

Role of Adjuvant and Neoadjuvant CT in resectable Lung Cancer

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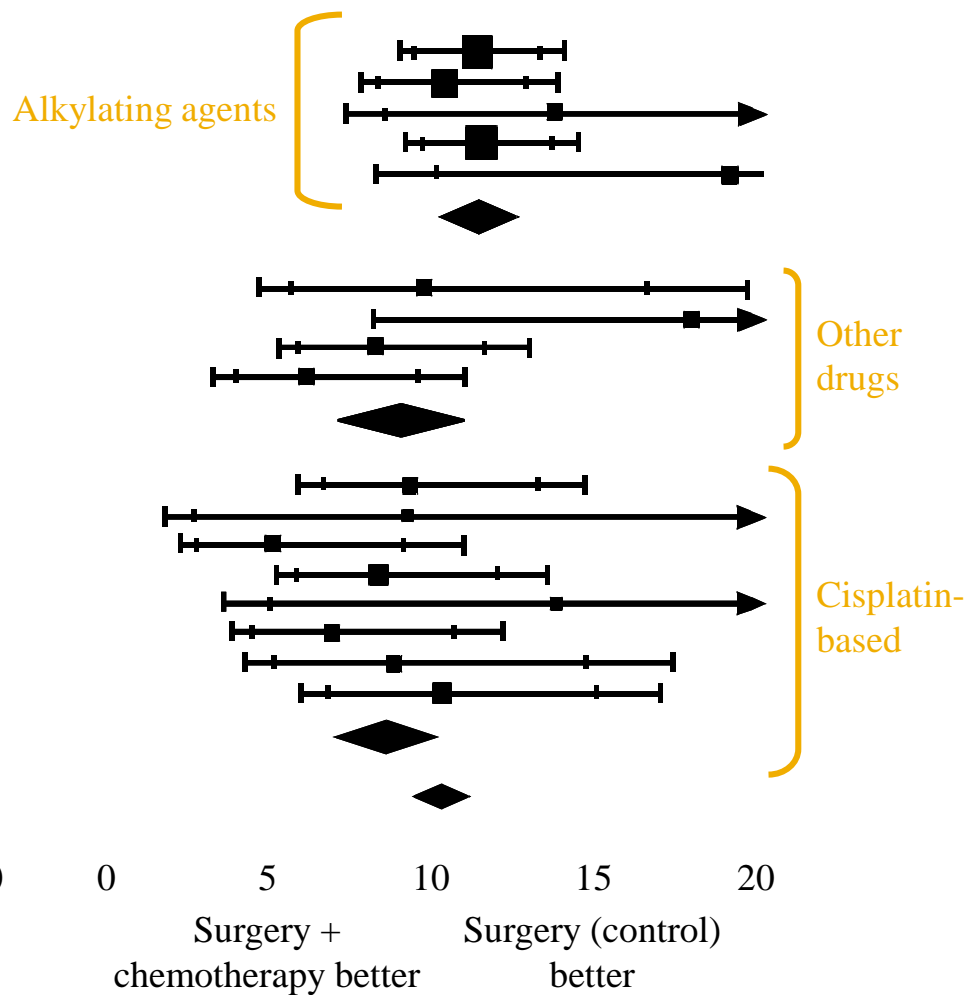
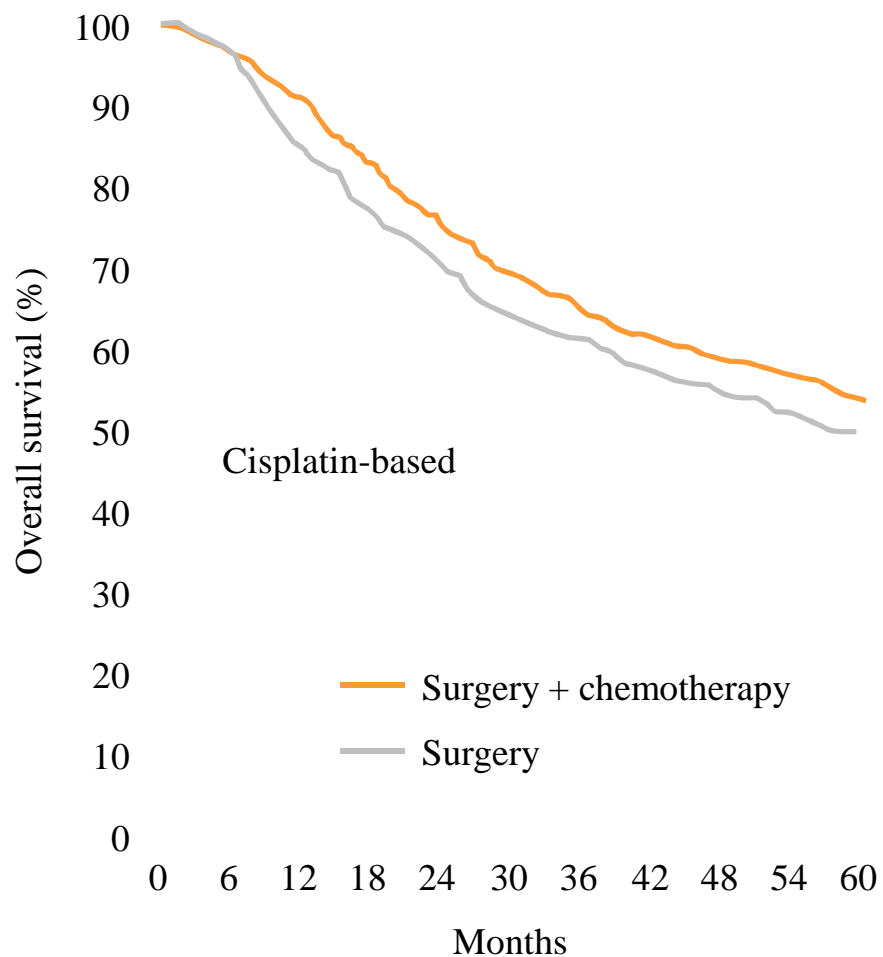
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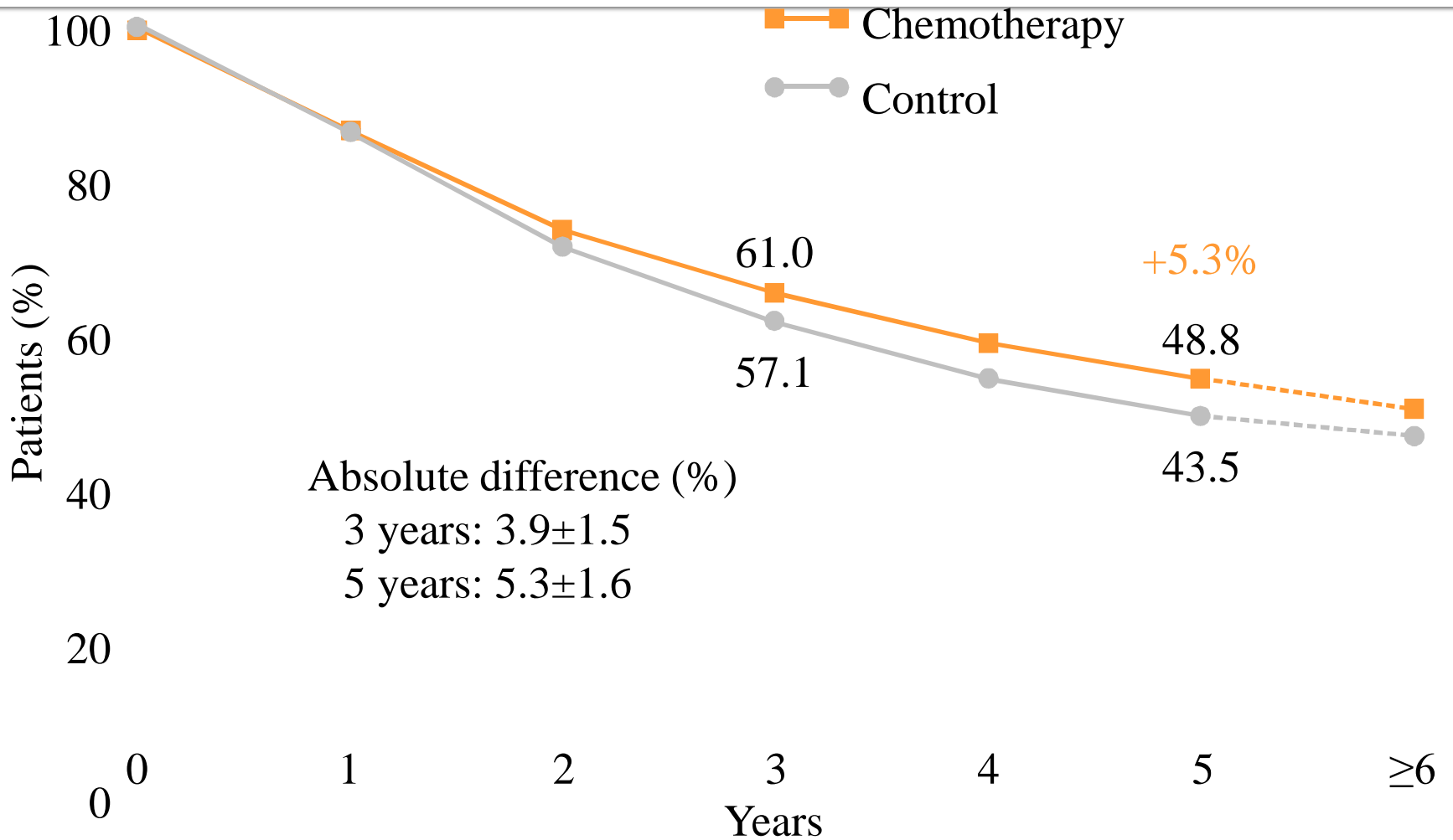
Adjuvant therapy: meta-analysis of the effect of chemotherapy



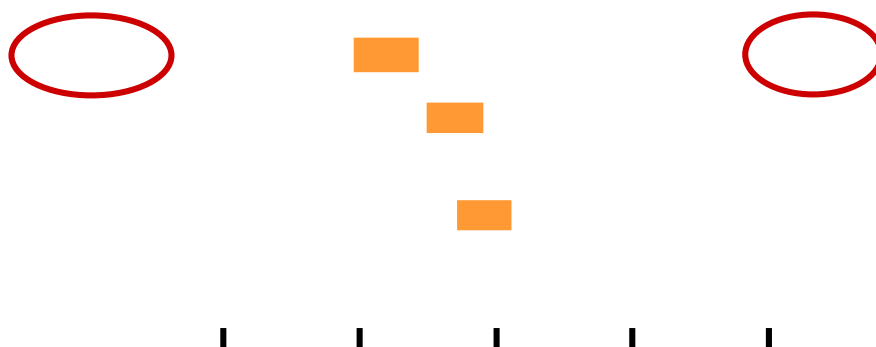
Adjuvant therapy: landmark trials

Study	Treatment	5-year survival		
		Observation	Active treatment	p value
International Adjuvant Lung Trial (IALT)	Surgery ± platinum chemotherapy	40.4	44.5	<0.03
Cancer and Leukemia Group B (CALGB 9633)	Surgery ± carboplatin/paclitaxel	57	59	0.38
National Cancer Institute of Canada (NCIC JBR.10)	Surgery ± vinorelbine/cisplatin	54	69	0.03
Adjuvant Navelbine International Trialist Association (ANITA)	Surgery ± vinorelbine/cisplatin	43	51	0.013
Tegafur-uracil (UFT) meta-analysis	Surgery ± UFT	77	82	0.001
LACE meta-analysis	Surgery ± cisplatin-based chemotherapy	43.5	48.8	0.004

LACE: overall survival

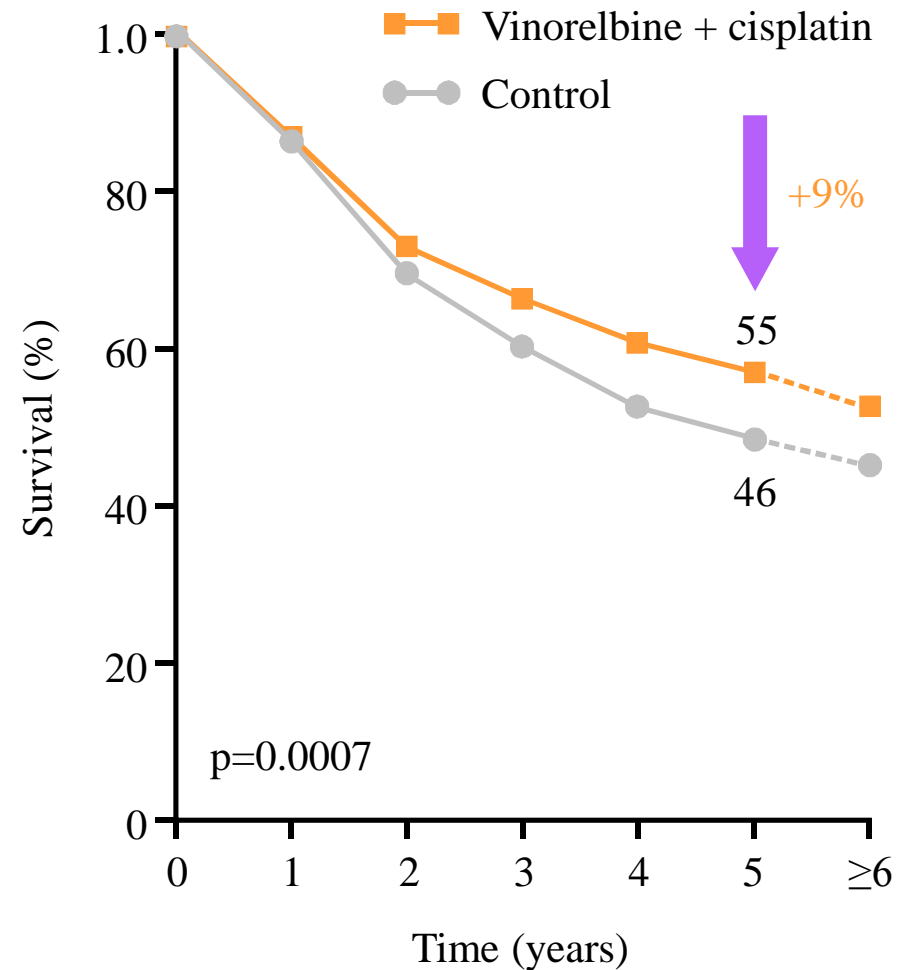
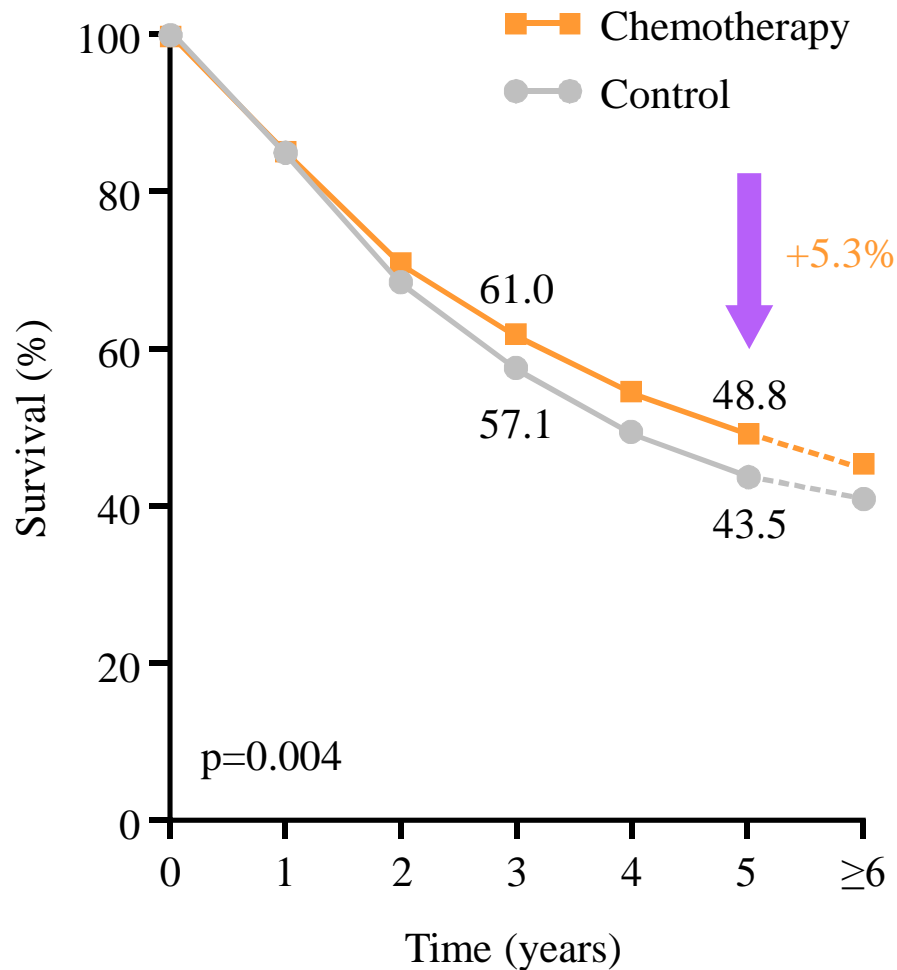


LACE: chemotherapy effect and associated drugs

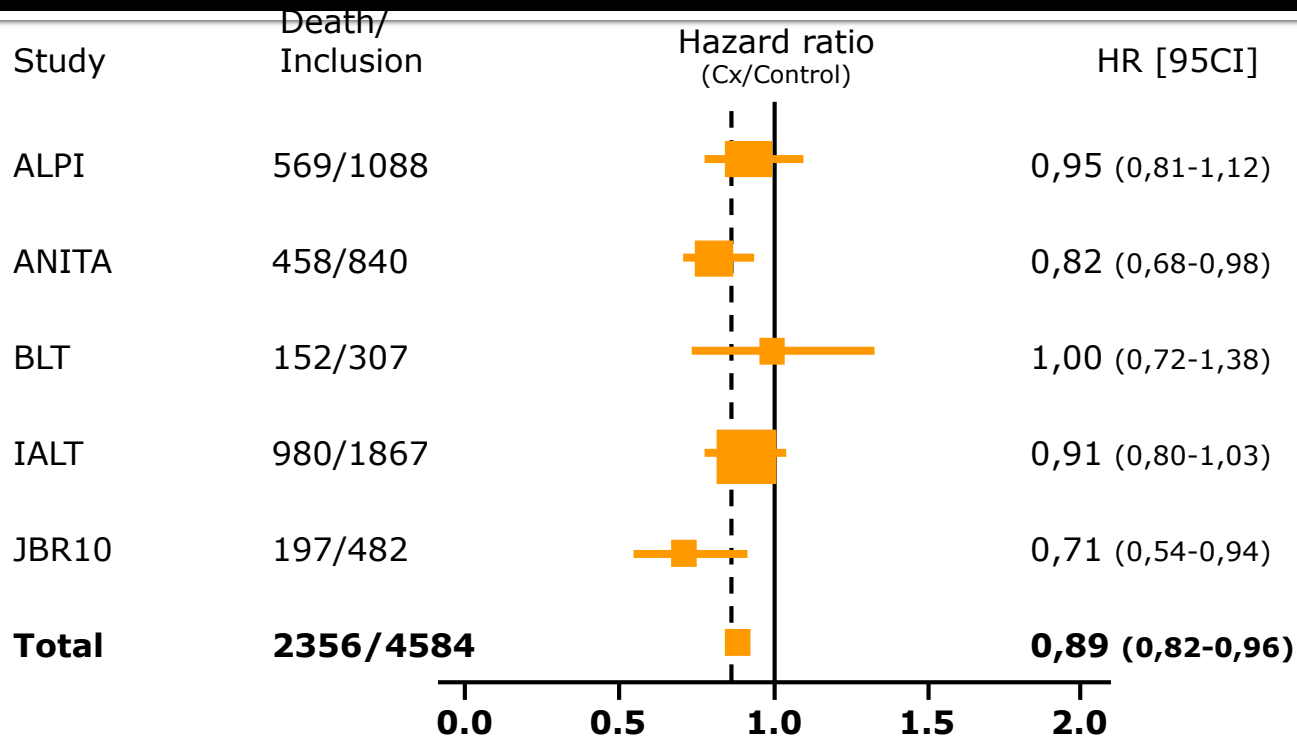


- The effect of **cisplatin + vinorelbine** was better than the effect of other drug combinations; this was significant when the other combinations were pooled ($p=0.04$, post-hoc analysis)

LACE: contribution of vinorelbine in adjuvant treatment of resected lung cancer



Standard of Care



+4.2% at 5 years for platinum-based adjuvant Cx

Case - Early operable NSCLC

- 65-year-old man
- 2 minor episodes of hemoptysis
- No other symptoms
- 4-cm mass right upper lobe on chest x-ray
- bronchoscopy and biopsy Sq Cell Ca
- Full Metastatic work-up is negative
- At surgery 1 microscopically positive hilar LN
- Right pneumonectomy with R0 resection

- The patient comes back for a follow-up visit. He has no symptoms and he is doing well
- What Next ?

Resectable Stage III – NSCLC

Predicting Mediastinal Disease – CT Scan

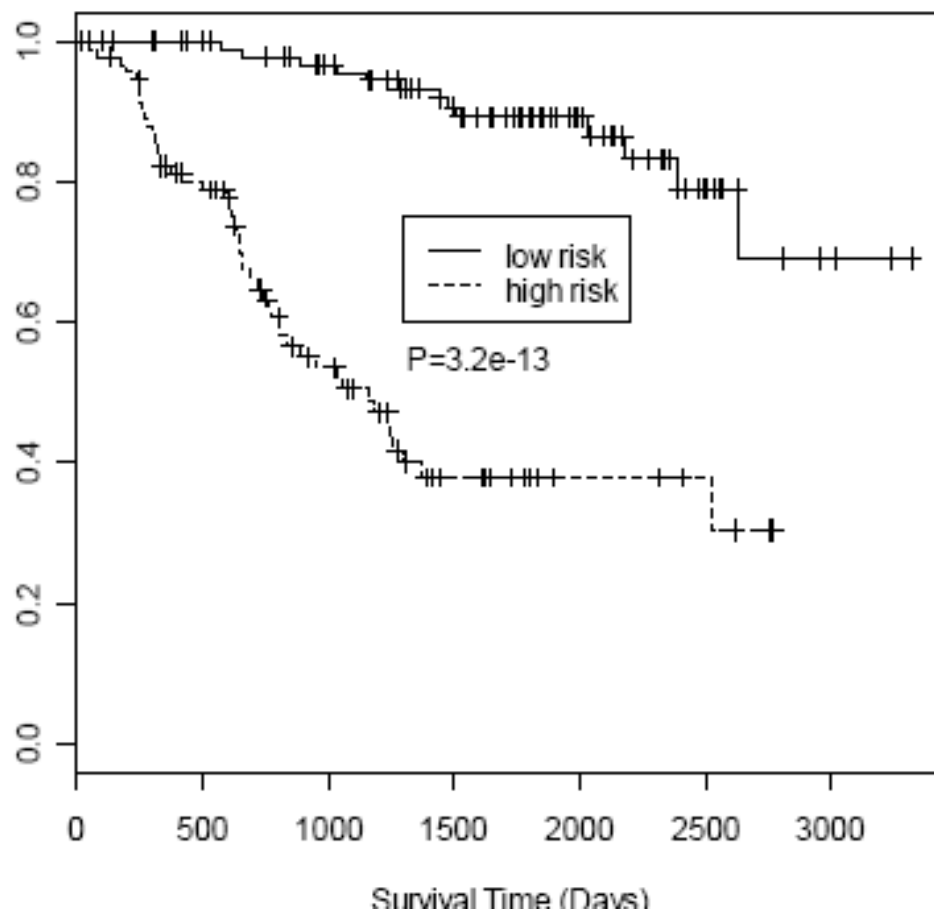
Node size, (cm)	Pathologic +vity %
<1	13
1-2	25
2-3	67

Markedly enlarged LNs with no tumor - 33%
Normal LNs with tumor - 13%

Majority of patients should have mediastinal LN Bx as part of staging

ASCO Clinical practice guidelines for Rx of NSCLC. JCO 1997; 15: 2996-3018

Expression Profiling to Predict Recurrence: Washington University Analysis Stage I NSCLC (N=172)



R0 resection rate

- The **goal** of oncological surgery
- **Open and close** thoracotomy <5%
- **Major impact on survival:**

Intervention	n	5-year survival	95%CI	Median survival (months)	Log rank
Complete i.e. R0	877	51%	47-55	+60	0.0002
Incomplete i.e. R1 or R2	60	29%	17-41	24	0.0004
Relatively incomplete i.e. no MLD ...	582	50%	46-54	59.5	

Notes. 95%CI: 95% confidence interval; survival differences between complete and relatively incomplete resections did not reach statistical significance: $P=0.67$.

Rami-Porta,

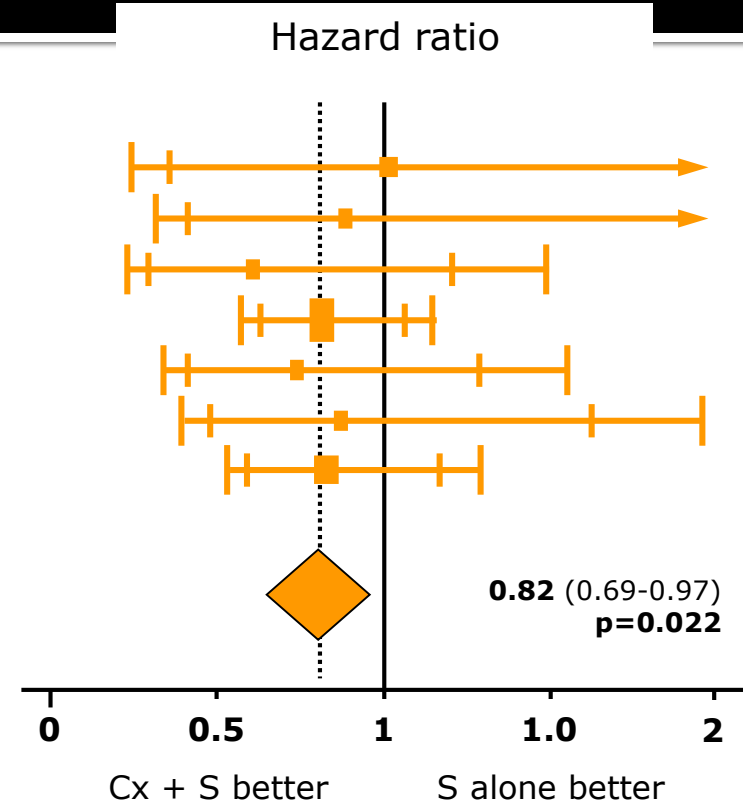
Eur J Cardio-Thorac Surg 2006

Impact on survival

	Number of patients	
	CT + surgery	Surgery alone
Dautzenberg	13	13
Roth	28	32
Rosell	30	30
Depierre	179	176
JCOG 9209	31	31
Sorensen	44	46
SWOG S9900	168	167
Total	493	495

Het $\chi^2_{(6)}=1.14, p=0.98$

+6% survival benefit at five years (3-7%)



Burdett, J Thorac Oncol 2006

Better than adjuvant Cx?

- **Neoadjuvant Cx:**

HR=**0.82** (95% CI 0.69-0.97), p=.02

- **Adjuvant Cx:**

HR=**0.89** (95% CI 0.82-0.96), p=.004

Burdett, J Thorac Oncol 2006

Pignon, ASCO 2006 (#7008)

Role of Neoadjuvant Rx in NSCLC

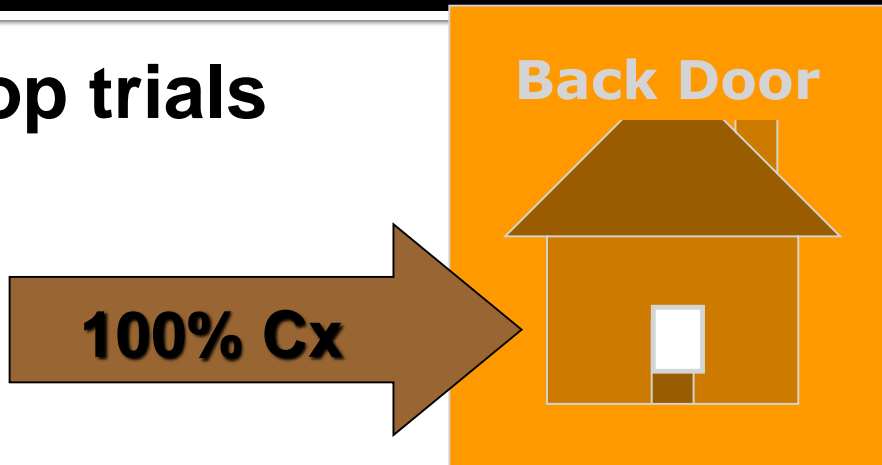
TABLE 3. Five-Year Survival by Stage*

Stage	5-Year Survival (%)	Absolute Benefit (%)	New 5-Year Survival (%)
Ia	75	4	79
Ib	55	6	61
IIa	50	7	57
IIb	40	7	47
IIIa	15–35	6–7	21–42
IIIb	5–10	3–5	8–15

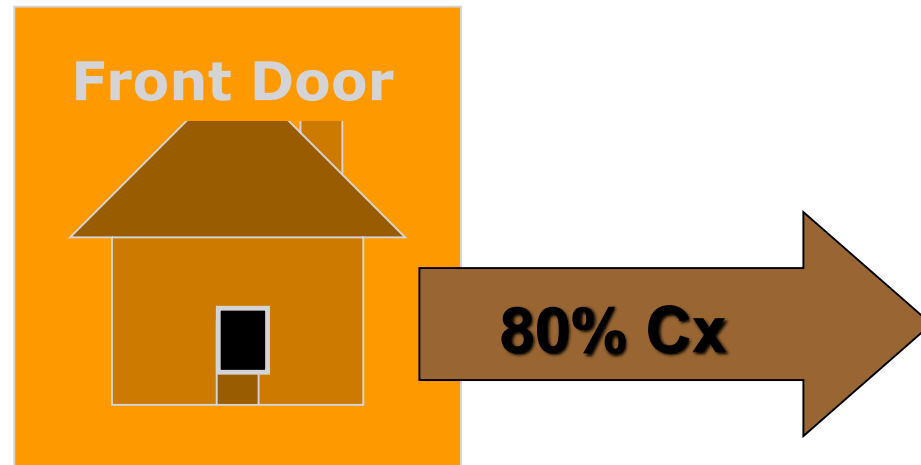
*Figures for 5-year survival by stage as reported by van Zandwijk.⁴

“Front Door vs. Back Door hypothesis”

- Pre-op trials



- Post-op trials



Conclusions

We are NOT happy with outcome of Surgery alone
outcomes in early NSCLC

Adjuvant and Neoadjuvant CT have documented
benefit in such NSCLC patients

Prognostic Factors help select high risk patients –
likely to benefit most from such approaches

Absolute Improvement in OS can be improved by
finetuning strategy in the light of revised staging