



# ADVANCING GI PATIENT CARE

APRIL 28–30, 2023  
Frisco, Texas

This activity is supported by educational grants from  
Mallinckrodt Pharmaceuticals, Pfizer Inc., and Salix Pharmaceuticals.



An aerial photograph of the New Orleans skyline, featuring various skyscrapers and buildings. The image is overlaid with a semi-transparent blue geometric shape that covers the top and right portions of the frame. The text is centered within this blue area.

# The GE Junction

Updates, Challenges and Surgical Perspectives

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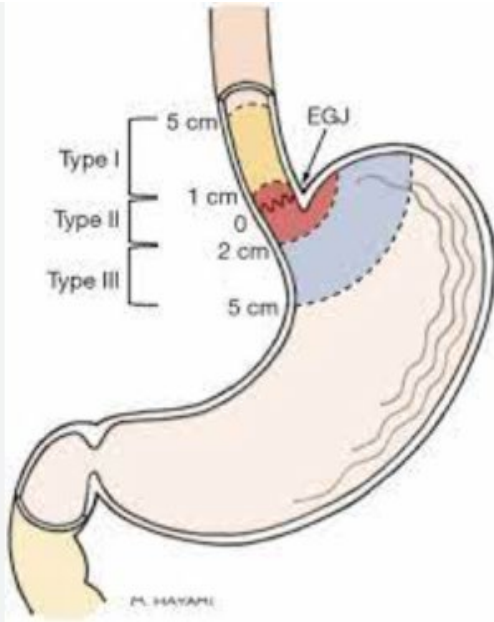
# Disclosure

- I have no relationships to disclose.

# The GE Junction

- Surgical anatomy of the GEJ
- GEJ Adenocarcinoma Staging Workup – Role of Advanced Endoscopy
- Updates in Clinical Trial Data
- Surgical and Perioperative Perspective
- Ochsner Experience

# The GEJ Junction



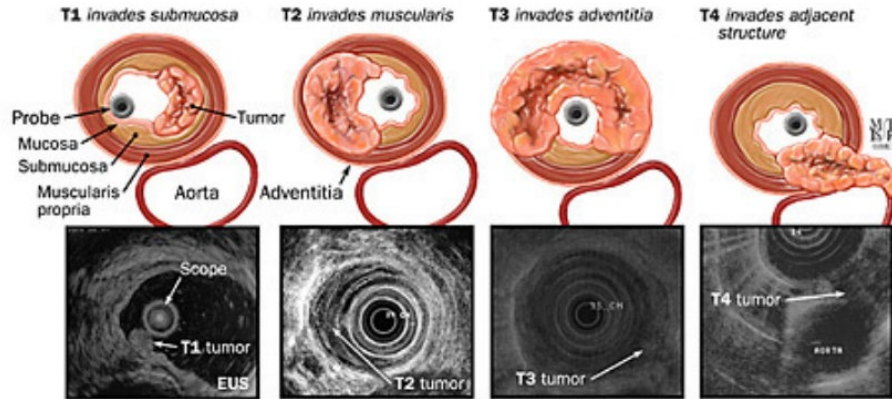
**Table 1. Siewert classification of EGJ tumors**

Siewert	Description	Surgical approach
I	Tumor center located between 5 and 1 cm proximal to the anatomical cardia	Approached as esophageal or EGJ cancer
II	Tumor center located between 1 cm proximal and 2 cm distal to the anatomical cardia	Approached as esophageal or EGJ cancer
III	Tumor center located between 2 and 5 cm distal to the anatomical cardia	Approached as gastric cancer

# The GEJ Junction

Siewart II

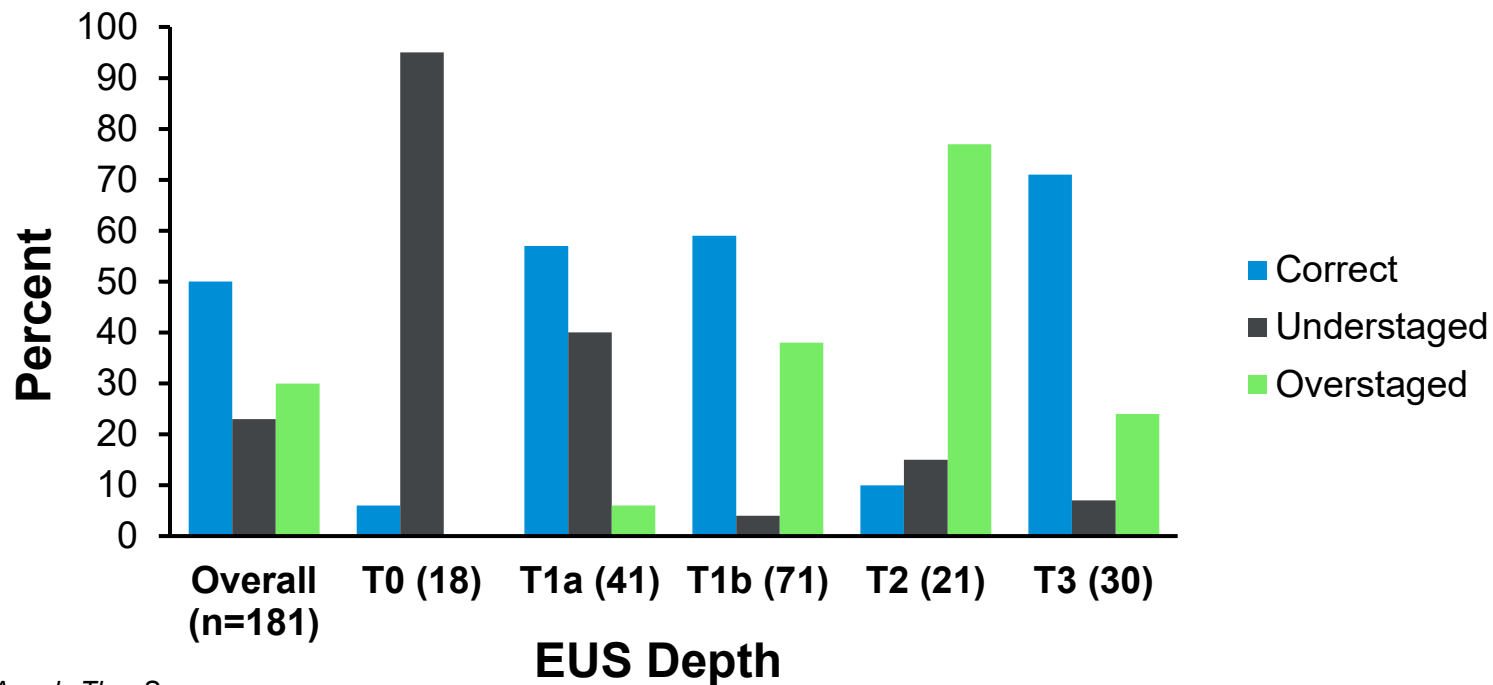
# EUS Staging – The Surgeon’s View



	Pooled sensitivity (%)	Pooled specificity (%)	Pooled LR+	Pooled LR-	Pooled DOR
T1	81.6 (77.8-84.9)	99.4 (99.0-99.7)	44.4 (15.5-127.4)	0.2 (0.2-0.4)	221.5 (118.5-413.9)
T2	81.4 (77.5-84.8)	96.3 (95.4-97.1)	16.6 (9.3-29.7)	0.2 (0.2-0.3)	90.7 (48.3-170.5)
T3	91.4 (89.5-93.0)	94.4 (93.1-95.5)	12.5 (7.7-20.3)	0.1 (0.1-0.2)	145.2 (90.3-233.4)
T4	92.4 (89.2-95.0)	97.4 (96.6-98.0)	25.4 (13.7-47.0)	0.1 (0.1-0.2)	250.0 (145.2-430.5)

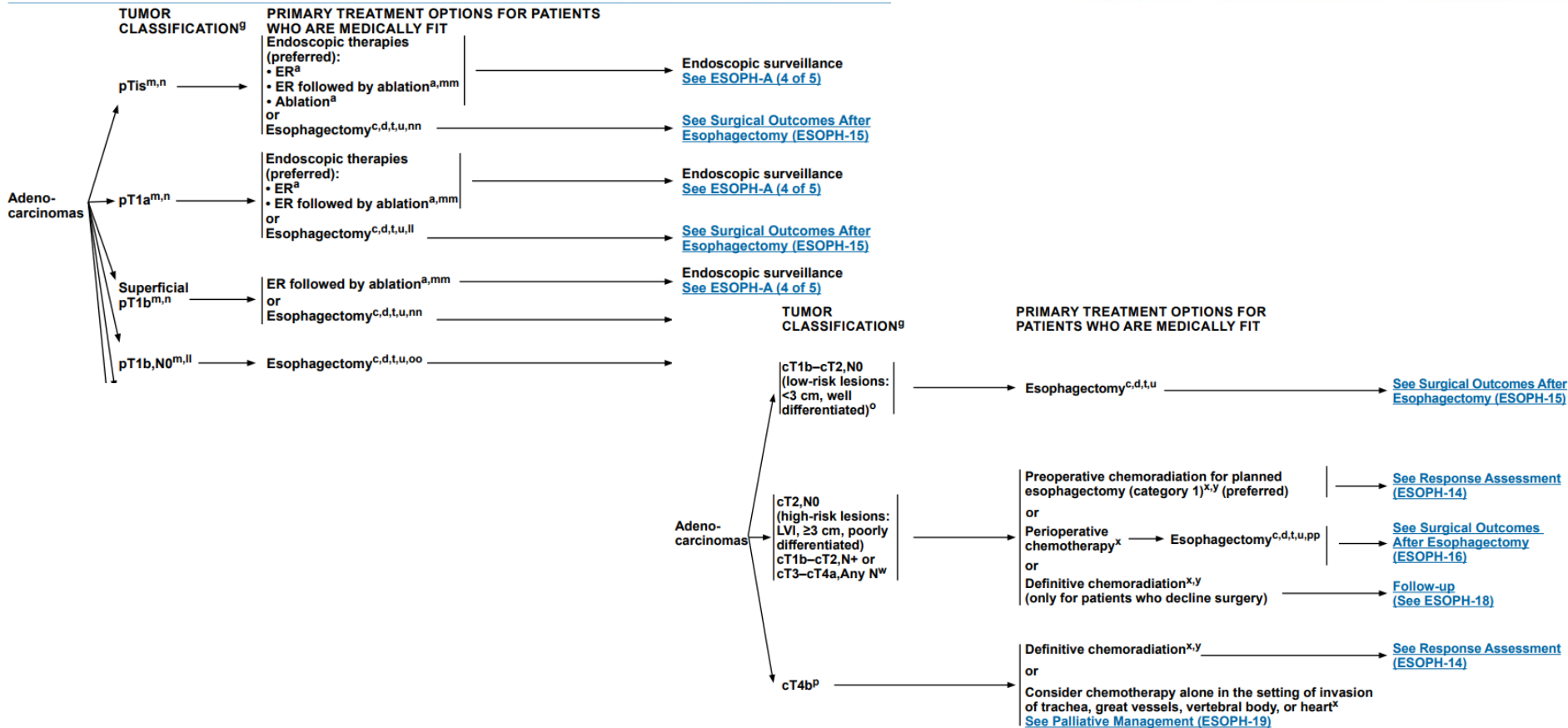
LR+: Positive likelihood ratio; LR-: Negative likelihood ratio; DOR: Diagnostic odds ratio.

# Is the GEJ Different?



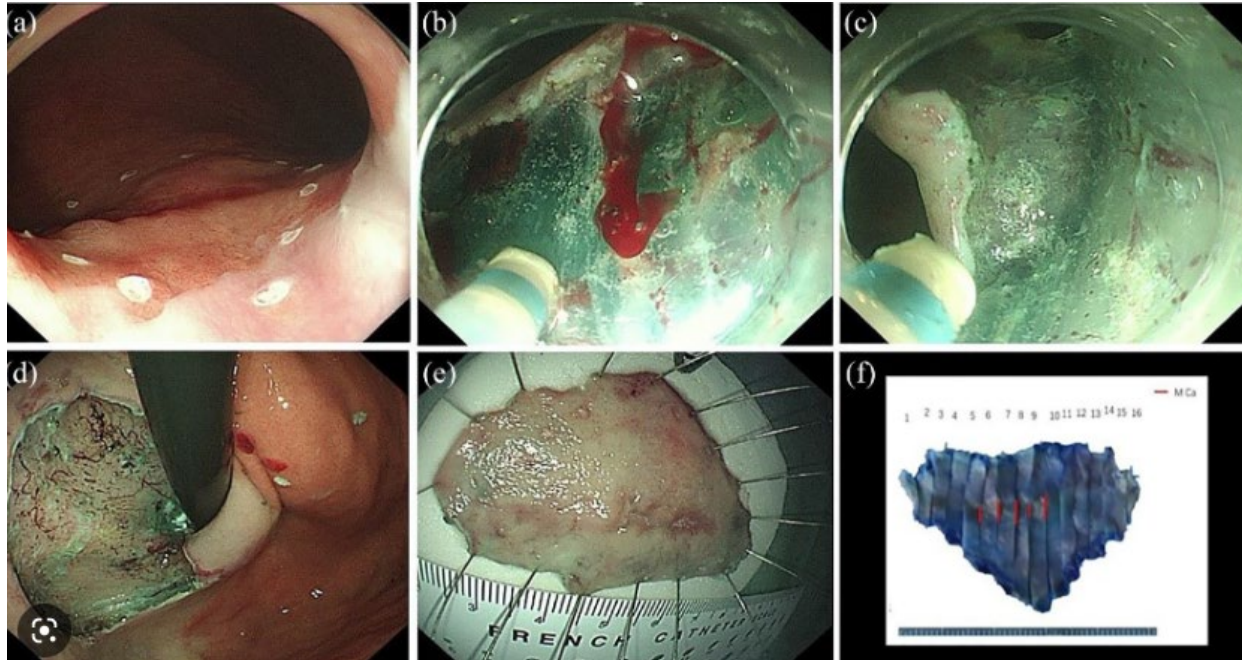


# Why Does It Matter?



# EMR/ESD

- How can we definitively stage early GEJ Cancer?



# EMR/ESD

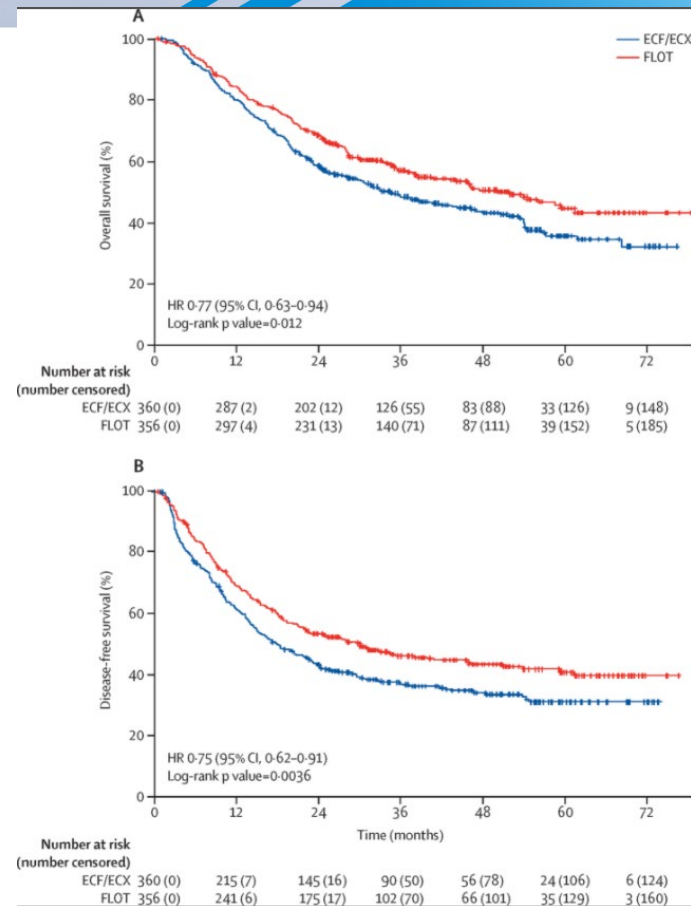
- What do we do with the information?
  - T1a?
  - $\geq$ T1b?
    - LVI? Grade?
  - Margin positive?

# Updates in Neoadjuvant and Adjuvant Therapy

- FLOT
- CROSS
- Checkmate 577
- NEO-AEGIS
- ESOPEC

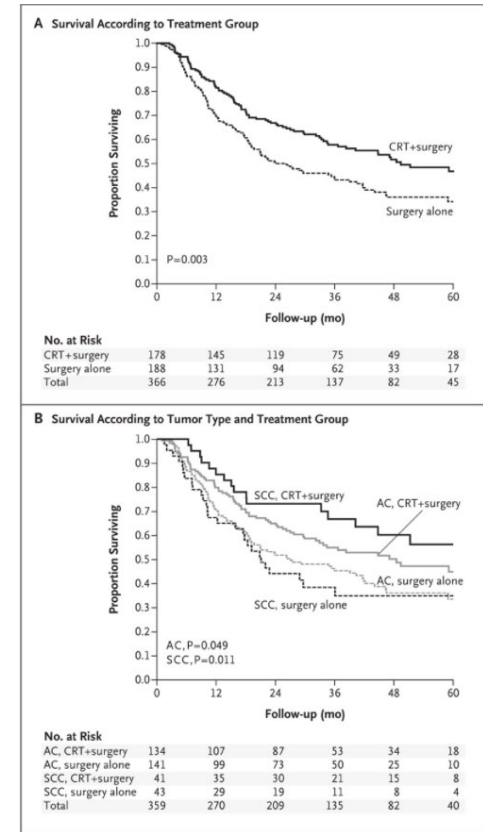
# Treatment – Early Stage

- FLOT4-AIO Trial
  - FLOT vs ECF
  - Docetaxel 50 mg/m<sup>2</sup> + oxaliplatin 85 mg/m<sup>2</sup> + leucovorin 200 mg/m<sup>2</sup> + infusional 5-FU 2600 mg/m<sup>2</sup> over 24 hours administered every 2 weeks
  - Studied FLOT x 4 cycle → Surgery → FLOT x 4 cycles
  - FLOT compared to ECF:
    - Higher pCR (16% vs 8%) in phase II portion
    - mOS 50m vs 35m (HR 0.77)
    - 3-year OS: 57% vs 48%



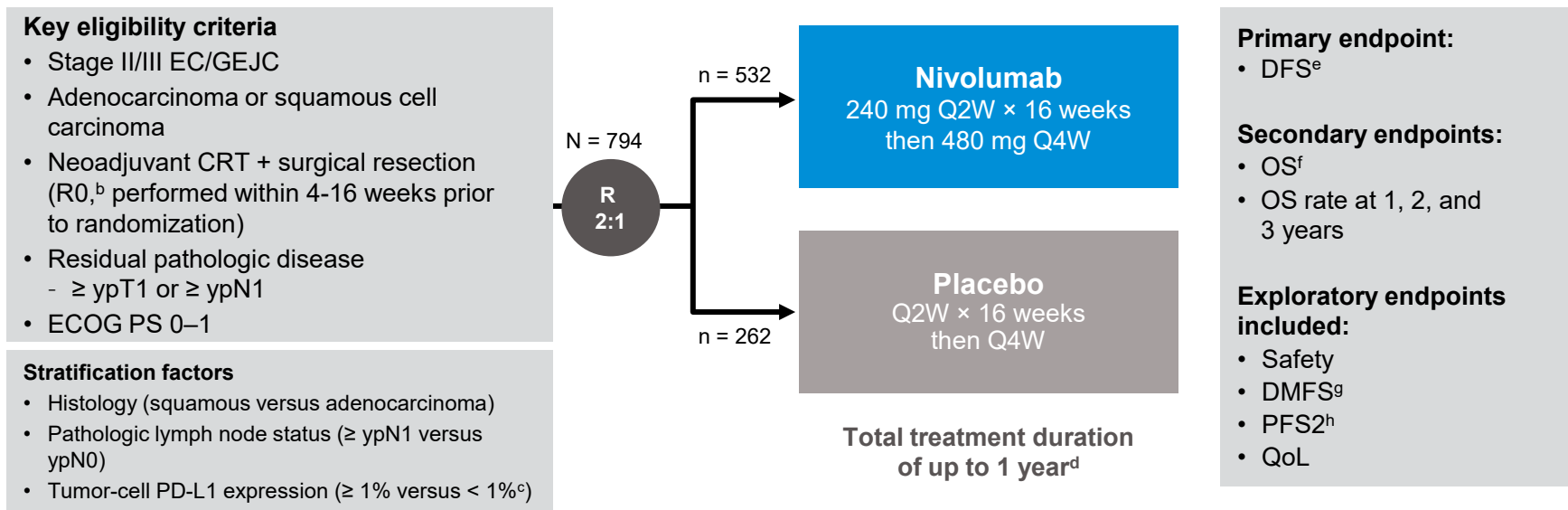
# Treatment – Early Stage – Esophageal

- CROSS Trial
  - Randomized resectable esophageal and GEJ patients to surgery alone or chemoradiation
  - Used carboplatin AUC 2 + paclitaxel 50 mg/m<sup>2</sup> weekly x 5 weeks with 41.4 Gy XRT
  - 75% adenocarcinoma
  - R0 resection 92% vs 69% (P<0.001)
  - pCR 29% of neoadjuvant CRT group
  - mOS: 49.4 m vs 24.0 m (HR: 0.657, P=0.003)



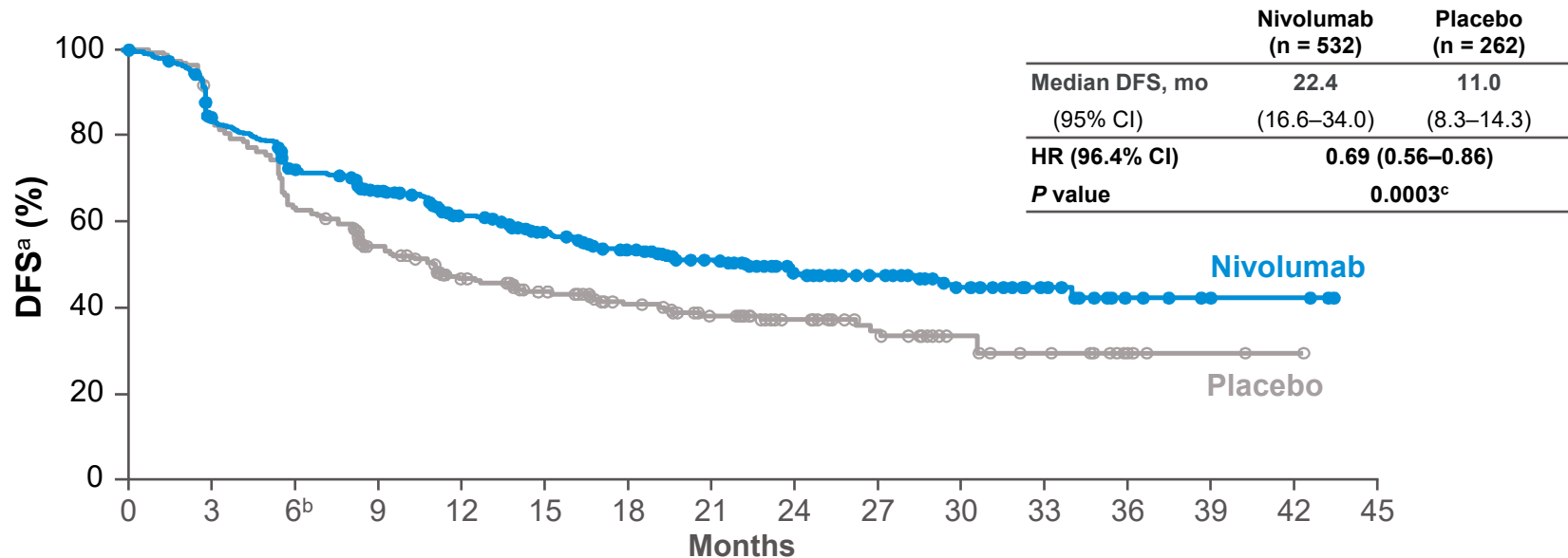
# CheckMate 577 Study Design

- CheckMate 577 is a global, phase 3, randomized, double-blind, placebo-controlled trial<sup>a</sup>



- Median follow-up was 24.4 months (range, 6.2–44.9)<sup>i</sup>
- Geographical regions: Europe (38%), United States and Canada (32%), Asia (13%), rest of the world (16%)

# Disease-Free Survival (DFS)



No. at risk	0	3	6 <sup>b</sup>	9	12	15	18	21	24	27	30	33	36	39	42	45
Nivolumab	532	430	364	306	249	212	181	147	92	68	41	22	8	4	3	0
Placebo	262	214	163	126	96	80	65	53	38	28	17	12	5	2	1	0



# Treatment – Early Stage

**Standard of care for early stage ( $\geq T2$  or N+, M0) gastric or GEJ (Siewart 3 +/- 2) adenocarcinoma is:**

**FLOT x 4 → SURGERY → FLOT x 4**

\*\* Only for most fit patients

\*\* For less fit patients, consider perioperative FOLFOX or CAPOX based on CLASSIC trial

- Data extrapolated from adjuvant CLASSIC trial

**Standard of care for early stage esophageal ( $\geq T2$  or N+, M0) or GEJ (Siewart 1 +/-2) SCC or adenocarcinoma is:**

**Chemoradiation (carboplatin + paclitaxel) → SURGERY → NIVOLUMAB**

\*\* For patients who do not achieve pCR

# Treatment – Early Stage

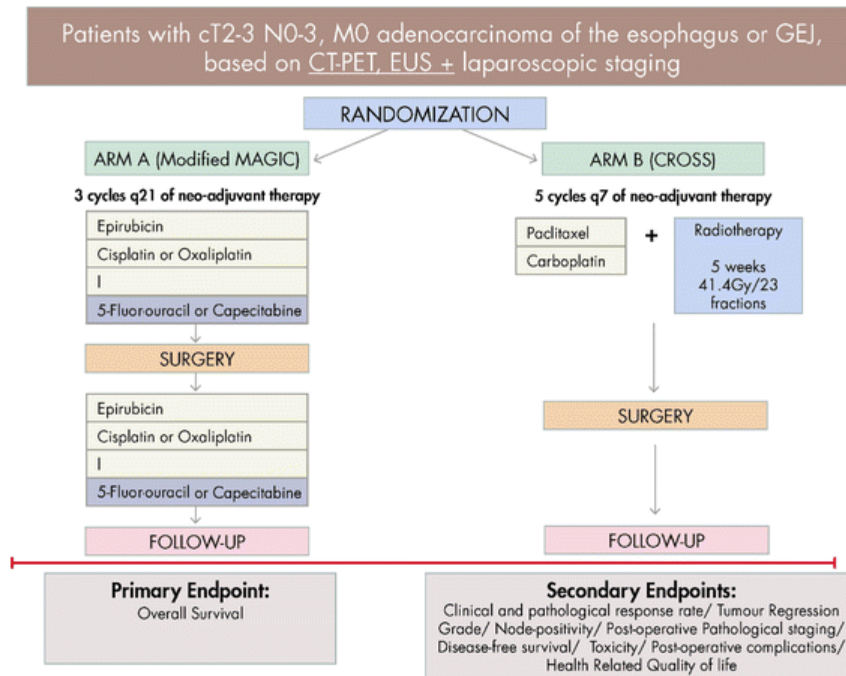
Unanswered questions:

**Is perioperative chemotherapy (i.e. FLOT) superior to neoadjuvant chemoradiation (i.e. CROSS regimen) for GEJ tumors?**

# Treatment – Early Stage

## Neo-AEGIS trial:

- Patients with **adenocarcinoma of esophagus or GEJ**
- Most patients in chemotherapy arm received MAGIC regimen (ECF) vs FLOT (157 vs 27).



# Treatment – Early Stage

## Neo-AEGIS trial:

- Estimated 3 year survival of ChemoRT vs chemo:
  - 56% vs 57%, HR 1.02 (95% CI: 0.74-1.42)
- Authors concluded there was non-inferiority between two approaches

	Arm A (Magic/FLOT)	Arm B CROSS
R0 (negative margins)	82%	95%
ypN0	44.5%	60.1%
Tumor regression grade 1 & 2	12.1%	41.7%
Pathologic complete response	5%	16%
Neutropenia (Gr 3/4)	14.1%	2.8%
Neutropenic sepsis	2.7%	0.6%
Postoperative in-hospital deaths	3%	3%
Postoperative Pneumonia/ARDS	20%/0.6%	16%/4.3%
Anastomotic Leak	12%	11.7%
Clavien-Dindo > III<V	23.6%	22%

# Treatment – Early Stage

Still unanswered question:

**Is perioperative chemotherapy (i.e. FLOT) superior to neoadjuvant chemoradiation (i.e. CROSS regimen)?**

Well...

If FLOT > MAGIC (FLOT4-AIO)

And MAGIC = CROSS (Neo-Aegis)

Then FLOT > CROSS ??

OR

FLOT = CROSS + Nivolomab??

# Surgical and Perioperative Perspective

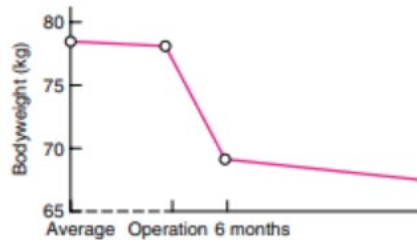
- Lots of operations to choose from...
- Which is best?

# Surgical and Perioperative Perspective

- Lots of operations to choose from...
  - Total Gastrectomy
  - Ivor Lewis Esophagectomy
  - Mckeown Esophagectomy
  - Open
  - Lap
  - Robotic
  - Hybrid
  
- Which is best?

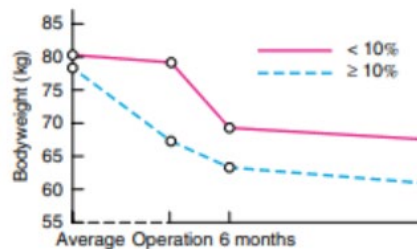
# Surgical and Perioperative Perspective

All are tough...



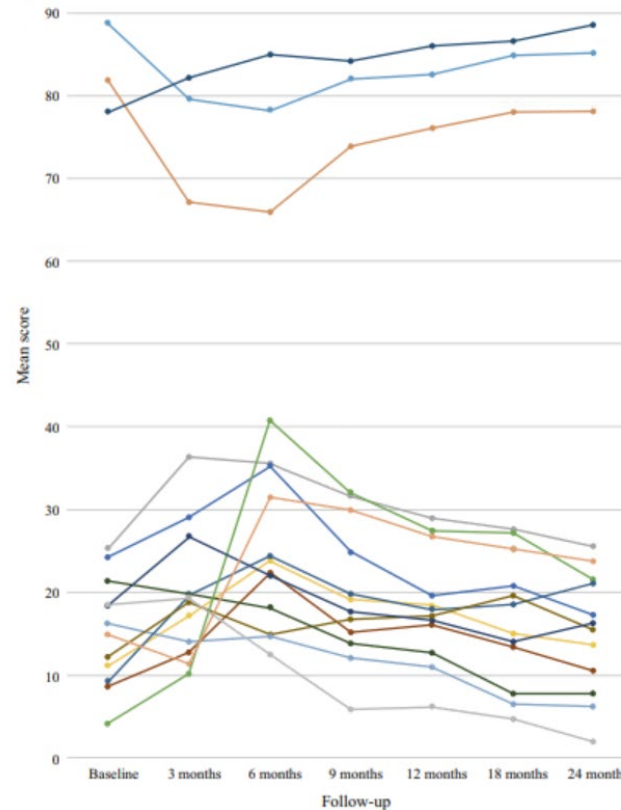
No. of patients 164 176 176

**a** Whole group



No. of patients  
 < 10% 132 132 131  
 ≥ 10% 31 31 31

**b** By preoperative weight loss



**(a)** HR-QoL domains with a significant decline in short-term HR-QoL score compared to baseline, that recovered to baseline level at 12 months follow-up:

- Physical functioning
- Role functioning
- Fatigue
- Dyspnea
- Appetite loss
- Dry mouth
- Trouble with taste

**(b)** HR-QoL domain with a significant decline in long-term HR-QoL score compared to baseline.

- Reflux

**(c)** HR-QoL domains with a significant improvement in long-term HR-QoL score compared to baseline:

- Emotional functioning
- Diarrhea

**(d)** HR-QoL domains with a significant improvement in short-term HR-QoL score compared to baseline, that remained significantly improved after long-term follow-up:

- Dysphagia
- Odynophagia

**(e)** HR-QoL domain with a significant improvement in short-term HR-QoL score compared to baseline, that became significantly impaired after long-term follow-up:

- Anxiety

**(f)** HR-QoL domain with a significant improvement in short-term HR-QoL score compared to baseline, that recovered to baseline level during the short-term follow-up:

- Trouble talking

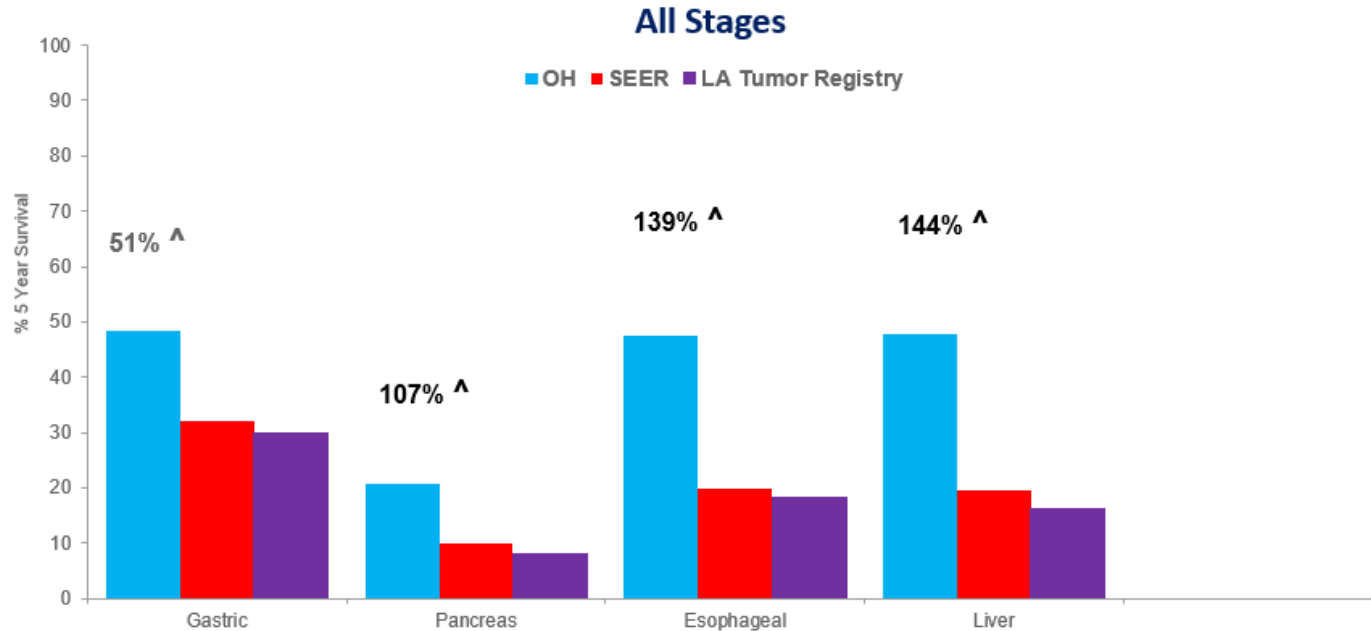


# Surgical and Perioperative Perspective

- Prehab
- Perioperative ERAS
- GI Survivorship
- Continued Shifting of Multimodal Therapy to the Neoadjuvant Setting

# GI Cancer at the Benson Cancer Center

## Saving More Lives: Relative 5-Year Cancer Survival



Ochsner UGI Surgical Oncology Outcomes vs. National and Louisiana

# Surgical Oncology at the Ochsner Clinic



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