995-99
Laurence Collette, MSc	Belgium	1995-98
Eugenio Donato di Paola, MD	Italy	1995-2000
Francesco Pignatti, MD	Italy	1995-96
Henk-Jan van Slooten, MD	The Netherlands	1995-96
Jan Bussels, Health Economist	Belgium	1995-96
Petra J. Timmers, MD	The Netherlands	1995-97
Michèle van der Heyden, Health Economist	Belgium	1995-98
Sandra Kalman, ADCLT	Australia	1996-97
Gabriele Calaminus, MD	Germany	1996-97
Josée Anne Roy, MD	Canada	1996-97
Sibel Akhan, MD	Turkey	1996-97
Debora Goran, RN	United Kingdom	1996-98
Ines Adriaenssen, Health Economist	Belgium	1996-99
Simon Cleall, MSc	United Kingdom	1997-98
Maryam Bigdeli, Pharm. MPH	Belgium	1997-98

Pascal Piedbois, MD	France	1991
Lisa Tyndall	Australia	1997-98
Sabine Steimle, MA	Germany	1997-99
Benoît Baron, MSc	Belgium	1997-98
Pieter Clahsen, MD	The Netherlands	1998
Helena Wagenaar, MD	The Netherlands	1998-2000
Anastasia Anastasopoulou, MSc	Greece	1998-99
Susan Caleo	Australia	1998-99
Ioannis Lainas, MS, Pharm.	Greece	1998-99
Sofie Van Impe	Belgium	1998-2001
Catherine Legrand, MSc	Belgium	1998-99
Kristel Van Steen, MSc	Belgium	1998-99
Conny den Hertog-Vrieling, MD	The Netherlands	1999
Elizabeth Gray	Australia	1999-
Alfredo Zurlo, MD	Italy	1999-2000
Thomas Roy, MS	France	1999-
Dritan Bejko, MD, MS	Albania	1999-2000
Florence Duffaud, MD	France	1999-2000
Jos van der Hage, MD	The Netherlands	1999-2000
Sandrine Marreaud, MD	France	1999
Griet Boon, MS	Belgium	1999-2001
Nina Bijker, MD	The Netherlands	1999-2000
Kay Roche, PhD	Ireland	1999-2000
Peggy Hugo, MD	Belgium	2000
Heidy vanWijk, MD	The Netherlands	2000-
Marlies Landheer, MD	The Netherlands	2000-2001
Liliana Baila, MD	Romania	2000-2001
Xavier Paoletti, MS	France	2000-2001
Gary Collins, MS	United Kingdom	2000-
Natasa Djurasinovic, MD	Yugoslavia	2000-

#### THE EORTC LADY GRIERSON RESEARCH FELLOWSHIP PROGRAM

Ingvar Rosendahl, BA	Sweden	1996-97
Jocelyn Kramer, MD	United Kingdom	1999-2000

#### THE EMMANUEL VAN DER SCHUEREN FELLOWSHIP PROGRAM

Vassilios Kouloulas, MD, PhD	Greece	2001
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## EORTC / EUROPEAN COMMISSION COOPERATION

E.U support was provided between 1986 and 1990, for the EORTC Data Center to coordinate high-quality clinical research in oncology in Europe and for the establishment of a comprehensive quality assurance program.

More recently, the European Commission (Directorate-General for Health and Consumer Protection, Directorate-General for Research, Directorate-General for Information Society) provided support to other innovative research projects including cost evaluation of treatment modalities in cancer patients, quality of life assessments of cancer patients including childhood cancer, quality assurance programs, leukemia research, supportive care of cancer patients, as well as projects on telematics, biological response modifiers, pharmacokinetics, management of clinical trials in radiotherapy, meta-analysis of cancer clinical studies, and fellowships for medical doctors, statisticians and other scientists.

Core support is indeed crucial to pursue a strong European-scale effort in the field of clinical research in oncology with the aim of establishing on an independent basis state-of-the art treatment strategies to rapidly improve cancer care at European level.

Significant progress will only result from international cooperation. Consistent with the principle of subsidiarity, therefore, the central structure of the EORTC should be regarded as the vital key to harmonizing and monitoring high-quality cancer clinical research in Europe and as such deserves recognition and support at a European level as a network of excellence contributing to both the EU research effort and to the protection and improvement of public health.



# EORTC / U.S NATIONAL CANCER INSTITUTE (NCI) EUROPEAN COLLABORATION

The **National Cancer Institute** (NCI) is the leading U.S. agency for cancer research and treatment in the United States and is part of the National Institutes of Health (NIH). The NCI was established by the U.S. Congress in 1937 and its programs were intensified in 1971 after passage of the National Cancer Act. The vast majority of NCI funds (80%) goes to grants and contracts to universities, medical schools, cancer centers, research laboratories and private firms. The NCI supports scientists all over the world in a broad spectrum of research activities.

## EUROPEAN-NCI COLLABORATIVE ACTIVITIES

A history of nearly three decades of co-ordinated cancer treatment research between the EORTC and the NCI has brought great opportunities for more efficient development of new cancer therapeutics. As part of the NCI's global strategy, the NCI Liaison Office in Brussels was created in 1972, to search for potential new anti-cancer substances from European sources. The Office expanded quickly and has been pivotal in moving Europe and North America closer to a common linked network.

A European Collaborative Program initiated with the EORTC in the early seventies continues to be highly successful in promoting the exchange of information on new drugs for both pre-clinical and clinical evaluation. The compound acquisition, selection, screening, formulation, toxicology, and the clinical evaluation are now well integrated between Europe and the USA. Much of this success in new drug development has been facilitated by the close working relationship between the NCI, the EORTC, and the British Cancer Research Campaign (CRC) in London.

## EUROPEAN COLLABORATIVE AGREEMENT

A trilateral Collaborative Agreement signed between NCI, EORTC and CRC, and a bilateral Agreement between NCI and the Southern Europe New Drugs Organisation (SENDO) in Italy defines the role of each organisation in the clinical development of new anti-cancer drugs. This expanded international collaboration also includes the exchange of information and new drug candidates of mutual interest at all stages of pre-clinical and clinical evaluation. High priority drug candidates may, by mutual agreement, be assigned to any appropriate CRC, EORTC, SENDO or NCI laboratory or clinic that can aid in or carry out a necessary step in the development of the agent. Drugs are now developed in such a way that they may enter clinical trials on either side of the Atlantic. Initial clinical trials are conducted according to mutually-agreed protocols and in compliance with appropriate standards for the testing of experimental agents, so as to facilitate the acceptability of data on Phase I results by the appropriate regulatory authorities. Joint guidelines on pharmaceutical formulation were published in the European Journal of Cancer and Clinical Oncology. Based on the current state-of-the-art, joint guidelines on pre-clinical toxicology are available and updated as necessary.

By mutual agreement this collaboration has been extended to provide new compounds of European origin from the NCI in-vitro anti-cancer screening program to the European collaborative groups. A review and selection committee composed of members of EORTC, CRC, and SENDO has so far reviewed the data on more than 1 000 compounds, of which 64 have been considered as being of interest for potential further anti-cancer evaluation in Europe.

With the registration by the EORTC and CRC of their Drug Master Files with the FDA, and thus the recognition by the FDA of the leading European centers, it is now well recognized that the pre-clinical studies as well as the clinical trials carried out under the collaborative program meet the requirements of the various regulatory agencies both in Europe and the United States. Over the past several years, it has become common practice for the FDA to approve INDs based on European studies carried out under these guidelines, as is documented by numerous examples. Very recently (March 2001) the US FDA published a document "Guidance for Industry- Acceptance of Foreign Clinical Studies". This is an important official recognition of what the NCI Liaison Office has been promoting for European clinical studies carried out by NCI's collaborators.

The granting of an International Project Assurances Certificate (ICPA) from the US Agency for Health Research Protections (AHRP) to the EORTC and the CRC (UK), are remarkable achievements which will add a new dimension to the transatlantic cooperation. It is anticipated that other national/regional organisations will join this network. By combining resources, key questions in the diagnosis and prevention of cancer may be answered. A "core" of leading world experts, now well linked, has the potential of expanding globally in the new Millennium.

#### THE NCI LIAISON OFFICE

The NCI Liaison Office in Brussels, Belgium, situated adjacent to the EORTC Central Office/Data Center, is part of the Office of the Director, Division of Cancer Treatment and Diagnosis, NCI, and is an integral part of the NCI. Its role is to act as a European-based link to NCI cancer research and treatment programs in the United States. It facilitates the interchange of information, ideas, experimental drugs, scientific expertise and scientists between Europe and the US NCI. It works in close collaboration with the EORTC, the British Cancer Research Campaign (CRC) and the Southern Europe New Drugs Organisation (SENDO) in Italy, as well as with other European cancer research institutes and pharmaceutical/chemical industries. Its role is to help create a network of cancer experts and cancer centers between Europe and the US NCI which work towards a common goal, to enable rapid progress in cancer research on an international scale.

Through the NCI Liaison Office, the NCI is represented on numerous European committees involved in new drug development, as well as on the EORTC Board and Council and the CRC Phase I/II clinical trials committee. The Office participates in working groups that disseminate cancer research and drug development information throughout Europe, and is also an observer on the European Drug Development Network (EDDN).

The Office assists with the acquisition of new agents from Europe for NCI's screening programs, and supports an international exchange of experimental drugs for pre-clinical and clinical evaluation. It keeps contacts with more than 600 European suppliers, and until the recent change to a web-based submission procedure acquired approx. 2 000 compounds per year from European sources for NCI's in-vitro anti-cancer screening program. Pre-clinical collaborative agreements with European institutions, administered by the Office, are providing important expertise on experimental tumor

models development, human tumor cell lines, and xenografts. These collaborative groups (e.g. EORTC Screening & Pharmacology and Pharmacology & Molecular Mechanisms Groups) also provide secondary evaluation of potentially effective anti-cancer drugs originating from the NCI in-vitro screening program.

The Office also assists other NCI divisions and programs with their European activities, such as exchange and support programs of the Office of International Affairs. Furthermore, the Office collects European cancer research protocols for the NCI Cancer Information Products and Systems (CIPS) Program, Office of Communications, NCI, for inclusion in NCI's clinical database PDQ/CancerNet (Internet address: <http://cancertrials.nci.nih.gov/>) PDQ/CancerNet is a database which contains cancer treatment research information. PDQ/CancerNet allows investigators to have access to both ongoing US and European protocols. In addition to the clinical studies under EORTC auspices, the inclusion of investigational protocols was extended to national groups in the early 90s. These include protocols from e.g. CRC, MRC, SCTN and SIOP from the UK, NKB from the Netherlands, SAKK from Switzerland, the German Cancer Society, FNCLCC from France, and from other national groups. The NCI Liaison office actively seeks new European groups with an interest to submit their research protocols to PDQ/CancerNet.

### **Long-term and Short-term Exchange Programs**

The NCI Liaison continues to co-ordinate several programs for the exchange of experts in the field of cancer research between Europe and the United States.

So far, 76 fellows have been appointed through the EORTC/NCI Exchange Program (see chapter: The EORTC/NCI Exchange Program). The Office of International Affairs (OIA), NCI, has overall responsibility for this program, the duration of which ranges from one to three years. Another 44 fellows have also participated in the Developmental Therapeutics and Division of Cancer Biology (and the former Division of Cancer Etiology) Exchange Programs, which are generally for a duration of two weeks to two months. With few exceptions the fellows were all from EORTC institutions receiving training in the United States. Both of these programs facilitate the collaboration between the European Oncology Community and the NCI, as well as other cancer research institutes in the United States. It is expected that these programs will continue and could probably be expanded in view of the enthusiastic reception on both sides of the Atlantic.

### **THE EORTC / NCI EXCHANGE PROGRAM**

The Exchange Program originated in an agreement between the EORTC and the US National Cancer Institute signed in April 1985 by virtue of which European research scholars with at least three years of postdoctoral research may apply for an EORTC/NCI exchangeship to do fundamental research in NCI laboratories in the US, and US cancer researchers to work at EORTC-related institutions in Europe.

All candidates had completed three years of research related to oncology at the time they left for the US or for Europe; all had been accepted in specific laboratories of interest to them, and with few exceptions all were assured that they would be welcomed back by their former employers after their research experience.

Selected fellows receive one half of their subsistence from a European source, most often their home institution or a European foundation, the other half is provided by the NCI or one of its extramural institutions. Dr. Federico Welsch, Director of the Office of International Affairs, NCI, has executive responsibilities for the NCI part of the program, in collaboration with the selection committee of the EORTC. The NCI Liaison Office is responsible for administering the program from Brussels. The Chairperson of the EORTC/NCI Exchange Program is Dr. Françoise Meunier, Director General of the EORTC.

The EORTC Selection Committee considers candidates from all EORTC member countries, Eastern European countries, and from the United States. As part of the agreement, qualified American researchers recommended by the NCI could also be assigned to EORTC approved laboratories.

Details of the program, qualification requirements and instructions for application should be obtained from the NCI Liaison Office, EORTC/NCI Exchange Program, 83, Av. E. Mounier, Bte. 12, 1200 Brussels, Belgium, Phone (2) 772 22 17, Fax (2) 770 47 54. Internet site <http://www.eortc.be>, see job opportunities.

Candidates are invited to apply for the Exchange competition which takes place in June and December each year. Applications should be received as soon as possible before the deadlines (April 15 and October 15.)

**THE EUROPEAN JOURNAL OF CANCER**  
**John Smyth, Editor-in-Chief**

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The European Journal of Cancer, published since 1965, is the official journal of the EORTC, the Federation of

European Cancer Societies (FECS), the European Association for Cancer Research (EACR) and the European School of Oncology (ESO) and, new since January 2000, the European Society of Mastology (EUSOMA).

It is an international, oncology journal, publishing original research, review articles, editorial comments and controversies. The 1999 Impact Factor (published in 2000) was 2.5 which compares favourably with the competitor journals.

The EJC published 18 issues in 2000, including three Special Issues on "Tumor Prevention and Genetics, Invasion and Metastasis, and Cervical Cancer Screening in the European Union". A number of supplements were also produced, including the abstract books of major European Cancer Conferences.

In 2000 there were approximately 840 manuscripts submitted and the acceptance rate was 38%. 64% of the latter were original papers. The journal continues to have a vast time to first decision (7 weeks) and the editorial board are committed to trying to continuously improve the total time taken in review acceptance and publication.

EJC Online was successfully launched in 1998 (<http://www.elsevier.com/locate/ejconline>) giving complete access to the journal's contents. While this service was free until mid 1999, there is now the possibility to join the EJC-Club and subscribe to the EJC at a very attractive personal annual fee.

There have been significant changes in the editorial board since the beginning of 2001, with Prof. Jaap Verweij and Prof. Maurizio D'Incalci, joining a strong board. This new correction of editors are committed to trying to promote the activities of EORTC and to improve communication around the ever expanding community, of scientists and clinicians working on cancer research throughout Europe.

All correspondence and manuscript submissions should be addressed to:

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# CURRENT RESEARCH AND STRATEGIES





**Information on all ongoing EORTC protocols is available on the EORTC web site, at <http://www.eortc.be>.**

**Patients can be randomized in all EORTC protocols via the EORTC web site, at the same address,  
or by phone at  
+32 2 774 16 00  
From Monday to Friday, from 9 a.m. to 5 p.m.**

# EORTC OPEN PROTOCOLS as of April 2001

Study	Target Accrual	TITLE
<b>EORTC Boron Neutron Capture Therapy Group</b>		
11961	30	<i>Trial Coordinator : W. Sauerwein, Essen</i> Postoperative Treatment of Glioblastoma with BNCT at the Petten Irradiation Facility – Phase I Clinical Trial.
<b>EORTC Biological Therapeutics Development Group</b>		
13001	30	<i>Trial Coordinator: S. Aamdal, Oslo</i> Phase I Clinical trial of recombinant viscumin (rViscumin, rMistletoe Lectin, rMI) administered twice weekly by the subcutaneous route in patients with solid tumors after failure of standard therapy.
13992	20	<i>Trial Coordinator: G. Jayson, Manchester</i> A Phase I, open label multiple dose, safety and pharmacokinetic study of intravenously administered humanized anti-VEGF monoclonal antibody (HuMV833) to patients with relapsed or refractory solid tumors.
<b>EORTC Brain Tumor Group</b>		
26981	520	<i>Trial Coordinator: R. Stupp, Lausanne</i> Concomitant and adjuvant Temozolomide and Radiotherapy for newly diagnosed glioblastoma multiforme. A randomized Phase III study. Joint with EORTC RT 22987, NCIC CYG CE.3, SAKK.
26951	350	<i>Trial Coordinator: M.J. Van Den Bent, Rotterdam</i> Phase III study of adjuvant Procarbazine, CCNU and Vincristine chemotherapy in patients with highly anaplastic oligodendroglioma (randomized) Joint with MRC BR 11.
26991	605	<i>Trial Coordinators: B. Baumert, Zurich, M. Brada, Sutton</i> Focal fractionated conformal stereotactic boost following conventional radiotherapy of high-grade gliomas: A randomized Phase III study. (Joint study of the MRC and EORTC Radiotherapy Group and the Brain Tumor Group) EORTC 22972/26991-MRC BR10.
<b>EORTC Breast Cancer Group</b>		
10925	3780	<i>Trial Coordinators: H. Bartelink, Amsterdam, H. Struikmans, Utrecht, A. Fourquet, Paris, W.F. Van Den Bogaert, Leuven</i> Phase III randomized trial investigating the role of internal mammary and medial supraclavicular (IM-MS) lymph node chain irradiation in stage I-III breast cancer (Joint study of the EORTC Radiotherapy Group and the EORTC Breast Cancer Group EORTC 22922/10925).
10951	768	<i>Trial Coordinator: R. Paridaens, Leuven</i> Randomized Phase II – III study in first line hormonal treatment for metastatic breast cancer with Exemestane or Tamoxifen in postmenopausal patients.
10967	4400	<i>Trial Coordinator: R. Paridaens, Leuven</i> Randomized double-blind trial in postmenopausal women with primary breast cancer who have received adjuvant Tamoxifen for 2-3 years, comparing subsequent adjuvant Exemestane treatment with further Tamoxifen.

Study	Target Accrual	TITLE
10981	3485	<i>Trial Coordinator: E.Rutgers, Amsterdam</i> After Mapping of the Axilla: Radiotherapy Or Surgery AMAROS.
10983	2500	<i>Trial Coordinator: M. Piccart, Brussels</i> A Phase III randomized double blind study of letrozole versus placebo in women with primary breast cancer completing five or more years of adjuvant Tamoxifen (NCIC CTG MA.17, EORTC study 10983). Intergroup trial with the Cancer and Leukemia Group B, the Eastern Cooperative Oncology Group, the International Breast Cancer Study Group, the National Cancer Institute of Canada-Clinical Trial Group and with the Southwest Oncology Group and North Central Cancer Treatment Group.
10992	1300	<i>Trial Coordinator: Janusz Jaskiewicz, Warsaw</i> Habits Hormonal replacement therapy after breast cancer diagnosis - is it safe? Protocol for randomized clinical study concerning hormonal replacement therapy (HRT) after previous radical breast cancer treatment. Intergroup trial with the International Breast Cancer Study Group and the Scandinavian Breast Group.
10993	100	<i>Trial Coordinator: R.Coleman, Sheffield, C. Dittrich, Vienna</i> A randomised Phase II study of two different schedules of Caelyx in metastatic breast cancer. Intergroup trial with the EORTC Early Clinical Studies Group.
10994	1440	<i>Trial Coordinator: H. Bonnefoi, Genève</i> First prospective Intergroup Translational Research Trial assessing the potential predictive value of p53 using a functional assay in yeast in patients with locally advanced/inflammatory or large operable breast cancer prospectively randomised to a taxane versus a non taxane regimen. Intergroup collaboration with Schweizerisches Arbeitsgemeinschaft Klin. Krebsforschung Swedish Breast Cancer Group.
		<b>EORTC – IDBBC studies</b>
10993	100	<i>Trials Coordinators: R. Coleman, UK (IDBBC Coordinator), C.Dittrich (ECSCG Coordinator), Austria. A randomised Phase II study of two different schedules of caelyx in metastatic breast cancer.</i>
<b>EORTC Children's Leukemia Group</b>		
58921	310	<i>Trial Coordinators: C. Behar, Reims, E. Vilmer, Paris, Y. Bertrand, Lyon</i> Randomized Phase III study comparing IDA versus MTZ in induction and intensification treatment of AML or MDS in children.
58951	1500	<i>Trial Coordinators: J. Otten, Brussels, N. Phillippe, Lyon</i> Dexamethasone versus prednisolone during induction and maintenance therapy, prolonged versus conventional duration of L-Asparaginase therapy during consolidation and late intensification, corticoid + VCR pulses during maintenance in ALL and NHL of childhood. A Randomised Phase III study.
58953	50	<i>Trial Coordinator: A. Thyss, Nice</i> Phase II Study of Fludarabine + Idarubicine + Aracytine in Refractory or Relapsed Acute Lymphocytic Leukemia in Children.
<b>EORTC Chronotherapy Group</b>		
05962	200	<i>Trial Coordinator: F. Lévi, Villejuif</i> Infusional 5-Fluorouracil with or without cisplatin and with or without chronomodulation against locally-advanced or metastatic pancreatic cancer. A multicenter randomized Phase III trial.

Study	Target Accrual	TITLE
05963	554	<i>Trial Coordinator: S. Giacchetti, Villejuif</i> First line infusional 5-Fluorouracil, Folinic Acid and Oxaliplatin for metastatic colo-rectal cancer or loco-regional recurrence. Role of chronomodulated delivery upon survival. A multicenter randomized Phase III trial.
05971	80	<i>Trial Coordinator: B.P.J. Coudert, Dijon</i> A multicenter randomized trial, to determine the optimal circadian time of Vinorelbine administration combined with chronomodulated infusion of 5-Fluorouracil in previously treated patients with metastatic breast cancer.
<b>EORTC Early Clinical Studies Group</b>		
16001	27	<i>Trials Coordinators: P. Fumoleau, Nantes, T. Cufer (IDBBC representative)</i> Phase II study of oxaliplatin single agent in patients with metastatic breast cancer after failure of Anthracycline/Taxanes based chemotherapy.
16002	30	<i>Trial Coordinator: P. Schöffski, Hannover</i> Phase I Clinical Trial of recombinant Viscumin (rViscumin, rMistletoe lectin, rml) administered twice weekly by the intravenous route in patients with solid tumors after failure of standard therapy.
16992	33	<i>Trial Coordinator: V. Dieras, Paris</i> Phase I study to determine the safety of MS-209 in combination with docetaxel in patients with a solid progressive tumor.
16996SL	49	<i>Trial Coordinator: C. Punt, Nijmegen</i> Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment in advanced small cell lung cancer.
16996U	25	<i>Trial Coordinator: M. de Jonge, Rotterdam</i> Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment in advanced/metastatic urothelial tract tumors.
1696O	50	<i>Trial Coordinator: P. Kerbrat, Rennes</i> Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment in advanced ovarian cancer.
16997	31	<i>Trial Coordinator: R.de Wit, Rotterdam</i> Phase II Study on SCH 66336 (Farnesyl Protein Transferase inhibitor) and gemcitabine as second line treatment in advanced /metastatic urothelial cancer.
<b>EORTC Gastrointestinal Tract Cancer Group</b>		
40954	540	<i>Trial Coordinator: U. Fink, München</i> Randomized Phase III study of preoperative chemotherapy followed by surgery versus surgery alone in locally advanced gastric cancer (cT3 and cT4NxM0).
40963	1600	<i>Trial Coordinator: J.A. Wils, Roermond</i> Pan-European Trial in Adjuvant Colon Cancer- PETACC-2 Randomised Phase III intergroup trial of high-dose infusional 5-FU (+ or – Folinic Acid) versus Standard bolus 5-FU/Folinic Acid.

Study	Target Accrual	TITLE
40973	370	<b>Trial Coordinators: T. Conroy, Vandoeuvre-les-Nancy, J. Blazeby, Bristol</b> An international field study of the reliability and validity of the EORTC QLQ-C30 and a disease specific questionnaire module (the EORTC QLQ-OES24) in assessing quality of life of patients with oesophageal cancer (15961/40973).
40983	330	<b>Trial Coordinator: B. Nordlinger, Boulogne - Billancourt</b> Pre-and Post-Operative Chemotherapy with Oxaliplatin 5FU/LV versus Surgery alone in Resectable Liver Metastases from Colorectal Origin- Phase III Study.
40984	82	<b>Trial Coordinator: M. Lutz, Ulm</b> Randomized Phase II study of docetaxel/gemcitabine Vs docetaxel/cisplatin in metastatic or locoregionally advanced pancreatic carcinoma.
40986	430	<b>Trial Coordinator: C.H. Koehne, Rostock</b> CPT-11 in combination with weekly 24h infusion 5-FU plus FA relative to weekly 24h infusion 5-FU plus FA alone in patients with advanced colorectal cancer.
40991	2100	<b>TrialCoordinator: P. Rougier, Paris</b> Phase III randomized study of adjuvant immunotherapy with monoclonal antibody 17-1A versus no adjuvant therapy following resection for stage II (modified Astler-Coller B2) adenocarcinoma of the colon.
<b>EORTC Genito-Urinary Tract Cancer Group</b>		
30904	1300	<b>Trial Coordinator: H. Van Poppel, Leuven</b> A Prospective Randomized Phase III study Comparing Radical Surgery to Elective Kidney Sparing Surgery for Low Stage Renal Cell Carcinoma.
30955	550	<b>Trial Coordinators: H. Van Poppel, Leuven, P.H.M. De Mulder, Nijmegen</b> Phase III adjuvant trial: Interleukin-2, Interferon-alpha and 5-Fluorouracil for patients with high risk of relapse after surgical treatment for RCC
30962	1288	<b>Trial Coordinator: Van den Meijden, 's Hertogenbosch</b> Comparative study of intravesical BCG standard dose long-term maintenance versus BCG 1/3 dose long-term maintenance versus BCG standard dose short-term maintenance versus BCG 1/3 dose short-term maintenance in intermediate and high risk Ta- T1 Papillary Carcinoma of the Urinary Bladder.
30974	222	<b>Trial Coordinator: G. Daugaard, Copenhagen</b> A randomized Phase III study of sequential high-dose Cisplatinum/Etoposide/Ifosfamide plus stem cell support versus BEP in patients with poor prognosis germ cell cancer.
30982	1200	<b>Trial Coordinator: H. Von Der Maase, Aarhus</b> TE 19/30982: Carboplatin Vs Radiotherapy in the adjuvant treatment of stage I Seminoma.
30983	498	<b>Trial Coordinator: R. De Wit, Rotterdam</b> Randomized Phase II/III study of Taxol-BEP versus BEP in patients with intermediate prognosis germ cell cancer.
30985	1512	<b>Trial Coordinator: A. Akdas, Istanbul</b> Intermittent androgen deprivation in patients with stage D2 prostate cancer-Phase III.

Study	Target Accrual	TITLE
22911	1000	<b>Trial Coordinators: H. Van Poppel, Leuven, M. Bolla, Grenoble</b> Phase III study of post-operative external radiotherapy in pathological stage T3N0 prostatic carcinoma (Joint study of the EORTC Radiotherapy Group and the EORTC Genito-Urinary Tract Cancer Group).
22961	966	<b>Trial Coordinator: M. Bolla, Grenoble</b> Long-term adjuvant hormonal treatment with LHRH analogue versus no further treatment in locally advanced prostatic carcinoma treated by external irradiation and a six months combined androgen blockade - A Phase III study. (Joint study of the EORTC Radiotherapy Group and the EORTC Genito-Urinary Tract Cancer Group).
30986	136	<b>Trial Coordinator: G. Kaiser, Nurnberg</b> Randomized Phase II/III study assessing Gemcitabine/Carboplatin and Methotrexate/Carboplatin/Vinblastine in previously untreated patients with advanced urothelial cancer ineligible for Cisplatin based chemotherapy.
30991	1266	<b>Trial Coordinator: G.H.J. Mickish, Rotterdam</b> Randomized Phase III step-up study on initial antiandrogen monotherapy in comparison with watchful waiting in asymptomatic T1-3 any G (any Gleason) N0 or NxM0 prostate cancer patients without local treatment with curative intent.
<b>EORTC Gynecological Cancer Group</b>		
55874	224	<b>Trial Coordinator: N. Einhorn, Stockholm</b> Phase III study to evaluate the role of adjuvant radiotherapy in the treatment of uterine sarcomas stages I and II.
55955	400	<b>Trial Coordinator: M.E.L. Van Den Burg, Rotterdam</b> A randomised trial in relapsed ovarian cancer: Early treatment based on CA 125 levels alone Vs. Delayed treatment based on conventional clinical indicators - MRC OV05 and EORTC/GCCG 55955.
55963	700	<b>Trial Coordinator: G. Favalli, Italy, M.E.L. Van Der Burg, Rotterdam</b> A randomized Phase III study for the treatment of recurrent epithelial ovarian cancer: Chemotherapy alone versus chemotherapy followed by secondary cytoreductive surgery in patients with a treatment-free interval of more than 12 months-trial 55963.
55971	704	<b>Trial Coordinator: I. Vergote, Leuven</b> Randomized Phase III study comparing upfront debulking surgery versus neo-adjuvant chemotherapy in patients with Stage IIIc or IV epithelial ovarian cancer.
55981	800	<b>Trial Coordinator: I. Vergote, Leuven</b> A randomized trial of Paclitaxel/Epirubicin/Carboplatin Combination (TEC) versus Paclitaxel/Carboplatin (TC) in the treatment of women with advanced ovarian cancer.
55991	400	<b>Trial Coordinator: C.F. De Oliveira, Coimbra</b> A randomized trial of adjuvant treatment with radiation plus chemotherapy versus radiation alone in high risk endometrial carcinoma.

Study	Target Accrual	TITLE
<b>EORTC Head and Neck Cancer Group</b>		
24954	564	<i>Trial Coordinator: J-C Horiot, Dijon, J-L Lefebvre, Lille</i> Phase III study on larynx preservation comparing induction chemotherapy and radiotherapy versus alternating chemo-radiotherapy in resectable hypopharynx and larynx cancers (Jointly with the EORTC Radiotherapy Cooperative Group).
24971	348	<i>Trial Coordinator: J-B. Vermorken, Edegem</i> A randomized Phase III multicenter trial of neoadjuvant docetaxel (Taxotere) plus cisplatin plus 5-fluorouracil versus neoadjuvant cisplatin plus 5-fluorouracil in patients with locally advanced inoperable squamous cell carcinoma of the head and neck.
22931	338	<i>Trial Coordinators: J-L. Lefebvre, Lille, F. Cognetti, Roma, J. Bernier, Bellinzona</i> Phase III randomized study on postoperative radio- and chemotherapy in patients with locally advanced head and neck carcinomas (Joint study of the EORTC Radiotherapy Group and the Head and Neck Cancer Group).
<b>EORTC International Antimicrobial Therapy Group</b>		
46951	370	<i>Trial Coordinators: A.Cometta, Yverdon, W.Kern, ULM</i> Oral empirical antibacterial therapy in selected febrile granulocytopenic patients with solid tumor, lymphoma or chronic leukemia: A prospective, randomized, multicenter trial comparing oral ciprofloxacin plus amoxicillin/clavulanic acid with ceftriaxone plus amikacin.
<b>EORTC Invasive Fungal Infections Group</b>		
19951	450	<i>Trial Coordinators: C. Viscoli, Genova, P. Ljungman, Huddinge</i> A Strategic Study to Determine the Optimal Moment to Initiate Systemic Antifungal Therapy with AmBisome in Granulocytopenic Cancer Patients with Unexplained Fever Refractory to Empirical Antibacterials.
<b>EORTC Leukemia Group</b>		
06951	308	<i>Trial Coordinator: P. Stryckmans, Brussels, B. Labar, Zagreb</i> A randomized Phase III trial comparing Dexamethasone with Prednisone in induction treatment and peripheral blood progenitor cell (PBPC) translation with intensive maintenance treatment in adolescent and adult acute Lymphoblastic leukemia and lymphoblastic lymphoma (ALL-4) (in collaboration with LALA).
06952	100	<i>Trial Coordinators: G Avisati, Roma, F. Mandelli, Roma, P. Muus, Nijmegen, C. Petti, Roma</i> Induction with All-Trans Retinoic Acid in combination with Idarubicin followed by intensive consolidation followed by bone marrow transplantation or a randomized maintenance treatment depending upon the amount of minimal residual disease in collaboration with GIMEMA-AIEOP Cooperative Groups).
06954	710	<i>Trial Coordinator: U. Jehen, München</i> Randomized Phase III study to evaluate the value of rHuG-CSF in induction and of an oral schedule as consolidation treatment in elderly patients with acute myelogenous leukemia (AML-I 3 protocol) (Jointly with the GIMEMA).

Study	Target Accrual	TITLE
06956	60	<b>Trial Coordinator: P. Muus, Nijmegen</b> Treatment of relapsed Acute Myelogenous Leukemia consisting of intermediate dose Cytosine Arabinoside (Ara-C) plus interspaced continuous infusion Idarubicine, followed by continuous infusion of low dose Ara-C, a Phase II study.
06961	300	<b>Trial Coordinators: T. de Witte, Nijmegen, U. Hess, St Gallen, F. Mandelli, G.E.G. Verhoef, Leuven</b> Autologous peripheral blood stem cell transplantation (PSCT) versus a second intensive consolidation course after a common induction and consolidation course in patients with bad prognosis MDS and sAML to MDS of more than 6 months duration. A randomised Phase III intergroup study of the EORTC LG, the EMBT chronic leukemia working party, GIMEMA, SAKK and HOVON.
06962	308	<b>Trial Coordinators: T. de Witte, Nijmegen, F. Mandelli, Roma</b> A randomized Phase III study to assess intensification of the conditioning regimen for allogeneic and autologous stem cell transplantation myeloid and lymphoid malignancies with a high risk of relapse.
06964	100	<b>Trial Coordinator: R. Willemze, Leiden</b> Phase II study of the efficacy of rH Interleukin-2 in patients with slowly progressing acute myelogenous leukemia (AML) and with limited bone marrow blastosis after autologous stem cell transplantation or chemotherapy.
06991	1320	<b>Trial Coordinators: R. Willemze, Leiden, F. Mandelli, Roma</b> The value of high dose versus standard dose Ara-c during induction and of IL-2 after intensive consolidation/autologous stem cell transplantation in patients (age 15-60) with acute myelogenous leukemia. A randomized Phase III trial of the EORTC and GIMEMA Leukemia Groups (AML-12).
06993	83	<b>Trial Coordinators: S. Amadori, Roma, Mandelli, Roma, Willemze, Leiden</b> Gemtuzumab Ozogamicin (CMA-676) followed or not by intensive chemotherapy as initial treatment for elderly patients with acute myeloid leukemia: an EORTC-LG pilot Phase II study.
<b>EORTC Lung Cancer Group</b>		
08941	640	<b>Trial Coordinators: T.A.W. Splinter, Rotterdam, G.W.P. Kremer, Arhem, P. Van Schik, Edegem</b> Randomized trial of surgery versus radiotherapy in patients with stage IIIa non-small cell lung cancer after a response to induction-chemotherapy. Amendment 2 – 15/9/2000.
08965	70	<b>Trial Coordinators: A. Ardizzoni, Genova, P.E. Postmus, Amsterdam</b> Study on Temozolomide in advanced non-small cell lung cancer with and without brain metastases: Phase II.
08971b	500	<b>Trial Coordinator: G. Giaccone, Amsterdam</b> Survival in an international Phase III prospective randomized LD small cell lung cancer vaccination study with adjuvant BEC2 and BCG. Amended 4 <sup>th</sup> October 31, 2000. Joint Study of the Groupe Français de Pneumo- Cancérologie, Independent Centers in Europe, USA & Australia /New Zealand, Memorial Sloan Kettering Cancer Center, Schweizerische Arbeitsgemeinschaft Klin. Krebsforschung, Spanish Lung Group Veterans' Administration.



Study	Target Accrual	TITLE
08972	418	<b>Trial Coordinators: A.L.J. Uitterhoeve, Amsterdam, J.S.A. Belderbos, Amsterdam, N. van Zandwijk, Amsterdam.</b> A randomized Phase III study comparing induction chemotherapy to daily low dose cisplatin both combined with high dose radiotherapy in patients with inoperable non-small cell lung cancer stage I, II and (low volume stage) III. (Joint study of the EORTC Lung Cancer Group and EORTC Radiotherapy Group) – EORTC 08972/22973. Amended 2, March 7, 2001.
08983	240	<b>Trial Coordinators: J. Van Meerbeeck, Rotterdam, Manegold, Heidelberg, G. Giaccone, Amsterdam.</b> Phase III study of Tomudex and Cisplatin versus Cisplatin in Malignant Pleural Mesothelioma. Joint Study of the Eastern Cooperative Oncology Group and the National Cancer Institute of Canada-Clinical Trial Group.
08984	40	<b>Trial Coordinator: C. Manegold, Heidelberg</b> Taxotere and Cisplatin as induction chemotherapy in patients with stage IIIaN2 non-small cell lung cancer.
08992	24	<b>Trial Coordinators: A. Ardizzoni, Genova, P. Baas, Amsterdam,</b> Phase II study on Tomudex in malignant mesothelioma.
<b>EORTC Lymphoma Group</b>		
20884	615	<b>Trial Coordinator: J. Raemaekers, Nijmegen</b> Prospective randomized controlled trial of adjuvant involved field radiotherapy after MOPP/ABV hybrid chemotherapy in advanced Hodgkin disease. H3-4 Trials. Closed for new patients entry.
20962	50	<b>Trial Coordinator: P. Poortmans, Tilburg</b> Evaluating the MBVP chemotherapy schedule followed by consolidating radiotherapy in non AIDS related primary CNS lymphoma (NAPCL) (in cooperation with the EORTC Brain Group).
20981	600	<b>Trial Coordinators: A. Hagenbeek, Utrecht, M.H.J. Van Oers, Amsterdam</b> Chimeric anti-CD20 monoclonal antibody (Mabthera*) in remission induction and maintenance treatment of relapsed follicular non-Hodgkin's lymphoma: a Phase III randomized clinical trial – Intergroup Collaborative Study.
20982	1626	<b>Trial Coordinators: J. Thomas, Leuven, H. Eghbali, Bordeaux, E.M. Noordijk, Leiden, C.F. Ferme, Bris sous Forge</b> Prospective controlled trial in clinical stages I-II supradiaphragmatic Hodgkin's disease. Evaluation of treatment efficacy, (long term) toxicity and Quality of Life in two different prognostic subgroups.
<b>EORTC Melanoma Group</b>		
18951	390	<b>Trial Coordinator: U. Keilholz, Berlin</b> Randomized Phase III trial. Treatment of metastatic melanoma with DTIC, CDDP and IFN-alpha with or without IL-2. Patients are randomized to Arm A: 2-4 x DTIC + CDDP + IFN-alpha or Arm B: 2-4 x DTIC + CDDP + IFN-alpha + IL-2 AMENDMENT, Dec. 12, 1999. Corrected version, February 22, 2000. Patients are randomized to Arm C : 2-4 x DTIC + CDDP + IFN-alpha + IL-2 or Arm D : 2 x DTIC followed by 2-4 x DTIC + CDDP + IFN-alpha + IL-2.
18991	900	<b>Trial Coordinator: A.M.M. Eggermont</b> Post-operative adjuvant Pegylated-interferon-alpha2b (PEG-Intron) vs Observation after surgery for regional lymphnode metastases in stage III melanoma patients. A 2-arm randomized Phase III trial.

Study	Target Accrual	TITLE
<b>EORTC Quality of Life Group</b>		
15961	370	<b>Trial Coordinators: T. Conroy, Vandoeuvre-lez-Nancy, J. Blazeby, Bristol</b> An international field study of the reliability and validity of the EORTC QLQ-C30 and a disease specific questionnaire module (the EORTC QLQ-OES24) in assessing quality of life of patients with oesophageal cancer (15961/40973).
15982	280	<b>Trial Coordinator: A. Cull, Edinburgh</b> An international field study of the reliability and validity of a disease specific questionnaire module (the QLQ-OV28) in assessing the quality of life of patients with ovarian cancer.
<b>EORTC Radiotherapy Group</b>		
22911	1000	<b>Trial Coordinators: H. Van Poppel, Leuven, M. Bolla, Grenoble</b> Phase III study of post-operative external radiotherapy in pathological stage T3N0 prostatic carcinoma (Joint study of the EORTC Radiotherapy Group and the EORTC Genito-Urinary Tract Cancer Group).
22921	1000	<b>Trial Coordinator: J-F. Bosset, Besançon</b> Four arms Phase III clinical trial for T3-T4 resectable rectal cancer comparing pre-operative pelvic irradiation to pre-operative irradiation combined with fluorouracil and Leucovorin with or without post-operative adjuvant chemotherapy.
22922	3780	<b>Trial Coordinators: H. Bartelink, Amsterdam, H. Struikmans, Utrecht, A. Fourquet, Paris, W.F. Van Den Bogaert, Leuven</b> Phase III randomized trial investigating the role of internal mammary and medial supraclavicular (IM-MS) lymph node chain irradiation in stage I-III breast cancer (Joint study of the EORTC Radiotherapy Group and the EORTC Breast Cancer Group EORTC 22922/10925).
22931	338	<b>Trial Coordinators: J-L. Lefebvre, Lille, F. Cognetti, Roma, J. Bernier, Bellinzona</b> Phase III randomized study on postoperative radio- and chemotherapy in patients with locally advanced head and neck carcinomas (Joint study of the EORTC Radiotherapy Group and the Head and Neck Cancer Group).
22952	340	<b>Trial Coordinator: R.P. Müller, Koeln</b> Convergent beam irradiation of cerebral metastases.
22961	966	<b>Trial Coordinator: M. Bolla, Grenoble</b> Long-term adjuvant hormonal treatment with LHRH analogue versus no further treatment in locally advanced prostatic carcinoma treated by external irradiation and a six months combined androgen blockade - A Phase III study. (Joint study of the EORTC Radiotherapy Group and the EORTC Genito-Urinary Tract Cancer Group).
22971	43	<b>Trial Coordinator: M. Bolla, Grenoble</b> A Phase II feasibility study of combined accelerated external radiation and chemotherapy with 5FU and CDDP following transurethral resection in patients with muscle invasive transitional carcinoma of the bladder.
22972	605	<b>Trial Coordinators: B. Baumert, Zurich, M. Brada, Sutton</b> Focal fractionated conformal stereotactic boost following conventional radiotherapy of high-grade gliomas: A randomized Phase III study. (Joint study of the MRC and EORTC Radiotherapy Group and the Brain Tumor Group) EORTC 22972/26991-MRC BR10.

Study	Target Accrual	TITLE
22973	426	<b>Trial Coordinators: L. Schuster-Uitterhoeven, Amsterdam J.S.A. Belderbos, Amsterdam, N Van Zandwijk, Amsterdam</b> Randomized Phase III study comparing induction chemotherapy to daily low dose cisplatin both combined with high dose radiotherapy using concomitant boost technique in patients with inoperable non-small cell lung cancer stage I, II and low volume stage III. (Joint study of the EORTC Lung Cancer Working Party and EORTC Radiotherapy Group) - EORTC 08972/22973.
24954	564	<b>Trial Coordinators: J-L. Lefebvre, Lille, J-C. Horiot, Dijon</b> Phase III study on larynx preservation comparing induction chemotherapy and radiotherapy versus alternating chemo-radiotherapy in resectable hypopharynx and larynx cancers (EORTC Head and Neck Cancer Group jointly with the EORTC Radiotherapy Group).
<b>EORTC Soft Tissue and Bone Sarcoma Group</b>		
80931	500	<b>Trial Coordinators: I. Lewis, Leeds, M. Nooij, Leiden, W.P. Steward, Leicester</b> EORTC/MRC/SIOP/UKCCSG/CSG collaborative Phase III randomized trial of chemotherapy with or without granulocyte colony-stimulating factor in operable osteosarcoma.
62005	600	<b>Trial Coordinator: J. Verweij, Rotterdam</b> Phase III randomized, intergroup, international trial assessing the clinical activity of STI-571 at two dose levels in patients with unresectable or metastatic gastrointestinal stromal tumors (GIST) expressing the KIT receptor tyrosine kinase (CD 117).
62931	340	<b>Trial Coordinator: P.J. Woll, Nottingham</b> Randomized Phase III trial of adjuvant chemotherapy with high-dose doxorubicin, ifosfamide and lenograstim in high grade soft tissue sarcoma.
62961	340	<b>Trial Coordinator: R.D. Issels, München</b> Randomized study comparing neoadjuvant chemotherapy Etoposide + Ifosfamide + Adriamycin (EIA) combined with regional hyperthermia (RHT) Vs neoadjuvant chemotherapy alone in the treatment of high-risk soft tissue sarcomas in adults. An Intergroup study with the European Society for hyperthermic oncology.
62971	780	<b>Trial Coordinator: P. Lorigan, Sheffield</b> Randomized Phase III trial of two investigational schedules of Ifosfamide versus standard dose Doxorubicin in patients with advanced or metastatic soft tissue sarcoma.
62981	200	<b>Trial Coordinator: I.R. Judson, London</b> EURO-EWING 99 - EUROpean Ewing tumor Working Initiative of National Groups.
62993	45	<b>Trial Coordinator: I.R. Judson, London</b> A Phase II study to evaluate the role of weekly Cisplatin with oral Etoposide in Ewing's sarcoma and primitive neuroectodermal tumor (PNET) with bone and/or bone marrow metastatic disease.

# REPORTS FROM THE EORTC GROUPS AND TASK FORCES

## BIOLOGICAL THERAPEUTICS DEVELOPMENT GROUP

### **Structure of the group:**

Chairman:	H. Zwierzina, Innsbruck
Vice-Chairman:	P. de Mulder, Nijmegen
Secretary:	L. Hakansson, Linköping
Research coordinator:	H. Hendriks, Pumerend
Treasurer:	V. Nuessler, München

The members of the BTDG are composed of preclinical and clinical research scientists in order to meet the following aims:

- Examining the clinical efficacy and safety of biologically active agents, which have been developed as having potential value in the treatment of patients with malignancies. This aim is met by the organisation of Phase I and Phase II trials with these agents, according to EC rules for Good Clinical Practice (GCP), in the institutions of members of the Group and in collaboration with the appropriate disease-oriented Group(s).
- Designing and coordinating of studies looking at the effects (others than safety, toxicity and antitumor response) of biologically active agents in vivo in patients with malignancies. Special emphasis is paid to effects on the immune system and to problems of targeting.
- Coordinating preclinical evaluation of biological agents such as cytokines, antibodies, vaccines and therapeutic genetic approaches. Special emphasis is laid on the set-up of research programs around clinical trials.
- Exchanging of knowledge among preclinical and clinical scientists in the field of biological therapy.

The BTDG welcomes initiatives from the members of disease-oriented groups of the EORTC and from other preclinical and clinical research institutions. Contacts between the participants and companies involved in the development of biological agents are encouraged in order to build up collaboration for future early clinical trials.

### **Recent Achievements:**

One of the first European clinical trials applying a genetically-modified organism (recombinant vaccinia virus) in a multicenter setting in cervical cancer patients was presented at the 91<sup>st</sup> Annual AACR Meeting in San Francisco in April 2000. Further trials closed during 2000 comprised a Phase I trial with the immunomodulatory compound Kirin7000 and a Phase II trial with a humanized monoclonal antibody directed against CD33 in patients with myelodysplastic syndromes. Like all BTDG trials, these studies were surrounded by a comprehensive ex vivo research program. Further ongoing early clinical trials comprise biological approaches with humanized antibodies, immunomodulators, and vaccination with genetically modified organisms / gene therapy.

**Projects and Strategies for the coming years:**

The BTDG will keep focusing on the development of new biological agents. It will be important, to attract more academic labs dealing with preclinical research. One major goal is to further improve collaboration with academic labs preferentially from the preclinical groups of the EORTC Laboratory Research Division.

Throughout the coming years the BTDG will perform a limited number of non-sponsored trials with drugs such as anti-cancer vaccines. These drugs are frequently owned by rather small biotech companies that may not have the financial back-up for rapid clinical development. A grant application will be forwarded to the European Commission.

**Collaboration with other groups:**

Major emphasis is put on interaction with disease-oriented groups of the EORTC. Since the BTDG was founded, disease-oriented groups have been continuously encouraged to send an official representative to the BTDG meetings. Up to now the GU, Leukemia, Lung, Lymphoma, Melanoma, and Sarcoma Group demonstrated their interest and participated in meetings. Furthermore all preclinically-oriented EORTC groups have represented in the BTDG.

A regular exchange of experience on a preclinical level as well as concerning the results of ongoing Phase I and early Phase II trials is accomplished with the Cancer Research Campaign (CRC) in the UK and the National Cancer Institute (NCI) in the USA.

## BORON NEUTRON CAPTURE THERAPY GROUP

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### Structure of the group:

Chairman:	W. Sauerwein, Essen
Secretary:	J-P. Pignol, Villejuif
Treasurer:	H. Fankhauser, Lausanne
Quality Assurance Officer:	R. Moss, Petten

### Recent Achievements:

The Boron Neutron Capture Therapy (BNCT) Group was set up four years ago to foster European fundamental and clinical research on treatment of cancer using neutron capture therapy. Preceded by the accumulation of pharmacological, radiobiological and dosimetric data on animal models then on humans, the group successfully launched the EORTC 11961 protocol: "Post operative on Treatment of Glioblastoma with BNCT at the Petten Irradiation Facility, Phase I Clinical Trial". This project is funded under the frame of the EU BIOMED II program.

The start of the third patient cohort, after the completion, without any evidence of side effects, of the two first cohort, being part of the four steps dose escalation trial.

Following the successful European Commission 5th Framework Program funding of the project "Therapeutic Strategies for Boron Neutron Capture Therapy: Boron Imaging" (QLK3-CT-1999-01067), the submission to the EORTC Protocol Review Committee of a new research trial entitled: "10B-uptake in different tumors using boron compounds BSH and BPA". This project, coordinated by the University of Essen (D), aims at defining new targets, i.e. new tumor sites, candidate for BNCT.

The finalization of the Status of the EORTC BNCT Group and the renewal of board members following elections. A Quality Assurance Committee has been set-up in order to review all the patient accrual procedures, dosimetry and treatment issues, data collection, maintenance and review.

The world leadership of our group in the field of BNCT enabled the Group Chairman and the QA Officer to be elected respectively President and Secretary/Treasurer of the International Society for Neutron Capture Therapy (ISNCT).

In November 2000, the BNCT Study Group was successful in its first audit with the EORTC Scientific Advisory Audit Committee.

The EORTC BNCT group aims to conduct, develop, coordinate and stimulate research in Europe on the experimental and clinical basis of treatment of cancer using neutron capture reactions.

BNCT is a binary treatment, based on the ability of the non-radioactive isotope 10B to capture thermal neutrons and to disintegrate instantaneously producing two highly energetic particles, He and Li nuclei, with a kinetic energy of about 2.5 MeV and a very short range in tissue of about 10mm. Such reaction, when produced selectively in tumor cells, opens an effective new modality for cancer treatment.

In the late 1950s and early 60s, patients, in the USA, were irradiated by BNCT, leading effectively to a complete failure. In the late 60s and during the 70s, the treatment was performed in Japan, with the investigators claiming that BNCT does benefit patients. However the reported results were difficult to interpret, because the treatment was not carried out in a controlled manner. Nevertheless, such reports stimulated a resurgence of BNCT activity, both in the USA and Europe, leading to the start in 1994 of new trials at Brookhaven National Laboratory and Massachusetts Institute of Technology. In Europe effective research into introducing BNCT began in the late 1980s, following the injection of financial support from the Biomedicine and Health Research Program (Biomed I) of the European Commission. This led with further funding from the Biomed II Program to the start of the ongoing EORTC trial. The trial is a Phase I study with the principal aim to establish the maximum tolerated radiation dose and the dose limiting toxicity derived from the irradiation itself or from the drug under defined conditions. The treatment facility used by the group is situated at Petten (The Netherlands) at the High Flux Reactor of the European Commission.

### **Projects and Strategies for the coming years:**

The strategies for the next years focus on two main directions.

- The development of new irradiation facilities in Finland, United Kingdom and Czech Republic requires the establishment of International Standards dedicated to BNCT dose prescription and reporting, the definition of minimal beam characteristics and Quality Assurance protocols.
- Another application of neutron capture reactions relates to Boron Neutron Capture Enhancement of Fast Neutron irradiations (BNCEF<sub>N</sub>). This technique showing promising theoretical advantages over FN therapy may be performed at cyclotrons already used for patient treatment in Essen (D), München (D) Nice (F) and Orléans (F). Translational research is currently under way regarding the engineering of thermal neutron enhancer systems and experimental dosimetry.

The main aims of the EORTC 11961 protocol: "Post operative Treatment of Glioblastoma with BNCT at the Petten Irradiation Facility, Phase I Clinical Trial", is to demonstrate the safety of BNCT applied to a tumor site within a very critical structure, here the brain. However, using a highly selective and efficient irradiation like BNCT could be an asset for other tumor sites showing high degree of local recurrence/normal structure radiosensitivity. It is expected from the project "Therapeutic Strategies for Boron Neutron capture Therapy: Boron Imaging" to define new targets for further clinical trials.

### **Collaboration with other groups:**

International Society of Neutron Capture Therapy ISNCT, EORTC Brain Tumor Group, International Commission on Radiation Units and Measurements ICRU, IAEA.

## BRAIN TUMOR GROUP

### **Structure of the group:**

Chairman:	Ch. J. Vecht, Den Haag
Vice-Chairman:	J-Y Delattre, Paris
Secretary:	M. J. van den Bent, Rotterdam
Treasurer:	M. J. B. Taphoorn, Utrecht
Quality Control:	A.A. Brandes, R.D. Kortmann
Pathology section:	J.M. Kros

### **Recent Achievements:**

In 2000, the results became available of the EORTC study 26952. This study on Primary CNS Lymphoma in patients over 60 years of age investigated the efficacy of chemotherapy with high dose methotrexate in this tumor type. Between 1/97 and 3/99, 55 patients were included. In 39% of patients a complete response was obtained, in another 4% a partial response. 61% and 51% were still free from progression after 6 and 12 months respectively. Cognitive functions were preserved or improved in all patients that survived more than 1 year. This regimen compares favorably with radiation therapy alone, especially in terms of neurotoxicity.

In the fall of 2000, an interim analysis of EORTC study 20962/26002 took place. This study investigates the value of a high dose methotrexate based regimen followed by radiation therapy in patients with a primary CNS lymphoma. Because more than 16 responses were observed in the first 33 patients, the trial is being continued.

In 2000 EORTC study 26972, 'Second line chemotherapy with temozolomide in recurrent oligodendroglioma after PCV chemotherapy' was completed. A full analysis is expected in the spring of 2001.

In the spring of 2000, the EORTC study 26882 was closed. This study investigates the effect of adjuvant BCNU and dibromodulciterol in anaplastic astrocytomas, and is an extension of a study in high-grade glioma. In that study (Neurology 1994;44:1479-1483) it was shown that this adjuvant chemotherapy regimen resulted in a small increase in survival, but a clinically significant increase in survival in the subgroup (of limited size) with anaplastic astrocytomas. The goal of the extension of the study was to confirm this increase in a larger group of patients. A first analysis is expected in 2002.

### **Projects and Strategies for the coming years:**

In 2000, a Pathology Section of the BTG has been created. The objectives of this group are to organize the pathology review within studies, to create more clear guidelines for the inclusion of patients in trials, and to set up translational research. This group has started with reviewing tumor material of patients included within EORTC study 26951, on oligodendroglioma. The histological diagnosis of these tumors is a notoriously difficult one. It is expected that together with new efforts on translational research this will bring more clarity in the inclusion criteria of trials, and will reduce the interobserver variation at the time of pathology review.



In cooperation with the EORTC ECSG a network has been created for early Phase II trials in GBM. The goal of this network is to test promising new agents in multicenter trials allowing rapid accrual. Within a period of 12 months, a first study has been completed and analyzed, a second one has completed its accrual. The results of both trials will be available in 2001. A third study is expected to begin its accrual in the first months of 2001. It is expected that this cooperation will allow the investigation of more new and potentially interesting drugs in the coming years.

In cooperation with the EORTC Radiotherapy group a working party has been set up to facilitate the developments of new trials and new initiatives for trials in brain tumors. This project will start in early 2001.

Efforts are being made to assure that in ongoing and new trials translational research is set up. For this, additional funding must be obtained and new cooperation with fundamental research groups is being sought.

#### **Collaboration with other groups:**

In cooperation with the EORTC Early Clinical Studies Group the BTG has setup a network for early Phase II studies with new drugs in glioblastoma multiforme. This project brings together the experience of the ECSG in investigating new agents, and the experience of the BTG in investigating and treating these tumors.

The EORTC Radiotherapy Group and the EORTC Brain Tumor Group are collaborating closely together on all projects in which radiation therapy of brain tumors is involved. This has now resulted in a new study on adjuvant chemotherapy with temozolomide in newly diagnosed glioblastoma multiforme. The new working party with members of both groups is expected to lead to several new trials.

Together with the EORTC Lymphoma Group, the EORTC BTG is investigating a high dose methotrexate regimen in combination with radiation therapy in patients under 65 years of age with a Primary Central Nervous System Lymphoma.

The EORTC study 26981, which investigates adjuvant and concomitant temozolomide chemotherapy with radiation therapy in glioblastoma multiforme, is being carried out in cooperation with NCI Canada.

## BREAST CANCER GROUP

### Structure of the group:

Chairman:	J. Jassem, Gdansk
Secretary:	E. Rutgers, Amsterdam
Treasurer:	R. Coleman, Sheffield

#### *Steering committee Members:*

C.J.H. van de Velde, Leiden; L. Mauriac, Bordeaux; J. Jassem, Gdansk; M. Piccart, Brussels; E. Rutgers, Amsterdam; R. Paridaens, Leuven; L. Cataliotti, Florence; P. Therasse, Brussels; H. Magdalenat, Paris; R. Coleman, Sheffield.

<i>Quality Assurance chairman:</i>	R. Paridaens, Leuven
<i>I.D.B.B.C chairman:</i>	M. Piccart, Brussels
<i>Medical Advisor:</i>	P. Therasse, Brussels

#### *Fellows:*

- Vito Distante, surgeon, for teaching and workshops in the AMAROS study
- Rob Bourez, fellow for the organisation of quality assurance in the AMAROS study
- Jos van de Hage, fellow for the POCOB and POP trials
- Nina Bijker, fellow on DCIS and Paget.

### Recent Achievements:

In 2000 the EORTC Breast Cancer Group organized together with European Society of Mastology (EUSOMA) and EUROPA DONNA (the European Breast Cancer Coalition) the 2<sup>nd</sup> European Breast Cancer Conference (EBCC 2) in Brussels.

The decision of organizing joint conferences with the two other breast cancer organisations was taken a few years ago. These three organisations have different, yet complementary aims: the EORTC Breast Cancer Group main task is the development and conduct of clinical trials, EUSOMA's main role is to unify and apply the results of research. EUROPA DONNA is a coalition of organisations with the aim of mobilizing the support of European women for education, treatment and research.

The aim of the joint meetings was to create the platform for closer cooperation between these three parties, in order to stimulate both scientific progress and to provide better standard care for this most common female malignancy. The Brussels conference, chaired by Martine Piccart from the Institut Jules Bordet, was attended by 3150 participants.

On the occasion of this conference the fourth edition of the "Manual for clinical research in breast cancer" was published in print and on CD-Rom. These materials were distributed among conference participants.

According to the tradition of the 1<sup>st</sup> European Breast Cancer Conference held in Florence in 1998, the 2<sup>nd</sup> conference developed a consensus entitled "Brussels statement on breast cancer 2000", addressing several key issues. This document sets the agenda for the future activities of the three major groups involved in breast cancer research, treatment prevention and advocacy. The major issues addressed in the statement include breast cancer screening, quality assurance in breast cancer

research, risk assessment, treatment tailoring and participation in clinical trials.

It is hoped that the objectives outlined in this document will stimulate much-needed change in the field of breast cancer. EORTC-BCG, EUSOMA, together with the breast cancer advocacy activities of EUROPA DONNA, will work towards these goals by lobbying European Governments and the European Commission and by mobilising health-service providers, the scientific communities and the healthcare industry. These measures called for by EBCC-2 delegates will be assessed and reviewed at EBCC-3 to be held in Barcelona in March 2002.

In 2000, eight studies were open for patient entry.

- **10925-22922:** Phase III randomised trial investigating the role of internal mammary and medial supraclavicular (IM-MS) lymph node chain irradiation in stage I-III; 53 patients.
- **10951:** Randomised Phase II-III study in first line hormonal treatment for metastatic breast cancer with Exemestane or Tamoxifen in postmenopausal patients; 35 patients.
- **10967:** Randomised double-blind trial in postmenopausal women with primary breast cancer who have received adjuvant Tamoxifen for 2-3 years, comparing subsequent adjuvant Exemestane with further Tamoxifen – an inter co-operative group study; 139 patients.
- **10983:** A Phase III randomised double blind study of letrozole versus placebo in women with primary breast cancer completing five or more years of adjuvant tamoxifen (open in Nov 2000, 1 patient).
- **10991:** Phase I study of cyclophosphamide and epirubicin with capecitabine in Metastatic Breast Cancer: (closed in Dec 2000, 23 patients).
- **10992-HABITS:** Hormonal replacement therapy after breast cancer diagnosis – is it safe? (open in Oct 2000, 0 patients).
- **10963-PEAT:** Perioperative Endocrine Adjuvant Treatment (open in Nov 2000, 0 patients).
- **10993:** A randomised Phase II study of two different schedules of caelyx in metastatic breast cancer (IDBBC only); 36 patients.

### Projects and Strategies for the coming years:

The main focus of the EORTC Breast Cancer Group will remain the conduct of high quality clinical trials with increased emphasis on translational studies aiming at treatment individualization. According to the Florence and Brussels statements the following tasks will be undertaken or continued:

For translational research and treatment tailoring:

1. Incorporation of tissue banking and translational research in clinical trials.
2. Designing optimal treatment strategies for individual breast cancer patients on the basis of predictive factors and micro-array analysis profiles of the primary tumor.

For better management of hereditary breast cancer patients (performed by the EORTC Breast Cancer Group Hereditary Task Force):

1. Registration study for mutation carriers treated by prophylactic or therapeutic intervention.
2. Integration and facilitation of mutation assays for breast cancer genes in former and ongoing EORTC studies; analysis of the prognostic impact of these alterations.
3. With Europa Donna: establishing protective legislation for genetic testing.
4. With EUSOMA: development of guidelines for treatment.

For better protection of breast cancer patients:

- I. Particular focus on quality control of diagnosis and treatment. The quality assurance programs, previously addressing radiotherapy and chemotherapy will now be extended to surgery, pathology and diagnostic radiology.

The following trials are ready to be activated (final protocol approved):

- 10974: Conservative local treatment versus mastectomy after induction chemotherapy in locally advanced breast cancer: a randomised Phase III study.
- 10981:-AMAROS: After mapping of the axilla: radiotherapy or surgery.
- 10994-p53: A Phase III study comparing anthracycline based regimen versus an anthracycline docetaxel regimen and first prospective EORTC translation research trial assessing the potential predictive value of p53 using a functional assay in patients with locally advanced/inflammatory breast cancer

The following new trials are in preparation:

- 10995: A randomised Phase II-III study of CMF in combination with anti c-erbB2 antibody (Herceptin) in women with metastatic breast cancer.
- 10997: Randomised study comparing 6 x CMF with 3 x CMF followed by 4 x Taxol (Paclitaxel) in high risk node negative patients with operable breast cancer: comparison of efficacy and evaluation of clinico- pathological and biochemical markers as risk selection criteria.
- 10001: A randomised Phase II-III trial evaluating the efficacy of capecitabine and vinorelbine in anthracycline and taxane pre-treated metastatic breast cancer.
- 10002: A cross-sectional survey of the BIG to assess the attitude toward the risk of loss of fertility related to adjuvant therapies for patients with early breast cancer aged less than 35 years.
- 10003: A Phase II study of paclitaxel with the multi-drug resistance reversor, R101933, in patients with paclitaxel refractory metastatic breast cancer (IDBBC only).
- HERA TRIAL: BIG 1-01: a randomized, two-arm, open label study of the efficacy, safety and tolerability of Herceptin compared to observation in women who have completed standard adjuvant treatment of HER2 positive primary breast cancer.

### Collaboration with other groups:

- The EORTC Radiotherapy Group.
- The EORTC Quality of Life Group.  
The EORTC Breast Cancer Group is a member of the Breast International Group (BIG). The purpose of this structure is to collaborate with other international groups in large Phase III trials (in particular adjuvant studies) to recruit the number of required patients more effectively.
- The Scandinavian Breast Group and the International Breast Cancer Study Group for the participation in the HABITS trial: Hormonal replacement therapy after breast cancer diagnosis – is it safe? (coordinator: Dr. L. Holmberg, Uppsala, Sweden).  
The BIOMED-2 group (coordinator: Dr. C. Thomssen, Hamburg, Germany) for the conduct of a Chemo- NO-Europ trial: a trial on risk-adapted adjuvant chemotherapy in node-negative breast cancer based on selection by tumor biological prognostic factors.

## CLINICAL RESEARCH COORDINATORS GROUP

### **Structure of the group:**

Chairman:	K. Fishwick, Newcastle upon Tyne
Secretary:	P. di Giulio, Milan
Treasurer:	to be appointed

The Clinical Research Coordinators Group (CRCG) is an umbrella organisation, compiled from four existing groups, namely the Oncology Nurses Group, the Data Management Group, the Radiation Technologists Group and the Early Clinical Studies Research Nurses Group. From the existing steering committees a new board has been formed and will consist of two members per group. The chairperson, secretary and treasurer will be elected from the board. Elections take place every three years. The four existing groups will continue as individual groups that will link into and collaborate with the other CRCG groups. Each group will continue to have their own membership.

The CRCG will create conditions and standards for implementing and conducting clinical protocols according to Good Clinical Practice within the EORTC.

Aims:

1. To make a positive impact upon quality of clinical trials by improving the involvement of the clinical research coordinator at international, national and local level.
2. To stimulate, improve and expand the collaboration of the different skills, roles and knowledge of those working within the CRC Group.
3. To improve the conditions for patients who participate in cancer clinical trials.

Objectives:

1. To improve the standard and quality of EORTC Clinical Trials by enhancing participation in clinical trials at a local level and improving knowledge of the involved professionals.
2. To promote, stimulate and organize the education of the various disciplines involved in cancer clinical trials at all levels.
3. To initiate and conduct (companion) studies.

### **Recent Achievements:**

The CRCG was formed in 2000. The group has defined and set out its statutes.

Work has begun on a project to develop a workload measurement tool for cancer clinical trials, and an application for funding the study has been made to the European Commission. The aim of the study is to measure the workload of the clinical research personnel involved in clinical trials and to develop an instrument for measuring it.

### **Projects/Strategies for the next year**

1. Organisation of a course for clinical research coordinators.
2. Organisation of a joint symposium open for all members.
3. Initiation and implementation of a research project.
4. Development of instruments to facilitate the conduct of clinical trials.
5. Development of common standards for practical on-site modalities to conduct clinical trials.

### **Collaboration with other groups:**

The workload measurement tool will be designed to accompany EORTC clinical trials in centres working on Phase I, II and III studies. Thus the group will be collaborating with the clinical groups running the various studies.

The chairman of the CRCG is taking over as chairman of the British Oncology Data Managers Association (BODMA), thus ensuring close ties between all groups.

## CHILDREN'S LEUKEMIA GROUP

### **Structure of the group:**

Chairman:	E. Vilmer, Paris
Secretary:	N. Philippe, Lyon
Treasurer:	P. Lutz, Ulm

The group is composed of 31 pediatric centers from Belgium, Portugal and France. Subcommittees on molecular biology, cytogenetics, immunology and cytology conduct independent reviews.

### **Recent Achievements:**

Final analyses have been performed in the ALL protocol (58881) closed to patient entry. This included the study of isolated CNS relapse, the value of 6 MP IV during maintenance treatment, the outcome of patients with translocation (12,21) and hyperdiploidy according to treatment received. The prognosis of hyperdiploid patients is dependent on the potency of Asparaginase treatment. A maintenance treatment without the addition of 6 MP IV allows to improve the prognosis of patients with t(12,21). The outcome of very high-risk patients receiving only intensive chemotherapy or allogeneic bone marrow transplantation was compared. Cytogenetic studies on the overall cohort of 2000 patients were performed and allowed to describe many subgroups and their clinical characteristics. Asparaginase pharmacology was studied and methods of detection of antibodies to Asparaginase was developed in many centers.

In 1999 protocol 58951 has been initiated for newly diagnosed ALL/NHL with the following objectives:

- to assess the value of dexamethasone (DXM) vs prednisolone (PDN) during induction and maintenance regarding the outcome of children with ALL and with lymphoblastic NHL.
- to assess the value of increase of the number of administrations of L-Asparaginase during consolidation and during late intensification regarding the outcome in children without high risk features.
- to assess the value of vincristine + corticosteroid (DXM or PDN) pulses during maintenance therapy in patients with average risk characteristics.

*Other objectives:*

- To compare the response rate to the prePhase of corticosteroids + i.t MTX in patients randomised on day 1 for receiving either PDN or DXM.
- To evaluate the long-term effects of the different regimes on height, weight, and incidence of clinically overt aseptic bone necrosis.

*Minimal residual disease:*

The previous study had shown that a high level of residual disease (10<sup>2</sup> after induction) is highly predictive for relapse. Thus this threshold can be obtained using simpler and more rapid techniques. We designed a semi- quantitative and simplified technique, fluorescent PCR analysis of gene

rearrangements. This technique is developed in four reference laboratories in France and one in Belgium with the goal of adapting the chemotherapy in patients with a high level of residual disease after induction therapy. This technique is validated in these different laboratories and is currently used for the adaptation of treatment. The objectives are to define the frequency of these patients presenting a persistent high level of residual disease and their outcome with intensified treatment

**Projects and Strategies for the coming years:**

We would like to focus our efforts on the new ALL trial and promote some biological studies in ALL regarding the molecular aspects and the pharmacology.

On the basis of collaboration with other multicenter groups a new AML trial is planned.

The strategy will also be to develop cooperation with other French groups (FRALL).

**Collaboration with other groups:**

The Group has very close contacts with the international BFM study group with a joint randomised study in the maintenance treatment of ALL protocol. Some members of the Group participate on an individual basis to the INTERFANT protocol (an international protocol including infants with ALL) and, for relapse patients, some members participate to the COPRALL protocol.



## CHRONOTHERAPY GROUP

### **Structure of the group:**

Chairman:	F. Lévi, Villejuif
Secretary:	B. Coudert, Dijon
Secretary-adjunct:	C. Mormont, Villejuif
Treasurer:	C. Focan, Liège

As of October 1<sup>st</sup>, 1999, the group structure has been modified and new officers have been elected for a 3-year term. The board includes all the active members – i.e. a representative of each center which has registered 10 patients or more per year to the group's trials, the study coordinators and the 3 EORTC Data Center representatives working with the group. Board meetings have taken place every 3 months and 2 full group meetings are organised on a yearly basis.

#### *Committees, and respective officers in charge*

Education and web :	L. Dogliotti, Torino E. Donato Di Paola, Brussels (Medical advisor at the EORTC Data Center)
Quality assurance :	S. Giacchetti, Villejuif R. Smaaland, Bergen
Pharmacoeconomics :	Ch. Focan, Liège N. Tubiana-Mathieu, Limoges
Translational research :	R. Smaaland, Bergen G. Bjarnason, Toronto
Quality of life :	C. Mormont, Villejuif P. Chollet, Clermont-Ferrand

#### *Other board members :*

B. Baron, Brussels; C. Garufi, Rome; M-A. Lentz, Brussels; T. Rich, Charlottesville (USA) and R. Zidani, Villejuif.

Full group meetings occurred in March (Dijon, F.) and September (Valescure, F.). This latter meeting was the 2<sup>nd</sup> strategy meeting of the Group, with topics relating to biological rhythms, quality of life and survival. The communications were assembled in a brochure for internal use by group members.

The Chronotherapy study group comprises 40 centers in 13 countries.

### **Recent Achievements:**

#### *On-going studies*

The group is currently conducting 3 trials (EORTC 05962, 05963 and 05971). Two studies of patient rhythms have been added to protocols EORTC 05963 and 05971 last year. A fourth trial is planned for activation early 2001. A major effort has been undertaken by the group in order to implement procedures for site visits, real time inclusion data monitoring and on site monitoring visits.

Protocol EORTC 05962 (F Lévi, coordinator) aims at demonstrating a survival advantage from both cisplatin addition to 5-FU and chronomodulation of drug delivery in patients with locally advanced or metastatic pancreatic cancer. This international multicenter randomized study plans to register 200 patients in 10 centers. It is supported by the Association pour la Recherche sur le Cancer (ARC, Villejuif, France).

Protocol EORTC 05963 (S Giacchetti, coordinator) aims at demonstrating a survival advantage from the chronomodulated infusion of 5-FU-LV-I-OHP in patients with metastatic colorectal cancer. Thirty two centers are active in this international multicenter randomized trial which plans to register 554 patients.

Protocol EORTC 05971 (B Coudert, coordinator) assesses the role of vinorelbine dosing time upon the tolerability of combined vinorelbine-chronomodulated 5-FU in patients with metastatic breast cancer, receiving this treatment as 2<sup>nd</sup> or 3<sup>rd</sup> line chemotherapy. This international multicenter randomized study plans to register 100 patients in one of 8 schedules. The new methodology of this "time finding study" has been especially designed by the statisticians at the EORTC Data Center. This study design may subsequently develop as a master protocol for subsequent investigations of this kind with other drugs.

Addenda to protocol EORTC 05963 and 05971 (C. Mormont, coordinator) aims at measuring the rest-activity cycle and the cortisol rhythm upon inclusion and every 2 months in patients with metastatic colorectal or breast cancer, as a function of treatment schedule. The goal is to assess the role of circadian rhythmicity upon patient outcome and quality of life and the role of treatment schedule upon circadian rhythmicity.

Protocol EORTC 05991 (T. Rich, coordinator) aims at assessing the rate of pathologic complete responses in patients with unresectable primary biliary cancer receiving concurrent radiation therapy and chronomodulated 5-FU infusion. This study has been approved and should be activated early 2001.

*Educational aspects:*

A web site of the Chronotherapy Group has been set up, with information on clinical trials and on scientific and organisational aspects ([www.eortc.be/home/chrono](http://www.eortc.be/home/chrono)). Applying to become a member of the Chronotherapy Group is possible through the website.

A booklet on Cancer Chronotherapy has been prepared and is under revision, so that it should reflect the group's recommendations for Chronotherapy implementation in patients and should appear in 2001 (L. Dogliotti et al., in preparation.).

### **Projects/strategies for the next years**

The projects of the group will develop along the following lines set out in the 2<sup>nd</sup> strategy meeting of the group with intergroup cooperation inasmuch as possible :

- Relations between circadian rhythms and quality of life (with QoL group)
- Surrogate markers and survival in the chronotherapy trials
- Host rhythms and tumor molecular markers for translational research
- Chronopharmacology of new cytotoxic and non cytotoxic agents

Scientific exchange in view of future cooperation has been established with American, Canadian, Chinese, Israeli and Polish cancer institutions.

- The group is planning to perform a pooled analysis of its unique data base involving nearly 1200 patients registered in a chronotherapy trial and to report on these data.
- Planned studies: Two outlines were approved by the group :
  - Time finding study of chronomodulated irinotecan, 5-fluorouracil, leucovorin and oxaliplatin as second to third chemotherapy line against colorectal cancer (EORTC 05011, C. Garufi, coordinator): submitted to the PRC
  - Role of dosing time upon tolerability of gemcitabine in patients with lung cancer (C. Focan, coordinator): to be submitted to the PRC.

#### *Educational aspects*

A special issue of Chronobiology International scheduled for 2001 will bring an update on the various aspects of cancer chronotherapy, from basics to clinical and economic aspects. Many group members will contribute to this issue (F. Lévi, guest editor).

#### **Collaboration with other groups:**

- EORTC Quality of life group : strategy meeting and projects.
- EORTC Receptor and Biomarker group : preparation of translational research projects.
- Radiation Therapy Group : protocol EORTC 05991.

## DATA MANAGEMENT GROUP

### Structure of the group:

Chairman:	K. Fishwick, Newcastle-upon-Tyne
Secretary:	A. Marinus, Brussels
Treasurer:	A. Marinus, Acting Treasurer

#### *Full members*

- Should be *actively involved* in data management and work in an institution which *participates in EORTC trials*
- Are prepared to attend the group meeting at least every 2 years
- Should *actively respond* to the mailings and group meeting invitations

#### *Corresponding members*

- Not fulfilling the criteria of Full Member but interested in the group activities
- Will be invited for the group meetings and can receive proceedings upon request.

### Recent Achievements:

The Data Management Group has joined forces with the Oncology Nurses Group, the Radiation Technologists Group and the ECSG Research Nurses Group to form the Clinical Research Coordinators Group (CRCG). Whilst the individual groups will continue to function as before, this new group will concentrate on joint projects and strategies to improve the conduct of clinical trials in EORTC centres, and focus on issues pertinent to "non-clinical" research staff in the clinical groups.

EORTC has enlisted the help of experienced data managers in several countries to help with site audits. They accompany EORTC monitors and quality control staff during site visits.

### Projects and Strategies for the coming years

It is planned to hold the next group meeting in October to coincide with ECCO 11 in Lisbon. As well as the Data Management meeting we hope to hold a joint meeting with the Oncology Nurses Group, the Radiation Technologists Group and the ECSG Research Nurses Group (see collaboration with other groups).

It is hoped that data managers will continue to be encouraged to accompany investigators and attend the clinical group meetings in 2001.

#### *Training program:*

For a number of years the Data Management Group has been actively involved in the organisation and running of a biannual course: "Data Management in Cancer Clinical Trials". With the formation of the CRCG, we now intend to restructure this course. Our aim is to broaden the areas covered and encompass other aspects of clinical trials, thus encouraging participation from a wider audience. For information on the organisation please consult the EORTC Web site.

*Quality Control*

With the current increase of quality control in clinical trials, the Data Management Group continues to support and maintain the quality control procedures within the EORTC Groups by inviting data managers involved in specific EORTC groups to the group meetings.

*Other group matters*

The Data Management Group will be looking to developing a web page over the next year, updating it regularly and using it as a forum to pass on news, developments and matters of interest to its members. We will also look to set up a mailbase and encourage members to use e-mail to discuss and share problems.

**Collaboration with other groups:**

The formation of the Clinical Research Coordinators Group will ensure close ties between Data Managers, Research Nurses and Radiation Technologists. The CRCG is currently working on a project to develop a workload measurement tool for cancer clinical trials. Further details can be found in the CRCG section.

The chairman of the data management group is taking over as chairman of the British Oncology Data Managers Association (BODMA), thus ensuring close ties between the two groups.

## EARLY CLINICAL STUDIES GROUP

### Structure of the group:

Chairman:	P. Fumoleau, Nantes-Saint Herblain
Vice-Chairman:	C. Twelves, Glasgow
Secretary:	N. Pavlidis, Ioannina
Treasurer:	P. Kerbrat, Rennes

Until September 1998, monitoring of ECSG studies was conducted through the New Drug Development Office (NDDO) in Amsterdam. After the decision of the Board of the NDDO to discontinue exclusivity for the EORTC (September 23, 1998), the EORTC has established a New Drug Development Program (NDDP) located at the EORTC Data Center in Brussels. Since that time, the EORTC/NDDP has been very successful in the accrual of new studies in collaboration with the ECSG. Clinical studies which were started or which were finally negotiated before the separation of the NDDO from the EORTC are being completed in cooperation with the NDDO.

The ECSG and NDDP are now providing the mechanisms necessary to satisfy the requirements of industry, which presently provides more than 90% of interesting compounds for clinical studies.

The changes implied by the organisational move to Brussels and the integration of the NDDP into the daily study acquisition activities proceeded smoothly.

The membership of the ECSG presently consists of 45 principal investigators and 6 probationary members and covers 15 European countries including Israël.

- Due to the increase in size of the group through the merger with the former EORTC/CSG, the acceptance of new members was on hold for most of 1997 and 1998. However, at the end of 1998 and in 1999 one institution could be accepted as full member, three institutions as new probationary members and the ECSG continues to enjoy an increasing number of excellent centers on the waiting list for membership acceptance. In 2000 one institution was accepted as a full member and four as new probationary members.
- Following application for membership, a prospective new member may be invited to present relevant material at the next Group meeting. A site visit is then conducted at his/her institution and if the outcome is satisfactory, he/she is granted "probationary member" status. This may be upgraded after 24 months to "full member" status if a minimum of 15 patients/two years are entered into ongoing trials, provided that after conducting site visits the group is satisfied that the quality of data provided is appropriate. Similar criteria for continued principal investigator status - apply to existing principal investigators.

### Recent Achievements:

ECSG assesses new anti-cancer agents at an early stage of clinical development. It is widely represented in Europe, and through its specifically-adapted infrastructure it aims to provide the highest standards of clinical research.

The aims of the EORTC Early Clinical Studies Group (ECSG) are:

- to provide preliminary assessment of the activity of new anti-cancer drugs, including novel structures and analogues of particular interest (Phase I and early Phase II studies). This assessment should include correlations between clinical activity and pharmacokinetics in each case; in addition, whenever possible pharmacodynamic/pharmacokinetic interactions will be evaluated and molecular target end-points investigated;
- to provide guidelines for further detailed study of specific tumor types.

Phase I and Phase II studies by definition should be of short duration requiring an efficient mechanism for the generation of high-quality data. When these are conducted on a multicenter, multinational basis, the organisational problems are considerable. They have been added to the increasingly stringent requirements of industry and regulatory authorities.

To satisfy these requirements, the professional group structure has been improved and expanded by employing full-time clinical monitors.

### Quality assurance

Quality control is a key element in Phase I and Phase II trials of the ECSG, continuous and close monitoring of the data is performed by the clinical monitors and data managers of the NDDP. Forms are checked and returned with queries within two weeks, and outstanding problems are discussed at regular site visits (approximately every two months). These are occasionally being conducted in conjunction with company representatives. If the compliance with ICH/GCP guidelines by participating centers fails, the ECSG Chairman will formally warn the center and consider removal of the institution from the group if necessary. Reevaluation of the members is done every two years with regard to compliance with accepted standards, whereas the number of patients accrued by different institutions is evaluated yearly.

The filing of ECSG and NDDP standard operating procedures as EORTC Drug Master File (DMF) with the Food and Drug Administration (FDA) has been received with great interest by industry.

In 2000, 372 patients were entered into ECSG studies, 59 into Phase I and 313 into Phase II trials.

The ECSG has successfully completed five Phase I studies according to the protocol with the following compounds: E 7070 (a novel apoptosis-inducing agent, 4 schedules); MEN 10755 (a new anyhracycline, weekly schedule).

Two Phase I studies with the following compounds were conducted but have not yet been completed: CHS 828 (a cyanoguanidine with a mechanism of action still unknown); MS 209 (a dihydroquinoline agent which inhibits the anti-cancer agent's efflux by binding to P-glycoprotein) in combination with Docetaxel and one were initiated with Viscumin (a recombinant mistletoe lectin)

In addition to the Phase I studies, the ECSG has completed six Phase II studies have been completed including: Docetaxel in germ cell cancer; S-1 in gastric cancer; ISIS 352 in non small cell lung cancer; XR 5000 (a topo I-II inhibitor) in colorectal cancer, glioblastoma multiforme and in ovarian cancer. Nine Phase II studies were conducted but have not yet been completed: ET-743 in breast cancer and malignant melanoma; XR 5000 in non small cell lung cancer; glufosfamide in non small cell lung and pancreas cancers; RFS 2000 (an oral camptotecin analog) in small cell lung, ovarian cancers, glioblastoma and urothelial tract tumor. The ECSG has further actively participated in a BIOMED program studying pharmacokinetic/pharmacodynamic correlations in patients receiving Adriamycin/cyclophosphamide in breast cancer; carboplatin in ovarian cancer and carboplatin/paclitaxel in ovarian cancer.

Finally, 2 Phase II studies were initiated: SCH 66336 (Farnesyl protein transferase inhibitor) in combination with Gemcitabine in urothelial tract tumor and Oxaliplatin in breast cancer.

#### *Phase I Trials*

##### **16970**

Phase I study to determine the safety of MEN 10755 in patients with a solid tumor on a short i.v. infusion given once every week for 3 consecutive weeks followed by one week rest.

Sponsor: Menarini Ricerche, S.p.A., Italy  
Trial Coordinators: E. de Vries, Groningen, The Netherlands  
 J. Vermorken, Antwerp, Belgium  
Accrual: 1998: 8 patients  
 1999: 14 patients  
 2000: 3 patients – closed

##### **16973**

Phase I study to determine the safety of E7070 in patients with a solid tumor on a single IV infusion every 3 weeks

Sponsor: Eisai Ltd-London UK  
Trial Coordinators: J.P. Armand, Villejuif, France  
 J. Schellens, Amsterdam, The Netherlands  
Accrual: 1998: 17 patients  
 1999: 18 patients  
 2000: 5 patients – closed

##### **16974**

Phase I study to determine the safety of E7070 in patients with a solid tumor as a daily iv infusion repeated for 5 days every 3 weeks

Sponsor: Eisai Ltd-London UK  
Trial Coordinators: P. Fumoleau, Nantes, France  
 C. Punt, Nijmegen, The Netherlands  
Accrual: 1998: 15 patients  
 1999: 18 patients  
 2000: 2 patients – closed

##### **16975**

Phase I study to determine the safety of E7070 in patients with a solid tumor as a single iv infusion weekly x 4, repeated every 6 weeks.

Sponsor: Eisai Ltd-London UK.  
Trial Coordinators: A. Hanauske, Munich, Germany  
 C. Dittrich, Vienna, Austria  
 H. Calvert, Newcastle, United Kingdom  
Accrual: 1998: 12 patients  
 1999: 22 patients  
 2000: 11 patients – closed

##### **16976**

Phase I study to determine the safety of E7070 in patients with a solid tumor on a continuous infusion for 5 days, repeated every 3 weeks.

Sponsor: Eisai Ltd-London UK



Trial Coordinators: H. Roche, Toulouse, France  
J.P Droz, Lyon, France  
Accrual: 1998: 11 patients  
1999: 18 patients  
2000: 2 patients – closed

**I6985**

Phase I and Pharmacokinetics study to determine the safety of CHS 828 in patients with a solid tumor on a single oral dose repeated every 3 weeks

Sponsor: Leo pharmaceuticals, Germany  
Trial Coordinators: Th. Cerny, St Gallen, Switzerland  
A. Ravaud, France  
Accrual: 1999: 7 patients  
2000: 17 patients – ongoing

**I6992**

Phase I to determine the safety of MS-209 in combination with Docetaxel in patients with a solid progressive tumor

Sponsor: Mitsui Pharmaceutical Inc., Japan  
Trial Coordinators: V. Dieras, Paris, France  
M. E. Bonnetterre, Lille, France  
2000: 14 patients – ongoing

**I6002**

A Phase I clinical trial of recombinant Viscumin administered twice weekly by the intravenous route in patients with solid tumors after failure of standard therapy

Sponsor: Madaus, Germany  
Trial Coordinators: P. Schöffsky, Hannover, Germany  
P. Fumoleau, Nantes, France  
2000: 5 patients – ongoing

*Phase II Trials***I6945T**

Phase II trial with Docetaxel in patients with relapsing germ cell tumors

Sponsor: Avantis, France  
Trial Coordinators: E. de Vries, Groningen, The Netherlands  
Accrual: before 1998: 15 patients  
1998: 3 patients  
1999: 4 patients  
2000: 2 patients – closed

**I6972 G**

Phase II trial with S-I in patients with gastric cancer

Sponsor: Tahio, Japan  
Trial Coordinator: A. Ravaud, Bordeaux, France  
Accrual: 1998: 7 patients  
1999: 12 patients  
2000: 7 patients – closed

**I 6977 N**

Phase II trial with ISIS 3521 (CGP 64128A) in patients with non-small cell lung cancer.

Sponsor: ISIS Pharmaceutical Inc., US  
Trial Coordinator: U. Bruntsh, Nuremberg, Germany  
Accrual: 1998: 4 patients  
 1999: 7 patients  
 2000: 5 patients – closed

**I 6982 A (Biomed 2 Project PK/PD analysis)**

Phase II and pharmacokinetic trial with doxorubicin plus cyclophosphamide in patients with breast cancer

Trial Coordinator: J. Schellens, Amsterdam, The Netherlands  
 2000: 17 patients – ongoing

**I 6982 C (Biomed 2 Project PK/PD analysis)**

Phase II and pharmacokinetic trial with carboplatin in patients with ovarian cancer

Trial Coordinator: J. Schellens, Amsterdam, The Netherlands  
 2000: 4 patients – ongoing

**I 6982 T (Biomed 2 Project PK/PD analysis)**

Phase II and pharmacokinetic trial with paclitaxel plus carboplatin in patients with ovarian cancer

Trial Coordinator: J. Schellens, Amsterdam, The Netherlands  
 2000: 55 patients – ongoing

**I 6989**

Phase II trial with ET-743

Sponsor: Pharmamar, Spain

**I 6989 B**

Phase II trial with ET-743 in patients with advanced or metastatic breast cancer

Trial Coordinator: H. Cortes-Funes, Madrid, Spain  
Accrual: 2000: 12 patients – ongoing

**I 6989 M**

Phase II trial with ET-743 in patients with advanced or metastatic malignant melanoma

Trial Coordinator: S. Aamdal, Oslo, Norway  
Accrual: 2000: 21 patients – ongoing

**I 6991**

Open label Phase II study on XR 5000 administered as a 5 days infusion

Sponsor: Xenova Ltd., United Kingdom

I 6991C Open label Phase II study on XR 5000 administered as a 5 days infusion in advanced colorectal cancer

Trial Coordinator: G. Comella, Naples, Italy  
Accrual: 1999: 8 patients  
 2000: 12 patients – closed

I 6991G Open label Phase II study on XR 5000 administered as a 5 days infusion in patients with glioblastoma multiforme

Trial Coordinator: C. Twelves, Glasgow, United Kingdom

Accrual: 1999: 7 patients  
2000: 9 patients – closed

I6991N Open label Phase II study on XR 5000 administered as a 5 days infusion in advanced non small cell lung cancer.

Trial Coordinator: C. Dittrich, Vienna, Austria  
Accrual: 2000: 15 patients – ongoing

I6991O Open label Phase II study on XR 5000 administered as a 5 days infusion in advanced ovarian cancer.

Trial Coordinator: V. Dieras, Paris, France  
Accrual: 1999: 5 patients  
2000: 11 patients – closed

### **I6994**

Open label Phase II study on glufosfamide administered as a 60 minute infusion every 3 weeks.

Sponsor: ASTA Medica, Germany

I6994N Open label Phase II study on glufosfamide administered as a 60 minute infusion every 3 weeks in advanced non small cell lung cancer.

Trial Coordinator: G. Giaccone, Amsterdam, The Netherlands  
Accrual: 2000: 31 patients – ongoing

I6994P Open label Phase II study on glufosfamide administered as a 60 minute infusion every 3 weeks in pancreas cancer.

Trial Coordinator: N. Pavlidis, Ioannina, Greece  
Accrual: 2000: 25 patients – ongoing

### **I6996**

Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment

Sponsor: Supergen, US

I6996SL Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment in advanced small cell lung cancer

Trial Coordinator: C. Punt, Nijmegen, The Netherlands  
Accrual: 2000: 15 patients – ongoing

I6996U Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment in advanced/metastatic urothelial tract tumors

Trial Coordinator: M. de Jonge, Rotterdam, The Netherlands  
Accrual: 2000: 7 patients – ongoing

I6996G Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment in glioblastoma multiforme

Trial Coordinator: E. Raymond, Villejuif, France  
Accrual: 2000: 17 patients – ongoing

I6996O Open label Phase II study on RFS 2000 (9-Nitro-Camptothecin, 9 NC) administered as a "5 days on-2 days off" oral treatment in advanced ovarian cancer

Trial Coordinator: P. Kerbrat, Rennes, France  
Accrual: 2000: 28 patients – ongoing

**I 6997**

A Phase II study of SCH 66336 (Farnesyl protein transferase inhibitor) in combination with Gemcitabine as second line treatment in patients with advanced/metastatic urothelial tract tumor

Sponsor: Schering Plough, US  
Trial Coordinators: R. de Wit, Rotterdam, The Netherlands  
 2000: 9 patients – ongoing

**I 6001**

Phase II study of Oxaliplatin in patients with metastatic breast cancer after failure of anthracycline/taxane based chemotherapy

Sponsor: Debioclinic, Switzerland  
Trial Coordinators: P. Fumoleau, Nantes, France  
 2000: 5 patients – ongoing

**Projects and Strategies for the coming years:**

- to continue the implementation of Phase I and early Phase II studies in collaboration with the pharmaceutical companies and also academic institutions. These studies will include new cytotoxic agents and new biological therapies (in cooperation with BTDG).
- to improve collaboration with other EORTC groups
- to promote translational research

In order to strengthen the links with the groups of the Laboratory Research Division, the ECSG board has decided:

a/ to support combined meetings with presentation to members of both groups. A joint meeting with the PAMM group has been arranged in Leicester on January 2000. Following this joint Leicester meeting, J. Schellens, from Amsterdam, as PAMM & ECSG member has been chosen to be the PAMM representative.

b/ to recommend that ECSG pharmacokinetic and translational studies should be done in group labs of the Laboratory Research Division.

- Studies on cytokines can be performed in cooperation with the EORTC Biological Therapeutics Development Group (BTDG). There is no official representative from BTDG, but since 1999, a close collaboration between the two chairmen has been initiated with frequent joint meeting at the EORTC Data Center through NDDP.
- In the same way, a close collaboration between IDBBC (M. Piccart, A. Awada), the Genito-Urinary Tract Cancer Group (R. de Wit, P. de Mulder), the Brain Tumor Group (M. Van Den Bent), the Melanoma Group (C. Punt) has been encouraged to conduct joint Phase II studies.

**Collaborations with other groups:**

Collaborations with EORTC Genito-Urinary Tract cancer Group, the Breast Cancer Group, the Pharmacology and Molecular Mechanisms group (PAMM group), the Biological Therapeutics Development group and the Brain Tumor group were continued and also initiated with the melanoma group. Contacts with the NCI and NCI-C have been further pursued.

## EUROPEAN OSTEOSARCOMA INTERGROUP

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### Structure of the group:

Chairman:	A. H. M. Taminiau, Leiden
Chairman Surgery Sub-committee:	R. J. Grimer, Birmingham
Chairman Pathology Sub-committee:	P. C.W. Hogendoorn, Leiden
Chairmen Chemotherapy Sub-committee:	M. A. Nooy, Leiden/ I. Lewis, Leeds

### Recent achievements:

The Intergroup's main activity is the 80931 study comparing cisplatin/doxorubicin given at conventional three-weekly intervals or two-weekly intervals with GCSF. Already 420 patients have been entered into the trial (target 450).

- A paper from the Surgery Sub-committee entitled 'The effect of local recurrence on survival in resected osteosarcoma' has been accepted for publication in the European Journal of Cancer.
- A paper from the Surgery Sub-committee entitled 'Surgical outcomes and prognostic factors' has been submitted to the Journal of Bone and joint Surgery.
- A paper entitled 'Received dose and dose-intensity of chemotherapy and outcome in nonmetastatic extremity osteosarcoma' has been published in the Journal of Clinical Oncology.
- An abstract entitled 'Long-term survival in localised extremity osteosarcoma: mature follow-up from two randomised trials of the European Osteosarcoma Intergroup' has been published in the Proceedings of ASCO 2000.

An abstract entitled 'Does the histologic subtype of high-grade central osteosarcoma influence the response to treatment with chemotherapy and does it affect overall survival? A study based on the material of two consecutive trials of the European Osteosarcoma Intergroup (EOI) consisting of 570 patients', was presented at the 6th Annual scientific meeting of the Connective Tissue Oncology Society held in Amsterdam, 2000.

### Projects/strategies for the next years:

The pathology Sub-committee is carrying out two projects to consider cases of late relapse in relation to tumor type, response, special events; further, the histology of all old cases will be considered in relation to survival and tumor type. Future publications on both these projects are planned.

### Collaboration with other groups:

- Medical Research Council (MRC)

## FUNCTIONAL IMAGING GROUP (FORMERLY PET GROUP)

### Structure of the group:

Chairpersons:	
PET	P. Price, Manchester
MRS	J. Griffiths, London
MRI	M. C. Knopp, Heidelberg
Secretary:	O. Hoekstra, Amsterdam
Treasurer:	U. Cremerius, Aachen
MR sub-groups:	Officers to be elected

### Recent Achievements:

Since the group's change of name (formerly PET Group) to encompass a wider range of research techniques, we have sought to expand membership to representatives from other areas of functional imaging. We now have a chairperson for each of the following disciplines: Positron Emission Tomography (PET), Magnetic Resonance Spectroscopy (MRS), Magnetic Resonance Imaging (MRI).

The focus of the EORTC Functional Imaging Group to date has been to explore with EORTC PET methodologists and oncologists the role of positron emission tomography (PET) for pharmacodynamic and pharmacokinetic measurements in translational oncology research, with the ultimate aim of improving the efficacy of the early clinical trials process.

The group acts primarily as a forum for the exchange of ideas, developments and results. In September 2000 our meeting in Brussels brought together EORTC laboratory research groups, oncology clinicians and members of the pharmaceutical industry, for a day of education and discussion on the role and value of PET in anti-cancer drug development.

We continue to work on a program of standardisation and refinement of methodology for PET measurements (particularly in respect of [<sup>18</sup>F]-fluorodeoxyglucose ([<sup>18</sup>F]-FDG) studies), to enable effective comparison of clinical trials data. To date we have had success with the study guidelines on FDG to measure tumor response, to the extent that the NCI are to use our model as a basis for devising their own criteria for such studies. Our findings were published in the European Journal of Cancer.

*Work progressed on two studies:*

A joint project of the PET and clinical groups of Amsterdam and Leuven to assess the clinical value of FDG PET as a prognostic and restaging tool after neoadjuvant chemotherapy in non-small cell lung cancer. The 64 patient study is now almost completed.

A two centre parallel study of an EORTC Phase I trial, in Brussels and München, on 'PET during LU79553'. A reproducibility paper has been published by Munich. The scan data is currently being analysed, with final publication awaited.

**Projects/strategies for the next years:**

We plan to hold a meeting of the Functional Imaging Group prior to the EORTC Translational Research meeting in Brussels on June 6<sup>th</sup> 2001.

PET sub-group

We aim in the future to expand the program of standardisation and refinement of methodology for PET measurements to encourage consensus on further PET techniques and applications; areas under consideration include standardisation of criteria for measurements of proliferation in FLT studies, and consensus on criteria for endpoint assessment, such as blood flow.

We plan to collaborate with the Genito-Urinary Tract Group on a Phase II study to investigate whether the use of PET in patients with non-seminomatous germ cell tumors (NSGCT) and vascular invasion can identify patients with a high risk, and/or a low risk, of relapse.

MRS & MRI sub-groups

We aim to contact interested MRS groups within Europe who have either ongoing or potential clinical or scientific oncology interests.

We aim to facilitate an active exchange of information as well as the availability of standardized processing capabilities, to allow for a more uniform post-processing of studies performed within clinical oncology trials. We are evaluating the feasibility of open source using shareware software modules to facilitate this.

We hope for a positive response from around Europe to the restructuring of our Group, and to encourage members, contributions and discussion from various areas of functional imaging as applied to cancer research.

**Collaboration with other groups:**

The Amsterdam/Leuven study is partially allied to the EORTC Lung Cancer Group study, protocol ref. 08941.

The Denmark study will be conducted with the participation of the EORTC Genito-Urinary Tract Cancer Group.



## GASTROINTESTINAL TRACT CANCER GROUP

### Structure of the group:

Chairman:	B. Nordlinger, Boulogne-Billancourt
Secretary:	E. Van Cutsem, Leuven
Treasurer:	D. Nitti, Padova
Chair of the chemotherapy subcommittee	H-J. Wilke, Essen
Chair of the surgery subcommittee;	J. G. Dos Santos, Porto
Chair of subcommittee for laboratory research	U. Vanhoefer, Essen

### Recent Achievements:

#### *Adjuvant studies*

##### 1. Colorectal cancer

Protocol 40911, launched in 1993, was closed to entry in July 1998 with 1859 patients randomized by the FFCD and the EORTC and was the largest trial ever organized by the group. This study assesses the role of "early" locally directed perioperative treatment (intraportal or intraperitoneal) added to "late" systemic chemotherapy". First analysis is planned in 2001 if a sufficient number of events have been observed.

In collaboration with national groups from Canada, Egypt, France, Germany, Italy, Portugal, Spain, The Netherlands and the UK, two intergroup adjuvant trials in Colon Cancer (PETACC 1-2; EORTC GI 40962/3), have been launched in 1998. PETACC-1 which looked for equivalence between Mayo regimen and Tomudex was closed to entry in July 1999, after randomization of 1918 patients. The PETACC-2 trial is ongoing and its aim is to demonstrate a benefit of high-dose infusional 5-FU over the Mayo regimen. More than 650 patients have now been randomized in PETACC-2. These two trials demonstrate that intergroup collaboration can accrue a large number of patients in a short period.

##### 2. Rectal cancer

EORTC 40971 : the Group joined the Dutch Colorectal Cancer Group (DCRCG) to evaluate the role of pre- operative radiotherapy in patients receiving Total Mesorectal Excision (TME) for primary rectal cancer. The study will soon be analysed.

#### *Advanced disease*

##### 1. Colorectal cancer

A phase III trial (40952), in collaboration with AIO, was launched in 1995 and closed in September 1998. This trial compared weekly infusional high-dose 5-FU plus/minus leucovorin versus bolus 5-FU plus leucovorin. 498 patients have been entered. The first results were presented at the ASCO 2000 meeting.

##### 2. Other trials in advanced disease

EORTC 40953 was a randomized phase II trial assessing the activity of high-dose infusional 5-FU-based regimens in gastric cancer; 153 patients have been entered. The trial was closed in 1999.



## New Trials

EORTC 40983 was opened to accrual in September 2000. It is randomized phase III trial comparing pre- and post-operative oxaliplatin 5FU/FU with surgery alone in resectable liver metastases from colorectal origin. It is an intergroup trial organized by EORTC with the participation of ACHBT, AGITG, ALM-CAO, CRC, ECOG FFCD, GOIRC, SFCD.

EORTC 40984 is a randomized phase II study designed to compare docetaxel/gemcitabine to docetaxel/cisplatin in metastatic or locoregionally advanced pancreatic carcinoma. This trial has now reached its target population and as a consequence is closed.

EORTC 40986 is a randomized phase III trial comparing CPT-11 in combination with weekly 24 hour infusion 5-FU plus Folinic acid with weekly 24 hour infusion 5-FU plus Folinic acid alone in patients with advanced colorectal cancer. Accrual is very rapid.

EORTC 40961; a phase II trial assessing the activity of HD-FU+FA in pancreatic cancer was closed to patient entry in 1998 (37 patients)(poster presented at ASCO 2000).

EORTC 40955: a randomized phase II trial assessing the activity of HD-FU vs. HD-FU/FA+ cisplatin in biliary tract cancer. It has been closed since 1999 (58 patients).

EORTC 22953: a phase II trial joint with the EORTC Radiotherapy Group. Shortened irradiation scheme, continuous 5 Fluorouracil and fractionation of Mitomycin C in locally advanced anal carcinoma. It has been closed since 1999 (44 patients). The subsequent trial is under discussion. .

EORTC 40902: Final results of this randomized phase III trial of sequential high-dose methotrexate, fluorouracil and doxorubicin versus etoposide, leucovorin and fluorouracil versus infusional fluorouracil and cisplatin in advanced gastric cancer were published in The Journal of Clinical Oncology, July 2000.

EORTC 40941: Final results are submitted for publication of the study vinorelbine and cisplatin in metastatic squamous cell carcinoma of the esophagus.

### *Scientific meetings/activities*

The fifth and the sixth GI Newsletter's, edited by E. Van Cutsem and M. Lutz, were published.

## Projects and Strategies for the coming years:

Pancreatic cancer: Following the closure of protocol 40891 recently published, a new study will be initiated. This trial (EORTC 22995/40992) will evaluate high dose radiotherapy and concomitant continuous infusion of 5-FU versus control after pancreaticoduodenectomy for resectable pancreatic head cancer.

In colon cancer stage III: our group will participate in a new intergroup trial (PETACC III in collaboration with Aventis, EORTC 40003), comparing high-dose infusional 5-FU alone to high-dose infusional 5-FU plus CPT11. This trial is approved by the PRC.

Oesophageal cancer: A joint study with the Radiotherapy Group (EORTC 22001/40001) and the FFCD (FFCD 9901) CLOCC is being prepared. This trial will assess preoperative chemoradiotherapy versus surgery alone in stage I - II squamous cell cancer and adenocarcinoma of the oesophagus.

*Strategy 2000 - 2001 EORTC Gastrointestinal Tract Cancer Group*

The main objectives for the coming years are to complete ongoing protocols exploring new strategies in advanced GI tract cancers, verify the principle of neoadjuvant chemotherapy particularly in resectable liver metastases and resectable gastric cancer. The group will increase its implication in intergroup studies and play a major role in developing and leading such studies in association with national groups in Europe as well as in the US (CALGB, ECOG...).

It will actively contribute to ongoing adjuvant trials in colon cancers through the PETACC network and prepare future intergroup studies to test newly developed drugs. Our group is organizing the possibility of doing translational research. Translational research will be associated with all new trials developed by the group. In a near future, it is likely that treatment of patients with GI malignancies will be tailored to biologic parameters. To prepare this, we will now associate preservation of resected specimens to all new trials.

**Collaboration with other groups:**

The "Gastrointestinal Tract Cancer Liaison Office" GITCLO founded by Harry Bleiberg in 1993, aiming to promote international collaboration, resulted in a booklet which includes different Groups and trials with the aim to promote necessary communication between scattered Groups. A third edition has been edited in 1999. It is also available on the net: [GITCLO@bordet.be](mailto:GITCLO@bordet.be).

Collaboration has been established or continued with other EORTC Groups, such as EORTC Radiotherapy and Quality of Life Groups, but also several non-EORTC research groups including: ICGG, AIO/CAO, FFCD, GIVIO, GISCAD, INTACC, GOCCI, ICMTG, TTD, QUASAR, GCCD-APIO, ECS, CGCRC, CRC and American groups, AGITG, CALGB and ECOG.

## GENITO-URINARY TRACT CANCER GROUP

### **Structure of the group:**

Chairman:	A. Bono, Varese
Vice-Chairman:	A. Van der Meijden, 's Hertogenbosch
Secretary:	Z. Kirkali, Izmir
Treasurer:	H. van Poppel, Leuven

At the beginning of 2000, some important changes occurred within the GU Group. A new Executive Committee came into office, with a new chairman. Some changes also occurred at the Data Center with a new Medical Advisor for the Group and Dr A. Zurlo. Adrian van der Meijden is a member of the PRC and Sophie Fossa, Trevor Roberts and Cora Sternberg are members of the NTC.

Within the GU Group the following Committees and Disease Orientated Groups (DOGs) are active, meeting 2 – 4 times a year:

Prostate Cancer: Chairman: Theo De Reijke, Amsterdam; Secretary: Tony Verbaeys, Gent

Superficial Bladder Cancer: Chairman: A. van der Meijden, 's Hertogenbosch; Secretary: Wim Oosterlinck, Gent

Advanced Bladder Cancer: Chairman: Karl-Heinz Kurth, Amsterdam.

Kidney Cancer: Gerald Mickisch, Rotterdam; Secretary: Jon A Lovisolo, Varese

Penis Cancer: Chairman: Christine Theodore, Villejuif; Secretary: Tim Oliver, London

Chemotherapy Committee: Chairman: Ronald de Wit, Rotterdam; Secretary: G.Daugaard, Copenhagen

Pathology Committee: Chairman: Wolter Oosterhuis, Rotterdam; Secretary: Leendert Looijenga, Rotterdam

Quality Control Committee: Chairman: Donald Newling, Amsterdam.

Quality of Life Committee: Chairman: George van Andel, Amsterdam.

### **Recent Achievements:**

a) The GU Group now has more than 200 members. Important studies were closed having reached the foreseen level of patient accrual, others have been finalized and some other projects have been accepted by the PRC. The new Pathology Committee has reached its complete functional status. The GU Group registered more than 1 200 new patients during the year 2000, and thousands of patients are in follow-up making it one of the most active groups within the EORTC.

b) New studies.

Several important studies were opened at the end of 2000 or will be activated during the first few months of 2001. All these studies look relevant because they either will test the activity of fairly new drugs or will check the efficacy of new strategies (30991 and 30993). Many of them are intergroup studies with the participation of international and national groups.

Study	Title	Coordinator	Participating groups
30993	A randomised Phase III trial of sequential chemo-immunotherapy versus immunotherapy alone in carcinoma in situ of the urinary bladder	A.V. Bono, Varese	AURO AUO FINNBLAD DER
30004	Chemoresection with 4 weekly instillations versus TUR + 1 single immediate instillation in small single papillary Ta-T1 bladder tumors	W. Oosterlinck, Gent	
30986	A randomised Phase II/III study assessing Gemcitabine/Carboplatin and Methotrexate/Carboplatin/Vinblastine in previously untreated patients with advanced urothelial cancer ineligible for Cisplatin based chemotherapy.	G. Kaiser, Nurnberg	
30987	A randomised Phase III study comparing Cisplatin/Gemcitabine and Cisplatin/Gemcitabine/Paclitaxel in patients with metastatic or locally advanced urothelial cancer without prior systemic chemotherapy suitable for receiving CDDP-based schedules.	J. Bellmunt, Barcelona	SWOG, NCIC, CUETO, GETUG, RTOG, SAKK, CECOG, SEUG, UKCCCR, SOGUG.
30994	A Randomised Phase III trial comparing immediate versus deferred chemotherapy after radical cystectomy in patients with pT2-pT4, and /or N+M0 transitional cell carcinoma (TCC) of the bladder.	C. Sternberg, Rome	SWOG, ECOG, NCIC, CALGB.
30992	Feasibility multicenter study of Irinotecan (CPT 11) and Cisplatin (CDDP) in metastatic or locally advanced penile carcinoma.	C. Theodore, Villejuif	
30991	Randomised Phase III step-up study on initial antiandrogen monotherapy in comparison with watchful waiting in asymptomatic T1-3 any G (any Gleason) N0 or Nx prostate cancer patients without local treatment with curative intent.	G. Mickisch, Rotterdam	

c) Ongoing studies.

Among the ongoing studies, the following have had a very good recruitment rate: 22911 (post-operative RT in pT3 Prostate Cancer); 22961 (RT plus hormonal treatment followed by hormonal treatment or observation in locally advanced prostate cancer); 30962 (BCG full dose versus 1/3 dose and long-term maintenance versus short-term maintenance in intermediate and high risk superficial bladder cancer); 30982 (carboplatin versus radiotherapy in stage I seminoma); 30951 (IFN 2-a plus cis-retinoic acid versus IFN 2- a in metastatic renal cancer). It is foreseen that these studies will close within the next year.

d) Closed studies.

Studies closed to recruitment during 2000 were: 30921 : Strontium <sup>89</sup> versus palliative local field radiotherapy in hormone escaped prostate cancer; 30971: transurethral resection and escalated dose M-VAC as primary treatment of T2-3 M0 bladder cancer. The final analyses of 30846 (delayed vs. immediate endocrine treatment for patients with pN1-3M0 carcinoma of the prostate and 30891 (early vs. delayed hormonal treatment in asymptomatic T0-4N0-3M0 prostate cancer) are underway.

**Projects and Strategies for the coming years:**

The vitality of the group is clearly apparent looking at the number of ongoing studies and also considering the importance and scientific interest of the new studies. Currently the group is discussing or analysing several other study projects. Among the most interesting are: use of PET in testicular cancer, metalloproteinase inhibitors and thalidomide in renal cell cancer, radical prostatectomy in clinical T3 prostate cancer.

Other initiatives, besides the clinical trials, are under development within the group. The Rare Tumor Registry is operative and the Pathology Committee is examining all the pathological slides of benign testicular tumors. The database for prostate biopsies is now ready at the Varese center in order to centralise the maximum possible amount of data of negative biopsies in men with suspected prostate cancer. Telepathology will be introduced in the prostate studies for standardizing grading. An interactive website is also under development by the Pathology Committee for teaching, training and consultation.

The Quality Control Committee is working hard to improve the quality of clinical performance within the group. The quality of trans-urethral resection of superficial bladder tumors was carefully assessed, and the conclusions are reported in an article which will be published soon. Another program on assessment of the side effects of bladder instillations is being prepared. A study of the quality of radical prostatectomy, based on the analysis of the surgery and hospitalisation data, is ongoing.

**Collaboration with other groups:**

Intergroup collaboration has been taken to new lengths. As well as collaborating with other EORTC groups, the GU Group participates on a regular basis in the meetings of the Global Group discussing and sharing new ideas with other international groups. The secretary of this Global Group is Richard Sylvester, who acts as a scientific advisor to the GU Group. Collaboration with UKCCCR, SWOG, NCI Canada, ECOG, RTOG etc. started in 1998 and has led to important achievements. Among these: participation of American groups in EORTC GU study 30984 (nephron sparing surgery versus radical nephrectomy in renal cell cancer) and participation of the GU Group in SWOG study 9346 (EORTC 30985) of intermittent hormonal therapy in advanced prostate cancer and in MRC study TE 19 in stage I seminoma testis (EORTC 30982).

Study	Groups collaborating	Disease	Regimens	EORTC GU Group Coordinator/s
30985	SWOG ECOG CALGB NCIC EMMES	Metastatic prostate cancer	Intermittent hormonal therapy vs continuous hormonal therapy (Complete androgen blockade)	A. Akdas Istanbul
22911	EORTC Radiotherapy Group	Locally advanced prostate cancer previously operated on	Post-operative radiotherapy vs no treatment	H. van Poppel Leuven
22961	EORTC Radiotherapy Group	Locally advanced prostate cancer	Radiotherapy plus 6 months maximal androgen blockade then LHRH analogue (30 mos) versus no further treatment	T.de Reijke Amsterdam
30974	GTCSG	Poor prognosis germ cell testis cancer	1 cycle standard VIP + 3 cycles HD VIP versus 4 cycles BEP	G. Daugaard Copenhagen
30982	UKCCCR	Stage I seminoma testis	Carboplatin single administration vs radiotherapy	H. von der Maase Aarhus
30983	GTCSG	Intermediate prognosis germ cell tumors	T-BEP versus BEP	R. de Wit Rotterdam
30904	ECOG	Low stage renal cell carcinoma	Radical surgery versus nephron sparing surgery	H. van Poppel Leuven

The collaboration with the European Association of Urology is continuing and the group now has its own official meeting during the annual EAU Congress. At the 2000 Congress the Prostate Cancer DOG organised a round table on prostate cancer and at the 2001 Congress the Kidney Cancer DOG will organise a round table. The group has also assured its collaboration with the EORTC Cancer in the Elderly Task Force.

## GYNECOLOGICAL CANCER GROUP

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### Structure of the group:

#### Executive Committee

Chairman	I. Vergote, Leuven
Secretary	N. Reed, Glasgow
Treasurer	C. F. De Oliveira, Coimbra
Ad hoc person	J. Vermorken, Antwerp
Medical Advisor	I. Teodorovic, Brussels
Members :	G. Bolis, Milan
	M. Van der Burg, Rotterdam
	N. Colombo, Milan
	P. Zola, Turin

#### Protocol Committee

Ovarian Tumor-site Committee	Chair : G. Bolis, Milan
Cervix Tumor-site Committee	Chair : M. Van der Burg, Rotterdam
Endometrium Tumor-site Committee	Chair: N. Colombo, Milan
Surgery Committee	Chair: P. Zola, Turin
Radiotherapy Committee	B. Trimbos, Leiden
Chemotherapy Committee	E. Van Limbergen, Leuven
Quality of life	C. Mendiola, Madrid
Quality Control	E. Greimel, Vienna
Translational Research	Chair: G. Favalli, Brescia
Hereditary Cancers	J. Green, Merseyside
	S. Greggi, Roma

### Recent Achievements:

One of the major trials of the EORTC-GCG has been the ACTION-trial (Randomized controlled trial to evaluate Platin-based chemotherapy as an adjuvant to surgery in early ovarian cancer). This trial is pivotal since this trial together with the ICON-1 trial of MRC has included about 940 patients with early ovarian cancer. The patients were randomized between a Platin-treatment or a no-treatment arm. The results will first be presented during the April-meeting of the group and afterwards during the ASCO 2001 meeting, and will possibly finally establish the role of adjuvant chemotherapy in early ovarian cancer.

One of the most important studies of the EORTC-GCG, which has been started recently, is a study evaluating neo-adjuvant chemotherapy in advanced ovarian cancer versus primary debulking surgery. In this trial the patients are randomized between neoadjuvant chemotherapy (three courses Platin- and Paclitaxel-based) followed by interval debulking surgery and again three courses chemotherapy versus primary debulking surgery followed by six courses of Platin- and Paclitaxel-based chemotherapy. We recently received support from the National Cancer Institute of Canada Gynaecological Group for this study. The accrual has increased substantially during the year 2000.

Another joint effort with the National Cancer Institute of Canada and also the Nordic Society of Gynaecological Oncology, is the randomized trial 55981. In this trial patients with advanced ovarian carcinoma are randomized between Paclitaxel-Epirubicin-Carboplatin versus Paclitaxel/Carboplatin. The accrual has been very good and in the summer of 2001 the required number of 800 patients

will be randomized. An earlier trial in the same subgroup of patients comparing Taxol-Cisplatin with Cyclophosphamide-Cisplatin showed, as in the earlier GOG III- study, that a combination of Taxol-Cisplatin is superior to Cyclophosphamide-Cisplatin in the treatment of advanced epithelial ovarian cancer (Journal of the National Cancer Institute 2000, 92 (9) : 609-708). In addition our group together with the Gynaecological Cancer Intergroup also proposed new guidelines for response evaluation including CA-125 serum levels in this group of patients (Journal of the National Cancer Institute 2000, 92 (15) : 34-35).

It has long been questioned whether the follow-up of ovarian cancer patients after first-line chemotherapy CA-125 increases has an influence on survival or not. There is no doubt when sampling serum CA-125 levels that the relapses will be discovered earlier but whether this improves survival remains unknown. Therefore, the EORTC-GCG launched a trial together with the MRC, in which the patients and doctors are blinded for the CA-125 results. In half of the patients the investigators will be informed about the increase in CA-125 levels during the follow-up, while in the other half of the patients the CA-125 results will be blinded, and the patient will only be treated when she has symptoms or when a relapse is discovered based on clinical findings.

Another trial which closed in 2000 was a Phase III study, investigating the usefulness of pelvic drains after radical hysterectomy and pelvic lymph node dissection. The results of this trial will be published and presented during 2001.

The group also paid much attention to quality control. This resulted in a paper in the European Journal of Cancer (2000, 36 : 1125- 1133).

Projects and Strategies for the coming years:

- Collaboration with other groups on rare tumors.
- Translational Research program in all new trials.
- One of the most interesting new concepts is neoadjuvant chemotherapy in advanced cervical cancer : two randomized trials (one Italian and one Argentinian) suggest that neoadjuvant chemotherapy before surgery might result in better survival rates than primary radiotherapy. A randomized Phase III study comparing these two treatment modalities will be started early 2001.
- Furthermore, a new Phase III randomized trial was developed together with the National Cancer Institute of Canada. In this trial patients with advanced ovarian cancer will be randomized between 4 courses of Topotecan-Cisplatin, followed by 4 courses of Taxol-Carboplatin versus 8 courses of Taxol-Carboplatin. It is expected that this randomized trial can be started in the summer of 2001.
- Several projects are under development, investigating the role of hormonal replacement therapy in gynaecological cancer.

#### **Collaboration with other groups:**

The EORTC Gynaecological Cancer Group has substantially increased its collaboration with other different groups. We collaborate with the following groups : EORTC Clinical Studies Group, NCIC-Canada, Scottish Gynaecological Cancer Group, Nordic Society of Gynaecological Cancer (NSGO), Medical Research Council (MRC, UK), Gynaecological Oncology Group (GOG-US), Arbeitsgemeinschaft für Gynäkologische Onkologie (AGO – Germany). Representatives from each group usually attend the meetings and this is reciprocal whenever possible.

In addition the EORTC-GCG is one of the founding members of the Gynaecological Cancer Intergroup. In this group most multicentric groups, studying gynaecological cancer, are represented and meet twice a year.



## HEAD AND NECK CANCER GROUP

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### Structure of the group:

Chairman:	J. Bernier, Bellinzona
Secretary:	J.B. Vermorken, Antwerp
Treasurer:	G. Andry, Brussels
Past Chairman:	J.L. Lefebvre, Lille
Subcommittee chairmen	
Chemotherapy:	L. Licitra, Milan
Radiotherapy:	H. Langendijk, Amsterdam
Surgery:	C. Grandi, Milan
Pathology:	J. Woolgar
EORTC Data Center representatives	
Medical Advisor	C. Debruyne, Brussels
Statistician	L. Collette, Brussels

### Recent Achievements:

There has been a gradual increase in the activity of the group over the past five years when taking the number of patients recruited in trials as a measure (see below). However, it has also become clear that the radiotherapy subcommittee is functioning in a better way and that the pathology subcommittee has been reactivated.

#### Accrual by year

1995	1996	1997	1998	1999	2000
80	96	152	185	189	221

Protocol 22931 (Phase III study on postoperative CRT vs RT in patients with locally advanced head and neck cancer) has been closed since October 2000 and follow-up of the trial is taking place.

The group was reviewed by the SAC in November 1999 and received an overall positive review; development of novel therapies has to be encouraged, translational research has to be promoted.

**Projects and Strategies for the coming years:**

New activities in 2001 concern the role of the sentinel node in patients with T1-T3/N0 oral cavity cancer, the EPO trial (protocol 22996), selective vs extensive RT in patients with squamous cell cancer metastatic to cervical lymph nodes from an unknown primary site, neoadjuvant chemotherapy followed by chemoradiation +/- amifostine in locoregionally advanced UNPC (with a translational research project connected to it) and studies in salivary gland tumors.

*Quality control*

Quality control is an integrated part of Phase II combined modality protocols with QA programs for surgery, radiotherapy and chemotherapy, as implemented in protocol 24954. QL studies will only be part of selected studies.

**Collaboration with other groups:**

NCI Canada; Dösak; Federation of French Cancer Centers; Radiotherapy Group; Quality of Life Study Group; Scandinavian Society of Head and Neck Oncology; British Association of Head and Neck Oncology.

## INTERNATIONAL ANTIMICROBIAL THERAPY

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### Structure of the group:

#### Advisory Board

Chairman:	C. Viscoli, Genova
Secretary:	J. Klustersky, Brussels
Treasurer:	H. Gaya, London
Members:	T. Calandra, Lausanne
	S. Zinner, Rhode Island
	M. Glauser, Lausanne

#### *Management Board*

Claudio Viscoli, Genova (Chairman)  
Thierry Calandra, Lausanne (Chairman-elect)  
Robrecht De Bock, Antwerpen (Member-at-large)  
Winfried Kern, Ulm (Member-at-large)  
Jean Klustersky, Brussels (Member-at-large) Marianne Paesmans, Brussels (Statistician) (ex-officio)

#### *Financial sub-committee*

Harold Gaya, London (Treasurer)  
Andrew Padmos, Halifax (Deputy Treasurer; appointed by the Management Board)  
Stephen Zinner, Cambridge (MA) (Advisor; appointed by the Management Board)

#### *Council*

Harold Gaya, London  
Michel Glauser, Lausanne  
Jean Klustersky, Brussels  
Stephen Zinner, Cambridge (MA)

#### *Chairman's Secretariat*

Thomas Wiley, Genova

#### *Data Center/Clinical Trials Operations Committee*

Alain Cometta, Yverdon (Co-coordinator)  
Robrecht De Bock, Antwerpen (Co-coordinator)  
Marialle Paesmans, Brussels (ex officio)  
Michelle Vandenberg, Data Manager, Brussels (ex officio)

#### *Research Committee*

Thierry Calandra, Lausanne (Chairman)  
Murat Akova, Ankara  
Marianne Paesmans, Brussels (ex officio)  
Michelle Vandenberg, Brussels (ex-officio)

#### *Pediatric subcommittee*

Elio Castagnola, Genova  
Dan Engelhard, Jerusalem  
Ian Hann, London

*Communication and Education Committee*  
Web site development sub-group  
Françoise Crokaert, Bruxelles (Coordinator)  
Giorgio Zanetti, Lausanne  
Tom Wiley, Genova  
Enrica Villa, Genova

### **Recent Achievements:**

*Revision of statutes/membership criteria.*

Towards the end of 2000, the Group began work aimed at revising its Statutes and criteria defining Group membership. Of the two tasks at hand, the first has yet to be completed, while the second is already being achieved according to the following working proposal for individual investigators:

- a) Active Members: all Group Officials, foreseen positions (e.g. Data Manager) and participants in the most recently closed Group trial (Active status is retained even if not participating in ongoing trial);
- b) Probationary Members: participants in the ongoing Group trial who did not participate in any of the previous 2 trials (Active status is achieved with launch of subsequent trial);
- c) Corresponding Members: participants in past Group trials (but not in most recent or ongoing trials).

For centers and institutions, the affiliations of individual Members (defined according to the above) automatically assume the corresponding status.

*Group Protocol*

Trial XIV (protocol 46971) closed at the end of June, 2000. The protocol was a prospective, randomized placebo-controlled study addressing the question of the impact of early addition of a glycopeptide in the treatment of high-risk febrile neutropenic cancer patients with persisting fever after 48 to 60 hours of empirical broad spectrum monotherapy (piperacillin/tazobactam). As a corollary, during the study serum samples were centralized c/o the participating center in Ulm (D) to evaluate the cytokine kinetics in febrile neutropenic patients. Preliminary analysis performed on 670 patients treated with monotherapy suggests that piperacillin/tazobactam monotherapy is effective for the treatment of febrile episodes in granulocytopenic cancer patients. The randomized part of the study on vancomycin plus placebo is still being evaluated.

The Group will seek to publish and report Trial XIV findings and outcomes through one full study focusing on the entire trial, as well as through the submission to different conferences/meetings of abstracts focusing on single aspects of the protocol, namely the piperacillin/tazobactam monotherapy component of the study and the randomized study with vancomycin/placebo. The serum cytokine kinetics analysis will be published separately.

*Web site*

The EORTC-IATG officially launched its own web site during 2000 ([www.eortc-iatcg.org](http://www.eortc-iatcg.org)). Directly accessible from the EORTC web site, the Group's Home Page is still in its developmental stages but will become fully operational during 2001. At present, items and information of general interest are available from a publicly accessible area, while information of a more confidential nature (members' data, full protocols, standard operating procedures, Data Review Committee reports, Group published articles) will be posted under a password-protected area.

### *Harmonization of SOPs*

One of the Group's priority initiatives over the past two years has been the drafting of revised EORTC-IATG Data Center Standard Operating Procedures (SOPs). The work began in 1996 with the systematic implementation of on site monitoring visits, according to European GCP guidelines, and the writing of SOP's for the conduct of these site visits. Exhaustive standard operating procedures for all the activities done at the IATG for the conduct of clinical trials will be the result of an ongoing collaborative effort between staff members of the Group's and the EORTC's Data Center. Thus far, six specific SOPs have been drafted, namely, (i) CRF design, (ii) data entry, (iii) data monitoring (at the Data Center), (iv) monitoring site visits, (v) SAE (severe adverse effects) management and (vi) statistical analysis, representing one-third of a total of 18 so far planned. Once reviewed and approved by Data Center/Clinical Trials Operations Co- coordinators and the EORTC-IATG Management Board, these SOPs will be submitted to the EORTC Data Center. This ongoing effort is emblematic of the Group's intention to fully comply with EORTC policies and procedures, while still maintaining its own Data Center primarily because of the composite nature (i.e., infectious diseases in cancer) of the Group's activities.

### **Projects and Strategies for the coming years:**

#### *Trial XV*

Oral Empirical Therapy of Fever in Low-Risk Neutropenic Cancer Patients: A Prospective, Double-Blind, Randomized, Multicenter Trial Comparing Monotherapy (Single Daily Dose Moxifloxacin) with Combination Therapy (Ciprofloxacin plus Amoxicillin/Clavulanic Acid).

The primary objective of the study is to show equivalence in efficacy between oral monotherapy and oral combination therapy in low-risk febrile neutropenic patients with the intention to treat on an outpatient management basis. A second goal will be to validate sensitivity, specificity and predictive values of the Multinational Association for Supportive Care in Cancer (MASCC) score for the prediction of complications in febrile neutropenic cancer patients.

The two-page outline of the Group's proposed Trial XV (EORTC protocol 46001) was submitted to the EORTC Protocol Review Committee (PRC) on October 30, 2000. Comments of the PRC were received shortly thereafter, and a revised outline addressing major issues and points raised by the PRC was re-submitted in early January, 2001. Negotiations between the Group, the EORTC and the trial's sponsor were stepped up early in the year with a view to officially launching the trial before May, 2001.

#### *Jointly sponsored symposia*

The Group's Education and Communications Committee pursued its attempts to propose a joint symposium of the EORTC-IATG/IFIG (Invasive Fungal Infections Group) at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) (Chicago, 2001). Despite promising contacts in 2000, it was learned in early 2001 that the proposal, "New approaches to the diagnosis of infections in febrile neutropenic patients", would not be feasible, and that a proposal taking into greater account the topical groups of the ICAAC program would have to be re-submitted in November, 2001.

A similar effort was made to include the Group in the sponsorship of the EORTC-IFIG symposium to be held at the next European Conference on Clinical Medicine and Infectious Diseases (ECCMID-11) (Istanbul, 1 - 4 April, 2001). The Group was notified that further modification of the planned symposium was not possible. Nevertheless, the Group will soon begin talks with the

organizers of this and other important venues (e.g., the annual meetings of the International Congress of Chemotherapy and the American Society of Clinical Oncology) for similar initiatives.

#### *Research proposals*

A number of proposals for research actions have been circulated throughout the Group. These include both prospective randomized clinical trials, as well as corollary studies aiming to tap the wealth of information held by the Group in its two operational structures: the EORTC-IATG Data Center (Institut Jules Bordet, Brussels) and the Microbiology Reference Center (CHUV, Lausanne).

Proposals for full-fledged protocols comprise:

- A joint trial with EORTC Invasive Fungal Infections and Leukemia Groups focusing on voriconazole versus fluconazole as antifungal prophylaxis in acute leukemia patients;
- A prospective randomized trial investigating the role of new quinolones in the treatment of febrile neutropenia in children with cancer;
- A prospective randomized trial on the early discontinuation of antibiotic therapy in neutropenic patients responding to initial empirical therapy;

Proposals for corollary research actions include:

- A study on the incidence and clinical characteristics of catheter-related infections in patients randomized in past EORTC-IATG trials;
- Infections in elderly cancer patients, following contacts with the EORTC Task Force on Cancer in the Elderly;
- Studies on the rate and clinical characteristics of superinfections in patients randomized in EORTC-IATG Trials IX and XI;
- A study on the incidence and clinical characteristics of pneumococcal infections in patients randomized in past Group trials;
- The epidemiology of gram-negative bacteremia and quinolone resistance in febrile neutropenic cancer patients recruited in past Group trials.

Still another long term proposal regards the development of a standardized data assessment procedure and CRF for all patients with febrile neutropenia or antibiotic resistant neutropenic fever ultimately aimed at the creation of a large database and registry of cases regardless of the inclusion of those cases in an ongoing Group trial.

#### **Collaboration with other groups:**

- EORTC Invasive Fungal Infections Group
- EORTC Leukemia Group
- GIMEMA (Gruppo Italiano Malattie Ematologiche dell'Adulto)

## INVASIVE FUNGAL INFECTIONS GROUP

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### Structure of the group:

Chairman : B. E. de Pauw, Nijmegen  
Secretary: C. Cordonnier, Creteil  
Treasurer: to be appointed

Other members of the Steering Committee:

J. Bille, Lausanne  
D. Denning, Manchester  
B-J. Kullberg, Nijmegen  
P. Ribaud, Paris  
C. Viscoli, Genova  
A. Marinus, Brussels  
R. Sylvester, Brussels

### Recent Achievements:

Invasive fungal infections have become the most prominent cause of death of both remitting and unremitting patients with a malignant disease. Facing this challenge, the Invasive Fungal Infections Group (IFIG) was created in 1991 on the initiative of Françoise Meunier. In 1997 it was decided that after stratification also patients with an invasive fungal infection who do not suffer from a malignant disease can be entered into trials that are conducted by the Group to enable a more rapid and reliable conclusion on the antifungal capacities of new agents and strategies.

The clinical definition criteria for invasive fungal infections that were developed in cooperation with the Mycoses Study Group in the USA has found worldwide acceptance for both research purposes and clinical practice. A full publication of this paper is expected in 2001.

Most of the newly developed antifungal agents are still not available for company-independent clinical research. The randomized trial of voriconazole, a new triazole developed by Pfizer Inc, for the treatment of proven and probable invasive aspergillosis was terminated slightly prematurely. This was due to the fact that voriconazole's activity against aspergillosis became obvious from compassionate need usage and therefore it appeared unethical to withhold the drug from patients in the trial who did not respond to amphotericin B. However, with more than 250 patients entered it became the largest randomized trial ever performed for this indication. Moreover, a similar protocol ran in North-America and enrolled half of the number of patients as a result of the registration of the lipid formulations of amphotericin B on the other side of the Atlantic ocean. It was decided to merge the data of both trials to increase the power of the eventual conclusions; to accomplish this the American data were transferred to the EORTC's Data Center. Joint data review committees were appointed under the guidance of a combined Steering Committee chaired by the chairman of the IFIG.

The second major trial that used liposomal amphotericin B to investigate the appropriate moment to start empiric antifungal therapy, was finally launched and started to accrue patients in 2000. The final results of the Phase II study on liposomal nystatin as rescue therapy for patients with invasive

fungal infections who did not respond to licensed antifungal drugs was presented at the annual ICAAC conference which was held in Toronto, Canada. A full publication will be prepared in 2001 which also applies to the comparison between fluconazole and itraconazole for oropharyngeal candidiasis in non- neutropenic cancer patients.

#### **Projects and Strategies for the coming years:**

Negotiations on a new trial designed to explore the options and limitations of voriconazole as a drug for prophylaxis against aspergillosis in patients treated for acute myelogenous leukemia and recipients of allogeneic bone marrow transplants were started. The IFICG is aiming at intergroup enterprise that comprises EORTC's International Antimicrobial Trial and the Leukemia Groups as well as the GIMEMA from Italy, the Medical Research Council from the United Kingdom, and the Canadian National Cancer Institute.

In 2001 a new chairman will be elected who will join the present chairman as a chairman-elect for a period of 18 months, whereafter the new chairman takes office and is joined by the previous official as a past-chairman for another 18 months, when a new election will replace the past-chairman by a chairman- elect to start a new cycle.

#### **Collaboration with other groups:**

The official cooperation with the Mycoses Study Group in the USA had to be kept at a low level as a result of an ongoing rescheduling of financial and administrative reorientation of the National Institutes of Health in the USA.



## LEUKEMIA GROUP

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### Structure of the group:

Chairman:	T. De Witte, Nijmegen
Secretary:	J-P. Marie, Paris
Treasurer:	P. Muus, Nijmegen

The EORTC Leukemia Group comprises more than 45 qualified hematology centers in Europe. During the last few years several centers from Eastern Europe have also joined our group. Subcommittees on cytogenetics and molecular biology, and immunology, shared by experts in the field, are rather active and have meetings on a twice a year basis.

### Recent achievements and Strategies:

The aim of our group is to organize Phase II and Phase III trials for patients with acute and chronic myeloid and lymphoid leukaemia, myelodysplastic syndromes and myeloma. In 2000, 330 patients have been included in 9 trials of the group. Presently more than 2,600 patients included in previous and current studies are alive and under continuous follow up allowing us to plan studies on long term results.

#### *Phase III studies in AML*

The AML 10 study for AML patients up to the age of 60 was activated in 1994 and closed in 1999. This is a joint study between the EORTC Leukemia Group and the Italian GIMEMA. In this trial three types of anthracyclines are randomized in induction and consolidation courses. After achievement of complete remission and a high dose consolidation course, an autologous or an allogeneic stem cell transplantation is planned to be performed in all patients. Those patients who were supposed to undergo autologous stem cell transplantation are randomized between a marrow or a peripheral blood stem cell transplantation. During the first five years of this trial the accrual was 380 - 400 patients per year, which means that at the end of the study 2,210 patients from 75 centers are registered. For the second question almost 300 patients were randomized.

The new protocol (AML-12) includes a randomization at diagnosis for a remission induction using high dose ARA-C compared to the "best" remission induction schedule of the AML-10 trial. For patients reaching a complete remission, this is followed by intensive consolidation and an autologous peripheral blood stem cell transplantation and a second randomization for maintenance with low dose subcutaneous interleukine-2 or no further treatment. Patients with an HLA identical family donor will be excluded for the autologous transplantation but will undergo an allogeneic transplantation. Monitoring of minimal residual disease by molecular techniques will be part of the study. This will be done in a recently formed EORTC/GIMEMA network of laboratories in The Netherlands, Belgium, France and Italy.

In 1996 the AML-13 trial comprising of patients over the age of 60 was initiated. In a randomized fashion the effect of G-CSF on remission induction rate and duration of remission is studied. A second randomization is performed on patients in complete remission to study the question of consolidation course in the hospital or on the almost identical consolidation course to be given outside the hospital using i.v. or oral idarubicine. Accrual is approximately 150 patients per year from

± 50 centers. At this moment 667 patients are registered, and 297 are randomized for the second question. It is anticipated that the study will be closed in the forthcoming months, as the targeted number of patients for the second question will then be reached (i.e. 315). So a new AML-15 trial for elderly AML will be necessary in the near future.

In the meantime a Phase II trial AML-15/P over the age of 60 has been initiated. This trial aims to assess the feasibility, toxicity and antileukemic activity of Myelotarg®(anti-CD33+calicheamycin) as a front-line therapy in elderly patients with previously untreated AML.

In 1996 the EORTC joined the GIMEMA protocol for acute promyelocytic leukemia (AIDA). This trial is based on the use of ATRA- and idarubicine for induction followed by intensive consolidation and a stratification on the basis of PCR analysis of minimal residual disease. The study was closed to patient accrual in November 2000 after achieving the required number of patients.

For relapsed patients one Phase II study has been closed due to a too low accrual, and another one is still open. Intermediate dose IL-2 can be given to slowly progressing leukemia patients relapsing or not after autologous stem cell transplantation (trial 06964). A new study for relapsed patients is under preparation.

In fact all AML trials are joint ventures between the Italian Leukemia Group GIMEMA and the EORTC Leukemia Group. In this way it is possible to perform AML studies for patients from the age of 15 years up to 75 years in about 600 patients per year.

#### *Myelodysplastic syndromes.*

For patients with so-called low risk myelodysplasia a Phase II study using Amifostine combined with erythropoietin in patients who showed no response concerning the erythropoieses has recruited 29 patients and closed prematurely in 1999 due to the low response rate. For patients with so-called "high risk" myelodysplasia and secondary AML under the age of 60 years a trial (06961) was initiated in December 1996. Remission induction is performed with combination of idarubicine, Ara-C and etoposide. After achievement of complete remission a consolidation follows using intermediate doses Ara-C and idarubicine. When the patient is still in remission and an allogeneic donor is not available, a randomisation follows comparing peripheral blood stem cell transplantation and a second consolidation. The second consolidation includes high dose Ara-C. The accrual is ± 60 patients per year from 31 centers. At this moment 234 patients are registered, and only 49 randomized for the second question. A Biomed grant (CRIANT) has been provided to study Europe-wide the molecular follow-up in these patients. At this moment a new protocol with a DNA demethylating agent is in preparation for high-risk MDS patients over the age of 60.

#### *Chronic myeloid leukemia*

The CML Phase II study (06941) using -Interferon and ATRA recruited 20 patients. Some cytogenetic conversions were reported. However the trial was closed in 1999 due to the lack of interest of the group members. Too many competing trials in Europe are available.

#### *Acute lymphoblastic leukemia*

For acute lymphoblastic leukemia, a new ALL-4 trial was initiated in 1995. This trial compares the effects of prednisone versus dexamethasone in the remission induction Phase and in the consolidation Phase. A second randomisation compares continuous intensive maintenance chemotherapy courses versus autologous stem cell transplantation followed by low dose maintenance courses. The second question is similar to the one addressed by the French LALA group. A prospective meta-analysis has been planned. The accrual of the EORTC Group is

disappointing however (< 40 patients per year) and only 169 and 42 patients were randomized respectively for the two questions.

An intergroup study for patients with positive bcr/abl-positive ALL in collaboration with GIMEMA and the French LALA group has been very successful this far. A total of 231 patients were registered by these three groups. The final analysis has been performed, and a paper is in preparation. A new trial with randomization of STI571 + chemotherapy during consolidation is planned by the same groups and other French groups in this subgroup of ALL.

#### *Chronic lymphocytic leukemia and myeloma.*

The randomized Phase II study on the effect of high dose chlorambucil versus fludarabine in previous untreated progressive B-CLL has been almost finalised. 88 patients were randomized by 16 centers. A new randomized Phase III study 06992 (CLL-3) comparing low dose chlorambucil maintenance versus no-maintenance in CLL patients with a good partial or complete remission after high dose chlorambucil induction has been accepted by the PRC. The study will soon be open to patient entry. For young patients with CLL a combined study with the EBMT comparing autologous stem cell transplantation and no further treatment in patients who have reached a good partial or complete remission has been planned. An intergroup study in myeloma coordinated by the ECOG which compares VAD versus VAD plus PSC-833, has been closed prematurely due to the low accrual rate.

#### *Quality assurance*

This is mainly based on the review of patients for eligibility and evaluability performed by the study coordinators along with the methodological approach of the Leukemia Unit according to the EORTC Data Center quality assurance procedures. Independent review of cytology cytogenetics, molecular biology and immunology by three subcommittees, and occasional site visits to participating centers have led to improvement in the quality of the studies of the group.

#### **Collaboration with other groups:**

The Leukemia Group has a very close relationship with the Italian GIMEMA group. Many leukemia studies are joint studies. This combination is very advantageous for both groups since it forms the largest group for leukemia treatment research in the world. Our group also has regular contacts with the EORTC Children's Leukemia Group and the Lymphoma Group. There are also joint studies with the French LALA Group and the European Blood and Bone Marrow Transplantation Group.

The EORTC Leukemia group is a member of the AML Collaborative Group, which comprises all groups performing randomized trials and AML in collaboration with the MRC and HOVON. The EORTC/GIMEMA plays a major role in conducting meta-analysis with the support of a Biomed grant.

## LUNG CANCER GROUP

### Structure of the group:

Chairman:	C. Manegold, Heidelberg
Secretary:	A. Ardizzoni, Genoa
Treasurer:	P. Baas, Amsterdam

### Steering Committee:

C. Manegold, A. Ardizzoni, P. Baas, G. Giaccone (Past-Chairman), P. Lianes (sub-chairperson chemotherapy), P. Van Schil (Sub-Chairman surgery), E. Van Marck (sub-Chairman pathology), C. Koning (sub-chairperson radiotherapy), J. Van Meerbeeck (sub-Chairman quality assurance), T. Splinter, V. Tjan-Heijnen, M. O'Brien, J. Belderbos, S. Senan, G. Kramer, E. Smit, N. Van Zandwijk, J. Jassem, C. Legrand (statistician) and C. Debruyne (medical advisor).

The Group officers include the secretary, treasurer and sub-chairmen of different specialties such as chemotherapy, radiotherapy, surgery and pathology. A Lung Cancer Group Quality Assurance will be implemented in the year 2000.

### Recent Achievements:

In 2000, two studies were closed and are being analyzed. At the present time, seven trials are open to accrual and another eight are expected to be activated in 2001. More than 500 patients were entered in the EORTC Lung Cancer Group trials during 2000.

- *Non-small cell lung cancer (NSCLC)*

Randomized trial of surgery versus radiotherapy in patients with stage IIIa NSCLC after response to induction - chemotherapy (08941).

This is a Phase III trial in which patients with stage IIIa (N2) disease, who respond to neo-adjuvant chemotherapy, are randomized between radical radiotherapy or surgery. Three cycles of neo-adjuvant platinum-based chemotherapy are required before randomization. Two sequential Phase II studies of new combinations have been inserted as neo-adjuvant regimen: 08955 gemcitabine-cisplatin, and 08958 carboplatin-paclitaxel. Both regimens have produced approximately a 70% major response rate in over 50 patients enrolled in each study. A new Phase II study with neo-adjuvant regimen taxotere-cisplatin has started in 2000. More than 500 patients have so far been registered in the Phase III study and more than half of those have been randomized.

*Taxotere and Cisplatin as induction chemotherapy in patients with stage IIIa N2 non-small cell lung cancer (08984)*

A new regimen of taxotere-cisplatin will be tested in the setting of neoadjuvant chemotherapy prior to locoregional treatment in stage IIIa N2 NSCLC (08941).

*A randomized Phase III study comparing induction chemotherapy to daily low dose Cisplatin both combined with high dose radiotherapy in patients with inoperable non-small cell lung cancer stage I, II and (low volume) stage III (08972)*

An accelerated radiotherapy with daily cisplatin, previously piloted in two institutions in Amsterdam, is being compared to the administration of two cycles of gemcitabine-cisplatin followed by the same radiation without daily cisplatin. This study is being jointly run with the EORTC Radiotherapy Group.

*Phase II study of Temozolomide in advanced NSCLC with and without brain metastases (08965).*

Untreated patients with NSCLC with and without brain metastases are eligible for this Phase II study assessing the activity of temozolomide. This trial has almost completed accrual. Major side-effects of this oral cytotoxic agent are emesis and thrombocytopenia.

- **Small cell lung cancer (SCLC)**

*Survival in an international Phase III prospective randomized LD SCLC vaccination study with adjuvant Bec2 and BCG (08971b)*

Patients with limited disease in response after chemo-radiation are randomized between Bec2/BCG vaccination or follow-up. Bec2 is an anti-idiotypic antibody directed against GD3, a ganglioside present in 100% of SCLC tumors, with biological activity in preclinical models. The provocative results of a small study performed at the Memorial Sloan Kettering in New York in SCLC stimulated the present international study, coordinated by the EORTC. This is a large international study involving the US, Europe and Australasia. The study has been recently amended to simplify the design and the conduct of the trial.

- **Mesothelioma**

*Phase II study on Tomudex in malignant mesothelioma (08992)*

Patients with measurable and previously untreated pleural mesothelioma are eligible for this Phase II trial assessing the activity of tomudex in this chemorefractory tumor. The trial will be closed to recruitment in the near future.

*Phase III study of Tomudex and Cisplatin versus Cisplatin in malignant pleural mesothelioma (08983)*

This randomized study is aimed at assessing the impact of tomudex / cisplatin on survival of patients with advanced pleural mesothelioma as compared to cisplatin alone. This study is being carried out in collaboration with NCIC and ECOG.

**Among the two studies that were closed the preliminary results are available for the following:**

*08975: Randomized study with new combination chemotherapies in advanced NSCLC.*

This trial was designed to compare the standard arm cisplatin (P)-paclitaxel (T) (T 175 mg/m<sup>2</sup>/3h dl + P 80 mg/m<sup>2</sup> dl) with cisplatin-gemcitabine (G) (G 1250 mg/m<sup>2</sup> d 1, 8 + P 80 mg/m<sup>2</sup> dl) and the non-cisplatin- based regimen of T 175/mg/m<sup>2</sup>/3 hrs dl + G 1250 mg/m<sup>2</sup> d 1, 8. All 3 schedules were repeated every 21 days. Eligible patients (pts) were required to have measurable disease; PS = 0-2; and Stage IIIB (malignant pleural effusion and /or supraclavicular nodes) or Stage IV. 480 pts were randomized between 8/98 and 7/00 (T+P 159; G+P 160; T+G 161; PS0=27%; PS1=61%; PS2=12%; IIIB=21%, IV=79%; squamous cell=24%, adeno=41%; undiff=31%; other 4%). In general, the 3 regimens were well tolerated. Gr 4 thrombocytopenia was more common with G+P. Severe nausea/vomiting were least common in arm T+G and sensory neuropathy in arm T+P. At the time of the 11/00 analysis, 191 of the 378 deaths needed for final analysis have occurred. The response rate & survival results of the individual arms will be available for presentation at ASCO in May 2001.

**Projects and Strategies for the coming years:**

1) The current objective of the Group is to promote large randomized studies on important questions in the treatment of lung cancer. This objective is also addressed by extensive collaboration outside the EORTC. In particular, various intergroup studies have been successfully initiated in recent years with a number of national groups (e.g. NCIC, Spanish Lung Group, SAKK, GFPC, ECOG, MRC and NVALT). Another objective is to explore new treatment strategies through Phase II trials with new agents or treatments for lung cancer and mesothelioma, with the limited participation of specific centers. Furthermore, at the end of 2000 a collaboration with MRC was established for a Phase three trial of surgical resection with or without pre-operative chemotherapy in patients with operable NSCLC of any stage. This trial is already open for recruitment in the United Kingdom and the Group is expecting to join the trial in the year 2001.

2) New trials to be activated in 2001:

Chemotherapy followed by surgery in selected stage IIIB NSCLC (08981)

This study will investigate the feasibility of surgery in stage IIIB after neoadjuvant chemoradiation. This small study will be first piloted by a small group of centers with particular interest in aggressive surgery.

Phase III study: CDE versus Carbo/Taxol in ED SCLC (08001)

This study will compare in terms of survival outcome the standard EORTC chemotherapy regimen cyclophosphamide-doxorubicin-etoposide vs one of the most active new regimens carboplatin-taxol

Phase III study: Reinduction versus Taxotere/CPT11 in sensitive SCLC (08002).

This study will answer the question of whether the best treatment option for relapsed SCLC is reinduction with first-line chemotherapy or the use of a non-cross resistant regimen including taxotere and CPT-11.

Phase III study of PCI in extensive disease small cell lung cancer (22993/08993).

This trial will assess if PCI can reduce the incidence of symptomatic brain metastases in patients with ED SCLC after response to chemotherapy.

Randomized double blind trial to compare ZD 1839 in combination with docetaxel versus placebo with docetaxel in patients with advanced NSCLC who failed previous chemotherapy (08011)

This trial would be the first to explore the continuous use of Iressa in combination with standard dose of docetaxel chemotherapy in the second-line setting.

High dose versus standard dose of prophylactic cranial irradiation in LD SCLC (EULINT1/22003 / 08004)

A meta-analysis has been performed including all randomized trials of PCI in SCLC in response after first line treatment. The positive results on survival found at this analysis constitute a recommendation for routine PCI in SCLC patients with limited disease. A new study comparing different doses of PCI is being prepared as a European Intergroup effort (EULINT).

Randomised trial of surgical resection with or without pre-operative chemotherapy in patients with operable NSCLC of any stage (MRC trial LU22)

The trial is designed to detect an improvement in 3-year survival of 15%, that is from 40% in the surgery alone group compared to 55% in the pre-operative chemotherapy group.

3) The Group is also trying to establish new projects on translational research by collecting tumor specimens and blood samples in specific tumor types like mesothelioma and bronchoalveolar carcinoma.

4) Finally, the group has established a quality assurance committee to further improve the quality of the group performance.

**Collaboration with other groups:**

EORTC Radiotherapy Group, EORTC Head and Neck Cancer Group, EORTC Quality of Life Group, EORTC Early Clinical Studies Group, Dutch Lung Cancer Group, Spanish Lung Group, SAKK, Groupe Français de Pneumo-Cancérologie, FONICAP, NCIC, ECOG, MRC, NVALT.

## LYMPHOMA GROUP

### Structure of the group:

Chairman:	J. Raemaekers, Nijmegen
Scientific Secretary:	H. Kluin-Nelemans, Leiden
Treasurer:	J. Thomas, Leuven

### Executive committee

It acts as daily board, handles business matters, prepares the semi-annual business and general group meetings, discusses, proposes and monitors the scientific strategy of the group.

It consists of:

- present chairman, secretary, and treasurer.
- past chairmen: P. Carde, E. Noordijk, C. Meerwaldt
- last secretary: J. Thomas
- medical advisor Data Center: I. Teodorovic

#### *Pathology committee*

- Hodgkin's disease (HD): a panel of expert pathologists is chaired by J. Bosq, Villejuif. The panel meets twice yearly to discuss central histologic review data and problem cases. Independent external experts in the panel: K. MacLennan (London), J. Diebold (Paris).
- Non-Hodgkin lymphoma (NHL): the central pathologist is D. de Jong, Amsterdam. The former central pathologist, C. de Wolf-Peters, Leuven, is still in charge for past studies.

#### *Radiotherapy*

In 2000 a radiotherapy committee was formed that will focus on new strategies in RT and develop quality control and assurance programs for the ongoing and new studies.

Chairman:	T. Girinsky, Villejuif
Members:	C. Meerwaldt, E. Noordijk, P. Richaud, R. vander Maazen, P. Poortmans, B. Aleman.

#### *New drugs*

In 2000 a new drug committee was formed that will propose and launch Phase-2 studies.

Chairman:	J. Thomas, Leuven
Members:	U. Tirelli, J. Baars, H. Eghbali, A. Pinto, I. Teodorovic, M. van 't Veer.

#### *Biological theme*

The biological theme group focuses on the quality control on quantitative t(14;18) analysis using Taqman technology. In December 2000, the blinded test samples have been sent to participating reference laboratories. After having established adequate, comparable and reproducible results in the reference labs, serial prospective analysis in future low-grade NHL trials will be incorporated. J. Meijerink (Nijmegen) left the group and was replaced by B. van der Reijden (Nijmegen)



Chairman: P. Soubeyran, Bordeaux  
 Members: B. van der Reijden, M. van t Veer, J. Baars, D. de Jong, J. Jancar, V. Gattei, A. Bennaceur, A. Buijs, J. Sliedlecki, J. Meder, J. Raemaekers.

#### *Quality-of-life theme*

Prospective and sequential QOL-monitoring is incorporated in early stages HD trials (H8 and H9) and is performed by H. Flechtner, Cologne, and M. Henry-Amar, Caen. The study coordinators of H8 and H9 trials are closely involved, as is the chairman of the group: C. Meerwaldt, A. Mellink, H. Eghbali, C. Ferme, J. Raemaekers.

#### *Group liaison persons communicating with other groups*

EORTC Biological Therapeutics Development Group	M. van 't Veer
EORTC Cancer in the Elderly Task Force	P. Soubeyran, U Tirell
EORTC Radiotherapy Group	P. Poortmans
International Cochrane Review group	C. Meerwaldt
EBMT Lymphoma Working Party	J. Raemaekers
German Hodgkin Study group	C. Meerwaldt
	J. Raemaekers
	J. Baars

#### **Recent Achievements:**

The executive committee has had a fruitful brainstorming session in June in Leuven. A plan of action for the next three years was defined and presented at the fall general meeting in Amsterdam. The radiotherapy committee and the Phase-II committee were formed to improve on the decisiveness in new developments and to increase active commitment of the members. The structure of the semi-annual group meetings will be reorganised by restricting the business meeting to purely business matters in a restricted time schedule. Then, the general meeting can be made more appealing by increasing the opportunity, also in time, to discuss past, ongoing and new trials. The cooperation with other groups in combined studies and intergroup initiatives will become increasingly important, thus requiring a smooth and transparent structure of cooperation. Especially, the collaboration with GELA and HOVON asks for good and smooth procedures. First and important steps have already been made by providing the opportunity to have double counting for centers participating in several groups concomitantly. A fruitful discussion on performing combined studies with GELA board members with the executive committee members and representatives of the Data Center in Brussels was held in November. For the coming years new Phase-III studies for advanced untreated and relapsed HD are planned; an absolute priority will be given to new protocols on patients with untreated aggressive NHL and the development of Phase-II studies with new drugs.

In July, the first meeting was held in Brussels to prepare and accompany the transfer of the HD database from Villejuif and Caen to Brussels. M. Henry-Amar, I. Teodorovic, A. Anastopolos and P. Therasse made good progress and it was decided that the database from the past studies was to be transferred first, also serving as a test case for compatibility of database structure. The first transfer, trial H2, has already been transferred. Appropriate statistical cross-checks will be run in the Caen and Brussels Data Centers to fulfill the quality assurance requirements, i.e. to check that databases on both sites are 100% matching. The same procedure will be performed for every transferred study.

### Closed trials

H7 (E. Noordijk, P. Carde): an update of data of the H7 trial on early stages HD has been finalised. The final report is being prepared and will be submitted early 2001.

#20884 (J. Raemaekers, B. Aleman, M. Henry-Amar): this long-running trial on the benefit of additional involved-field RT (IF-RT) after chemotherapy-induced CR in advanced stages HD, reached the target accrual in May 2000. The study is now closed for entry; definite analysis is expected in 2001 on this group of 750 patients.

#20901 (H. Kluin-Nelemans, J. Thomas): this study on high-dose treatment versus standard chemotherapy in untreated aggressive stage I bulky, II, III and IV NHL patients, closed in 1998, was submitted and accepted in the JNCI and will be published early 2001. In this trial on 311 entered patients no benefit of consolidation with high-dose treatment after standard chemotherapy could be demonstrated as compared to standard chemotherapy + iceberg RT.

#20921 (Dr Hagenbeek, Dr Marcus): Fludarabine versus CVP in patients with stages III and IV low grade NHL. The database is being extensively checked and final analysis is planned early summer 2001.

#### *On-going trials*

#20982 (J. Thomas, E. Noordijk, H. Eghbali): the H9- trial, in cooperation with GELA, on early stages HD concerning EBVP +/- IF-RT in favourable patients and ABVD 4 versus 6 cycles versus 4 baseline BEACOPP cycles +IF-RT in unfavourable patients, is running extremely well with >700 patients already accrued (in 2000 a total of 211 patients by EORTC).

#20962 (P. Poortmans, H. Kluin-Nelemans): the first interim analysis of the trial on MBVP chemotherapy+ RT in primary CNS NHL has been performed in November after the first 31 patients had been entered. Response rates and toxicity were encouraging and acceptable respectively, implying that the study will continue.

#20981 Intergroup trial (A. Hagenbeek, R. van Oers): the trial on CHOP chemotherapy +/- Mabthera followed by maintenance with Mabthera or no maintenance in relapsed low-grade NHL, is steadily increasing its accrual rate after a very slow start. A total of 120 patients have been included, 19 of them being from EORTC members.

#20995 (H. Kluin-Nelemans): the mantle cell NHL international study has been accepted as EORTC study with a target accrual overall of 210 patients. In this randomised study, high-dose treatment is compared to standard chemotherapy in untreated mantle cell NHL patients.

#20971 (C. Meerwaldt, P. Richaud): the randomised Phase-III study on low-dose TBI + involved-field RT versus low-dose involved field RT alone in localised untreated low-grade NHL patients was accepted and will start soon.

**Project for the next five years:***Forthcoming trials*

#20991/#20992 (P. Soubeyran): the randomised twin trials on aggressive NHL in elderly patients will probably start in the first half of 2001 focusing on the randomised comparison of standard CHOP versus CHOP + prolonged oral etoposide in good performance patients (20991). For the poor performance elderly patients, a performance status-based treatment schedule with adapted number of cycles of CVP will be tested in a Phase-II setting (#20992). Extensive quality-of-life analysis is foreseen in this trial.

A consensus was reached to start a large intergroup and intercontinental study on patients with untreated advanced stages HD with poor prognostic features. In this randomised Phase-III study 8 cycles of ABVD will be compared to 4 cycles of escalated BEACOPP followed by 4 cycles of baseline BEACOPP. The EORTC Lymphoma Group coordinates this study (P. Carde, J. Raemaekers) in close cooperation with GELA (M. Divine, E. Lepage) and includes cooperation with Nordic Lymphoma Group, Catalan Group, SAKK, NCI Canada. Protocol will be submitted to the PRC in early 2001.

A combined trial with the German Hodgkin Study Group has been discussed and agreed upon. This randomised trial on sequential high-dose treatment versus conventional single high-dose treatment in relapsed HD, will start in Germany early 2001. Submission to the PRC is planned early 2001 (J. Baars).

A large intergroup study on radio-immunotherapy in low-grade NHL is planned (D. Bron, A. Hagenbeek). Zevalin, anti-CD20 coupled to Yttrium, will be randomised as a single consolidation treatment versus no consolidation after chemotherapy-induced remission in previously untreated low-grade NHL patients.

Another intergroup study will be initiated on the randomised comparison of low-dose IF-RT versus chlorambucil chemotherapy in advanced stages previously untreated elderly low-grade NHL patients (R. Haas). The study will be performed together with HOVON and possibly other groups.

Absolute priority will be given to new protocols on patients with untreated aggressive lymphomas. There is a need for new avenues, especially incorporating biological markers in the treatment design as a guide to tailor treatment strategies. Results from central pathology review and biologic marker studies will become increasingly important and constitute one of the priority developmental areas for our group. Improvement of outcome of patients is likely to be modest, therefore urging the need for even more collaboration with other groups in large intergroup studies. However, the development of Phase-II studies with new drugs are also needed and this will be one of the priority areas for the lymphoma group during the coming years.

The quality of life (QOL)-studies, so closely related to the early stages HD trials (H8 and H9) and coordinated by M. Henry-Amar, Caen and H. Flechtner, Cologne, will reveal a wealth of data in the next years. We are just very slowly beginning to understand what short and long-term impact our treatment causes in patients. The establishment of the clinical significance of these data is a priority for the coming years in order to obtain possible reproducible QOL end-points for use in the design of new trials.

Late toxicities both in HD and in NHL trials, will be analysed in the data bases of our past trials. Grants have been pursued and a group of actively interested members of the group will take the

initiative to start analyses (M. Henry-Amar, H. Kluijn-Nelemans, P. Carde, J. Cosset, E. Lugtenburg, M. MacKenzie, B. Aleman, J. Raemaekers).

The recently closed #20884 trial on advanced stages HD, will be analysed on the main end-points in 2001. In this study quality control on the IF-RT is of utmost importance. This retrospective analysis on over 150 patients will be performed in 2001 in close cooperation with the RT group and the experience already gained in France and The Netherlands (T. Girinsky, P. Poortmans). Furthermore, an ultimate effort will be made to have a radiologic central review of CT scans pre- and post-chemotherapy. A grant submission has been approved (J. Raemaekers, B. Aleman).

**Collaboration with other groups:**

Within the EORTC, contacts have been made between our group and the Cutaneous Lymphoma Task Force, the Radiotherapy Group, the Brain Tumor Group, the Biological Therapeutics Development Group and the Cancer in Elderly Task Force.

A strong cooperation with GELA and HOVON has been established. Combined studies/projects with the German Hodgkin Study Group have been initiated. Increasing numbers of requests emerge from other groups to cooperate in specific intergroup studies. Formal collaboration has been already established with the Nordic Lymphoma Group, the SAKK, the Catalan Lymphoma Group, and recently also the NCI of Canada.

## MELANOMA GROUP

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### Structure of the group:

Chairman:	D. Liénard, Lausanne
Secretary:	U. Keilholz, Berlin
Treasurer:	G. Ghanem, Brussels

The MG has eight committees concerned with the management of melanoma, the development of new immunotherapy strategies and basic science carrying out immunological, pathological and epidemiological studies on melanoma. Epidemiology has become a new key program for the group next to an extensive Phase III trial program regarding treatments in virtually all stages of melanoma. Immunotherapy based on specific tumor antigens and T cell responses will be increasingly explored in the future. A new committee structure adapted to the sharply increased activities of the group is now working as follows:

<i>Chairman Adjuvant Therapy Strategies Committee:</i>	A.M.M. Eggermont, Rotterdam
<i>Chairman Epidemiology Committee:</i>	P. Autier, Luxembourg
<i>Chairperson Genetics Committee:</i>	V. Bataille, London
<i>Chairman Immunotherapy Committee:</i>	U. Keilholz, Berlin
<i>Chairman New Drugs Committee:</i>	C.J.A. Punt, Nijmegen
<i>Chairman Pathology subgroup:</i>	D.J. Ruiter, Nijmegen
<i>Chairman Surgery Committee:</i>	DA. Testori, Milan
<i>Chairman Vaccine Development Committee:</i>	D. Schadendorf, Mannheim

### Recent Achievements:

Clinical trials:

- **18952** -Randomized Phase III study : Post-operative adjuvant Interferon alpha 2b in resected high risk primary (> 4mm) and/or regionally metastatic melanoma. One year intermediate-high dose versus two years intermediate-low dose versus observation. (A. M. M. Eggermont, Rotterdam).

The trial investigates whether following an induction treatment period of daily administration of 10 MU of IFN alpha 2, maintenance therapy of one year intermediate-high dose (10MU) or two years intermediate-low dose (5MU) of IFN alpha 2b can statistically reduce mortality in high risk melanoma without excessive toxicity associated with very-high dose. This protocol was activated in April 96 and thanks to an excellent accrual (1418 pts included within 4 years) the trial was closed by June 2000. It was immediately followed up by trial 18991 « Long Term Adjuvant PEG-Intron versus Observation in Stage III Melanoma ». The first analysis of the 18952 trial is expected early 2001.

- **18951** -Randomized Phase III study of DTIC, CDDP, INF alpha with or without IL-2 in disseminated melanoma (U. Keilholz, Berlin and A. M. M. Eggermont, Rotterdam).

The trial was open to selected centers with experience in high-dose IL-2, 363 pts have been included. Objectives: survival, time to progression, duration of response, quality of life. Accrual was completed by March 2000 and was followed up by an amendment to the study which evaluates DTIC (2 courses) vs DTIC, CDDP, IFN alpha + IL2, followed in both arms by biochemotherapy (except in rapid progressors) to determine whether DTIC «pretreatment» results could be used as a «chemoselection» (to identify rapid progressors and spare them the toxicity of biochemotherapy). The first step of the Simon design was reached in December 2000 and the continuation will depend on the interim analysis. A first analysis of the 18951 trial was presented at the ESMO 2000 Meeting.

- **18991** -Randomized Phase III : Adjuvant PEG Intron (5 years) versus observation after regional lymph node dissection in AJCC Stage III (TxN1M0) melanoma patients (A. M. M. Eggermont, Rotterdam).

The trial investigates the effect of a long term (5 years) therapy with the long acting Pegylated interferon alpha 2b vs observation on apparition of distant metastasis, survival and disease free survival in high risk melanoma patients. The protocol was activated in June 2000, 900 pts expected.

#### **Committees activities :**

##### *Epidemiology :*

Population-based case-control study of melanoma and exposure to sunlamps/ sunbeds. This study including 900 melanoma cases and 900 controls is funded by the BIOMED 2 program of the European Commission. The final report is scheduled for April 2001.

##### *Immunotherapy:*

Workshop was organized during the Spring meeting about a minitransplant project. A protocol is being developed to test the efficacy of allogeneic blood stem cell transplantation after reduced conditioning in selected melanoma patients.

The results of the ELISPOT assays quality exchange program has been published in J. of Immunol Methods (C. Scheibenbogen).

##### *Pathology and surgery:*

Sentinel node technique is nowadays largely applied as a staging procedure in skin melanoma, nevertheless, standardization of the surgical technique, the definition of micro-metastases and improvement in their detection methods are necessary. A project addressing these questions will start during 2001 and will serve as an appendix to the 18961 and 18991 protocols.

Manuscript on prognostic factors in thin (<1mm Breslow) melanoma was submitted for publication (M. Cook).

#### **Projects/Strategy for the next five years:**

New trials regarding almost all stages of melanoma have been activated or will be activated soon :

**Stage II : 18961**.- *Post-operative adjuvant ganglioside GM2-KLH/QS21 vaccination treatment after resection of high risk primary melanoma (> 1.5mm) (TNM: T3-4N0M0: stage II). A 2-arm multicenter randomized Phase III trial.* (A. M. M : Eggermont, Rotterdam).

This trial will investigate whether following excision of a high risk primary melanoma (>1.5mm) treatment with the ganglioside vaccine GM2-KLH/QS21 for a period of 3 years will improve DFS and OS. This trial is complementary to the I8952 trial for the lower Breslow melanomas and for node-negative patients.

**Stage IV: I8981** - *Temozolomide vs Temozolomide + whole brain radiation in stage IV melanoma patients with asymptomatic brain metastases* (J. Becker, Würzburg). This trial comparing the 2 treatment modalities has been activated very recently.

**Stage IV: I800X** - Another randomized trial is being prepared comparing the efficacy of «classical scheduling of Temozolomide vs Cyclic Scheduling (P. Patel, Leeds).

In collaboration with the Ocular Oncology Task Force a vaccine (peptides) trial based on specific antigen presentation by HLA A2 patients with high risk primary ocular melanoma will be initiated (Trial **I8001/88001**). The endpoint is improvement in DFS and OS in patients treated with the vaccine. (V. Brichard, Brussels).

Future trials for stage IV ocular melanoma are under developments.

#### **Collaboration with other groups:**

EORTC OOTF : cf. supra

EORTC ECSG : Trial I8002/I6005 - Open Phase II study of E7070 in patients with metastatic stage IV melanoma (S. Aamdal, Oslo).

Contacts with the ECOG Melanoma Study Groups have been established and the option of doing Intergroup Studies in the future is under study in stage IV ocular melanoma.

The minitransplant project in melanoma patients will be realized in close collaboration with hematologists of the EBMT. A collaborative study will start with the NCI on genetic characteristics determining susceptibility to UV radiation. The EORTC MG will take part in an international effort aimed at setting up a population-based randomized trial for determining in which circumstances sunscreens may protect against melanoma.

## ONCOLOGY NURSES GROUP

### **Structure of the group:**

Chairperson:	P. di Giulio, Milan
Secretary:	H. Gall, Amsterdam
Treasurer:	C. Molin, Stockholm
Liaison Member ECSG Research Nurses Group:	D. Batchelor, Amsterdam

### **Recent achievements:**

- Internet page for the Oncology Nurses Group (<http://www.algonet.se>)
- The Oncology Nurses Group initiated a meeting together with the Data Management Group, The Radiation Technologists Group and the Early Clinical Studies Group Research Nurses in March 2000 in which the Clinical Research Co-ordinators Group (CRC Group) was proposed. The CRC will function as an independent group within the EORTC and will promote the collaboration of the three groups in order to improve the quality of cancer clinical trials.
- Organise the nursing symposium entitled "Patients' participation in cancer clinical trials: the role of the nurse" during ECCO 11 Conference to be held in Lisbon. The content and the speakers for this symposium is a joint project with the ECSG Research Nurses.
- Current membership is about 60 nurses.

### **Projects/strategies for the next five years:**

- The Core Curriculum for Cancer Clinical Trials for Oncology Nurses: we are awaiting endorsement by the European Oncology Nursing Society.
- The Core Curriculum will then be published and will be used to develop a course (based on the Core Curriculum) on Cancer Clinical Trials for Oncology Nurses. The organisation of the course, regarding the planning, content and speakers, will be a joint project with the ECSG Research Nurses.
- The CRC Group plan to initiate a study to assess the workload of different members of the study team involved in clinical research trials.
- Repeat the 1994 survey on nurses involved in cancer clinical trials to discover the differences in the way that nurses are now working and to assess the areas that still require education and support. This will form the basis for future research projects.
- Continue to strengthen contacts with other collaborating centres to increase the network of nurses involved in clinical cancer trials.
- Be responsible for the nursing symposium on Clinical Cancer Trials during ECCO 11 Conference to be held in Lisbon.

### **Collaboration with other groups:**

- EORTC Data Management Group.
- ECSG Research Nurses Group.
- EORTC Radiation Technologists Group.
- Quality Assurance Committee.



## PATHOLOGY GROUP

### Structure of the group:

Chairman:	W. Oosterhuis, Rotterdam
Secretary and Chairman telematics committee:	A. Spatz, Villejuif
Treasurer:	S. Daugaard, Copenhagen
Chairman review process committee:	S. Banerjee, Manchester
Chairman research studies committee:	E. van Marck, Edegem
Fellow:	K. Lam, pathologist

### Recent achievements:

The project "Central support for Histology review and Tissue Banking in EORTC", which was funded by the Parthenon Trust, started effectively on October 1, 2000, under the leadership of a Steering Committee composed of J.W. Oosterhuis (chairman), A. Spatz, P. Therasse and I. Theodorovic. Mr. M. Isabelle was appointed to provide support to this project at the Data Center. He is setting up the logistics for support for a histology review in the four Disease Groups (Melanoma, Soft Tissue and Bone Sarcoma, Breast and Genito-Urinary), that were invited to propose one of their trials in the pilot Phase of the project. Mr. J. Tucker (Edinburgh) and K. Lam are involved as consultants to develop the software for the Virtual Tumor Bank in collaboration with the IT Department of the EORTC. Mr. E-B van Veen (Rotterdam), health lawyer, consultant, will study the legal and ethical aspects of tissue banking and the use of the collected tissue for research across Europe. This work will be carried out in close collaboration with experts at the Data Center in Brussels.

At the beginning of the project a null-measurement will be done regarding the status of histology review and tissue banking in the Disease Groups. At the end of the project the effects of it on these activities will be measured.

The Pathology Group participated in the CANTOR-project (Converging Agreement by Network Telematics for Object Recognition). This was a fourth framework European Union project with the aim to develop software for training in morphology. This encompasses, object recognition, reproducible classification of tumors - consensus diagnosis - quality control in pathology. This project ended in 2000 and has been highly relevant in furthering the goal of the Pathology Group i.e. to improve the quality of histology review in the Disease Oriented Groups. The EORTC has contributed to the CANTOR project in a number of work-packages of which work-package n°5, aiming at the construction of the image databases is the most important (being the Work Package leader) from the EORTC Pathology Group perspective. This was done using EORTC Melanoma Group and University Hospital Rotterdam cases.

The image database has been put on two CD-ROMs each containing around 300 images. They were distributed to the consortium together with reference classifications. The images are also used for the ongoing EORTC Pathology Group telematics activities. The deliverables of work-package 5 to the EU Commission were: D05.1 "Quality assurance procedures for image database", D05.2,

"Assessment plan" and D05.3, the actual image databases on CD-ROM. The EORTC has also made substantial contributions to work-package 1, 7, 8 and 9.

At the end of the project it was obvious that the software which has been developed was suitable for detecting discrepancies between observations of pathologists in terms of intra- and inter-observer variation. This makes the software usable in the EORTC PG for education, training and quality control. At this moment, the commercial partner in the CANTOR project is making the software ready for the market. It is expected that this effort will be successful.

A study was conducted on the use of telematics for melanocytic lesions. It aimed to assess the value of morphological criteria for the diagnosis of melanocytic lesions in terms of inter-observer viability at the expert level, and to define protocols for the capture of digitized images useful for the review process in the EORTC context. This study involved five pathologists and had a study web site that used cold fusion dynamic technology. A manuscript is in preparation.

Telepathology connections between experts in the realm of prostate cancer are established with the GU-Group. A project aiming at electronic publishing of case reports to be carried out in collaboration with IOS-Press.

#### **Projects and Strategies for the coming years:**

The tasks of the group are to increase the involvement of pathologists in the DGs and to streamline the review process, to facilitate translational research in EORTC Disease Oriented Groups, and to reinforce the representation of pathologists in scientific committees in accordance with EORTC objectives. Involvement of pathologists in EORTC-DGs has already been facilitated by the group in several groups. According to the group, these pathologists act as individuals or in pathology committees. However, this has to be pursued with the aim to have well-identified pathologists acting in every DG. Representatives of the Pathology Group have attended meetings of several Disease Groups, like the GI Group and the Gynecology Group to explain the recently started project and its potential role in translational research in the Group.

EORTC pathologists should also be able to make site visits for quality controls. It is obvious that the histology review process for EORTC clinical trials will be drastically facilitated by telematics. This implies that functional telepathology networks between expert pathologists are organized in each DG. This has already begun in EORTC Melanoma Group, Soft Tissue and Bone Sarcoma Group and GU Groups. It is now clearly stated that a pathologist should be systematically a member of the steering committee. They should be involved in the early negotiations with the pharmaceutical industry in order to get involved in the organisation of quality controls and to participate in the design of side studies involving pathology.

Translational research in the EORTC also depends on the availability of tumor material. As already mentioned the goals of the tissue bank project are to organize an office based at the Data Center collecting materials for histological review and an helpdesk for teleconsultation, to build a virtual tumor bank, to sort out legal and ethical problems, and to develop rules for access to tissues. Actually the success of such a collection depends very much on the rules for using the material. These rules should be tested before becoming EORTC standards in one or two pilot DGs. These collections would be administrated by a steering committee comprising the board of the group, chairpersons of the group subcommittees, and chairperson of Laboratory Research division. Translational research in DGs can be either side studies of clinical trials or specific research studies

outside the context of a clinical trial. The pathologists members of the steering committees of the DGs should be able to act both as an expert in the field and to deal with side studies. However, this also depends on the contacts in the board between the researchers and the clinicians. The natural link between the Pathology Group and Receptors and Biomarker Group should lead to common research studies. Both groups should develop collaborative work on prognostic factors and marker developments.

Representation of pathologists in scientific committees is an important task to facilitate transversal studies. This has been done in two European projects focused on pathology (EUROPATH and CANTOR) allowing hiring a fellow for the group. However, interactions between pathologist and pharmaceutical industry still need to be organized.

### **Collaboration with other groups:**

#### *In the EORTC*

Collaboration with the Melanoma Group, Soft Tissue and Bone Sarcoma Group, GU Group, Breast Group, Gynecology Group and Lung Cancer Group have been established. Collaboration with other Disease Groups will be pursued and pathologists from these groups are invited to participate in the Pathology Group. Joint studies with the Receptor and Biomarker Group will be designed and common networks of resources will be facilitated. Collaboration with the Laboratory Research Division in general should be reinforced.

#### *Outside the EORTC*

Collaboration with UICC are mainly focused on the UICC Telepathology Consultation Center. This project is co-organized by the WHO and AFIP (Armed Forces Institute of Pathology). The EORTC participates at the individual level. Several EORTC pathologists act as experts for difficult cases sent by telematics. Collaboration with the Pathology committee of the OECl are in the discussion process. Interactions with the NCI on repositories have recently started.

## PHARMACOLOGY AND MOLECULAR MECHANISMS GROUP

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### Structure of the group:

Chairman:	A.J. Gescher, Leicester
Secretary:	J.H.M. Schellens, Amsterdam
Treasurer:	J. Robert, Bordeaux

After consultation of its members, the PTMG (Preclinical Therapeutics Models Group) decided to merge with the PAMM group in 2000. As a consequence, all PTMG members become PAMM members and PTMG chairman and secretary become members of PAMM executive committee.

### Recent Achievements:

1. Merger with PTMG.
2. Launching of initiative: "PAMM faces the East". This is an attempt to invite viable research groups from Eastern and Central European countries to join PAMM activities.
3. Design of PAMM website in consultation with EORTC Headquarters.
4. Approach by Astra-Zeneca for organising workshop on preclinical in vivo models in new drug design (Verona, February 2001), provision of funds for workshop.
5. Support of ECSG in introduction of translational elements into trials (lurtotecan, mistletoe).

### Projects and Strategies for the coming years:

1. Establishment of website.
2. Increase in translational research collaboration with ECSG.

### Collaboration with the other groups:

1. Merger with PTMG.
2. Collaboration with ECSG.

## QUALITY OF LIFE GROUP

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### Structure of the group:

Chairman:	P. Fayers, Aberdeen
Secretary:	T. Young, London
Treasurer:	A. de Graeff, Utrecht
Module Development Committee:	J. Blazeby, Bristol
Joint Scientific Committee:	H. Fletchner, Cologne
Methodology Committee:	M. Groenvold, Copenhagen
Elected Representatives:	G. Velikova, Leeds, E. Greimel, Graz, J. Weis, Freiburg

The group has 59 members; 46 active, 4 probationary and 9 corresponding and up to 7 members of the QL Unit (QLU) at the EORTC Data Center (DC) in Brussels also attend Group meetings.

### Recent Achievements:

During 2000, 590 academic users have registered to use the QLQ-C30 and 45 pharmaceutical companies have signed agreements. The core questionnaire, the QLQ-C30 has now been translated into 42 languages. Recently acquired translations include 3 Indian languages, 3 African languages, French Canadian, Macedonian, Taiwanese and Korean. Validated disease or domain specific modules are now distributed from the DC and in addition to English most are available in Danish, Dutch, French, German, Italian, Norwegian, Spanish and Swedish.

In order to promote the EORTC approach to QL assessment and to facilitate communication with the QLU staff and QLG members the website has been expanded. In addition to information on the Group's activities and numerous contact details it is now possible for academic users to download the QLQ-C30 and the Lung, Breast and Head & Neck Modules on completion of a registration form which must be faxed to the EORTC Data Center. A number of QLG manuals are also available online, including the newly revised Scoring Manual, the Guidelines for Module Development, the Guidelines for QL in Clinical Trials and the Reference Data.

During 2000 the Group met twice, in Oslo and in Edinburgh. The format of recent meetings has changed with more time for scientific/strategic debate rather than factual reporting on current projects. In Oslo the main topics of discussion were 1) Fatigue and 2) Collaboration with developers of other QL instruments (e.g. FACT developed by Cella in the USA). In Edinburgh there were presentations on the 'Touch Screens' to collect QL data in routine clinical practice and on "Interpretation and the Clinical Significance of QL data." The QLG and QLU were represented at the annual ISOQOL meeting in Vancouver with a number of posters and presentations.

In collaboration with the QLU at the DC, the QLG has implemented an Internet based computerized database that include all items from all existing EORTC Quality of Life questionnaires along with their translations. The Item Bank is expected to help improve quality and speed of module development and this year is being used to provide ad hoc items for use in clinical trials.

Three committees continue to coordinate the Group's activities and are responsible for a wide-ranging research program:

*Methodology Committee*

There is still a need for increased knowledge about how to interpret the magnitude of changes in quality of life scores. Such knowledge is also useful for sample size calculation. A revised version of the Subjective Significance Questionnaire (Osoba D. et al., J Clin Oncol 1999; 16; 139-144) has been developed. This questionnaire will be used in clinical trials in conjunction with the QLQ-C30 and will elucidate how patients perceive specific changes in their quality of life.

Even though the QLQ-C30 is the standard questionnaire used in trials across cancer sites and in various stages of the disease, a need has been recognized to develop a shorter version of the questionnaire specifically designed for trials in palliative care. In this project funded by the Group we use modern statistical models (so called Item Response Theory) to shorten scales of the QLQ-C30. The ongoing project has shown that it is possible to do this while preserving full compatibility of the shortened questionnaire with the scores obtained by the full-length QLQ-C30.

As part of the project using Item Response Theory to develop a shortened version of the QLQ-C30 for palliative care we have explored the use of these techniques to test the quality of translations. The results are encouraging and suggest that these relatively new methods can be used to maximise the level of equivalence across translations of the QLQ-C30.

*Module Development Committee*

Development of questionnaire modules to supplement the EORTC QLQ-C30 has continued well over the past 12 months. Two large field studies examining the validity and reliability of the ovarian (Protocol 15982) and oesophageal cancer (Protocol 15961) modules have accrued good numbers of patients. Both will be completed in the next year.

A two page outline has been accepted by the PRC to internationally field-test the pancreatic module. The full protocol for validation testing of the gastric cancer module (the EORTC QLQ-STO22) was accepted by PRC and the study will open early in the new year.

Twenty-two questionnaire modules are at various states of development. Three have completed cross cultural validation (Lung, Breast and Head & Neck) and 11 modules are at an advanced stage of development. Bladder (2), Brain, Colorectal, Gastric, Myeloma, Oesophageal, Ovarian, Pancreatic, Prostate, Satisfaction with Care) The remaining modules include Carcinoid Tumors, Chronic Lymphatic Leukaemia, High Dose Chemotherapy, Ophthalmic Malignancies, Peripheral Neuropathy, Communication, Information and Decision Making and Supportive Care Symptoms.

*Joint Scientific Committee*

The Group aims to advise the EORTC about the assessment of the multidimensional aspects of patients' Quality of Life (QL) as a measurable outcome of cancer treatment; and to advise on the design, implementation and analysis of QL studies within EORTC trials, in cooperation with the QL Unit at the Data Center. This involves liaison with all the disease oriented Groups conducting QL evaluation in their clinical trials. The role of the former Liaison Committee is to develop models for this collaboration that take account of the need of the individual liaison representatives and the Groups. The QLG and QLU jointly carried out a major review of the liaison function in 1998. From this review it became clear that the liaison function works in those Groups which are very active in QL assessment. Other Groups only include QL assessment in some of their studies, and do not regularly rely on liaison activities. To further expand the liaison model as described in a recent paper in the European Journal of Cancer (Haes et al. 2000) and as outlined in the guidelines for assessing QL within EORTC Clinical Trials it will be necessary to allocate more resources to this activity. An attempt was made in 2000 to propose ways of action to the Board and the Chairmen of the Groups. The main part of the proposal being that the current liaison function should be divided into

1) mutual scientific projects between the QLG and the Groups and 2) routine service regarding QL assessment. Hence the change in name of the committee.

### **Projects and Strategies for the coming years:**

Over the past 10 years the QLQ-C30 questionnaire has been used extensively in cancer patients from many different cultures. The Group have recently funded a statistician to work in the QLU at the EORTC DC to investigate research questions on cross-cultural issues. The work is based on a large database which is being built up from existing datasets.

Over the next 12 months new protocols to internationally validate the prostate, bladder, pancreatic and satisfaction with care modules are planned.

The EORTC document/blue book describing methods for questionnaire development will be updated. A booklet describing EORTC Quality of Life Group methods for validating quality of life questionnaires will also be produced.

The QLG is looking at strategies to improve communications between group members and clinicians. These will include training programs and scientific discussions to develop mutual research interests.

Proposals for training programs:

- Introductory course to provide a basic concept of quality of life assessment (for clinicians and for new group members)
- Quality of life training sessions about implementing QL in clinical trials and clinical practice
- Interpreting quality of life results: how to communicate the meaning and importance of QL data to clinicians and decision makers.

These training sessions will be offered by members of the QLG in collaboration with clinicians interested in QL research. The QLG are considering collaborating with other research and oncology groups on some of these training programs.

The QLG appreciates the importance of informing interested researchers, clinicians and the pharmaceutical industry about the scientific achievements and products of the group as well as about ongoing research activities. During the next year we plan to start publishing a newsletter. It will provide factual update on modules, translations, list of manuals and documentations. It will also have short articles on exciting new projects and developments. The information from the newsletter will be accessible from the QL Website. We also plan to offer a number of new services via the website and hope these will include a FAQ section and the possibility to download 'touch screen' software for collecting QL data in clinics.

### **Collaboration with other groups:**

The Group continues to look for opportunities to work with other Groups, especially in the validation of disease specific modules. The oesophageal cancer module validation study has been a joint endeavour between the QLG and the Gastrointestinal Group. The international testing of the gastric cancer module will also form a joint study between the two Groups as will the testing of the

pancreatic module. Planned validation studies for modules addressing quality of life in patients with prostate and bladder cancer are joint endeavours between the QLG and the Genito-urinary Group.

Strong links are maintained with Canada where the NCI-C widely use the QLQ-C30. A representative from the NCI-C regularly attends Group meetings and they have acted in an advisory capacity during the development of the Item Bank. A reciprocal visit to Canada in 2000 by a representative of the QLU/QLG provided an opportunity to demonstrate the Item Bank and discuss common issues on assessing QL in cancer clinical trials.

The Group are also part of a multi-collaborative venture in the USA using Computer Adaptive Testing and Item Response Theory to evaluate a wide range of existing Cancer QL questionnaires. The aim is to develop a system for use in Managed Care where the questions patients are asked are determined by computer algorithms based on their answers to previous questions. Such systems may one day be considered commonplace in routine care.

Overall the QLG will continue to focus on further developing – together with the central bodies of the EORTC – a high standard of QL assessment and analysis within EORTC clinical trials, making best use of all the available resources within the QLG, the QLU and key players in the Groups.



## **RADIATION TECHNOLOGISTS GROUP**

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### **Structure of the group:**

Chairperson:	J. Berridge, Nottingham
Secretary:	M. Coffey, Dublin
Treasurer:	G. Vandeveldel, Leuven
Guideline Development Committee:	J. Berridge, M. Coffey, V. Vlaun, M. van Os, F. Duclos.

### **Recent Achievements:**

During this year the structure of our group and its membership were reorganised. We actively participated in the Radiotherapy Group meetings and asked the members to identify radiotherapy technologists from their department who would become active members in our group. This resulted in recruitment of several new members whose input to date has already proved to be very valuable.

### **Projects and Strategies for the coming years:**

The first Phase of our project on recording acute side effects was completed at the beginning of the year. The second Phase of the project saw the members taking a proactive role in reviewing the technique details of Prostate Trial 2299 I. A group of RTs from identified participating centres met to discuss and review the draft protocol. Each representative presented detail of the current techniques used to treat patients with prostate cancer and these were then discussed at length.

Guidelines for RTs in participating centres were then drawn up which included details of several variations of technique application with a recommendation on what would be considered ideal practice if resources allowed. An acute side effect evaluation sheet was also drawn up and a technique check list for quality assurance purposes. Julie Berridge and Mary Coffey produced a set of general guidelines for RTs participating in clinical trials and translations of all documentation into French, Italian and Portuguese was completed by Frederic Duclos, Gianfranco Brusadin and Miguel Ramalho. Other translations are currently being completed. The group has also reviewed the technique details for a new lung trial and have now developed a procedural strategy for implementation in any new trial which includes radiotherapy.

**Collaboration with other groups:**

At least two members of our group now regularly attend the Radiotherapy Group meetings and identify areas where our input may be of benefit. We continue to circulate information to all members on an ongoing basis. Regular contact is maintained with the Data Center.

In collaboration with the Data Managers and Oncology Nurses Groups we have made a submission to the Europe Against Cancer Program to evaluate the cost of participation in clinical trials and to prepare guidelines on cost evaluation for potential participating departments. We will continue to attend the Radiotherapy Co-operative Group meetings and to firmly establish the reviews of technical guidelines for radiotherapy trials.

The group has joined with the Data Managers and Oncology Nurses Groups to form the Clinical Research Co-ordinators Group. We will each retain our own identity but will work closely where appropriate. We will meet on a regular basis and facilitate joint education programs on areas of common interest to all members. If our submission is successful we will complete this joint project over the coming years.

## RADIOTHERAPY GROUP

### **Structure of the group:**

Chairman:	V. Budach, Berlin
Secretary:	R. Mirimanoff, Lausanne
Treasurer:	R.P. Müller, Cologne
Administrator:	F. Godson, Lausanne

### *Steering Committee:*

H. Bartelink, Amsterdam, J. Bernier, Bellinzona, M. Bolla, Grenoble, J.F. Bosset, Besancon, L. Cionini, Pisa, L. Collette, Brussels, J.B. Davis, Zürich, J.C. Horiot, Dijon, J. Lopez Torrecilla, Valencia, D.A.L. Morgan, Nottingham, P. Poortmans, Tilburg, W. Van den Bogaert, Leuven, M. van Glabbeke, Brussels; A. Zurlo, Brussels.

### **Recent Achievements:**

Four studies have been activated during the last 12 months: on newly diagnosed glioblastoma multiforme comparing radiotherapy alone with radiotherapy with concomitant and adjuvant Temozolomide – a joint study with the Brain Tumor Group and the NCIC (22981/16981); a Phase III randomised study comparing curative radiotherapy with or without erythropoietin in head and neck squamous cell carcinoma which is a joint study with the Head and Neck Cancer Group (22996); a Phase III randomised study on low dose total body irradiation and involved field versus involved field only in low grade non-Hodgkin lymphoma (22997/20971); a Phase II study on moderate dose radiotherapy for inoperable aggressive fibromatoses, a joint study with the Soft Tissue and Bone Sarcoma Group (62991/22998).

The results of the 22991/10882 study on “boost versus no boost” in the conservative treatment of breast cancer were presented at ECCO, ASTRO and at the European Breast Cancer Conference during 2000.

Protocol 22931 in head and neck cancer was closed to patient entry in October 2000 having accrued the required number of patients. Analysis is now underway.

### *Head and Neck Task Force*

It was decided to install a task force including different national radiotherapeutic task forces and a representative of the EORTC-Head & Neck Group. This group is intended to act as a discussion forum for the initiation of new trials in head & neck cancer. It is intended to have biannual meetings.

### *Quality Assurance*

In 1999 and 2000, main efforts in QA remained trial-bound. For every trial, a dedicated QA program is set up and conducted. Several presentations on the results of this work are made at international meetings. A paper on QA in trial 22931 was published and a manuscript on the dummy run procedure in 32 centres in trial 22922 was recently accepted for publication. Analysis has been started of the older QA data in trial 22881.

We received a limited number of responses to the electronic questionnaire, set up in cooperation

with ESTRO. Work on this will soon be activated again.

A first outline for QA in 3D conformal radiation therapy trials is developed in cooperation with the NCI/RTOG. This will very soon be activated in the new prostate and NSCLC studies.

The lymphoma group established, in cooperation with representatives of the radiotherapy group, a radiotherapy subgroup for QA in lymphoma trials. The first meeting will take place in January 2001.

The selection of the Emmanuel van der Schueren fellow has been made and Dr. Vassilis Kouloulis has started his work at the end of January 2001. His tasks will include:

- Early eligibility and treatment compliance checks in breast cancer study 22922.
- An overview of performed and planned QA checks in all Radiotherapy Group studies.
- Re-release of the electronic questionnaire on RT department infrastructure (equipment and staffing).
- Finalization of QA work on the nearly complete 22961 prostate cancer study

QA in the new conformal radiotherapy studies in prostate and lung cancer.

#### *Physics Quality Assurance Activities in 2000*

22911: The dummy run procedure has been done in the 11 largest participating institutes and evaluated for protocol compliance. The results are very good with 9 institutes being fully compliant. The data from one institute was incomplete and only one institute had some minor deviations such as the use of large fields and the absence of shielding blocks. The data was presented at the ESTRO Meeting in September in Istanbul by Michel Bolla. The dummy run has now been extended to a further 9 institutes and the data is still being collected for evaluation. A paper will be written for publication in 2001.

22961: The dummy run has been organised and circulated to the largest institutes. Data is being collected. Evaluation will be done in 2001 and the results will be presented at the group's autumn meeting.

22972: Questionnaire I (equipment and treatment technique) has been received from 9 institutes. The data from 8 institutes has been evaluated and presented at the group's meeting in Zurich. All institutes have been allowed to randomise patients. One institute is having its couch and beam penumbra checked. Questionnaire II (fractionation schedule) has been received from 6 institutes. The dummy run has been done by 6 institutes and has only partly been evaluated pending a decision on the future of the protocol.

22991: Forms, questionnaires and the dummy run procedure are being prepared for circulation in 2001.

#### **Projects and Strategies for the coming years**

- Elaboration of new randomised trials aiming at the most efficient integration of radiotherapy with other treatment modalities (i.e. surgery, chemotherapy, hormone therapy) in a whole spectrum of cancer sites, in close cooperation with other EORTC or international groups.
- Integration of innovative modalities into radiotherapy such as new classes of therapeutic agents (radiation modifiers, anti-angiogenesis compounds and gene therapy).
- Integration of novel radiation techniques such as IMRT, allowing dose-escalation studies.

To improve the efficacy of the group, a new format for the group meeting will be implemented from 2001, with the creation of working parties, led by expert clinicians in various cancers, such as brain, head and neck, gastro-intestinal and genito-urinary and breast tumors, lymphoma and lung tumors. Members of other EORTC groups will be invited to participate in these working parties in order to facilitate the elaboration of joint clinical studies. At the next meeting in Berlin in the Spring of 2001, two morning parallel sessions will accommodate four working parties which will then report during the afternoon plenary session of the group meeting. In Berlin, the working parties on Head and Neck cancer, Brain Tumors, Genito-Urinary and Gastro-Intestinal Tract Cancer will be meeting.

The following studies will soon be active: 3D conformal radiotherapy with or without hormonal therapy in prostate cancer (22991); fractionation study in squamous cell carcinoma of the vocal cord (22922); prophylactic cranial irradiation in extensive disease small cell lung cancer (22993/08993) and in limited disease small cell lung cancer complete responders (22003/08004); 3D conformal radiotherapy in inoperable or locally advanced non-small cell lung cancer (22994); postoperative high dose radiotherapy with concomitant 5FU in pancreatic head cancer (22995/40992); preoperative chemoradiotherapy versus surgery in stage I and II squamous cell and adenocarcinomas of the oesophagus (22001/40001); conservative local treatment versus mastectomy after induction chemotherapy in locally advanced breast cancer (22002/10974).

Work is also being carried out on development of studies in anal and operable pancreatic carcinoma.

A task force on prostate brachytherapy is working in cooperation with the GEC/ESTRO in developing guidelines for this therapy modality.

#### **Collaboration with other groups:**

Apart from collaboration with other EORTC groups (Head and Neck, Breast, Brain Tumor, Genito-Urinary Cancer, Gastro-Intestinal Tract Cancer and Lung) a joint protocol has been set up in cooperation with the following organisations: AKK/ARO, ARTSCAN, DAHANCA, GORTEC, TROG. The Medical Research Council also works together with the Radiotherapy Group on the brain tumor study in conformal stereotactic boost (22972). The French FFCD and GERCOR will be involved in the development of the new pancreatic head cancer protocol 2995.

There is cooperation with ESTRO on prostate brachytherapy and in the area of quality assurance. Also in the area of quality assurance, cooperation has been set up with the EORTC Radiation Technologists Group.

## RECEPTOR AND BIOMARKER GROUP

### Structure of the group:

Chairman:	H. Magdelénat, Paris
Vice Chairman:	M. Schmitt, München
Secretary:	N. Brüner, Copenhagen
Treasurer:	R. Leake, Glasgow

### Steering Committee:

President	M. Schmitt, München
Quality Assurance spokesman	F. Sweep, Nijmegen
Clinical spokesman	C. Thomssen, Hamburg

### Biomedical specialists

Steroid receptors	G. Leclercq, Brussels
Predictive tissue biology	J. Foekens, Rotterdam
Proliferation and cell cycle	F. Spyrtos, St. Cloud
Biomarkers	M. Gion, Venice
Molecular biology	PM. Martin, Marseille
	H. Magdelénat, Paris
Tissue banks and derivatives	U. Eppenberger, Basel
Education & training	N. Brüner, Copenhagen
	M.G. Daidone, Milano
Publications and Editing	M. Gion, Venice

### Representatives towards:

EORTC Clinical Research	C. Thomssen, Hamburg, Breast Cancer Group L. Beex, Nijmegen, Breast Cancer Group PM. Martin, Marseille, Breast Cancer Group
EORTC Laboratory Research	R. Leake, Glasgow (BTDG) F. Sweep, Nijmegen (SPG) H. Magdelénat (PAMM)
NCI/AACR/ASCO	N. Brüner, Copenhagen
BIOMED	C. Thomssen, Hamburg
	M. Schmitt, München
NTC	R. Leake, Glasgow

### The goals of the Group:

- Quality Assurance: to establish the most suitable method for any assay of biomarkers, under investigation, such that common (or at least equivalent) methodologies can be used throughout Europe and to organize Quality Assurance and Quality Control programs for institutions participating in EORTC clinical trials or translational research.

- Translational research: to actively contribute to the translational activities of the EORTC with our expertise in tumor biology and physiopathology, by participating "ab initio" to the design of clinical trials based on predictive biological hypotheses and by conducting retrospective or prospective studies in molecular physiopathology in homogeneously treated groups of patients, such as those included in EORTC clinical trials or in appropriate experimental models.

### **Recent Achievements:**

#### *Quality Assurance and Quality Control*

The major RBG activity on QC has now shifted to uPA/PAI-I assays in connection with clinical trials evaluating these new prognostic factors, and on VEGF. RBG has developed a VEGF assay using its own "4-span" technology.

Pr. Martin (Marseille) has developed gene expression assays (20 parameters) using quantitative RT-PCR. The use of artificial RNA constructs allows an absolute determination of gene copy numbers.

These assays will be available in 2001 to RBG members for interlaboratory validation and a methodology workshop will be organized as well as the organisation of a European QC.

#### *Translational research*

The Biomed I Study on the prognostic value of uPA/PAI-I has been completed it has established the high prognostic value of the combination of uPA and PAI-I in assessing the risk of recurrence of breast cancer, specially in node negative patients. This was the basis of the "German Chemo N0" trial.

Breast cancer trial Chemo N0 and factors of the plasminogen activator system on node negative breast cancer: this trial is now closed and the publication of the interim analysis is accepted in the J. Natl. Cancer Inst 2001. This trial was the first risk adapted adjuvant chemotherapy breast cancer trial based on tumor biological factors on uPA and PAI-I.

The pooled analysis of 8000 uPA (+/- PAI-I) assays performed in 15 RBG laboratories, on a well defined population of breast cancer patients (node negative, no adjuvant treatment) is completed and the publication of results scheduled in 2001. The results show a consistent prognostic value, globally or at the level of each laboratory, even with slight variations in the assay performed.

The retrospective studies on frozen collections of breast tumors have been completed for:

- 2800 breast cancer patients for uPA/PAI-I (J. Foekens et al., Cancer Res. 60: 636-643, 2000).
- 900 T1-T2, N0-N1, M0 breast cancers for TK and TS (S. Romain et al., Int. J. Cancer, 2000).
- Parameters Response Tamoxifen therapy in breast cancer (J. Foekens, S. Romain).

A retrospective study on serum markers has been completed:

- Prognostic value of serum uPAR in Colon Cancer (N. Brünner) (357 patients).

#### *Research activities*

G. Leclercq (Brussels) has investigated the implication of spontaneous and drug induced degradation pathways (ubiquitination) on the half life of steroid receptors and on their immunoreactivity, the latter explaining part of the discrepancies which could be observed between radioligand and immunoenzymatic assays.

A. Lykkesfelt (Copenhagen) has investigated resistance to antiœstrogens, in relation with the activation of erbB-2 and/or erbB-3 in genetically modified cell lines.

### Meetings

The RBG organized the first NCI/EORTC Meeting: "From Discovery to Clinical Practice: Diagnostic Innovation, Implementation, and Evaluation, June 28 - July 1, 2000, Nyborg, Denmark". The second one is already scheduled for June 2002 in Washington, USA.

### Projects/strategy for the next years:

- Micrometastasis: demonstration of usefulness of screening for micrometastatic cells in bone marrow aspirates and blood of cancer patients. Application of new technologies (ACIS, laser dissection, PCR) as diagnostic, prognostic and/or predictive marker
- uPAR and TIMP1 in plasma of cancer patients (colon).
- Resistance to chemotherapy: Y-Box proteins in breast cancer.
- Therapy related factors: HER/neu, Immunochimistry vs FISH vs ELISA.
- It was agreed with the Pathology Group that comparative studies should be performed and guidelines for the appropriate determination of HER/neu states should be proposed for use in EORTC Clinical trials.
- Development and validation of new reagents and assays for biological markers.

New antibodies to factors of the plasminogen activation controlled system. Epitope mapping

- Implementation of Quality Controlled (RT) PCR assays (by real time PCR) of gene alteration/ expression for translational research studies (40 parameters are available and will be validated in several RBG laboratories, before entering prospective translational research)
- Search for therapy related genes: genomics vs proteomics, biology of the micrometastatic cells
- Two clinical studies are under preparation

BCG 10997. Node Negative Breast Cancer.

Randomized study comparing 6 x CMF with 3 x CMF followed by 4 x Taxol (Paclitaxel) in high-risk node negative patients with operable breast cancer: Comparison of efficacy and evaluation of clinico-pathological and biochemical markers as risk selection criteria. Coordination: Pr Robert Paridaens.

BIOMED II. Node Negative Breast Cancer. (Subject to modifications):

Adjuvant chemotherapy in node-negative breast cancer patients guided by prognostic (uPA/PAI-I) and predictive (*c-erbB-2*, TS/TK) factors. A multicentric, prospective and randomized trial on the predictive value of *c-erbB-2* overexpression and TS/TK-activity in adjuvant chemotherapy of high-risk node-negative breast cancer patients defined by tumorbiological factors (uPA/PAI-I). Coordination: Priv. Doz. Dr. med. Christoph Thomssen Prof. Dr. med. Fritz Jänicke.



### **Collaboration with other groups:**

- Breast Cancer Group:* – RBG members actively participate in the Breast Cancer Group. The RBG Chairman has been elected as a BCG Steering Committee adviser.
- Chronotherapy Group:* – RBG was invited in fall 2000 by the Chronotherapy Group to discuss relevant markers in breast and colon cancer.
- Gastrointestinal Tract Cancer Group (GTC): RBG and discussion risk assessment
- PAMM:*
- representative invited to RBG Meeting in 1999
  - joint application to EORTC for a pharmacogenomic platform 1999
  - circulation of information regarding translational research in EORTC clinical trials
- Pathology Group:*
- collaboration starting on tissue banking
  - collaboration starting on guidelines for HER/determination.

## SCREENING AND PHARMACOLOGY GROUP

### Structure of the group:

Chairman : I. Fichtner, Berlin  
Vice-Chairman: L. Kelland, Sutton  
Secretary/Treasurer: P. Lelieveld, Moerkapelle

35 full and probationary members from 13 European countries and Canada.  
Recent Achievements:

The group was involved in the preclinical characterization of novel benzothiazoles and acridinones. This has led to the selection of two candidates for clinical trials:

1. Phortress; 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole L-lysylamide dihydrochloride; NSC 710305.
2. The imidzoacridinone C-1311.

Several members of the group actively contribute to the evaluation of NCI-compounds from European origin.

### Projects/strategies for the next years:

- To provide antitumor and toxicity testing systems to investigate new agents and study their mode of action, toxicity and other pharmacological properties.
- To establish and to characterize our model systems especially in terms of those "targets" that may be appropriate for the evaluation of "rationally designed drugs".
- To prepare drug dossiers on potential new clinical candidates for submission to the EORTC NTC.
- To attract chemists/biochemists with new ideas or new chemicals in order to organize joint rational developmental programs for novel drug candidates by using the various expertise available within the group.

### Collaboration with other groups:

- NDDP, NTC, PAMM, BTDG
- Several European research institutions, CESAR EWIV, CRC and NCI (USA)

## SOFT TISSUE AND BONE SARCOMA GROUP

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### Structure of the group:

Chairman:	O.S. Nielsen, Aarhus
Vice Chairman:	J. Verweij, Rotterdam
Secretary:	I. Judson, London
Treasurer:	A.T. van Oosterom, Leuven

### Subcommittees:

#### Local Therapy Subcommittee:

Chairman:	Martin Robinson, Sheffield
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#### Pathology and Biology Subcommittee:

Chairman:	to be appointed
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The Board is comprised of a Chairman, Vice Chairman, Secretary, Treasurer and the respective Chairmen of the Pathology and Local Treatment Subcommittees. The Group has 27 full and 10 probationary members in 12 countries. The Group has a strict membership policy with regard to study accrual and data quality. All radiological responses have to be confirmed by 2 independent investigators.

Two meetings are held each year and after a short business meeting to discuss membership and financial issues these are open to outside parties, such as collaborators from the pharmaceutical industry. Time is specifically made available to allow for discussion of future trials to ensure that all members feel they can make a contribution. In addition to the meeting of the Local Treatment Subcommittee, a recent innovation was the inclusion of a separate systemic treatment subgroup meeting to expand the time devoted to discussing chemotherapy issues.

Key members from other groups are invited on a regular basis to present the work of their group and take part in these discussions with the aim of improving communication and fostering Intergroup collaborations.

### Recent Achievements:

In total, more than 200 patients were entered by the Group into 6 clinical trials during 2000. An extensive study of the new agent ET-743 has confirmed the second-line activity of the drug in advanced Soft Tissue Sarcomas (STS). This represents one of the first new agents to demonstrate significant benefit in these tumors for 20 years and this promise is to be confirmed in the first-line setting. A new agent STI-571 has shown considerable promise in a dose-finding study of gastrointestinal stromal tumors (GISTs), a Phase II trial has been conducted and the Phase III is ongoing. This is a particularly exciting development for a disease that has hitherto proved totally untreatable.

The adjuvant study continues to accrue steadily and is anticipated to make a significant contribution to our knowledge of this form of treatment. The database of >2000 patients treated with anthracycline-containing chemotherapy for advanced STS continues to prove extremely valuable and further studies have been presented this year clarifying prognostic factors for survival and response to therapy.

**Projects and Strategies for the coming years:**

It is now possible to define certain individual disease subtypes according to the expression of specific receptors or tumor markers. In the case of GISTs the diagnosis is confirmed by demonstrating expression of c-kit, as measured by antibodies to CD117. This receptor is also the target for the receptor tyrosine kinase inhibitor STI-571. An international Intergroup Phase III study of GISTs with STI-571, together with the National Cancer Institute in the USA, is ongoing.

In some cases the likelihood of response to treatment can be defined for a subgroup of patients. For example, liposarcomas that express the peroxisome proliferator-associated receptor gamma (PPAR $\gamma$ ) may be induced to differentiate by PPAR $\gamma$  agonists, such as rosiglitazone. These agents have been developed for the treatment of diabetes and have the ability to overcome resistance to oral hypoglycaemic agents. A study is planned with this agent.

The Group is keen to collaborate with colleagues in the US on molecular profiling studies of sarcomas using DNA micro-array and proteomic technologies. A number of laboratories are already conducting such studies and it is anticipated that many Group members will be able to contribute frozen tissue samples. A study in radiation- induced sarcomas is underway.

A radiotherapy study in inoperable fibromatosis will commence soon and discussions are ongoing with regard to participation in the study being coordinated by the American College of Surgeons Oncology Group.

New studies are proposed include a Phase I, dose finding study with liposomal doxorubicin (CAELYX®/DOXIL®) plus ifosfamide, a Phase II study with the topoisomerase I inhibitor DX8951, a Phase II study in elderly patients with trosfosfamide and a Phase II study in liposarcoma with rosiglitazone.

**Collaboration with other groups:**

A study investigating the value of chemotherapy in addition to pulmonary metastasectomy was being conducted together with the Scandinavian Sarcoma Group. We were also joined by the Eastern Oncology Group and South West Oncology Group in the US, and the Scandinavian and French sarcoma groups in Europe. Unfortunately, despite these collaborative efforts, the study had to be closed owing to poor accrual. As discussed above, close collaboration on an international project on molecular profiling of sarcomas involves the STBSG and was coordinated by the Connective Tissue Oncology Society (CTOS).

In recognition of the contribution made by the STBSG to sarcoma research, the Group is well represented on the CTOS Board. Prof. Verweij is President of CTOS and the current STBSG Chairman, Dr. Steen Nielsen, who was responsible for preparing the scientific program of the meeting in 2000, is to be the next Treasurer.

Discussions between STBSG and the European Osteosarcoma Intergroup are likely to result in agreement on the joint conduct of bone tumor clinical trials.

## CANCER IN ELDERLY TASK FORCE

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### Structure of the Task Force:

Chairman:	M. S. Apro, Genolier
Treasurer:	L. Repetto, Genova
Medical advisor:	P. Therasse, Brussels

### *Aims of the Task Force*

The complexities of treatment decisions in cancer in the elderly (defined as patients above age 65 for regulatory purposes according to ICH-GCP guidelines) are multifaceted and variable. There is a clear need for evidence-based guidelines for diagnosis and treatment of this group of patients.

The Cancer in Elderly Task Force aims to improve EORTC coordination of old age-associated preclinical and clinical research. Special attention will be given to conditions that may complicate treatment. The Task Force wants to cover not only cancer chemotherapy, but also surgery and radiotherapy questions.

The rationale behind the creation by the Board of this Task Force was the idea that the scientific consideration of factors related to the age of patients should offer new therapeutic approaches in oncology, taking into account physiological and pathological processes. New research concepts in the elderly area must be developed and the effectiveness of clinical trials must be improved by closely relating them to basic research programs. The Task Force will have to promote the use of standardized risk-evaluation methodologies. Such techniques are validated in geriatrics, and cooperation with geriatric experts will be looked for. Specific nursing aspects will need to be worked upon with EONS.

### Recent Achievements:

The EORTC Task Force lead several of the discussions at the New-York meeting on the Elderly, on September 21-23, 2000. This meeting was the first of the International Society For Geriatric Oncology. The next meeting is planned for September 14-15 in Lyon, France. The organizing committee is under the direction of Prof J-P. Droz.

Independently of this Task Force, EORTC initiatives are active like the lymphoma study led by P. Soubeyran (EORTC Number 7800) and EORTC members are aware of the study coordinated by Dr J. Schellens, under the Biomed grant.

### Projects and Strategies for the coming years:

Several groups have developed protocols addressing the issues of treatment of elderly patients. It is obvious however that many specific issues relative to "senior citizens" are not taken into consideration in these protocols. In collaboration with EORTC NTC and PRC, the Task Force will have to find modalities to develop the multidimensional assessment of elderly patients within such protocols.

The EORTC Cancer in Elderly Task Force is promoting another pharmacology project developed by a group in which many EORTC members participate, coordinated by Brigitte Tranchand from Lyon. This group has written a grant application independently of the EORTC and has now joined the TF. The application has been sent to appropriate EU authorities under the Fifth Framework Program of the European Commission. The Pain and Symptom Control Task Force (Project leader A. Luebbe) is developing a project for evaluation of the Elderly along with the Elderly TF. The project will fit the area 7.2 (chronic and degenerative diseases) and will be submitted to the European Commission (deadline October 2001.)

Prof Dr K. Höffken (Jena – Germany), and Dr Ulrich Wedding (Jena – Germany) were invited together with M. Aapro, head of the EORTC Task Force "Cancer in the Elderly" and Executive Director of the "International Society of Geriatric Oncology" (SIOG), to a first international meeting of clinical researchers, interested in the field of geriatric oncology during the ESMO meeting in Hamburg, October 16, 2000. The aim of the meeting was the discussion of possible fields of combined research activities in the field of geriatric oncology. Participants included also K. Höffken, E. Späth-Schwalbe, Berlin – Germany; S. Zanetta, Lyon - France; G. Kolb, Lingen – Germany; C. Bokemeyer, Tübingen – Germany; C. Steer, London – UK ; Peter Harper, London – UK; O. Kloke, Recklinghausen – Germany. This meeting has lead to the ESMO Working Group on Geriatric Oncology under the chairmanship of K. Höffken; Secretary: Ulrich Wedding. A close cooperation with the EORTC TF has started and FECS will help in establishing a cooperation with EONS, ESSO, and ESTRO.

A group composed of R. Audisio (Liverpool), V. Zagonel (Roma), L. Repetto (Genova) will be writing the new chapter on Cancer in the Elderly for the 8<sup>th</sup> Edition of the Manual of Clinical Oncology of UICC.

The work in non-small cell lung cancer in the elderly by the group directed by Cesare Gridelli in Naples is well known. This group has decided to join the EORTC Task Force and will lead a project in this area, integrating all geriatric evaluation tools that they have recently been validated in a 750 patient prospective study.

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#### **Collaboration with other groups:**

A team lead by R.C.F. Leonard (UK), M. Aapro (CH) and R. Paridaens (BE) has started working on a project on adjuvant chemotherapy of breast cancer in the elderly. This project will lead wide international collaboration and thus contacts are already made with several groups. Last but not least, contact has been made with NCI-US and a meeting for coordination should be held in 2001.

## CUTANEOUS LYMPHOMA TASK FORCE

### **Structure of the Task Force:**

Chairman: R. Knobler, Vienna  
Secretary/Treasurer: S. Whittaker, London

### **Group Structure**

The group consists of a chairman, secretary/treasurer, national representatives and members defined by their submission of cases for the histopathology meeting or submission of cases for clinical trials. Two meetings per year are held consisting of histopathology and clinical meetings. The histopathology meeting is based on a specific subtype of cutaneous lymphoma with reviews of submitted material and review by an expert panel. The clinical meeting consists of a series of invited lectures, focus topics, open communications and a discussion of recently completed, ongoing and proposed clinical trials. Most of the meetings generate consensus documents on specific themes. Attendance is high with an average of 30-80 delegates attending the histopathology and clinical meetings respectively.

### **Recent Achievements:**

The recent publication of an EORTC classification system for cutaneous lymphomas now provides the opportunity for well designed clinical trials and pathogenetic studies.

Completion of several clinical trials in early stages of mycosis fungoides.

Establishment of a scientific committee consisting of national representatives and officers to develop a cohesive strategy especially with regard to clinical trials.

Identification of lead clinicians to develop protocols in conjunction with the EORTC Data Center. On-going consensus documents include a study of primary cutaneous pleomorphic T-cell lymphomas and the use of radiotherapy in the management of cutaneous lymphomas.

**Projects and Strategies for the coming years**

The critical aim for our task force in the next few years is to establish at least one clinical trial in each subtype of cutaneous lymphoma. One trial is set to start recruitment in Sept. 2001 and two other protocols are currently under consideration. It is also the aim of the Task force to develop translational research programs investigating prognostic markers. Two new drug products have been licensed in the US for the treatment of cutaneous T-cell lymphoma and the Task Force has made approaches to the company concerned in order to develop well designed trials to assess these products in EORTC trials.

**Collaboration with other groups:**

A pilot study involving TBI in advanced mycosis fungoides was planned at a small ad-hoc meeting in Oct. 1999 consisting of officers from the cutaneous lymphoma group and the lymphoma group. Participation in other ongoing trials of peripheral T-cell lymphoma was not felt to be feasible because most are nearing completion.

A collaboration is planned with the International Society for Cutaneous Lymphomas analysing staging and prognostic parameters in CTCL.



## OPHTHALMIC ONCOLOGY TASK FORCE

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### Structure of the group:

Chairman:	J. Prause, Copenhagen
Vice-Chairman:	J. Pe'er, Jerusalem
Secretary:	T. Kivela, Helsinki
Treasurer:	M. J. Jager, Leiden

### Group Structure

The Ophthalmic Oncology Group was changed into a Task Force. It maintained its five working subcommittees: Metastatic Uveal Melanoma, Adult Intraocular Tumors, Conjunctival and Adnexal Tumors, Retinoblastoma, and Basic Sciences, and its Quality Control Subcommittee.

A new Committee was elected: Prof. Jacob Pe'er continued as the Vice-Chairman, Dr. Tero Kivelä as the Secretary, and Dr. Martine Jager as the Treasurer and Basic Sciences representative, and Dr. Ian Cree was elected the Pathology Representative. New chairpersons for the subcommittees were elected as well.

A Medical Advisor, Dr. F. Lehmann at the Data Center, was allocated to this Task Force.

### Recent Achievements:

Results of the protocol 88941 "Recombinant alpha-2b-interferon with dacarbazine, vincristine, bleomycin, and lomustine (BOLD) in metastatic malignant uveal melanoma: a pilot study" were analysed and the manuscript will be submitted early next year. A translational research manuscript "Cell proliferation activity in posterior uveal melanoma after Ru-106 brachytherapy - An EORTC Ocular Oncology Task Force study" was submitted for publication.

The Ophthalmic Quality of Life Questionnaire module was further developed in collaboration with the EORTC Quality of Life Study Group. At the end of the year, the module was sent to centers in four member countries for field testing by trial and interview.

Protocols entitled "A randomised trial of Mitomycin C and 5-fluorouracil for treatment of intraepithelial neoplasia of conjunctiva and cornea" and "A randomised Phase II trial of treosulfan plus gemcitabine versus fotemustine in metastatic uveal melanoma" were processed in collaboration with the Statistician and Medical Advisor. In addition, a protocol proposal "Randomized Phase III study of adjuvant immunisation with the NA17.A2 and melanoma differentiation peptides in HLA-A2 patients with primary ocular melanoma at high risk of relapse" was drafted in collaboration with Dr. Vincent Brichard.

The group's homepage was temporarily discontinued in preparation of a major update in 2001.

**Projects and Strategies for the coming years:**

The group aims to launch a study on adjuvant vaccination therapy for patients with high risk uveal melanoma, and a stage IV chemotherapy study for patients who develop metastases, which could start enrollment in 2001. These protocols will be initiated in collaboration with the Melanoma Group.

**Collaboration with other groups:**

The Committee held a strategy meeting with the Committee of the Melanoma Group, and this meeting founded two joint Protocol Developing Committees, one for adjuvant studies and one for treatment of stage IV melanoma. An ophthalmic module was developed in collaboration with the Quality of Life Study Group.

The group participated in a joint meeting of cutaneous and uveal melanoma in Clermont-Ferrand, France, and held its Autumn Meeting as a satellite to the European Vision and Eye Research meeting at Palma de Mallorca, Spain.

## PAIN AND SYMPTOMS CONTROL TASK FORCE

### **Structure of the group:**

Chairman:	B. Van den Eynden, Mortsels
Secretary:	A. Lübke, Bad Lippspringe
Treasurer:	S. Amason, Reykjavik

### **Recent Achievements:**

1. *Towards a European standard for "best supportive care" for cancer patients.*

This is a 'coordinated activity' funded by a grant from the European Commission via DG V program. Coordinator: S. H. Ahmedzai. The final part of this project, the 'Patients' Charter', was completed at the Annual Scientific Meeting in Berlin. This will now be submitted, via the Director General, to the National Cancer Leagues of Europe for their ratification and translations.

2. *Survey of knowledge and attitudes regarding analgesia amongst European oncologists.*

Funded by an educational grant from Medtronic. Coordinator: S H Ahmedzai. This is a mailed questionnaire survey of the most active recruiting EORTC clinical trial participants. The purpose is to document the levels of knowledge, attitudes to different forms of analgesic interventions and actual clinical practice regarding cancer pain control among oncologists. This study has been completed and a poster was presented at the EAPC Scientific Meeting in Berlin, December 2000.

3. *Classification of symptoms and palliative oncology interventions.*

Non-funded project. Coordinator: A S Lübke. This project is aiming to develop a comprehensive logical taxonomy of symptoms and their palliative interventions in cancer patients, so that appropriate assessment methods can be chosen and documented for use in EORTC clinical trials.

### **Projects/Strategy for the next years:**

*Octreotide for the control of CPT-11 induced diarrhoea.* Coordinator: A. S. Lübke. This new project is being developed by the Task Force for submission to the PRC in early 2001. A randomised Phase III design is being used to compare 'standard' treatment loperamide versus octreotide.

*Cancer in the elderly.* Coordinators: A. S. Lübke and M. S. Apro. This is a joint project between the Pain & Symptom Control Task Force and the Task Force on Cancer in the Elderly. The aim is to develop a cohort of older cancer patients across several European countries to track symptoms and treatment outcomes and adverse events. It is hoped that the project will be submitted for funding under the DG Research program.

### **Collaboration with other groups:**

Cochrane Collaboration; WHO; European Association for Palliative Care; Multinational Association for Supportive Care in Cancer; German Society Group on Supportive Care  
British Psycho-oncology Society.

# EORTC DATA CENTER ANNUAL REPORT 2000

## Patrick Therasse, MD, MS

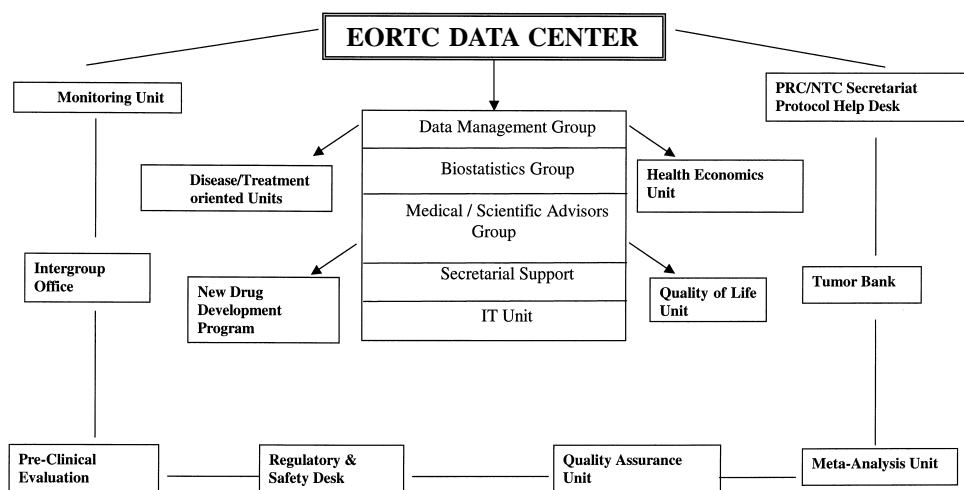
### A. SPECIFIC AIMS OF THE EORTC DATA CENTER

The core of the EORTC's work has been and is to conduct large scale, prospective, high-quality, randomized multicenter clinical trials on a European and worldwide basis in order to facilitate the passage of experimental discoveries into state-of-the-art-treatment. While the EORTC Central Office is the administrative link between the EORTC Groups, the EORTC Data Center is the scientific link. Established in 1974, the EORTC Data Center is a unique central facility in Europe that offers a comprehensive approach to cancer research and to the management of cancer clinical trials.

The main objective of the EORTC Data Center is to provide logistic and scientific support to the EORTC Committees and Groups with respect to the management of cancer clinical trials. This includes expertise in various areas such as protocol and case report form (CRF) development, regulatory requirements based on both national and international legislation, data management, computer, statistical and medical sciences as well as cancer related problems such as Quality of Life and Health Economics. It ensures from an independent, objective, academic point of view, the highest possible quality of the trial, from its design to the final analysis and publication of the final results.

To be able to provide optimal support, the EORTC Data Center is also a research center where the methods used to conduct cancer research are the subject of many research projects in the various areas previously mentioned. Finally, being a center of excellence, many staff members contribute to the education of health care professionals involved in cancer research through courses, workshops, and congresses as guest faculty or in those organized by the Data Center itself.

The EORTC has been the only European organisation bringing together European cancer experts from all disciplines to set up transnational collaboration to facilitate, speed-up and coordinate independent cancer research in Europe. Over the last four decades it has proven, beyond all expectations, that such collaboration is both successful and mandatory to generate important advances in the field of cancer treatment. The EORTC Data Center is a key element of the organisation, also playing the role of watchdog with regard to independence and standards of quality for conducting cancer research. The Data Center has adapted itself to the evolution of the research environment by increasing its capabilities and expertise in all areas of cancer research, constantly striving to improve the quality of the research performed within the organisation and trying to convince health authorities and legislators to consider non-commercial research as a key element for success leading to cancer cure.



## B. PROGRESS REPORT

### I. Structure of the Data Center

The structure of the Data Center is built around different groups of staff members with a specific expertise in data management, statistics, medicine/life science or administrative support. Representatives of these groups compose the core units of the Data Center whilst another set of specialty units provide support on an ad hoc basis.

The structure of the Data Center is described in detail in the figure above.

In the course of the year 2000, two new units have been created : the Intergroup Office and the Tumor Bank.

The Intergroup Office was set up with financial support from the Parthenon Trust to facilitate collaboration between different groups within Europe initially and worldwide subsequently.

The Tumor Bank unit, created in parallel to the EORTC pathology group, was also set up with financial support from the Parthenon Trust. As indicated by the name of the unit, it has focused its energy to set up an EORTC tumor bank of dry tissue at the Data Center, and also a virtual tumor bank of frozen tissue at the centers participating in EORTC trials. It is also extensively involved in the implementation of a telepathology system within the organisation.

## **2. Mode of operation**

The EORTC Data Center functions following a set of established Standard Operating Procedures (SOPs). These SOPs have been developed on the basis of the ISO 9000 concept with a Quality Manual, Procedures Manual and Working Procedures. It was finalized in June 1998 and then submitted to the regulatory department of NCI as well as to the FDA (DMF N° 059). The last revision was issued in June 2000. All procedures are available to all personnel through the Intranet in place at the Data Center. Data Center staff are trained in each procedure before it is implemented. Regular training sessions are organized when substantial modifications are made or new procedures are issued.

In 2000, the following SOPs were either issued for the first time or updated :

WP1107 "guidelines for writing and reviewing the patient information sheet and obtaining informed consent" (updated version) (Dec 2000)

WP1302 "reporting trial progress" (updated version) (Aug 2000)

WP2101 "collaboration between several EORTC groups" (new) (Feb 2000)

WP5103 "development of EORTC full protocols" (new) (Aug 2000)

WP5104 "implementation of amendments to protocols" (new) (Sept 2000)

WP5105 "medical fellows working at the DC" (new) (Sept 2000)

All important decisions and problems are discussed during the "Senior Staff Meetings" which are held on a regular basis with the coordinators of the different units, the Director of the Data Center and the Director General of the EORTC (in 2000, 8 senior staff meetings).

All other major groups have regular meetings to discuss the specific aspects of their respective activities :

Data Manager meetings : 5 in 2000

Stats club meetings : 17 in 2000

Medical advisors : 13 in 2000

All other units hold regular meetings to discuss the development of ongoing projects within their unit. Reports of these meetings are transmitted to the Director of the Data Center.

## **3. Personnel**

As of March 2001, there were 103 Data Center staff members (94 full-time, 9 part-time, 72 female, 31 male), 10 research fellows and 2 part-time volunteers. In total, 16 different nationalities are represented.

## 4. Activities

### 4.1. Management of clinical trials

The Data Center supports the management of clinical trials for 22 EORTC clinical research groups.

*Clinical Trials in 2000*

	On-going	New	Nb of patients
Phase I	13	5	291
Phase II	25	11	518
Phase III	63	9	5,700
<b>TOTAL</b>	<b>101</b>	<b>25</b>	<b>6,509</b>

*Recruitment*

EORTC institutions : 5 966 patients (91.7% of total) / 359 institutions

Foreign members : 543 patients (8.3% of total) / 187 institutions

### 4.2. Quality of Life Unit

During the last year, quality of life (QL) evaluation has been included in 12 clinical trials. Proposals for 11 new studies are under discussion. Four abstracts have been published and accepted for presentation (oral and poster) at scientific meetings, including ISOQOL, MASCC and ISCB. Five other articles have been published in journals such as the European Journal of Cancer, Statistics in Medicine and one book chapter has been published on quality of life methodology. A further three papers have been submitted and are under revision or are in preparation and two book chapters on methodology are presently in print.

The unit contributed to two European School of Oncology published Task Force Reports in the field of anemia and fatigue and provided lectures on these topics at the European School of Oncology.

A third edition of the EORTC Scoring Manual for the QLQ-C30, and a Manual of Reference Values for the QLQ-C30 (also available on CD-ROM) were prepared by staff of the Quality of Life Unit in collaboration with QLG, and will be available in early 2001.

In collaboration with the EORTC QLG, an important aspect of the Unit's work is development of disease-specific modules for evaluation of QL in conjunction with the QLQ-C30. There are currently three modules in use for breast, head and neck, and lung cancers. A further 15 modules are under development. The Unit has taken the lead in developing an additional fatigue module, working in close collaboration with the QLG. Large-scale validation studies are in progress for the oesophageal (QLQ-OES24) and ovarian (QLQ-OV28) cancer modules, which will close in early 2001. Four additional large-scale module validation studies for pancreatic (PAN26), gastric (STO22), prostate (PR25) and satisfaction with care (QLQ-SAT32) will be activated in early 2001. In the last year, the QLQ-C30 core questionnaire has been translated into an additional 4 languages. It is currently available in 42 languages and has been used in over 2000 studies worldwide. In

addition, over the last year the Unit's translation program has ensured that an additional 53 translations of the developing modules have been completed and validated using EORTC pilot testing.

In collaboration with the EORTC QLG, the Quality of Life Unit at the Data Center implemented the Item Bank. This innovative project has developed a state-of-the-art computerized Internet database application. All items from EORTC QL questionnaires will be stored and made available to EORTC researchers in the future, for trial-specific QL evaluation. Over 362 items are stored in the Item Bank. Additionally, over 5 400 individual translations of these items will be made available. The Item Bank also contains an extensive data set of information relating to individual items such as reliability, validity, and other critical information. The Item Bank is expected to improve the speed of module development and increase quality in the module development process. This year it has been used to help develop three Phase II modules (high dose chemotherapy, ophthalmic and chronic lymphocytic leukaemia) as well as being used for two EORTC trials (30986 and 55994) where no formal EORTC modules were available. In addition, we are considering further developmental use of the Item Bank, for example, linking data directly to items in order that we can investigate the use of individual items and their performance as possible scales or modules.

Working in collaboration with the QLG, an innovative project was initiated in late 2000, which will investigate the cross-cultural aspects of the QLQ-C30 measurement system. A research fellow has begun to undertake a detailed cross-cultural analysis of the QLQ-C30 with a view to exploring any cultural differences between patients across the European setting. This project will enable researchers to check the validity of pooling data, across cultures.

In addition, in early 2001 a new project will start which will be used to provide updated information to users of the QLQ-C30, providing representative scores based on longitudinal assessment of cancer patients from all disease sites and stages. Such information will be invaluable to researchers and users of the QLQ-C30 measurement systems.

#### 4.3. Health Economics Unit

During the last year, health economic evaluations have been integrated into four clinical trials. Currently, proposals for evaluations are under discussion or preparation for six new trials. Five past trials in which economic evaluation has been integrated are mature enough for analysis, which will be performed in 2001. In 2000, seven abstracts of economic evaluations and methodological work carried out by the unit have been accepted for presentation (oral and poster) at the scientific meetings of ASCO, ISTAHC, SMDM and the Second European Conference on the Economics of Cancer organised by the EORTC.

In addition to presentations at conferences, one peer-reviewed article on patient management strategies in stem-cell transplantation was published as well as two contributed chapters to books on the management of colorectal cancer and the use of erythropoietin for chemotherapy induced anemia in patients with cancer. Methodological work was started on 1) the development of statistical tools for the calculation of confidence intervals of ICER (incremental cost effectiveness ratios) and cost effectiveness acceptability curves, 2) assessment of alternative methods of estimating mean survival, and 3) improved methods of data collection within clinical trials.

The Second European Conference on the Economics of Cancer took place in Brussels (3 – 5 September 2000) with an attendance of more than 200 delegates and 113 abstracts were submitted. It proved to be a lively occasion for interesting scientific exchanges among the participants on methodology and application of economic studies in cancer. It is expected that a third conference will be arranged in 2003.



Although the randomized controlled clinical trial is the “gold standard” for evaluation of new therapies, it is clearly not a natural setting, and this is a well recognized criticism when assessments of the costs of treatments are based only on RCT data. Accordingly, in the future the Health Economics Unit intends to further investigate modelling as a complementary tool for economic evaluation of clinical data as well as continue to improve methods for collection of economic data within and outside clinical trials. In parallel, specific methodological studies will be undertaken to assess the following topics: 1) assess methods to deal with the problem of missing data often encountered when cost data are collected in trials, 2) assess various approaches to modelling in economic evaluation, especially evaluate the use of discrete event simulation, and 3) evaluate the use of the Bayesian approach to statistical analysis of economic and clinical data.

#### **4.4. Meta-analysis Unit**

Last year, four papers were published in cooperation with the Meta-analysis Unit: estimating the number of events from Kaplan-Meier curves for incorporation in literature based meta-analyses (Biometrics), the role of meta-analyses in assessing cancer treatments (European Journal of Cancer), the role and impact of pathology review in superficial bladder cancer (Journal of Urology), the role of adjuvant chemotherapy after cystectomy in locally advanced bladder cancer (Annals of Oncology) and a fifth was accepted for publication: comparison of LHRH agonists and LHRH agonists + Tamoxifen in premenopausal advanced breast cancer (Journal of Clinical Oncology). The Meta-analysis Unit has continued its work on individual patient data meta-analyses carried out in the following areas:

- Bone marrow transplantation in adult leukemia.
- Prognostic factors for the adjuvant prophylactic treatment of stage TaT1 bladder cancer.
- The role of accelerated and/or hyper fractionated radiotherapy in patients with squamous cell head and neck carcinomas (in collaboration with the Institut Gustave Roussy, Villejuif, France).

Although the EORTC Meta-Analysis Unit always performs individual patient data meta-analyses (MAP), most of the meta-analyses in cancer are based on the literature (MAL) as they take much less time to perform. The Meta-analysis Unit has therefore undertaken a comparison of MAP and MAL in an extensive meta-analysis of Chemotherapy in Head and Neck Cancer (MACH-NC), together with the Institut Gustave Roussy. A paper has been prepared and is being submitted for publication.

#### **4.5. Quality Assurance Unit**

The Quality Assurance Unit currently has three members: one coordinator, who is also the contact person and secretary to the EORTC Quality Assurance Committee, one person who dedicates most of her activities educating the Data Center Staff and check compliance to our SOP's at the Data Center level, and one person who is responsible for our external Quality Assurance Program. Besides its ongoing activities including support to both the EORTC groups and the Quality Assurance Committee, the Quality Assurance Unit has been actively involved in the organisation of 21 training courses for the Data Center staff with regards to EORTC Standard Operating Procedures Development and implementation of the EORTC Auditing procedure.

During the past year the Quality Assurance Unit performed 29 Audits / QA visits for various reasons: Affiliated Institutions, Intergroup collaboration, pre- industry / FDA audit, for cause.

The Data timelines procedure has been applied according to the normal schedule (January, April,

June, and October). Only a few centres were subject to temporary closure following persistent outstanding information, but could be re-opened shortly afterwards.

A Center was temporarily closed for problems with the Informed Consent (IC) procedure. Following this problem a letter was sent in December 2000 informing all EORTC investigators on the more stricter procedure which has been put in place in January 2001. During registration / randomisation of the patient, the date of IC must be provided as eligibility check. Informed consent dates must be prior to the registration / randomisation date. On-site monitoring / audits will pay special attention to the availability of the IC in the study master file, and any deviation / non-compliance with the ICH-GCP will be reported as a serious problem with the possibility of being excluded for further participation to EORTC research.

#### **4.6. Monitoring Unit**

Between January 2000 and December 2000, the EORTC Monitoring Unit (MU) has been involved in 62 trials from 21 different EORTC Groups. In total, 553 sites visits have been performed involving 167 different EORTC institutions. The information relative to all site visits (including the 29 audits performed by the Quality Assurance Unit) are stored in a central database accessible to the Quality Assurance Committee to monitor the performance of EORTC institutions.

The Monitoring Unit has started to co-operate with the pharmaceutical industry and CROs to develop a procedure to centralise monitoring and to outsource the on site monitoring for large Phase III trials. This project will be further developed during 2001.

#### **4.7. New Drug Development Program (NDDP)**

In 1998, the EORTC established at the EORTC headquarters, a New Drug Development Program (NDDP), to expand an already existing program of new anti-cancer agent development. This was a bold move to enhance new cancer drug development including both conventional as well as biological anti-cancer agents in Europe. The EORTC NDDP is organised in involving a full range of specialists with experienced EORTC Data Center support to carry out Phase I and Phase II trials. Such trials are essential steps after laboratory and animal studies towards clinical trials involving patients with cancer that will prove the true value of the new anti-cancer agent.

Today, the EORTC NDDP, conducts clinical trials with cytostatic and cytotoxic as well as biological/ immunological agents. These trials are performed within the EORTC groups focused upon early drug development: the EORTC Early Clinical Studies Group (ECSG) and the EORTC Biological Therapeutic Development Group (BTDG).

The NDDP is composed of two medical advisors appointed to each of the groups, one statistician, three data managers, four clinical research associates, one Phase I project leader, one pre-clinical project leader, one research fellow, one GCP filing assistant and one secretary. As of February 2001, the NDDP is conducting 15 Phase II trials and two Phase I trials. Four New Phase II and 1 Phase I trials are in preparation.

More than 250 patients have been included in these trials over a period of 17 months. Three Phase II trials have been accepted for poster presentations at ACCR 2001.

NDDP trials involve 13 new drugs representative of a large variety of drugs with various mechanisms of action such as DNA intercalating agents, MDR inhibitors, alkylating agents, camptothecin analogs and encapsulated topoisomerase inhibitors, farnesyl protein transferase inhibitor, platinum derivatives, new anthracyclines, inhibitors of cell cycle cyclins, new lectin

obtained from DNA recombinant technology as well as as antiangiogenesis compounds and collagenase inhibitors.

The NDDP has facilitated intergroup collaboration as three studies are performed in collaboration with the brain group, one with the GU group, one with the gynecological group, one with the lung group, one with the breast group, one with the BTDG and one with the melanoma group. Also, five studies have translational research components and are conducted in collaboration with the PAMM group.

#### **4.8. Intergroup office**

Taking into account the increasing number of intergroup collaborations (within Europe, North America and Australia), the EORTC Data Center created in September 2000 an Intergroup Office (IO). This office started dealing with a series of new logistic, legal and methodological problems, most of which have been addressed on an ad hoc basis, to enable specific inter-group collaboration to happen. It is obvious nowadays that intergroup studies are a key factor that may rapidly help the development of new anti-cancer treatments. On the basis of the expertise acquired at the Data Center, the IO will be organized as a service to European and/or US collaborative groups to help them to overcome the problems usually encountered when intergroup studies are discussed. It will also have the duty to investigate new possible pathways of collaboration to promote and facilitate intergroup collaboration.

The IO has already developed a series of standard documents to allow the rapid creation of specific appendices for intergroup trials. These include the proposed intergroup procedure followed by EORTC, a standard table of content for the specific group appendix and letter of agreement for collaboration between different groups.

#### **4.9. Tumor Bank**

The EORTC Pathology Group and the EORTC Data Center recently started a three-year pilot project on centralised collection and storage of paraffin blocks and slides for patients entered in EORTC clinical trials. This is not only to improve and harmonise the histological review and the use of telepathology, but to facilitate the translational research in the context of EORTC trials, by providing rapid access to the tumor tissues needed for side-studies. Experience coming from this Phase will serve as a basis for full implementation in EORTC trials as a whole.

The EORTC Data Center will provide dedicated logistic support in collection and storage of paraffin blocks/slides, pathology forms and digital images. This will be done through a close collaboration and interaction between the tissue banking administrator, trial data manager and (local and review) pathologist. The virtual tumor banking, containing frozen tissue, will remain at the clinical site. However, the information on tissue samples will be available in the central database at the EORTC Data Center.

The whole process, including legal and ethical issues, will be closely monitored by the steering committee, composed of representatives of the EORTC Pathology Group and EORTC Data Center.

#### **4.10. IT Unit**

The main objective of the IT developments in 2000 was to integrate Remote Data Entry into the existing VISTA environment. EForms is the application that has been developed to be installed on investigators PC to allow them to enter data directly into EORTC clinical trials. The other modules of VISTA have been adapted to make this new procedure almost transparent for the Data Manager and allow studies to go electronic, including queries, with no extra work. In parallel, new systems have been installed to help specialized units work. The Itembank is intended to dramatically reduce the work and the time for the set up of Quality of Life module questionnaires. The Safety desk also is now equipped with a system for SAE management. 2001 will see the migration from paper to electronic CRF's. Little by little eForms will be distributed to participating centers and become the main tool to send data to the EORTC.

#### **4.11. Specific research programs**

##### **4.11.1. Response Evaluation Criteria in Solid Tumors (RECIST)**

Together with representatives of the US NCI and NCI Canada, the EORTC Data Center has coordinated over the last 5 years the revision of the criteria used to evaluate the response to treatment with cytotoxic agents. The new guidelines have been published in the February 2000 issue of JNCI.

##### **4.11.2. Treatment Outcome**

Three large scale breast cancer trials have been re-analyzed to detect differences in treatment outcome according to treating institution and country. Based on the practical problems encountered, different approaches to fitting the frailty model have been studied in collaboration with the Limburgs Universitair Centrum and simulations were carried out to determine the influence of the number of centers and the number of patients per center on the results.

##### **4.11.3. Statistics**

In addition to conducting various prognostic factor analyses, statistical research has been carried out in a number of areas including: the design of chronotherapy trials, the design of Phase I trials, the design of combined Phase II/Phase III trials, the analysis of treatment outcome data using frailty models, the inclusion of literature data in individual patient data meta-analyses, the estimation of the number of events from Kaplan-Meier curves (for use in the comparison of literature based and individual patient data meta-analyses), methods for assessing the relationship between time to local recurrence and duration of survival, and use of the bootstrap in the analysis of the cost effectiveness ratio from censored survival data.

In February 2000, a new statistician started at the Data Center with the specific objective of reviewing the existing EORTC procedures with regards to the methodology of Phase I and Phase II trials. This person has been actively involved in the development of models to facilitate the development of new anti-cancer agents.

In collaboration with the Limburgs Universiteit Centrum (Diepenbeek, Belgium), research on the analysis of surrogate end-points is being carried out, most notably for the case where both the surrogate and the true endpoint involve time to event end-points. Particular applications of interest are the use of the disease free interval as a surrogate for survival in adjuvant trials of early breast cancer and the use of PSA progression as a surrogate for survival in metastatic prostate cancer.

#### **4.11.4. European Drug Development Network (EDDN)**

In 1999, the EORTC has negotiated an agreement with the UK Cancer Research Campaign (CRC) and the South East New Drug Development Office (SEND0) to create the European Drug Development Network (EDDN). This network has been set-up to facilitate at the European level the transfer of new discoveries into potential clinical applications for patients with cancer. Information, resources and expertise of the three organisations will be shared through the network to avoid competition, duplication of efforts, multiplying the channels to allow a rapid development of new anti-cancer agents. It is expected that the EDDN will grow with other national/regional organisations dedicated to the development of anti-cancer agents in Europe.

Six meetings of EDDN occurred in 1999-2000. EDDN has now structured itself through a joint venture agreement between the member organisations. A set of rules has been established to define the minimal requirements for member organisations and for potential new applications. Activities of EDDN have resulted in cross fertilized expertise between member organisations for operational and management aspects of early clinical trials. The forum of EDDN also allows member organisations to be fully aware of respective activities on anti-cancer agents being studied in order to avoid redundant and counterproductive actions between the major European academic organisations.

#### **4.12. Fellowship program**

The further broadening of the Data Center's scientific structure is being pursued by encouraging the one up to three-year stay of research fellows (medical doctors, biostatisticians, computer analysts, health economists and other scientists) linked either to a group, a specialty unit or specific research projects involving the EORTC Data Center's database. (See also section "EORTC Fellowship Programs").

In 2000, four new fellows joined the EORTC. Currently there are 12 fellows working at the Data Center and three others will be added during 2001.

#### 4.13. Scientific output

In 2000, Data Center staff members made presentations at various courses, symposia and congresses (ASCO, AACR, ESMO, AUA, etc.) and were (co)authors of publications as follows:

	2000
Peer-reviewed articles	99
Chapters in books	3
Books	1
Published abstracts	88
Communications/invited lectures	104

#### 4.14. Teaching and Organisation of Courses

In 2000, Data Center staff has been active through their participation in the activities organized by the EORTC Education Office. Data Center staff members were involved in the organisation and teaching of the following courses:

- Clinical Trial Statistics for Non Statisticians (Brussels, Belgium, 25-26 May 2000)  
This course is designed as an introduction to the statistical principles which form the basis for the design and analysis of Phase III cancer clinical trials. It concentrates on the philosophy and understanding of the statistical principles that are used on a day-to-day basis in conducting clinical trials and does not simply present statistical formulae in a cookbook fashion. This course is aimed at non statisticians (medical doctors, data managers, etc.) who are already working in the field of clinical trials and who have completed an introductory course in statistics, or at statisticians with little or no experience in clinical trials.
- One-Day Introduction to EORTC Trials (Brussels, Belgium, 6 October 2000)  
This course is dedicated to newly participating members (investigators, data managers, research nurses, etc.), and industry representatives. The purpose of this introductory workshop is to give guidance for participating in EORTC clinical trials activities and clinical trials. Participants receive information about the functioning of the EORTC and about clinical trial data management. Trial methodology, randomization procedures, quality control measures, protocol and case report form requirements are presented, as well as practical guidelines to facilitate the organisation of clinical research in the hospital. It also provides an opportunity to visit the EORTC Central Office - Data Center and to have informal discussions with the Data Center staff.

The Data Center staff has also been involved in the organisation of:

- The Second European Conference on the Economics of Cancer (Brussels, Belgium, 3-5 September 2000).
- PET for Anti-cancer Drug Development Conference (Brussels, Belgium, 15 September 2000).

The EORTC Education Office is currently organizing with the Data Center staff:

- The EORTC Translational Research Meeting (Brussels, Belgium, 7-8 June 2001)

Courses for 2001:

- Clinical Trial Statistics for Non Statisticians (Brussels, Belgium, 14-15 June 2001)
- One-Day Introduction to EORTC Trials (Brussels, Belgium, 28 September 2001)
- Cancer Clinical Trials: Methods and Practice (Brussels, Belgium, 5-9 November 2001)
- Data Management in Cancer Clinical Trials (Brussels, Belgium, 26-30 November 2001)

#### **4.15. Continuing Education at the Data Center**

The continuing education of staff members is given a high priority and includes:

- Courses on the fundamentals of cancer and its treatment (21 courses in 2000).
- Training sessions on Data Center SOPs (21 sessions in 2000).
- Computer courses organized on a regular basis using both a hands-on and a workshop approach. The courses cover the EORTC's in-house clinical trials management systems; Orta and Vista, the general administrative software; Microsoft Office '97 and Outlook, and the statistical analysis software; SAS.
- Stats Club Meetings (17 meetings in 2000). At the Stats Club meetings the statisticians keep abreast of the latest statistical methodology dealing with the design and analysis of clinical trials. In addition, new statistical software is presented and statistical policies within the Data Center are discussed.
- Data Manager meetings (5 meetings in 2000). These sessions are dedicated to the discussion of specific data management problems that are not addressed through existing SOPs or when existing SOPs are unclear and outdated. It addressed the relation between data managers and other Data Center groups.
- Medical Advisor meetings (13 meetings in 2000) are held at regular interval with representatives from the statisticians and data managers to exchange information about the decisions taken by the Data Center senior staff, the EORTC Board and the director of the Data Center. It is also a forum where the experienced acquired by each can be shared with others, problems can be discussed and solutions proposed.
- Monitors training session (8 meetings in 2000).

## Information Technology systems at the EORTC Central Office/Data Center

The configuration of the EORTC computer system is based on client/server technology mainly powered by Windows NT machines.

There are several servers, each dedicated to a certain category of service:

- Three Windows NT servers running the BackOffice suite provide the network services (file services, print services and application services)
- A Windows NT server running SQL Server handles the clinical database management system: VISTA (Visual Information System for Trial Analysis)
- A Linux server handles the Internet services
- Pentium PC's running Windows 95 have access to all the local resources and to the Internet.

VISTA is the Clinical Database Management and Reporting System used at the Data Center. It assists the complete clinical trial process, from form design to reporting of results. For more complex statistics, all PC's have access to the SAS system for Windows.

VISTA has been developed in-house to respond to the specific needs of the Data Center's everyday work. It takes full advantage of the 32-bits Windows environment, and provides the users with an easy-to-use interface. VISTA is a client/server-based system powered by an SQL server relational database.

The ORTA (On-line Access to Randomized Trials) system is used for patient registration. It allows complex eligibility checks and dynamic treatment allocation. Registered patients are automatically transferred into the VISTA system. ORTA is a web-based application using state of the art Java technology and available from any browser on the Internet.

EForms is the latest application developed at EORTC. It is a remote data entry system integrated into Vista allowing investigators to send their data in electronic format.



# EORTC EDUCATION OFFICE

In 2000, the Data Center staff has been active through their participation in the activities organized by the EORTC Education Office. Data Center staff members were involved in the organisation and teaching of courses and conferences:

- Clinical Trial Statistics for Non Statisticians (Brussels, Belgium, 25-26 May 2000)
- One-Day Introduction to EORTC Trials (Brussels, Belgium, 6 October 2000)
- The Second European Conference on the Economics of Cancer (Brussels, Belgium, 3-5 September 2000).
- PET for Anti-Cancer Drug Development Conference (Brussels, Belgium, 15 September 2000)

The EORTC Education Office is currently organizing:

- The EORTC Translational Research Meeting (Brussels, Belgium, 7-8 June 2001)

## **Courses scheduled for 2001**

- Clinical Trial Statistics for Non Statisticians (Brussels, Belgium, 14-15 June 2001)
- One-Day Introduction to EORTC Trials (Brussels, Belgium, 28 September 2001)
- Cancer Clinical Trials: Methods and Practice (Brussels, Belgium, 5-9 November 2001)
- Data Management in Cancer Clinical Trials (Brussels, Belgium, 26-30 November 2001)

**For further assistance, please contact: Danielle Zimmermann:**

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## EORTC CANCER COMMUNICATIONS OFFICE

In May 1997, a Cancer Communications Office was established in order to provide "cutting edge" information on a regular basis to the various Cancer Leagues supporting the EORTC activities through the EORTC Foundation, the scientific community, the patients, the press and the public.

Financial support for this program has been provided by several Cancer Leagues.

The EORTC Cancer Communications Office aims to promote the EORTC and its research activities in order to increase public awareness of the importance of cancer clinical research in Europe by disseminating research results. It also assists patients and the general public in locating EORTC experts in the oncology field.

The following material and information may be obtained upon request through the EORTC website <http://www.eortc.be>.

- EORTC Press kit.
- Background information about the EORTC and relevant recent scientific publications.
- The EORTC Report: Organisation Activities and Current Research 2001- 2002.
- Information about the EORTC Groups and their research activities, the EORTC Central Office, the Data Center and all specialty units.
- EORTC patient's booklet: What Are Cancer Clinical Trials All About? (updated version) (available in English, French and Dutch.)
- Information regarding meetings organised by the EORTC, the Education Office or organised under the auspices of the EORTC.

**For further assistance or for any information regarding the content of the  
EORTC website, please contact:**

**Samantha Christey, EORTC Communications Officer: [sch@eortc.be](mailto:sch@eortc.be)**

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