


NEOHX Study: Perioperative Treatment With Trastuzumab in Combination With Capecitabine and Oxaliplatin (XELOX-T) in Patients With HER-2 Resectable Stomach or Esophagogastric Junction (EGJ) Adenocarcinoma: 18 Months Disease-Free Survival (DFS) Analysis

Abstract 107

Rivera F, Jimenez P, García Alfonso P, Lopez C, Gallego J, Limón ML, Alsina M, López L, Galán MC, Falcó E, Manzano JL, Gonzalez E, Serrano R, Fernández E, Jorge M

Gastric Cancer: Introduction

Tumor type	New Cases (million)	Deaths (million)
Gastro- esophageal cancer	1.4	1.1
Lung cancer	1.4	1.2
Breast cancer	1.2	0.4
Colorectal cancer	1.0	0.5
Overall	10.8	7.0

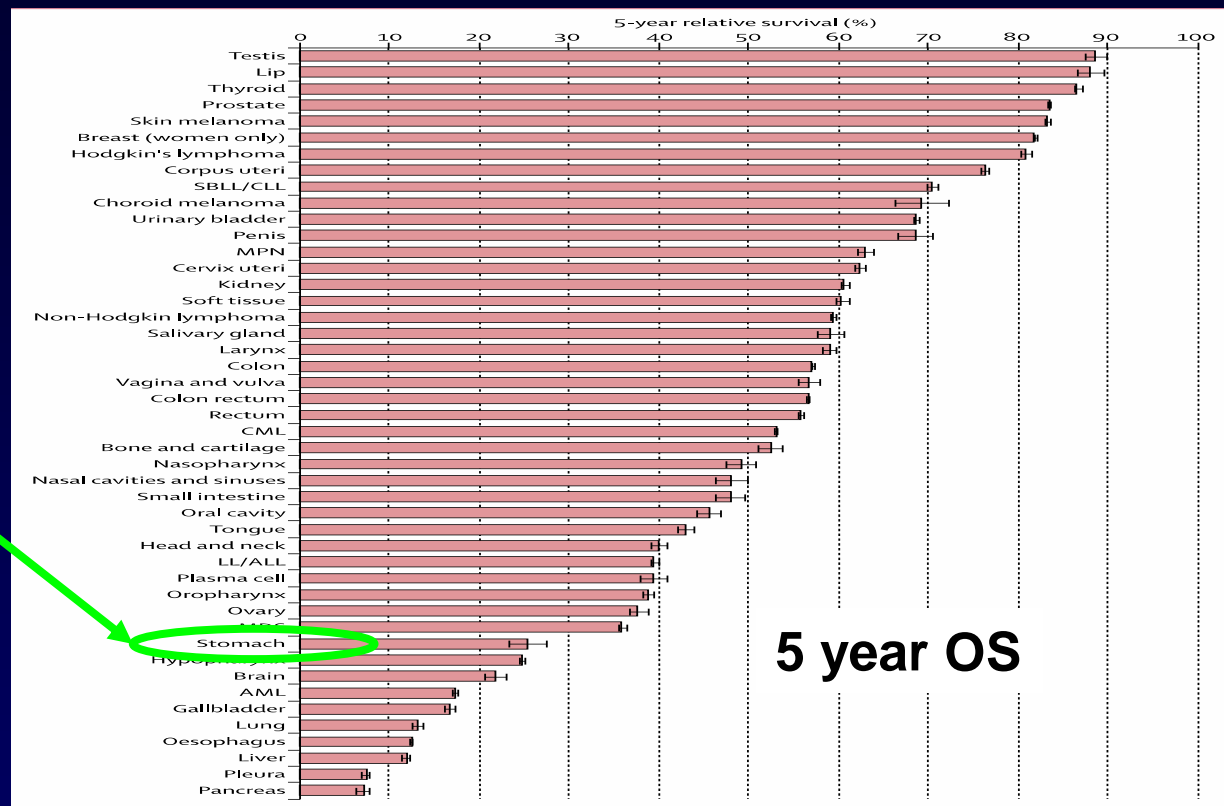


Kamangar F, et al. *J Clin Oncol*. 2006;24(14):2137-2150.

Rivera F, et al. *J Clin Oncol*. 2015;33(suppl 3): Abstract 107.

Gastric Cancer: Introduction

Gastric cancer
5 year overall
survival (OS) 25%¹



Stage

- Resectable early disease (T1-2, N0, M0) 10% → 5 year OS*: 70%
 - Resectable locally advanced disease (T3-4, N+, M0) 40% → 5 year OS*: 30%
 - Unresectable locally advanced disease 20% → Median OS: 13 months
 - Metastatic (M1; stage IV) 30% → Median OS: 10 months
- *with Surgery alone

1. De Angelis R, et al. *Lancet Oncol.* 2014;15(1):23-34.

Rivera F, et al. *J Clin Oncol.* 2015;33(suppl 3): Abstract 107.

Treatment Options in Resectable EGJ and Gastric Adenocarcinoma



Perioperative Chemotherapy: MAGIC-1

503 Patients (pts)

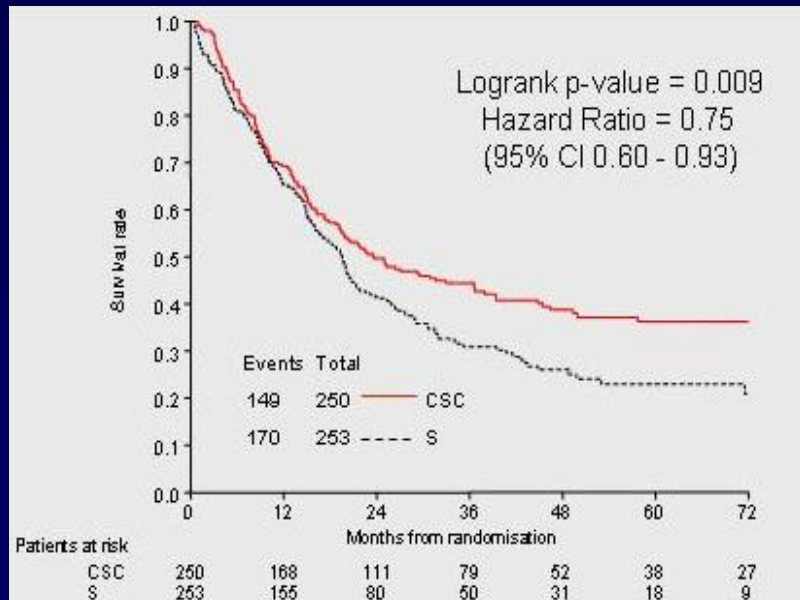
Resectable	Stage II-IV (M0)
Gastric	74%
EGJ	26%

Perioperative chemo

ECF x 3 → Surgery → ECF x 3
(44% of patients)

Surgery

Survival



Survival (3 years): 43% $P < .05$ 32%

Loc Rel (3 years): 29% $P < .05$ 44%

Dist Rel (3 years): 31% $P < .05$ 45%

Cunningham D, et al. *N Engl J Med.* 2006;355(1):11-20.

Rivera F, et al. *J Clin Oncol.* 2015;33(suppl 3): Abstract 107.

Perioperative Chemotherapy

Phase III FNLCC-ACCORD07-FFCD 9703

224 Patients

Resectable adenocarcinoma

Gastric (no EGJ) 25 %
EGJ 64 %
Distal esophagous 11 %

PS 0 / 1 (75% / 25%)

Perioperative chemo

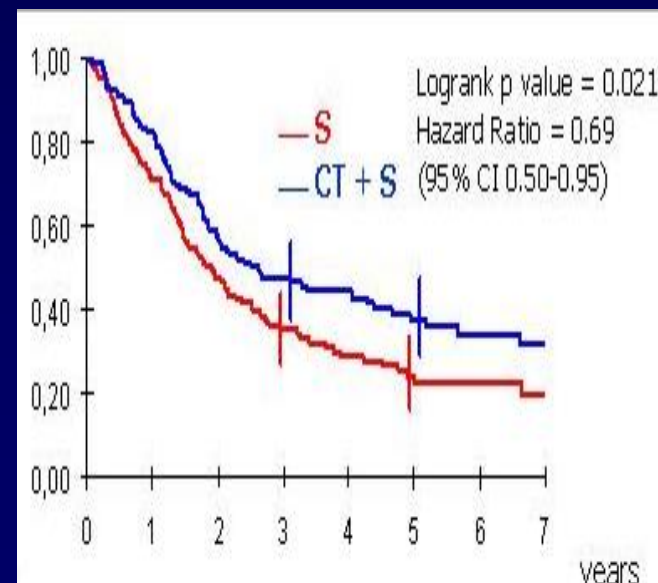
CFx2-3→Surgery

(→CF x 4 postSx if overall response or stable disease with pN+: 50% patients)

Surgery

Primary endpoint: Survival

	CF> Survival	Survival	HR	P value
Survival (5 year)	38%	24%	0.66	.01
DFS (5 year)	34%	21%	0.65	.003



Boige V, et al, *J Clin Oncol*. 2007;25(18S): Abstract 4510.

Rivera F, et al. *J Clin Oncol*. 2015;33(suppl 3): Abstract 107;

P. III TOGA (C-X/F vs C-X/F-Trastuzumab)

3807 screened pts → 810 HER2+ → **584 pts included**

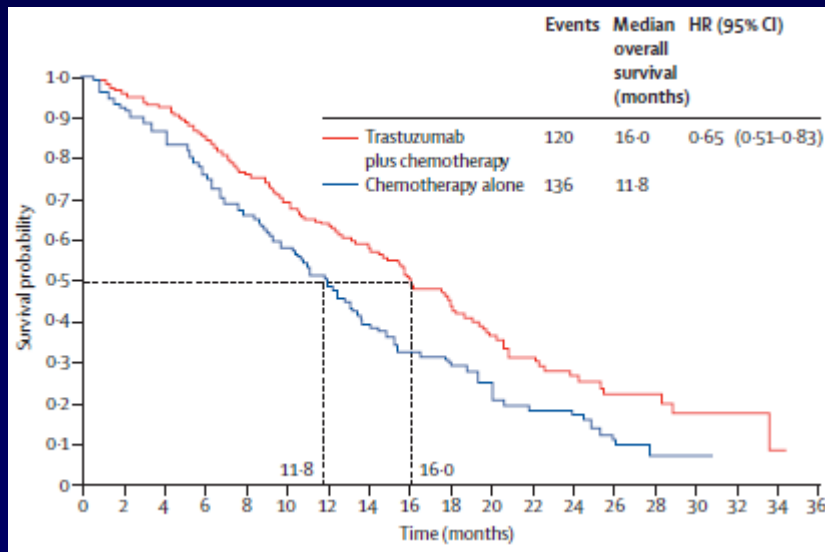
97% M1; 32% EGJ; 10% ECOG 2

CX_(87%)/F_(13%)

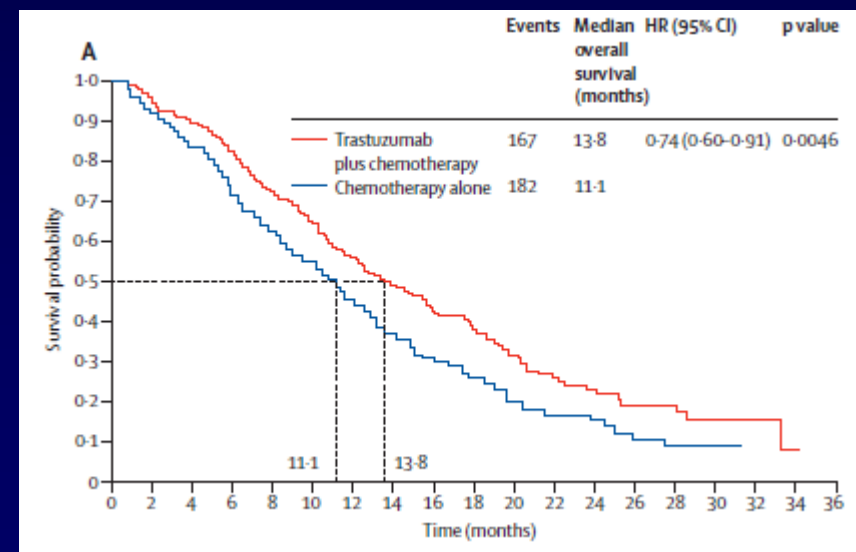
CX_(87%)-/F_(13%)-Trast

8→6mg/kg/3w

Primary endpoint OS



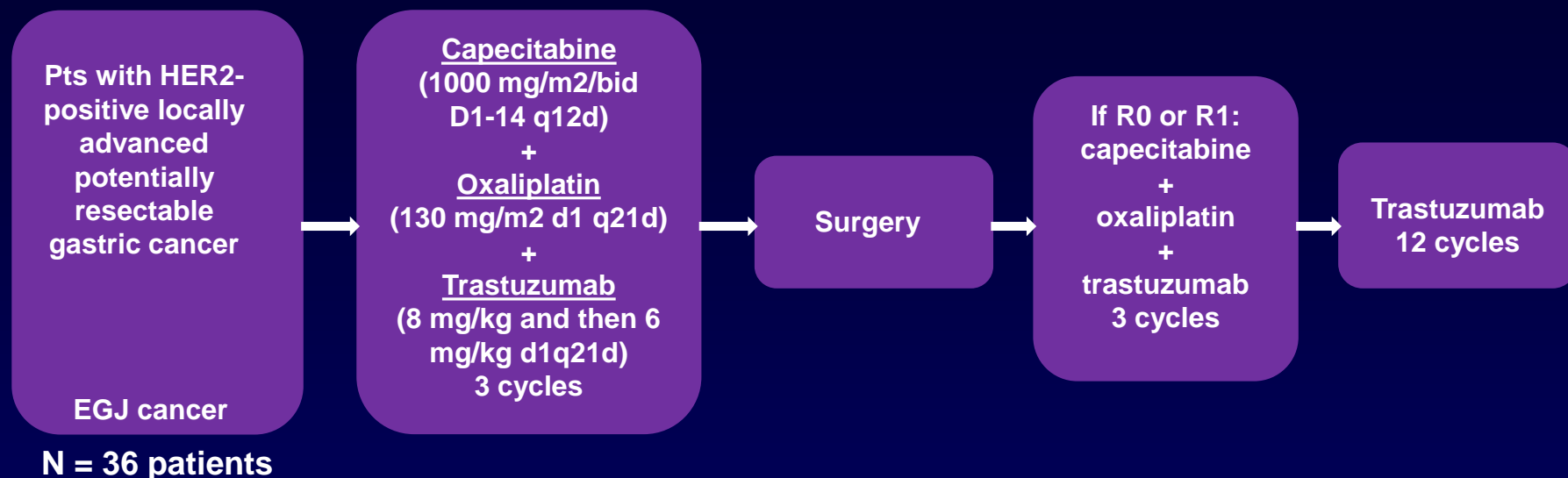
OS in IHC2+/FISH+ or IHC3+ (exploratory analysis)



Bang YJ, et al. *Lancet*. 2010;376(9742):687-697.

Rivera F, et al. *J Clin Oncol*. 2015;33(suppl 3): Abstract 107.

NEOXH: Design



Objective

The primary endpoint was 18 months DFS, secondary endpoints included pathologic CR, R0 resection rate, the safety profile of XELOX-trastuzumab combination and specifically trastuzumab monotherapy (maintenance treatment), surgical morbidity and mortality

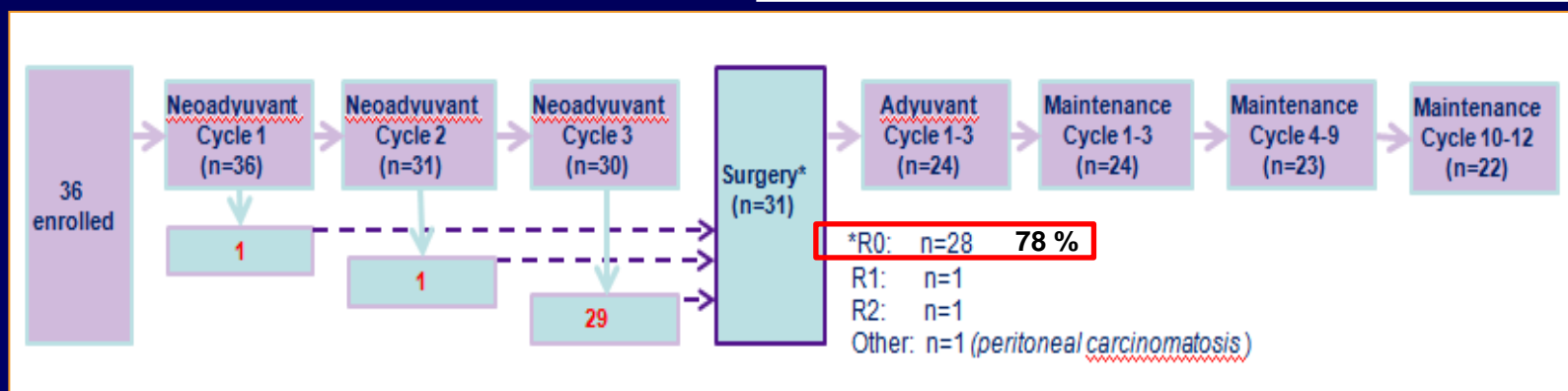
OS and biomarker analysis

Patient Characteristics

From June 2010 to March 2012, 36 patients were included in 15 Spanish hospitals

Baseline Charecteristics (n=36)		
Age, y	63.44	(±1.74)
ECOG	n	%
0	16	44.4
1	19	52.78
2	1	2.78
Gender		
Male	29	81
Female	7	19

Baseline Charecteristics (n=36)		
	N	%
Tumor location		
Stomach	21	58.33
EGJ	15	41.66
Stage		
IB-IIA	7	19.5
IIB-IIIC	29	80.5
N+	31	86.1
Type of adenocarcimona		
Intestinal	23	63.89
Mixed	1	2.78
Diffuse	4	11.11
Not available	8	22.22
HER2+		
HER2+++	29	80.56
HER2+++/ <u>FISH+</u>	7	19.44

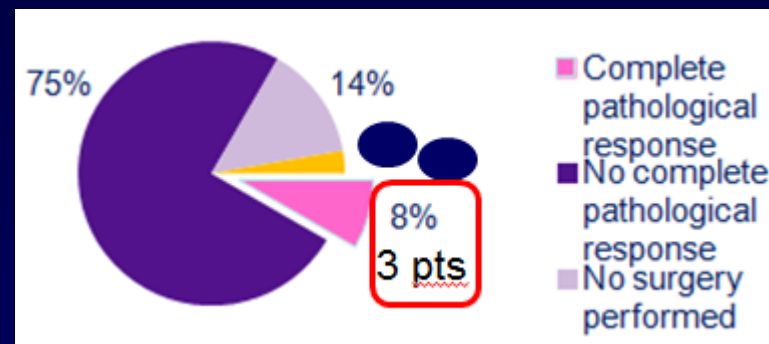


NEOXH: Response

Clinical response

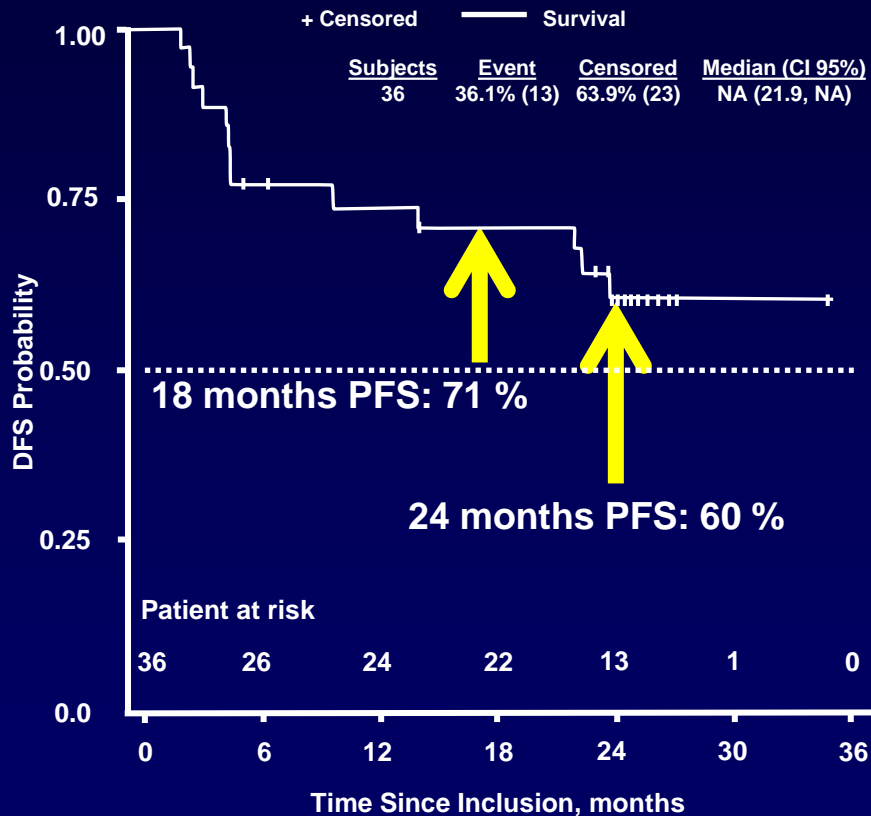
RECIST Response Evaluable population (n=32)	n	%
SD	18	56.25
PR	14	43.75

Pathological response (n = 36)

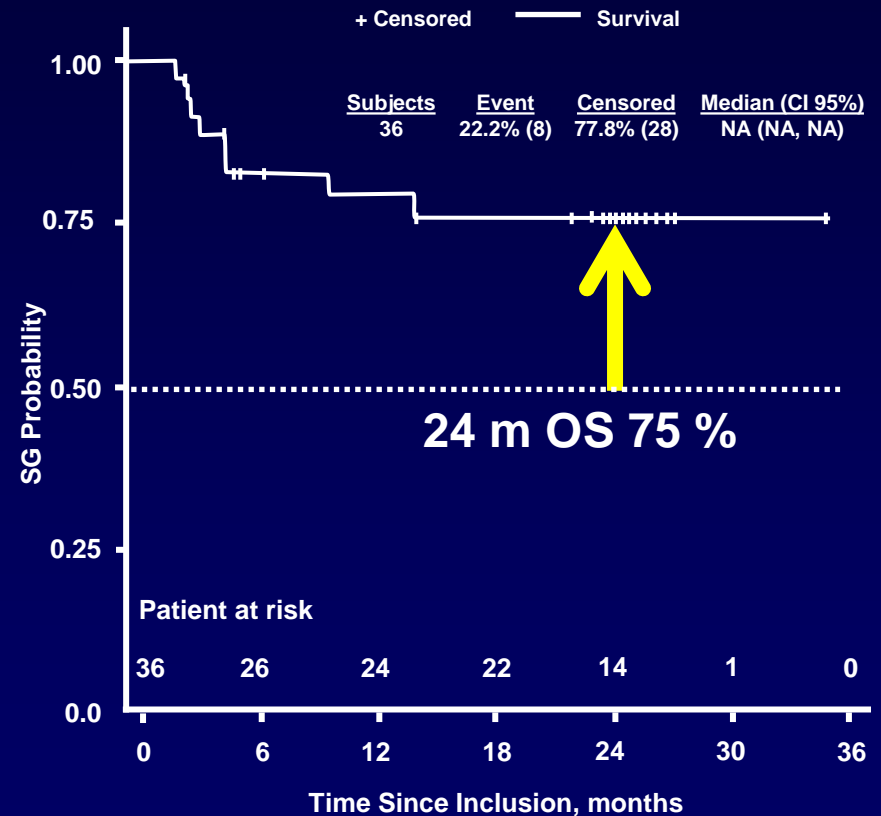


NEOXH: PFS and OS

Progression-free survival



Overall survival



NEOXH: Toxicity

Grade	1		2		3		4		Total
	n	%	n	%	n	%	n	%	%
Diarrhea	10	27.78	7	19.44	9	25.00	3	8.33	80.56
Asthenia	15	41.67	7	19.44	0	0	2	5.56	66.67
Nausea	11	30.56	3	8.33	3	8.33	0	0	47.22
Loss of appetite	9	25.00	4	11.11	1	2.78	1	2.78	41.67
Vomiting	6	16.67	6	16.67	3	8.33	0	0	41.67
Anemia	5	13.89	4	11.11	2	5.56	0	0	30.56
Pyrexia	8	22.22	1	2.78	1	2.78	1	2.78	30.56
Neurotoxicity	9	25.00	1	2.78	0	0	0	0	27.78
Abdominal pain	7	19.44	2	5.56	0	0	0	0	25.00
Mucosal inflammation	5	13.89	3	8.33	1	2.78	0	0	25.00

NEOHX vs MAGIC: Efficacy

Phase II NEOHX (Spain)

36 Patients

Resectable HER2+, gastric-EGJ Cancer
Primary endpoint: 18 m DFS



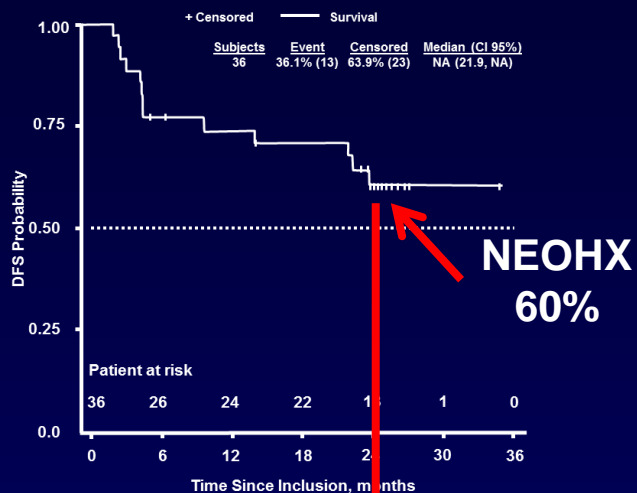
Perioperative xelox-trastuzumab

Xelox-T x3 → Surgery → Xelox-T x3 → Tx12

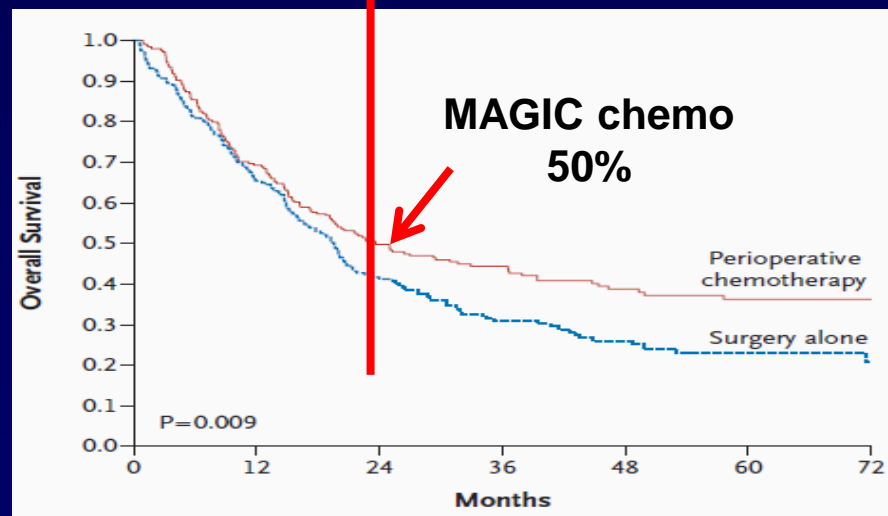
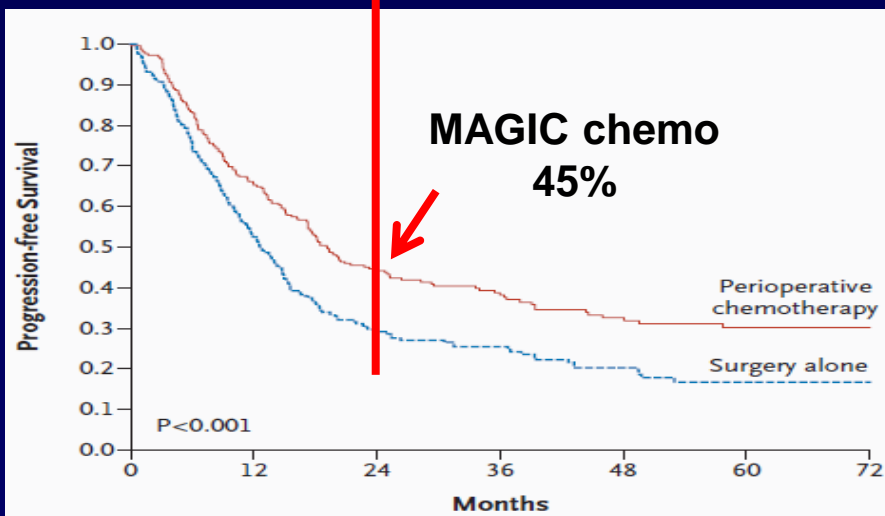
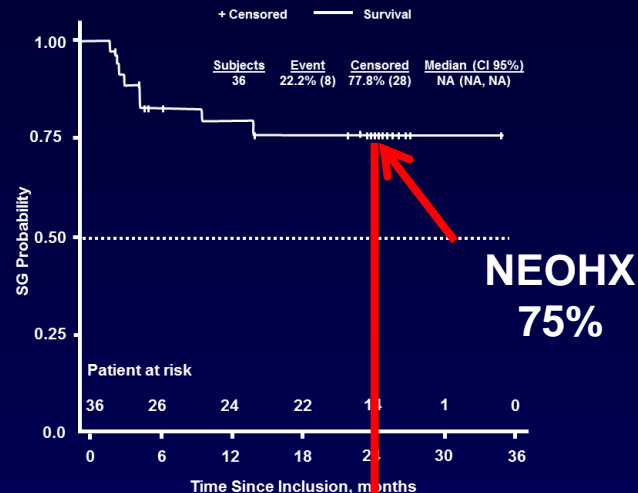
R0:	78%	(MAGIC: 69%)
pCR:	8%	(MAGIC: 0%)
24 m PFS:	60%	(MAGIC: 45%)
24 m OS:	75%	(MAGIC: 50%)

NEOHX vs MAGIC: PFS and OS

24 months PFS



24 months OS



NEOXH: Conclusion

- **NEOHX trial meets its primary endpoint, DFS at 18 months reaches the optimal cutoff (70%)**
- **Perioperative XELOX-trastuzumab in HER2-positive resectable stomach and esophagogastric junction adenocarcinoma is feasible and has a promising activity, showing:**
 - **R0: 78%**
 - **pCR 8%**
 - **18 m PFS; 71%; 24 m PFS: 60%**
 - **24 m OS: 75%**

Studies With Trastuzumab in Resectable HER2+ Esophago-Gastric Adenocarcinoma

Phase II NEOHX (Spain)

36 Pts
Resectable Her 2+, Gastric-EGJ Cancer
Primary endpoint: 18 m DFS

Perioperative xelox-trastuzumab

Xelox-T x3 → Surgery → Xelox-T x3 → Tx12

R0:	78%	(MAGIC: 69%)
pCR:	8%	(MAGIC: 0%)
24 m PFS:	60%	(MAGIC: 45%)
24 m OS:	75%	(MAGIC: 50%)

Phase II AIO-STO 0310 (Germany)

53 Pts
Resectable HER2+, Gastric-EGJ
cancer primary endpoint: pCR

Perioperative FLOT-trastuzumab

FLOT-T x4 → Surgery → FLOT-T x4 → Tx9

(Hofheinz R, et al.) R0: 93%; pCR: 22%

Hofheinz R, et al. *J Clin Oncol*. 2014;32(5S): Abstract 4073.

Rivera F, et al. *J Clin Oncol*. 2015;33(suppl 3): Abstract 107

Studies With Trastuzumab in Resectable HER2+ Esophago-Gastric Adenocarcinoma

Phase III RTOG 1010 (USA)

160 Pts

Resectable HER2+ esoph-EGJ
adenocarcinoma primary endpoint: DFS

Preoperative carb Tax-RT

Carb Tax/RT 50Gy→Surgery

Preoperative CarbTax RT+Periop.Trastuzumab

T-carbTax/RT 50Gy→Surgery→Tx13

Anti-HER2 Treatment Neoadjuvant Setting? INNOVATION Study – Europe + Korea

STAGE 1:

Randomized phase II
“pick the winner” of
two experimental arms
1:2:2 randomization

Chemo only

Chemo +
trastuzumab

Chemo +
trastuzumab +
pertuzumab

STAGE 2:

Randomized phase III with
the best experimental arm of
STAGE 1 1:3 randomization

Chemo only

Chemotherapy + trastuzumab
(+ pertuzumab)

IMAGE substudy in selected
centers!

What is the accuracy of
PDG_PET in targeted
(antibody) treatment