

# Chemotherapy in Locally Advanced Lung Cancer: NACT/Adjuvant

Dr. Rushabh Kothari

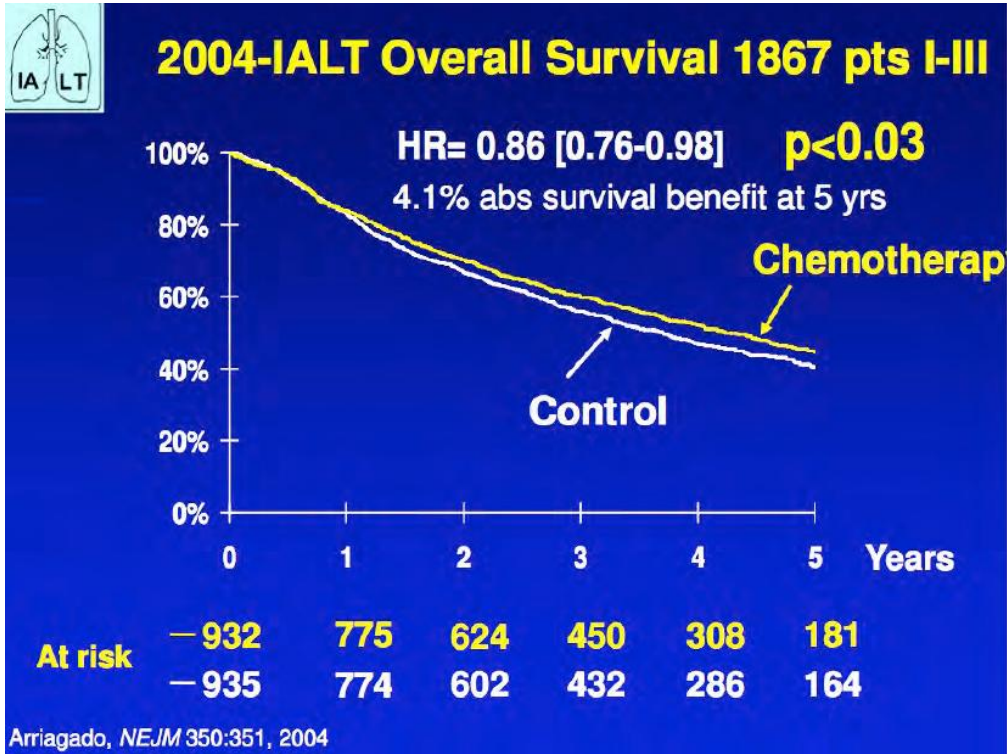
Director, Oncowin Cancer Center

Consultant Medical  
Oncologist, Narayana  
Multispeciality Hospital

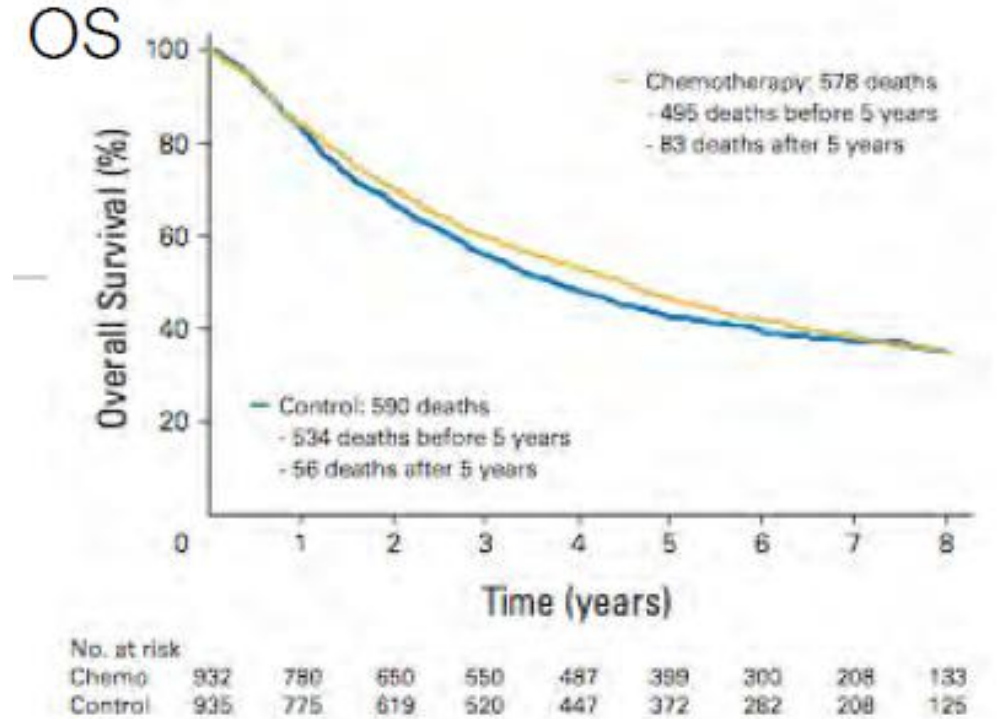
surgical stage (6th ed)	5-year survival (%)	relapse (%)	
		local	distant
IA T1N0M0	67	10	15
IB T2N0M0	57	10	30
IIA T1N1M0	55		
IIB T2N1M0	39	12	40
T3N0M0	38		
IIA T3N1M0	25	15	60
T1-3N2M0	23		

- High risk of failure
- Most recur within 2 years
- Distant failure > Local failure

# IALT

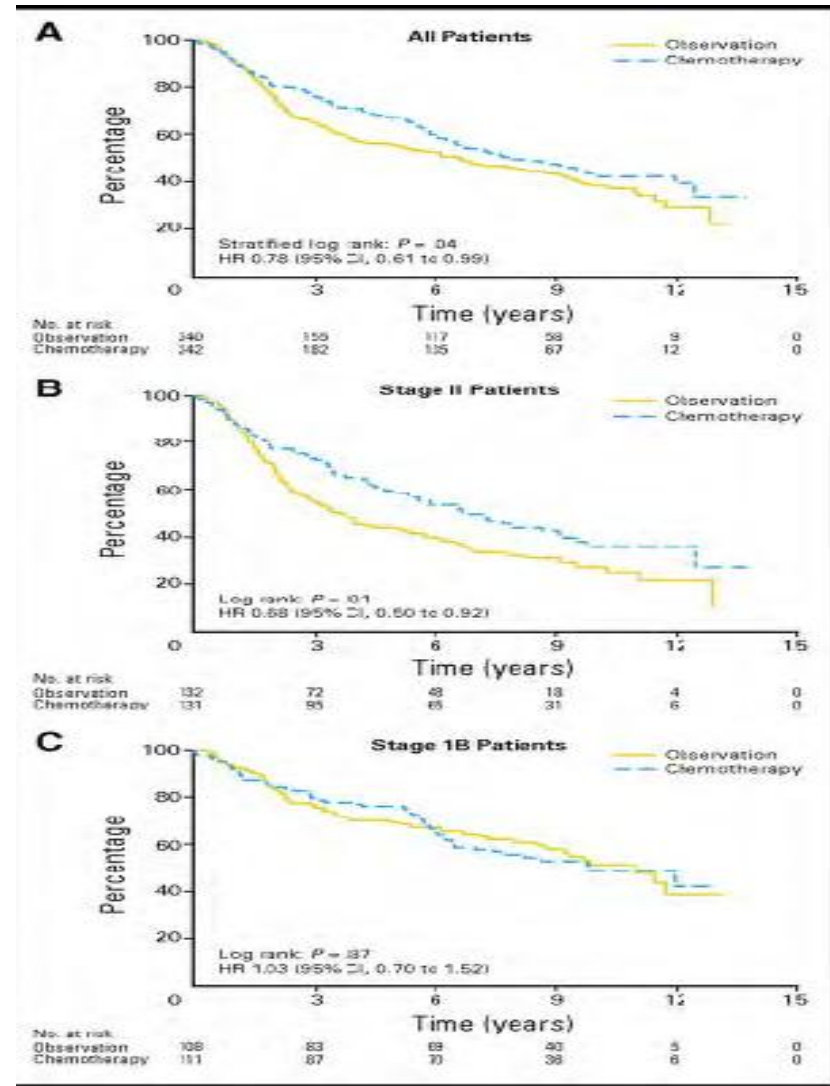
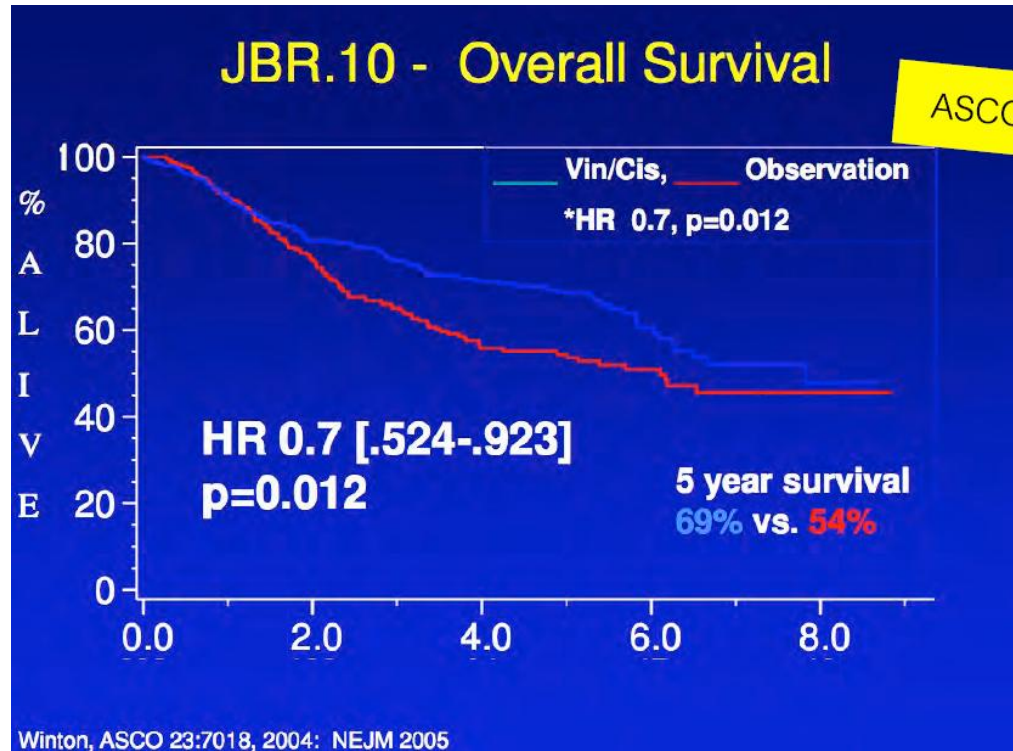


33% stage I patients



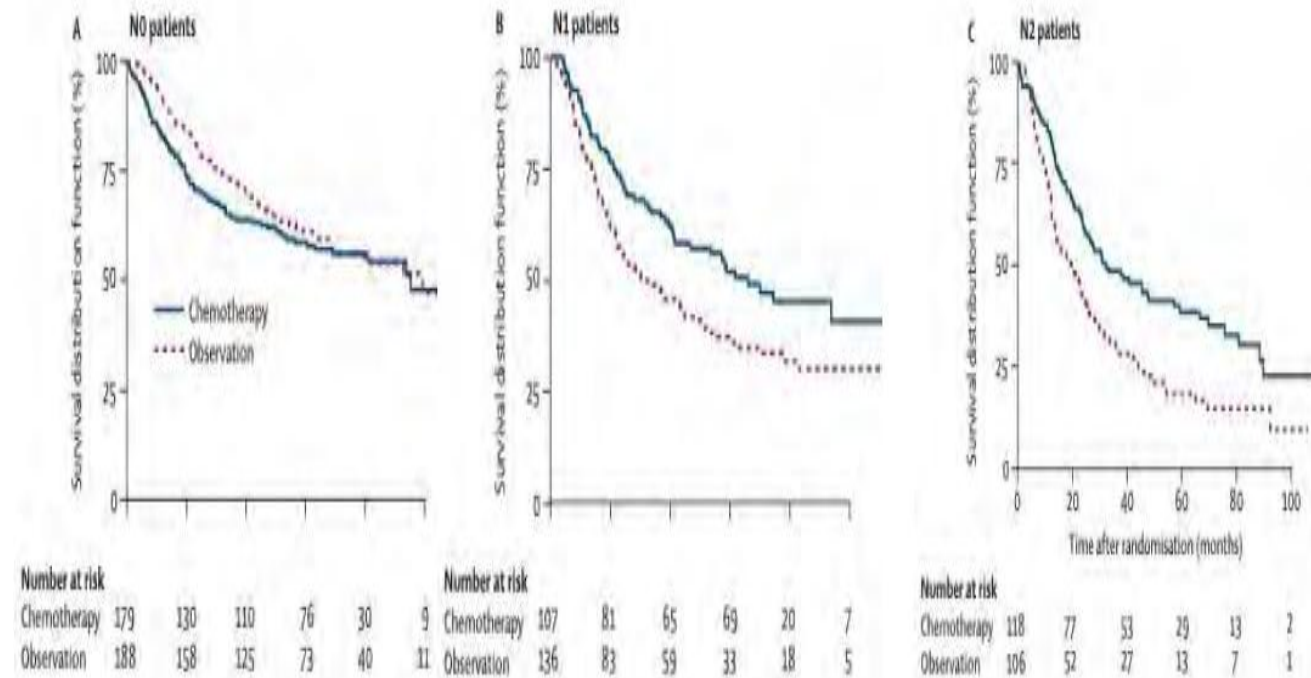
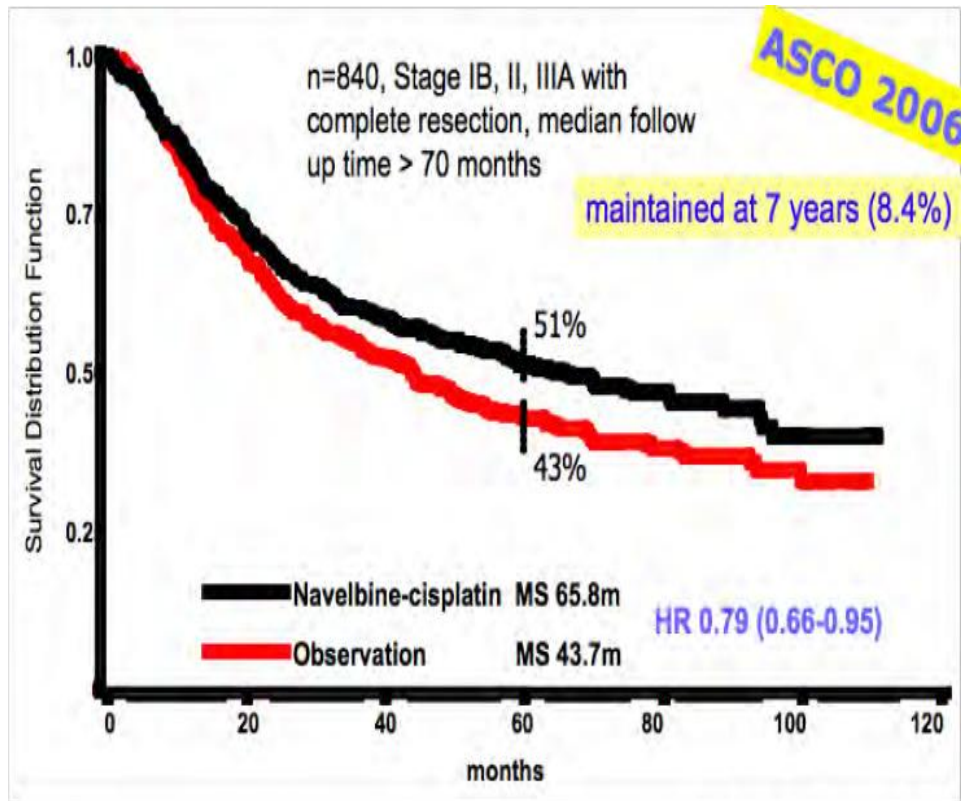
@ 7.5 years  
HR: 0.91(0.81-1.02)

# JBR 10



@ 9.3 years  
Stage II driven

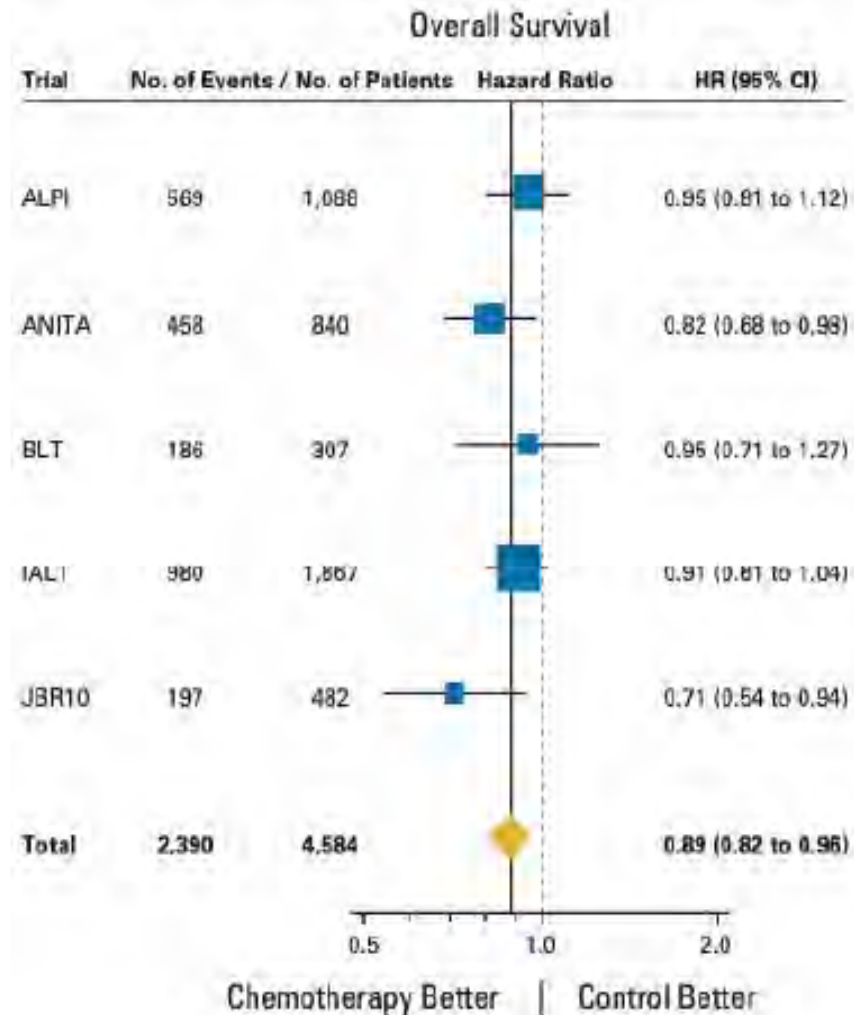
# ANITA



- Benefit in N+ disease only

# LACE meta-analysis: OS

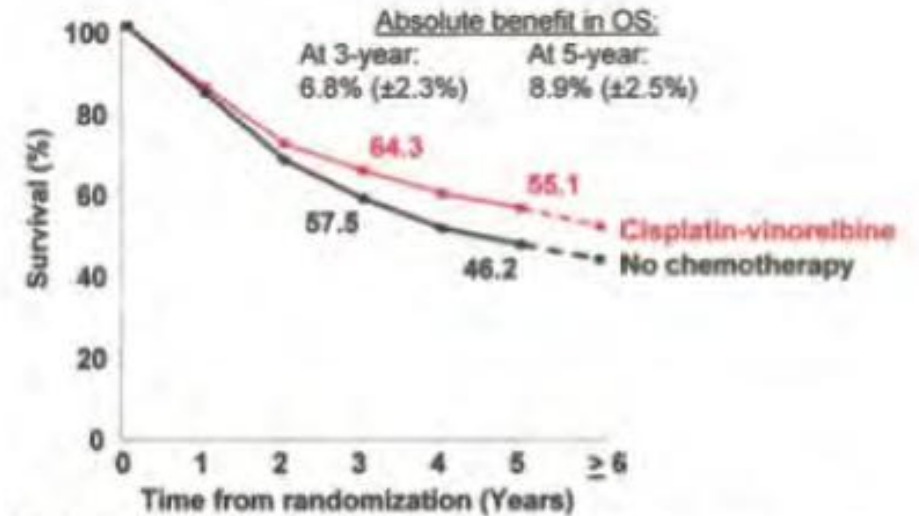
**ALPI:** cisplatin + vindesine or mitomycin **BLT:** cis + vindesine/vinorelbine/mitomycin+ifosfamide or mitomycin + vinblastine  
**IALT:** cis + vindesine/vinblastine/etoposide or vinorelbine **JBR10:** cis + vinorelbine  
**ANITA:** cis + vinorelbine



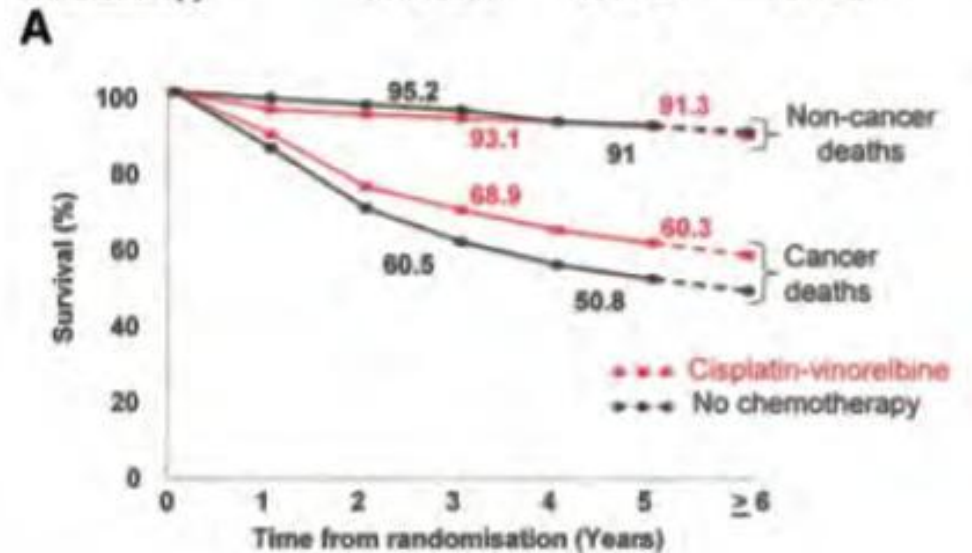
- individual patient data from 5 largest trials (n = 4584)
- median f/u 5.2 years
- 5-year absolute benefit 5.4% from chemotherapy
- benefit varied with stage
  - IA HR 1.40 [95% CI 0.95-2.06]
  - IB HR 0.93 [95% CI 0.78-1.10]
  - II HR 0.83 [95% CI 0.73-0.95]
  - III HR 0.83 [95% CI 0.72-0.94]
- trend to worse OS for stage IA
- effect higher for better PS patients
- effect of chemotherapy did not vary significantly according to drug

# LACE vinorelbine 2010

- subgroup analysis of cisplatin/vinorelbine
- 1888 pts. from 4 studies
- survival improvement at 5yr 8.9% HR 0.80 [95% CI 0.70-0.91]



Deaths / person years by period	Years 0-3	Years 4-5	Years ≥ 6
Control	401 / 2135	81 / 695	30 / 379
Chemotherapy	325 / 2171	63 / 794	35 / 412



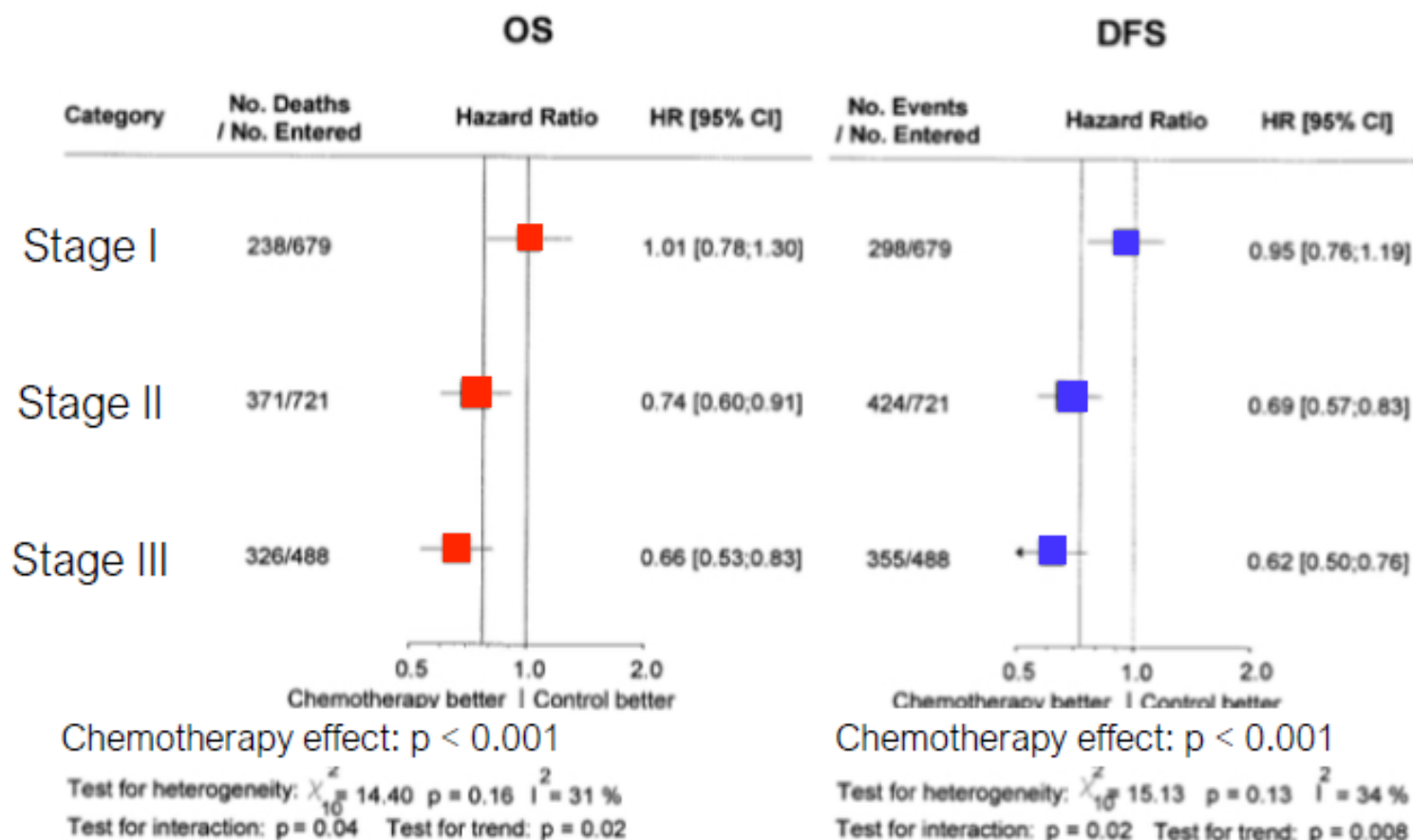
# chemotherapy effect according to stage: LACE

## cisplatin/vinorelbine

- 1888 pts. from 4 studies
- survival benefit at 5 years  
8.9% cf observation HR  
0.80 [95% CI 0.70-0.91]

## OS

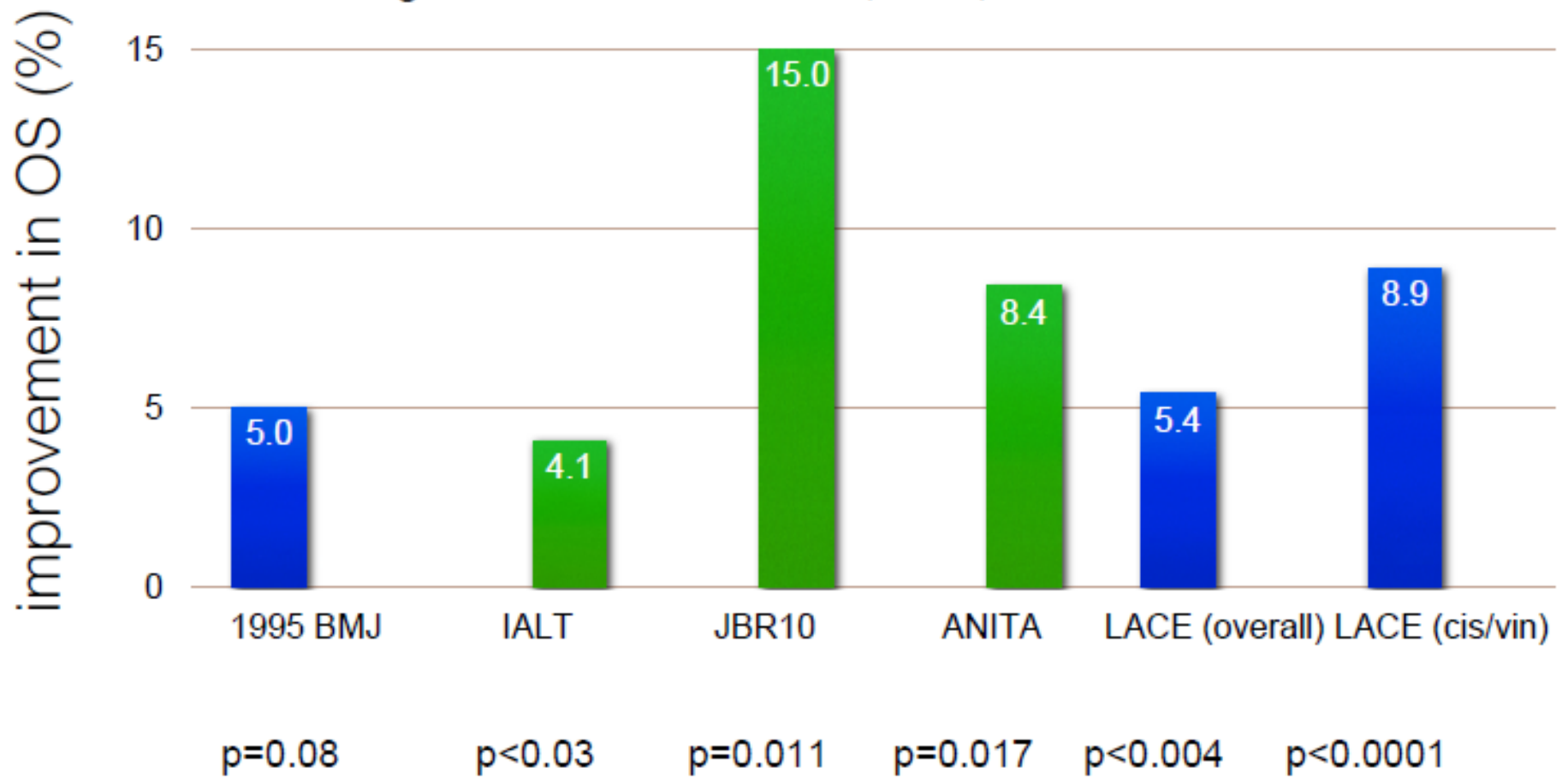
- stage I HR 5yr benefit of 1.8% HR  
1.01 [0.78 -1.30] (-1.2% at 3yr)
- stage II 5yr benefit of 11.6% HR  
0.74 [0.60 - 0.91]
- stage III 5yr benefit of 14.7% HR  
0.66 [0.53 - 0.83]





■ meta-analysis    ■ Trial

the results are astonishing” (Editorial comment on JBR10 study)  
New England Journal of Medicine, June, 2005



# Indications

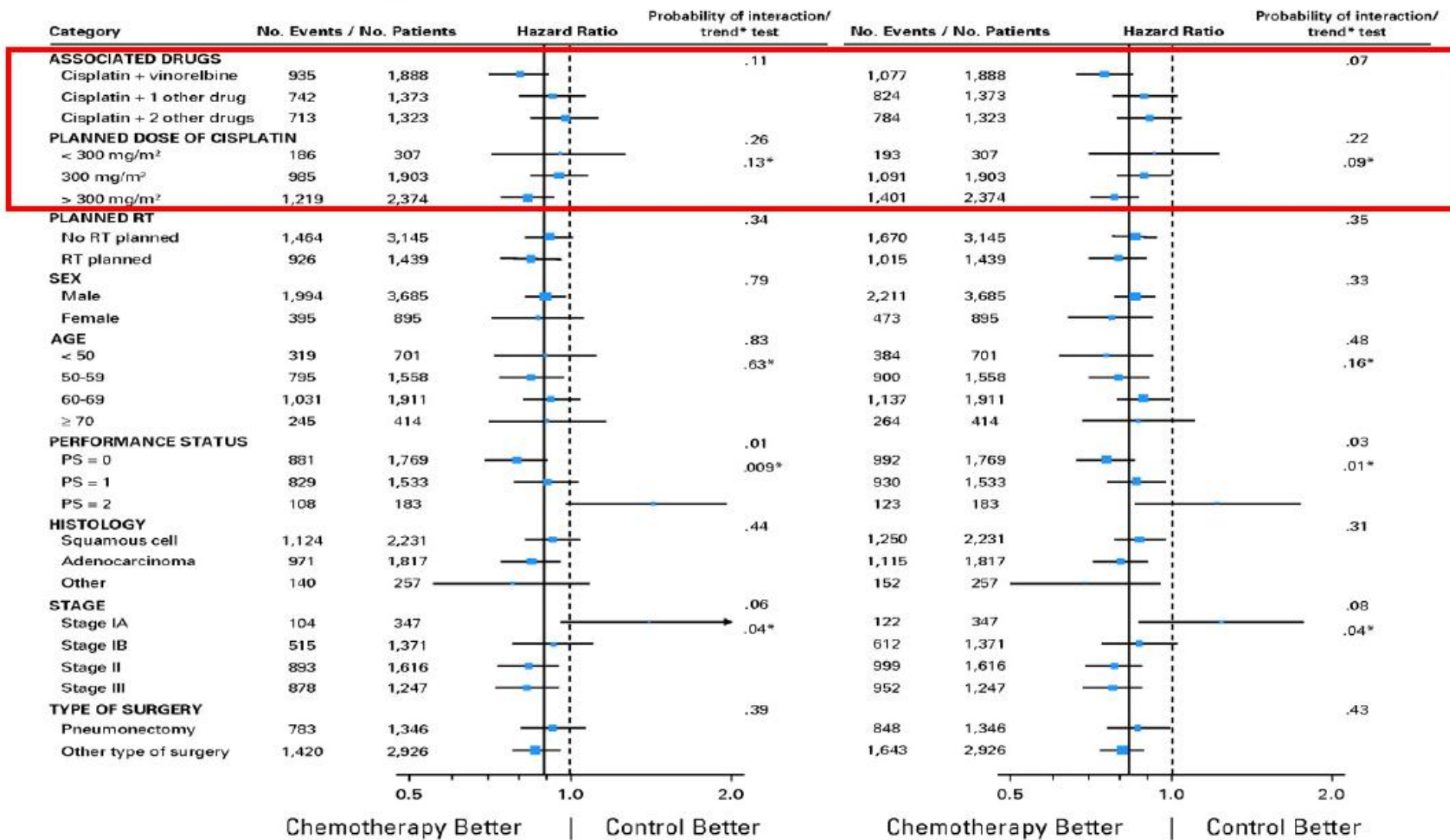
- Stage II
- Stage III
- Stage IB(>4cm, LVI, High grade, PET SUV, Visceral pleural involvement)
  
- Age: > 65 years(similar benefit), limited data for 70+
  
- PS

# Regimen

- Cisplatin Doublet
- Cisplatin  $\geq 300\text{mg}/\text{m}^2$
  
- Carboplatin (consensus for cisplatin ineligible, no positive study)

### Overall Survival

### Disease-Free Survival



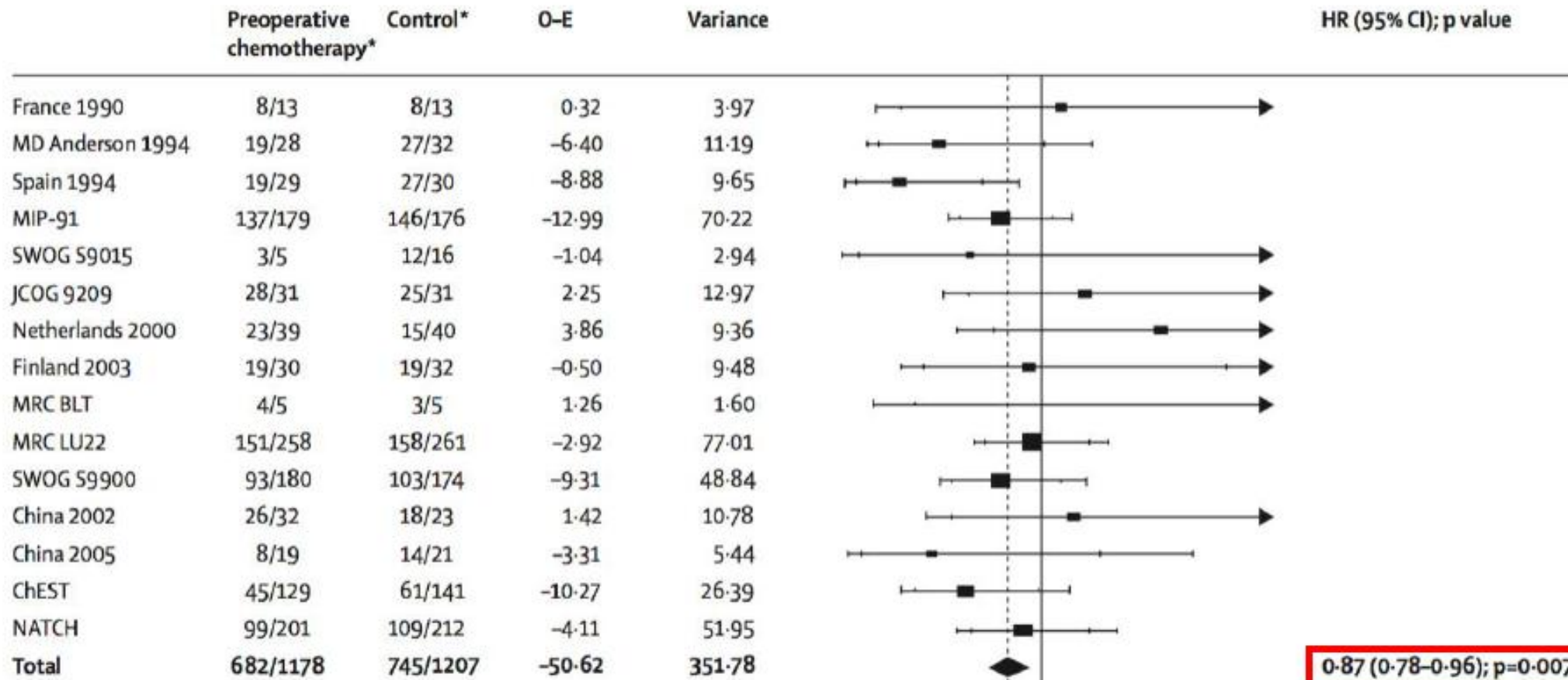
# Toxicity

G3-4 toxicity	IALT (%)	JBR.10 (%)	ANITA (%)
neutropaenia	17.5	73	85
febrile neutropenia	-	7	9
anaemia	-	7	14
thrombocytopenia	-	1	3
asthenia	-	15	28
peripheral neuropathy	-	7	3
emesis	3.3	17	27
constipation	-	3	5
treatment related deaths	0.8	0.8	2

# Regimens

- Vinorelbine, Gemcitabine, Etoposide, Taxanes, Pemetrexed(similar efficacy based on E1505 study)
  - Vinorelbine: Neutropenia(13%), FN
  - Gemcitabine: Thrombocytopenia(18%)
  - Pemetrexed: Less grade 3 or more toxicity(83% v/s 67%)
- Vinorelbine-Cisplatin: Most robust data(ANITA, JBR 10)
- Pemetrexed-Cisplatin: JIPANG(Gr 3/4 neutropenia: 0.3% v/s 12%)

# Neoadjuvant chemotherapy: Metaanalysis



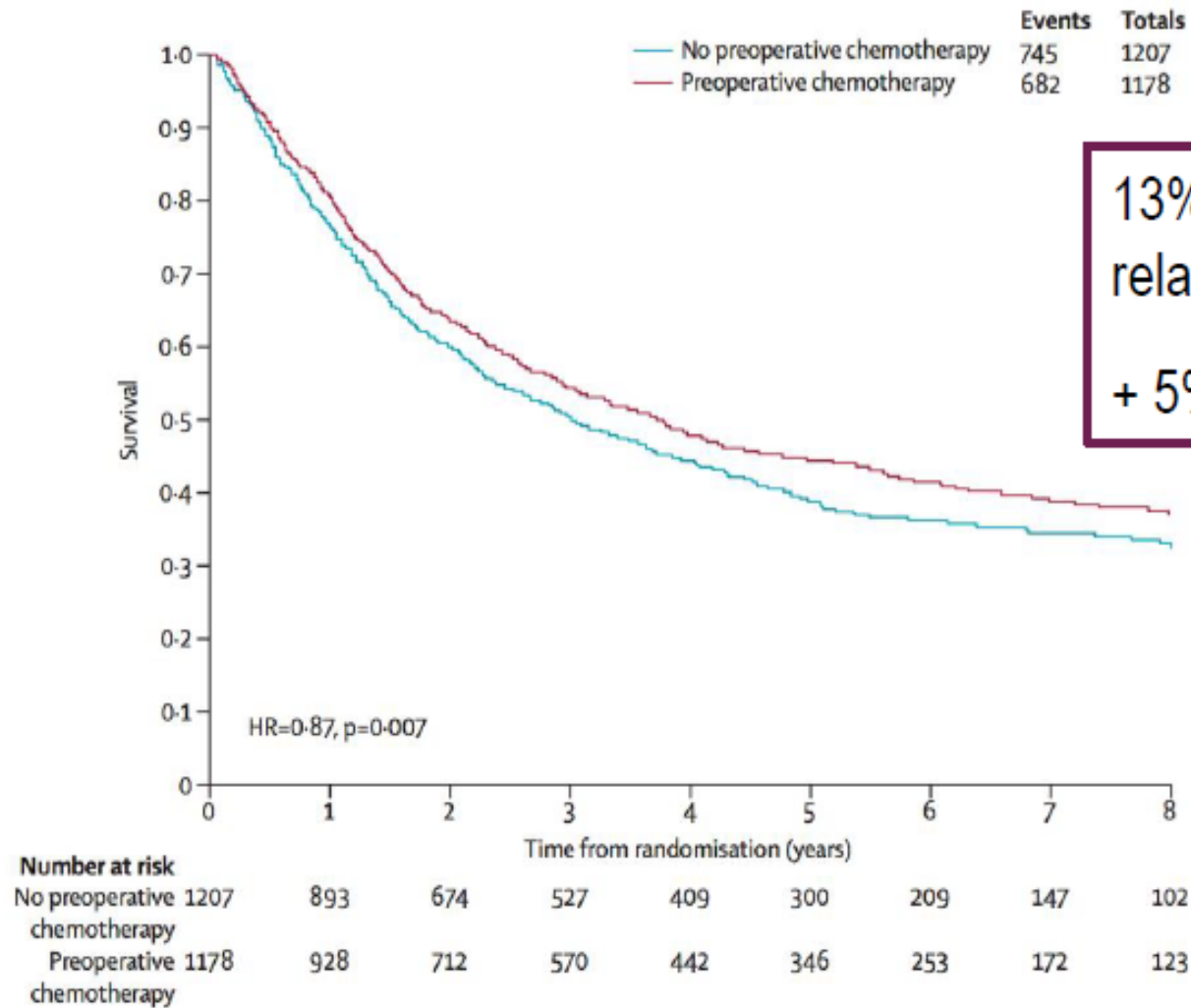
## Overall HR

0.87 (0.78-0.96), p=0.007 (fixed effect)

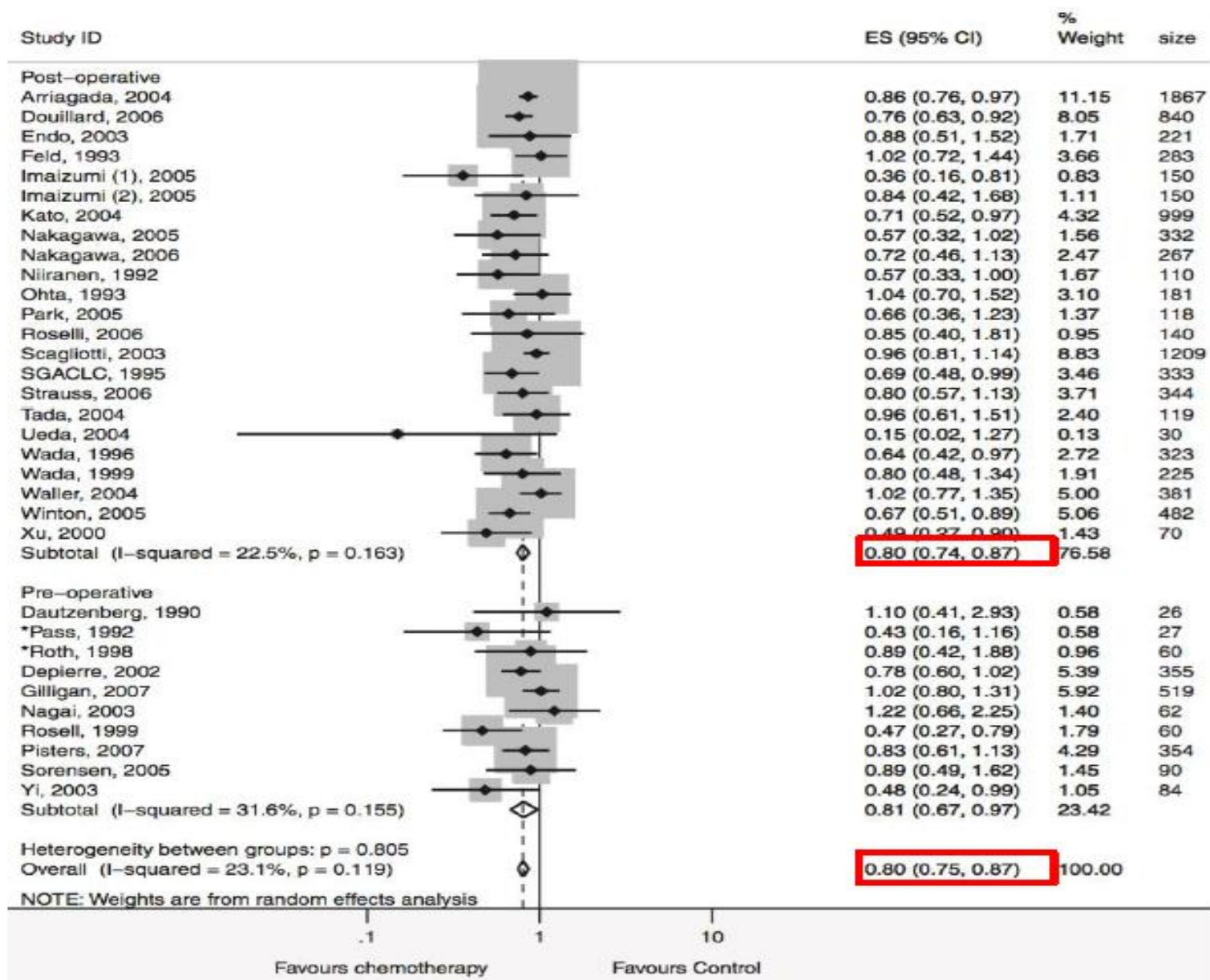
0.86 (0.75-0.98), p=0.03 (random effects)

Heterogeneity:  $\chi^2=18.75$ , df=14, p=0.18,  $I^2=25\%$

# Kaplan-Meier curves (non-stratified) of the effect of preoperative chemotherapy on time to survival







# Compliance

<b>Trials</b>	<b>At least 1 cycle</b>	<b>2 cycles</b>	<b>3 cycles</b>	<b>4 cycles</b>
ALPI	90%	ND	69%	NA
IALT	92%	ND	ND	ND
ANITA	90%	72%	61%	50%
JBR10	95.5%	64%	55%	45%
NATCH adj	66%	ND	61%	NA
Depierre	98%	90%	NA	NA
NATCH neoadj	97%	ND	90%	NA
Gilligan	96%	89%	96%	NA
SWOG 9900	ND	ND	79%	NA

# Adjuvant vs NACT

	Neoadjuvant	Adjuvant
Level of evidence		X
Staging		X
Earlier delivery	X	
Compliance	X	
Evaluation of tumour response	X	
<b>Research purposes</b>		
Tissue availability		X

# Modern options

- EGFR: ADAURA
- IO options: IMPOWER 010, CHECKMATE 816
- Many other trials with IO and Targeted agents are ongoing

THANK YOU