



NEWS RELEASE

20th EORTC-NCI-AACR SYMPOSIUM on “Molecular Targets and Cancer Therapeutics” Geneva, Switzerland, 20-24 October 2008

Embargoed: 12.00 hrs CEST, Wednesday 22 October 2008

Researchers identify pattern of gene expression that can predict how patients with advanced bowel cancer will respond to treatment

Geneva, Switzerland: Research by scientists in France has shown for the first time that identifying patterns of gene expression can be used to predict response to treatment in patients with advanced metastatic colorectal cancer.

Dr Maguy Del Rio, a scientist at the Institut de Recherche en Cancérologie de Montpellier (Montpellier, France), presented a study to the 20th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Geneva today (Wednesday) [1] in which she and her team had identified an 11-gene signature that could be used to separate those patients who would respond to a particular chemotherapy (FOLFIRI – leucovorin, fluorouracil and irinotecan) from those who would not. FOLFIRI is one of the most commonly used, first-line treatments for metastatic colorectal cancer.

Dr Del Rio said: “Gene expression signatures are a new class of molecular diagnostic tests for cancer. For cancer prognosis, three tests are commercially available, all for breast cancer. It is more difficult to predict responses to anticancer drugs than it is to predict prognosis. Few studies have been made in this field. This and our previous study [2] are the first that demonstrate the utility of gene expression profiling for the prediction of response in colorectal patients.”

About half of patients with colorectal cancer develop liver metastases during the course of their disease. Dr Del Rio said: “When this happens, it is critical for the success of overall treatment to choose a chemotherapy regime that is most likely to induce a maximal response during the first course of treatment. It is a major clinical challenge to identify a subset of patients who could benefit from a particular chemotherapy, and to identify those who will not and therefore need to be treated using an alternative treatment.”

The researchers used microarray analysis to identify gene expression levels in samples taken from 19 colorectal cancer patients with liver metastases who had not yet started chemotherapy. They followed the patients to see who responded to the chemotherapy and who did not, and, using this information, found a pattern of 11 genes that clearly separated responder and non-responder patients. They designed a mathematical model that was able to predict and classify the eight responding and 11 non-responding patients with 100% accuracy.

Dr Del Rio said: “The fact that we achieved 100% accuracy could be due to our small sample size of 19 patients. Obviously, it is essential to validate and, if necessary, to improve the gene signature in a larger independent cohort of patients. Until it is properly validated, the gene signature cannot be used in the clinic. However, in the future it could be used to identify a subset of patients who would benefit from chemotherapy and lead to an improvement in response to metastatic treatment for colorectal cancer.

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“For the subset of patients who are identified as non-responders to FOLFIRI, other treatments such as FOLFOX (leucovorin, fluorouracil and oxaliplatin) chemotherapy, or newer, targeted drugs such as cetuximab and bevacizumab could be added.”

At present, the test for the 11-gene signature takes about three days to run, with several steps involved: surgical removal of tumour tissue, histologic validation, RNA extraction, chip hybridization, comparative analysis of gene expression and patient’s classification. The researchers hope that this process could be speeded up, but the ability to choose the correct first-line treatment is a big step forward.

“For patients with metastatic colorectal cancer, time is an important factor and to make the good first-line treatment choice could be decisive in the overall success of the treatment,” said Dr Del Rio.

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Abstract no: 202. Poster session in the poster area, 12.00-15.00 hrs CEST, Wednesday 22 October.

Notes:

- [1] EORTC [European Organisation for Research and Treatment of Cancer, NCI [National Cancer Institute], AACR [American Association for Cancer Research].
[2] Del Rio et al., *J Clin Oncol.* 2007 1;25(7):773-80).

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From 09.00 hrs CEST Tuesday 21 October to 14.30 hrs CEST Friday 24 October

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