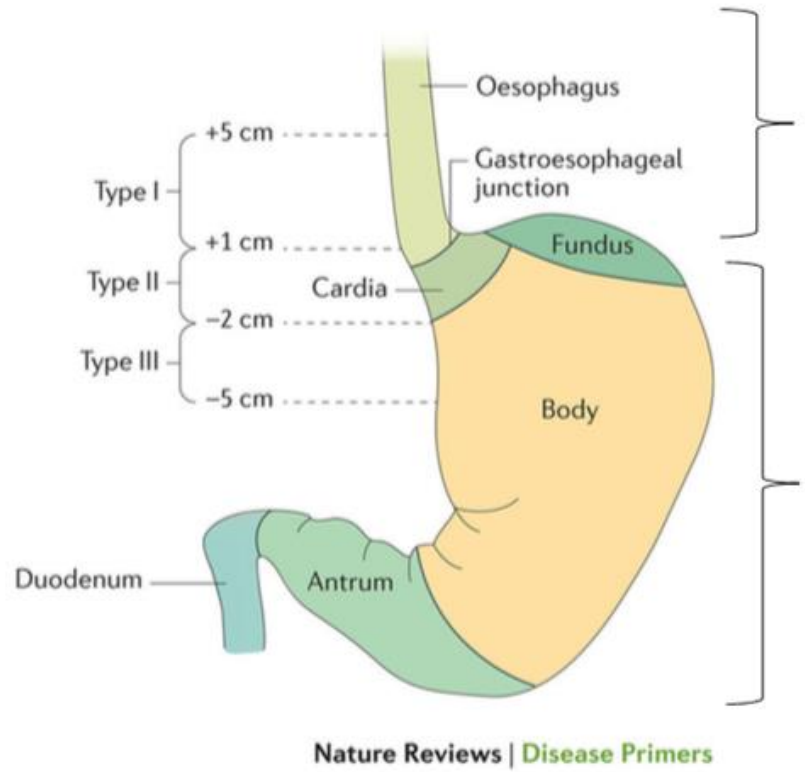
NEOADJUVANT AND ADJUVANT CHEMOTHERAPY FOR GASTRIC CANCER

DR. SHYAM AGGARWAL MD

MEDICAL ONCOLOGY

SGRH, DELHI

GASTRIC AND GASTROESOPHAGEAL CANCER NOMENCLATURE

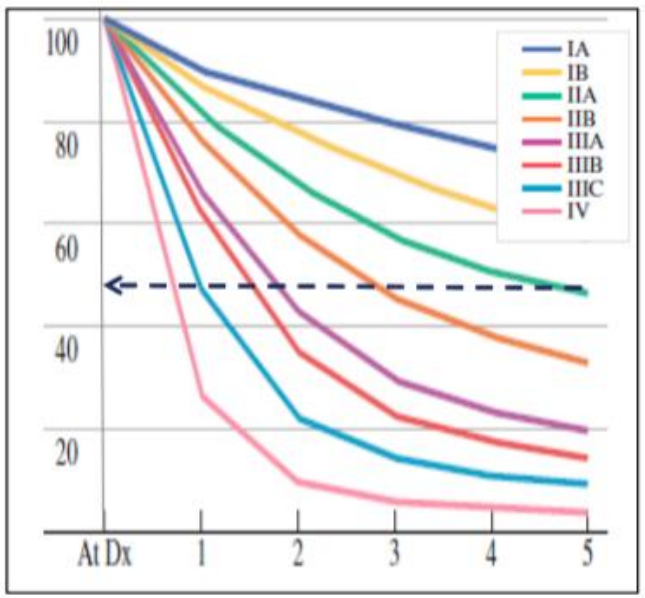


Nature Reviews | Disease Primers

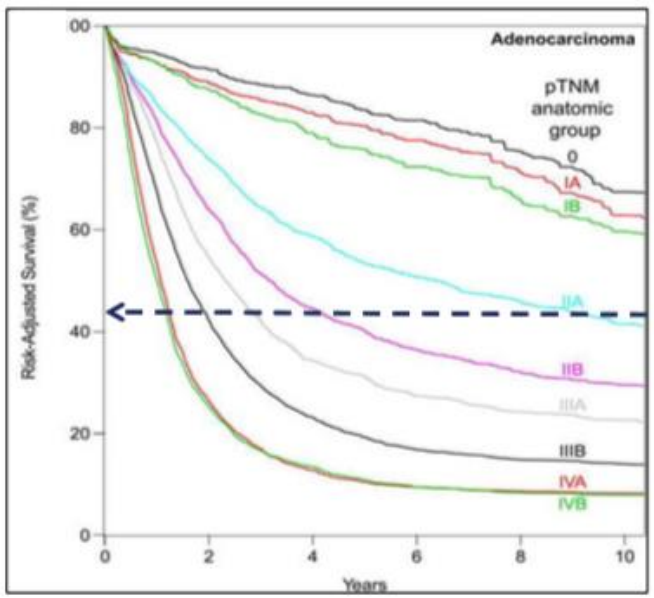
Lower oesophageal, gastroesophageal junction adenocarcinoma
→ ESMO Oesophageal Cancer Guidelines

Gastric cancer
→ ESMO Gastric Cancer Guidelines

SURVIVAL FROM OG CANCER WITH SURGERY ALONE



Gastric cancer OS surgery alone



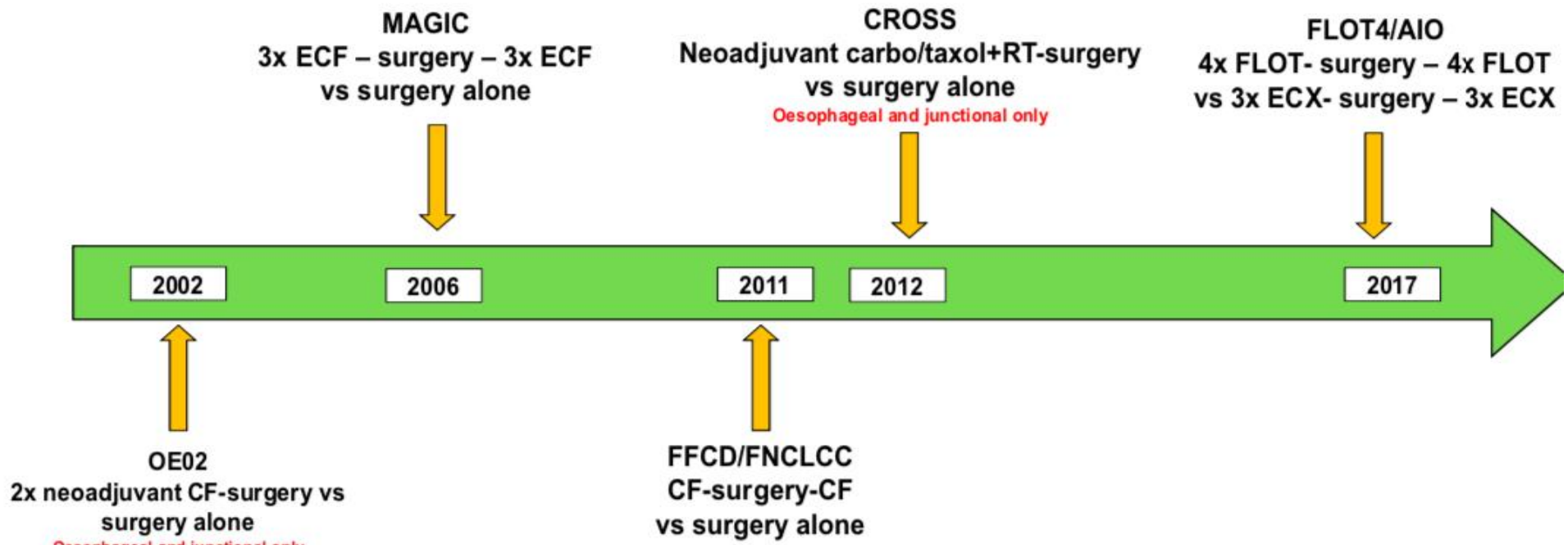
Oesophageal adeno OS surgery alone

Treatment in addition to surgery is required for most patients

NEOADJUVANT AND PERIOPERATIVE CHEMOTHERAPY

EVOLUTION OF NEOADJUVANT AND PERI-OPERATIVE

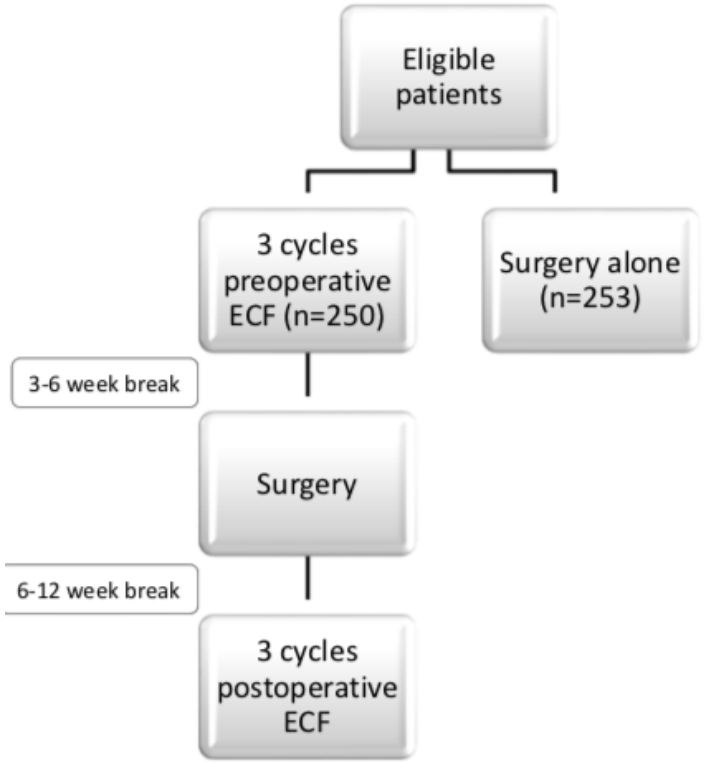
EVOLUTION OF NEOADJUVANT AND PERI-OPERATIVE (CHEMO)THERAPY 2002 - 2017



CF, cisplatin + 5-fluourouracil; ECF epirubicin + CF; FLOT. 5-fluororuraci, leucovorin, oxaliplatin, docetaxel

1. OE02 Trial Group, Lancet 2002
2. Cunningham D, *et al*. N Engl J Med 2006.
3. Ychou M, *et al*. J Clin Oncol. 2011
4. Van Hagen et al, N Engl J Med 2012
5. Al-Batran S, et al. ASCO Annual Meeting 2017

MEDICAL RESEARCH COUNCIL MAGIC TRIAL



Eligibility criteria

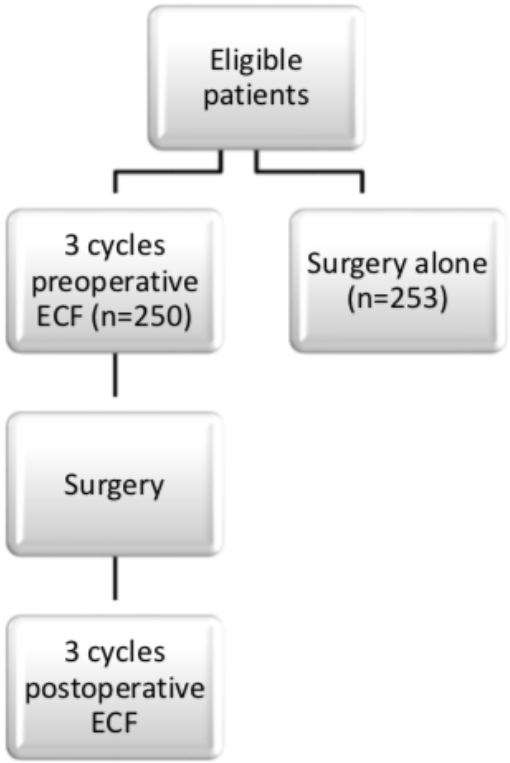
Stage ≥ II gastric, gastroesophageal junction, or lower oesophageal adenocarcinoma (after 1999)

No metastases

ECOG 0-1

MAGIC preoperative patient characteristics		
	Surgery alone	Chemo + surgery
Median age	62	62
Sex Male Female	 191 (75%) 62 (25%)	 205 (82%) 45 (18%)
Site of disease		
Gastric	187 (74%)	185 (74%)
Oesophagus	36 (14%)	37 (15%)
GOJ	30 (12%)	28 (11%)

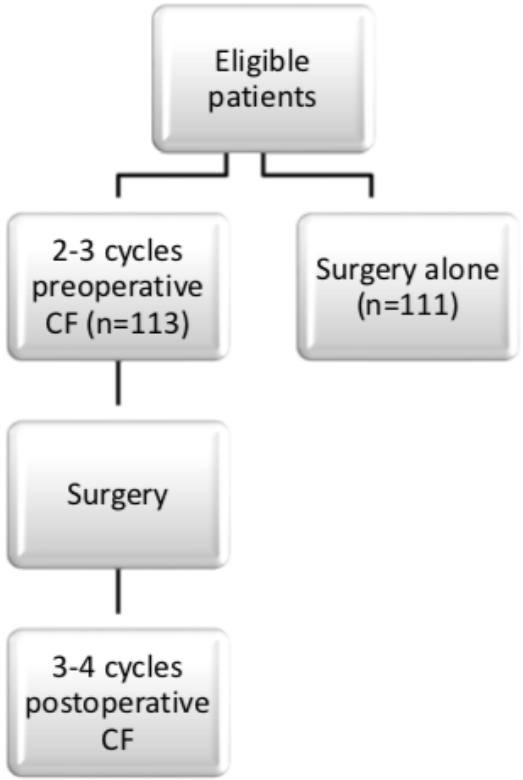
MEDICAL RESEARCH COUNCIL MAGIC TRIAL



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%)

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

FFCD/FNCLCC TRIAL

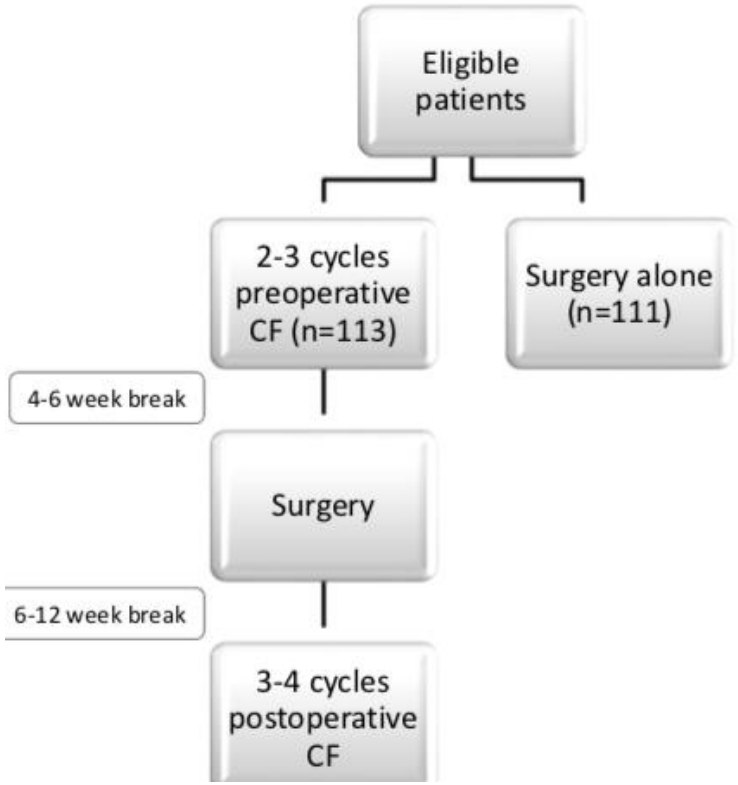


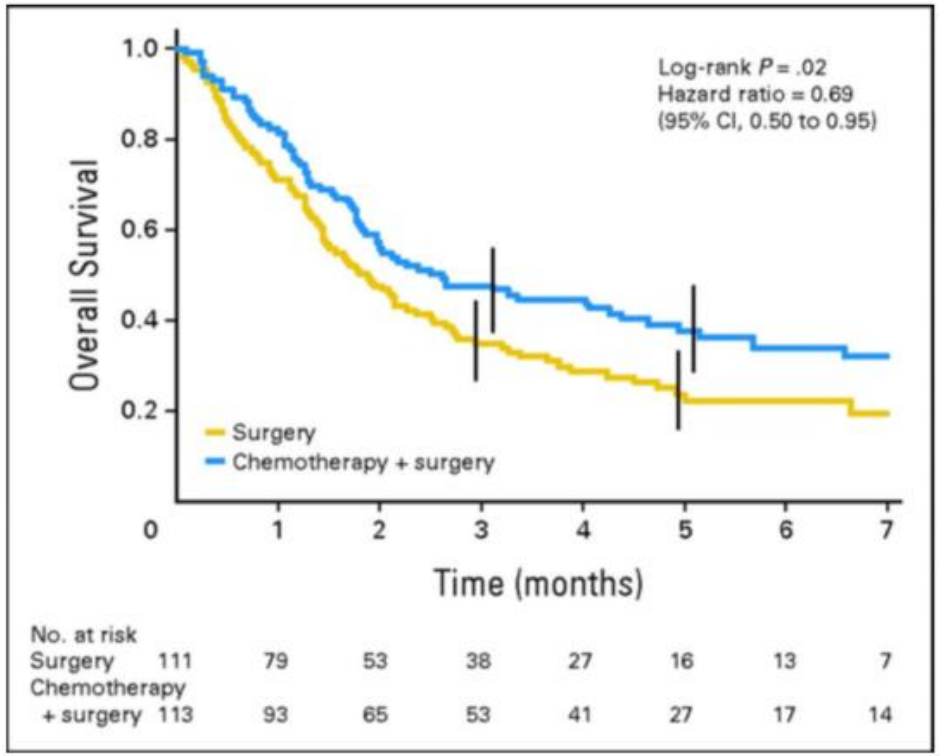
Eligibility criteria
Lower oesophageal or GOJ adenocarcinoma (gastric after 1998)
No metastases
ECOG 0-1

FFCD/ACCORD preoperative patient characteristics

	Surgery alone	Chemo + surgery
Median age	63	63
Sex Male Female	 91 (82%) 20 (18%)	 96 (85%) 17 (15%)
Site of disease Gastric Oesophagus GOJ	 28 (13%) 15 (25%) 70 (62%)	 27(9%) 10 (24%) 74(67%)

FFCD/FNCLCC TRIAL





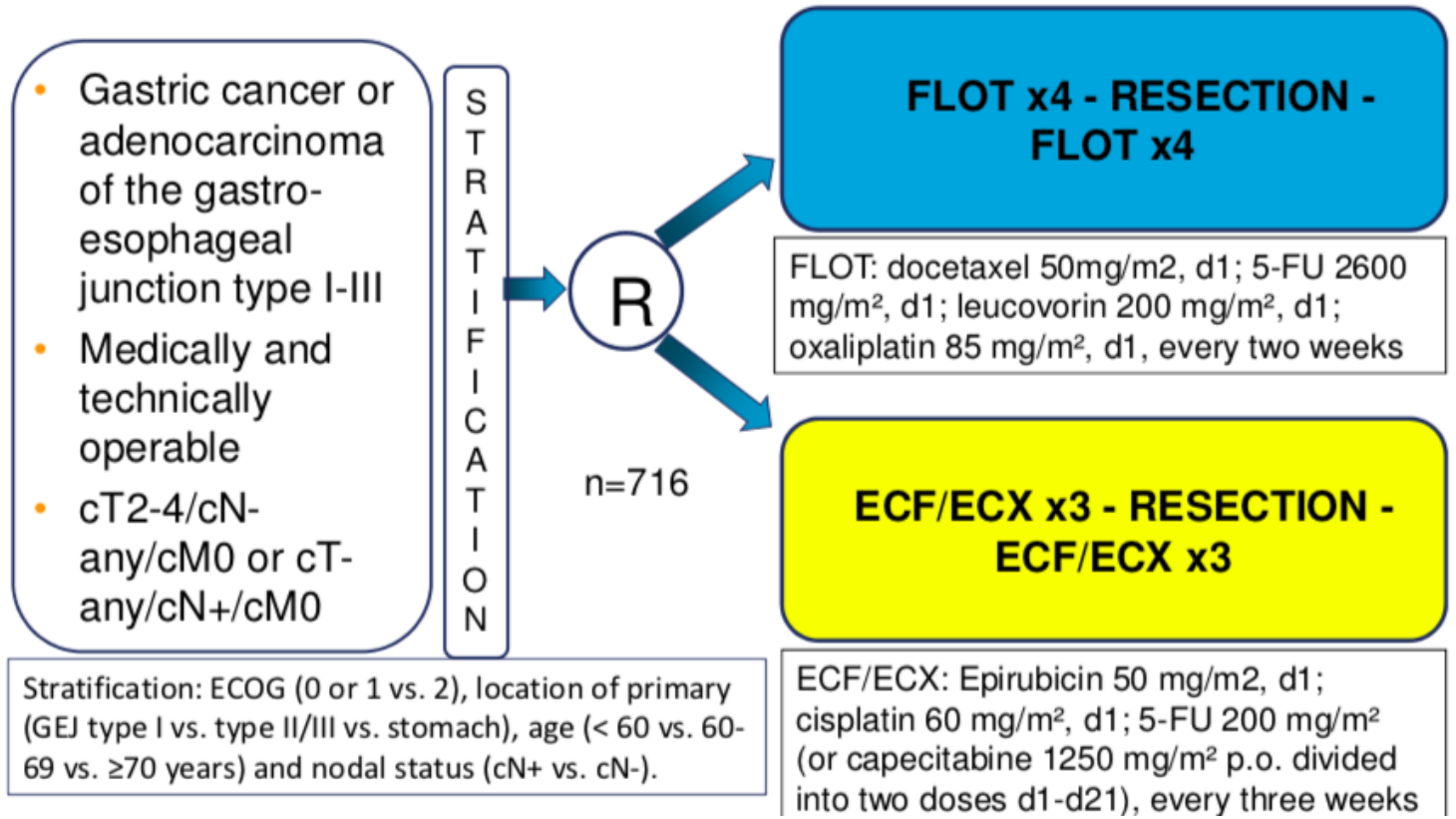
Absolute benefit in OS 14% (24% surgery vs. 38% chemo + surgery)

LESSONS FROM MAGIC AND FFCD TRIALS

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

	MAGIC 3 cycles ECF	FFCD/FNCLCC 2-3 cycles CF
Pre-operative chemotherapy	3 cycles: n= 215 (91%)	1 cycle: n=11 (10%) 2 cycles: n=85 (75%) 3 cycles: n= 13 (12%) 87% had minimum 2 cycles
Surgery	229 (92%)	109 (97%)
Post-operative chemotherapy	Any chemotherapy: n=137 (55%) 3 cycles: n= 104 (42%)	Any chemotherapy: n=54 (50%) 1 cycle: n=6 (6%) 2 cycles: n=7 (6%) 3 cycles: n= 16 (15%) 4 cycles: n=25 (23%)

NEW HORIZON IN PERI-OPERATIVE CHEMOTHERAPY



Primary endpoint
OS (ITT)

FLOT BASELINE CHARACTERISTICS

	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 or 3	115	32%	118	33%
Stomach	160	44%	158	44%

FLOT VS ECF/X 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%)	
Median duration hospital stay	16 days	15 days	
Death 90 days	26 (8%)	16 (5%)	

✓Peri-operative FLOT chemotherapy increases the proportion of patients who undergo surgical resection and increases the R0 resection rate compared to ECF/ECX

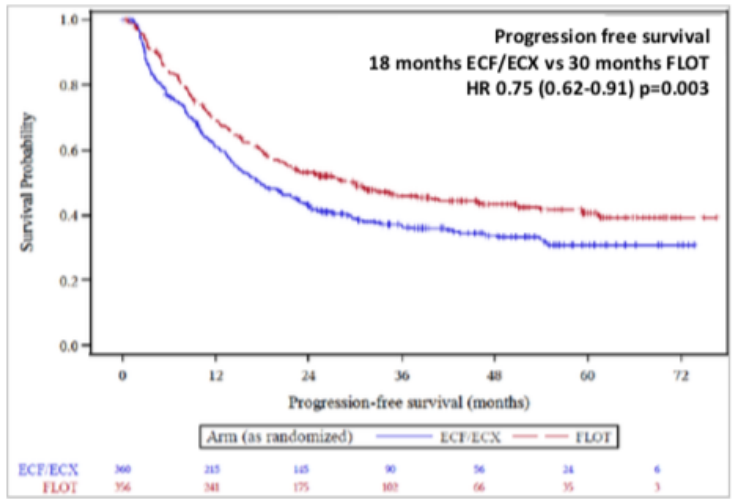
✓Surgical morbidity and mortality was not increased by use of FLOT chemotherapy

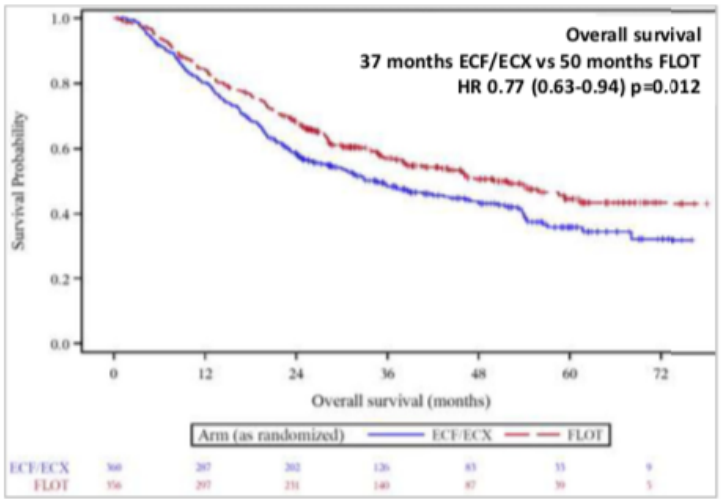
FLOT VS ECX PATHOLOGICAL OUTCOMES

	ECF/ECX (n=360)	FLOT (n=356)	
ypT stage			
≤T1	**53 (15%)**	**88(25%)**	**0.001**
T2	44 (12%)	44(12%)	
T3	175 (49%)	165(46%)	
T4	47(13%)	37(10%)	
NA	41(11%)	22(6%)	
ypN stage			
N0	**146(41%)**	**174(49%)**	**0.029**
N1	44(12%)	55(16%)	
N2	54(15%)	47(13%)	
N3	73(20%)	57(16%)	
NA	43(12%)	23(7%)	

✓Peri-operative FLOT chemotherapy increases the proportion of patients have pathological early stage tumours compared to ECF/X

FLOT IMPROVES PFS AND OS COMPARED TO ECF/X

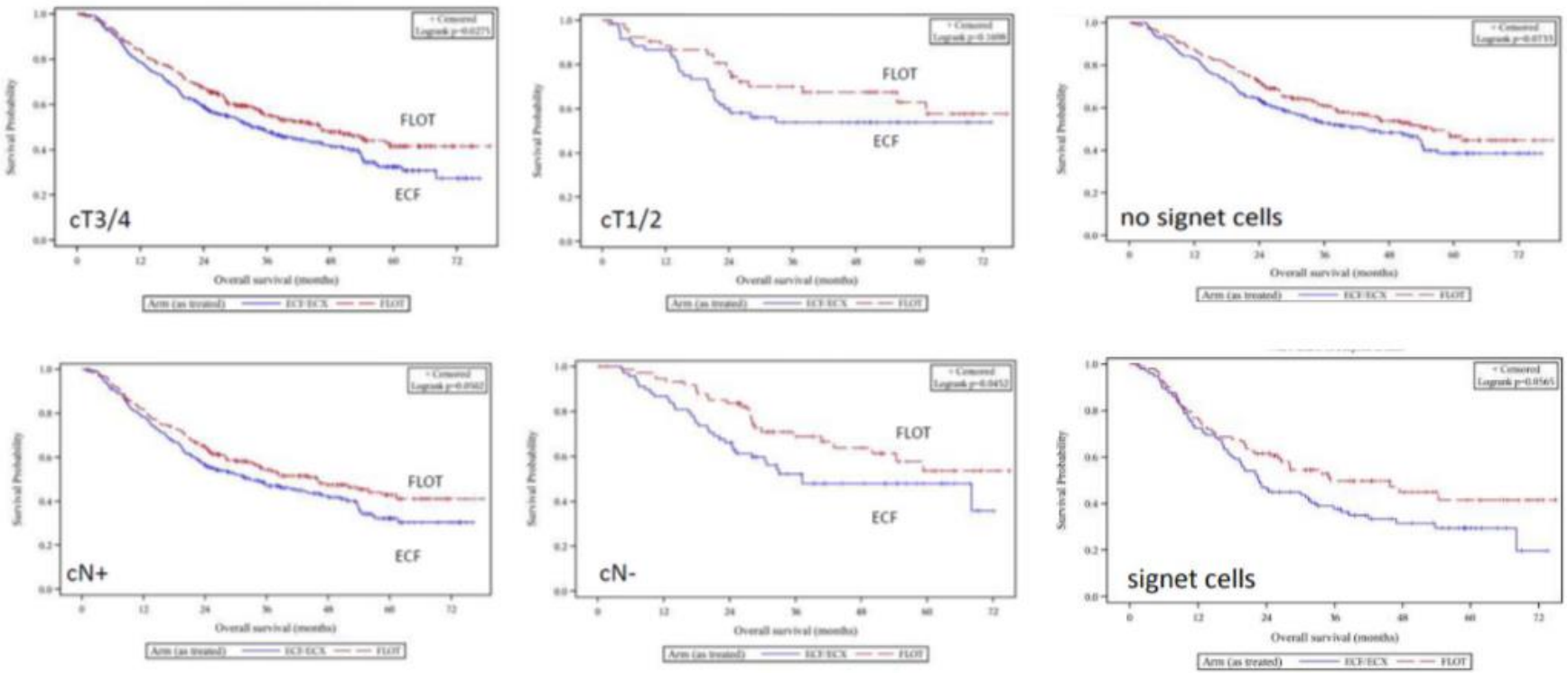




Projected PFS rates		
	ECF/X	FLOT
2 year	43%	53%
3 year	37%	46%
5 year	31%	41%

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

BENEFIT OF FLOT IN ALL PROGNOSTIC GROUPS



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
Fatigue	38 (11%)	25 (7%)	
Infections	30 (9%)	63 (18%)	<0.001
Leukopenia	75 (21%)	94 (27%)	
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 VS ECF/X TREATMENT TOLERABILITY

	ECF/ECX (n=360)	FLOT (n=356)
Completed pre-operative chemo	327 (91%)	320 (90%)
Surgery	340 (94%)	336 (94%)
Started post-operative chemo Completed protocol post-op chemo	187 (52%) 133 (37%)	213 (60%) 162 (46%)

✓Patients treated with FLOT were more likely to commence post-operative chemotherapy, and those who commenced post-operative FLOT were more likely to complete post-operative chemotherapy

PERI-OPERATIVE CHEMOTHERAPY: TAKE HOME MESSAGES

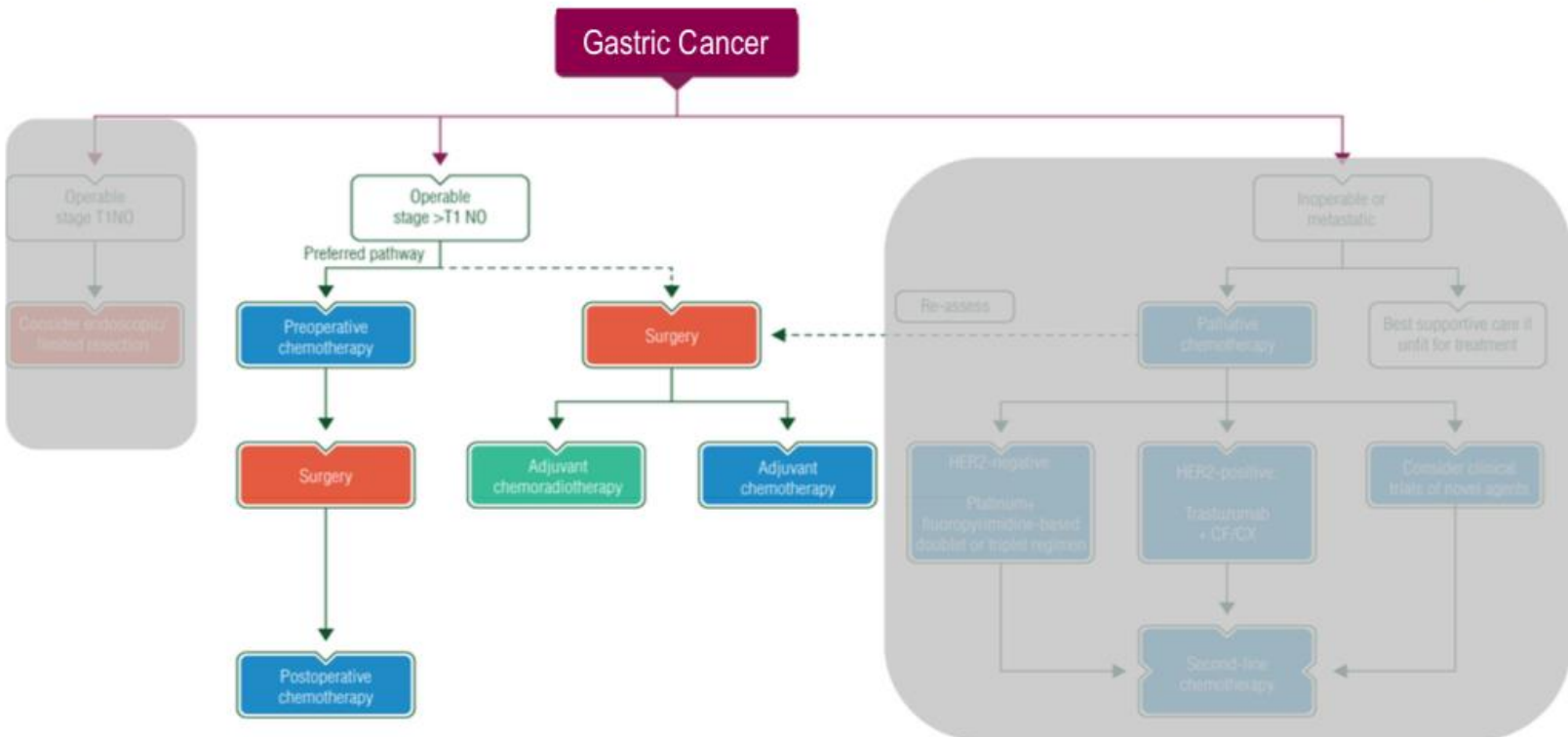
FLOT is the new gold standard treatment for patients who receive peri-operative chemotherapy and surgery for operable gastroesophageal cancer

- 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 CHEMOTHERAPY

ESMO GASTRIC CANCER GUIDELINES



Smyth et al, Ann Oncol. 2016;27(suppl_5):v38-v49. doi:10.1093/annonc/mdw350

The role of chemotherapy:
Main studied adjuvant modalities

SCIENTIFIC EVIDENCES…

Post-operative CT

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

...Meta-analyses

Author	N° of studies	ODDs Ratio/Hazard Ratio for death
Hermans, *JCO 1993*	11	**OR** 0.88 (**95% CI** 0.78-1.08)
Earle, *EJC 1999*	13	**OR** 0.80 (**95% CI** 0.66-0.97)
Mari, *Ann Onc 2000*	20	**OR** 0.82 (**95% CI** 0.75-0.89)
Gianni, *Ann Onc 2001*	17	**OR** 0.72 (**95% CI** 0.62-0.84)
Janunger, *Eur J Surg 2002*	21	**OR** 0.84 (**95% CI** 0.74-0.96)
Panzini**,** Tumori 2002	17	**OR** 0.72 (**95% CI** 0.62-0.84)

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

...Meta-analyses...What's the problem?

METHODOLOGICAL LIMITS OF META-ANAYSES:

1. Literature-Based (selection bias)
2. Heterogeneus criteria for selections of patients and for selections of studies
3. Studies with low statistical power
4. Old chemotherapy regimens

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

[274pts]
- **E**toposide-**A**driamycin-cis**P**latin* (x 2) → FU/LV (x 2)
- ***Surgery***

1992-97

[260pts]
- FU icp x 5 d → **FU** icp x 5 d - cis**P**latin* d 2 (x 4)
- ***Surgery***

1989-97

[258pts]
- cis**P**latin*-**E**pirubicin-**L**eucovorin-**F**U (x 4)
- ***Surgery***

1995-00

* *CDDP-based chemotherapy*

[228pts]
- **E**pirubicin-**L**ederfolin-**F**U-**E**toposide (x 6)
- ***Surgery***

1996-01

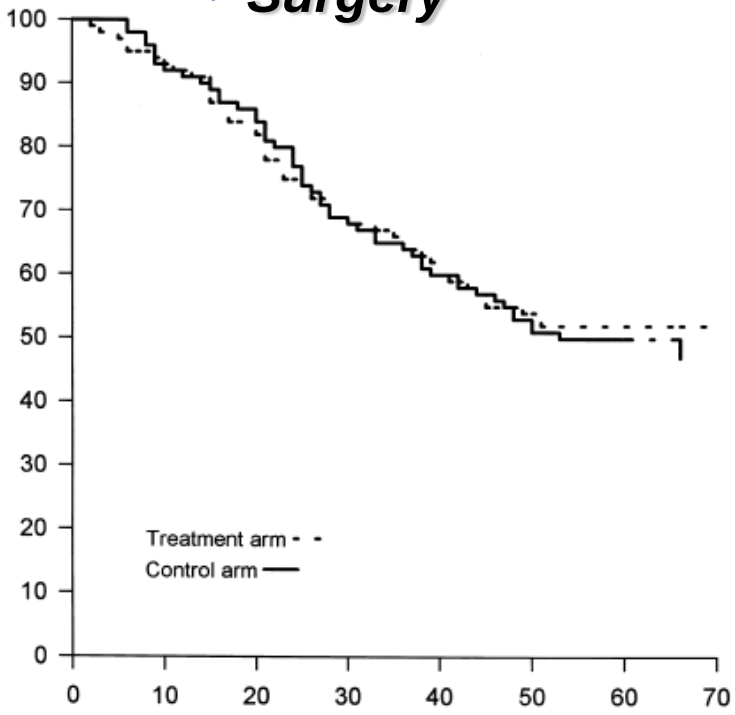
[400pts]
- cis**P**latin-**E**pirubicin-**L**eucovorin-**F**U (x 4)
- FU/LV (x 4)

1998-03

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

[274pts] → **E**toposide-**A**driamycin-cis**P**latin (x 2) → FU/LV (x 2)

→ ***Surgery***



P = 0.22

HR 0.93 [95% CI 0.65-1.34]

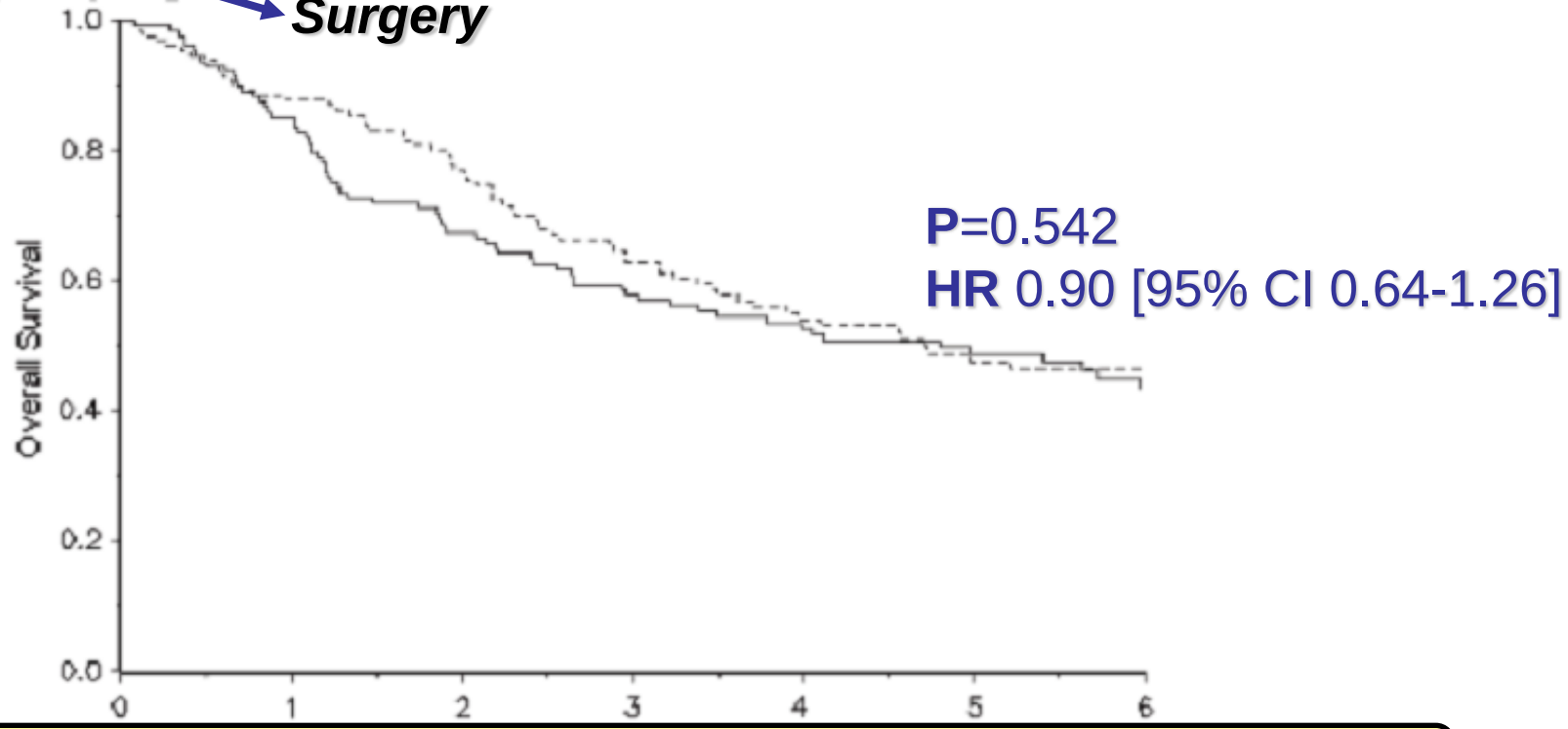
5-year OS: 52% (CT arm) **vs 48%** (f-up arm)

Bajetta, Ann Oncol 2002

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

[258pts] → cis**P**latin-**E**pirubicin-**L**eucovorin-**F**U (x 4)

→ ***Surgery***



P=0.542

HR 0.90 [95% CI 0.64-1.26]

5-year OS: 47.6% (CT arm) **vs 48.7%** (f-up arm)

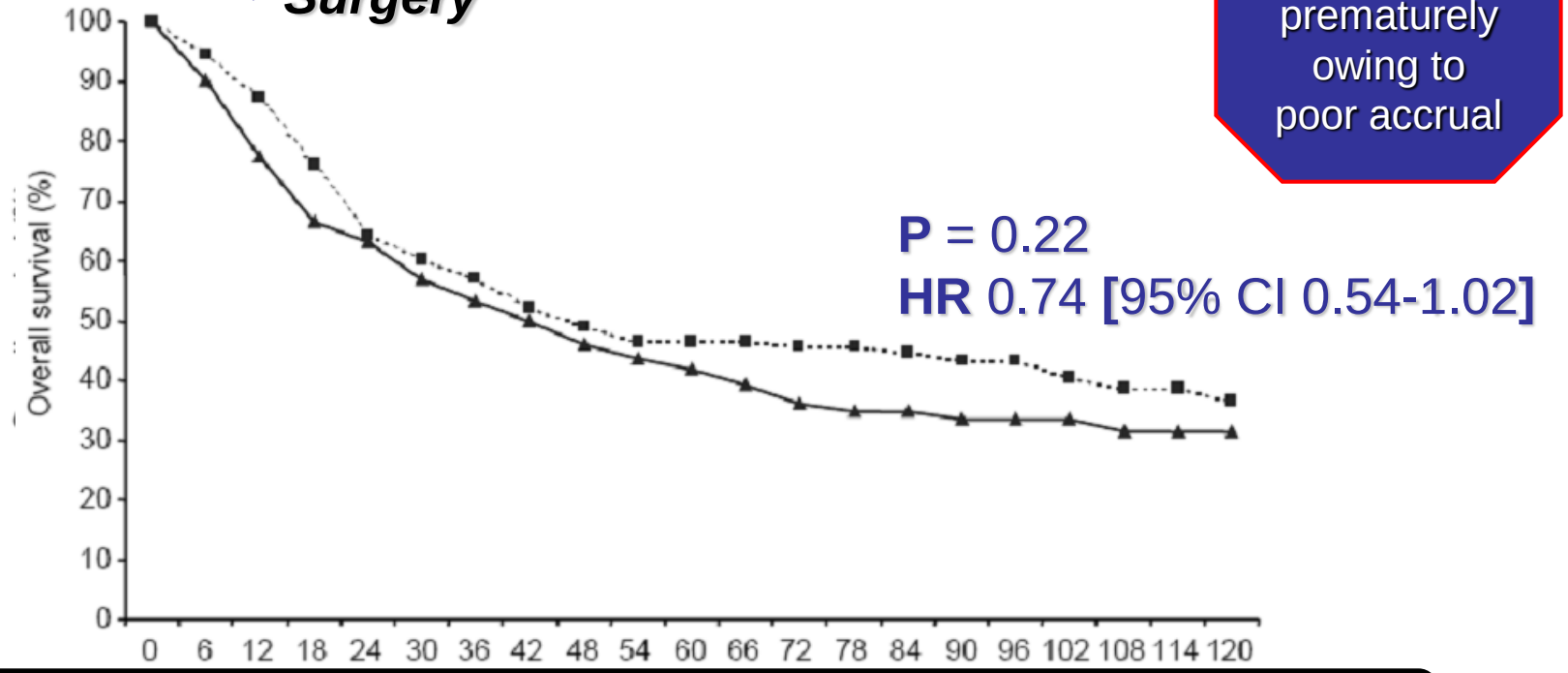
Di Costanzo, JNCI 2008

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

[260pts] → FU icp x 5 d → **FU** icp x 5 d - cis**P**latin d 2 (x 4)

→ ***Surgery***

Closed prematurely owing to poor accrual



P = 0.22

HR 0.74 **[**95% CI 0.54-1.02**]**

5-year OS: 46.6% (CT arm) **vs 41.9%** (f-up arm)

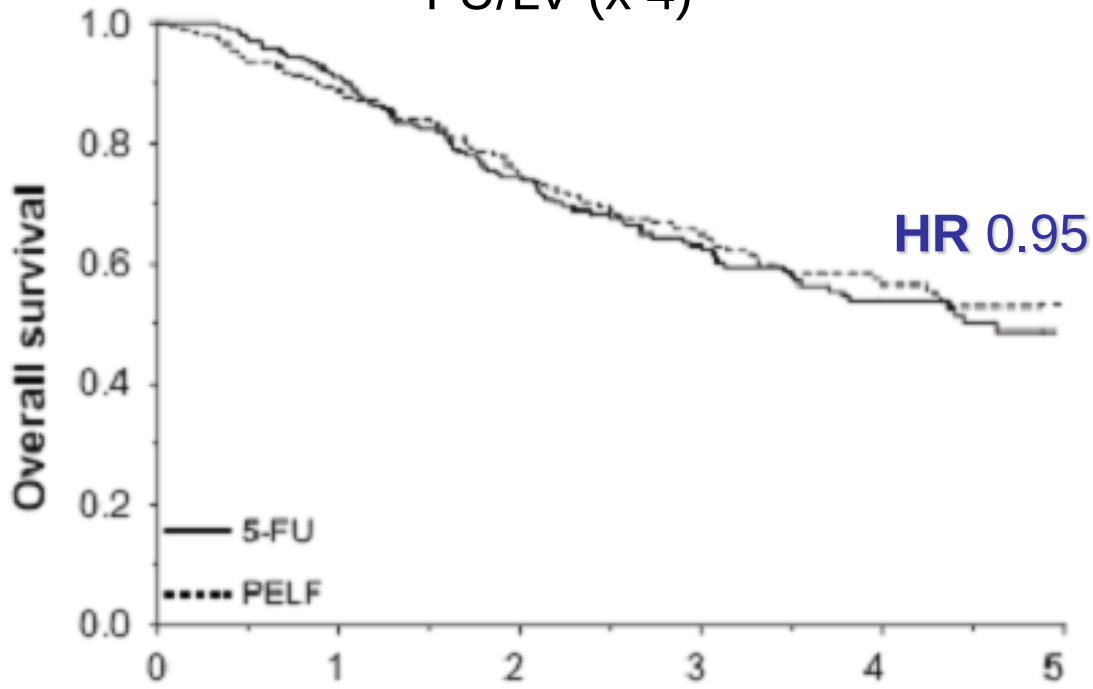
Bouchè, Ann Oncol 2005

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

GISCAD
Gruppo Italiano per lo studio dei Carcinomi Apparato Digerente

[400pts] → cis**P**latin-**E**pirubicin-**L**eucovorin-**F**U (x 4)

→ FU/LV (x 4)



HR 0.95 **[**95% CI 0.70-1.29**]**

5-year OS: 52% (PELFw) **vs 50%** (5-FU)

Cascinu, JNCI 2007

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

...After Meta-analyses

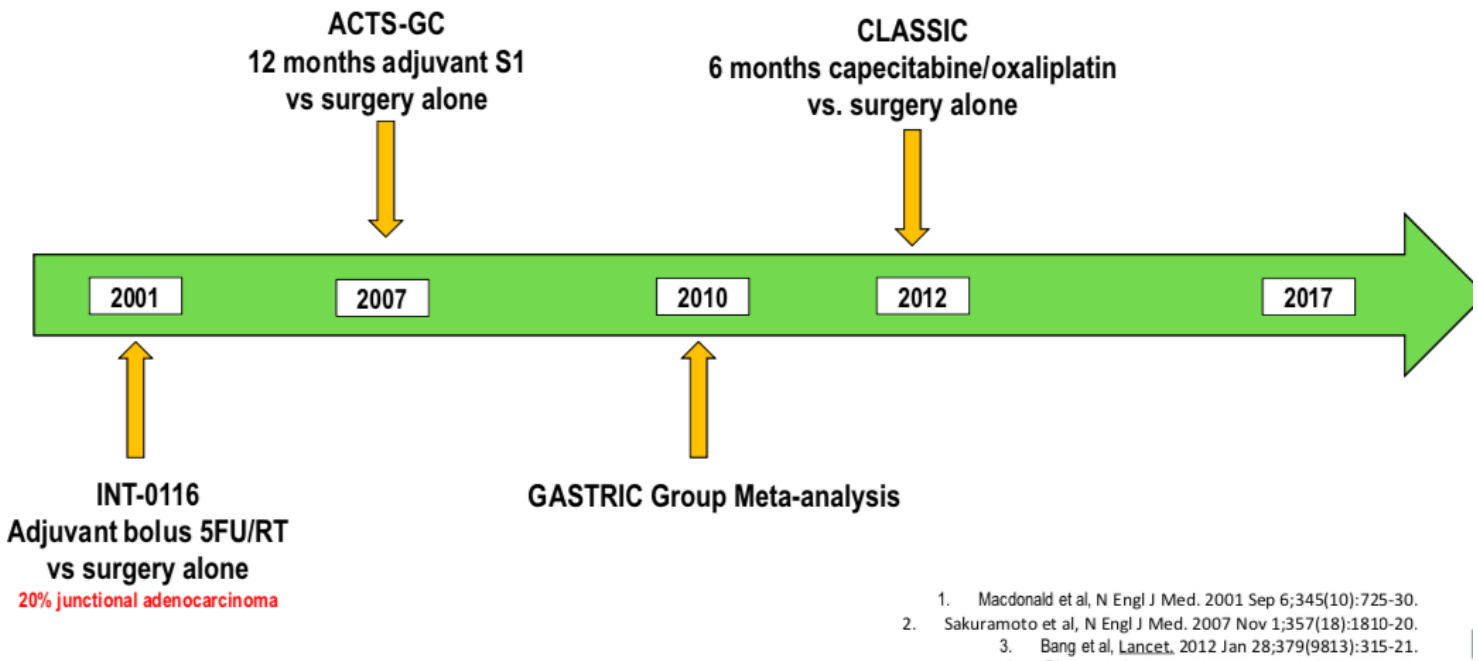
Trial	CT	N° p	↑ 5-OS rate	↑5DFS rate
ITMO	EAP→5-FU/LV	274	**4%** (p=0.7)	**5%** (p=0.29)
GOIRC	PELF	200	**1%** (p=0.54)	
FFCD	5-FU→FUP	278	**5%** (p=0.22)	**8%** (p=0.19)
GISCAD Gruppo Italiano per lo studio dei Carcinomi Apparato Digerente	PELFw **VS** FU/LV	400	**2%** (n.s.)	**1%** (n.s.)
GOIM	ELFE	228	**4,5%** (p=0.6)	**5%** (p=0.3)

SCIENTIFIC EVIDENCES ABOUT POST-OPERATIVE ADJUVANT CHEMOTHERAPY

...After Meta-analyses...What's the problem?

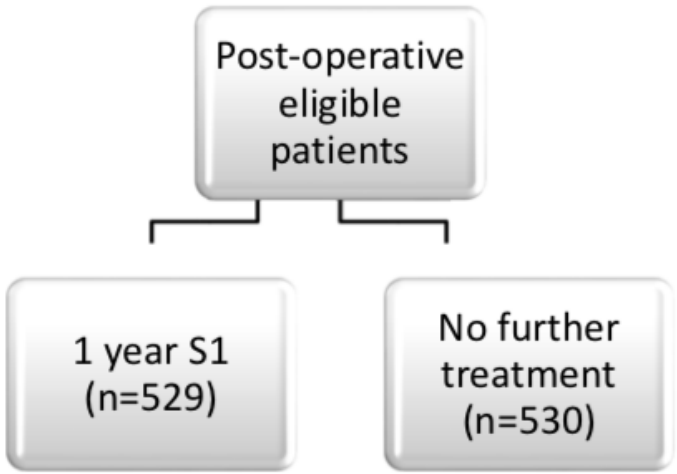
Trial	CT	N° p	↑ 5-OS rate	↑5DFS rate
ITMO	EAP→5-FU/LV	274	**4%** (p=0.7)	**5%** (p=0.29)
GOIRC	PELF	200	**1%** (p=0.54)	
FFCD	5-FU→FUP	278	**5%** (p=0.22)	**8%** (p=0.19)
GISCAD Gruppo Italiano per lo studio dei Carcinomi Apparato Digerente	PELFw **VS** FU/LV	400	**2%** (n.s.)	**1%** (n.s.)
GOIM	ELFE	228	**4,5%** (p=0.6)	**5%** (p=0.3)

EVOLUTION OF ADJUVANT (CHEMO)THERAPY FOR GASTRIC CANCER 2001 - 2017



1. Macdonald et al, N Engl J Med. 2001 Sep 6;345(10):725-30.
2. Sakuramoto et al, N Engl J Med. 2007 Nov 1;357(18):1810-20.
3. Bang et al, Lancet. 2012 Jan 28;379(9813):315-21.
4. Pignon et al, JAMA. 2010 May 5;303(17):1729-37.

ACTS-GC TRIAL



Primary Endpoint
Overall survival
Secondary endpoints
Relapse free survival & safety

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

ACTS-GC patient characteristics		
	Surgery alone	Chemo + surgery
Median age	63	63
Sex Male Female	 369 (70%) 161(30%)	 367 (71%) 162(29%)
Stage of cancer II III IV	 282 (53%) 213 (40%) 35 (7%)	 264 (50%) 224 (42%) 40(8%)

ACTS-GC TRIAL

Post-operative eligible patients

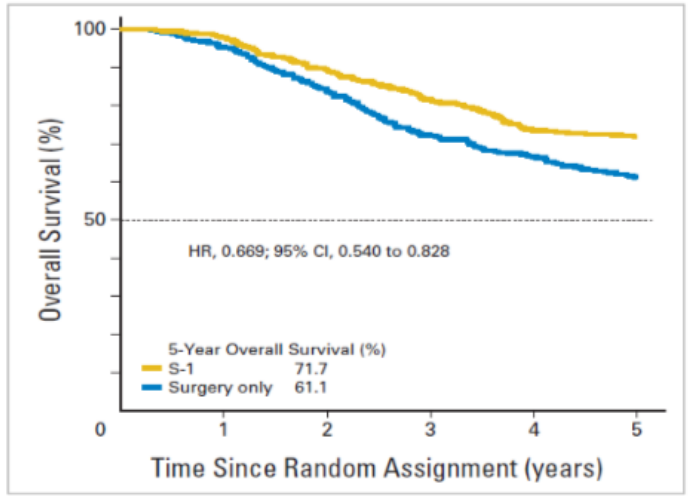
1 year S1 (n=529)

No further treatment (n=530)

Primary Endpoint
Overall survival
Secondary endpoints
Relapse free survival & Safety

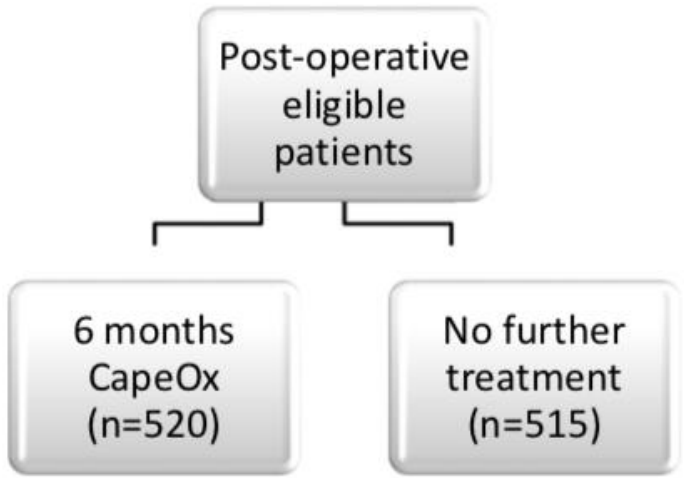
Update ESMO 2017 OPAS-1 study
6 months of S1 not inferior to 12 months

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%



Sasako et al, J Clin Oncol. 2011 Nov 20;29(33):4387-93.

CLASSIC TRIAL



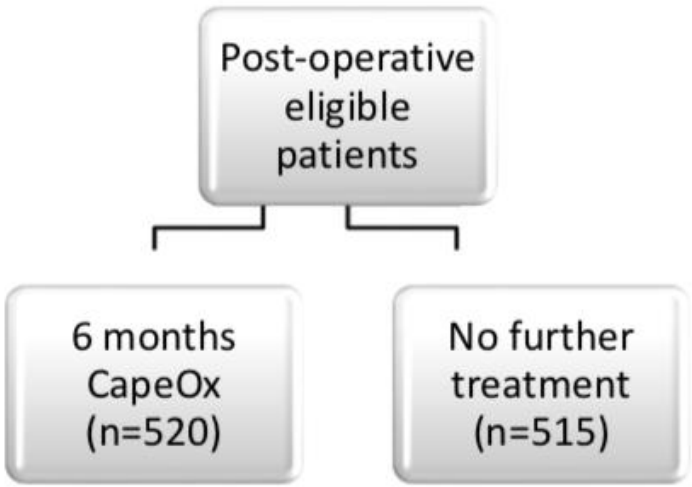
Primary Endpoint
3 year disease free survival
Secondary endpoints
Overall survival & safety

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

CLASSIC patient characteristics

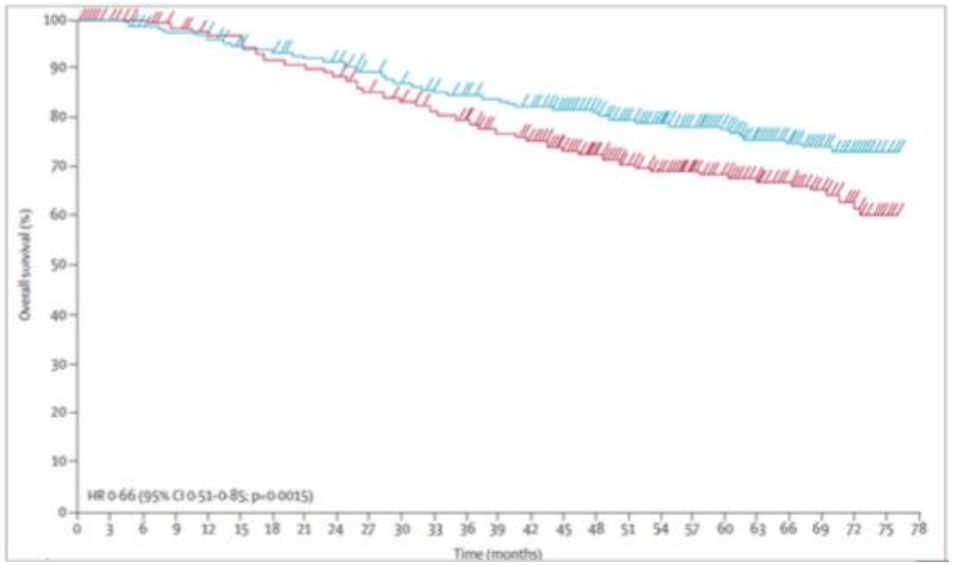
	Surgery alone	Chemo + surgery
Median age	56	56
Sex Male Female	 358 (70%) 157(30%)	 373 (72%) 147(28%)
Stage of cancer II III IV	 261 (51%) 253 (49%) 1 (<1%)	 253(49%) 266(51%) 0 (0%)

CLASSIC TRIAL



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

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%)



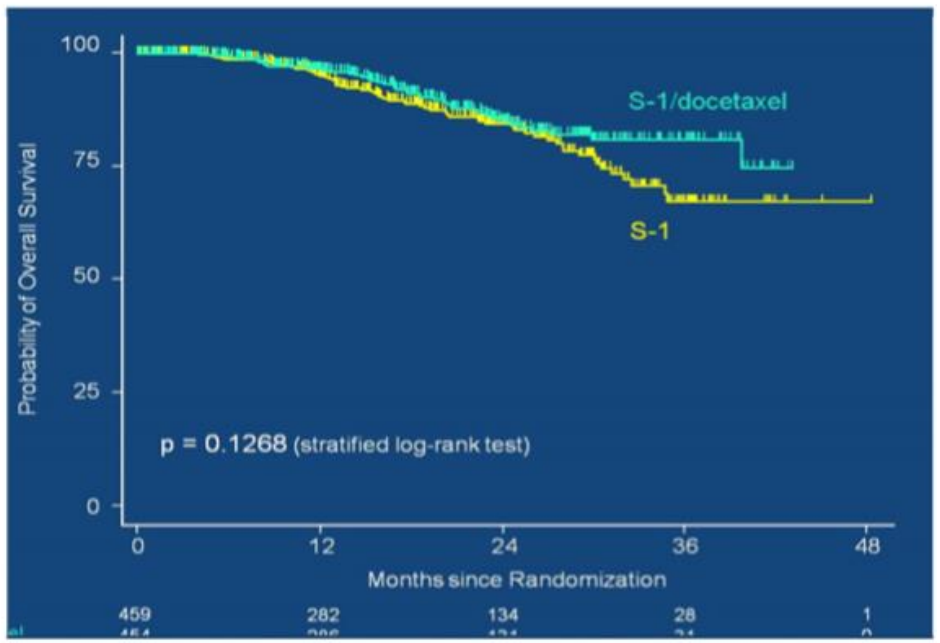
JACRO-07

Post-operative eligible patients

S1 80mg/m² d1-28 q 6 wks x 1 year (n=459)

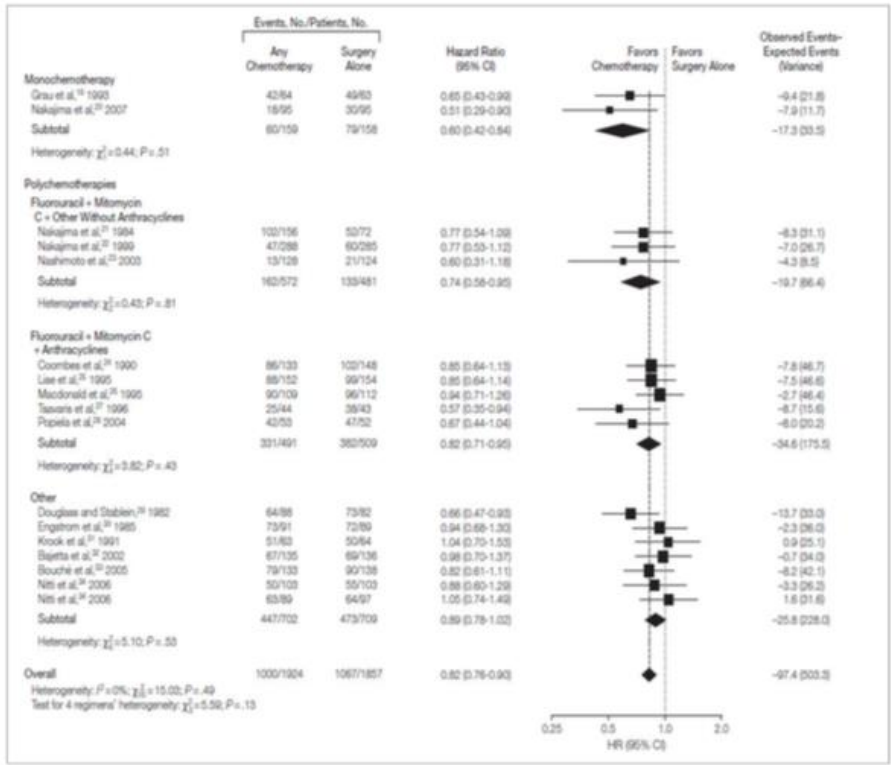
Cycle 1: S1 80mg/m² d1-14 q21d
Cycle 2-7: docetaxel 40mg/m² plus S1 80mg/m² d1-14 q21d
Then S1 x 6 months
(N=456)

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



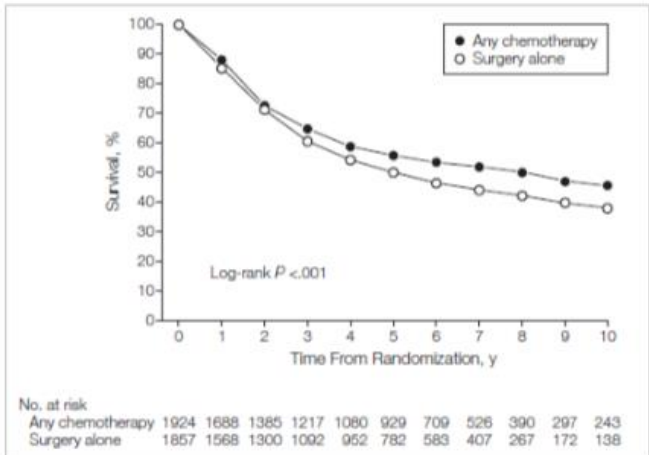
Overall survival

ADJUVANT CHEMOTHERAPY FOR NON-ASIAN PATIENTS



Neoadjuvant or peri-operative chemotherapy is preferred due to the downstaging effects associated with this.

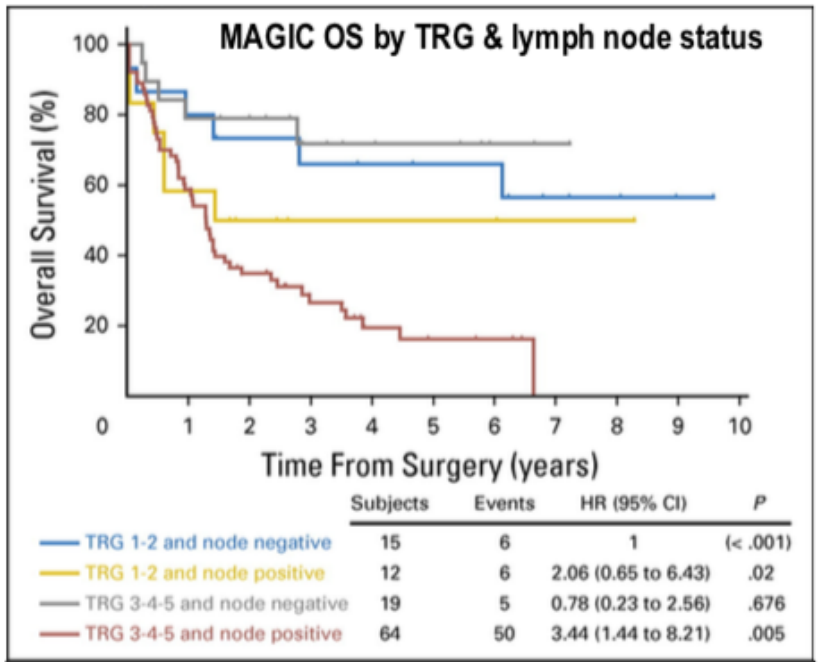
The GASTRIC group meta-analysis suggests a 5.8% absolute OS benefit at 5 years (55.3% to 49.6%) for patients treated with adjuvant chemotherapy .



Paoletti et al, JAMA. 2010 May 5;303(17):1729-37.

BIOMARKERS FOR PERIOPERATIVE CHEMOTHERAPY

RISK STRATIFICATION USING TUMOUR REGRESSION GRADING



	Subjects	Events	HR (95% CI)	P
TRG 1-2 and node negative	15	6	1	(< .001)
TRG 1-2 and node positive	12	6	2.06 (0.65 to 6.43)	.02
TRG 3-4-5 and node negative	19	5	0.78 (0.23 to 2.56)	.676
TRG 3-4-5 and node positive	64	50	3.44 (1.44 to 8.21)	.005

Lymph nodes are the most important prognostic marker following chemotherapy and surgical resection

EORTC VESTIGE Study design

CI: F. Lordick

Gastric or EGJ adenocarcinoma stage Ib-IV

Completed pre-operative chemo with a fluoropyrimidine-platinum containing regimen

Duration of neoadjuvant chemotherapy: 6 weeks - 12 weeks

Total or partial gastrectomy with at least D1 LND; Minimum of 15 lymph nodes evaluated

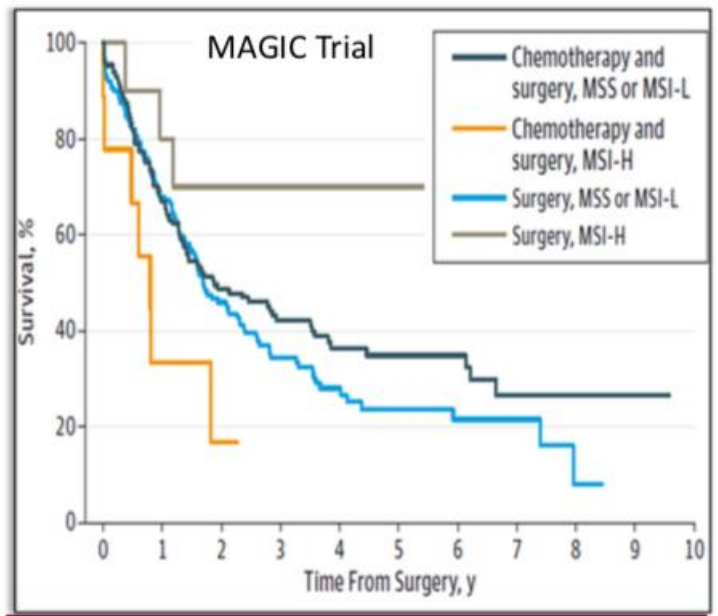
Age ≥ 18 years

Control arm: Postoperative chemotherapy (completion of the perioperative tx) according to standards:
Fluoropyrimidine/platinum based (CF/CX/ECF/ECX/EOX/FOLFOX/ CapeOx/FLOT/DCF).

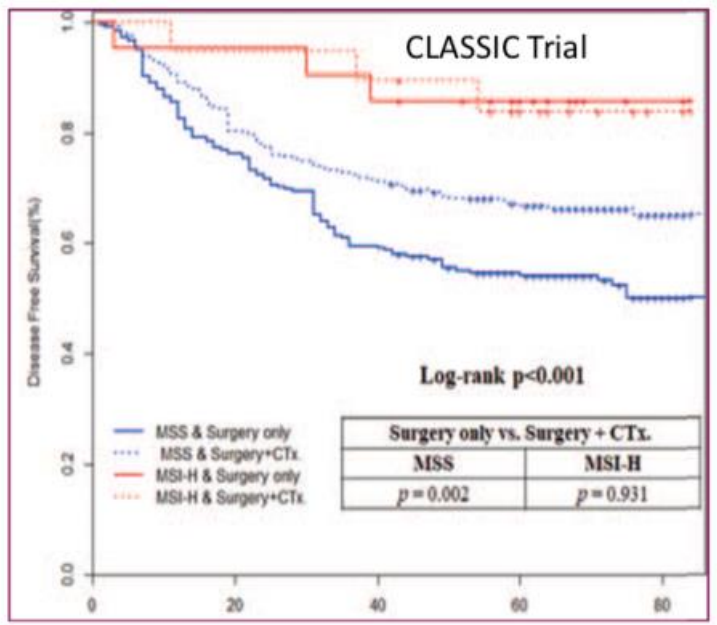
Experimental arm:
Nivolumab 3mg/kg q2w x 1y
Ipilimumab 1mg/kg q6wkx 1y

Follow-up:
- Clinical examination and CT scan of the chest and abdomen every 3 months during year 1 and 2 following randomization
- and then every 6 months until year 5 or death or documented recurrence

MSI FOR PERSONALISED TREATMENT IN RESECTABLE GC



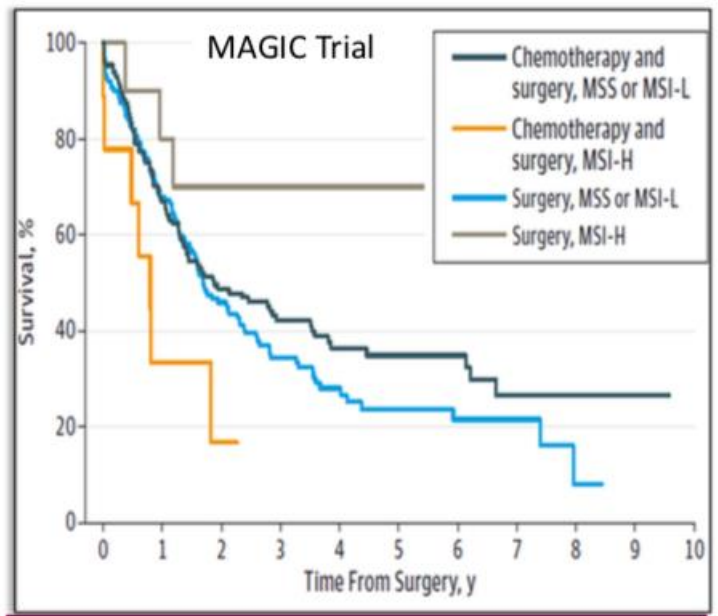
No benefit to perioperative chemotherapy in MSI-H gastric cancer, possible detriment observed (small numbers)



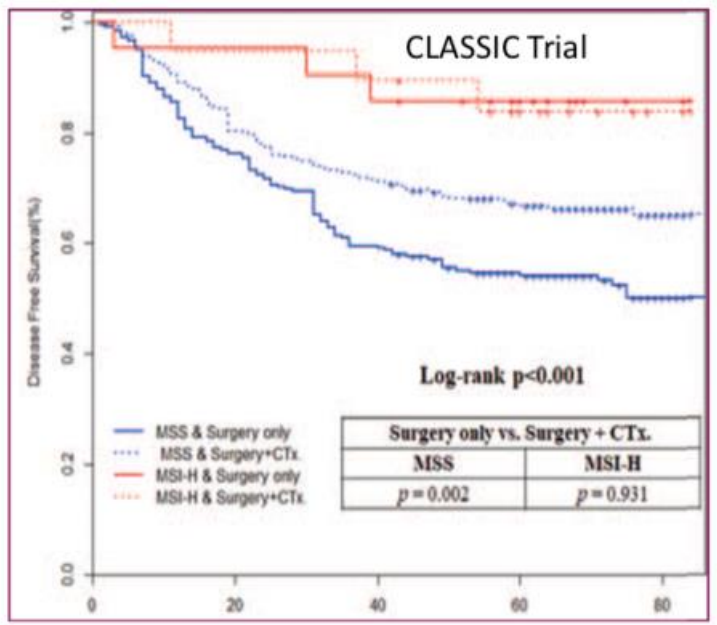
No benefit to adjuvant chemotherapy in MSI-H gastric cancer

Smyth et al, JAMA Oncol. 2017 Sep 1;3(9):1197-1203.,
Choi et al,. Ann Surg; 2018,

MSI FOR PERSONALISED TREATMENT IN RESECTABLE GC



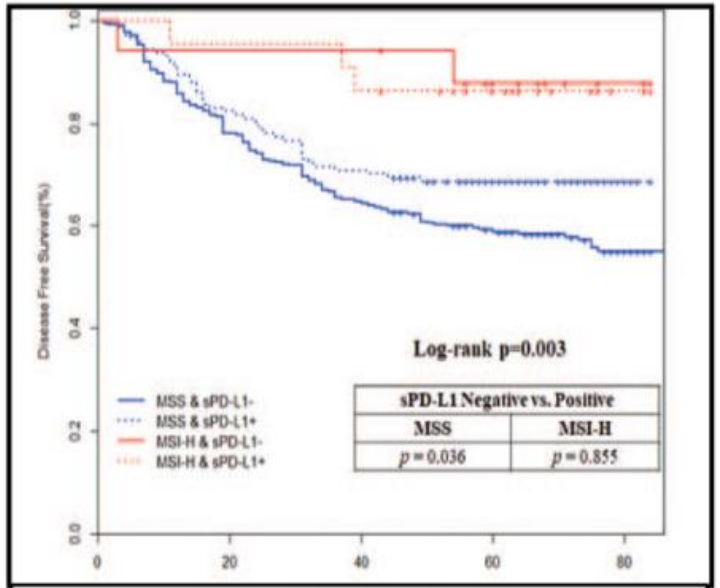
No benefit to perioperative chemotherapy in MSI-H gastric cancer, possible detriment observed (small numbers)



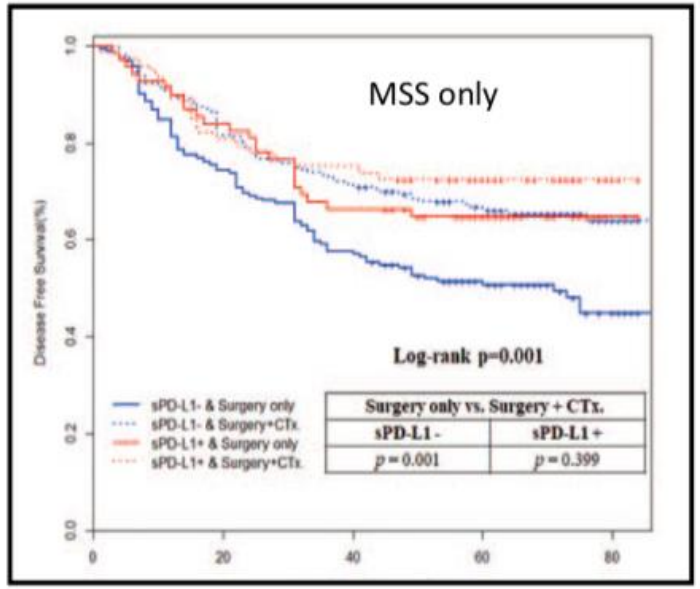
No benefit to adjuvant chemotherapy in MSI-H gastric cancer

Smyth et al, JAMA Oncol. 2017 Sep 1;3(9):1197-1203.,
Choi et al,. Ann Surg; 2018,

PD-L1 AS A BIOMARKER IN OPERABLE GC:
PROGNOSTIC AND PREDICTIVE EFFECTS OF MSI AND PD-L1 IN CLASSIC



PD-L1 is prognostic in MSS patients in the trial as a whole



Chemo appears to benefit MSS PD-L1 negative patients > MSS PD-L1 positive

Choi et al, Ann Surg 2018

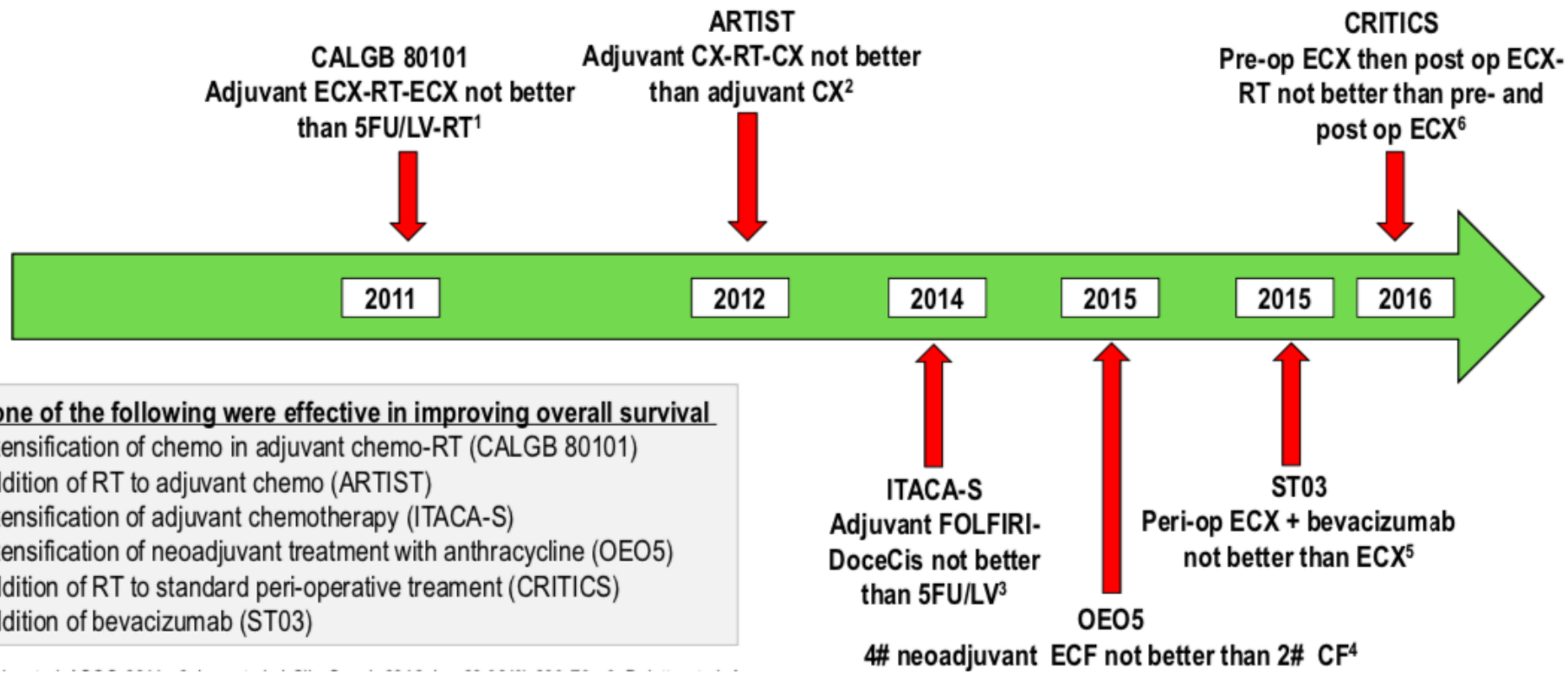
BIOMARKERS

Take home messages

- Lymph node metastases are a more important prognostic marker than tumour regression grade
- Mismatch repair deficient tumours do not appear to benefit from perioperative or neoadjuvant chemotherapy
- Gene signatures show promise for selection for chemotherapy, however require prospective validation.

NEGATIVE TRIALS OF (NEO)ADJUVANT TREATMENT 2012-2016

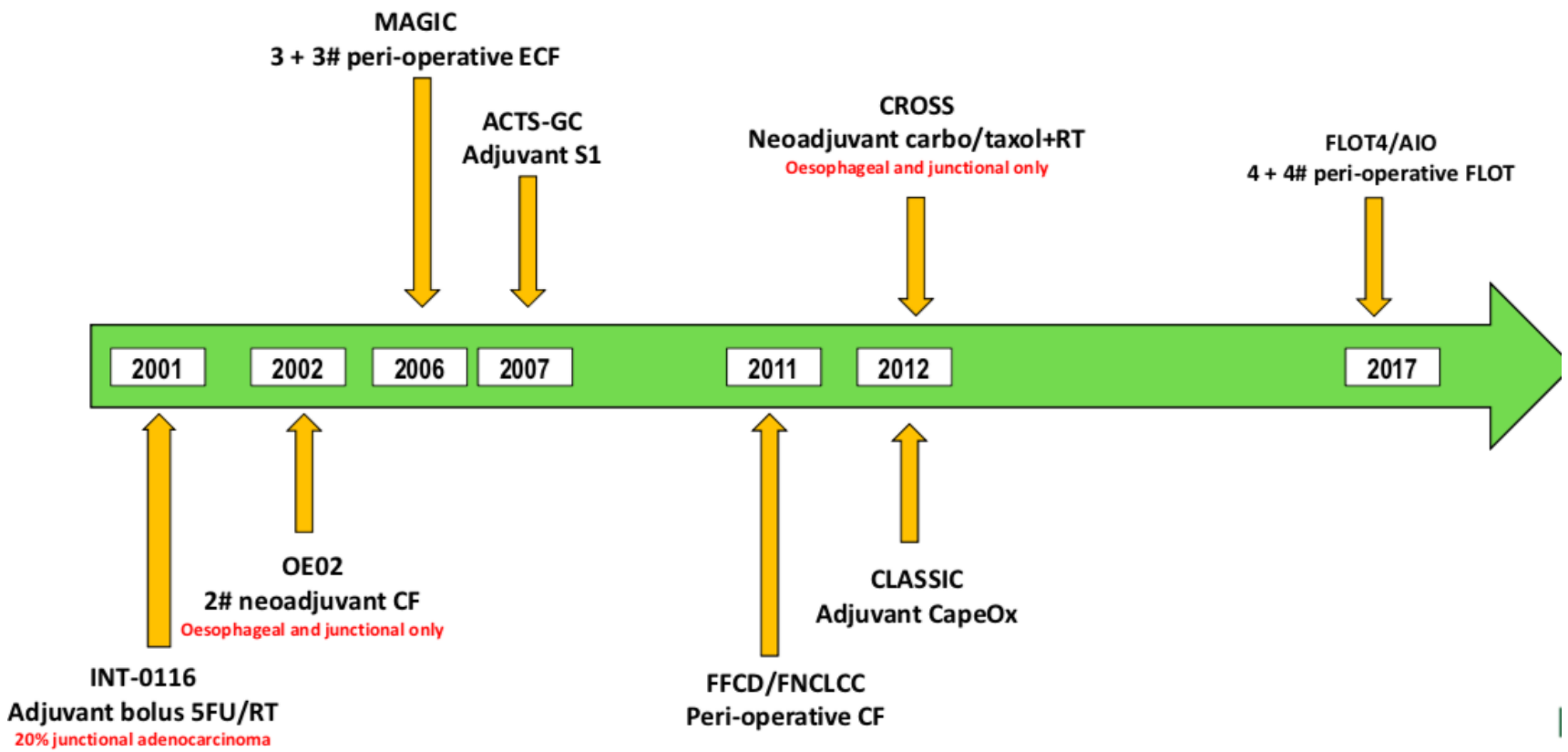
More is not always better



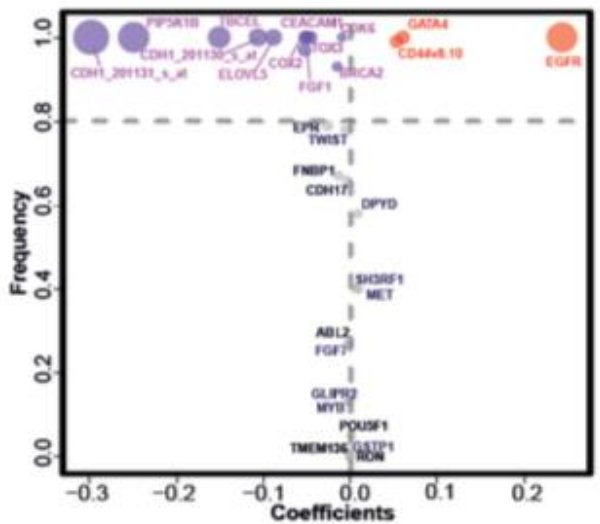
None of the following were effective in improving overall survival

Intensification of chemo in adjuvant chemo-RT (CALGB 80101)
Addition of RT to adjuvant chemo (ARTIST)
Intensification of adjuvant chemotherapy (ITACA-S)
Intensification of neoadjuvant treatment with anthracycline (OEO5)
Addition of RT to standard peri-operative treament (CRITICS)
Addition of bevacizumab (ST03)

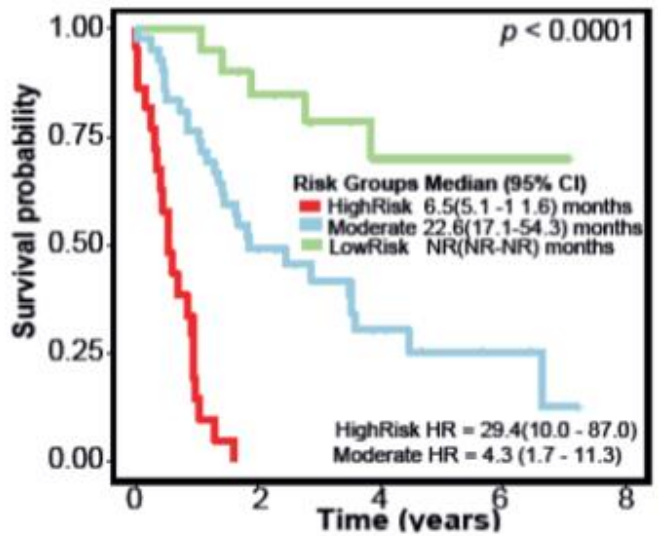
EVOLUTION OF (NEO)ADJUVANT TREATMENT 2002 - 2017

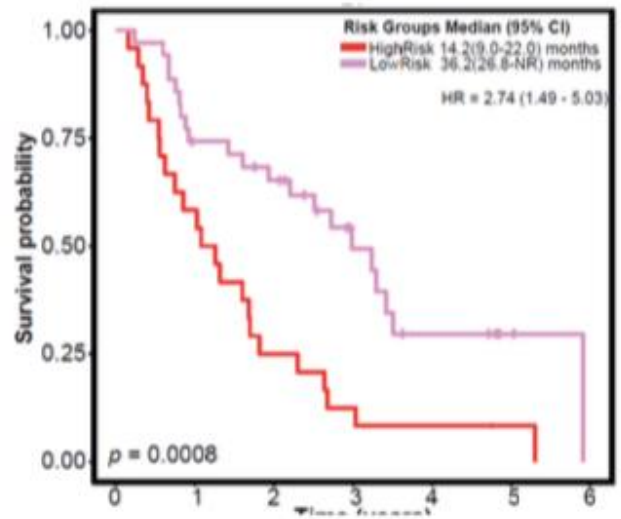


PROGNOSTIC POST-CHEMOTHERAPY GENE SIGNATURE MAGIC

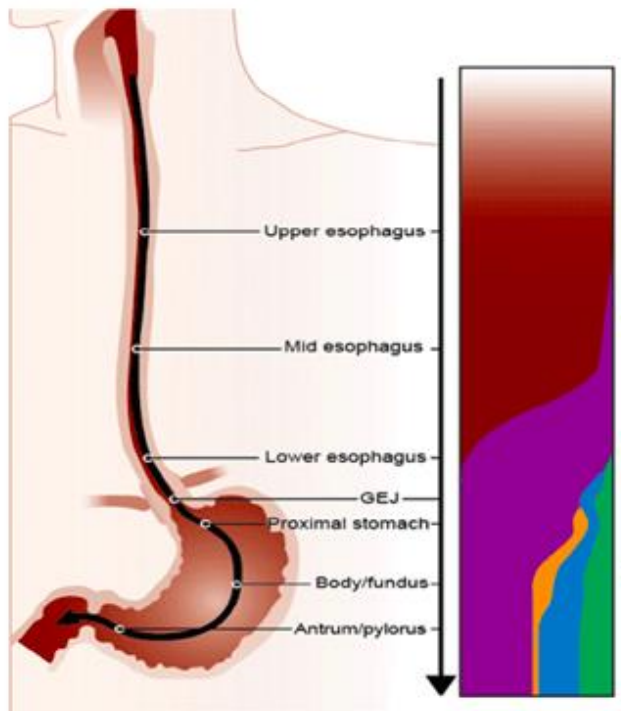


Prognostic gene selection





Gradations of Molecular Subclasses of Gastroesophageal Carcinoma[1]



ESCC	• *CCND1* amplification • *TP63/SOX2* amplification • *KDM6A* deletion
CIN	• *ERBB2* amplification • *VEGFA* amplification • *TP53* mutation
EBV	• EBV-CIMP • *PIK3CA* mutation • *PD-L1/2* overexpression
MSI	• Hypermutation • Gastric-CIMP • *MLH1* silencing
GS	• Diffuse histology • *CDH1, RHOA* mutations • *CLDN18-ARHGAP* fusions

CHEMOTHERAPY VS. CHEMORADIOTHERAPY

CHEMOTHERAPY VS CHEMORADIOTHERAPY

An ongoing debate

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.

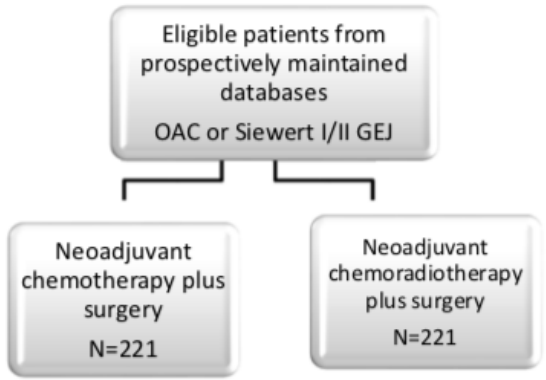
For **GASTROESOPHAGEAL JUNCTIONAL (Siewert Type I/II)** and **OESOPHAGEAL** adenocarcinoma

Perioperative chemotherapy and neoadjuvant chemoradiotherapy are both reasonable choices

Patients selection for treatment depends on the characteristics of the patient, the tumour and local expertise

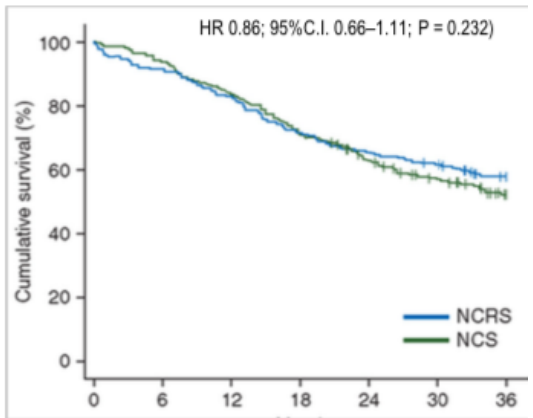
CHEMOTHERAPY VS CHEMORADIOTHERAPY

Propensity matched analysis neoadjuvant chemotherapy vs CRT



RETROSPECTIVE

Study Outcomes		
	nCT	nCRT
R0	165 (78%)	204 (92%)
Path CR	11 (5%)	59 (27%)
30 day mortality	1.4%	4.1%
Leak	6.8%	23.1%



This multicentre European analysis matched patients with resectable oesophageal and Siewert Type I and II junctional cancers treated with neoadjuvant chemotherapy or chemoradiotherapy.

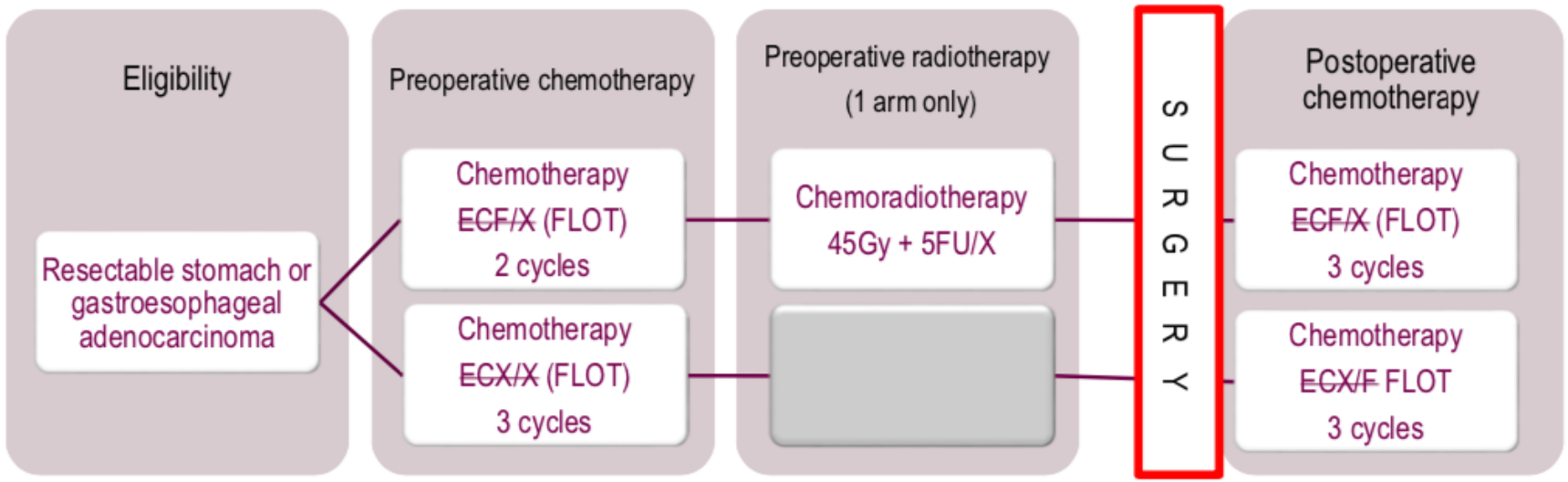
Compared with chemotherapy CRT is associated with improvements in R0 resection rates and pathological complete response, but not in overall survival.

With the exception of anastamotic leaks, morbidity and post-operative mortality were not different between the groups.

Markar et al, Ann Oncol. 2017 Mar 1;28(3):519-527.

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

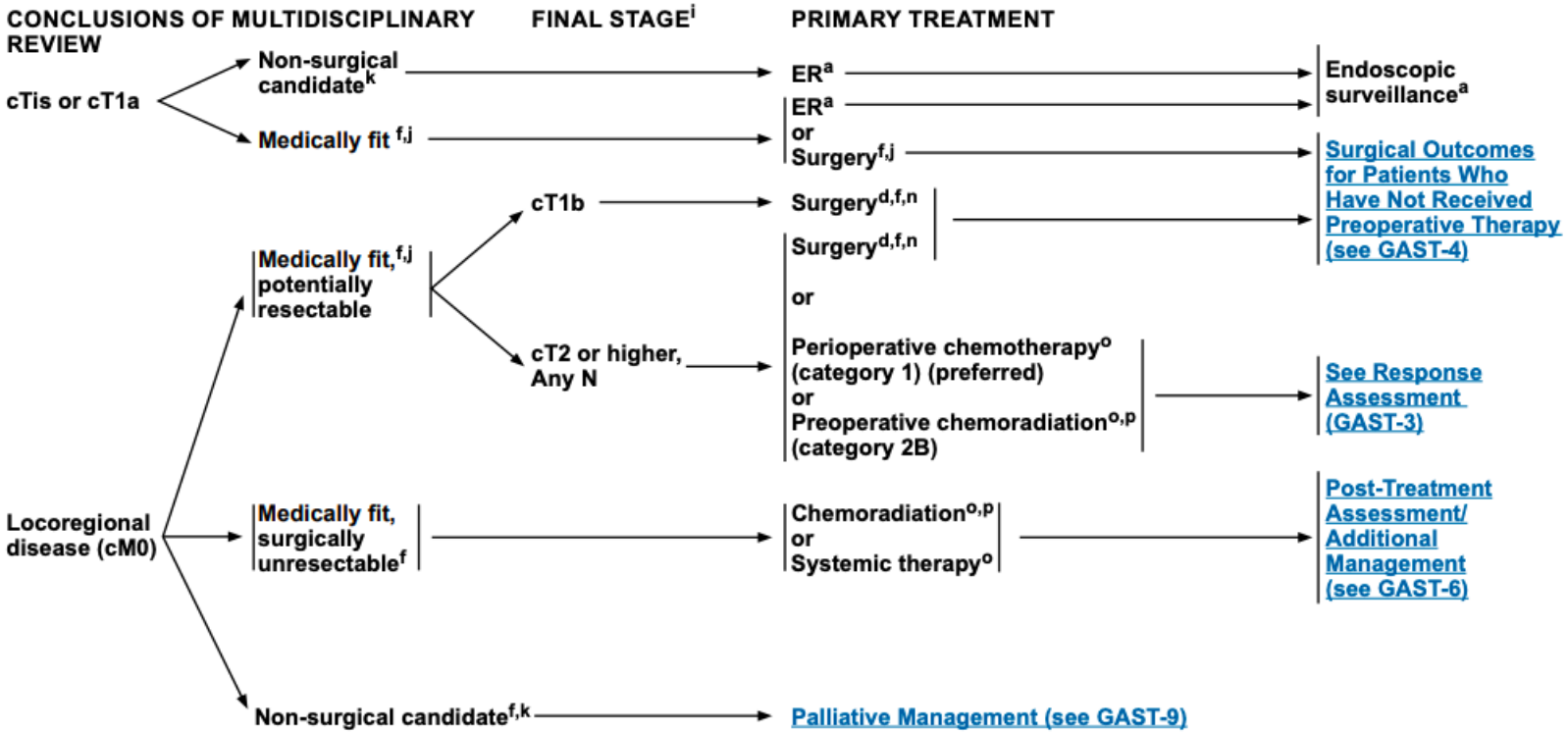
TOPGEAR



FLOT to replace ECF/X

NCCN Guidelines Version 3.2020
Gastric Cancer

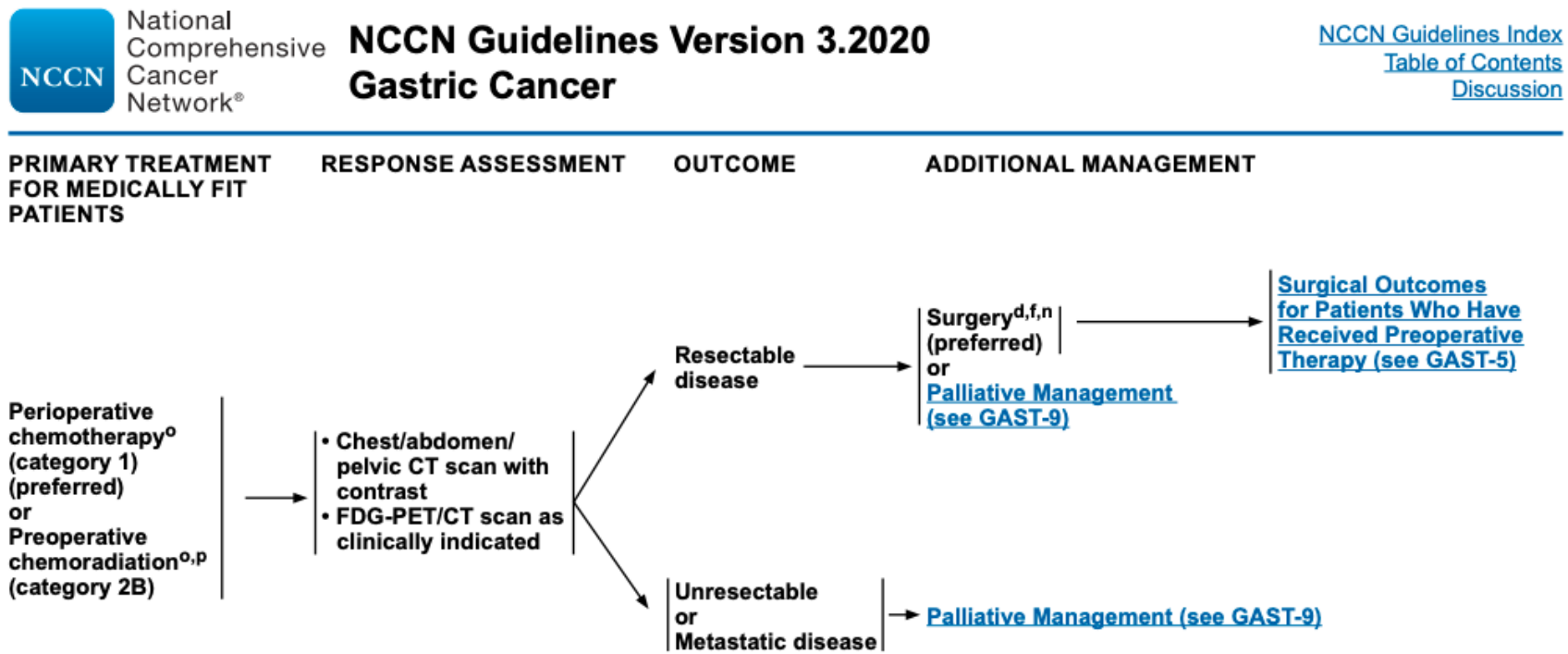
NCCN Guidelines Index
Table of Contents
Discussion



National Comprehensive Cancer Network®

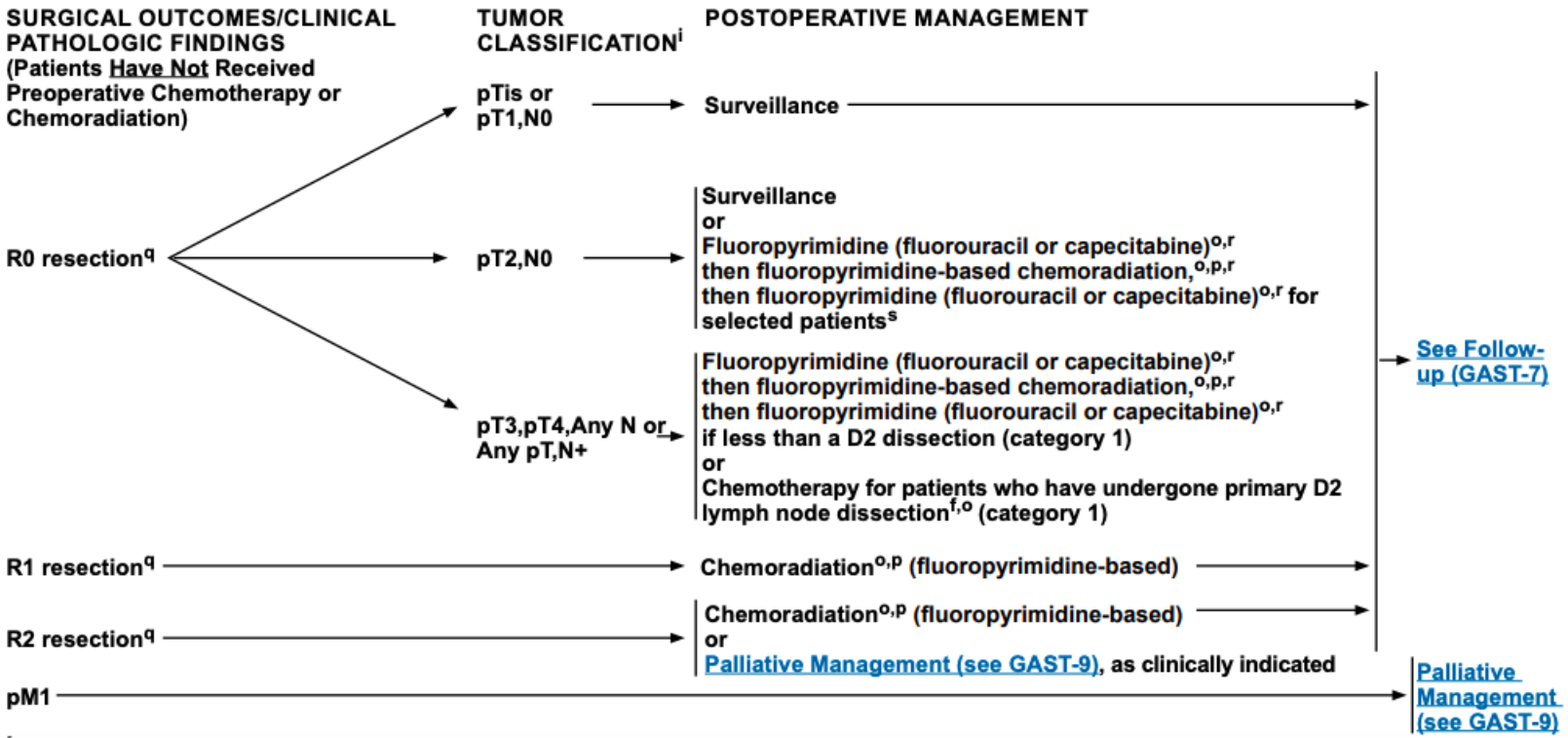
NCCN Guidelines Version 3.2020
Gastric Cancer

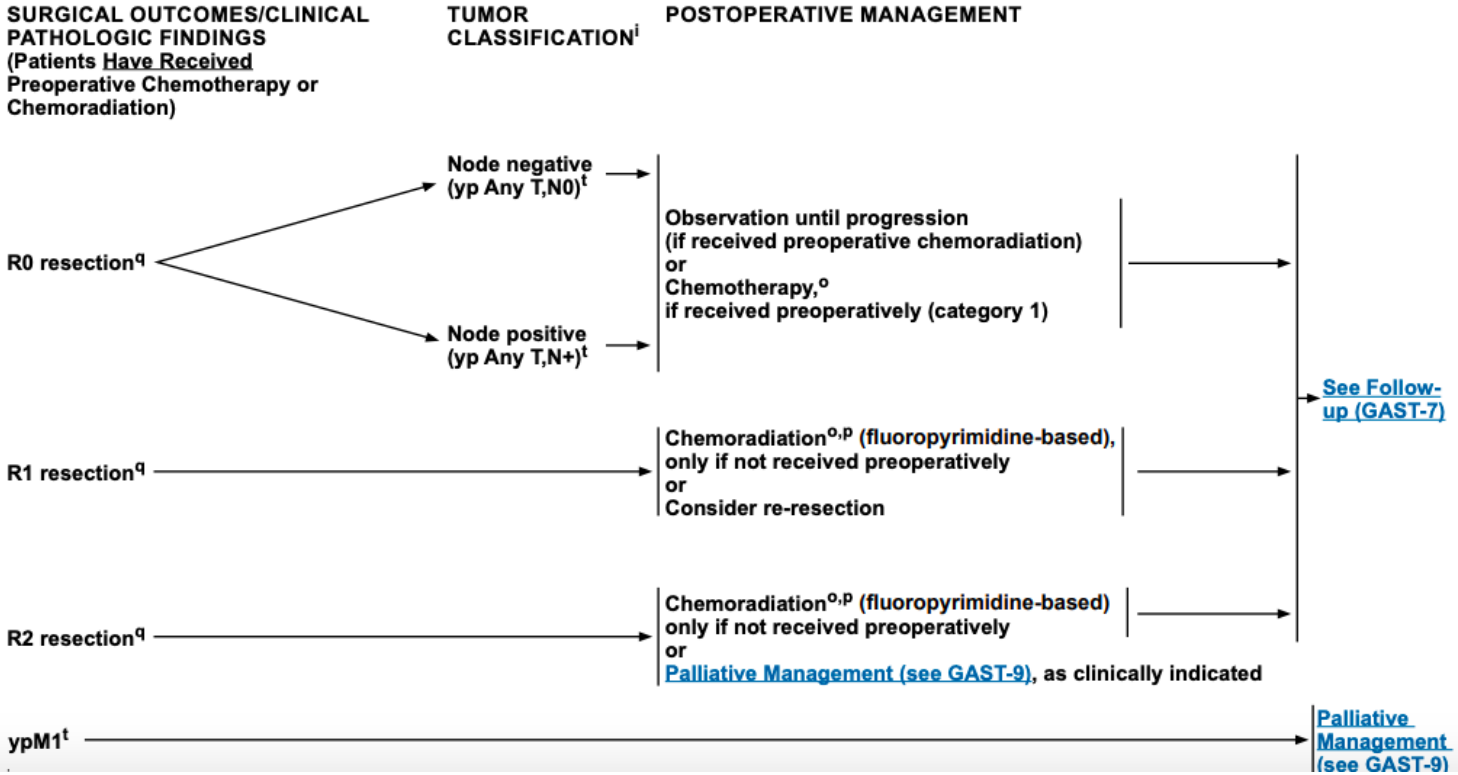
NCCN Guidelines Index
Table of Contents
Discussion



NCCN Guidelines Version 3.2020
Gastric Cancer

NCCN Guidelines Index
Table of Contents
Discussion




SURGICAL OUTCOMES/CLINICAL PATHOLOGIC FINDINGS (Patients Have Received Preoperative Chemotherapy or Chemoradiation)
TUMOR CLASSIFICATION[i]
POSTOPERATIVE MANAGEMENT
R0 resection[q]
Node negative (yp Any T,N0)[t]
Node positive (yp Any T,N+)[t]
Observation until progression (if received preoperative chemoradiation) or Chemotherapy,[o] if received preoperatively (category 1)
R1 resection[q]
Chemoradiation[o,p] (fluoropyrimidine-based), only if not received preoperatively or Consider re-resection
R2 resection[q]
Chemoradiation[o,p] (fluoropyrimidine-based) only if not received preoperatively or Palliative Management (see GAST-9), as clinically indicated
See Follow-up (GAST-7)
ypM1[t]
Palliative Management (see GAST-9)

ESMO 2019

Annals of Oncology

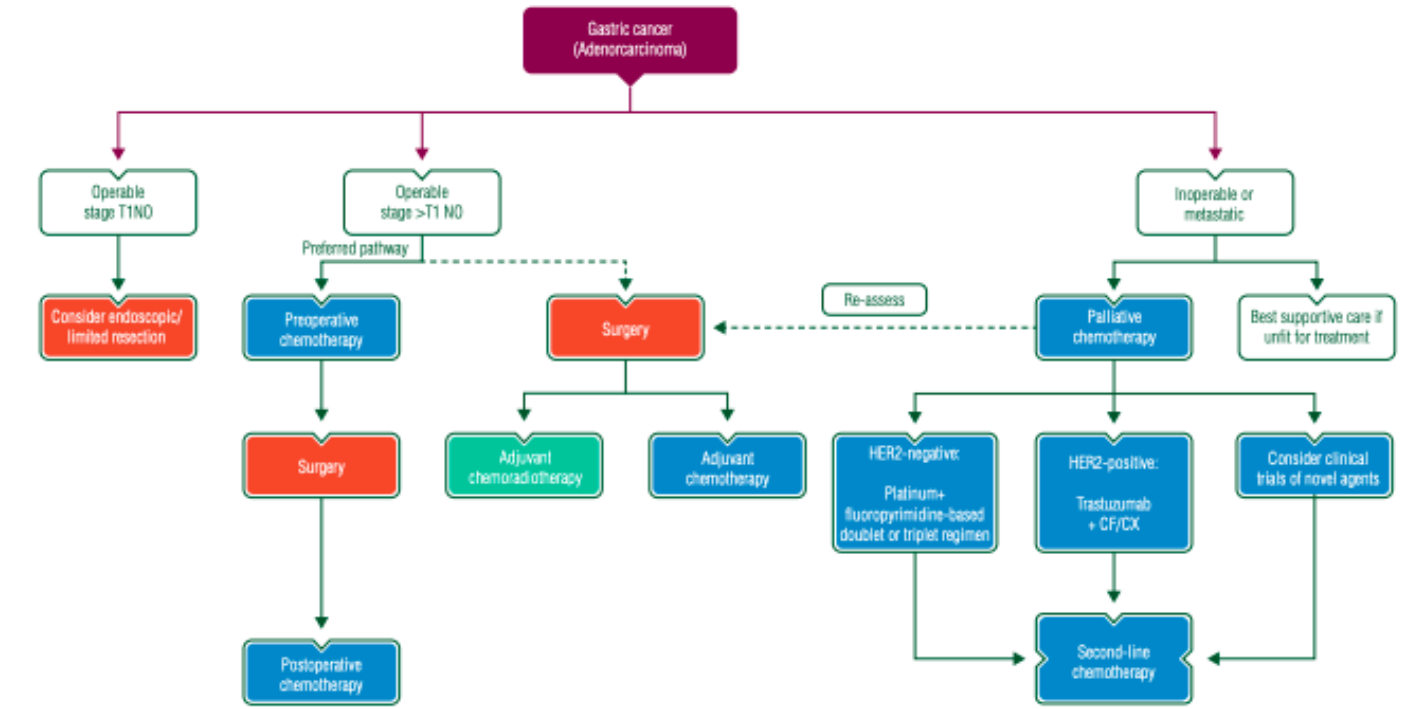
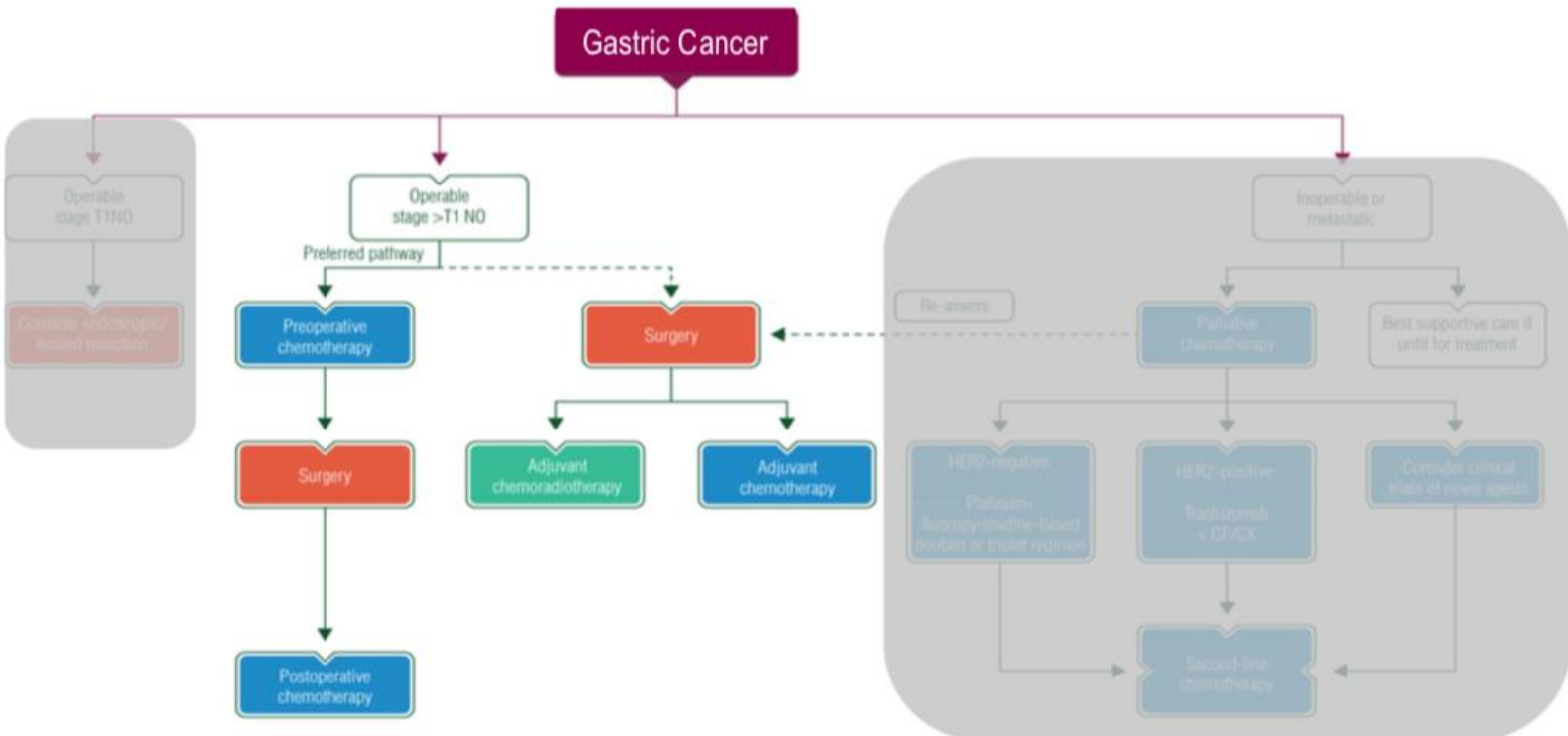


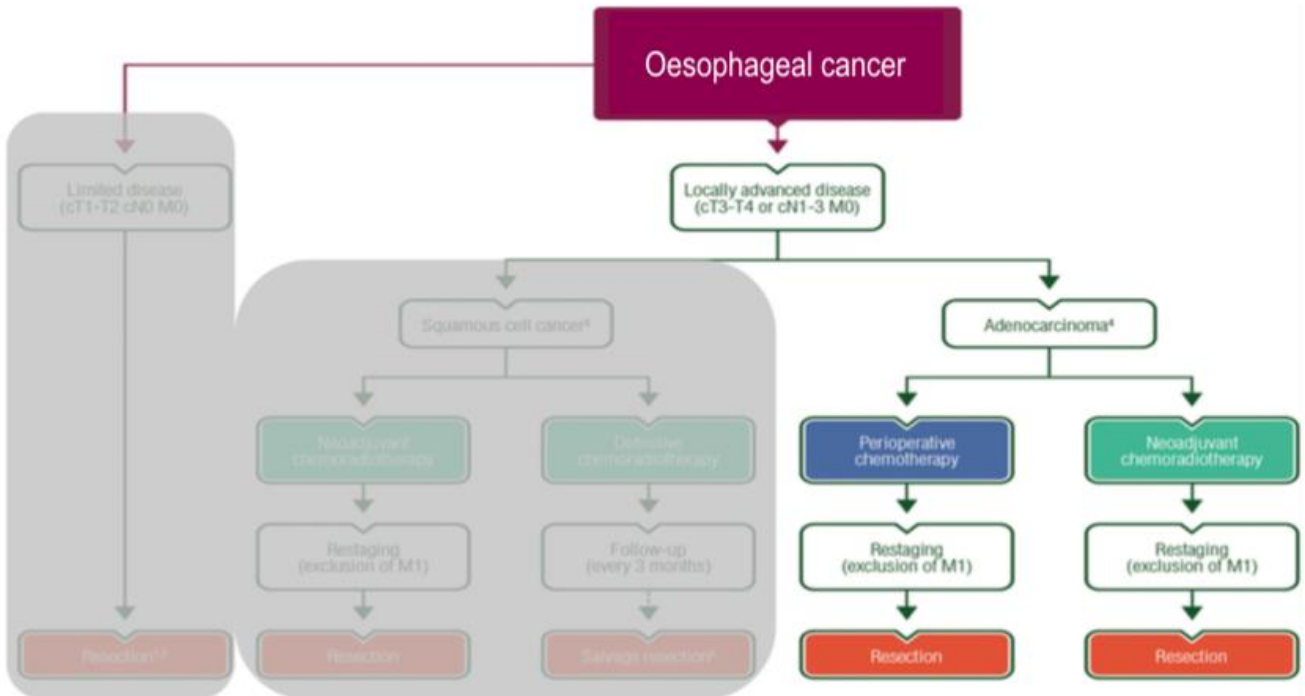
Figure 1. Gastric cancer treatment algorithm.
HER2, human epidermal growth factor receptor 2; CF, cisplatin and 5-fluorouracil; CX, cisplatin and capecitabine

ESMO GASTRIC CANCER GUIDELINES



Smyth et al, Ann Oncol. 2016;27(suppl_5):v38-v49. doi:10.1093/annonc/mdw350

ESMO OESOPHAGEAL CANCER GUIDELINES



Lordick et al, Ann Oncol. 2016;27(suppl_5):v50-v57. doi:10.1093/annonc/mdw329