PATHOLOGIC FACTORS PROGNOSTIC OF SURVIVAL IN PATIENTS WITH GI TRACT AND PANCREATIC CARCINOMA TREATED WITH NEOADJUVANT THERAPY
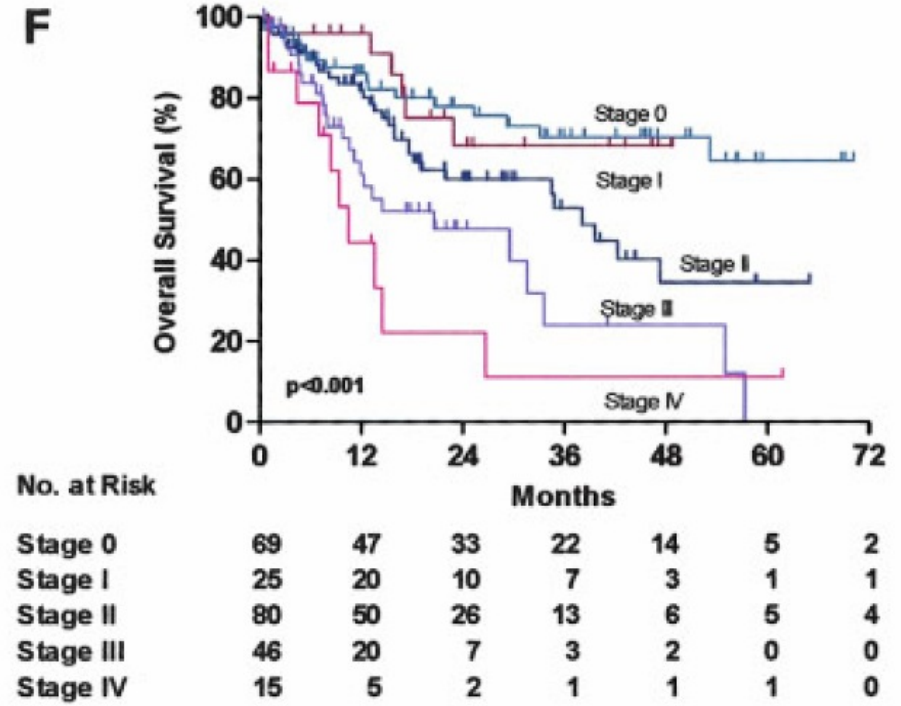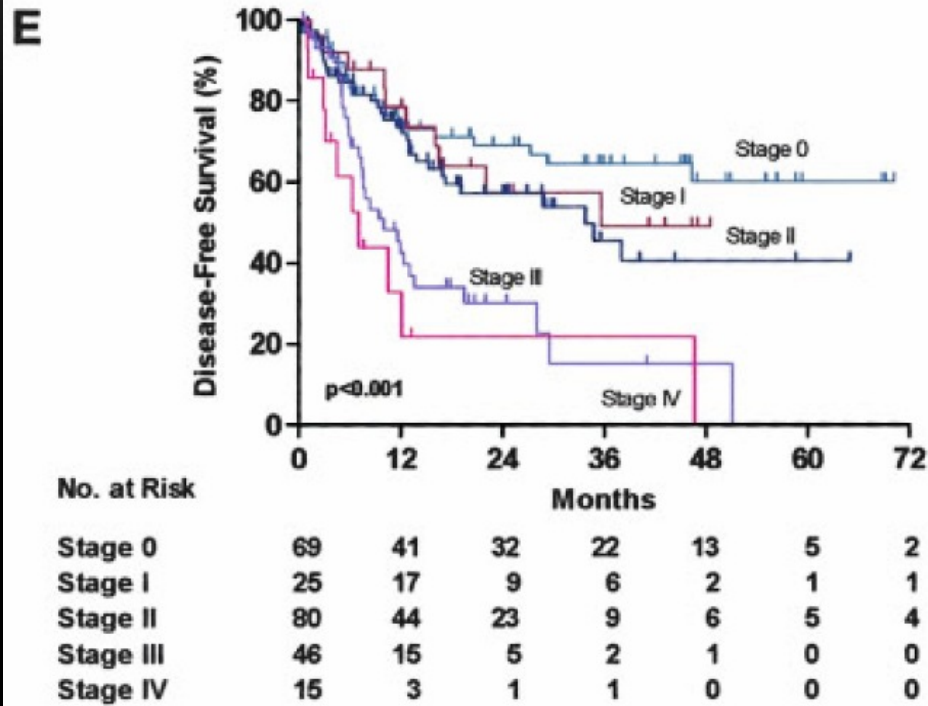
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Department of Pathology

The UT MD Anderson Cancer Center

ESOPHAGEAL ADENOCARCINOMA

ESOPHAGEAL ADENOCARCINOMA

MD Anderson
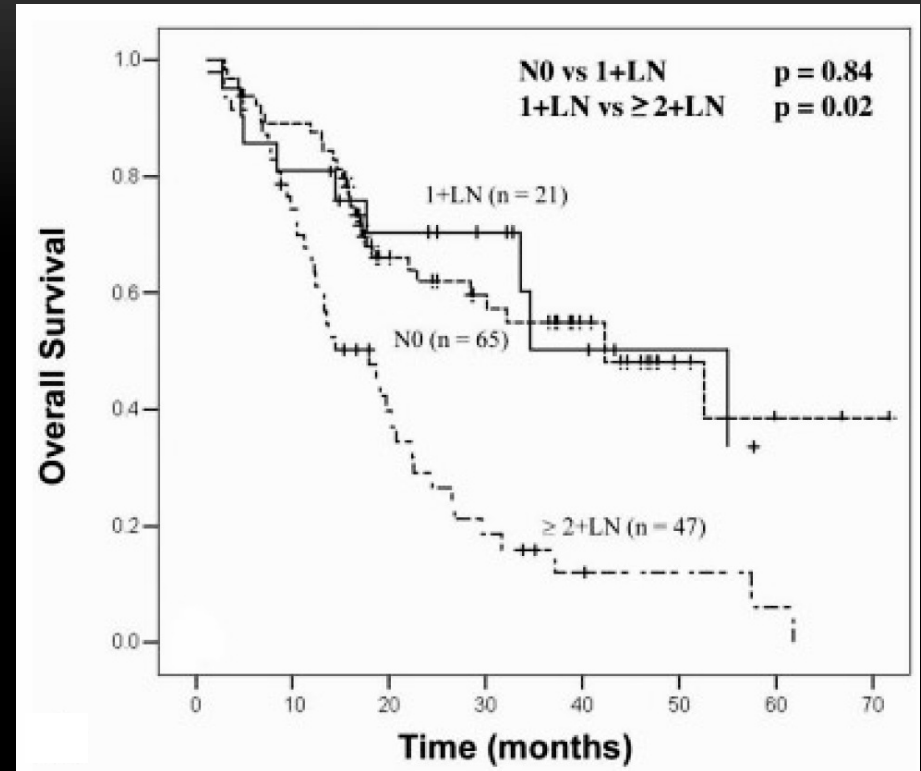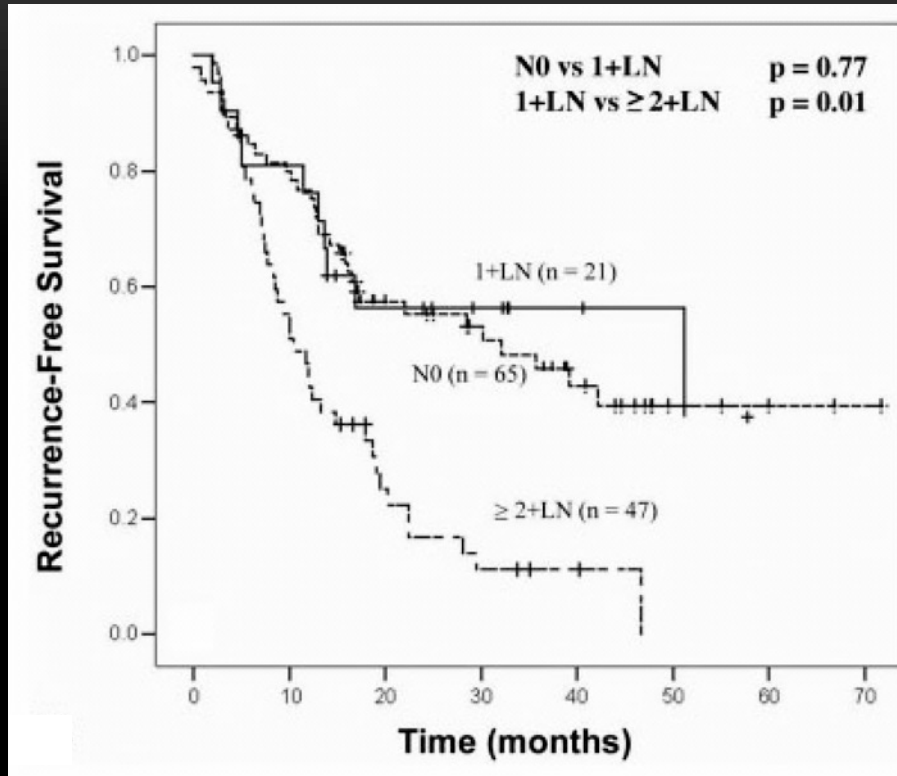- N=235 +neoadjuvant chemoXRT

ypTNM (AJCC 6th)

ESOPHAGEAL ADENOCARCINOMA

Results of Multivariate Cox Regression Analysis of Disease-Free Survival and Overall Survival

Variables	No. of patients (n = 235) (%)	Disease-free survival			Overall survival		
		HR	(95% CI)	P value	HR	(95% CI)	P value
Extent of residual carcinoma				0.08			0.04
0% (reference)	77 (33)	1.00			1.00		
1–10%	58 (25)	1.39	(0.40–4.79)	0.61	2.28	(0.51–10.14)	0.28
11–50%	43 (18)	1.15	(0.32–4.09)	0.83	2.03	(0.45–9.15)	0.36
> 50%	57 (24)	2.29	(0.67–7.87)	0.19	4.15	(0.95–18.25)	0.06
Pathologic (ypTNM) stage				0.02			0.02
0 (reference)	69 (29)	1.00			1.00		
I	25 (11)	0.92	(0.22–3.78)	0.90	0.42	(0.07–2.34)	0.32
II	80 (34)	1.06	(0.31–3.67)	0.93	0.88	(0.20–3.92)	0.87
III	46 (20)	2.03	(0.50–8.28)	0.32	1.34	(0.26–6.93)	0.73
IV	15 (6)	3.89	(0.85–17.71)	0.08	2.85	(0.51–16.13)	0.24
Downstage							
No (reference)	103 (44)	1.00			1.00		
Yes	132 (56)	1.16	(0.61–2.19)	0.65	1.34	(0.69–2.63)	0.39
Any margin positive							
No (reference)	211 (90)	1.00			1.00		
Yes	24 (10)	1.59	(0.88–2.86)	0.12	1.32	(0.71–2.48)	0.38

HR: hazard ratio; 95% CI: 95% confidence interval; ypTNM: posttherapy pathologic tumor/lymph node/metastasis stage.

ypTNM (AJCC 6th)

ESOPHAGEAL ADENOCARCINOMA

MD Anderson
- N=187 +neoadjuvant chemoXRT

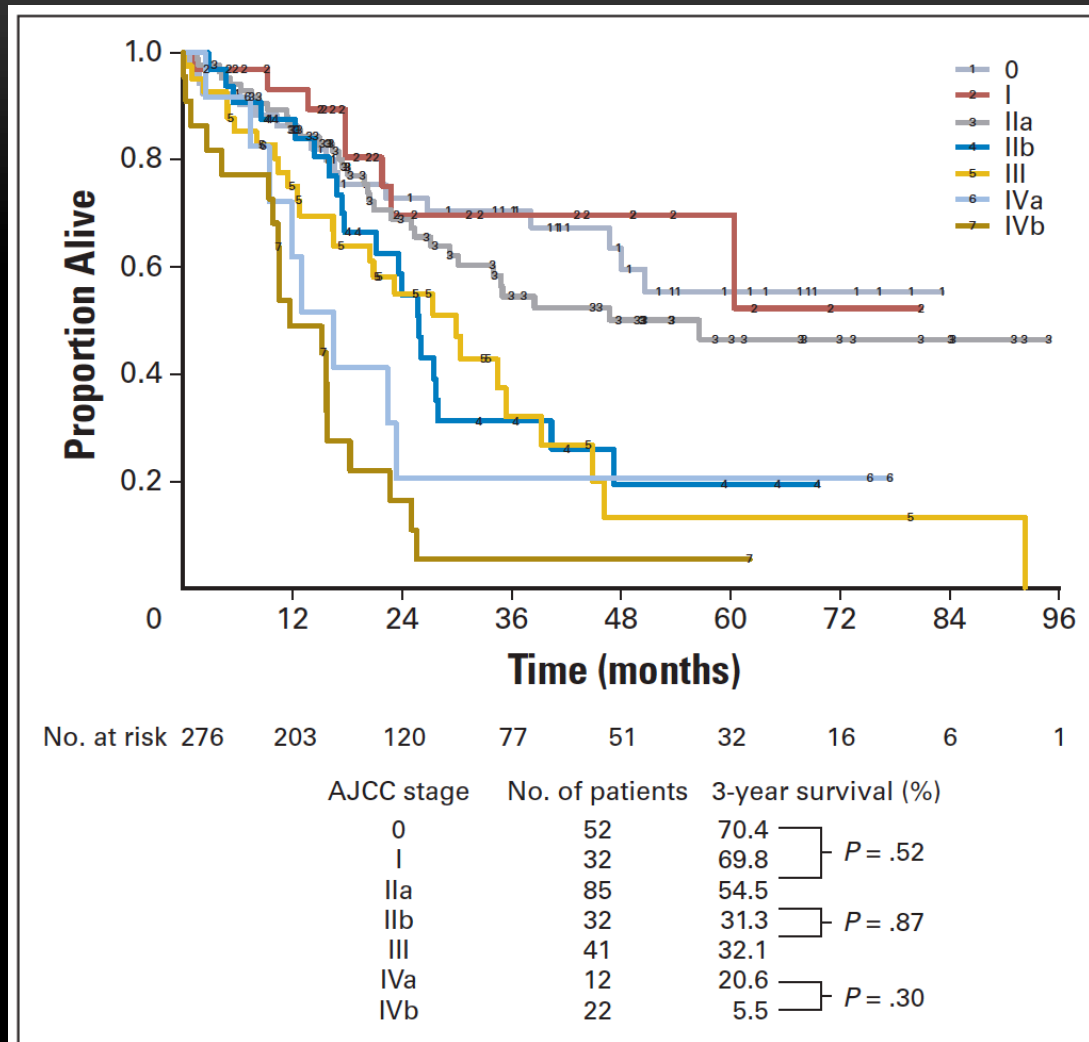## Number of +LN

ESOPHAGEAL ADENOCARCINOMA

Fig 1. American Joint Committee on Cancer (AJCC) staging system after chemoradiotherapy.

Memorial Sloan-Kettering
- N=276 +neoadjuvant chemoXRT
- Kaplan-Meier analyses:
  - 0 to IIA (P=0.52)
  - IIB to III (P=0.87)
  - IVA to IVB (P=0.30)

ypTNM (AJCC 6th)
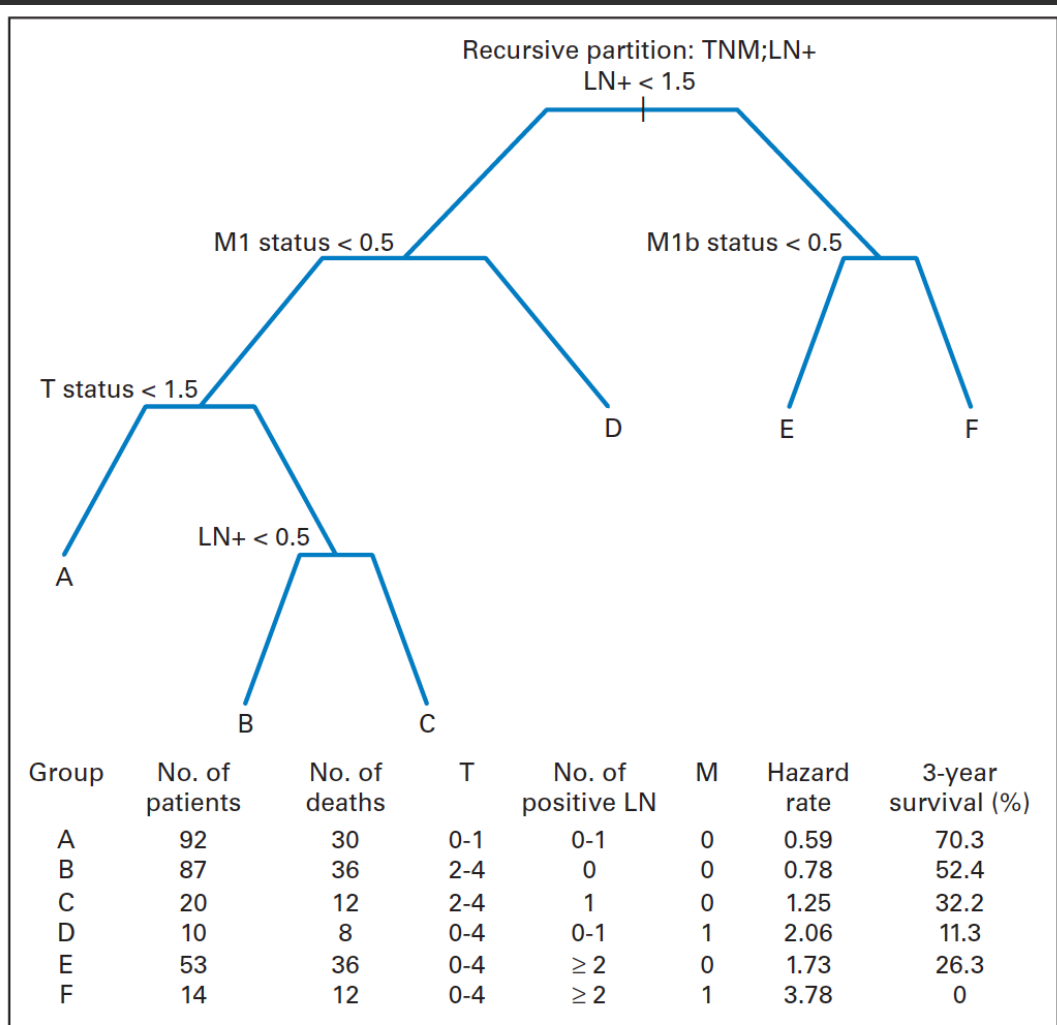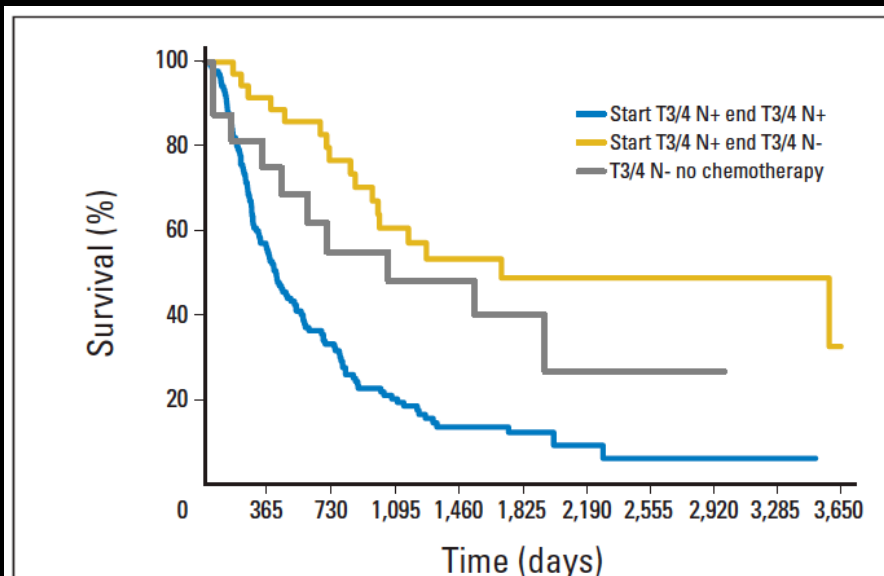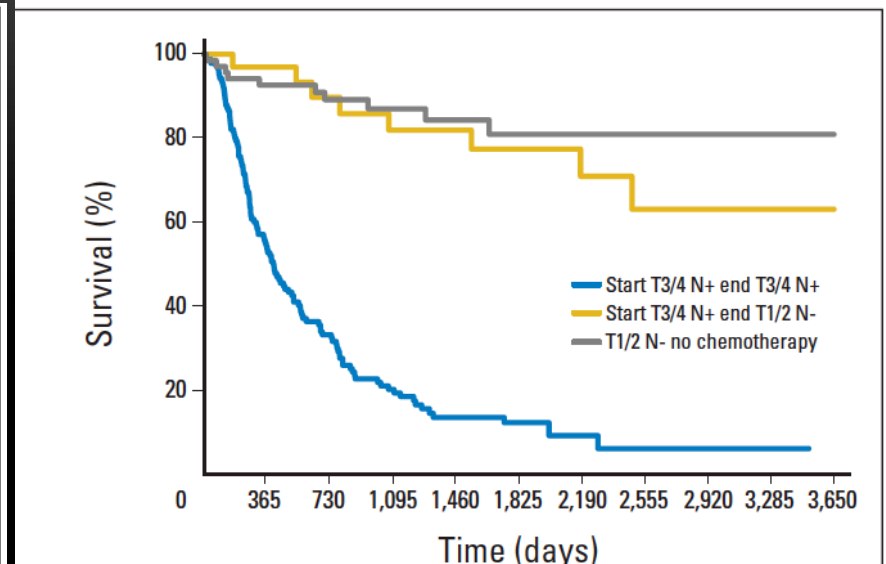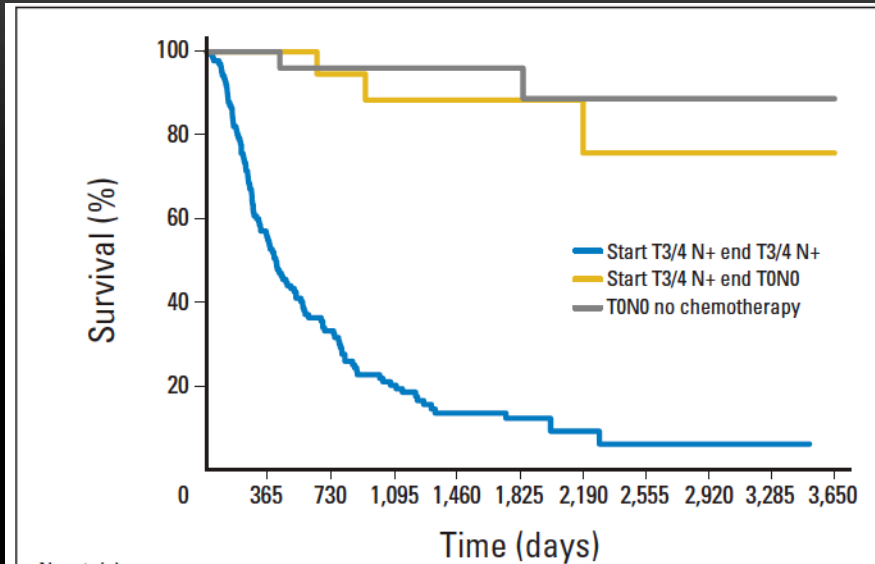
ESOPHAGEAL ADENOCARCINOMA

Recursive partition: TNM;LN+
LN+ < 1.5

M1 status < 0.5

M1b status < 0.5

T status < 1.5

D

E

F

A

LN+ < 0.5

B

C

Group	No. of patients	No. of deaths	T	No. of positive LN	M	Hazard rate	3-year survival (%)
A	92	30	0-1	0-1	0	0.59	70.3
B	87	36	2-4	0	0	0.78	52.4
C	20	12	2-4	1	0	1.25	32.2
D	10	8	0-4	0-1	1	2.06	11.3
E	53	36	0-4	≥ 2	0	1.73	26.3
F	14	12	0-4	≥ 2	1	3.78	0

Fig 4. Recursive partitioning using TNM and number of positive lymph nodes (LN) as variables.

Memorial Sloan-Kettering
- N=276 +neoadjuvant chemoXRT
- Best predictors
    LN status
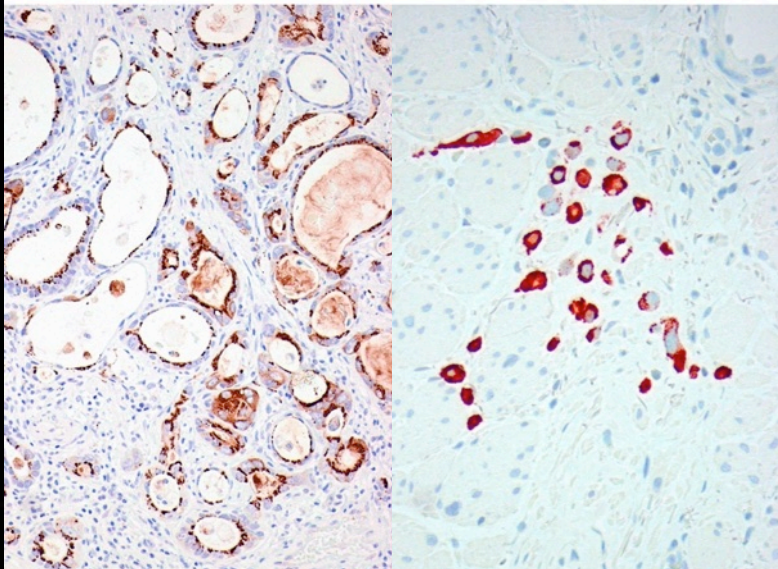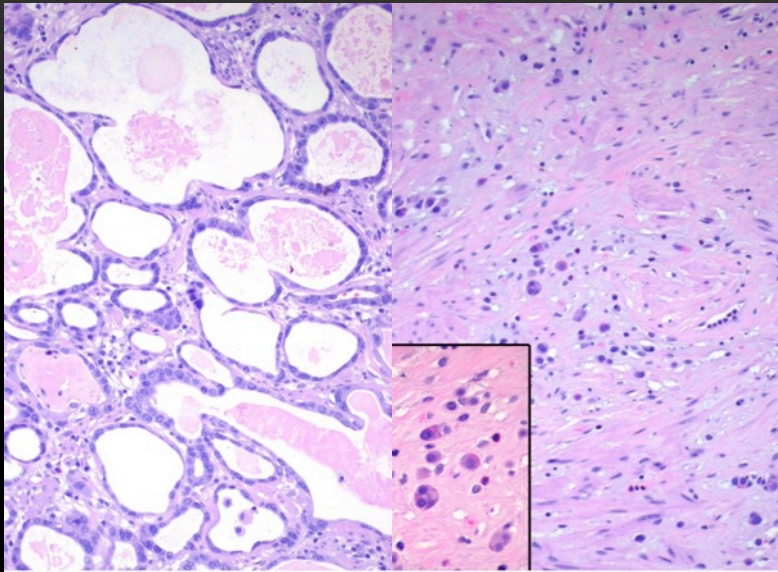   metastasis

ESOPHAGEAL ADENOCARCINOMA
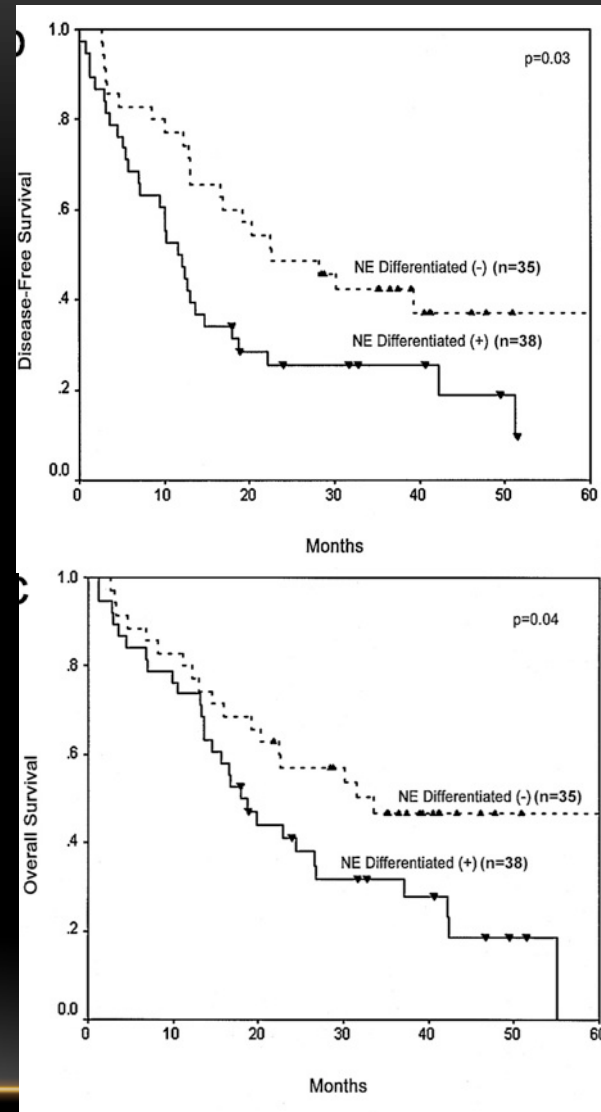

2 high-volume centers in London
- N=584 patients
- N=400 +neoadjuvant tx
- Downstaging:
    HR=0.43, 95%CI 0.31-0.59
    strongest independent predictor

Tumor downstaging
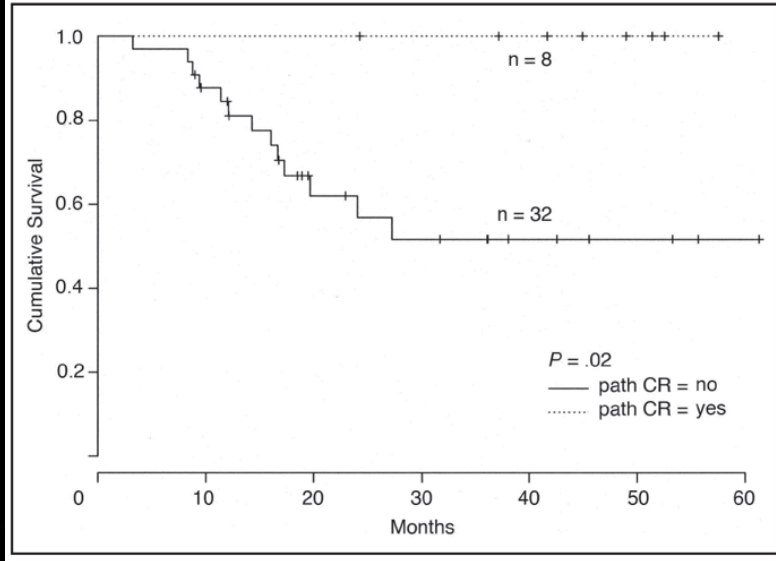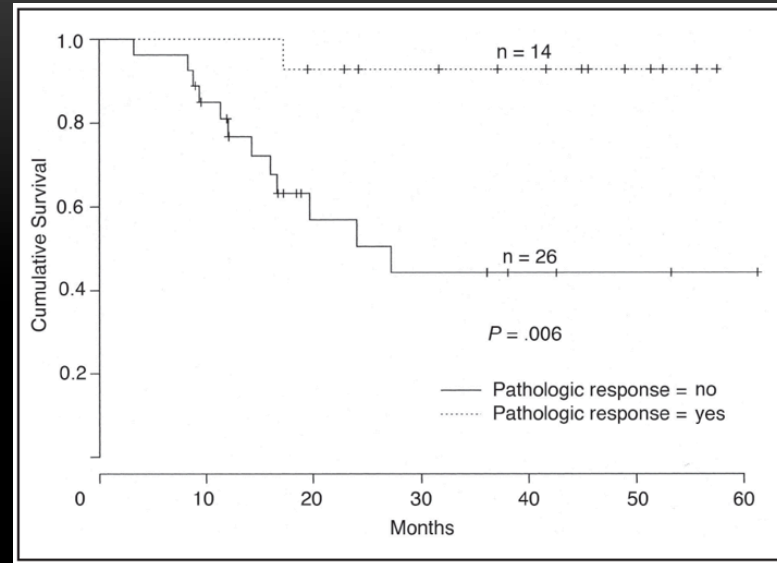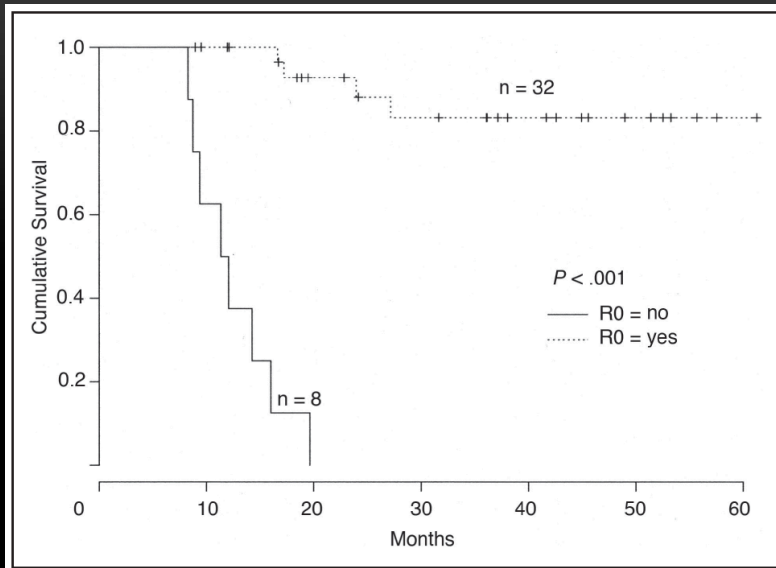
ESOPHAGEAL ADENOCARCINOMA

Neuroendocrine differentiation

GASTRIC CARCINOMA

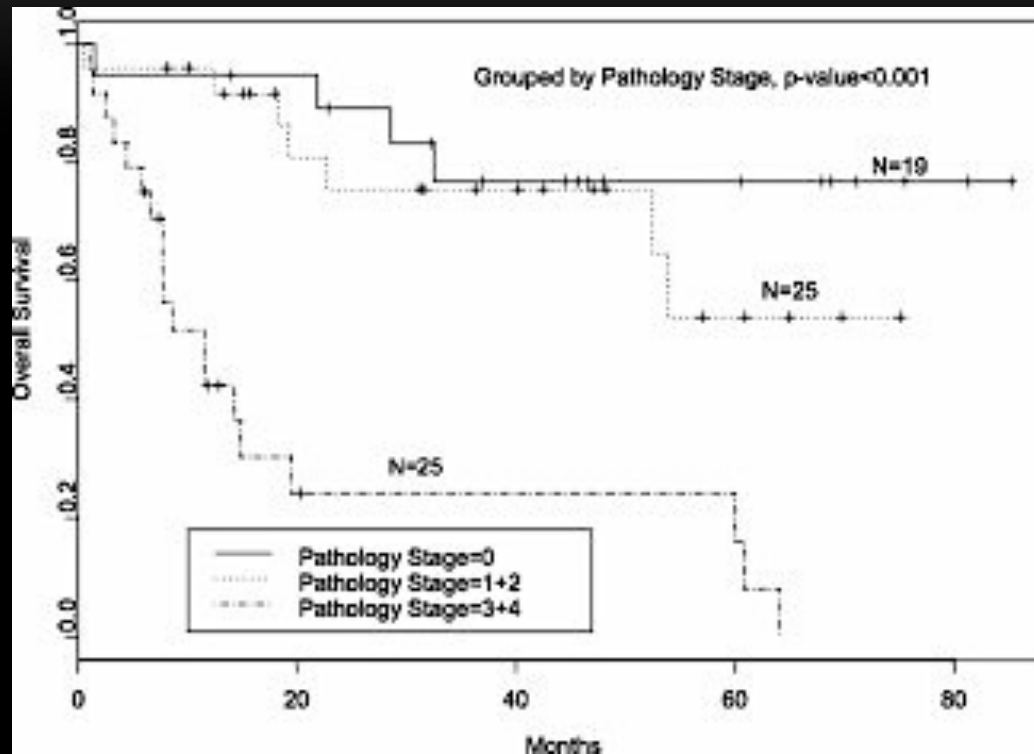# GASTRIC CARCINOMA

<10% residual tumor

MD Anderson
- N=41 +neoadjuvant chemoXRT localized gastric ca

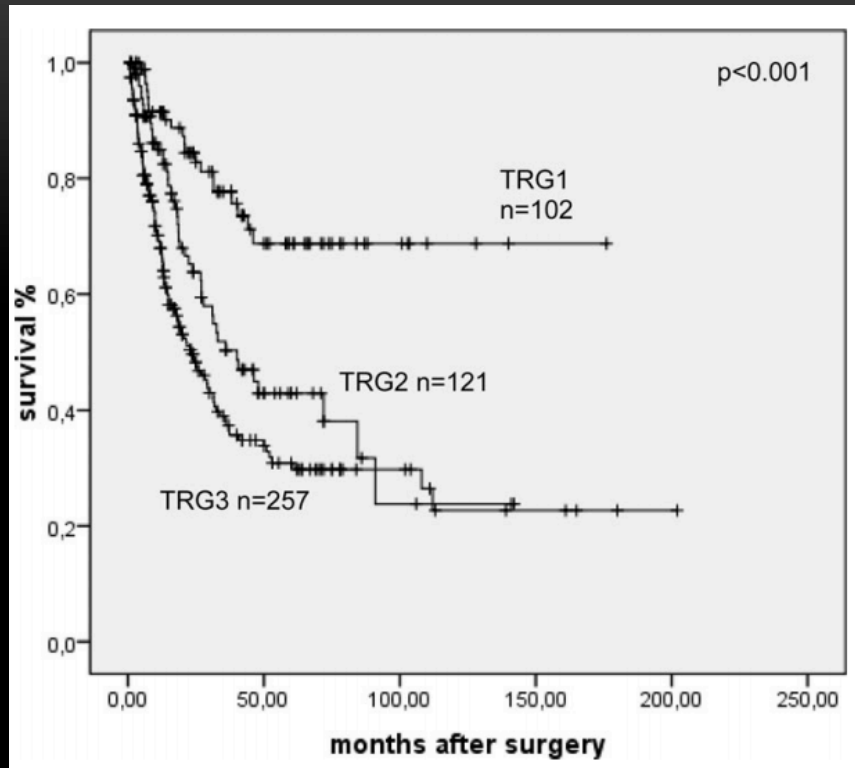Margin status, pathologic response
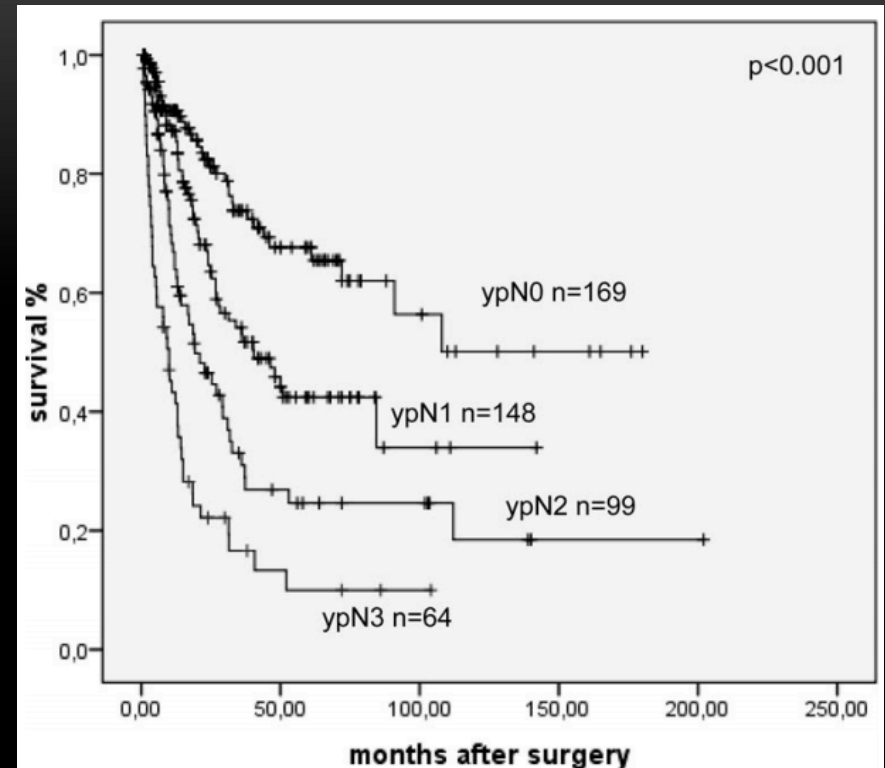
GASTRIC CARCINOMA

MD Anderson
- N=69 +neoadjuvant chemoXRT localized gastric ca

AJCC stage (6th)

GASTRIC CARCINOMA

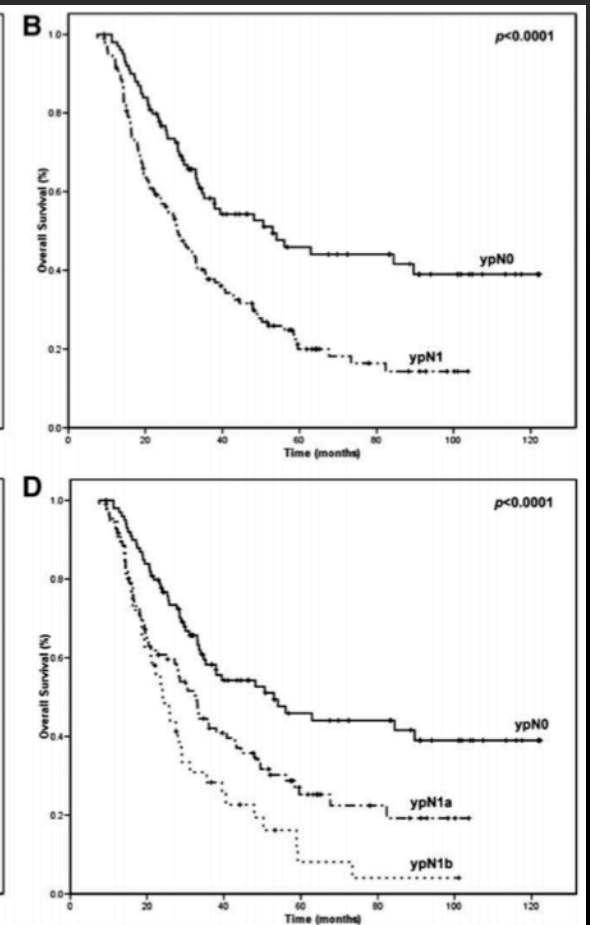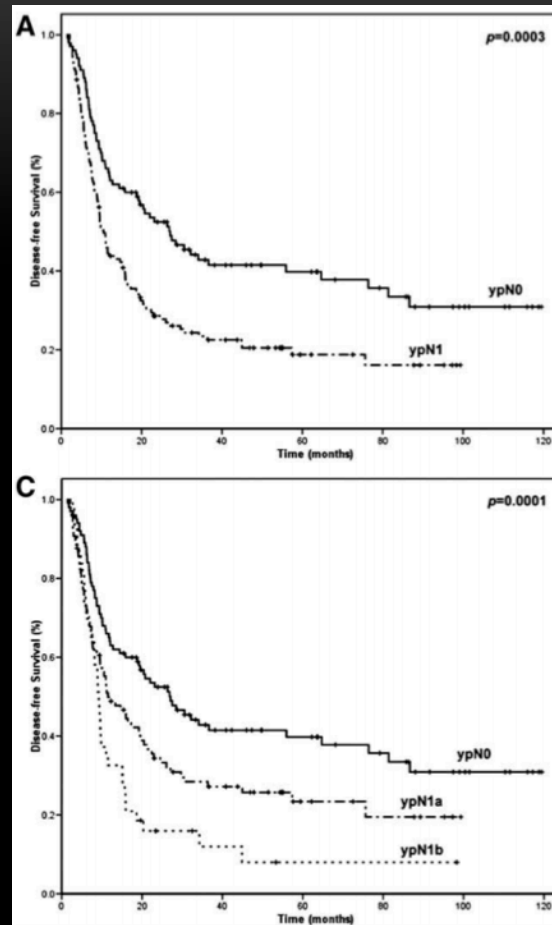

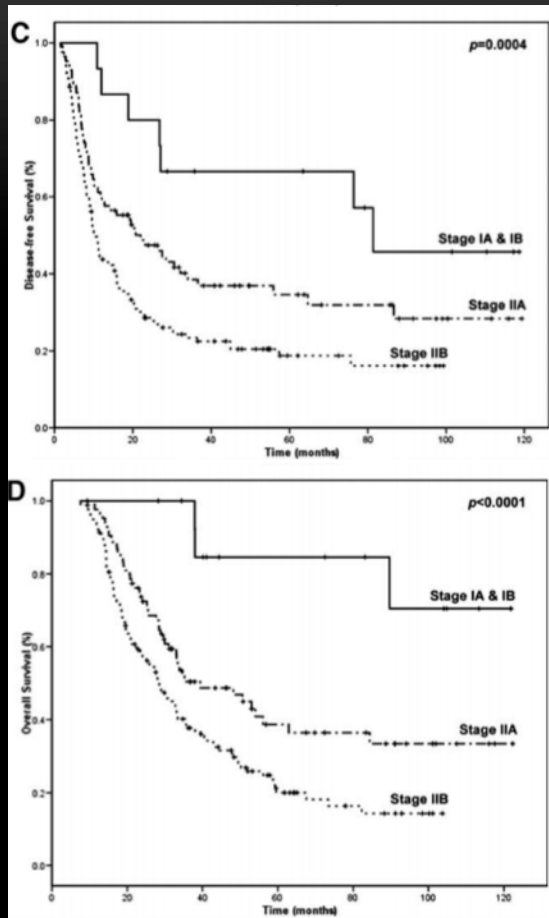TRG1 <10%, TRG2 10-50%, TRG3 >50%

UICC 2002 ypN

Technische Universitat Munchen
- N=440 +neoadjuvant chemo
  locally advanced gastric ca

Pathologic response, LN status

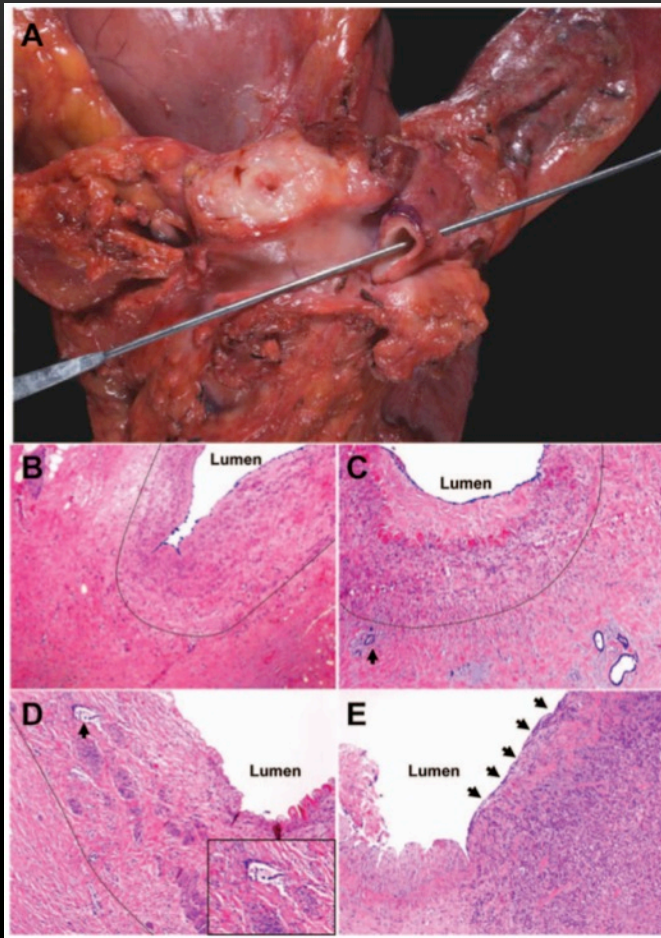# PANCREATIC DUCTAL CARCINOMA

PANCREATIC DUCTAL CARCINOMA

MD Anderson
- N=240 +neoadjuvant chemoXRT

ypN1a: 1-3 +LN, ypN1b: >3 +LN

AJCC stage (7th)
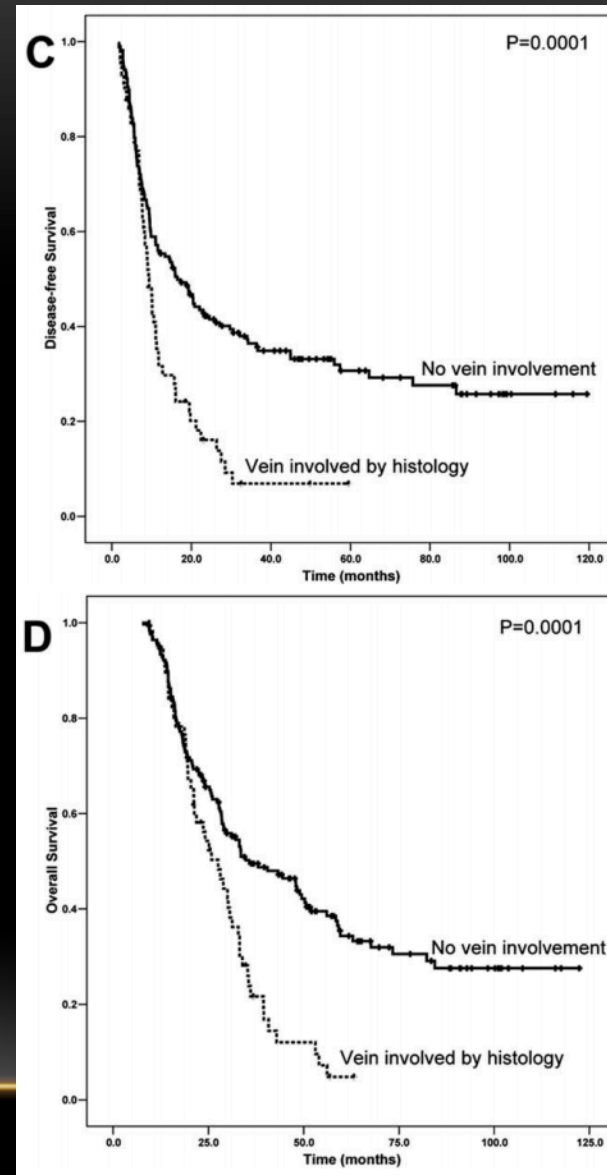
Cancer. 2012 Jan 1;118(1):268-77
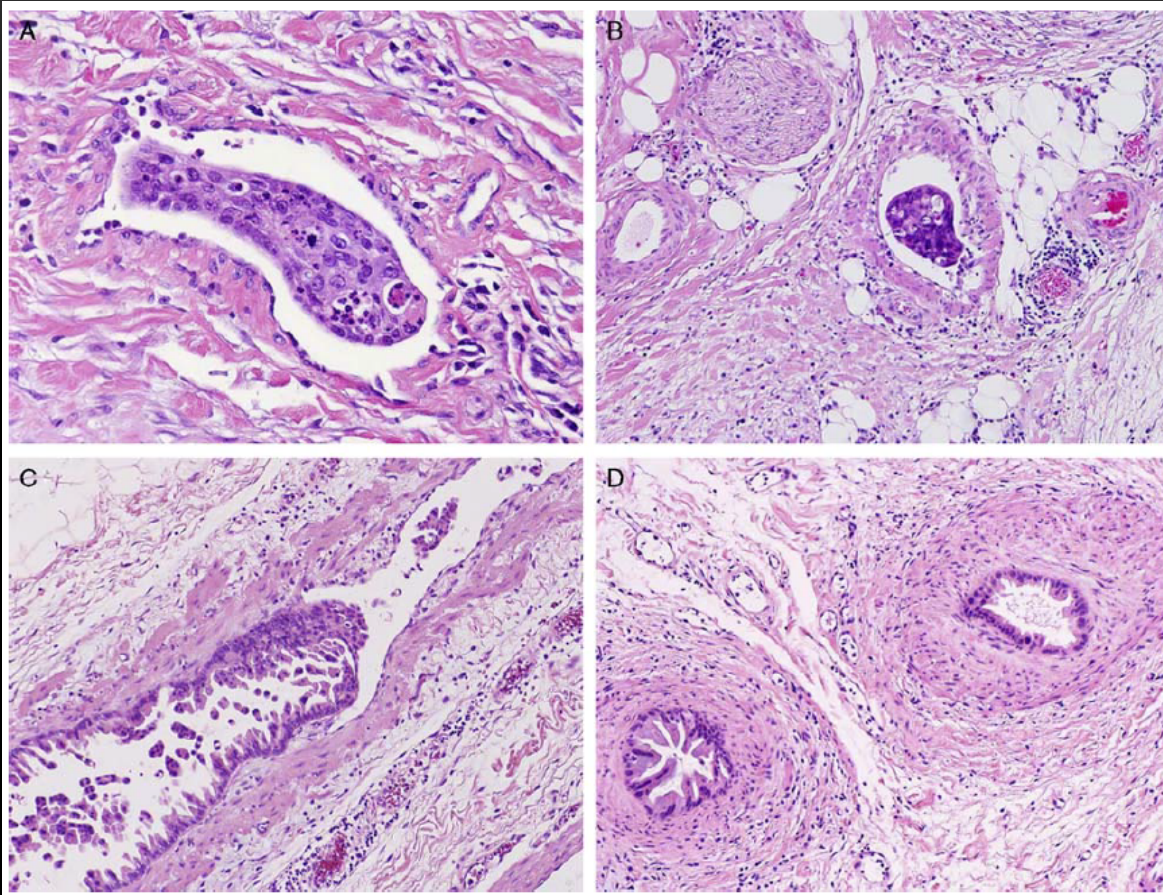
PANCREATIC DUCTAL CARCINOMA

MD Anderson
- N=225 patients +neoadjuvant chemoXRT

PV/SMV involvement

PANCREATIC DUCTAL CARCINOMA

MD Anderson
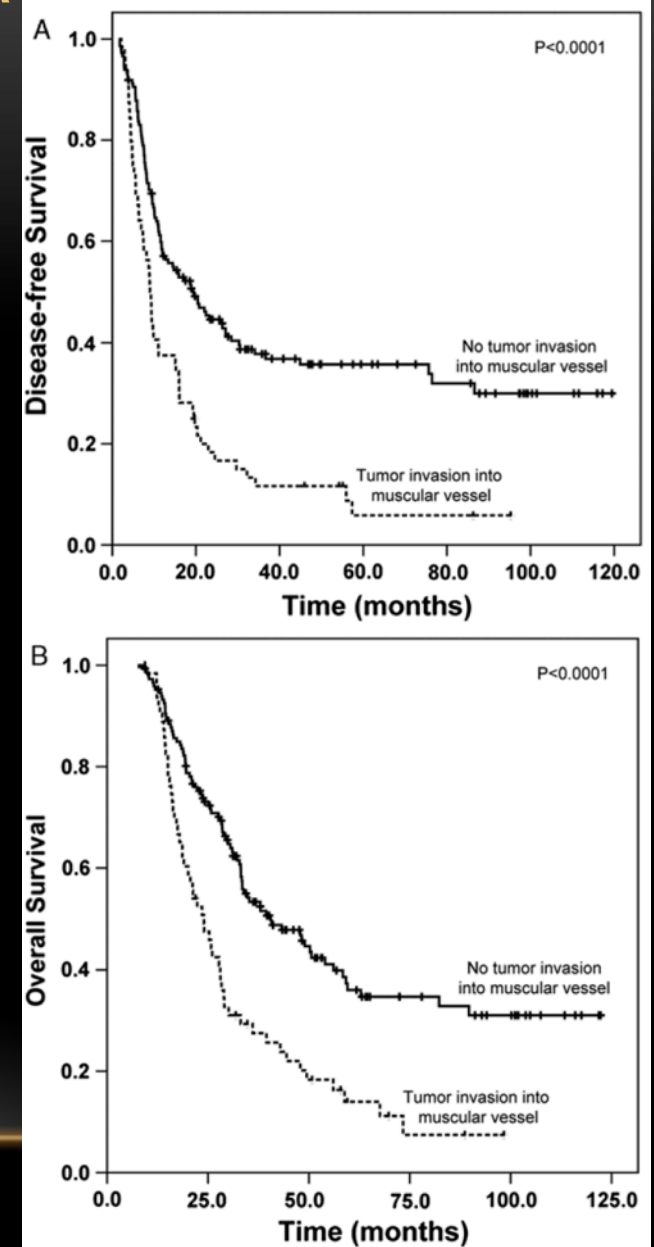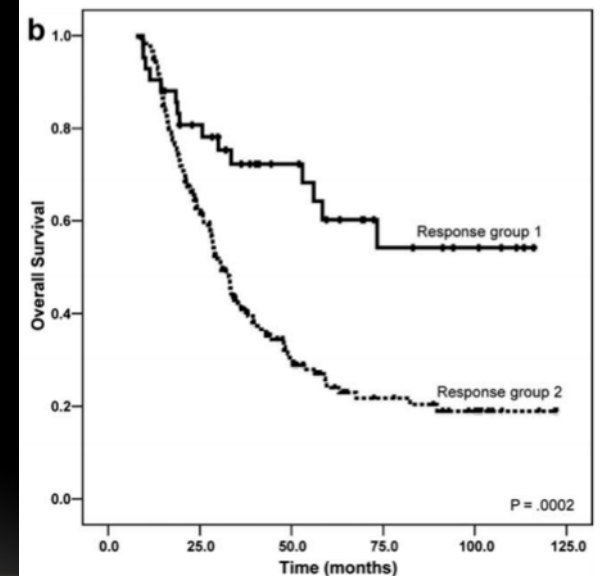- N=212 patients +neoadjuvant chemoXRT
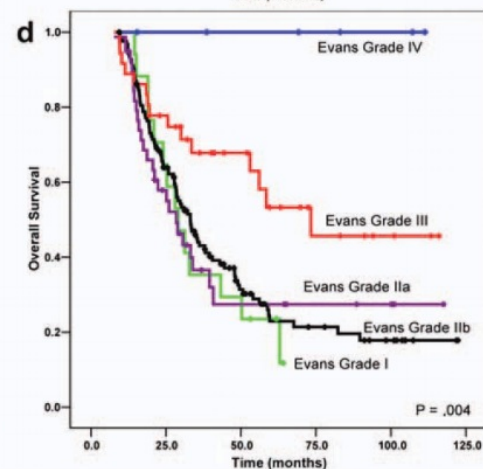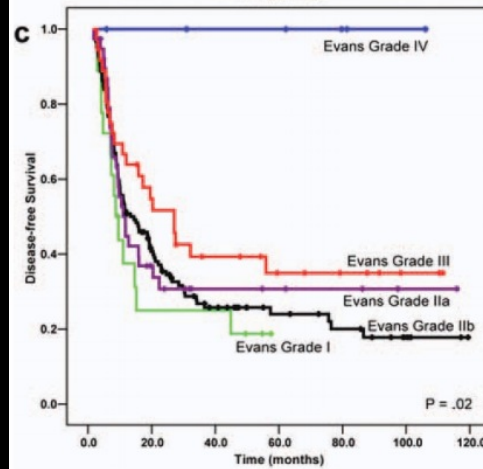
+Muscular vessel

PANCREATIC DUCTAL CARCINOMA
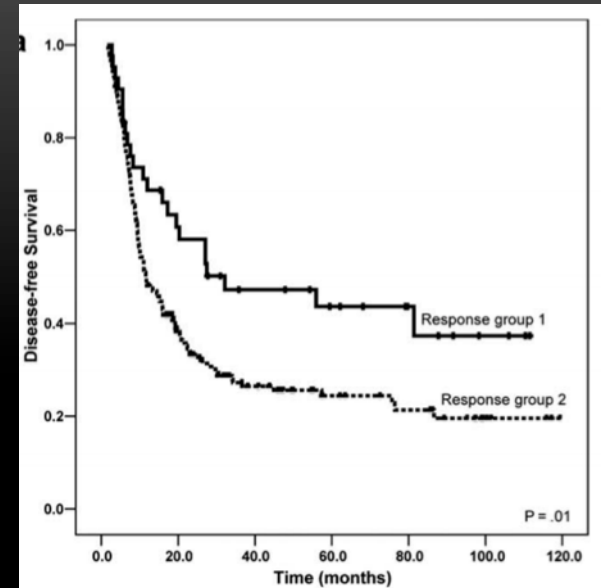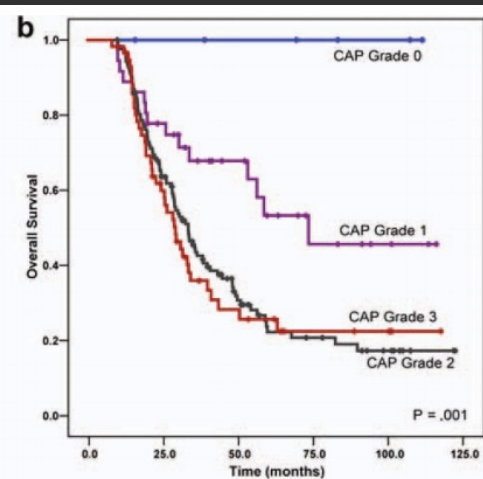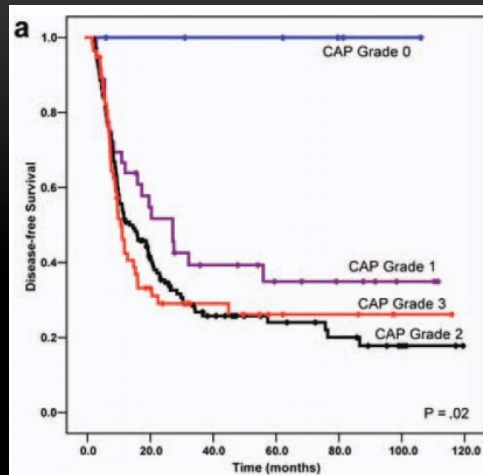
MD Anderson
- N=223 +neoadjuvant chemoXRT

Group 1: <5%, Group 2: ≥5%

Pathologic response

RECTAL CARCINOMA

RECTAL CARCINOMA
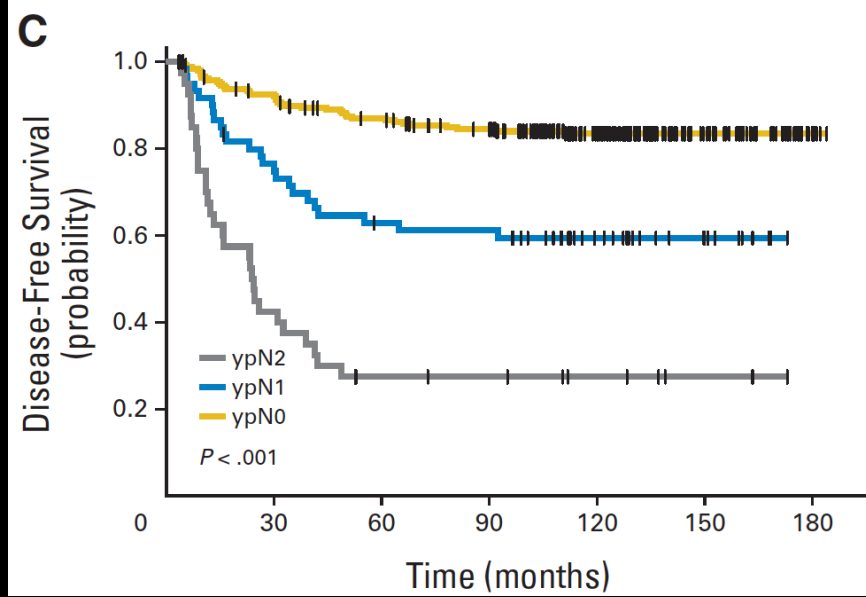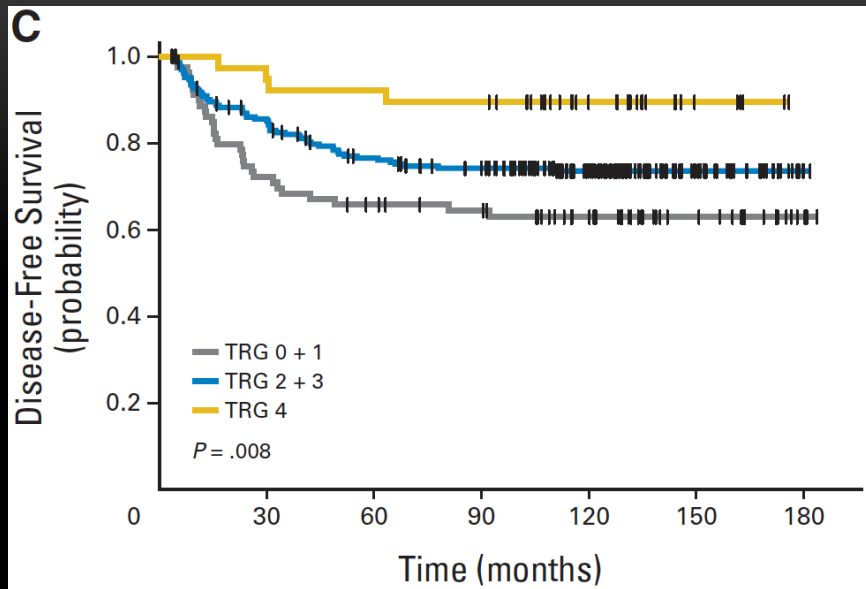
Variable Significant in Univariable Analysis	10-Year DFS		
	HR	95% CI	P^*
ypN category	2.50	1.95 to 3.22	< .001
Preoperative T category	—		
ypT category	0.93	0.81 to 1.08	.391
TRG	0.76	0.52 to 1.11	.039
Distance from anal verge	—		
Lymphatic invasion	1.29	0.81 to 2.05	.115
Venous invasion	1.89	0.93 to 3.82	.093
Local resection	—		

CAO/ARO/AIO-94 trial (multicenter randomized phase III study)
- N=402 +neoadjuvant chemoXRT
- Median follow-up: 132 months
- TRG: 0-no response, 1-≤25% fibrosis, 2-26-50% fibrosis, 3->50% fibrosis, 4-complete response

TRG, ypN

RECTAL CARCINOMA

Table 1 Definitions of categories within tumour regression grading (TRG) systems.

| System	Definition
Mandard five-point TRG system [7]	
TRG 1	(Complete regression) with absence of residual cancer and fibrosis extending through the wall
TRG 2	Presence of rare residual cancer cells scattered through the fibrosis
TRG 3	An increased number of residual cancer cells, but fibrosis is still predominant
TRG 4	Residual cancer outgrowing fibrosis
TRG 5	Absence of regressive changes
RCPath system [11]	
RCPath A	No residual tumour cells and/or mucus lakes only
RCPath B	Minimal residual tumour (i.e. only occasional microscopic tumour foci are identified with difficulty)
RCPath C	No marked regression
CAP system [12]	
TRG 0 (complete response)	No residual tumour
TRG 1 (marked response)	Minimal residual cancer
TRG 2 (moderate response)	Residual cancer outgrown by fibrosis
TRG 3 (poor or no response)	Minimal or no tumour kill; extensive residual cancer
Modified Mandard three-point TRG system by Ryan et al. [17]	
TRG 1	No cancer cells, or single cancer cells, or small group of cancer cells
TRG 2	Residual cancer outgrown by fibrosis
TRG 3	Fibrosis outgrown by cancer, or no fibrosis with extensive residual cancer
Modified Mandard four-point TRGN by Dhadda et al. [8]	
TRGN 1	(Complete regression) with absence of residual cancer and fibrosis extending through the wall
TRGN 2	Presence of rare residual cancer cells scattered through the fibrosis
TRGN 3	An increased number of residual cancer cells, but fibrosis is still predominant
TRGN 4	Macroscopic tumour; absence of regressive; any node positive within the irradiated volume

CAP, College of American Pathologists; RCPath, The Royal College of Pathologists; TRGN, new proposed tumour regression grade.

Beaumont Hospital, Dublin, Ireland

- N=153 +neoadjuvant chemoXRT +adjuvant chemo
- T3/T4 +LN (locally advanced)
- Evaluated all TRG systems
- By multivariate analysis:
  ypN and margin
  not TRG

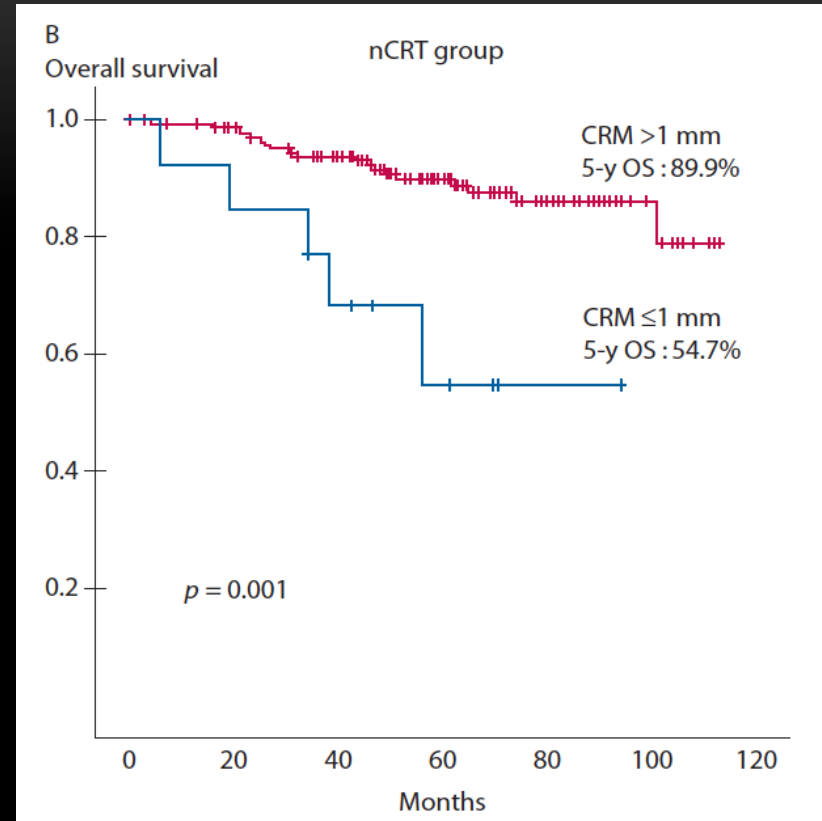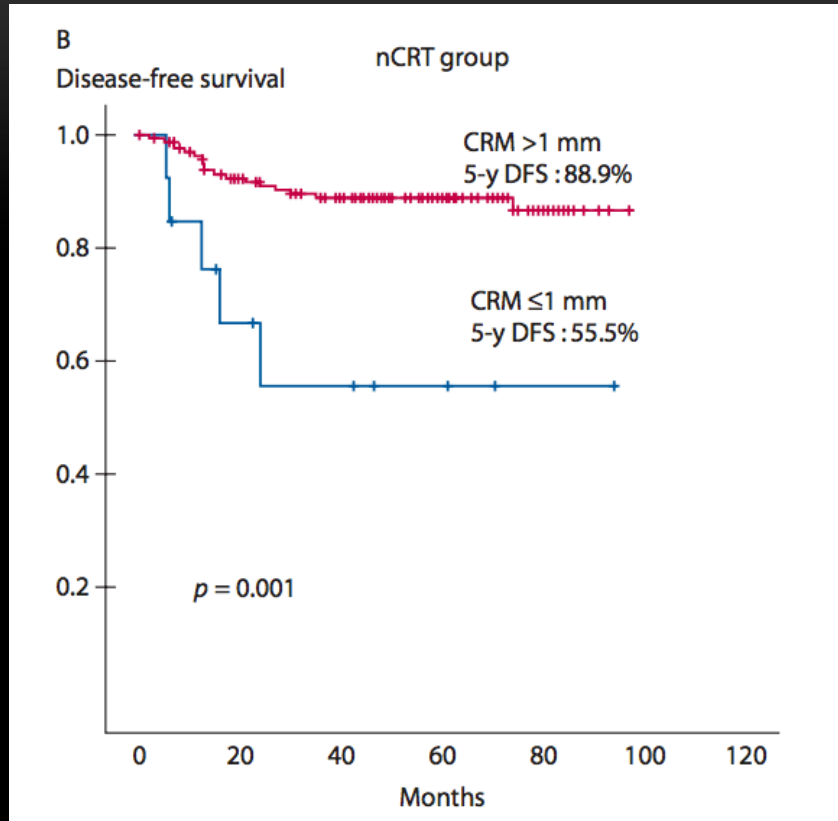ypN and margin

RECTAL CARCINOMA
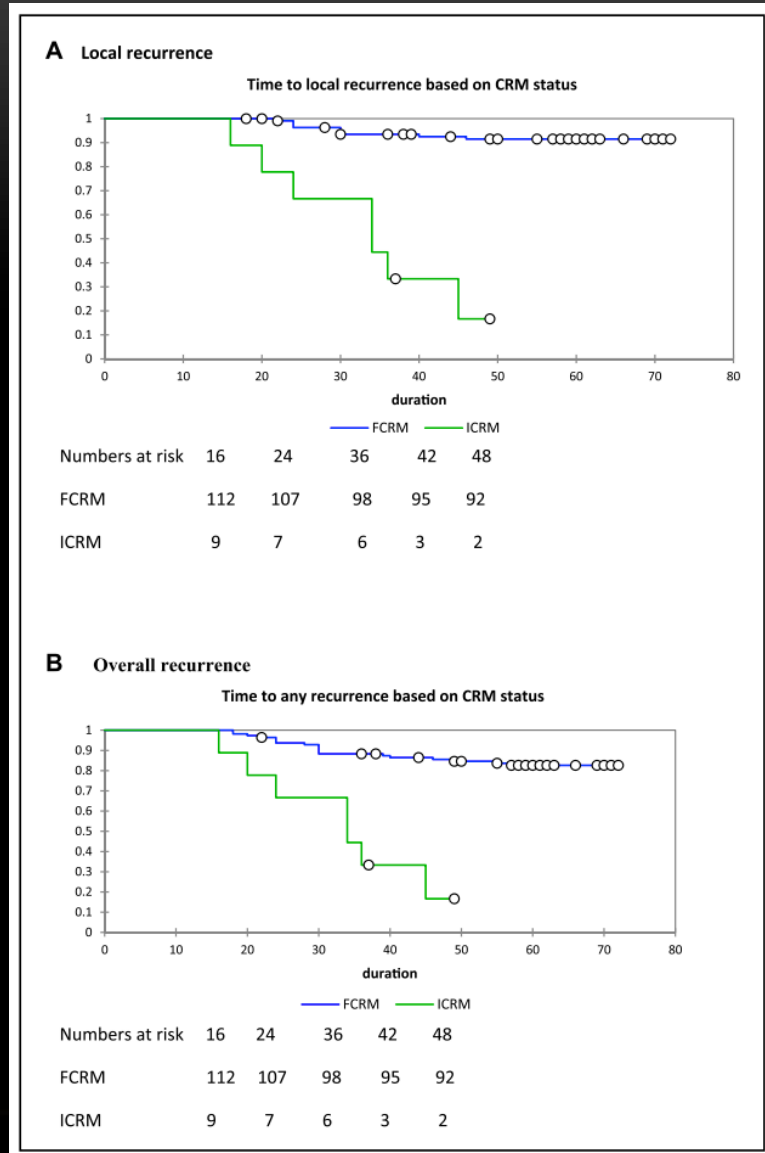
University of Alexandria, Egypt
- N=121 patients +neoadjuvant chemoXRT + adjuvant chemo
- Median follow-up: at least 5 years
- +margin: tumor extension (continuous and discontinuous) <2mm from ink
- Mesorectal resection status NOT a prognostic factor for recurrence

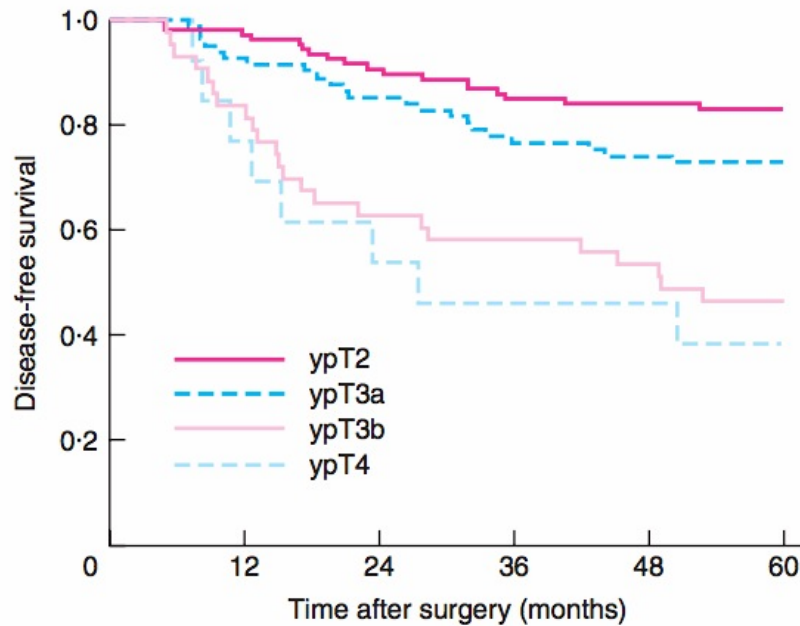## Circumferential margin <2mm

RECTAL CARCINOMA

Sungkyunkwan University School of Medicine, Seoul, Korea
- N=181 +neoadjuvant chemoXRT

Circumferential margin <1mm

RECTAL CARCINOMA

CAO/ARO/AIO-94 trial (multicenter randomized phase III study)

- N=124 +neoadjuvant chemoXRT
- Median follow-up: at least 5 years
- ypT3a: ≤5mm, ypT3b: >5mm
- ypT3b: HR 2.46, 95%CI 1.2-5.0, P=0.014 disease-specific survival

ypT3a versus ypT3b

PATHOLOGIC FACTORS PROGNOSTIC OF SURVIVAL

Esophageal adenocarcinoma

- ypTNM (AJCC 6th) – conflicting studies

- LN and distant metastasis

- Tumor downstaging

- NE differentiation

PATHOLOGIC FACTORS PROGNOSTIC OF SURVIVAL

Gastric carcinoma

- R0 resection

- Pathologic response
  - Complete and <10% residual tumor

- ypTNM (AJCC 6th)

- LN status (UICC 2002)

PATHOLOGIC FACTORS PROGNOSTIC OF SURVIVAL

Pancreatic ductal carcinoma

- ypTNM (AJCC 7th)

- LN status

  - 0 vs 1-3 +LN vs >3 +LN

- +tumor in resected vein

- +invasion into muscular vessel

- Pathologic response

  - <5% vs ≥5% residual tumor

PATHOLOGIC FACTORS PROGNOSTIC OF SURVIVAL

Rectal carcinoma

- Tumor regression grade – conflicting studies

- LN status

- R0 resection

  - 1 mm vs 2 mm

- ypT3a vs ypT3b