



XX Riunione Nazionale del Gruppo I.T.M.O.

# CA DELLO STOMACO: *terapia preoperatoria vs adiuvante*

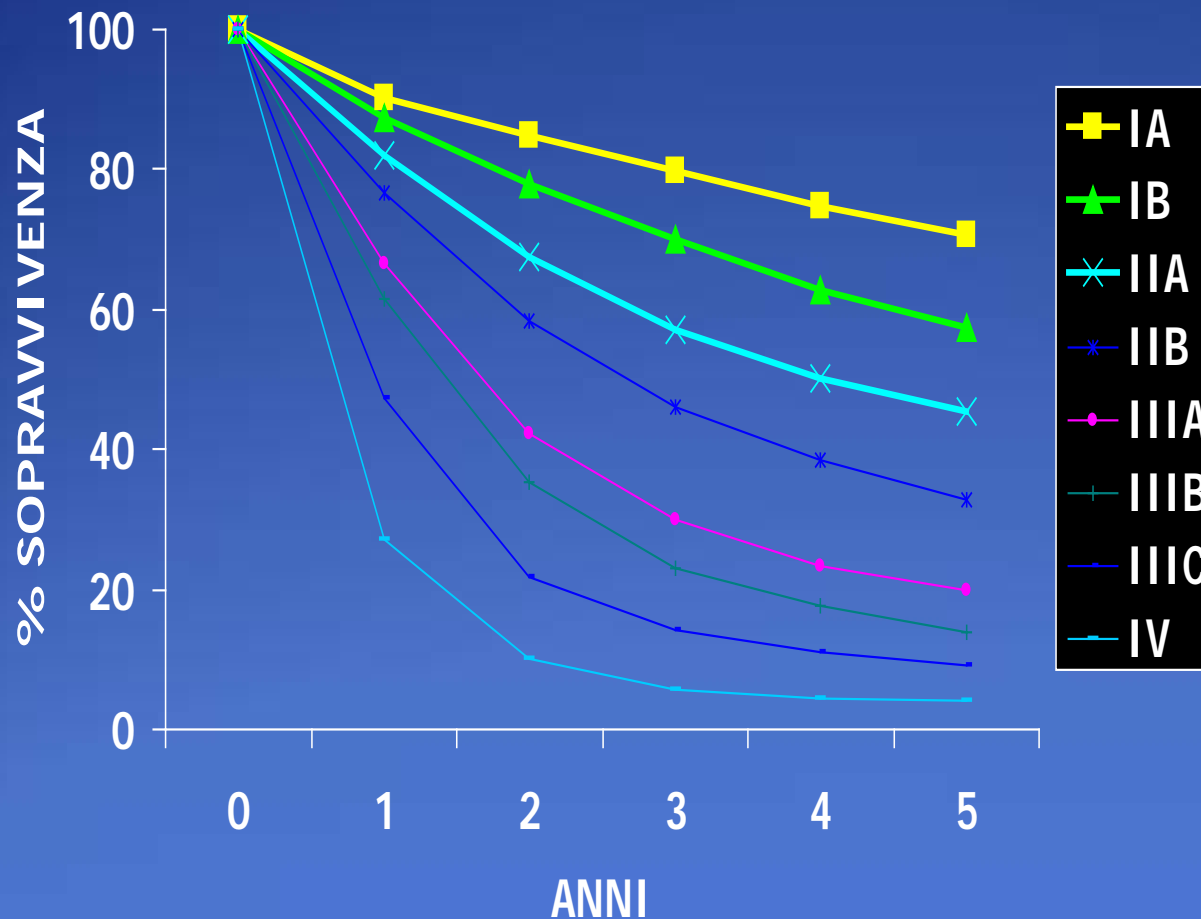


**Istituto  
di Oncologia**

Istituto di Ricovero e Cura ad Alta Specializzazione

*Dott.ssa Nadia Bianco  
Monza, 6 Maggio 2011*

# Prognosi stadio dipendente nel carcinoma gastrico radicalmente operato

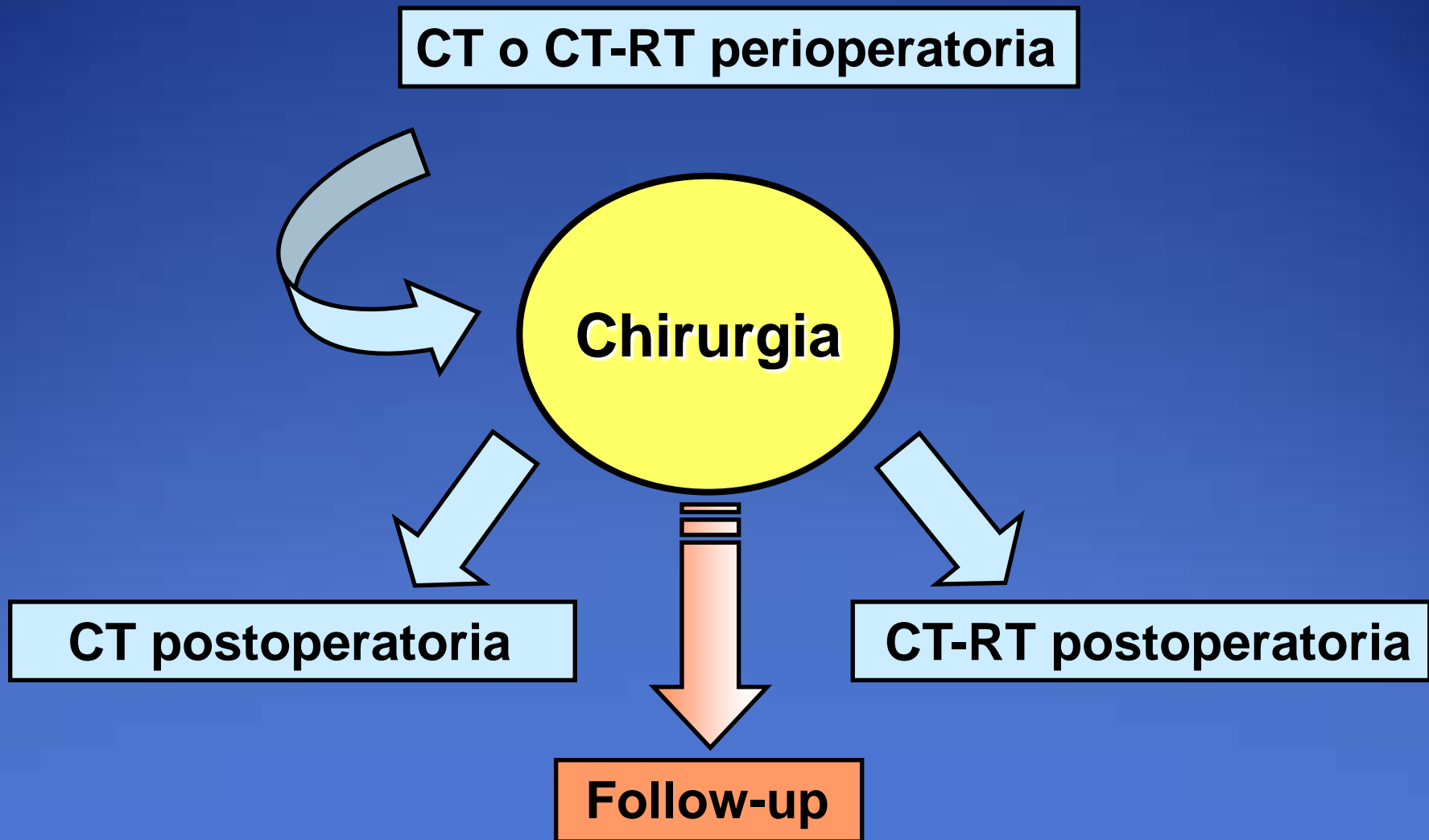


Stadio O	Tis No Mo
Stadio Ia	T1 No Mo
Stadio Ib	T2 No Mo; T1 No Mo
Stadio Iia	T3 No Mo; T2 N1 Mo; T1 N2 Mo
Stadio Iib	T4a No Mo; T3 N1 Mo; T2 N2 Mo; T1 N3 Mo
Stadio IIIa	T4a N1 Mo; T3 N2 Mo; T2 N3 Mo
Stadio IIIb	T4b No Mo; T4b N1 Mo; T4a N2 Mo; T3 N3 Mo
Stadio IIIc	T4a N3 Mo; T4b N3 Mo; T4b N3 Mo
Stadio IV	ogni T, ogni N, M1

TNM VII edizione  
AJCC 2010

SEER 1973-2005

# *Come migliorare la prognosi dei pazienti con carcinoma gastrico radicalmente operati*



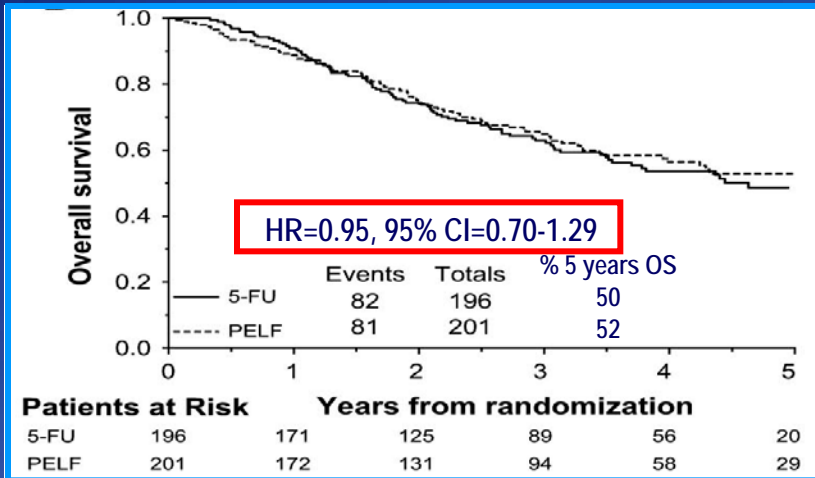
## CT postoperatoria

Meta-analyses	Studies (n)	Patients (n)	Odds ratio (CI)	Reduction of mortality (%)
Hermans 93	11	2096	0.82 (0.78-1.08)	18%
Earle 99	13	1990	0.80 (0.66-0.97)	20%
Mari 00	21	3658	0.82 (0.75-0.89)	18%
Janunger 02	21	3962	0.84 (0.74-0.9)	16%
Panzini 02	18	3118	0.72 (0.62-0.84)	28%

**Absolute benefit in OS at 5 years: 4%**

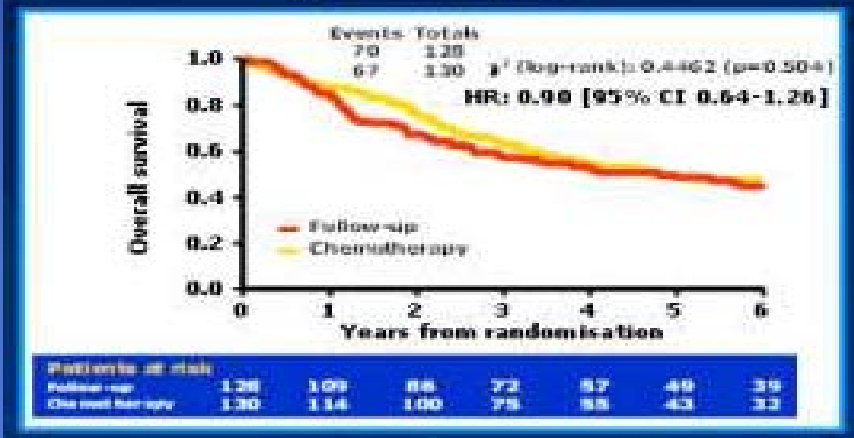
# CT postoperatoria

## Adjuvant Treatment of High-Risk, Radically Resected Gastric Cancer Patients With 5-Fluorouracil, Leucovorin, Cisplatin, and Epirubicin in a Randomized Controlled Trial



Cascinu S, JNCI 2007

GOIRC



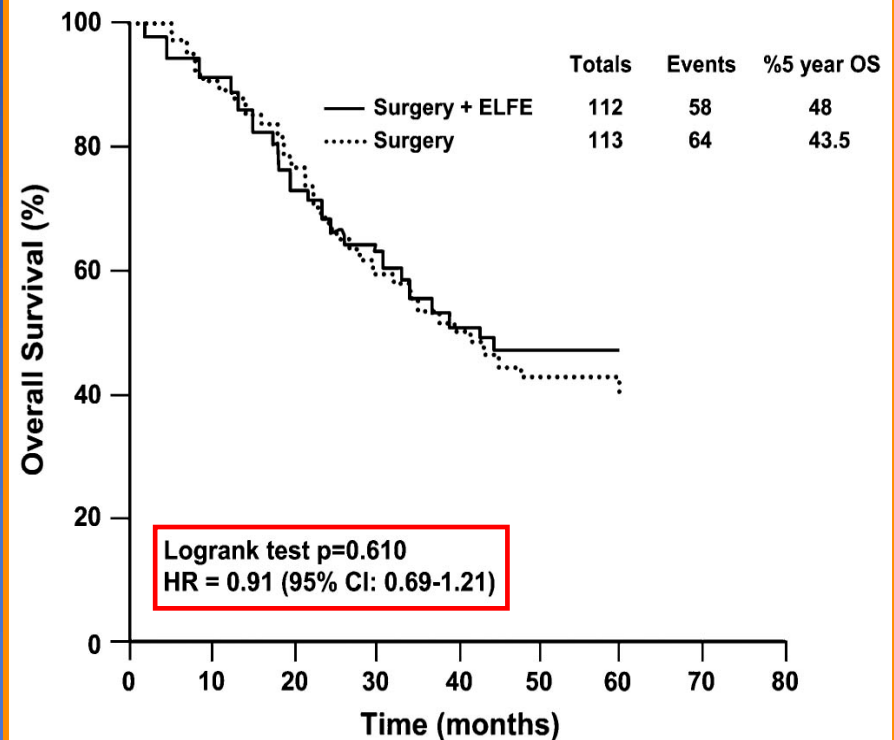
DI Costanzo F, JNCI 2008

original article

Annals of Oncology  
doi:10.1093/annonc/mdm128

## Adjuvant chemotherapy with epirubicin, leucovorin, 5-fluorouracil and etoposide regimen in resected gastric cancer patients: a randomized phase III trial by the Gruppo Oncologico Italia Meridionale (GOIM 9602 Study)

Overall survival by arm Intention-to-treatment population.



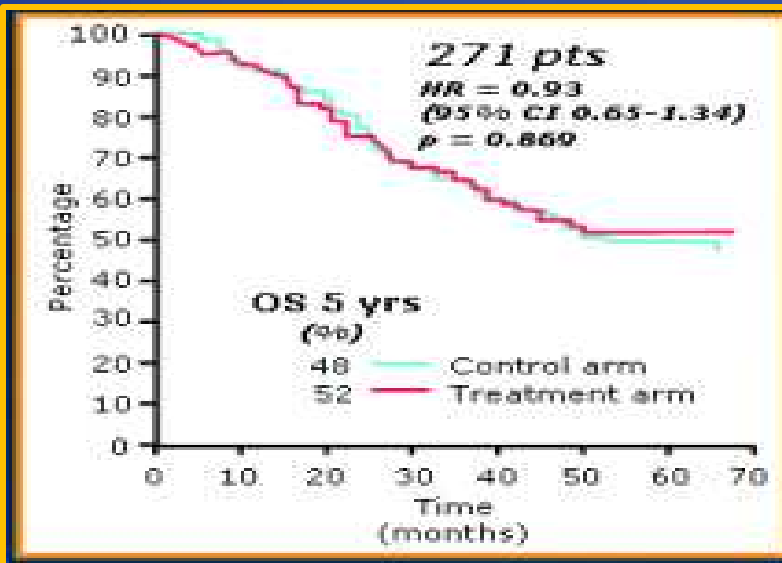
De Vita F, Ann Oncol 2007

# CT postoperatoria



Original article

Adjuvant chemotherapy in gastric cancer: 5-year results of a randomised study by the Italian Trials in Medical Oncology (ITMO) Group

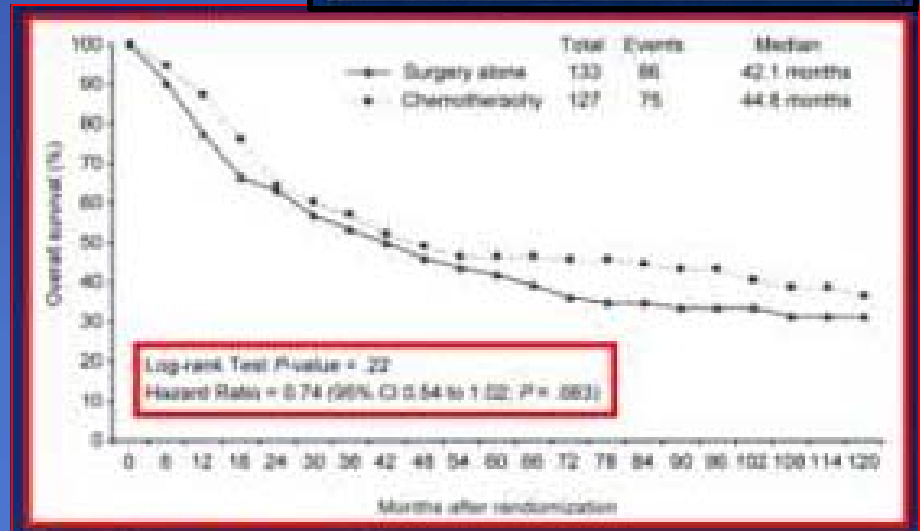


Bajetta E, Ann Oncol 2002



Original article

Adjuvant chemotherapy with 5-fluorouracil and cisplatin compared with surgery alone for gastric cancer: 7-year results of the FFCD randomized phase III trial (8001)



Bouchè O, Ann Oncol 2005

# CT postoperatoria

Trial	Control arm 5 year OS	Experimental arm 5 year OS
GOIM 9602	20	35
ITMO	30	45
FFCD 8801	40	55
GISCAD	20	35
GOIRC	30	50

**Increase in 5 year OS**

**15-20%**

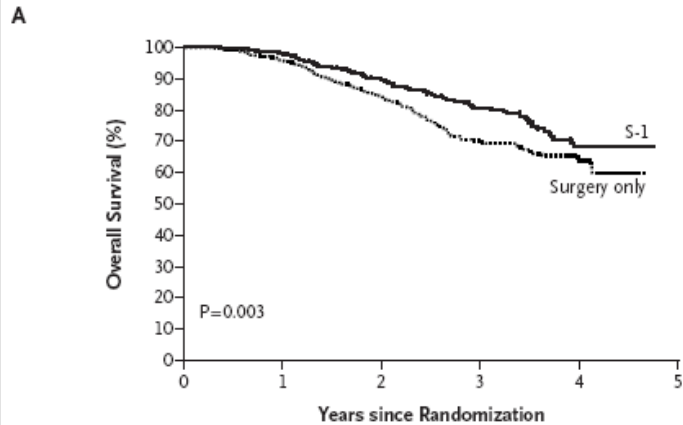
**Survival benefit from meta-analysis**

**4%**

## ORIGINAL ARTICLE

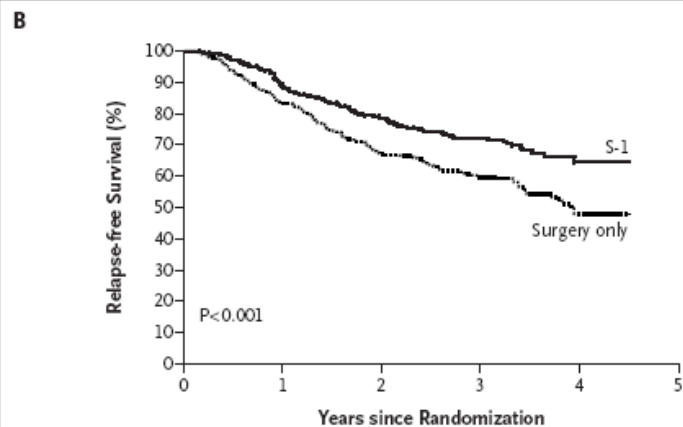
## Adjuvant Chemotherapy for Gastric Cancer with S-1, an Oral Fluoropyrimidine

Shinichi Sakuramoto, M.D., Mitsuru Sasako, M.D., Toshiharu Yamaguchi, M.D., Taira Kinoshita, M.D., Masashi Fujii, M.D., Atsushi Nashimoto, M.D., Hiroshi Furukawa, M.D., Toshifusa Nakajima, M.D., Yasuo Ohashi, Ph.D., Hiroshi Imamura, M.D., Masayuki Higashino, M.D., Yoshitaka Yamamura, M.D., Akira Kurita, M.D., and Kuniyoshi Arai, M.D., for the ACTS-GC Group\*



## No. at Risk

S-1	529	515	270	196	46
Surgery only	530	504	352	163	40



## No. at Risk

S-1	529	463	290	145	25
Surgery only	530	437	252	111	21

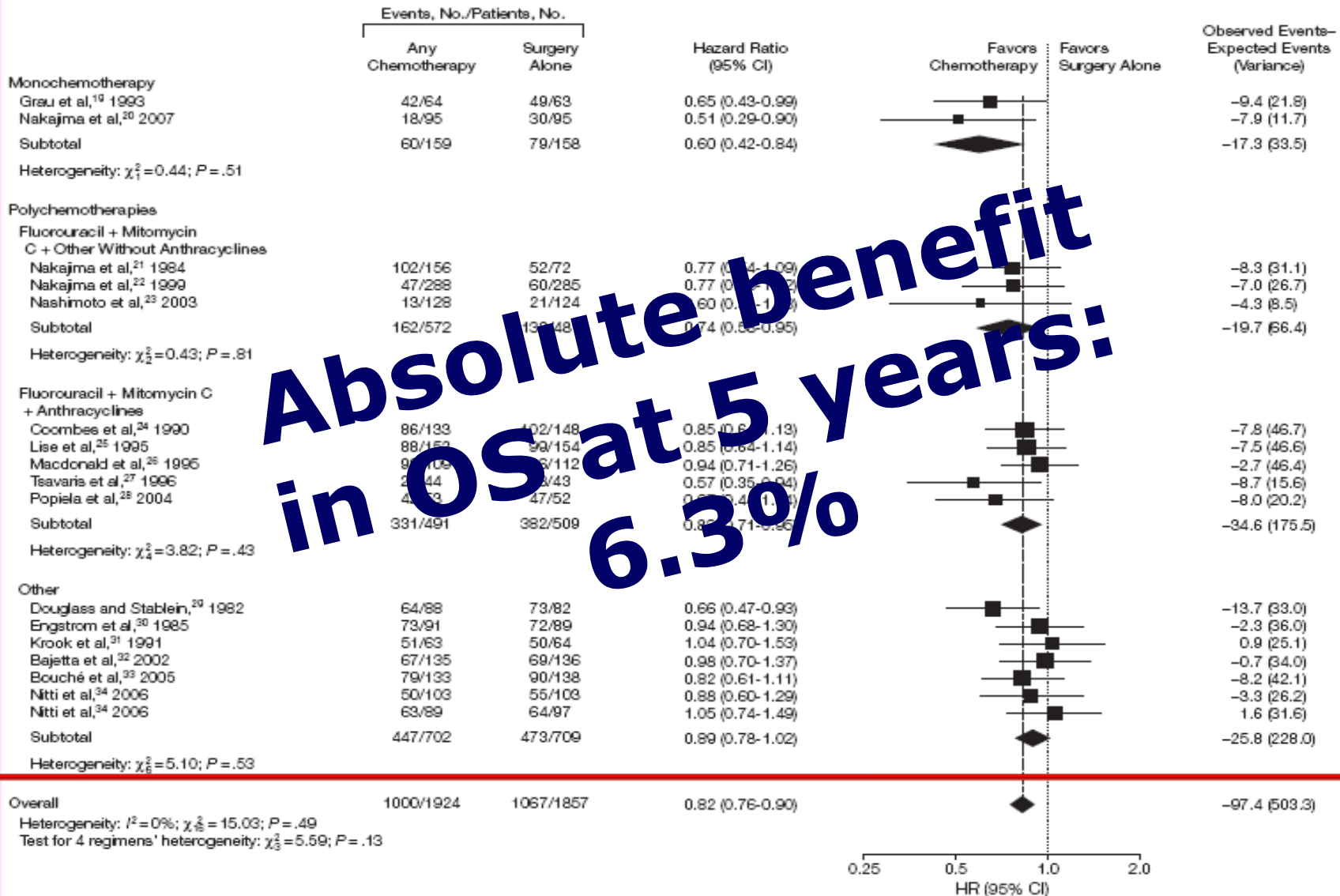
its success. These results for the use of S-1 should be interpreted with caution, however, particularly with regard to implications for clinical practice in a non-Japanese population. A Swedish meta-analysis, for example, found a small overall survival benefit with the use of adjuvant chemotherapy in Western and Asian studies, but when analyzed separately, no survival benefit was found in the subgroup of Western patients, whereas the magnitude of benefit in the treated Asian patients was greater and remained significant.<sup>8</sup>

## Attenzione ai polimorfismi enzimatici di popolazione!

Several considerations need to be taken in account before combination S-1 plus cisplatin is implemented as standard treatment in western countries. First, phase I/II trials of S-1 undertaken in the USA showed good activity and safety profiles, but also the need for a S-1 dose decrease because of polymorphic differences in the cytochrome P-450 2A6 enzyme (*CYP2A6*) gene between Asian and white patients.<sup>9</sup> Therefore, more cross-ethnic studies with common study design and assays are warranted, and caution should be used when interpreting findings between regions [A:OK?].



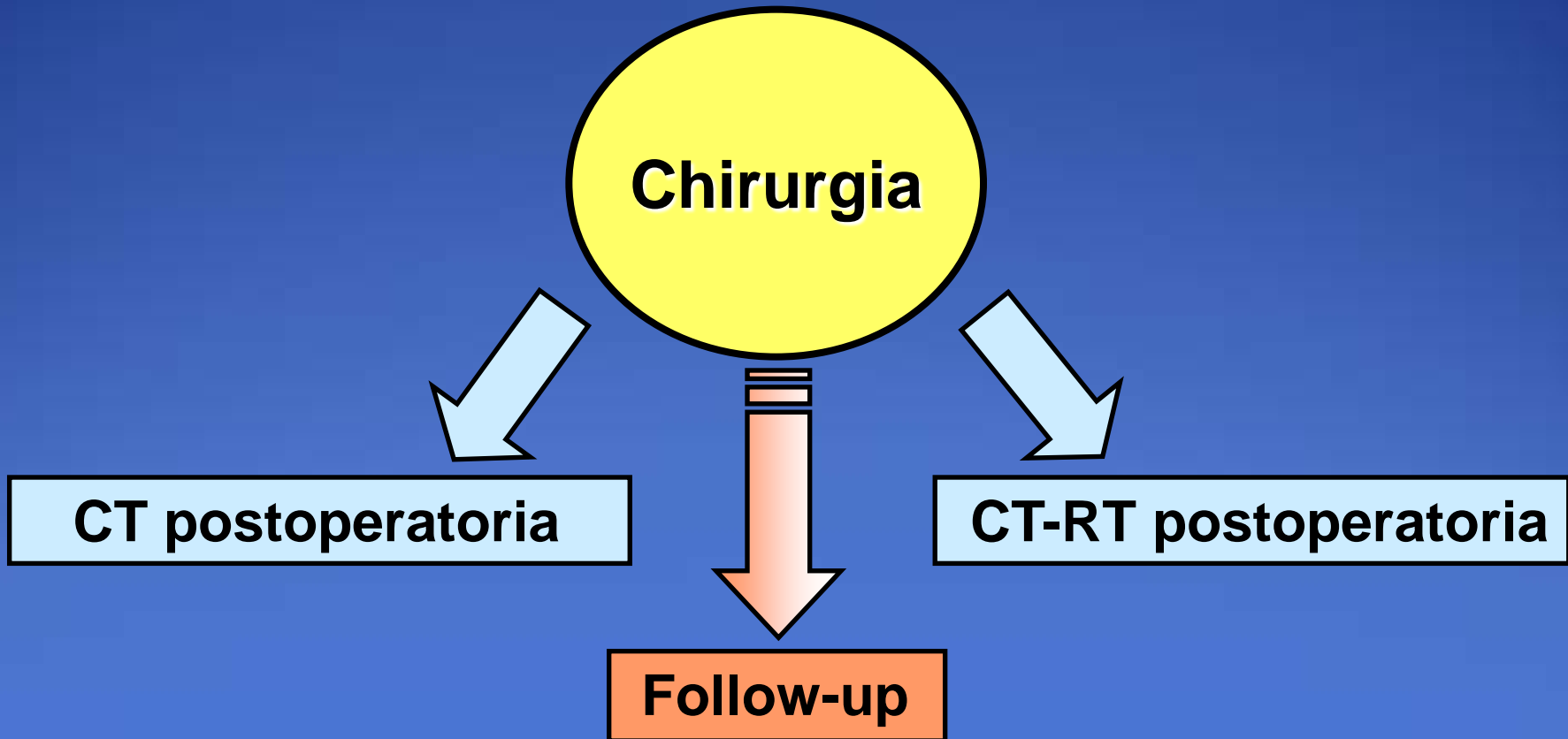
# GASTRIC project: meta-analisi su dati individuali di sopravvivenza e HR di terapia adiuvante vs chirurgia



# ITACA-S1: ...in attesa dei dati di efficacia

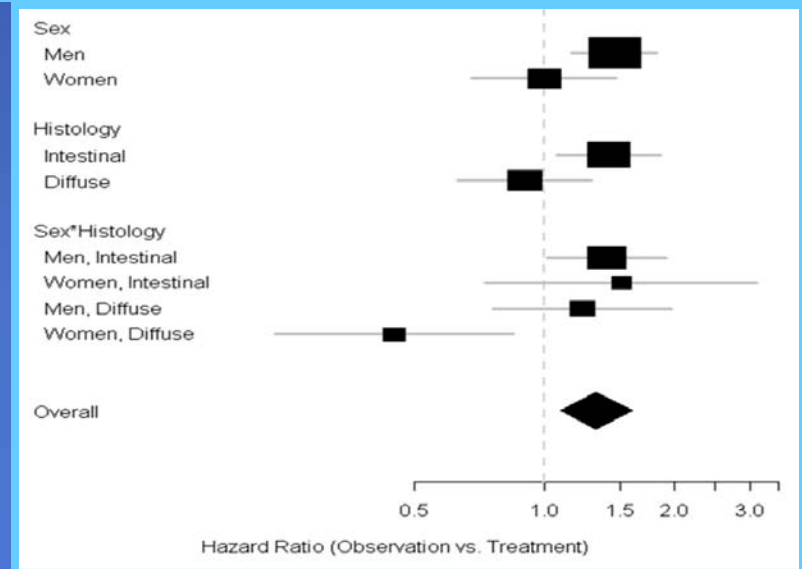
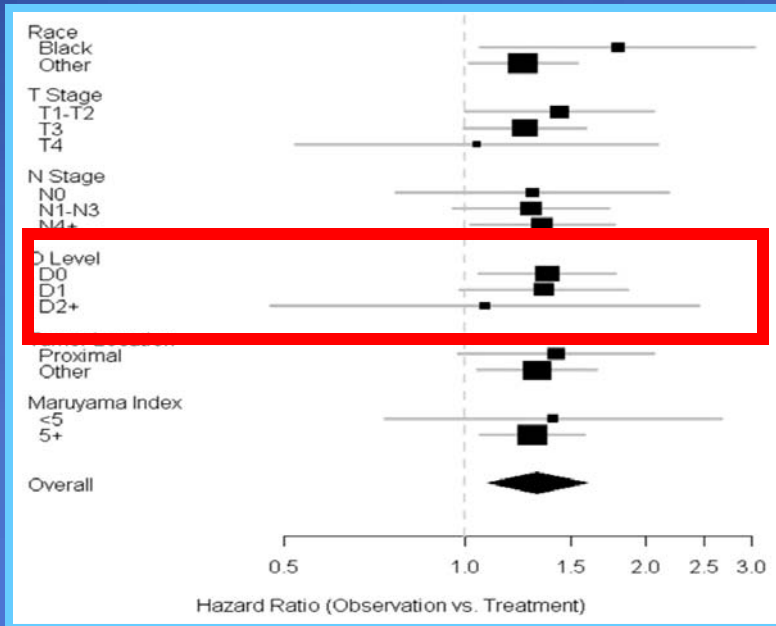
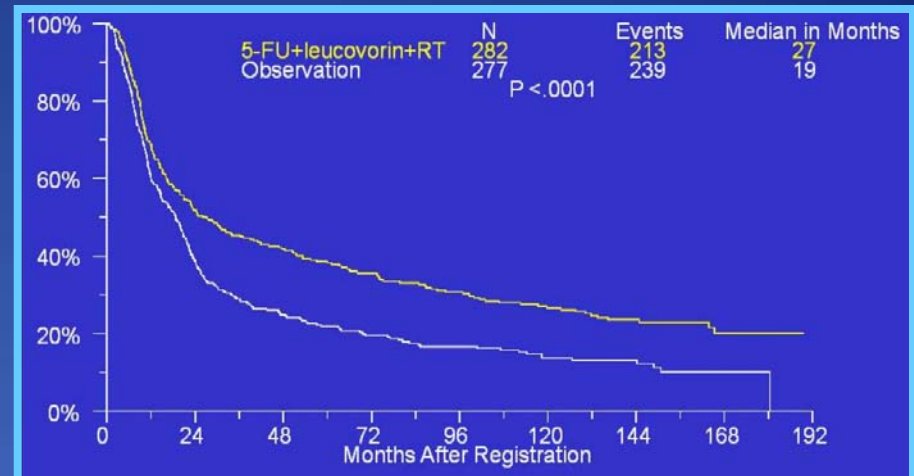
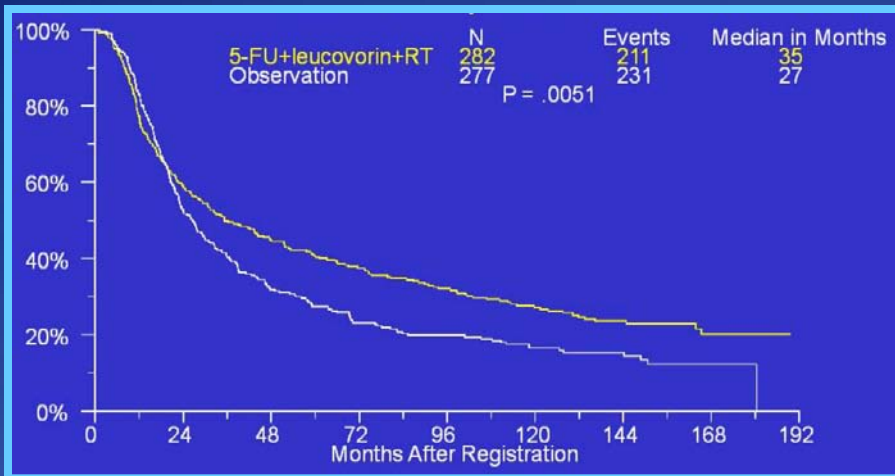


# *Come migliorare la prognosi dei pazienti con carcinoma gastrico radicalmente operati*

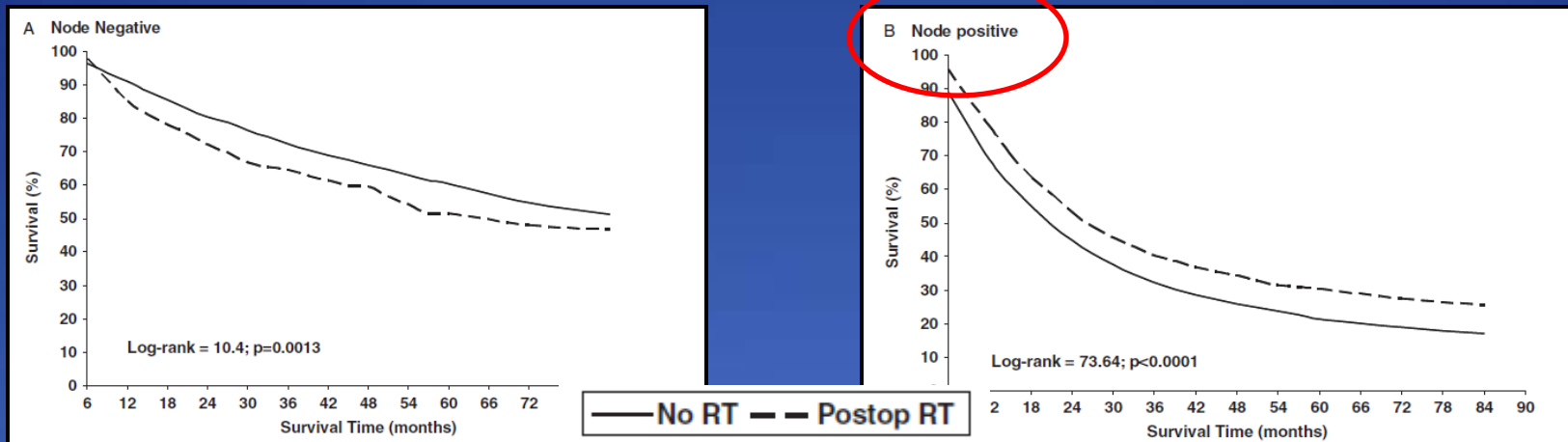


# CT-RT postoperatoria

## INT0016 trial: OS e DFS a 10 anni di follow up

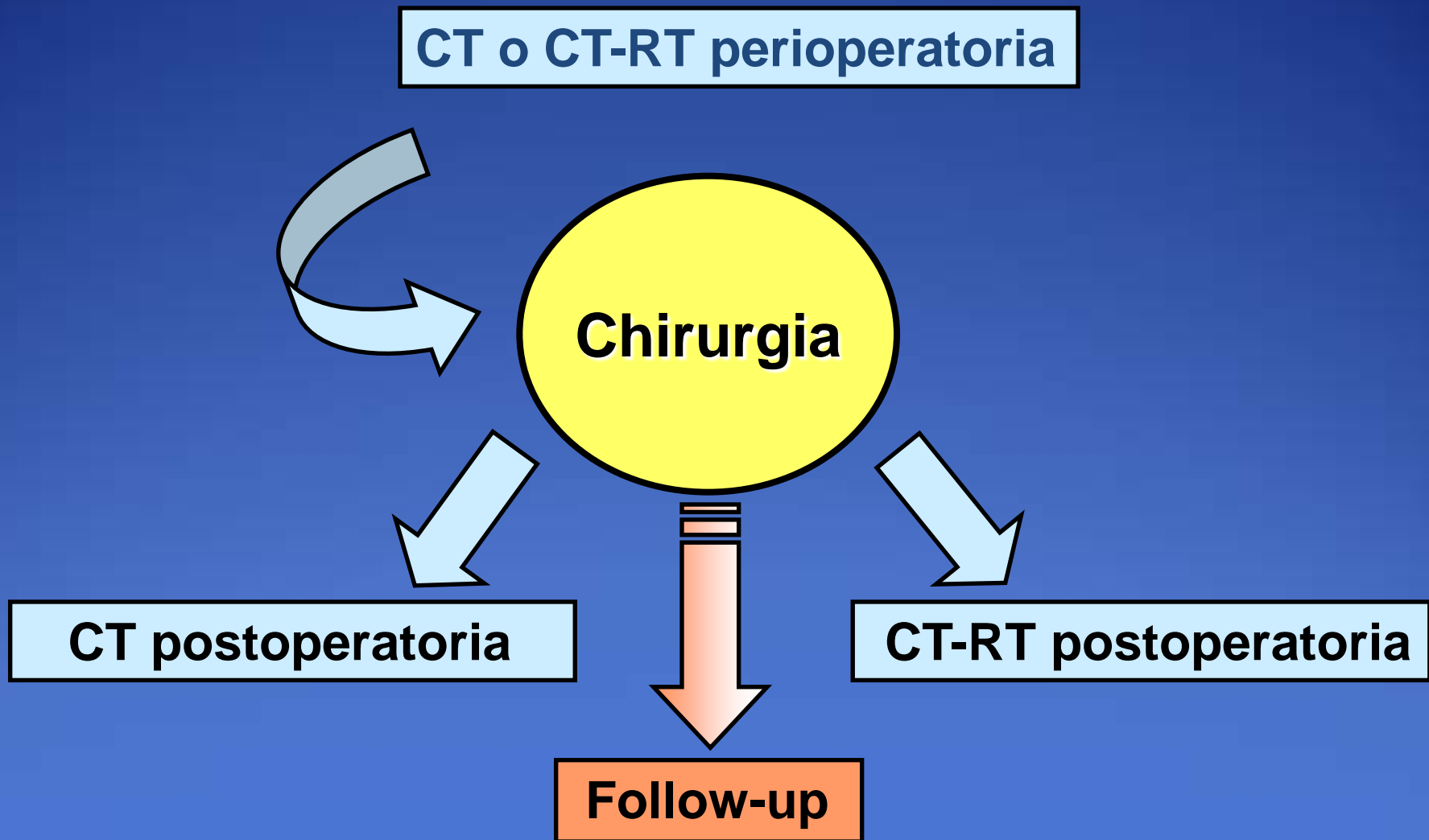


## Impatto della radioterapia adiuvante su OS: SEER database analysis



AJCC Stage	Median Survival (m)*		HR†	95% CI	P
	No RT	RT			
I	80	96	1.061	0.901-1.251	0.4828
IA	113	NR	1.182	0.611-2.285	0.6201
IB	56	96	0.824	0.693-0.979	0.0281
T2N0	58	95	0.921	0.756-1.118	0.4013
T1N1	43	100	0.548	0.377-0.796	0.0016
II	23	37	0.782	0.709-0.863	<0.0001
III	14	22	0.797	0.724-0.876	<0.0001
IIIA	16	23	0.795	0.715-0.885	<0.0001
IIIB	11	17	0.765	0.617-0.949	0.0147
IV	10	18	0.703	0.616-0.801	<0.0001

# *Come migliorare la prognosi dei pazienti con carcinoma gastrico radicalmente operati*



## *Razionale*

- *Aumentare il tasso di resecabilità chirurgica (downstaging/downsizing)*
- *Ridurre l'incidenza di metastasi a distanza*
- *Test di sensibilità al trattamento "in vivo"*
- *Controllo precoce dei sintomi*

# MAGIC-Trial

Cunningham D et al. N Engl J Med 2006

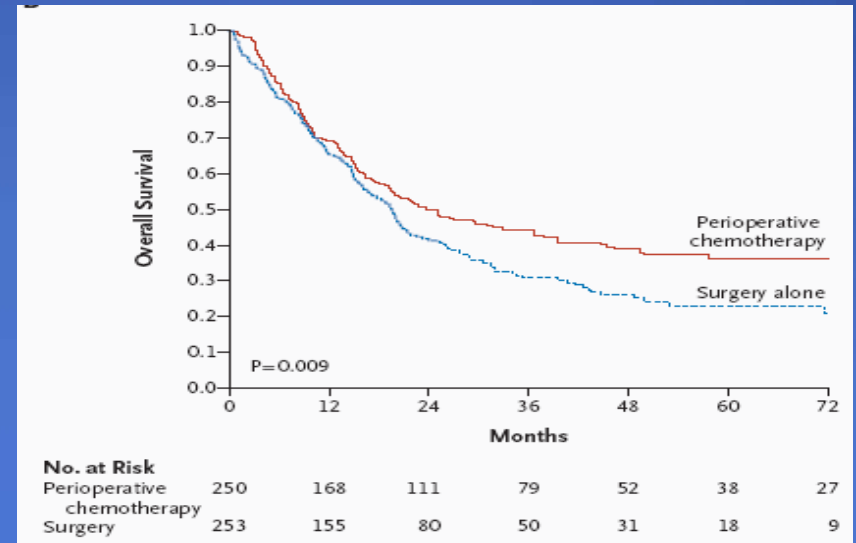
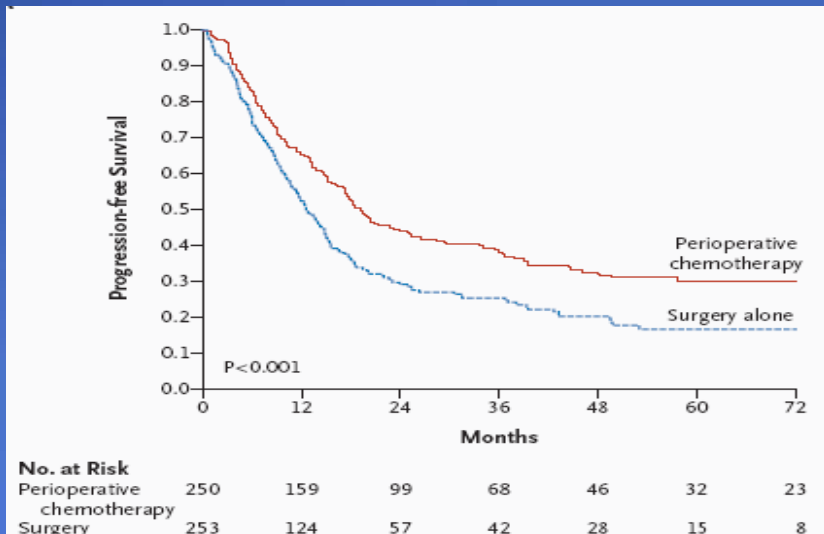
**St. II + III**  
**Stomaco +**  
**Giunzione +**  
**Esofago**  
**N = 503**  
**1994-2002**

**RANDOM**

**Chemioterapia:**  
**ECF x 3 → Chirurgia → ECF x 3**

**Obiettivo primario: OS a 5 anni**  
**23% → 36%**

**Chirurgia**





# FFCD 9703

Boige et al, ASCO 2007

**St. II + III**  
**Stomaco +**  
**Giunzione**  
**N = 224**  
**1995-2003**

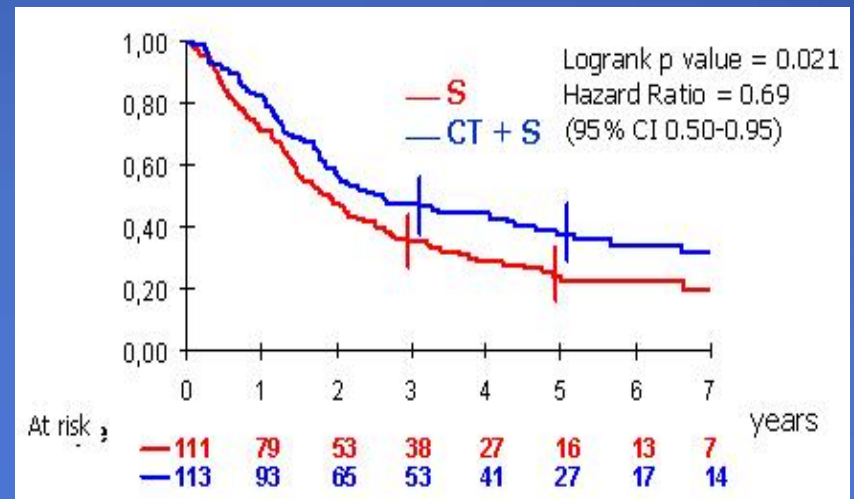
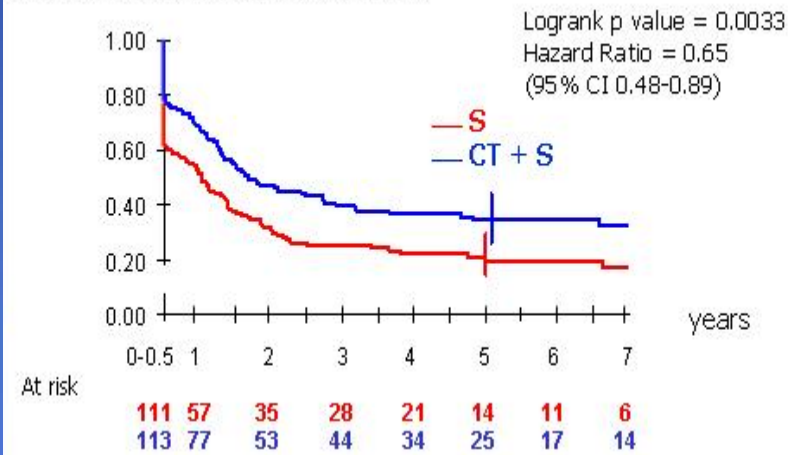
**RANDOM**

**Chemioterapia:**  
**CF x 2 → Chirurgia → CF x 4**

**Obiettivo primario: OS a 5 anni**  
**24% → 38%**

**Chirurgia**

DFS from landmark time of 6 months



# Studio ITACA-S2

## (Intergroup Trial in Adjuvant Chemotherapy for Adenocarcinoma of the Stomach)

ARM A

*CT peri-operatoria*

ARM B

*CT post-operatoria*

ARM C

*CT peri-operatoria +  
CT-RT post-operatoria*

ARM D

*CT post-operatoria +  
CT-RT post-operatoria*

CT: EOX/ECF regimens  
CT-RT: 5-FU/capecitabina

# *“Open questions” nel management multidisciplinare del cancro gastrico*

- ✓ Quali farmaci e quali combinazioni
- ✓ Ruolo delle terapie biologiche
- ✓ Approcci integrati con RT
- ✓ Adeguato staging preoperatorio
- ✓ Selezione dei pazienti

**Grazie per l'attenzione**