

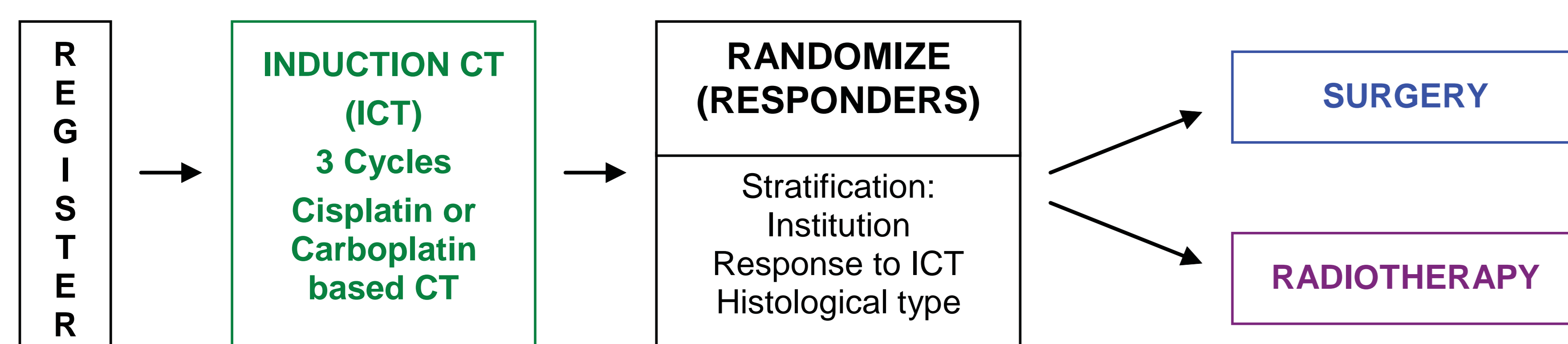


DOES DOWNSTAGING IN PATIENTS WITH IIIA-N2 NON-SMALL CELL LUNG CANCER (NSCLC) AND A RESPONSE TO INDUCTION CHEMOTHERAPY (ICT) INFLUENCE OUTCOME WITH SURGERY (S) OR RADIOTHERAPY (RT)? AN EXPLORATORY ANALYSIS OF EORTC TRIAL 08941.

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BACKGROUND

STUDY DESIGN



MAIN ELIGIBILITY CRITERIA

- Proven clinical stage IIIA (N2) NSCLC
- Considered unresectable by local surgeon
- Measurable primary tumour
- Fit for combined modality treatment
- Informed consent
- No previous CT, no previous RT to the chest

PRIMARY ANALYSES

The final analysis showed no difference in overall and progression-free survival in the 332 randomized patients with unresectable stage IIIA-N2 NSCLC, treated with either S or RT after a response to platinum-based ICT (van Meerbeeck, JCO 2005; 23, 1095s).

In the S-patients, non-randomized exploratory comparisons showed a statistically significant benefit in outcome for patients with (bi-)lobectomy vs. pneumonectomy (p= 0.0088) and for patients with downstaged mediastinal lymphnodes (MLN) vs. non-downstaged MLN (p= 0.0009).

No difference was observed between S-patients treated with/without postoperative radiotherapy (PORT).

RATIONALE FOR THE CURRENT EXPLORATORY ANALYSES

By randomizing after response to ICT, MLN-downstaging is assumed to be equally distributed among both treatment groups but cannot be formally retrieved in RT-patients.

In order to compare the influence of MLN-downstaging and extent of resection in each treatment arm, we estimated the outcome in subsets of S-patients and matched paired subsets of RT-patients.

METHODS

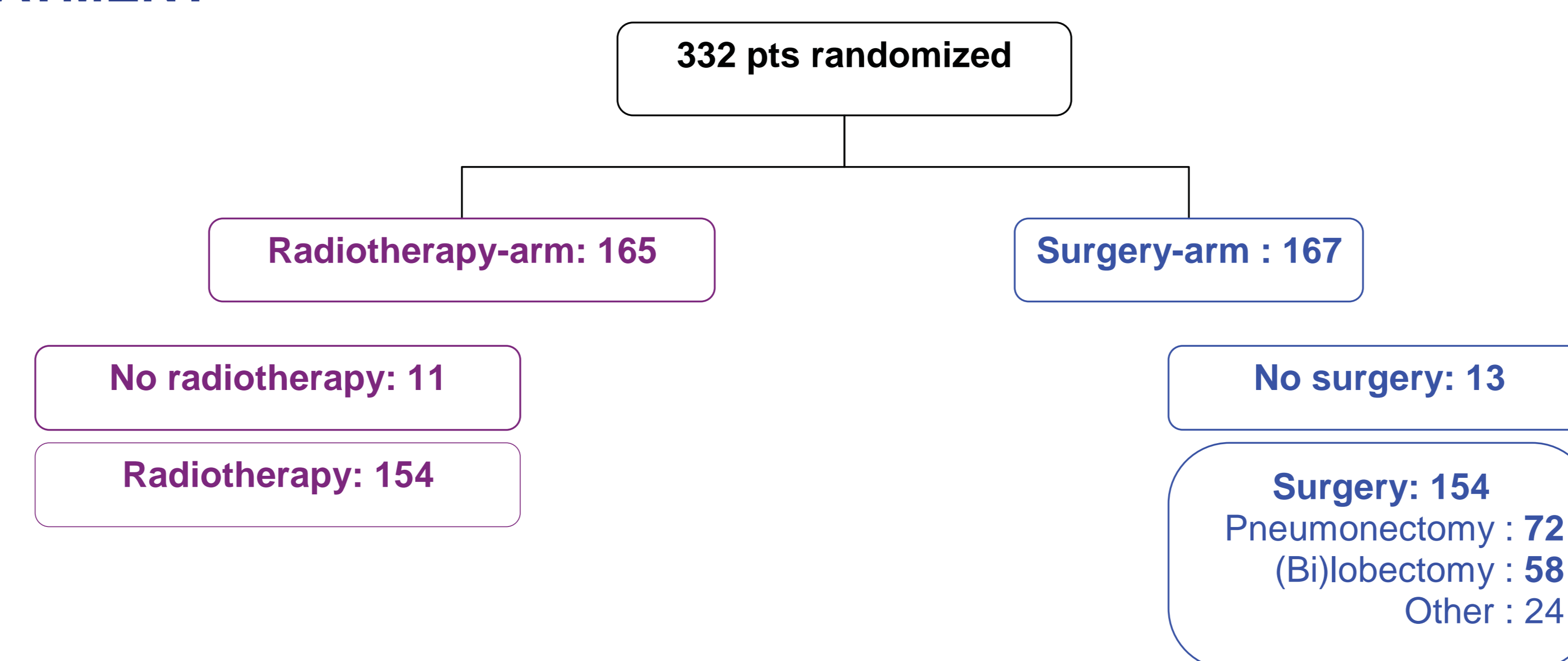
Subgroups of resected S-pats are defined as follows:

- (i) pts with MLN-downstaging at resection,
- (ii) pts without MLN-downstaging.
- (iii) pts who underwent a (bi-)lobectomy
- (iv) pts who underwent a pneumonectomy

Each subgroup was compared to a randomly selected subset of the irradiated RT-patients matched on 4 baseline factors: histological subtype, gender, T stage, response to ICT. Kaplan-Meier estimates for overall survival (OS) and logrank p-values were then computed.

RESULTS

TREATMENT



PATIENT POPULATION (Patients who actually received protocol treatment)

N (%)		Surgery (N=130)	Radiotherapy (N=154)	TOTAL (N=284)
Histological type	Squamous cell	48 (37)	63 (41)	111 (39)
	Adenocarcinoma	44 (34)	42 (27)	86 (30)
	Large cell	34 (26)	43 (28)	77 (27)
	Mixed cell	1 (1)	1 (1)	2 (1)
	Other	3 (2)	5 (3)	8 (3)
Sex	Male	99 (77)	118 (77)	217 (76)
	Female	31 (24)	36 (23)	67 (24)
cT	T1	15 (12)	20 (13)	35 (12)
	T2	100 (78)	110 (71)	210 (74)
	T3	15 (12)	23 (15)	38 (13)
	Unknown	0 (0)	1 (1)	1 (1)
	Overall clinical response	CR	10 (8)	8 (5)
	PR or min	119 (92)	139 (90)	258 (91)
	SD	1 (1)	6 (4)	7 (3)
	PD	0 (0)	1 (1)	1 (1)
Downstaging	pN0-pN1	61 (47)	-	-
	pN2	68 (53)	-	-
	Unknown	1 (1)	-	-

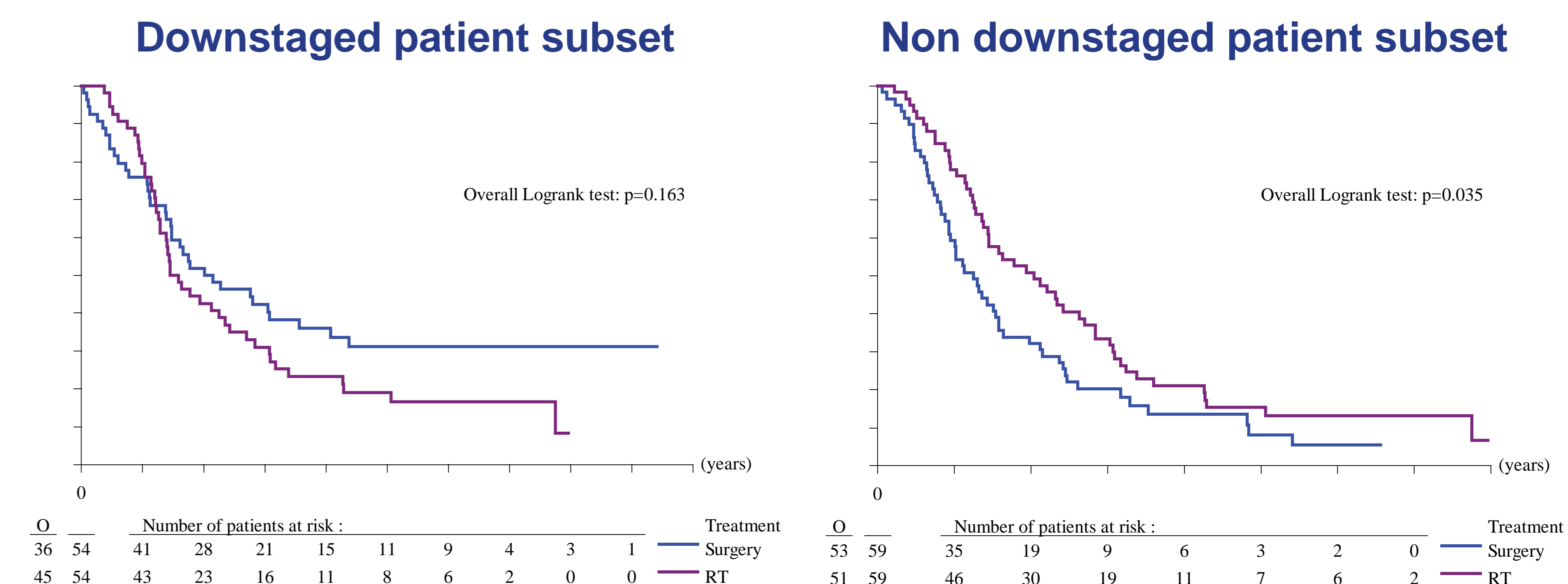
MATCHED PAIRS

A match was feasible for 54/61 downstaged patients, 59/68 non-downstaged patients, 50/58 lobectomies and 62/72 pneumonectomies.

Subset	Downstaged Patients		Non Downstaged Patients	
	S	RT	S	RT
OS/pair				
N	54	54	59	59
Median (m)	25 (18-49)	18 (17-32)	15 (11-19)	24 (17-34)
2 yr (%)	52 (38-64)	43 (29-55)	32 (21-44)	51 (38-63)
5 yr (%)	31 (19-44)	19 (10-31)	8 (2-18)	15 (7-26)
P value	0.16		0.035	
Subset	(BI-) LOBECTOMY		PNEUMONECTOMY	
	S	RT	S	RT
OS/pair				
N	50	50	62	62
Median (m)	24 (18-37)	19 (16-34)	13 (11-21)	24 (17-34)
2 yr (%)	52 (37-65)	46 (32-59)	34 (22-46)	50 (37-62)
5 yr (%)	27 (15-41)	10 (3-20)	14 (7-25)	16 (8-26)
P value	0.12		0.16	

Numbers between brackets are 95% confidence intervals

OVERALL SURVIVAL - Surgery versus matched RT patients



CONCLUSION

These exploratory analyses suggest that:

1. RT improves OS in MLN-non-downstaged patients as compared to S.
2. S does not improve OS in MLN-downstaged patients, as compared to RT.
3. S does not improve OS in patients who underwent a (bi-)lobectomy, as compared to RT