Neo-Adjuvant vs Adjuvant approach in gastric cancer

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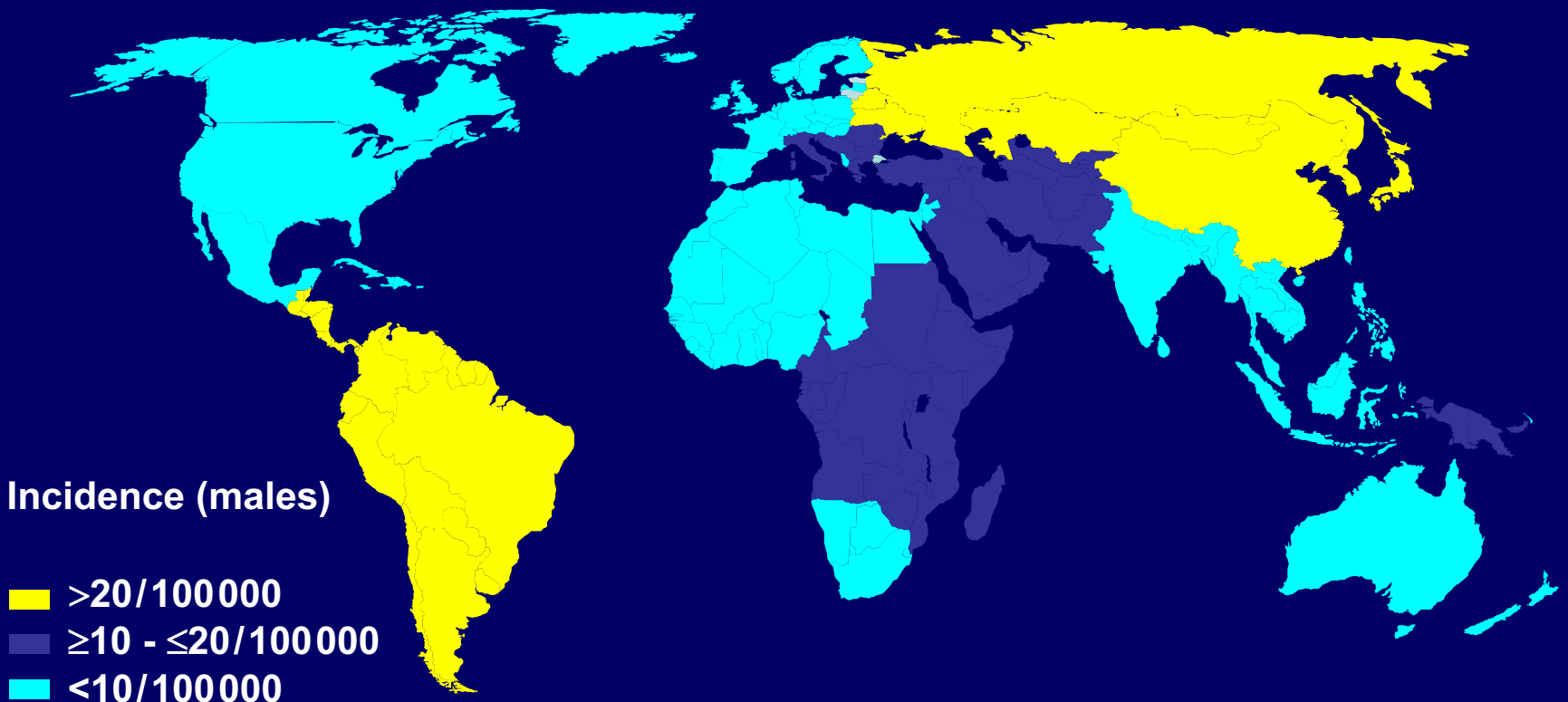
Gastric cancer: a global disease

- 4th most common malignant disease ~ 930,000
- 2nd most common cause of cancer-related death worldwide ~700,000
- Falling incidence of distal gastric cancer
- Increasing incidence of proximal gastric cancer
- Wide geographical variation



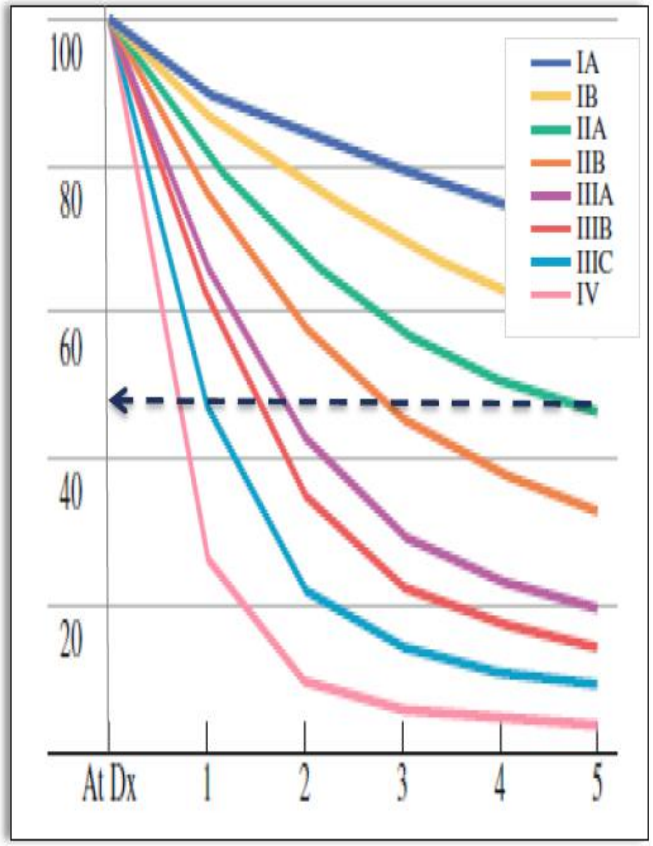
www.cancer.gov

Kamangar F et al. J Clin Oncol 2006;24:2137–50

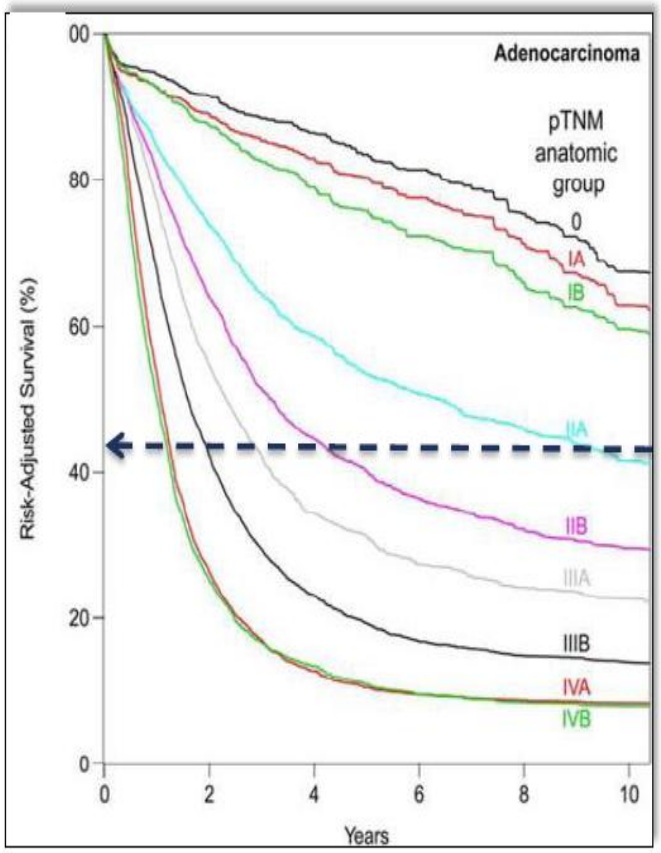
Gastric cancer stage and survival rates

Stage	TNM[1]	5-year survival rates (%)
0	Tis, N0, M0	89
IA	T1, N0, M0	78
IB	T1, N1, M0 or T2a/b, N0, M0	58
II	T1, N2, M0 or T2a/b, N1, M0 or T3, N0, M0	34
IIIA	T2a/b, N2, M0 or T3, N1, M0 or T4, N0, M0	20
IIIB	T3, N2, M0, T1–3, N3, M0, or T4, N1–3, M0 or	8
IV	any T, any N, M1	0

SURVIVAL FROM OG CANCER WITH SURGERY ALONE



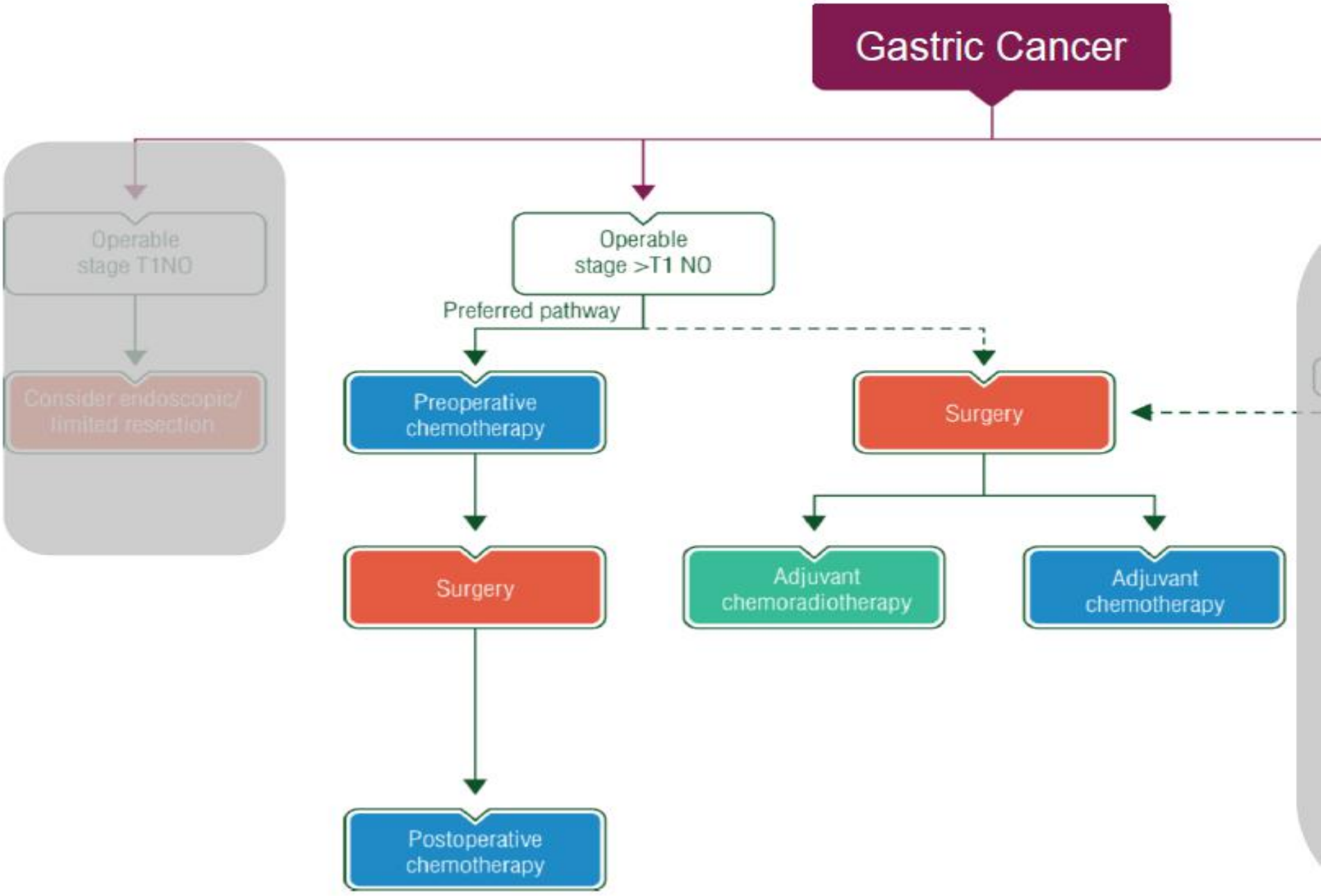
Gastric cancer OS surgery alone



Oesophageal adeno OS surgery alone

Treatment in addition to surgery is required for most patients

ESMO GASTRIC CANCER GUIDELINES



NEOADJUVANT AND PERIOPERATIVE CHEMOTHERAPY

AIMS OF NEOADJUVANT AND PERI-OPERATIVE CHEMOTHERAPY

- Downstage the tumour
- Increase R0 resection rate
- Treat micrometastatic disease
- Improve overall survival

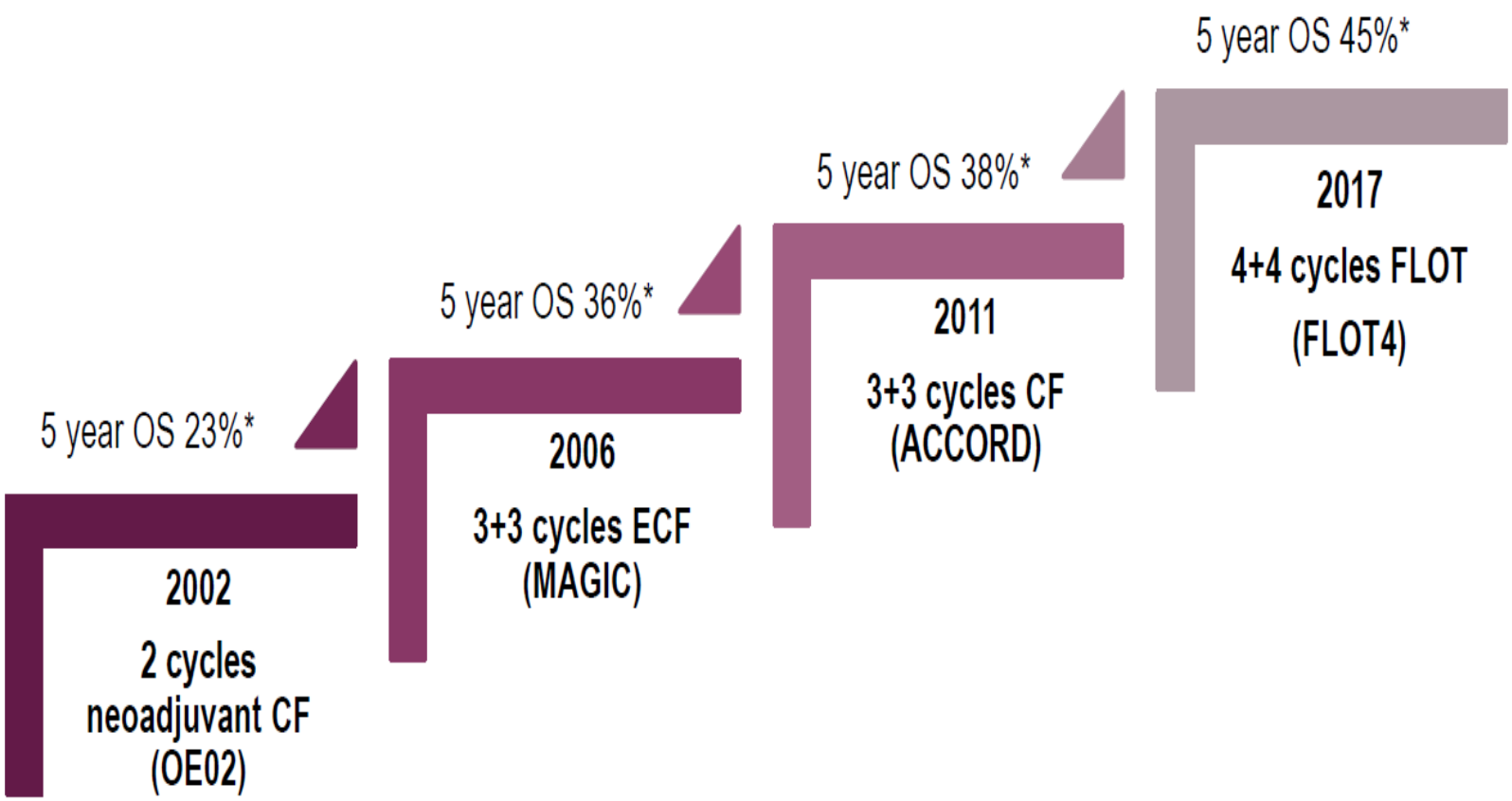
Neoadjuvant and perioperative chemotherapy is more commonly used in non-Asian countries where tumours are frequently locally advanced and require downstaging prior to successful resection

Peri-operative treatment in resectable patients

Disadvantages

- Risk of disease progression during pre-operative treatment
- Definitive surgery may be delayed if significant toxicity occurs
- Risk of increased peri-operative morbidity (NOT seen in MAGIC)

EVOLUTION OF NEOADJUVANT AND PERI-OPERATIVE CHEMOTHERAPY 2002 - 2019



PERI-OPERATIVE CHEMOTHERAPY VS. SURGERY ALONE MAGIC AND FFCD/FNLCC

Eligible patients

3 cycles preoperative ECF (n=250)

Surgery alone (n=253)

3-6 week break

Surgery

6-12 week break

3 cycles postoperative ECF

Eligibility criteria
Stage ≥ II gastric, GOJ, or lower oesophageal adeno (after 1999)
No metastases
ECOG 0-1

Eligible patients

2-3 cycles preoperative CF (n=113)

Surgery alone (n=111)

Surgery

3-4 cycles postoperative CF

Eligibility criteria
Lower oesophageal or GOJ adeno (gastric after 1998)
No metastases
ECOG 0-1

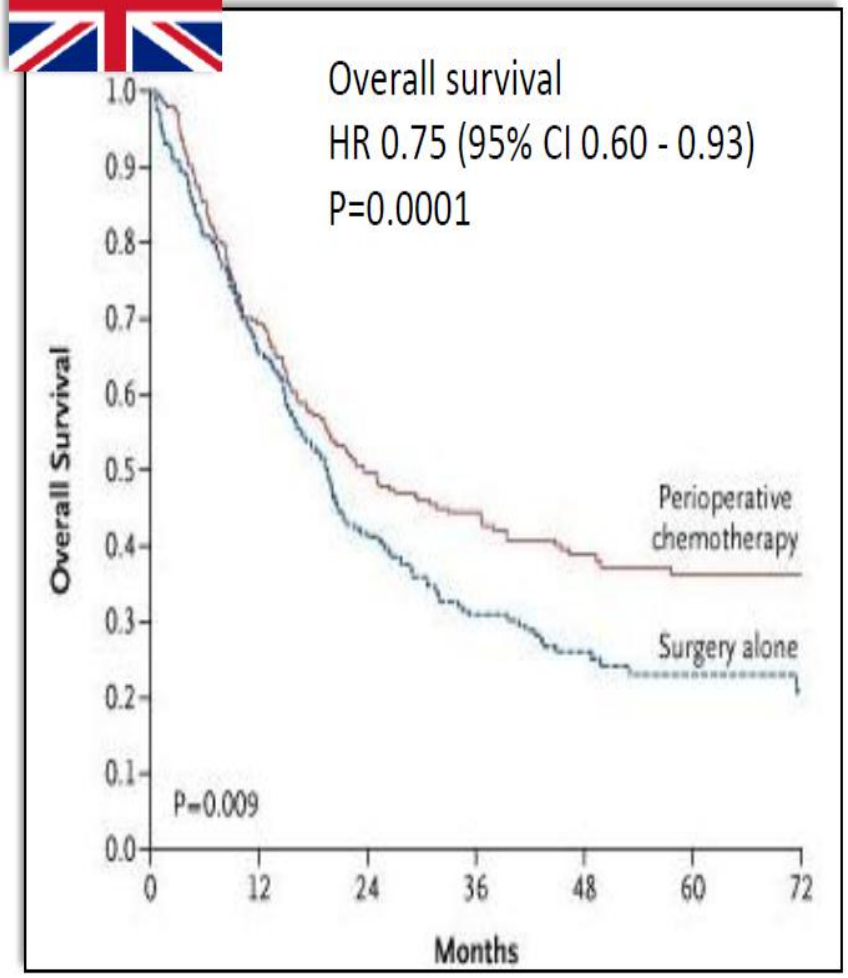
PERI-OPERATIVE CHEMOTHERAPY VS. SURGERY ALONE
EFFECT OF CHEMOTHERAPY ON POST-OPERATIVE STAGE

MAGIC post-operative patient characteristics		
	Surgery alone	Chemo + surgery
Surgery		↑ curative resections
Curative	66/250 (66%)	169/244 (69%)
Palliative	70/250 (28%)	44/244 (18%)
Other	17/250 (6%)	27/244 (13%)
ypT stage		↑ early T stage
T1	16/193 (8%)	27/172 (16%)
T2	55/193 (29%)	62/172 (36%)
T3	106/193 (55%)	75/172 (44%)
T4	16/193 (8%)	8/172 (4%)
ypN Stage (gastric)		↑ early N stage
N0	42/156 (27%)	42/135 (31%)
N1	68/156 (43%)	72/135 (53%)
N2	34/156 (23%)	19/135 (14%)
N3	12/156 (8%)	2/135 (2%)

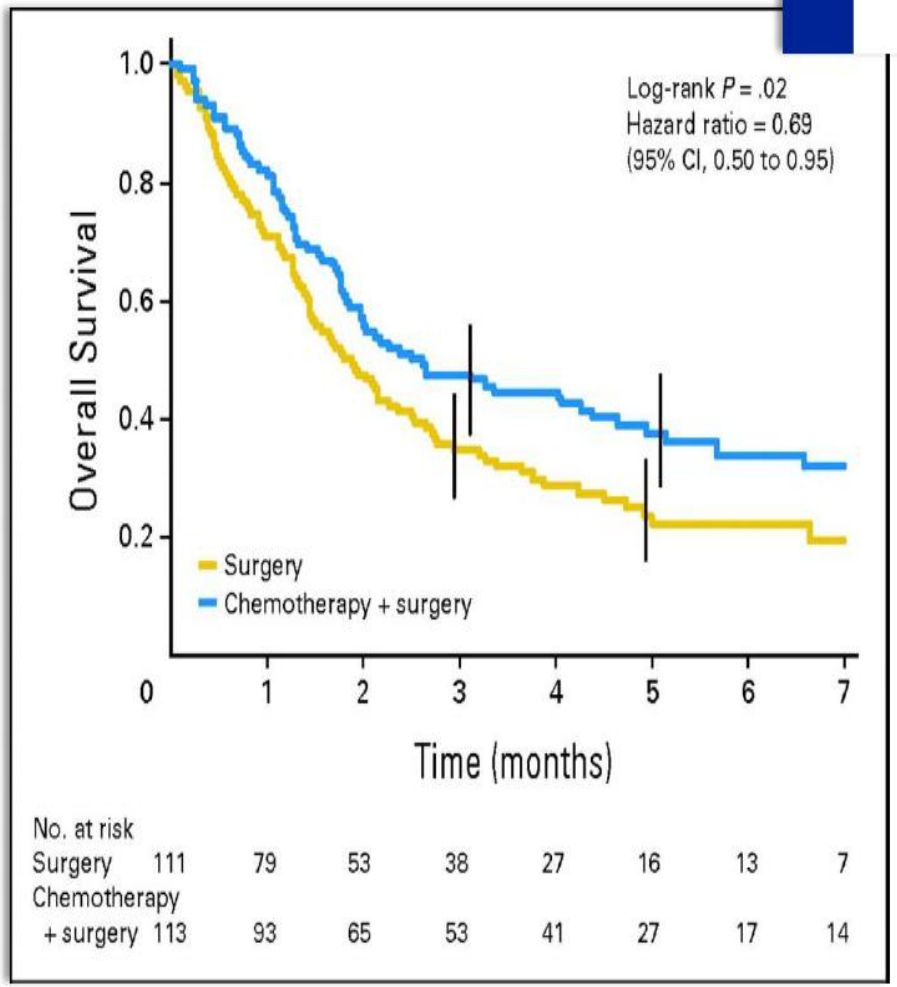
FFCD/FNCLCC post-operative patient characteristics		
	Surgery alone	Chemo + surgery
Surgery		↑ curative surgery
No resection	11 (10%)	7 (6%)
R0	81(74%)	95(87%)
R1	6 (5%)	4 (4%)
R2	11(10%)	2(2%)
Rx	1(1%)	1(1%)
ypT stage		↑ early T stage
T0	(8%)	3 (3%)
T1-2	(29%)	38 (39%)
T3-4	(55%)	57 (58%)
ypN Stage (gastric)		↑ early N stage
N0	17 (20%)	32(33%)
N+	68 (80%)	66(67%)

Peri-operative chemotherapy leads to tumour **downstaging**

PERI-OPERATIVE CHEMOTHERAPY VS. SURGERY ALONE
EFFECT OF CHEMOTHERAPY ON OVERALL SURVIVAL



Absolute gain in 5 year survival 13% (23% surgery alone to 36% chemotherapy plus surgery



Absolute benefit in OS 14% (24% surgery vs. 38% chemo + surgery)

AIO/FLOT4 TRIAL

- Gastric cancer or adenocarcinoma of the gastro-esophageal junction type I-III
- Medically and technically operable
- cT2-4/cN-any/cM0 or cT-any/cN+/cM0

STRATIFICATION

R

n=716

FLOT x4 - RESECTION - FLOT x4

FLOT: docetaxel 50mg/m2, d1; 5-FU 2600 mg/m², d1; leucovorin 200 mg/m², d1; oxaliplatin 85 mg/m², d1, every two weeks

ECF/ECX x3 - RESECTION - ECF/ECX x3

ECF/ECX: Epirubicin 50 mg/m2, d1; cisplatin 60 mg/m², d1; 5-FU 200 mg/m² (or capecitabine 1250 mg/m² p.o. divided into two doses d1-d21), every three weeks

Stratification: ECOG (0 or 1 vs. 2), location of primary (GEJ type I vs. type II/III vs. stomach), age (< 60 vs. 60-69 vs. ≥70 years) and nodal status (cN+ vs. cN-).

Primary endpoint OS (ITT)

WHO ARE THE PATIENTS IN FLOT4?

	ECF/ECX N=360		FLOT N=356	
Age				
median	62	-	62	-
>=70	87	24%	85	24%
Sex				
male	265	74%	268	75%
ECOG PS				
0	254	71%	246	69%
1	103	29%	109	31%
2	3	1%	1	<1%
Location				
GEJ Siewert type 1	85	24%	80	23%
GEJ Siewert type 2/3	115	32%	118	33%
Stomach	160	44%	158	44%

Median age 62, younger than most gastroesophageal patients

But...24% were >70 years

99%+ were PS 0-1

50:50 split stomach vs junctional adeno

FLOT IMPROVES SURGICAL OUTCOMES

	ECF/ECX (n=360)	FLOT (n=356)	
Resection surgery	313/360(87%)	336/356 (94%)	0.001
R0 resection rate	276/360 (77%)	300/356 (84%)	0.011
Any surgical complication	188/341 (55%)	188/345 (55%)	
Death 90 days	26 (8%)	16 (5%)	

FLOT chemotherapy increases...

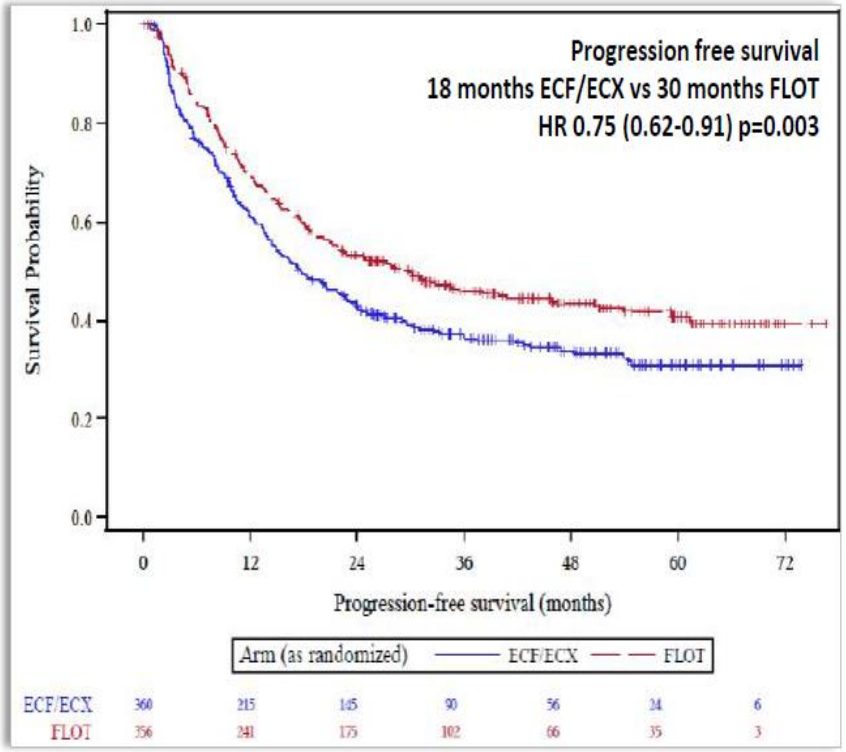
% patients who undergo surgery
% patients with R0 resection

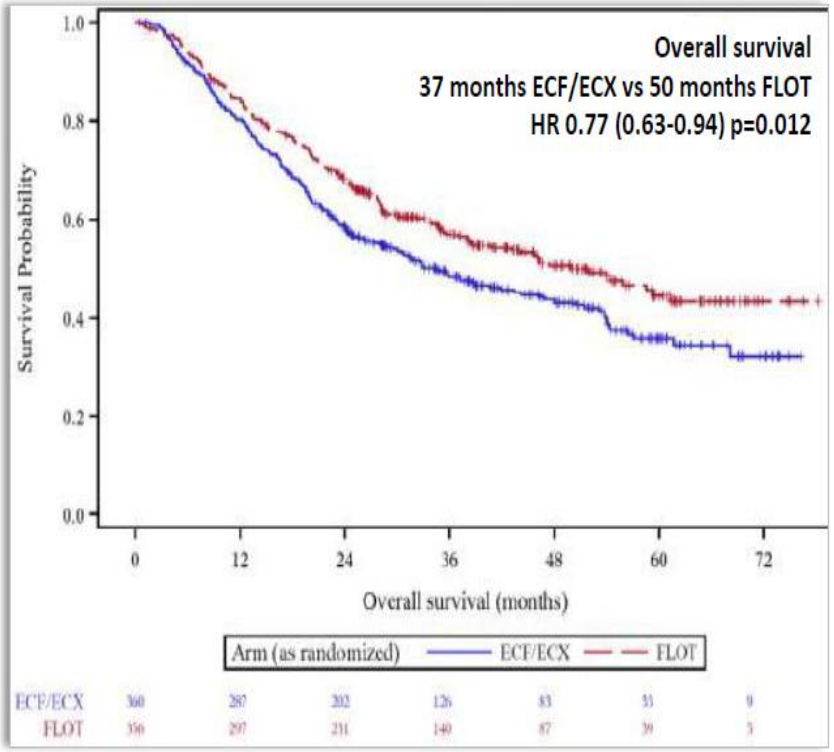
Surgical morbidity and mortality was not increased FLOT

	ECF/ECX (n=360)	FLOT (n=356)	
ypT stage ≤T1	53 (15%)	88(25%)	0.001
ypN stage N0	146(41%)	174(49%)	0.029

FLOT increases the % of patients have pathological early stage tumours compared to ECF/X

FLOT IMPROVES PFS AND OS COMPARED TO ECF/X





Projected PFS rates		
	ECF/X	FLOT
2 year	43%	53%
3 year	37%	46%
5 year	31%	41%

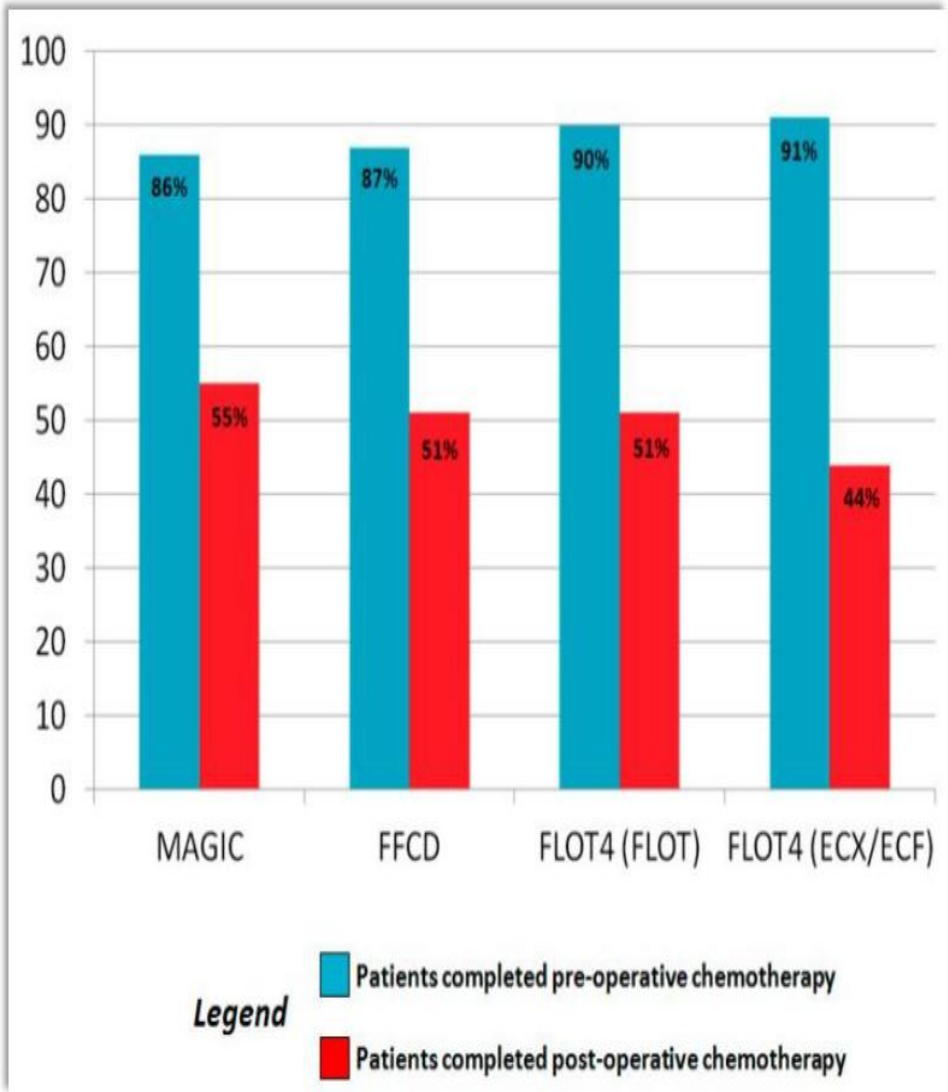
Projected OS rates		
	ECF/X	FLOT
2 year	59%	68%
3 year	48%	57%
5 year	36%	45%

FLOT VS ECF/X TOXICITY

Grade 3-4 >5%	ECF/ECX (N=354)	FLOT (N=354)	P-value (Chi-Square)
Diarrhea	13 (4%)	34 (10%)	0.002
Vomiting	27 (8%)	7 (2%)	<0.001
Nausea	55 (16%)	26 (7%)	0.001
Infections	30 (9%)	63 (18%)	<0.001
Neutropenia	139 (39%)	181 (51%)	0.002
Sensory	7 (2%)	24 (7%)	0.002
Thromboembolic	22 (6%)	9 (3%)	0.03
Anemia	20 (6%)	9 (3%)	0.04

FLOT increased diarrhoea, neutropenia and neuropathy
ECX increased nausea, anaemia and thromboembolic complications

PERIOPERATIVE CHEMOTHERAPY TOLERABILITY CF, ECF/X AND FLOT



1. ~10% of patients will not complete pre-operative chemotherapy
2. Approximately 50% of patients are not fit enough for post operative chemotherapy

A NEW HORIZON FOR PERIOPERATIVE CHEMOTHERAPY IN ASIA

PRODIGY TRIAL

CSC arm: Neoadjuvant Chemotherapy + Surgery + Adjuvant Chemotherapy
SC arm: Surgery + Adjuvant Chemotherapy

Key Eligibility Criteria

- Newly diagnosed locally advanced gastric or GEJ adenocarcinoma
- cTNM stage: cT2,3/N[+]M0 or cT4/N[any]M0 (AJCC 7th edition)
- ECOG PS 0 or 1
- Adequate organ function

R* → 1:1

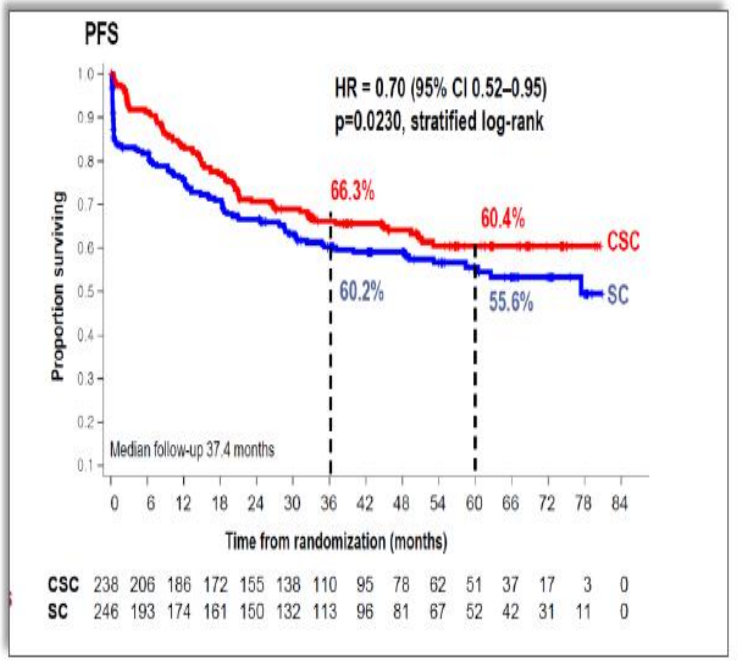
CSC → DOS (Neoadjuvant DOS, 3 cycles) → Surgery (Gastrectomy + D2 LN dissection) → S-1 (Adjuvant S-1 8 cycles)

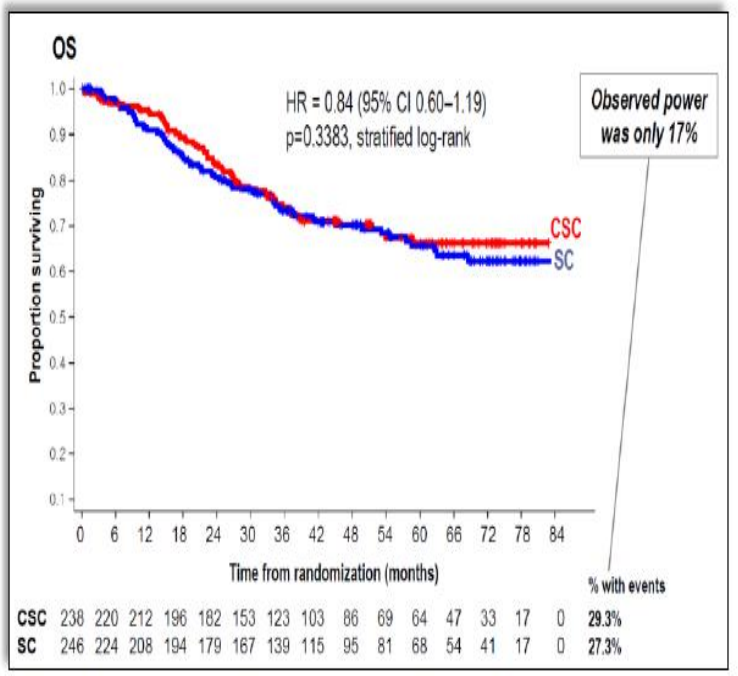
SC → Surgery → S-1

FOLLOW-UP‡
Progression
Death
End of study

*** Stratification factors**
1) Study site
2) cTNM stage (cT2/N+, cT3-4/N+, cT4/N-)

Primary endpoint	Secondary endpoints
• 3-year PFS in FAS	• R0 resection rate • Post-operative pathological stage • OS • Safety





Neoadjuvant DOS + adjuvant S1 could be an option for locally advanced GC in Asia

Kang et al. ESMO 2019

- Adjuvant CT after D2 gastrectomy is standard therapy for resectable advanced GC in Asia. We investigated whether added neoadjuvant (NA) CT can further improve outcomes.
- Methods
- 530 pts with newly diagnosed locally advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma (cT2,3/N[+]M0 or cT4/N[any]M0, AJCC 7th ed), ECOG PS 0-1, were randomized 1:1 to NA DOS then surgery and adjuvant S-1 (CSC; n = 266), or surgery and adjuvant S-1 (SC; n = 264). NA CT was D 50mg/m^2 iv and O 100mg/m^2 iv on day 1, S 40mg/m^2 twice po on days 1–14 every 3 weeks for 3 cycles. Standard surgery was D2 gastrectomy. Adjuvant CT was S 40mg/m^2 twice po on days 1–28 every 6 weeks for 8 cycles. Primary endpoint: 3-year progression free survival (PFS)
- Results
- With 46 pts excluded due to ineligibility or consent withdrawal, FAS was 484 pts (238 in CSC, 246 in SC). Baseline characteristics were balanced. In CSC arm, 214 pts (90.0%) completed 3 cycles of NA DOS. Main ≥grade3 toxicities: neutropenia in 12.6%, febrile neutropenia 9.2%, diarrhea in 5.0%, 1 treatment related death. 222 CSC (93.3%) and 246 SC (100%) pts underwent surgery. R0 resection rates: 96.4% vs 85.8%, $p < 0.0001$; lower pathologic stage in CSC with pathologic CR 10.4% vs 0%, $p < 0.0001$. Major surgical complication rates: 6.3% vs 8.5% with 1 surgical mortality in CSC arm. 204 CSC pts started adjuvant S-1, 170 (83.3%) completed 8 cycles; SC arm: 187 started, with completion of 8 cycles in 157 (84.0%). Main ≥grade3 toxicities: neutropenia (6.4% CSC, 5.4% SC), diarrhea (2.9% CSC, 3.2% SC). With median follow up of 37.4 months and 37.8% of PFS events, 3-year PFS rate (FAS) was 66.3% for CSC, 60.2% for SC; hazard ratio (HR) 0.70 (95% CI 0.52–0.95), stratified log-rank $p = 0.023$. Sensitivity analyses (intent to treat set and landmark analysis) confirmed these results.
- Conclusions
- Addition of NA DOS to D2 gastrectomy and adjuvant S-1 led to significant tumour downstaging and improved PFS with acceptable safety in PRODIGY study. Neoadjuvant DOS chemotherapy followed by D2 gastrectomy and adjuvant S-1 should be considered as a treatment option for resectable advanced GC.

RESOLVE TRIAL

Gastric or GEJ adenocarcinoma
cTNM stage: T4aN+ or cT4b

N=1022

R

Surgery → XELOX

cT4: 97% pT4 58% + 5% NA

cN+: 97% pN0 16% + 5% NA

Surgery → SOX

cT4: 97% pT4, 53% (+7% NA)

cN+ 97% pN0 19% (+5% NA)

SOX → Surgery → SOX

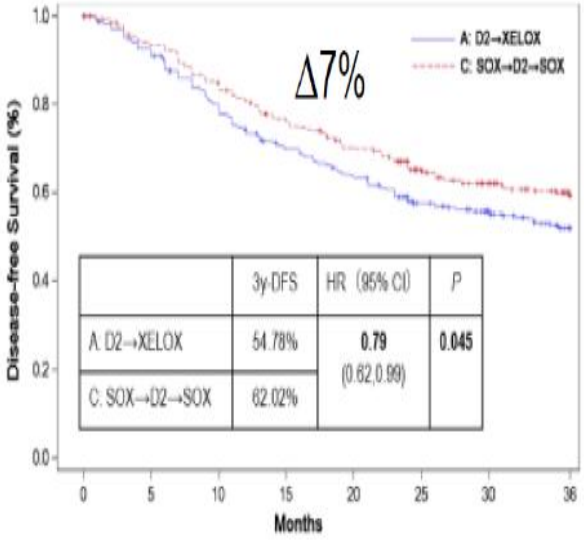
cT4: 97%

cN+: 96%

Superiority

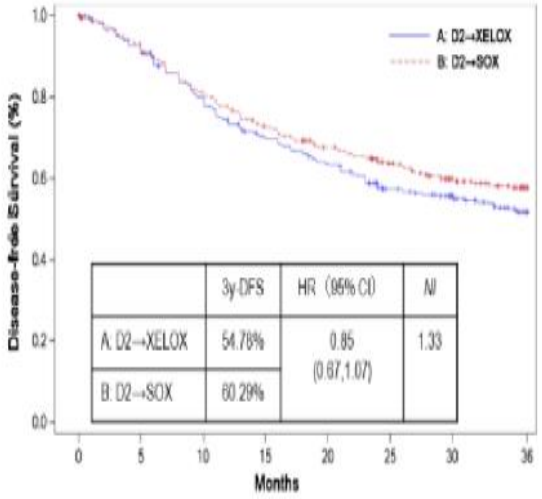
Non-inferiority

3-y DFS peri-op SOX vs. post-op XELOX



	3y-DFS	HR (95% CI)	P
A. D2→XELOX	54.78%	0.79 (0.62,0.99)	0.045
C. SOX→D2→SOX	62.02%		

3-y DFS post-op SOX vs. post-op XELOX



	3y-DFS	HR (95% CI)	NI
A. D2→XELOX	54.78%	0.85 (0.67,1.07)	1.33
B. D2→SOX	60.29%		

Perioperative SOX could be an option for locally advanced GC in Asia

SOX could replace XELOX for adjuvant treatment

- Surgery alone is not sufficient to achieve satisfactory prognosis for locally advanced gastric cancer (LAGC), and perioperative therapies have been proposed to improve survival outcome. However, the optimal modality and regimen of perioperative chemotherapy are yet to be identified. This study compared the efficacy and safety of SOX as perioperative chemotherapy versus SOX or XELOX as postoperative chemotherapy after D2 gastrectomy in patients with LAGC.
- Methods
- The RESOLVE Trial is a three-arm, randomized, multicenter, open-label phase III trial. Patients with stage cT4a/N+M0 or cT4bNxM0 gastric or gastro-esophageal junction adenocarcinoma were enrolled. All patients received standard gastrectomy with D2 lymphadenectomy. Arms A and B respectively received 8 cycles of adjuvant XELOX (capecitabine 1000 mg/m^2, bid, d1-14, oxaliplatin 130 mg/m^2, d1, q3W) or SOX (TS-1: 40-60 mg bid, d1-14, oxaliplatin: 130 mg/m^2 d1, q3W). Arm C received 3 cycles of neoadjuvant SOX and 5 cycles of adjuvant SOX followed by 3 cycles of TS-1. The primary endpoint was 3-year disease-free survival rate (3yDFS%) in the mITT population.
- Results
- A total of 1094 patients were randomized between 08/2012 and 02/2017, 364/365/365 in arm A/B/C, and 454 recurrences/deaths were observed by 07/2019. Baseline characteristics were similar between arms (overall, male 75.2%; median age 60.0 years; GEJ 36.5%). Peri-operative SOX improved 3yDFS% compared with post-operative XELOX (3yDFS%, 62.0% in Arm C, 54.8% in Arm A; HR 0.79, 95%CI [0.62-0.99]; p = 0.045). Post-operative SOX was non-inferior to post-operative XELOX (3yDFS%, 60.3% in Arm B, 54.8% in Arm A; HR 0.85, 95%CI [0.67-1.07]; p = 0.162). Resection rate was 90.4% in Arm A, 92.7% in Arm B, and 85.5% in Arm C, respectively. Thirty-day mortality rate was all 0.9% for Arms A, B and C.
- Conclusions
- Perioperative SOX is superior to post-operative XELOX while post-operative SOX is non-inferior to post-operative XELOX for LAGC after D2 gastrectomy. It provides the evidence of perioperative SOX in LAGC.

PERI-OPERATIVE CHEMOTHERAPY: TAKE HOME MESSAGES

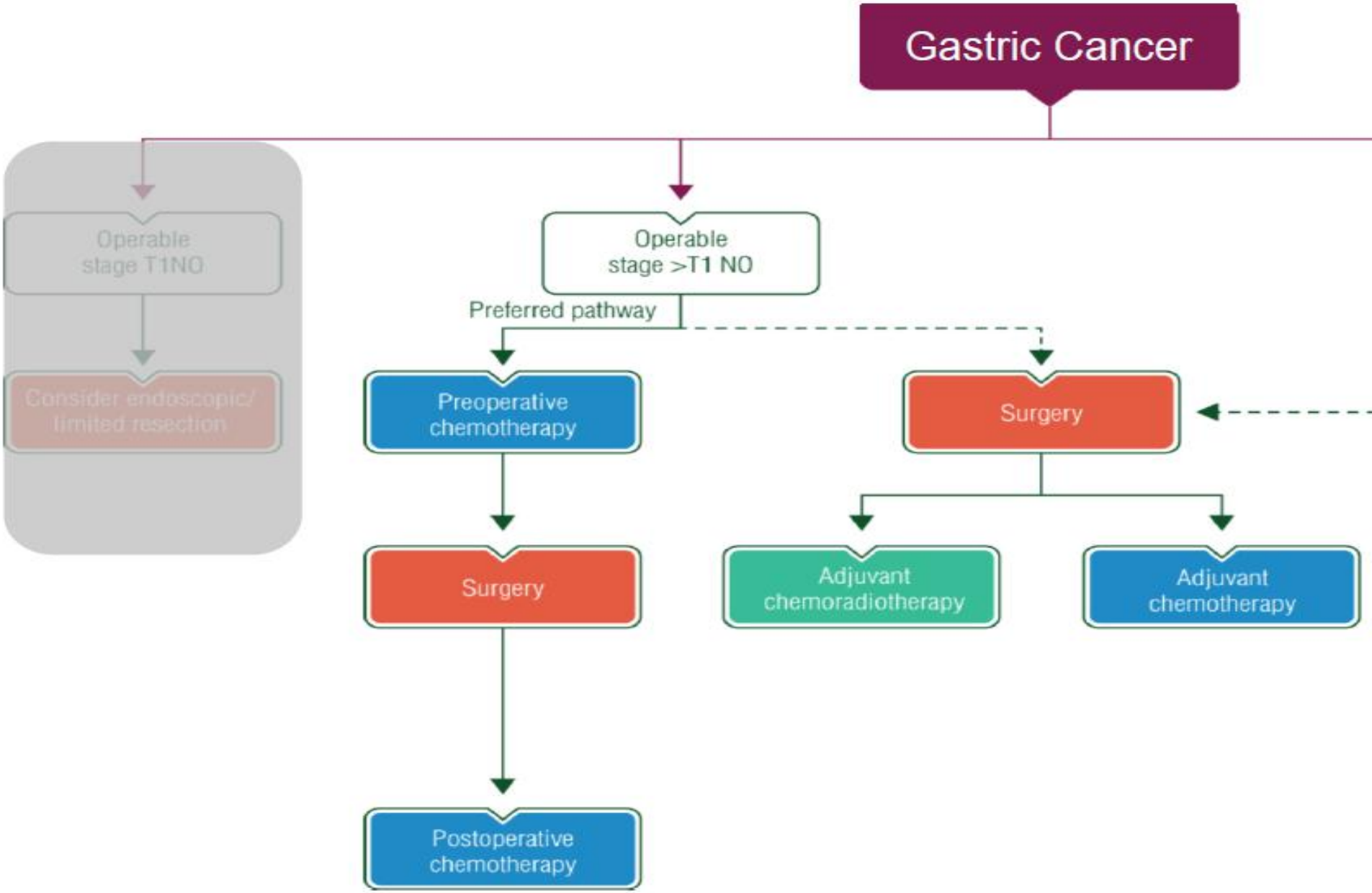
FLOT is the new gold standard treatment for patients who receive peri-operative chemotherapy and surgery for operable gastroesophageal cancer

- In patients are not suitable for triplet chemotherapy, doublet chemotherapy can be considered
- Doublets can be cisplatin or oxaliplatin based

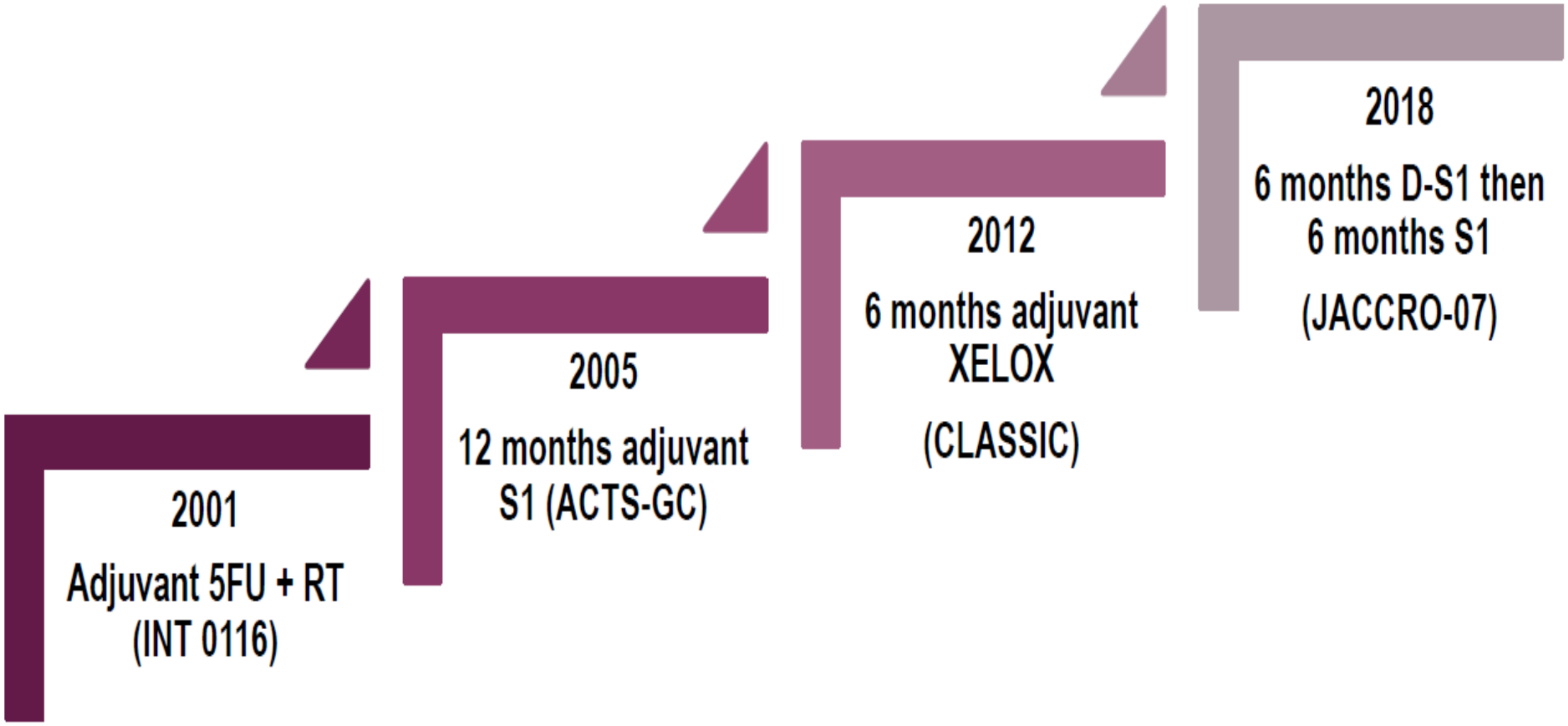
5 year projected OS with FLOT is **45%,** therefore there is still **more work** to do to improve survival for patients treated with peri-operative chemotherapy

Adjuvant Treatment

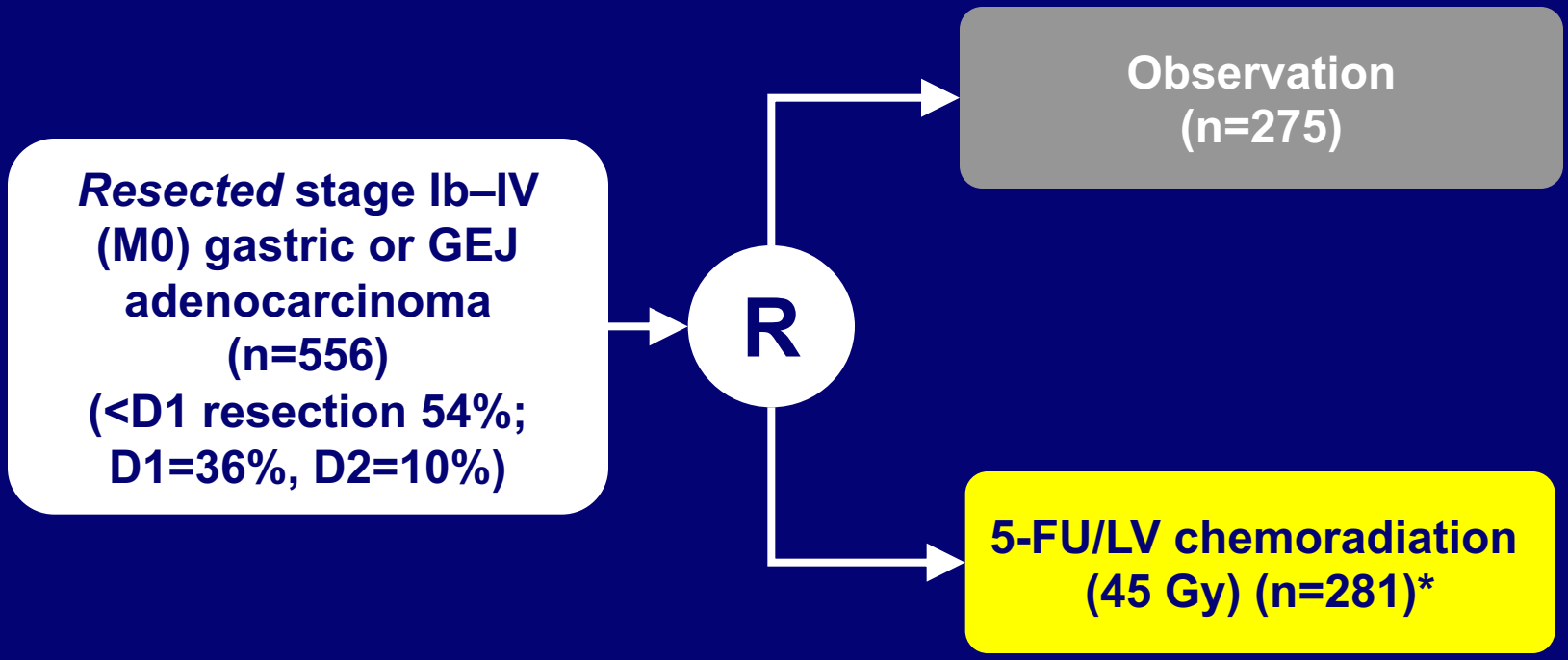
ESMO GASTRIC CANCER GUIDELINES



EVOLUTION OF NEOADJUVANT AND PERI-OPERATIVE CHEMOTHERAPY 2002 - 2019



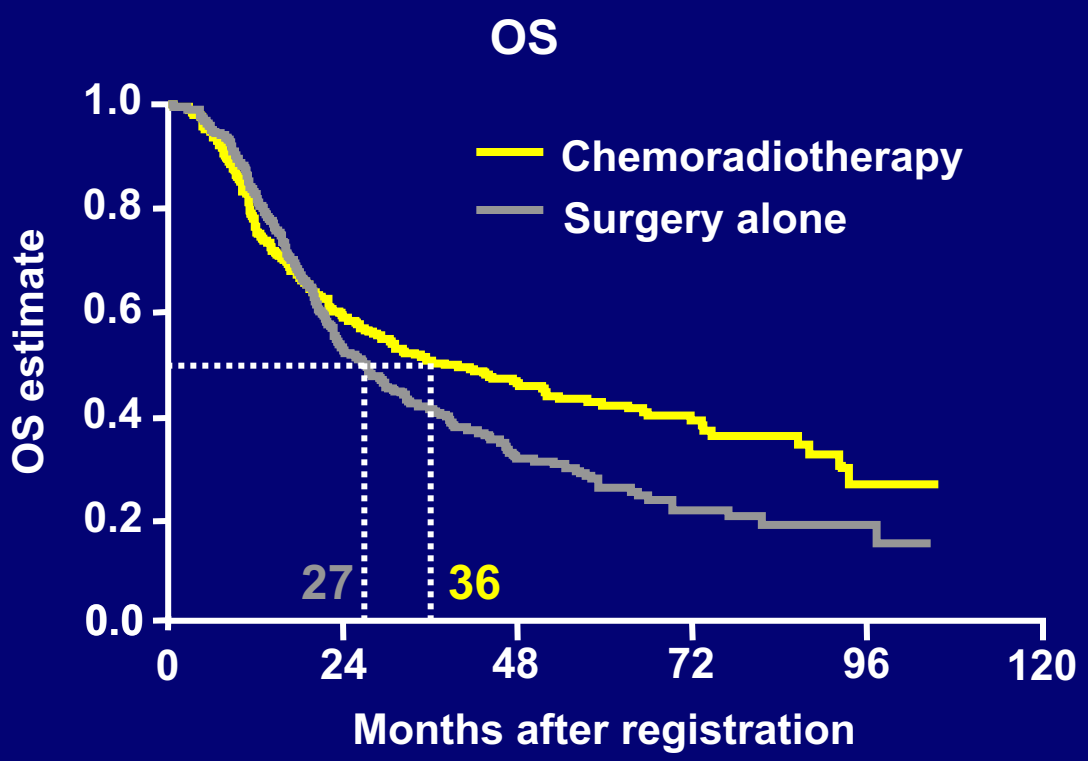
SWOG 9008/Intergroup 0116 trial: Phase III trial of postoperative adjuvant radiochemotherapy



- Primary endpoint: OS, RFS
- Secondary endpoints: safety

* Details of the regimen in the note page
Macdonald, et al. NEJM 2001

SWOG 9008/Intergroup 0116 trial: OS

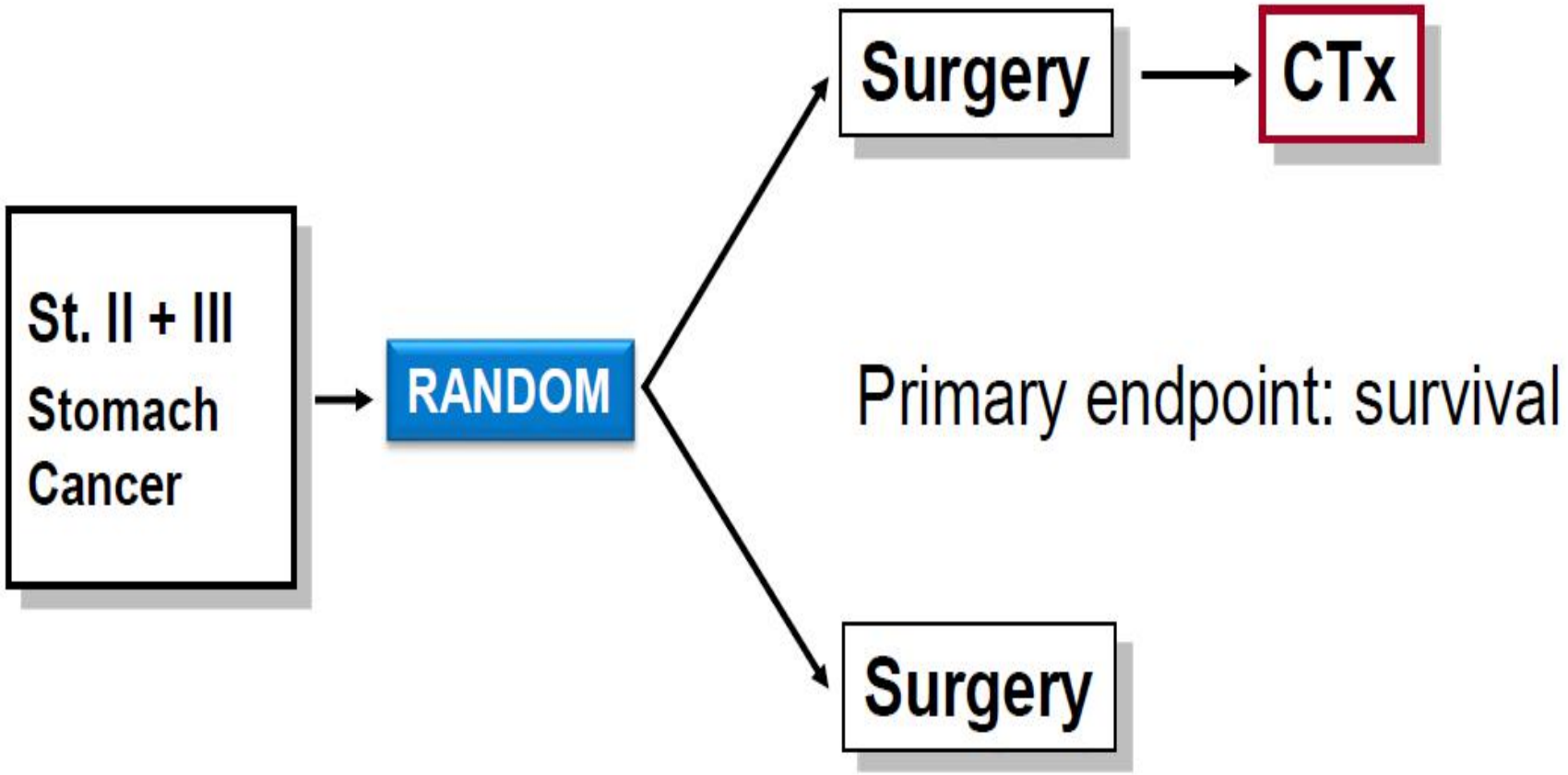


- HR for death: 1.35; 95% CI: 1.09–1.66; p=0.005
- Median OS: 27 vs 36 months
- Highly selected population (all had R0 resection and recovered from surgery)
  - only 64% completed treatment
- Significant treatment-related toxicity:
  - toxic death (1%)
  - grade 3/4 AEs (73%)

Post-operative chemoradiotherapy is perceived as the standard of care for resectable gastric cancer in the US

Macdonald, et al. NEJM 2001

Multiple Adjuvant Studies



ADJUVANT TRIALS IN GASTRIC CANCER

ACTS-GC

Post-operative eligible patients

1 year S1 (n=529)

No further treatment (n=530)

Primary Endpoint
Overall survival
Secondary endpoints
Relapse free survival & safety

Eligibility criteria
Stage ≥ II (no T1), IIIA or IIIB gastric adenocarcinoma
D2 resection minimum

CLASSIC

Post-operative eligible patients

6 months CapeOx (n=520)

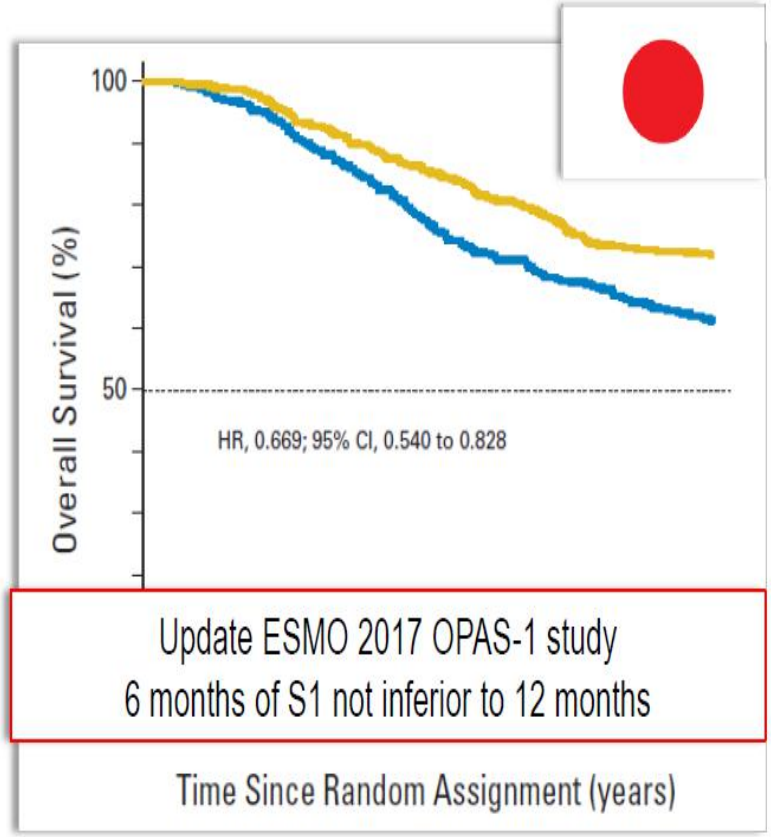
No further treatment (n=515)

Primary Endpoint
3 year disease free survival
Secondary endpoints
Overall survival & safety

Eligibility criteria
Stage ≥ II, IIIA or IIIB gastric adenocarcinoma
D2 resection minimum

IMPROVEMENTS IN SURVIVAL WITH ADJUVANT CHEMOTHERAPY

ACTS-GC

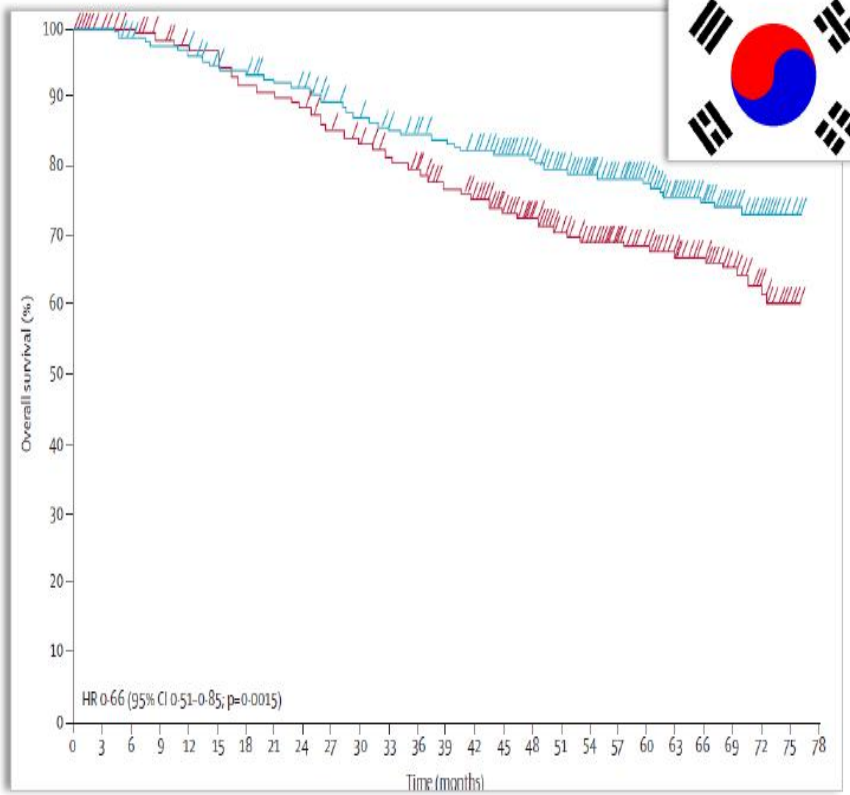


Update ESMO 2017 OPAS-1 study
6 months of S1 not inferior to 12 months

Updated 5 year survival S1 vs surgery alone

All patients 5 year OS 72% vs. 61%
Stage II 5 year OS 84% vs 71%
Stage IIIA 5 year OS 67% vs 57%
Stage IIIB 5 year OS 50% vs 44%

CLASSIC



5 year updated survival CapeOx vs surgery alone

All patients 5 year OS 78% vs 69%
Stage II 5 year OS 88% vs 79%
Stage IIIA 5 year OS 70% vs 63%
Stage IIIB 5 year OS 66% vs 45% (compare **ACTS GC 50% vs. 44%**)

S1 VS. S1-DOCETAXEL ADJUVANT CHEMOTHERAPY JACCRO-7

Post-operative eligible patients

S1 80mg/m^2 d1-28 q 6 wks x 1 year

(n=459)

Cycle 1: S1 80mg/m^2 d1-14 q21d

Cycle 2-7: docetaxel 40mg/m^2 plus S1 80mg/m^2 d1-14 q21d

Then S1 x 6 months

(N=456)

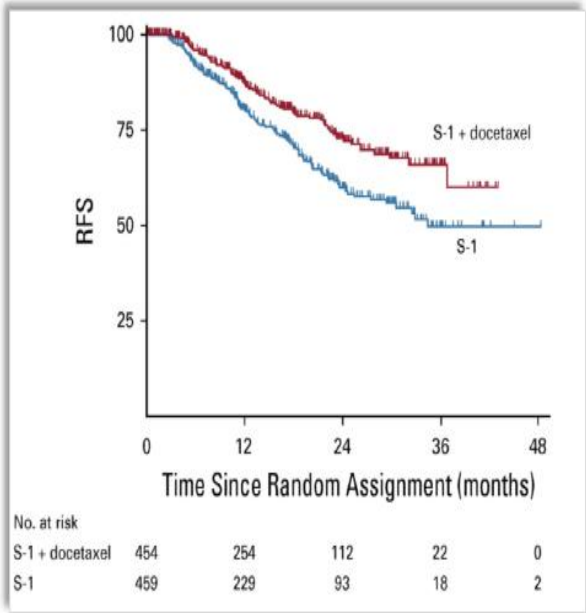
Primary Endpoint

3 year relapse free survival

Secondary endpoints

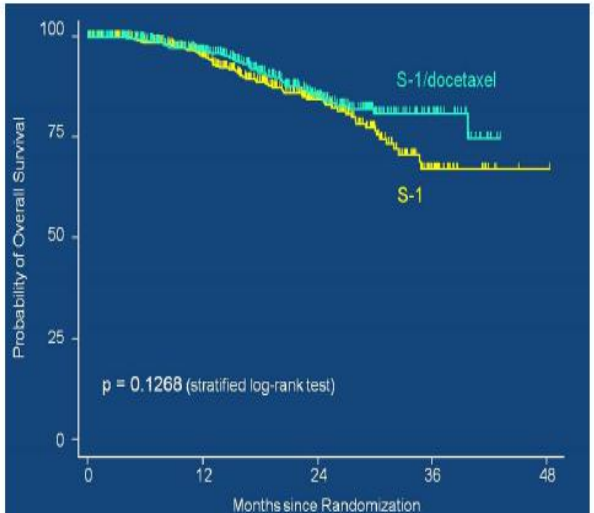
Overall survival & safety

Relapse free survival



HR, 0.632; 99.99% CI, 0.400 to 0.998; $P < .001$)

3-year RFS of 66% vs 50% in favour of docetaxel-S1



Overall survival not mature

Metaanalysis	Studies (n)	Patients (n)	Odds ratio (CI)
Hermans 1993	11	2096	0.88 (0.78-1.08)
Earle 1999	13	1990	**0.80 (0.66-0.97)**
Mari 2000	21	3658	**0.82 (0.75-0.89)**
Janunger 2002	21	3962	**0.84 (0.74-0.96)**
GASTRIC 2010	17	3838	**0.82 (0.75-0.90)**

- **5-year survival benefit ~ 5% (GASTRIC 2010)**
- **Some more benefit in node positive tumors (Janunger 2002)**

Adjuvant Intensification (Italian Trials)

Universitätsklinikum Leipzig
Anstalt öffentlichen Rechts

GISCAD

→ **5-FU (375mg/m² bolus) / LV (20mg/m²) d1-5; q4w x 6**

N = 400

→ **wPELF (weekly cisplatin, epirubucine, LV, 5-FU) x 8**

Cascinu et al., *J Nat Canc Inst* 2007; 99: 601-607

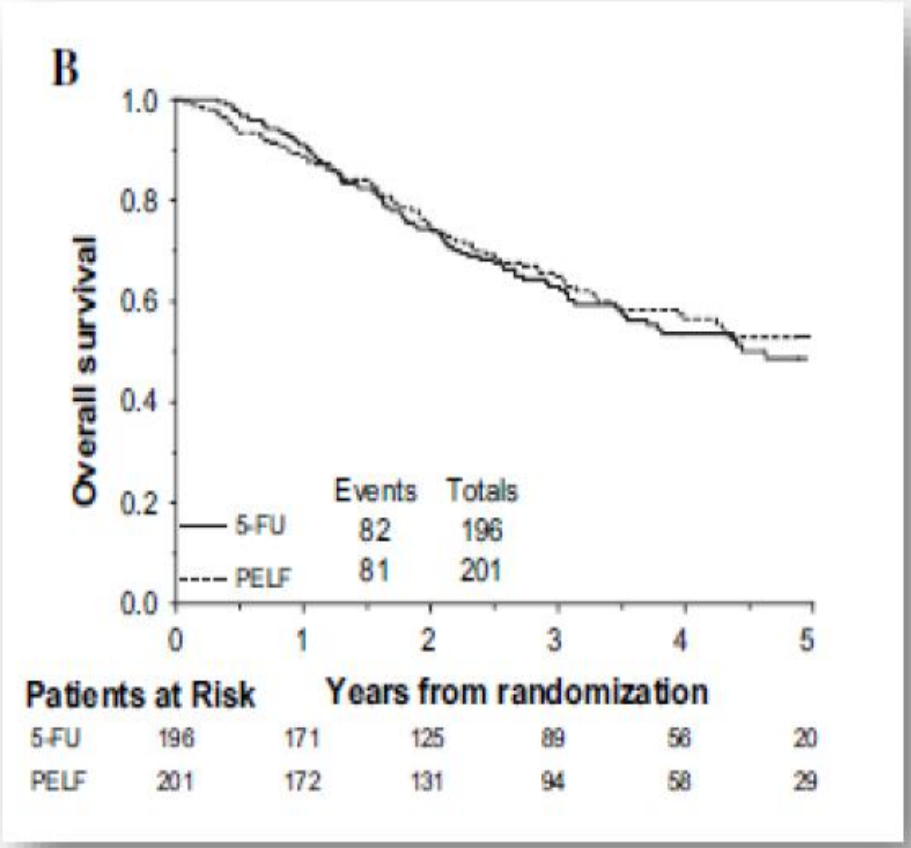
ITACA-S

→ **5-FU (400-600mg/m²) / LV (100mg/m²) d1-2; q2w x 9**

N = 1106

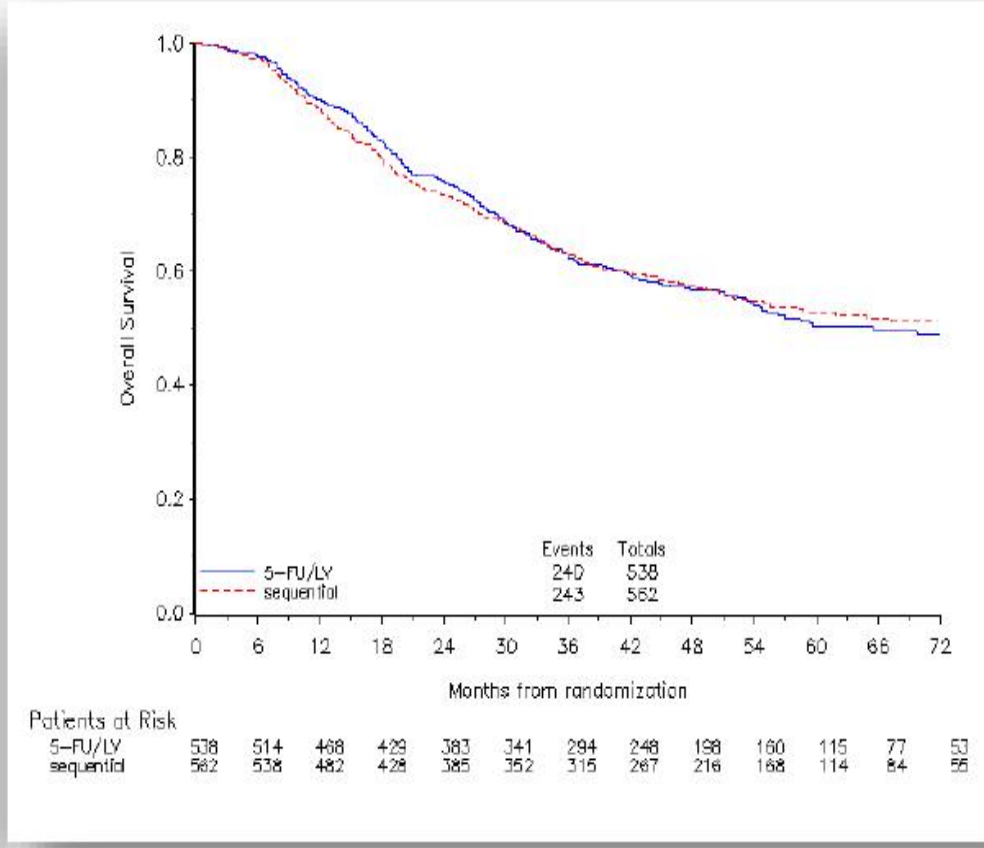
→ **FOLFIRI x 4 → Docetaxel/Cisplatin x 3**

GISCAD Study



Cascinu et al., *J Nat Canc Inst* 2007; 99: 601-607

ITACA-S Study



Bajetta et al., *Ann Oncol.* 2014; 25: 1373-8

Postoperative CTx intensification did not improve outcomes in EU

CHEMOTHERAPY VS. CHEMORADIOTHERAPY

A Multicenter Randomized Phase III Trial of Neo-adjuvant Chemotherapy Followed by Surgery and Chemotherapy or by Surgery and Chemoradiotherapy in Resectable Gastric Cancer

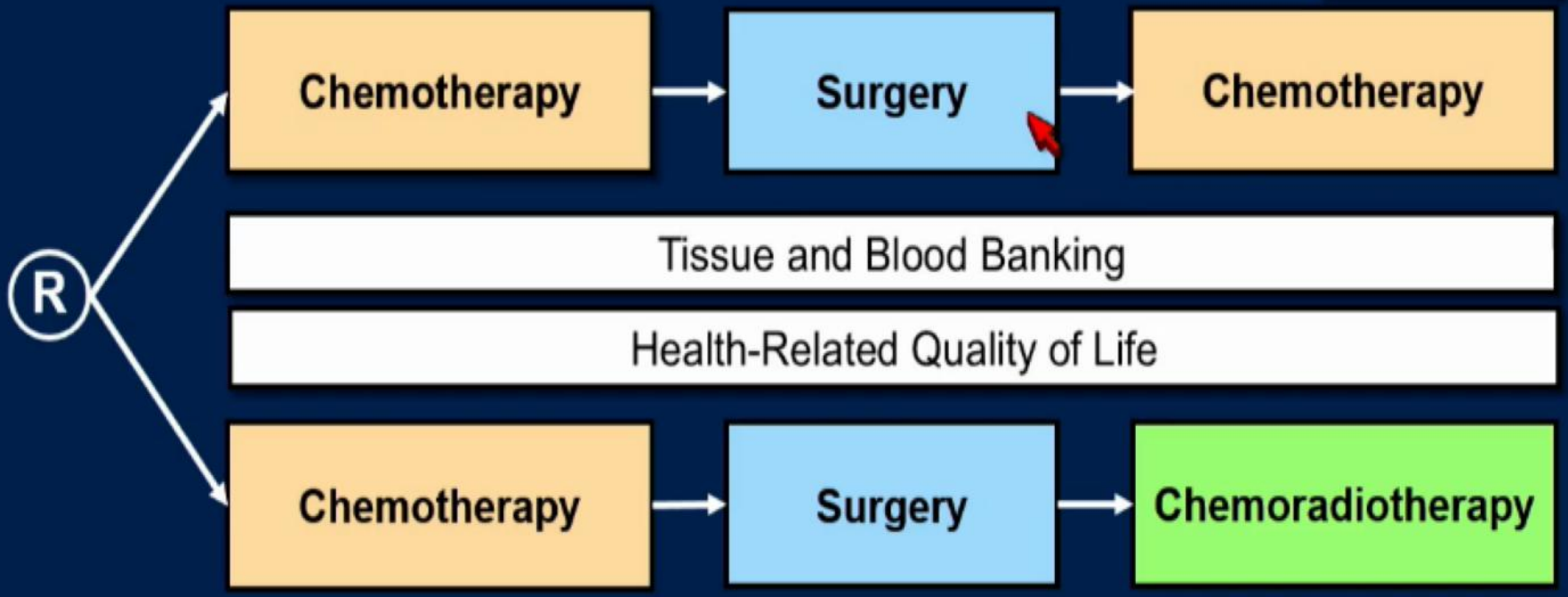
First results from the CRITICS study

Marcel Verheij[1], EPM Jansen[1], A Cats[1], NCT van Grieken[2], H Boot[1], PA Lind[3], E Meershoek-Klein Kranenbarg[4], M Nordsmark[5], HH Hartgrink[4], H Putter[4], AK Trip[1], JW van Sandick[1], K Sikorska[1], H van Tinteren[1], YHM Claassen[4], CJH van de Velde[4], on behalf of the CRITICS Investigators

[1]Netherlands Cancer Institute, [2]VU University Medical Center, [3]Karolinska University Hospital, [4]Leiden University Medical Center, [5]Århus University Hospital

PRESENTED AT: ASCO ANNUAL MEETING '16

Trial design



Stratified for: Center, Histological type, Tumor localization

Treatment Details

Chemotherapy: Pre-operative and post-operative: 3x ECC or EOC q3 wks

Epirubicin 50 mg/m² day 1; Cisplatin 60 mg/m² day 1; Capecitabine 1000 mg/m² b.i.d. 1-14
Epirubicin 50 mg/m² day 1; Oxaliplatin 130 mg/m² day 1; Capecitabine 625 mg/m² b.i.d. 1-21

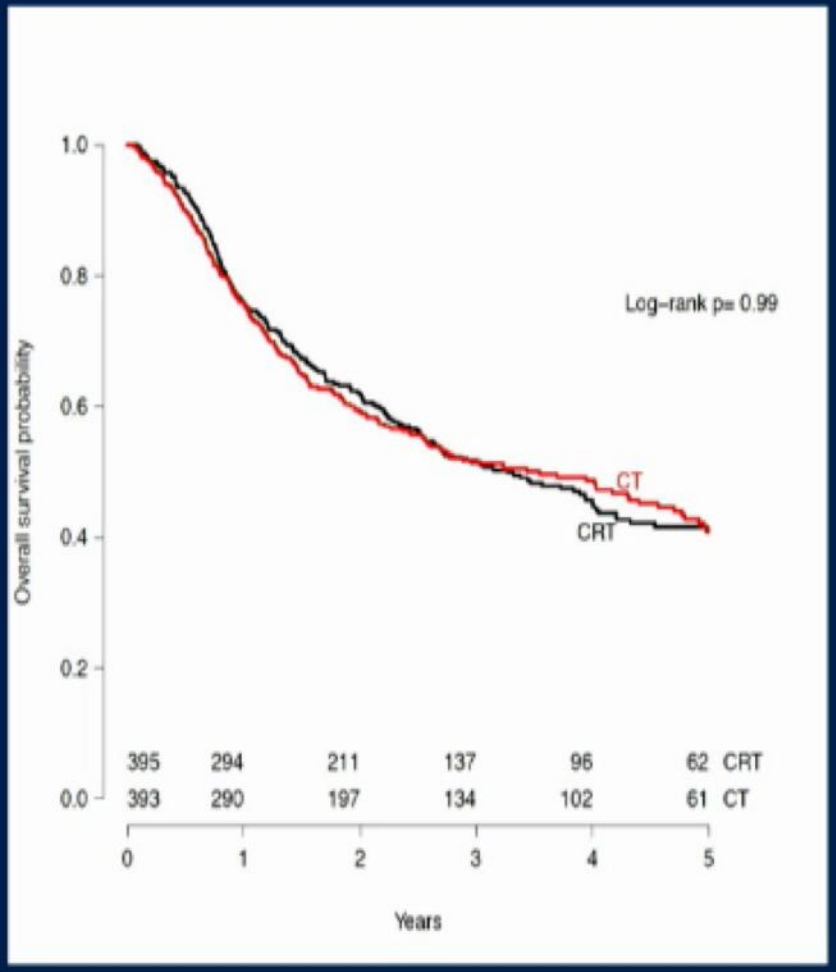
Surgery: Total / partial gastrectomy + *en bloc* N1 and N2 lymph nodes

D1⁺ resection: lymph node stations 1-9 and 11; no splenectomy or pancreatectomy
Removal of ≥15 lymph nodes
Quality assurance: Maruyama Index

Chemoradiotherapy: Post-operative: 45 Gy in 25 fractions combined with CC

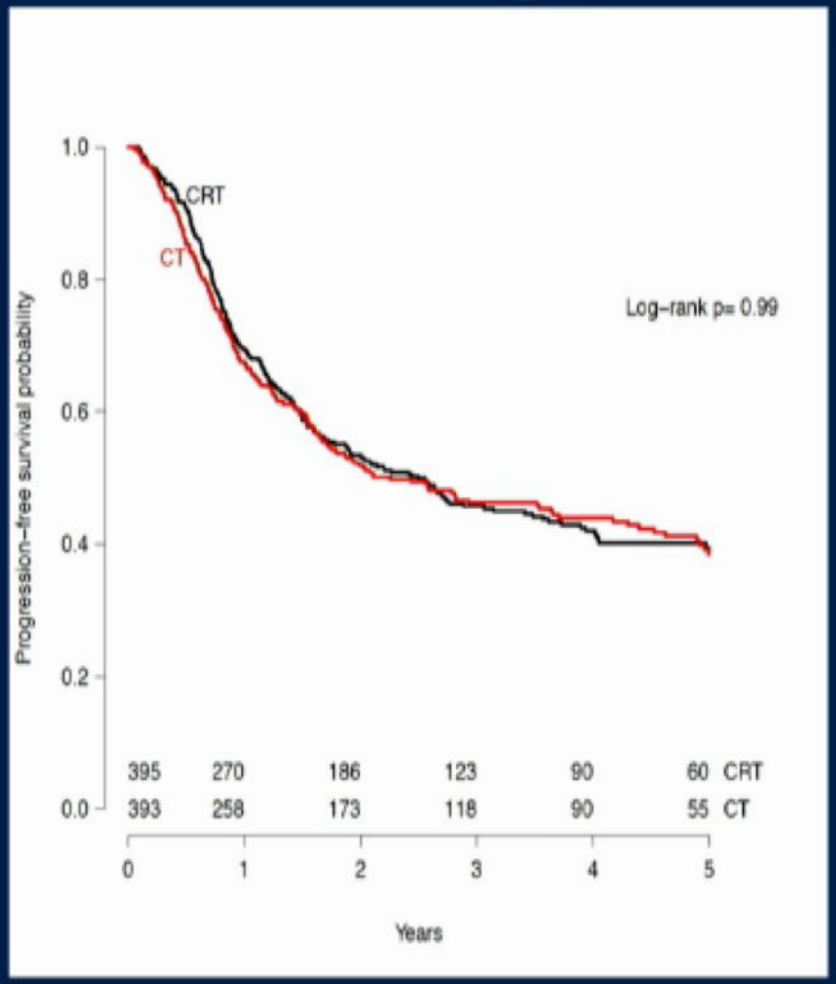
3D-CRT or IMRT; CTV includes tumor bed, anastomoses, draining lymph node stations
Concurrent during RT: Cisplatin 20 mg/m² weekly; Capecitabine 575 mg/m² b.i.d./d.d.w.d.
Quality assurance: central review of RT plans

Results: Overall Survival



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

Results: Progression-Free Survival



	CT	CRT
5-year PFS (%)	38.5	39.5
Median PFS (yrs)	2.3	2.5

Conclusions

- The expected treatment difference in overall survival has not been observed
- 5-year overall and median survival are comparable with other studies in Western countries
- Based on the currently available data, no advise can be given on the preferred adjuvant strategy
- Ongoing analyses may identify treatment benefits in specific subgroups
- As less than 50% of patients could complete full treatment, more emphasis on pre-operative strategies should be considered

CHEMOTHERAPY VS CHEMORADIOTHERAPY

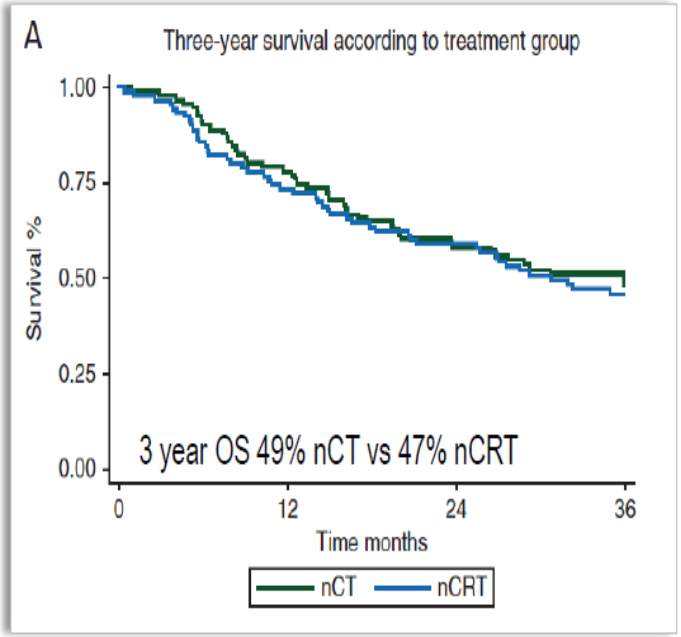
NeoRes Study

Pre-operative eligible patients (ADC and OSCC)

- Cisplatin 100mg/m^2 + 5FU 750mg/m^2 D1-5 q3w x3 (n=90)
- SAME CHEMOTHERAPY + RT 40Gy (20 x 2Gy) (n=91)

Primary endpoint: pathological CR

NeoRes Study Outcomes	CT	CRT
R0	58 (74%)	68 (87%)
Path CR	7(9%)	22 (28%)
30 day mortality	0 (0%)	1(1%)



The NeoRes study treated patients with oesophageal SCC and adenocarcinoma including gastroesophageal junction

Although underpowered for survival, no difference was suggested in OS for chemotherapy vs chemoradiotherapy treated patients, nor in subgroup analysis

Surgical complications were more severe, but not more frequent in patients treated with chemoradiotherapy

Trials which will answer this question
Chemo vs CRT

ESOPEC

N=438

T1N1M0
or
T2–4aN0–1M0

RANDOM

Neoadjuvant Radio-CTX – CROSS Regimen
RESECTION

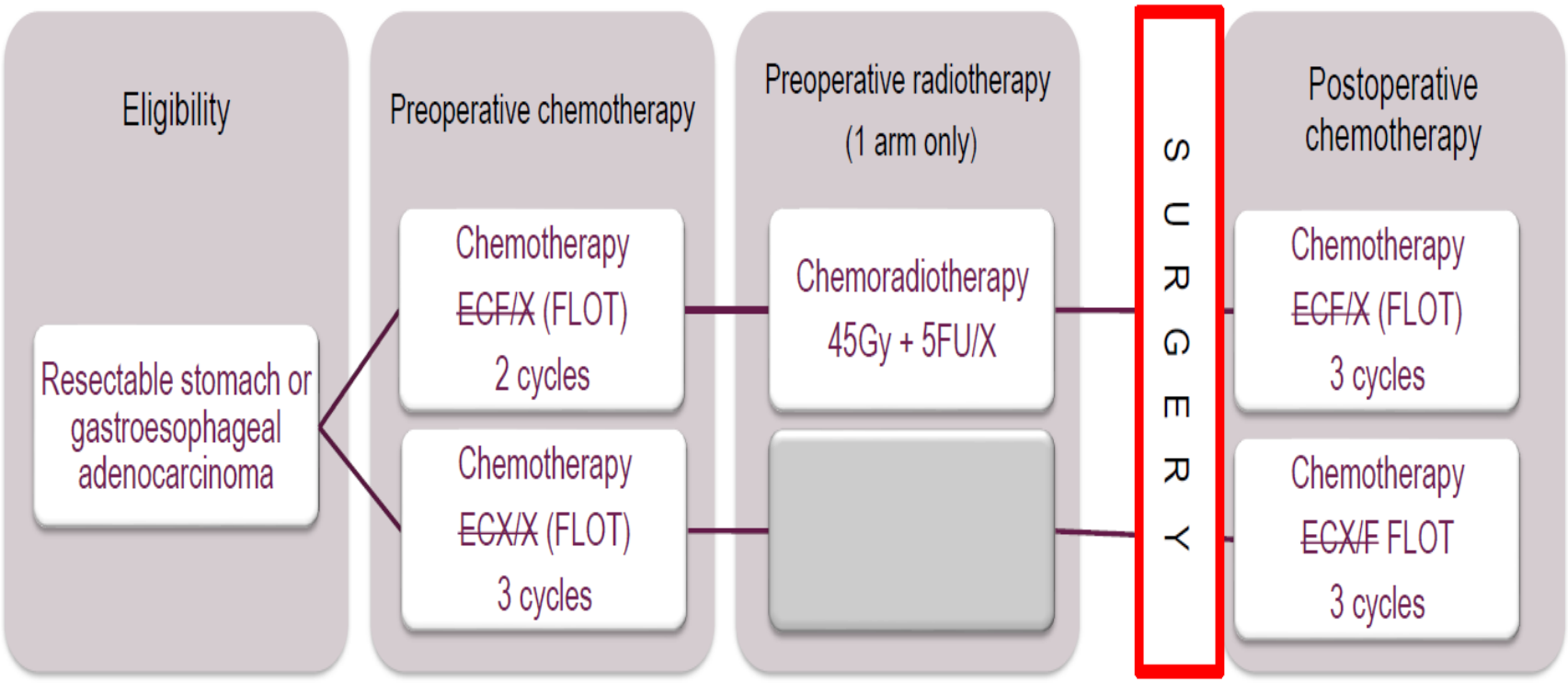
Primary endpoint: survival
3-year-OS-rate
55% CROSS vs. 68% FLOT)

Perioperative CTX: FLOT* 4 x pre and post
RESECTION

Neo-Aegis (NCT01726452): Same design (n=594)

Trials which will answer this question
Peri-operative chemo vs peri-operative chemo +RT

TOPGEAR



FLOT to replace ECF/X

Take home messege

For **GASTRIC** adenocarcinomas **peri-operative chemotherapy (FLOT)** is preferred to post-operative chemotherapy or post-operative chemoradioatherapy because:

- More patients are able to receive chemotherapy before surgery than afterwards.
- Downstaging due to chemotherapy increases rates of R0 resections

However, in cases where surgery has been performed without neoadjuvant chemotherapy, adjuvant treatment may be considered.

Assuta Ashdod Public Hospital

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THANK YOU