

Neoadjuvant / Adjuvant Treatment in Gastric Cancer

The Surgical Point of View

William Allum

William Allum

Conflict of Interest

Honoraria

Lilly

Nestle

Taiho



R0 Resection

A surgical procedure in which there is no evidence of macroscopic residual tumour in the tumour bed, lymph nodes and/or distant sites with microscopic negative resection margins



Surgery in Gastric Cancer

Surgery is the primary curative treatment of gastric cancer

Extended lymph node dissection (D2) is of benefit

Following curative resection the incidence of locoregional recurrence is high

Neoadjuvant Therapies

Surgery Issues

Advantages

- Enhance resection
- Better tolerance / compliance
- Improved nutrition / performance status
- Improved survival

Disadvantages

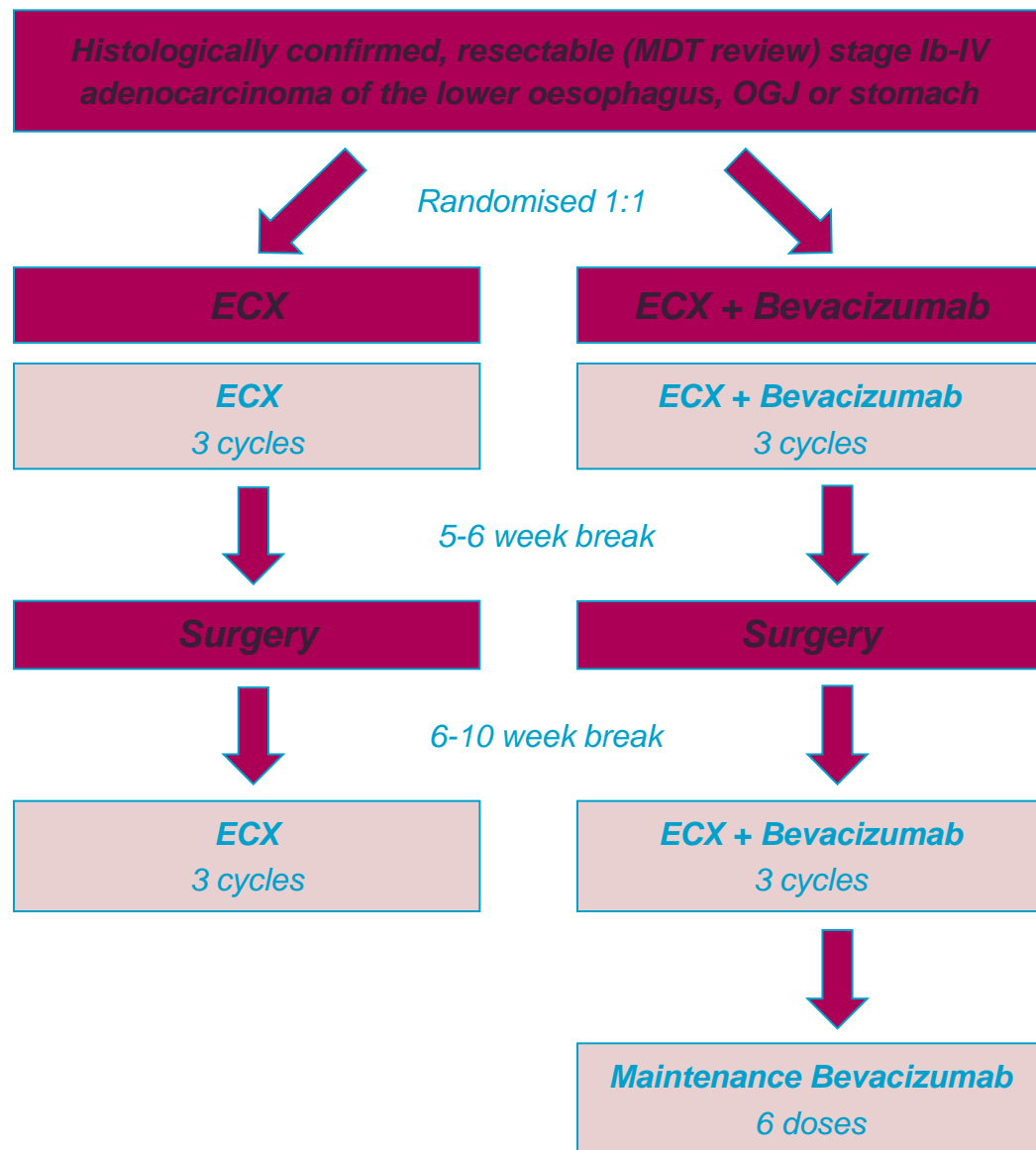
- Toxicity
- Postoperative complications
- Non-response
- Disease progression

Gastric Cancer Neoadjuvant - Results

	Ro Resection		Pathology Stage	
	Treated	Control	Treated	Control
MAGIC	79%	70%	T1/2: 52% No/1: 84%	T1/2: 38% No/1: 76%
FFCD 9703	87%	74%	T1/2: 39% No: 33%	T1/2: 32% No: 20%
EORTC 40954	82%	67%	T1/2: 66% No: 38.6%	T1/2: 50% No: 19%



ST03 trial design



Chemotherapy regimens

21-day cycles

ECX

- Epirubicin 50mg/m² IV on day 1
- Cisplatin 60mg/m² IV on day 1
- Capecitabine 1250mg/m² PO daily

ECX + Bevacizumab

- Bevacizumab 7.5mg/kg IV on day 1 added to each ECX cycle

Surgery in ST03

Resectability

		ECX (n=533)	ECX+B (n=530)
Resection performed	Yes	447 (84%)	425 (80%)
Reason for no resection	Found to be inoperable	25 (5%)	30 (6%)
	Disease progression	20 (4%)	18 (3%)
	Death	10	15
	Withdrawal / refusal	8	13
	Not fit / comorbidity	6	6
	Other reason	17	23



Surgery in ST03

Radicality of Resection

		ECX (n=533)		ECX+B (n=530)		p-value
Extent of resection	R0	315	(74%)	301	(75%)	0.844
	R1	108	(26%)	100	(25%)	
	No resection	86		105		
	Unavailable	24		24		
Lymph node dissection	<15 nodes	79	(19%)	62	(15%)	
	15-24 nodes	143	(34%)	134	(33%)	
	25+ nodes	204	(48%)	206	(51%)	
	Unavailable	21		23		

Common serious toxicities

	ECX	ECX+B
Pre-operative chemotherapy	N=527	N=525
Any grade 3+ toxicity	47%	50%
Any fatal toxicity	<1%	<1%
Neutropenia	27%	26%
Lethargy	8%	8%
PPE	6%	6%
Nausea	7%	4%
Infection with neutropenia	6%	5%
Diarrhoea	5%	6%
Vomiting	6%	3%



Toxicities reported during chemotherapy, at grade 3 or above, in at least 5% of patients

Post-operative Morbidity & Mortality

	ECX		ECX+B		Total	
	Overall	LT	Overall	LT	Overall	LT
Any complication	48%	7%	56%	8%	52%	8%
Revisional operation	8%		9%		9%	
Wound healing complications	7%	<1%	12%	1%	10%	<1%
Wound infection (superficial)	8%	<1%	9%	<1%	9%	<1%
Cardiac complications	5%	2%	7%	1%	6%	2%
Intra-abdominal sepsis	4%	1%	4%	2%	4%	1%
Wound infection (deep)	3%	1%	3%	1%	3%	1%
Haemorrhage requiring transfusion	3%	1%	3%	2%	3%	1%
PE	1%	0%	2%	0%	2%	0%
DVT	1%	0%	2%	0%	1%	0%
TOTAL	440		426		866	

LT = life-threatening

Post-operative mortality	Death within 30 days	14 / 447 (3%)	10 / 425 (2%)
	Death within 90 days	21 / 447 (5%)	21 / 425 (5%)

Anastomotic leaks

Surgical procedure	ECX	ECX+B	Total
	Leaks / Patients (%)	Leaks / Patients (%)	Leaks / Patients (%)
Oesophago-gastrectomy	20 / 229 (9%)	51 / 218 (23%)	71 / 447 (16%)
Total gastrectomy	17 / 137 (12%)	19 / 129 (15%)	36 / 266 (14%)
Sub-total gastrectomy	0 / 15 (0%)	1 / 16 (6%)	1 / 31 (3%)
Distal gastrectomy	1 / 43 (2%)	2 / 41 (5%)	3 / 84 (4%)
Other procedures	1 / 16 (6%)	2 / 22 (9%)	3 / 38 (8%)
TOTAL	39 / 440 (9%)	75 / 426 (18%)	114 / 866 (13%)

- 30-day mortality: 2 / 39 ECX (5%), 8 / 75 ECX+B (11%)
- Revisional operations: 20 / 39 ECX (51%), 24 / 75 ECX+B (32%)
- 39% occurred within 5 days of surgery, 78% within 10 days
- No other clinical factors identified (no centre/surgeon effect)



Adjuvant Therapies

Surgery Issues

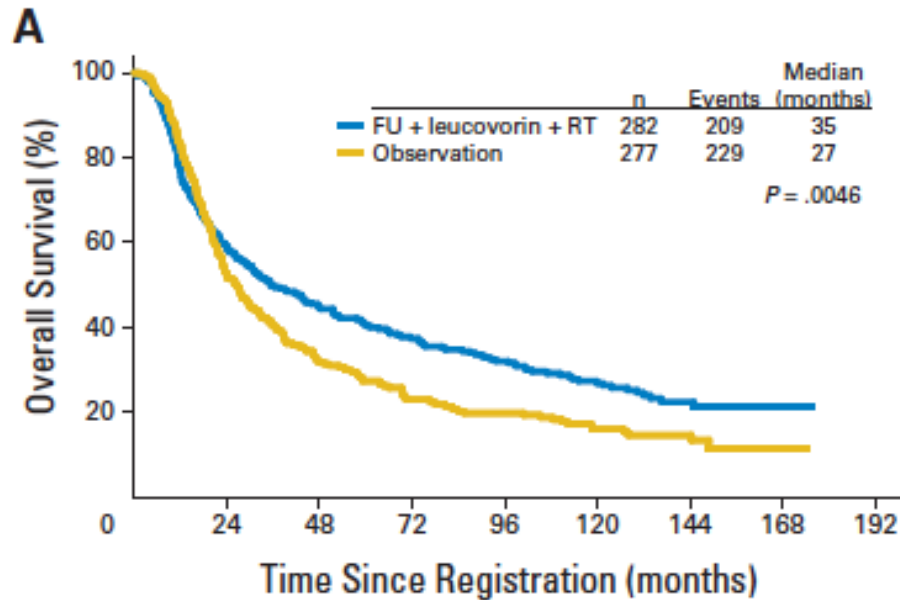
Advantages

- Stage known
- Low tumour volume

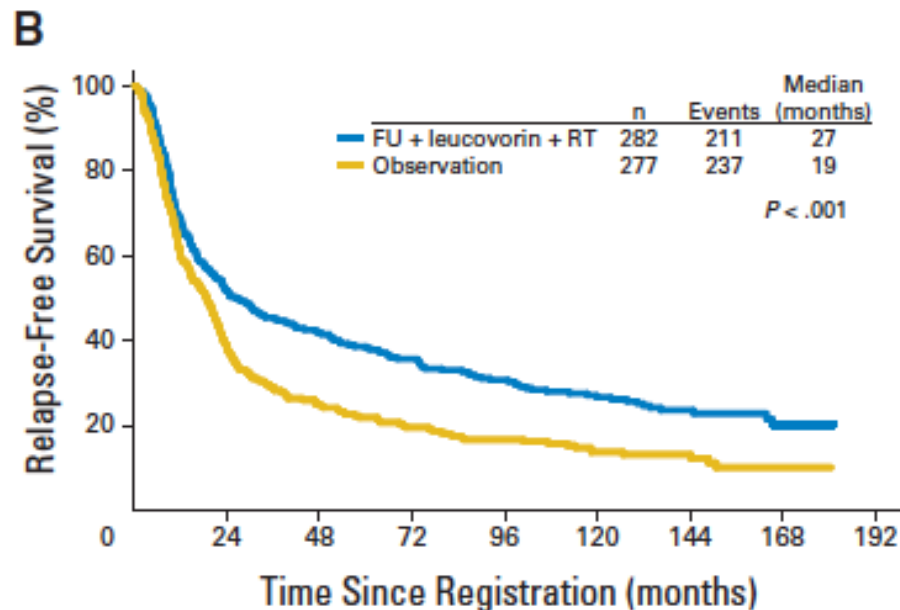
Disadvantages

- Postoperative complications
- Treatment planning
- Toxicity / tolerance

Inter¹⁴group 0116 chemoradiation in resected gastric cancer



A: Overall Survival



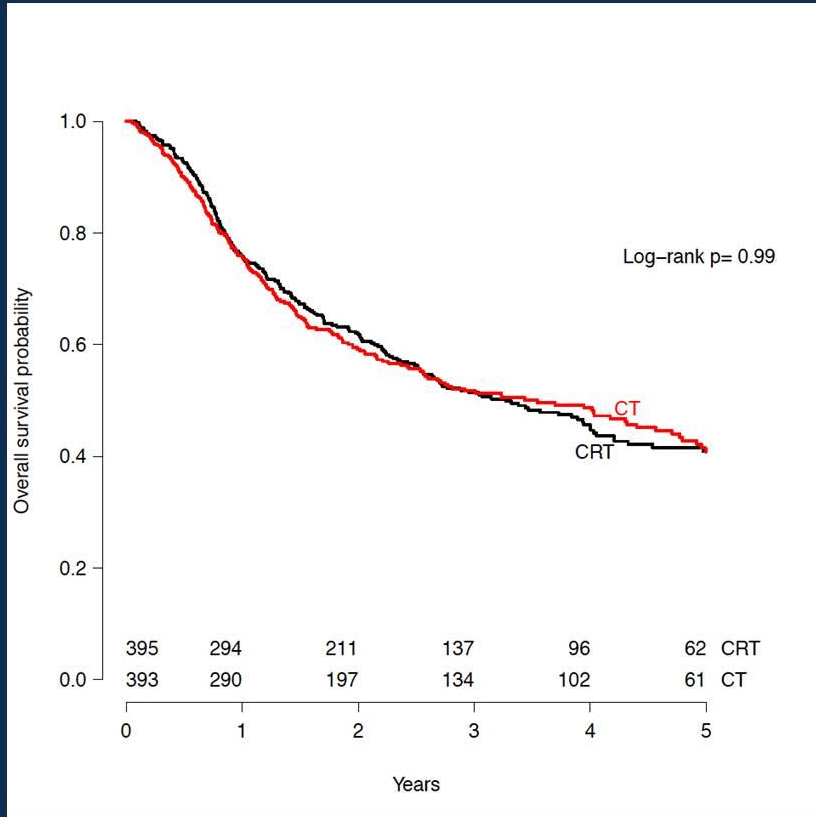
B: Relapse free survival

Intergroup 0116

Gastric Resection

PROCEDURE	PROPORTION IN STUDY
D0	54%
D1	36%
D2	10%

Results: Overall Survival



	CT	CRT
5-year OS (%)	40.8	40.9
Median OS (yrs)	3.5	3.3

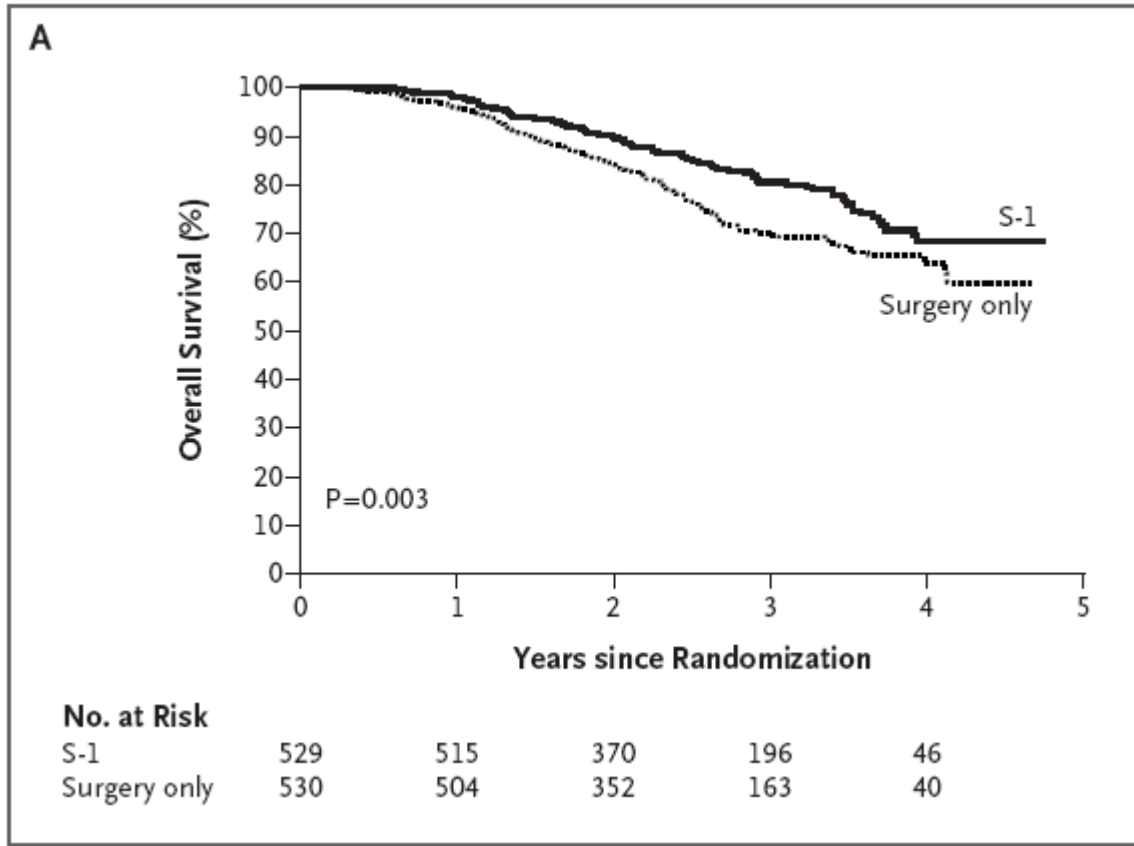
PRESENTED AT: **ASCO ANNUAL MEETING '16**

Slides are the property of the author. Permission required for reuse.

Completion of Planned Adjuvant Treatment

	Proportion
MAGIC	Chemo 41%
FFCD	Chemo 50%
STo3	Chemo 37%; Chemo +Bevacizumab 37%
INT 0116	CRT 65%
ARTIST	Chemo 75%; CRT 81.7%
CRITICS	Chemo 47%; CRT 52%

Gastric Cancer Adjuvant Trials



Median follow-up: 3 years

3 year survival

S-1 80.5%

Surgery 70.1%

HR 0.62 (0.50 – 0.77)

P<0.0001

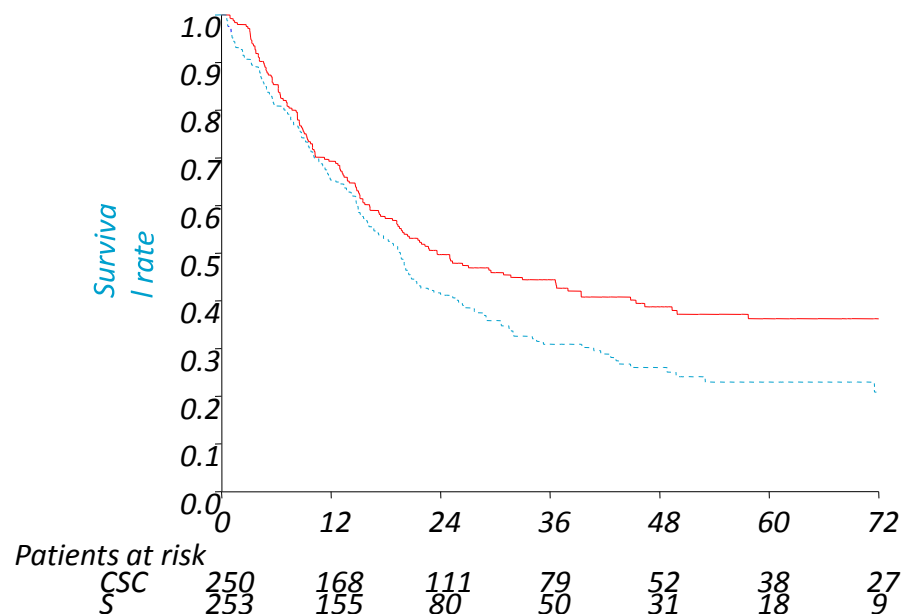


Sakuramoto et al 2007

Surgery Outcomes

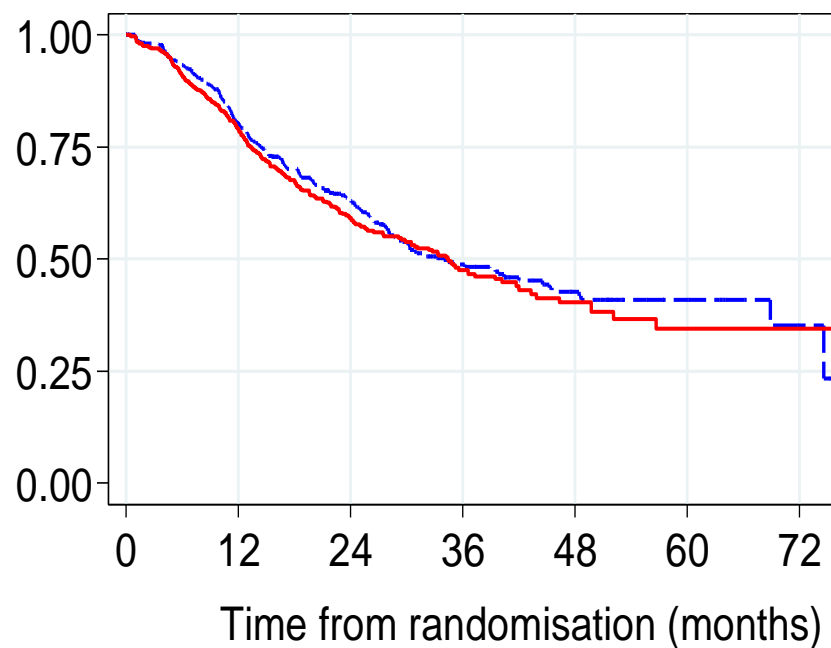
MAGIC

Median Survival: 20 / 24mo



STO3

Median Survival: 34 mo

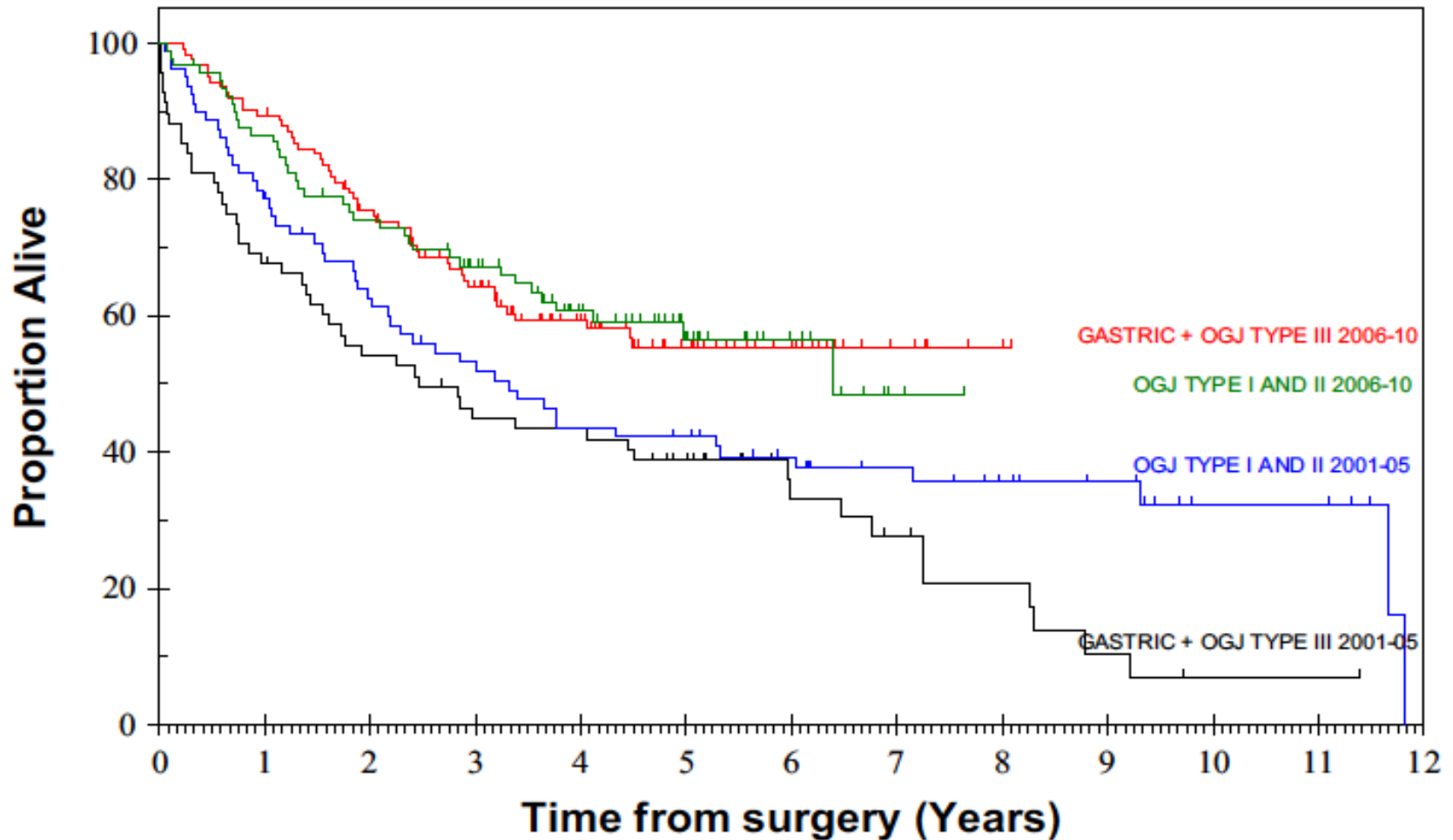


N							
CX	533	394	226	97	49	17	5
+B	530	383	208	98	41	14	6

--- ECX — ECX+B

RMH Overall Survival 2001-2010

Overall Survival by Site and Period of Surgery



Summary

- Preoperative chemotherapy
 - Better compliance – preferred dose
 - Better response evaluation
 - Better tolerance
 - More R0 resections
- Postoperative therapy
 - High risk for loco-regional relapse (R1)
 - High risk for distant metastases
 - Limited pathological response
- Optimal surgery in high volume centres



Tailored Treatment

Treatment modality varies:

- Stage
- Patient risk
- Surgical volume
- Available chemotherapy
- Quality of radiotherapy

“the result of treatment for locally advanced gastric cancer is the sum of the effect of local tumour control by surgery, with or without radiotherapy and / or systemic chemotherapy”

Takeshi Sano 2007

Thank you for your attention

