Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Gastroesophageal Cancers

Saturday, April 12, 2025

12:15 PM – 1:45 PM

Faculty

Sunnie Kim, MD
Brooke Parker, MSN, FNP
Michal F Segal, BSN, RN, OCN
Manish A Shah, MD

Moderator

Neil Love, MD

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Faculty

Brooke Parker, MSN, FNP
Gastrointestinal Oncology Nurse Practitioner
UCHealth Cancer Care
Aurora, Colorado

Sunnie Kim, MD
GI Medical Oncologist
Associate Professor
University of Colorado Cancer Center
Aurora, Colorado

Michal F Segal, BSN, RN, OCN
Clinical Trials Nurse II
Memorial Sloan Kettering Cancer Center
New York, New York

Manish A Shah, MD
Professor of Medicine
Bartlett Family Professor of Gastrointestinal Oncology
Chief, Solid Tumor Oncology
Weill Cornell Medicine/NewYork-Presbyterian Hospital
New York, New York

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Dr Kim — Disclosures

Consulting Agreements	Amgen Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol Myers Squibb, Gilead Sciences Inc, I-Mab Biopharma, Merck
Contracted Research	Merck
Data and Safety Monitoring Boards/ Committees	Jazz Pharmaceuticals Inc

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Ms Parker — Disclosures

No relevant conflicts of interest to disclose

Ms Segal — Disclosures

Consulting Agreements	Astellas

Dr Shah — Disclosures

No relevant conflicts of interest to disclose

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Commercial Support

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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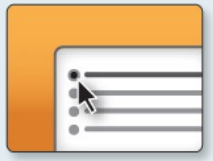
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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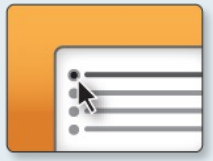
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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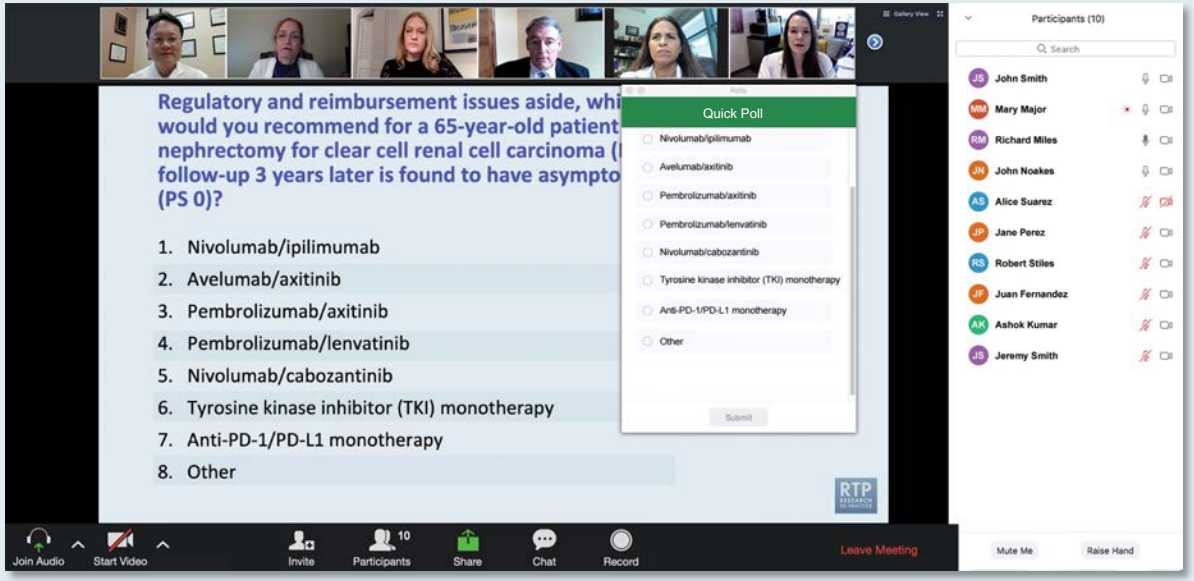
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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ONCOLOGY NURSING UPDATE WITH DR NEIL LOVE

Bispecific Antibodies in Lymphoma Part 1 — An Interview with Ms Robin Klebig for Oncology Nurses

MS ROBIN KLEBIG
MAYO CLINIC

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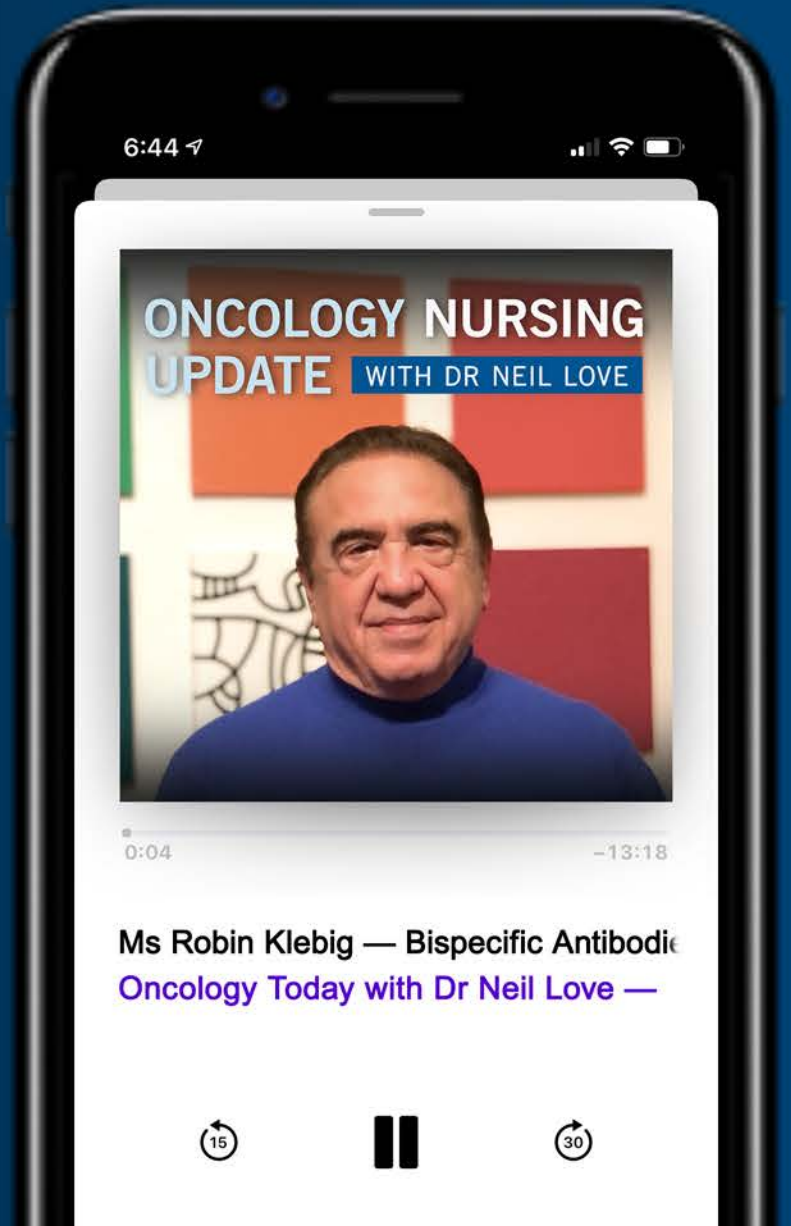
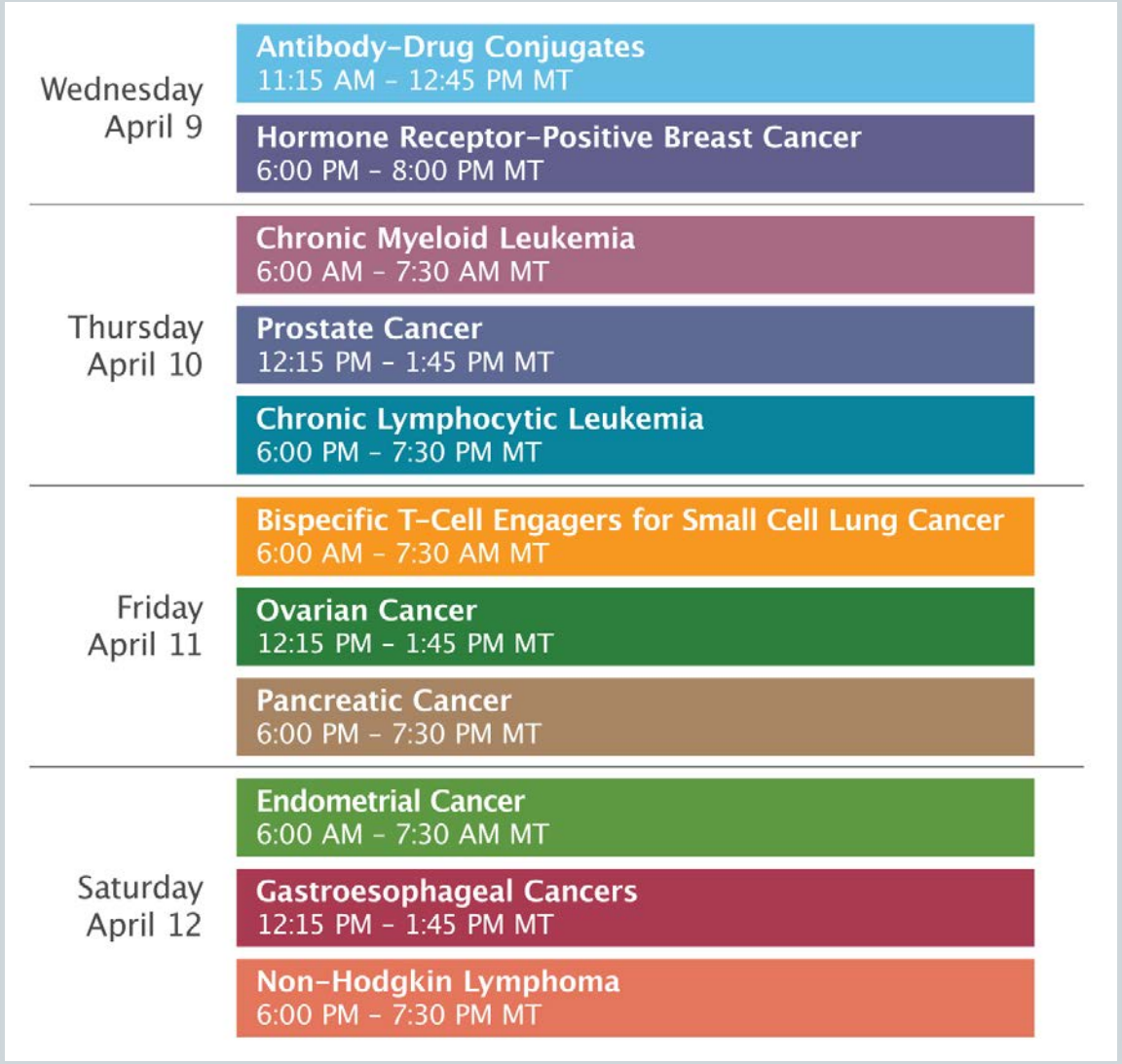


“Understanding the Current Paradigm and New Approaches”
Seventeenth Annual RTP-ONS NCPD Symposium Series



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Understanding the Current Paradigm and New Approaches
RTP Faculty at ONS 2025

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Agenda

Introduction: Clinical Presentation of Gastroesophageal Cancer

Module 1: Management of Localized or Locally Advanced Gastroesophageal Cancers; Current and Future Role of Immune Checkpoint Inhibitors

Module 2: Incorporation of Immunotherapeutic Strategies for HER2-Negative Metastatic Gastroesophageal Tumors

Module 3: Role of Therapy Targeting CLDN18.2 in Advanced Gastric/Gastroesophageal Junction Adenocarcinoma

Module 4: Considerations in the Care of Patients with HER2-Positive Gastroesophageal Cancers

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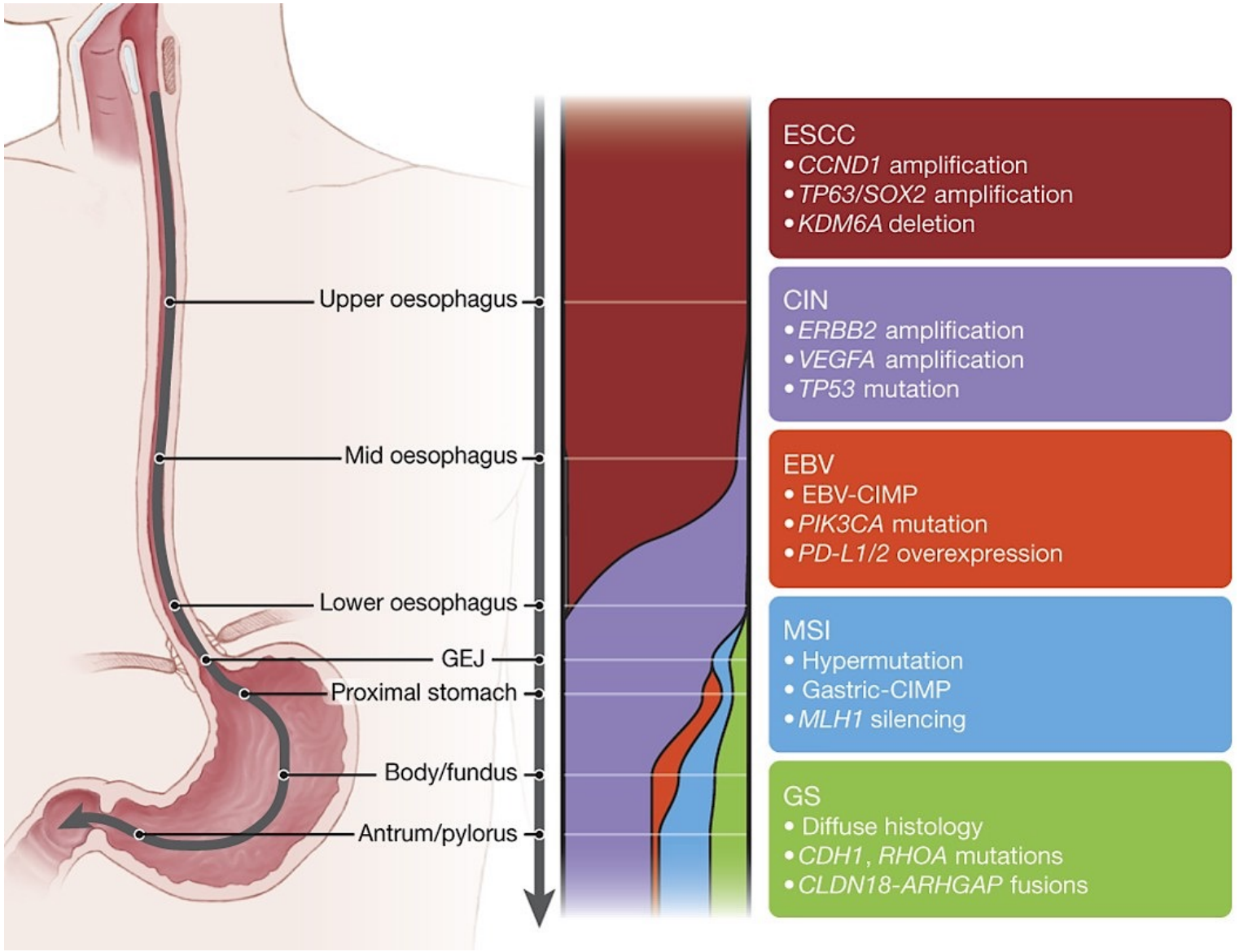
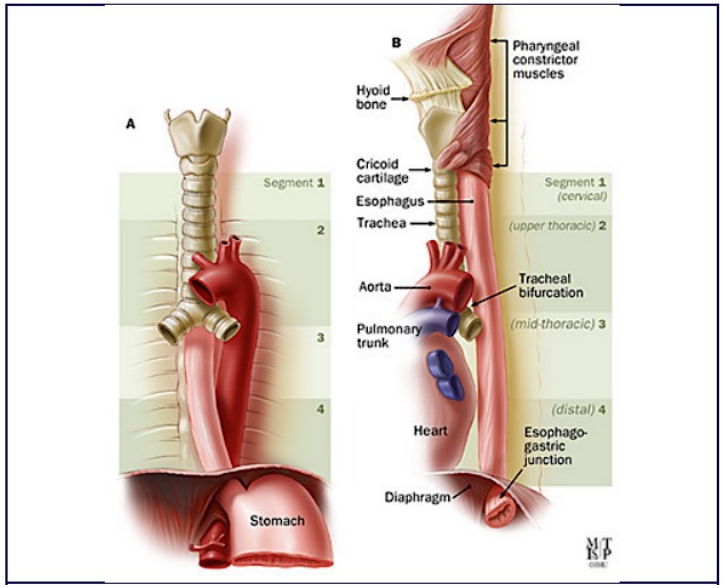
Esophago-gastric cancer subclasses



The Cancer Genome Atlas Research Network. *Nature.* 2017;541:169-175

Adenocarcinoma v. Squamous Cell Cancer?



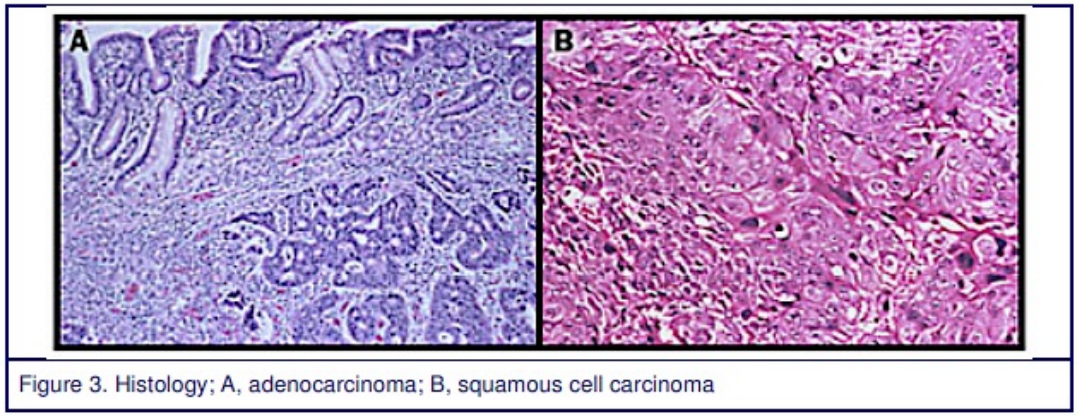
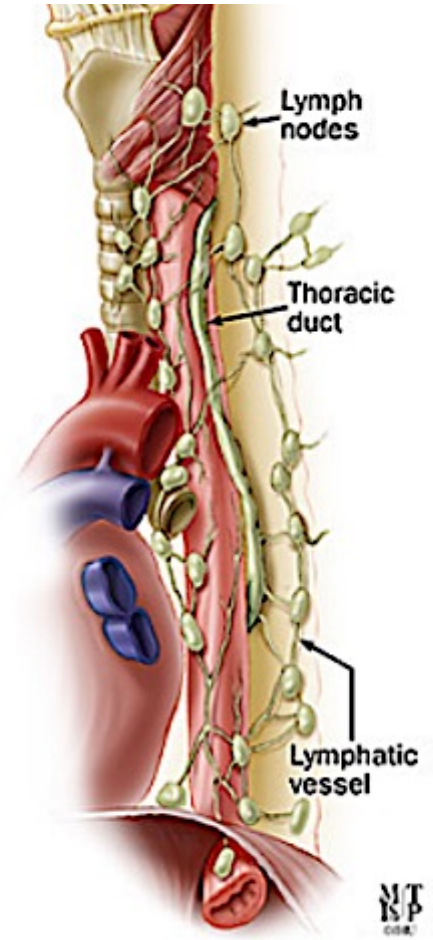


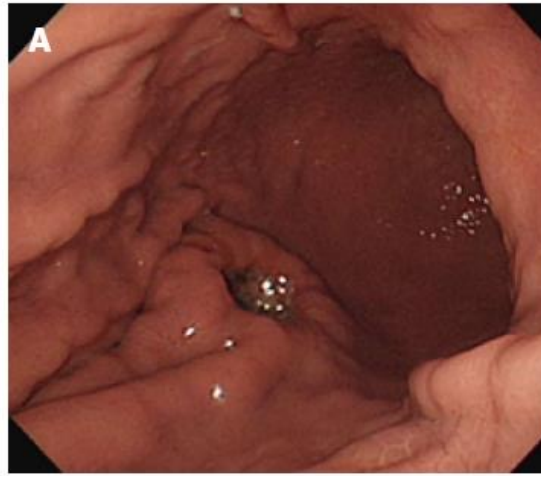
Figure 3. Histology; A, adenocarcinoma; B, squamous cell carcinoma



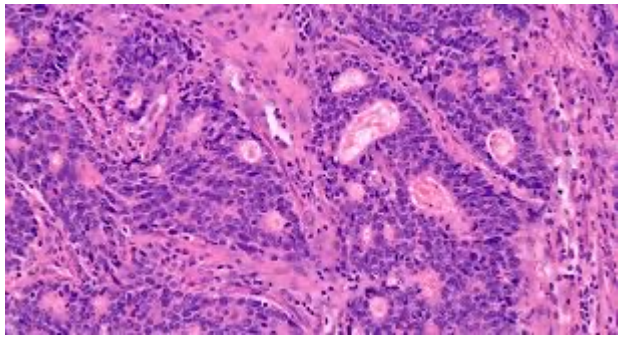
Esophageal Cancer can present as Squamous Cell Carcinoma (SCC) or Adenocarcinoma

Case Presentation: Dr Shah

- 67-year-old male presents with anemia and pain after eating. He continues to work as a lawyer but is finding he needs to rest in the afternoons.
- Work up reveals pallor on exam, Hb 7.4, LFT WNL

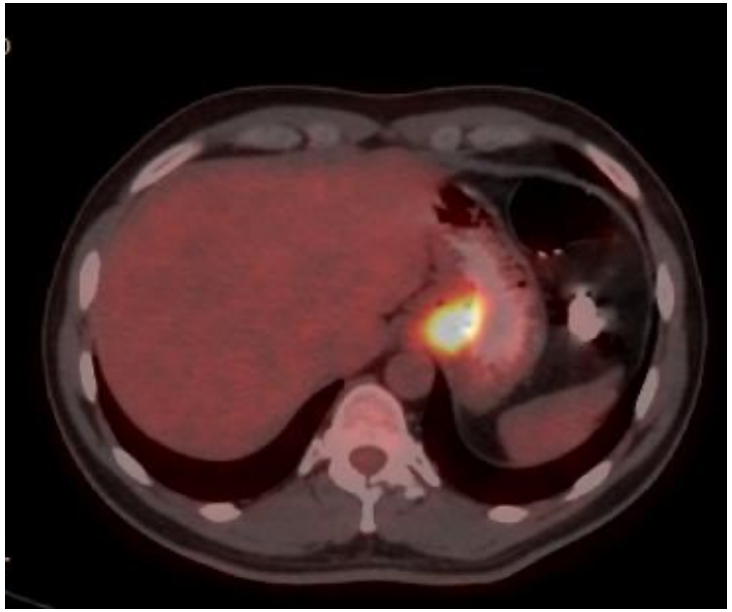


- EGD reveals a mass in the gastric cardia
- Pathology is consistent with adenocarcinoma, intestinal type, moderately differentiated

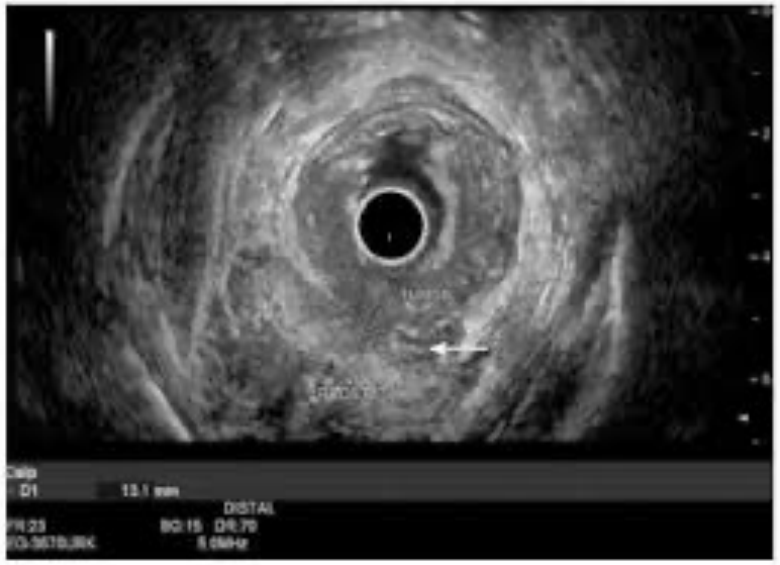


Case Presentation: Dr Shah

- CT/PET is without evidence of metastatic disease



- EUS reveals tumor invading into submucosa, 2 lymph nodes, FNA of the node is positive for adeno ca - cT3N1M0



- Laparascopic evaluation is without evidence of disease, cytology washings are negative
- Molecular testing reveals the following profile:
  - PD-L1 tumor area positivity (TAP) >10%, HER2-negative, microsatellite stable (MSS)

Case Presentation: Dr Shah

- 67-year-old male presents with anemia and pain after eating. He continues to work as a lawyer but is finding he needs to rest in the afternoons.
- Work up reveals pallor on exam, Hb 7.4, LFT WNL
- EGD reveals a mass in the gastric cardia, adenocarcinoma, moderately differentiated
- Pt received perioperative FLOT chemotherapy
- Resection – rare cancer cells, consistent with major pathologic response. TRG 1. ypT3N0. (0/18 lymph nodes).

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Clinical Scenario

A patient with newly diagnosed esophageal cancer that is amenable to surgical resection

Locally Advanced Esophageal Cancer

Manish A. Shah, MD, FASCO

Weill Cornell Medicine/NewYork-Presbyterian

mas9313@med.cornell.edu

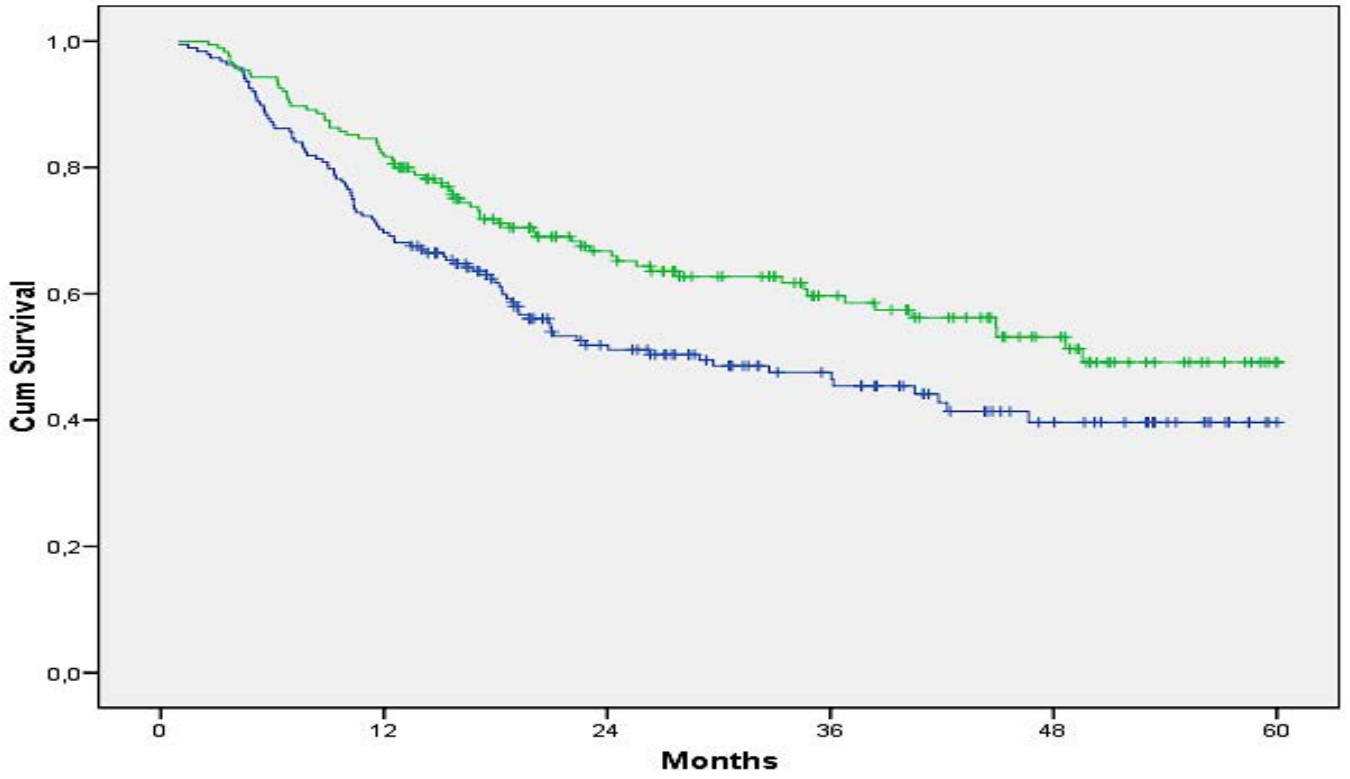
Epidemiology

- Esophageal cancer is the 7th leading cause of cancer deaths
- 1% of all malignancy and 6% of all GI malignancy
- Most common in China, Iran, South Africa, India and former Soviet Union
- Incidence rises with age, reaching a peak in the 6th to 7th decade of life
- Male:female 3.5:1
- In the US African-American males:white males 5:1

CROSS Trial: Major Results

- 93% received all courses chemotherapy
  - 95% went to operating room
  - ~23% had >grade 3 toxicity from pre-op therapy
- R0 resection rate: 92% versus 67% $p<0.001$
  - ~26% had pathologic complete remissions
- Post-operative morbidity and mortality almost identical

CROSS Trial: Overall Survival



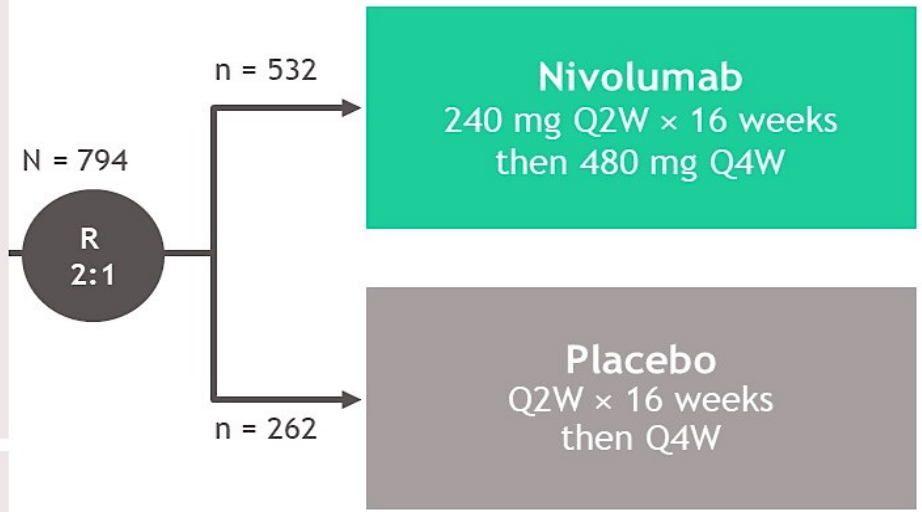
- 1-year survival 82 versus 70%
- 2-year survival 67 versus 52%
- Median survival 49 versus 26 months

CheckMate 577 study design

- CheckMate 577 is a global, phase 3, randomized, double-blind, placebo-controlled trial[a]

Key eligibility criteria
- Stage II/III EC/GEJC
- Adenocarcinoma or squamous cell carcinoma
- Neoadjuvant CRT + surgical resection (R0,[b] performed within 4-16 weeks prior to randomization)
- Residual pathologic disease
  - ≥ ypT1 or ≥ ypN1
- ECOG PS 0-1

Stratification factors
- Histology (squamous versus adenocarcinoma)
- Pathologic lymph node status (≥ ypN1 versus ypN0)
- Tumor-cell PD-L1 expression (≥ 1% versus < 1%[c])



Total treatment duration of up to 1 year[d]

Primary endpoint:
- DFS[e]

Secondary endpoints:
- OS[f]
- OS rate at 1, 2, and 3 years

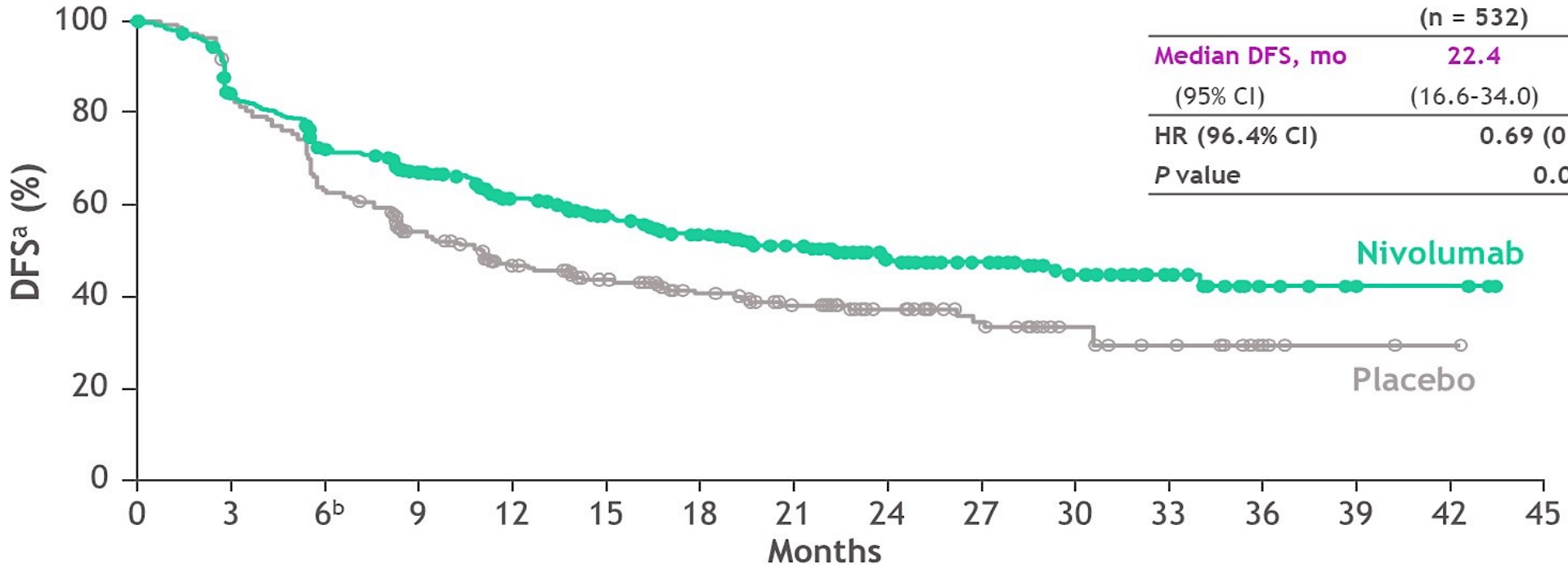
Exploratory endpoints included:
- Safety
- DMFS[g]
- PFS2[h]
- QoL

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

[a]ClinicalTrials.gov. NCT02743494; [b]Patients must have been surgically rendered free of disease with negative margins on resected specimens defined as no vital tumor present within 1 mm of the proximal, distal, or circumferential resection margins; [c]< 1% includes indeterminate/nonevaluable tumor cell PD-L1 expression; [d]Until disease recurrence, unacceptable toxicity, or withdrawal of consent; [e]Assessed by investigator, the study required at least 440 DFS events to achieve 91% power to detect an average HR of 0.72 at a 2-sided α of 0.05, accounting for a prespecified interim analysis; [f]The study will continue as planned to allow for future analysis of OS; [g]DMFS is defined as the time between randomization and the first distant recurrence or death, whichever occurs first; [h]PFS2 is defined as the time from randomization to progression after the first subsequent systemic therapy, initiation of second subsequent systemic therapy, or death, whichever is earlier; [i]Time from randomization date to clinical data cutoff (May 12, 2020).
Kelly RJ, et al. *N Engl J Med* 2021;384:1191-1203.

Disease-free survival (DFS)

	Nivolumab (n = 532)	Placebo (n = 262)
Median DFS, mo	22.4	11.0
(95% CI)	(16.6-34.0)	(8.3-14.3)
HR (96.4% CI)	0.69 (0.56-0.86)	
P value	0.0003[c]	

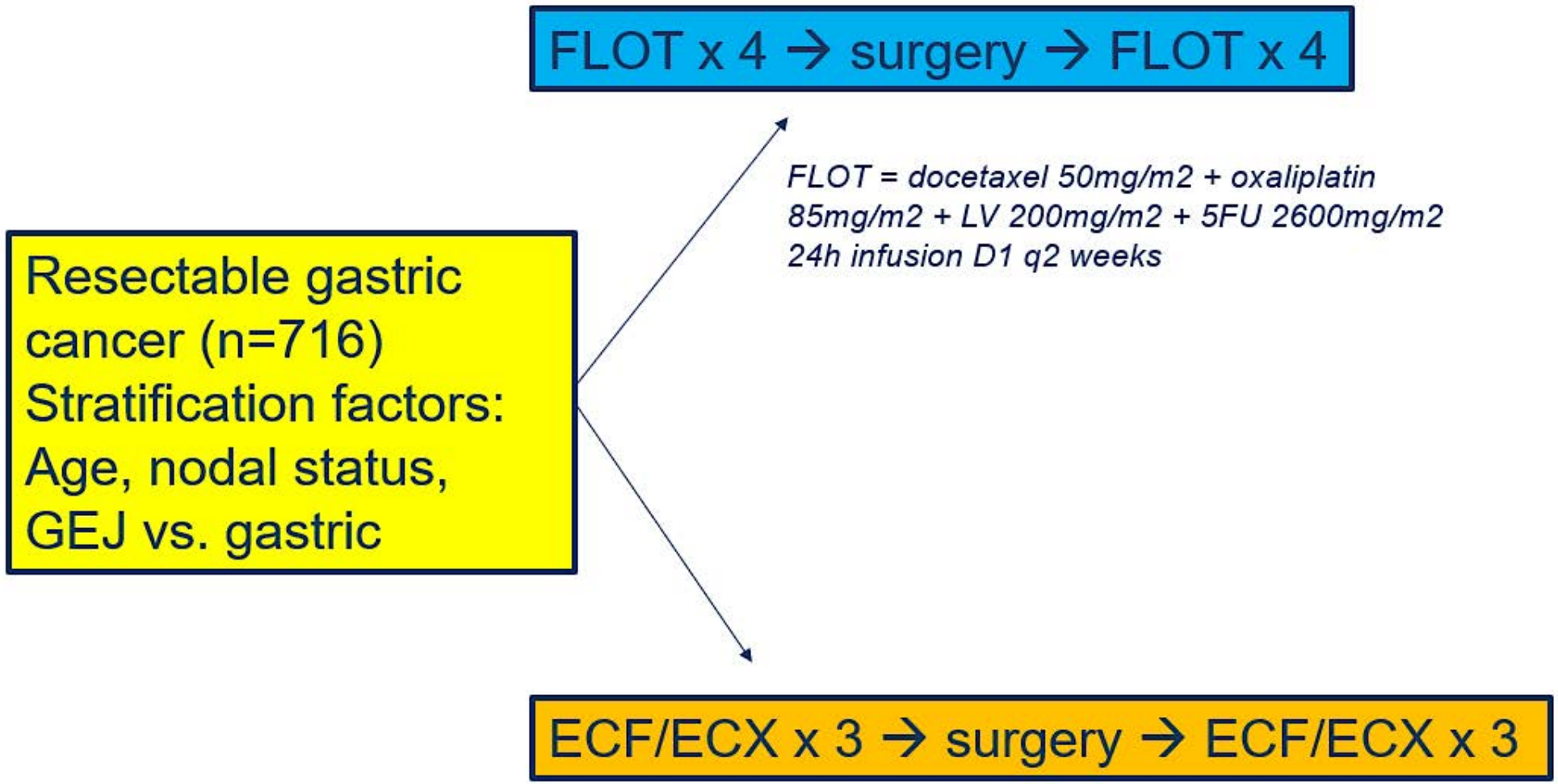


No. at risk																
Nivolumab	532	430	364	306	249	212	181	147	92	68	41	22	8	4	3	0
Placebo	262	214	163	126	96	80	65	53	38	28	17	12	5	2	1	0

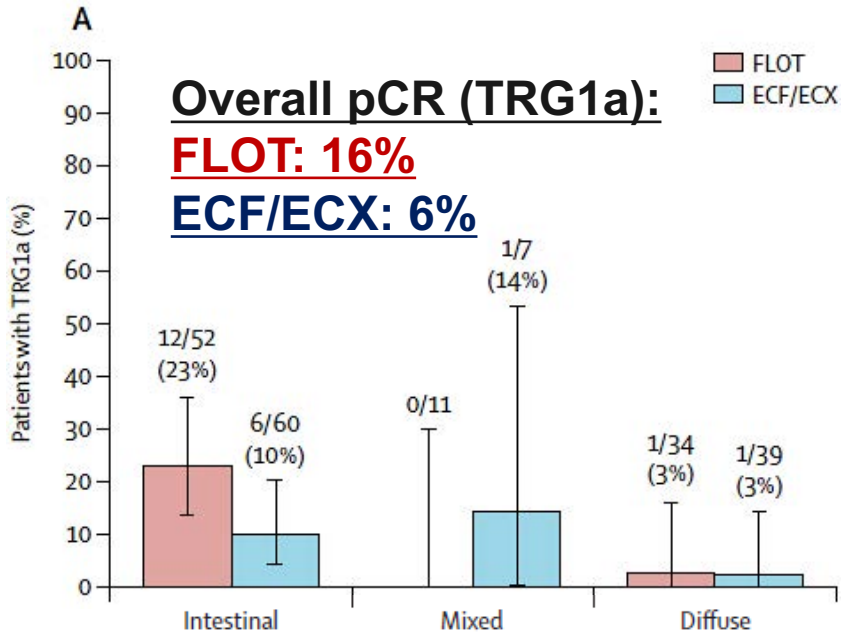
- Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo

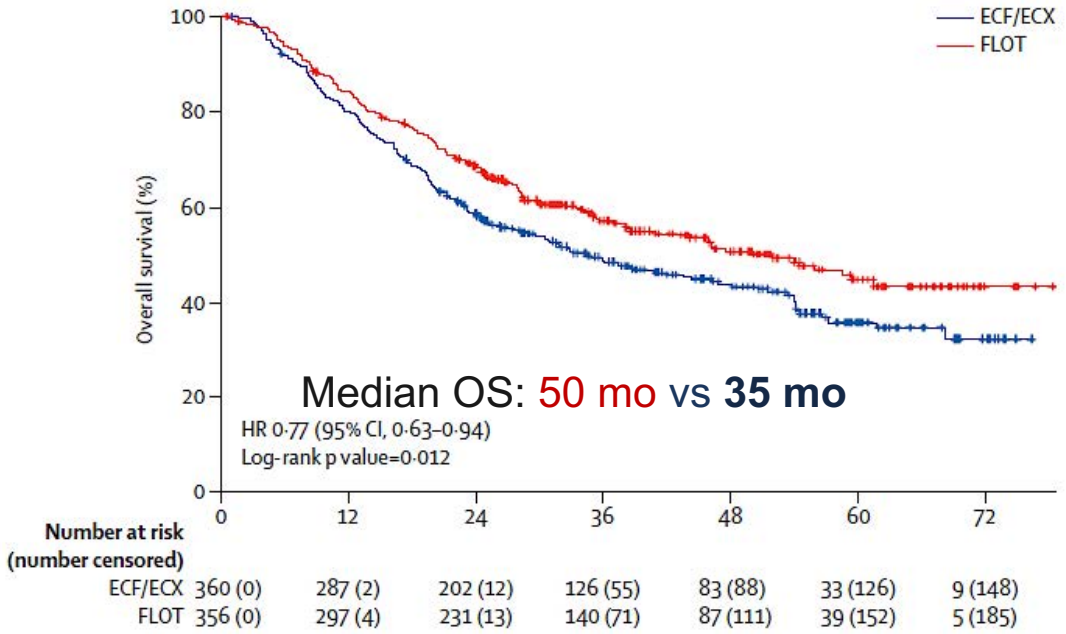
[a]Per investigator assessment; [b]6-month DFS rates were 72% (95% CI, 68-76) in the nivolumab arm and 63% (95% CI, 57-69) in the placebo arm; [c]The boundary for statistical significance at the prespecified interim analysis required the *P* value to be less than 0.036.
Kelly RJ, et al. *N Engl J Med* 2021;384:1191-1203.

FLOT4-AIO: Perioperative FLOT vs ECF/ECX



FLOT4-AIO: Perioperative FLOT improves OS vs ECF/ECX





Adverse events

Grade 3-4 >5%	FLOT (n=354)
Neutropenia	51%
Infections	18%
Diarrhea	10%
Nausea	7%
Fatigue	7%
Anemia	3%
Vomiting	2%

OS rate*, %	ECF/ECX	FLOT
2-year	59	68
3-year	48	57
5-year	36	**45**

Median DFS: 30 mo vs **18 mo**

Al-Batran SE et al. *Lancet.* 2019;393(10184):1948-1957;
Al-Batran SE et al. *Lancet Oncol.* 2016;17(12):1697-1708;
Tables extrapolated from Dr. Burguete-Torres' presentation, ASCO GI 2024

Durvalumab-based regimen demonstrated statistically significant and clinically meaningful improvement in event-free survival in resectable early-stage gastric and gastroesophageal junction cancers

Press Release: March 7, 2025

Positive high-level results from the MATTERHORN Phase III trial showed perioperative treatment with durvalumab in combination with standard-of-care FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) chemotherapy demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of event-free survival (EFS).

Patients were treated with neoadjuvant durvalumab in combination with chemotherapy before surgery, followed by adjuvant durvalumab in combination with chemotherapy, then durvalumab monotherapy. The trial evaluated this regimen versus perioperative chemotherapy alone for patients with resectable, early-stage and locally advanced (Stages II, III, IVA) gastric and gastroesophageal junction (GEJ) cancers.

For the secondary endpoint of overall survival (OS), a strong trend was observed in favour of the durvalumab-based regimen at this interim analysis. The trial will continue to follow OS, which will be formally assessed at the final analysis.

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https://www.astrazeneca.com/media-centre/press-releases/2025/imfinzi-improved-efs-in-early-stage-gastric-cancer.html

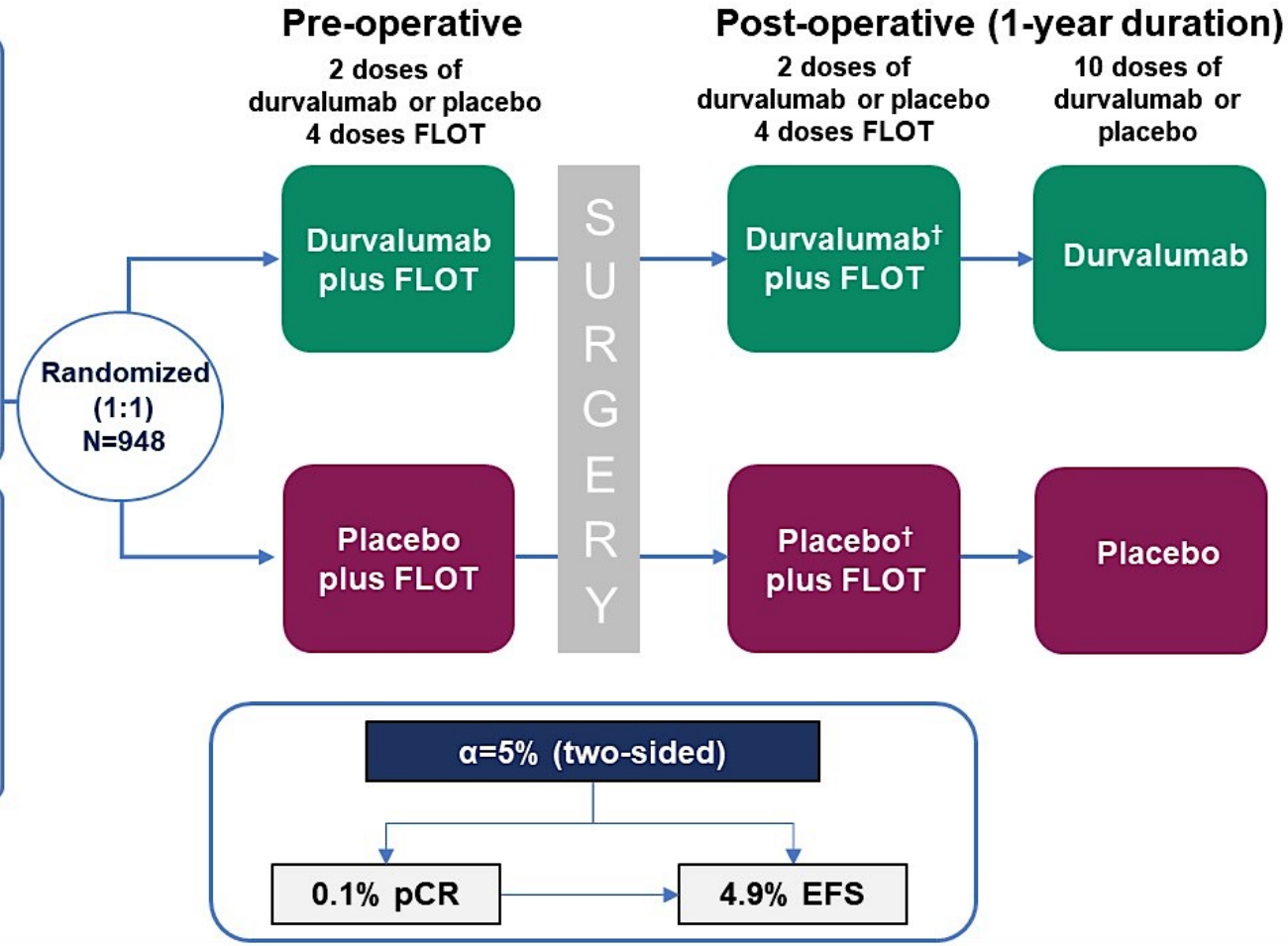
MATTERHORN is a global, Phase 3, randomized, double-blind, placebo-controlled study

Study population

- Gastric and GEJ adenocarcinoma
- Stage II, III and IVA (>T2 N0-3 M0 or T0-4 N1-3 M0)
- No evidence of metastasis
- No prior therapy
- ECOG PS 0 or 1
- Global enrolment from Asia, Europe, North America, and South America

Stratification factors

- Geographic region: Asia versus non-Asia
- Clinical lymph node status: positive versus negative
- PD-L1 status: TAP <1% versus TAP ≥1%*



Primary objective:

- EFS

Key secondary objectives:

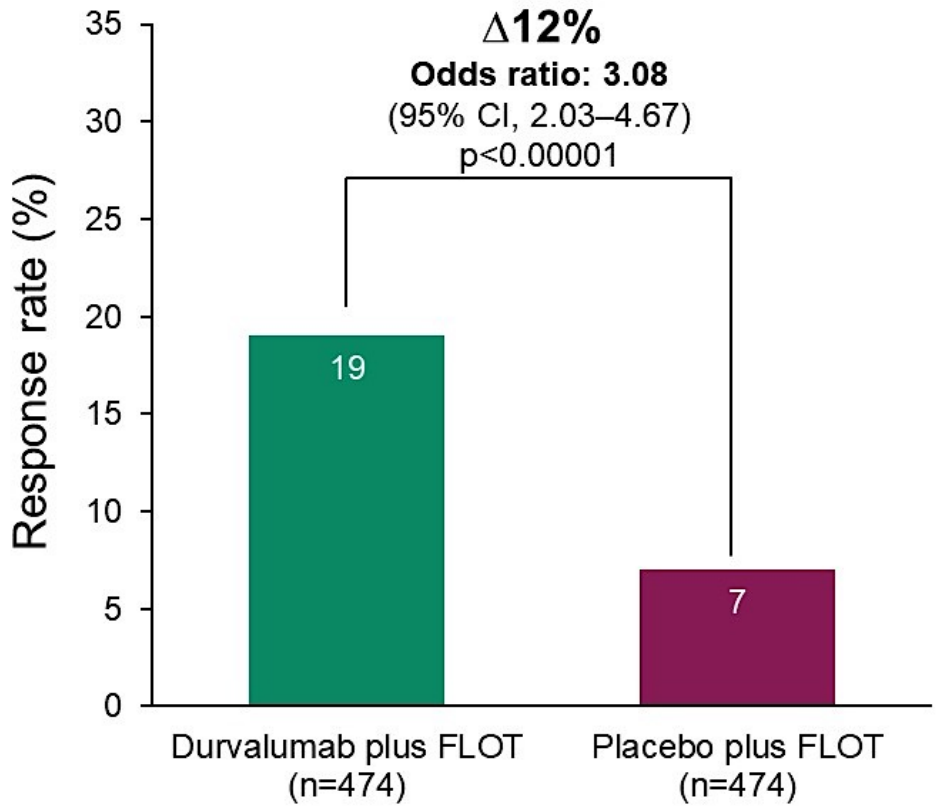
- Central review of pathological complete response by modified Ryan criteria
- OS

pCR = no residual viable tumor cells found at primary tumor and resected lymph nodes at the time of resection

Janjigian YY, et al., Annal Oncol 2023, 34:S1315-S1316

Pathological complete response

Durvalumab plus FLOT showed statistically significant improvement in pathological complete response



Janjigian YY, et al., Annal Oncol 2023, 34:S1315-S1316

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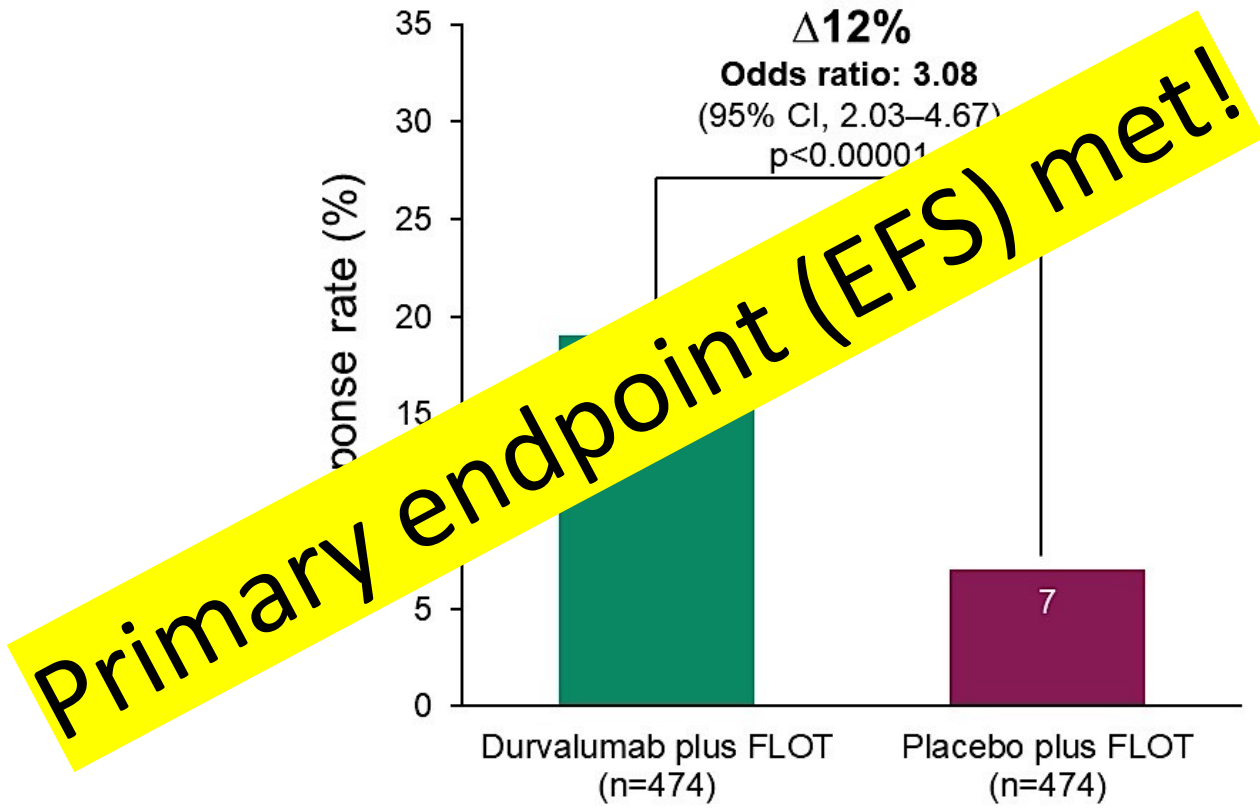

Primary endpoint (EFS) met!

Janjigian YY, et al., Annal Oncol 2023, 34:S1315-S1316

Summary

- FLOT remains standard of care in perioperative MSS esophagogastric cancer
  - ESOPEC
  - Checkmate 577
- MSI H/dMMR disease IO
- The addition of IO to perioperative chemotherapy has improved pCR but not impacted OS
  - Matterhorn is positive for EFS
- The role of radiation limited to R1 disease

Roundtable Discussion

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MANAGEMENT OF LOCALIZED/LOCALLY ADVANCED GASTROESOPHAGEAL CANCERS

NURSING CONSIDERATIONS

MICHAL F SEGAL, BSN, RN, OCN

Known Risk Factors

Esophageal Squamous Cancer	Esophageal/GEJ Adenocarcinoma
• Tobacco • Alcohol • HPV • Ingestion of corrosives (lye), hot beverages, or nitrosamines • Prior head/neck/chest radiation • Plummer-Vinson syndrome • Tylosis palmaris • Achalasia	• Tobacco • Obesity • GERD • Barrett's esophagus

Esoph/GEJ/Gastric

- Age
- Sex
- Race

Source: Enzinger PC, Mayer RJ. Esophageal cancer. *N Engl J Med*. 2003;349(23):2241-2252.

Known Risk Factors

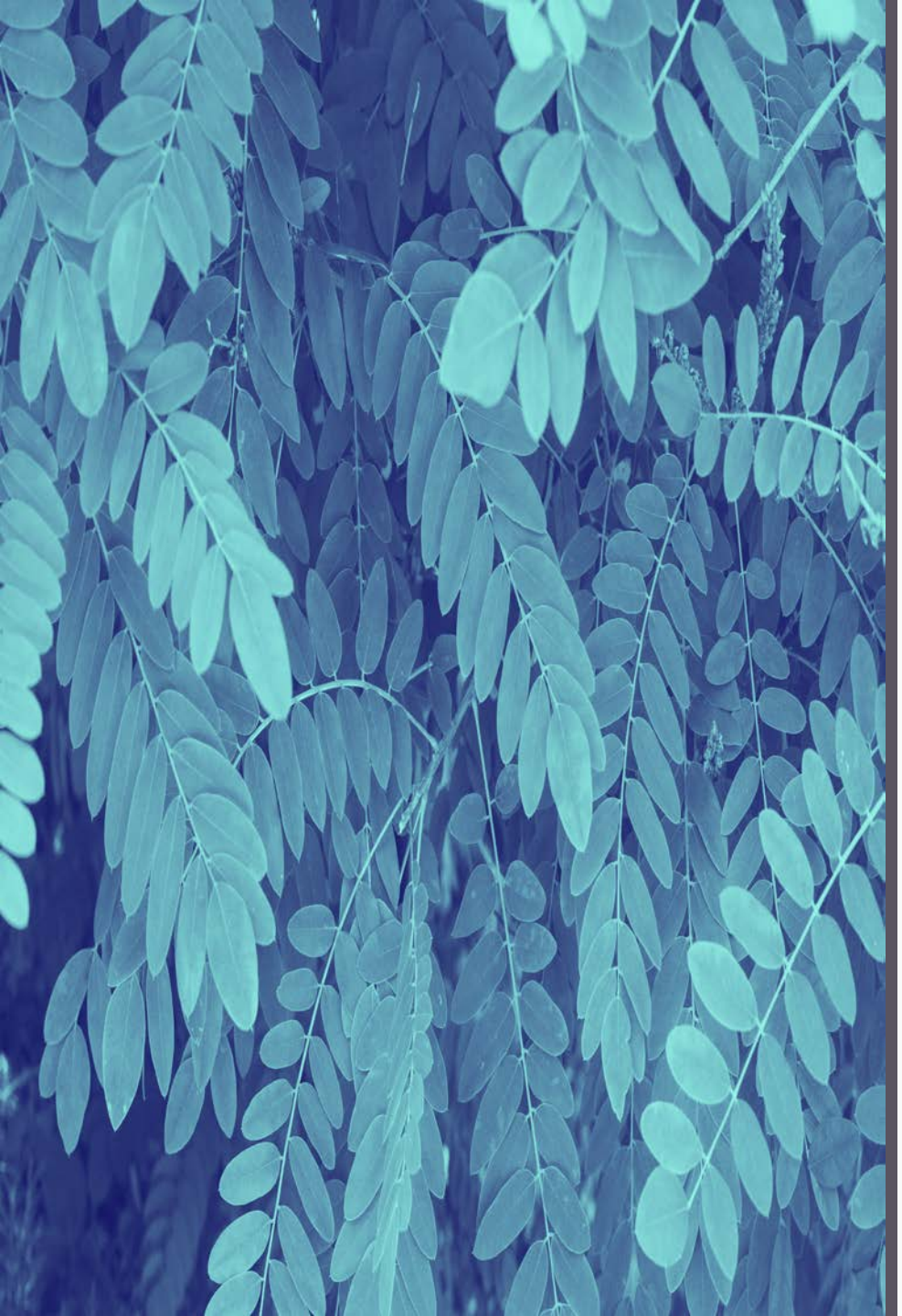
Gastric Adenocarcinoma

- Fried foods, salted meats, low fiber, nitrates, pickled vegetables
- *H. pylori*
- Tobacco
- Atrophic gastritis
- Intestinal metaplasia
- High Body Mass Index
- Coal mining, lumber, rubber
- Low vitamin C
- Previous gastric ca surgery

Genetic Risk Factors

- Lynch syndrome
- Menetrier disease
- FAP (Familial adenomatous polyposis)
- Hereditary diffuse gastric Ca: (CDH1) E-cadherin mutations

Salted foods: (Int J Cancer. 2004;108(4):606-12)
Vit C use: Cancer Epidemiol Biomarkers Prev. 2002;11(1):35-41. :
Occupation: Scand J Work Environ Health. 1991 Aug;17(4):240-7.
Smoking: Smoking: Int J Cancer. 2003 Nov 20;107(4):629-34.
J Gastroenterol Hepatol. 2003 Nov;18(11):1257-1263
Pernicious anemia Gut. 2003 Jul;52(7):938-41.



Common Presenting Symptoms

- Dysphagia/Odynophagia
- Weight loss
- Abdominal pain
- Supraclavicular adenopathy
- Other
  - Cough
  - Hoarseness

Typical Side Effects: Chemotherapy, Immunotherapy and/or Radiation

Chemotherapy and Immunotherapy	Radiation
• Fatigue, weakness • Nausea, vomiting, loss of appetite • Weight loss • Constipation, diarrhea • Mouth sores • Hand-foot syndrome • Photosensitivity • Hair loss (paclitaxel) • Effects from supportive medications • IO: “Itis’s” (colitis, gastritis, etc.)	• Fatigue • Nausea • Skin changes • Dysphagia/odynophagia

Side Effect Prevention and Management

All Modalities

- Pre-medication
- Take home PRN – Proactive with Rx and OTC
- Weight management – stress caloric intake, protein
- Small, frequent meals, liberalize food choices and textures
- IV hydration as needed
- Rest/time off from work
- Manage activities/physical expectations
- Reporting symptoms
- Mouth care prevention
- Skin care prevention
- Hygiene/avoid sick people
- Movement/light exercise
- Support system

Monitoring Tools

- Food tracking
- Scale for weight
- Blood test
  - Albumin
  - Metabolic panel

Post Op Management

- Manage expectations
- PEG/PEJ tube (short-term)
- Hydration – with calories (limit during meals)
- Supplements (Shakes, meal-replacement)
- Slow, small, frequent meals
- Soft, avoid spicy, avoid fatty, avoid carbonated
- Mindset adjustment, food schedule
- Pain management
- Dumping syndrome – sugary, fatty
- Reflux management

Supportive Care

- **Nutritionist**
- **Registered Dietician**
  - **Meal Plans**
  - **Recipe ideas**
  - **Tips/tricks**
- Support Groups
- Resources for Life After Cancer (RLAC) Program (MSK)

Integrative Medicine

- Acupuncture
- Acupressure
- Yoga
- Tai chi
- Massage therapy
- Dance and movement therapy
- Meditation and other mind-body relaxation therapies
- Music therapy
- Exercise

60-year-old male with a history of GERD presents with 2 months of progressive dysphagia accompanied with 10-pound weight loss. Endoscopy last week revealed partially obstructing mass at the gastroesophageal junction extending into the cardia. Pathology confirmed poorly differentiated adenocarcinoma.

What are next steps?

Case Study

Preparation and Education

- Complete work up (imaging, EUS)
- Mediport, EKG, basis labs
- Discuss adjuvant and neoadjuvant therapy
- Investigate available support system
- Introduce nutrition and social work
- What to expect, manage anxiety
- Help guide disability leave, or accommodations
- Cancer center navigation

Case Study

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Clinical Presentation of Gastroesophageal Cancer

Module 1: Management of Localized or Locally Advanced Gastroesophageal Cancers; Current and Future Role of Immune Checkpoint Inhibitors

Module 2: Incorporation of Immunotherapeutic Strategies for HER2-Negative Metastatic Gastroesophageal Tumors

Module 3: Role of Therapy Targeting CLDN18.2 in Advanced Gastric/Gastroesophageal Junction Adenocarcinoma

Module 4: Considerations in the Care of Patients with HER2-Positive Gastroesophageal Cancers

Clinical Scenario

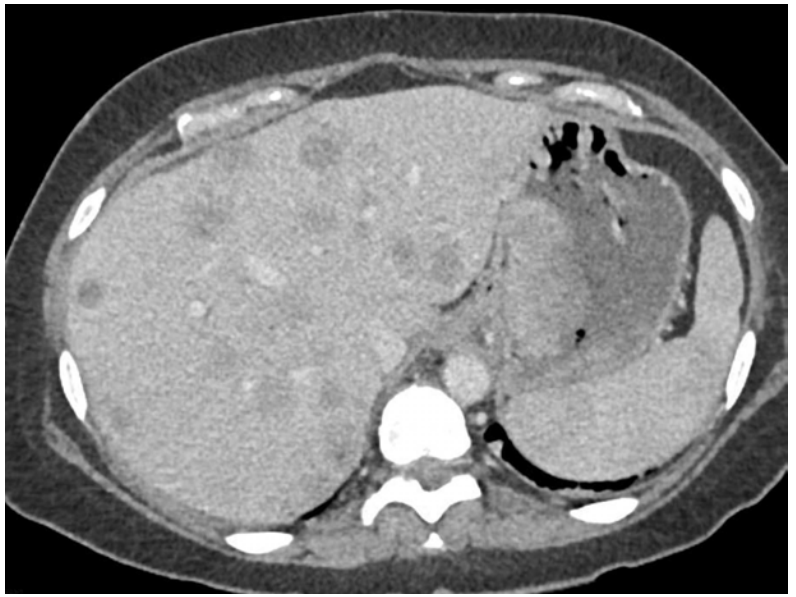
A patient with newly diagnosed metastatic gastric cancer who is about to begin first-line treatment with chemotherapy in combination with an anti-PD-1/PD-L1 antibody

Incorporation of Immunotherapeutic Strategies for Patients with HER2-Negative Metastatic Gastroesophageal Tumors

Sunnie Kim, MD

Patient Case

- 67-year-old woman presents with abdominal pain, anemia and weight loss
- EGD shows fungating mass in gastric body
- Pathology reveals moderately differentiated adenocarcinoma with signet ring features
- CT CAP shows liver lesions, lung nodules, and peritoneal thickening consistent with metastatic disease



Next steps?

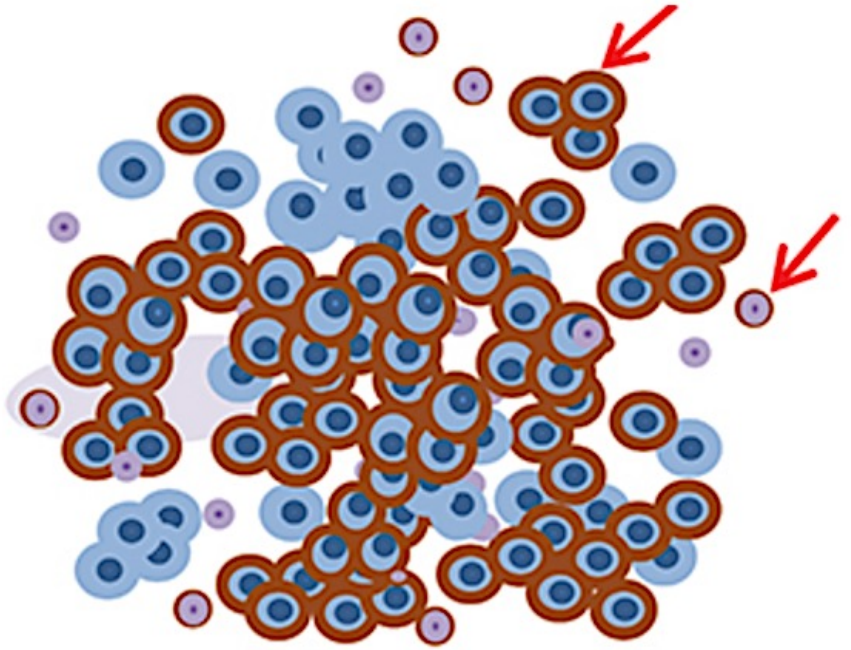
Growing List of Biomarker Testing in GE Cancers

★PD-L1

★MMR/MSI

- HER2
- Claudin 18.2
- Rarer alterations (NTRK, EBV, EGFR, BRAF V600E, RET)

PD-L1 Combined Positive Score (CPS)



CPS

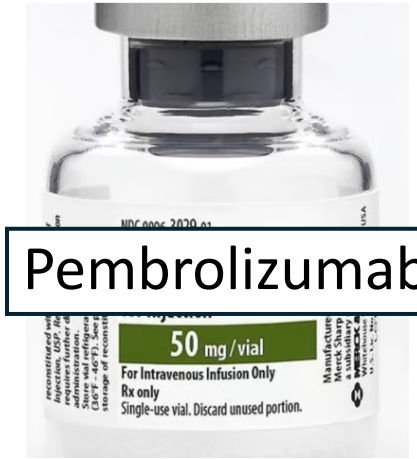
$$\text{CPS} = \frac{\text{PD- L1 staining} \begin{cases} \text{Tumor cells} \\ \text{Lymphocytes} \\ \text{Macrophages} \end{cases}}{\text{viable tumor cells}} 100$$

Epistola R, Cancer Management Research 2023

Patient Case

- 67-year-old woman with Stage 4 gastric cancer
- Biomarker testing as follows:
  - pMMR
  - PD-L1 CPS: 10
  - HER2 negative
  - Claudin 18.2 negative
- Started FOLFOX+nivolumab

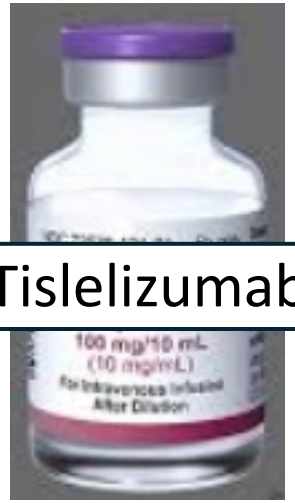
Phase 3 trials of 1L chemo+PD-1 inhibitor versus chemo in advanced gastric/GEJ cancer



Pembrolizumab

KEYNOTE-859

OS: 12.9 months *v* 11.5 months



Tislelizumab

RATIONALE-305

OS: 15.0 months *v* 12.9 months

Nivolumab

CheckMate 649

OS: 13.7 months *v* 11.6 months

Ra, SY G ASCO 2024
Qiu, MZ BMJ 2024
Janjigian YY GI ASCO 2025

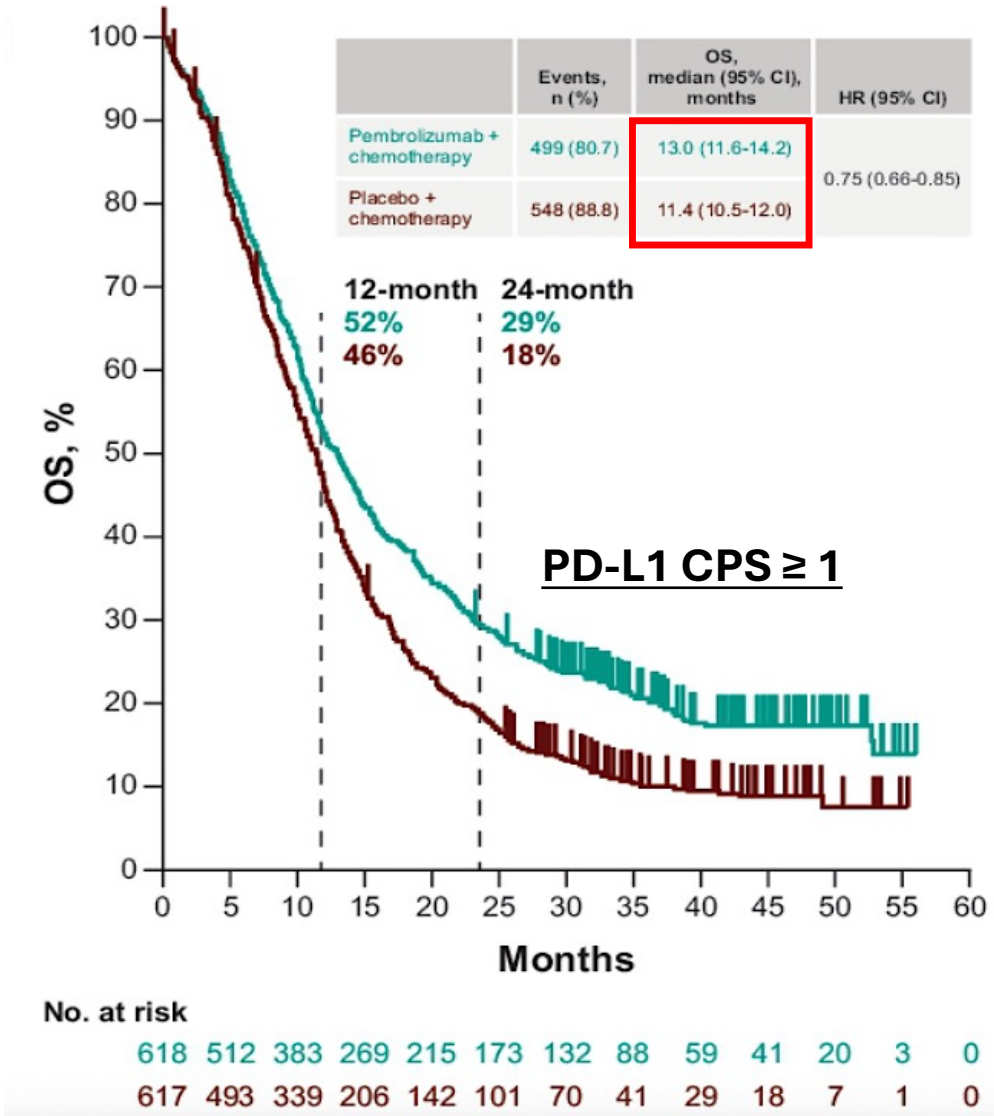
How does a PD-L1 score affect clinical outcomes?

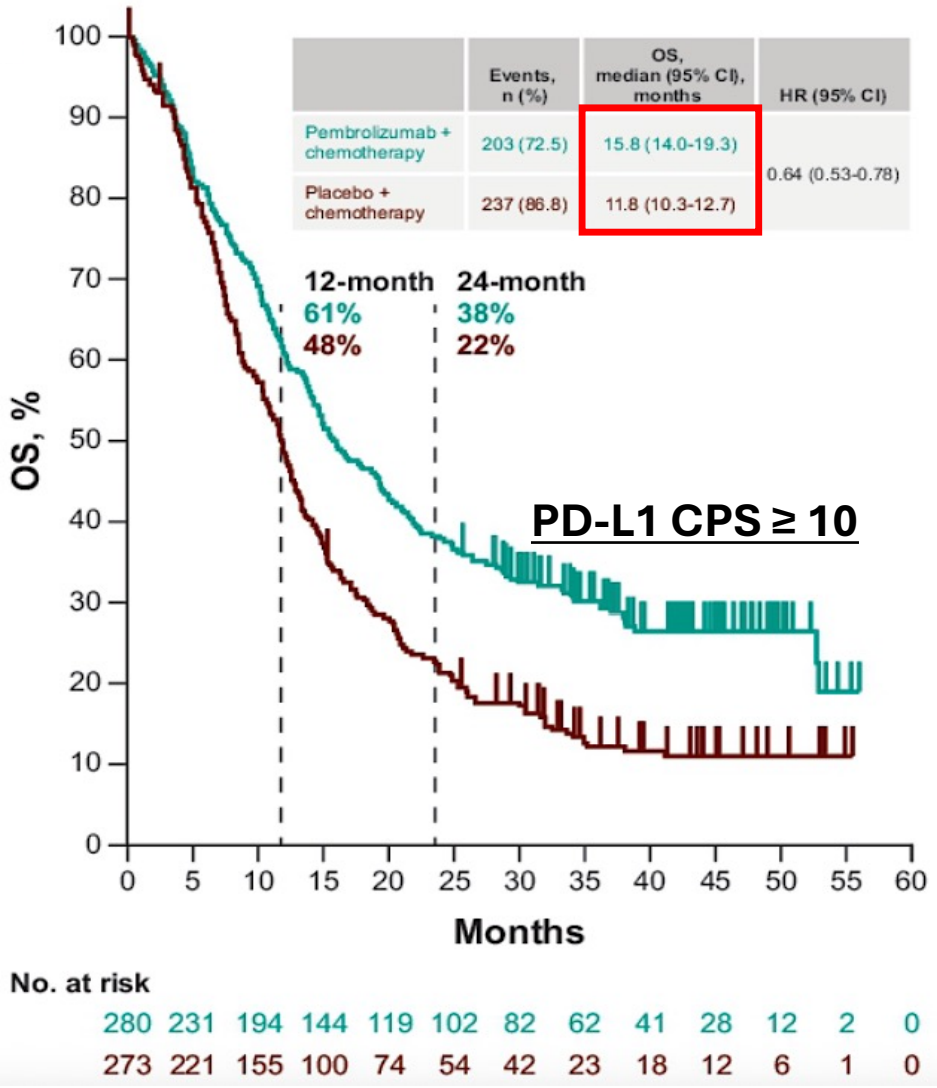
CheckMate 649

Efficacy	PD-L1 CPS ≥ 5		PD-L1 CPS ≥ 1		All randomized	
	NIVO + chemo (n = 473)	Chemo (n = 482)	NIVO + chemo (n = 641)	Chemo (n = 656)	NIVO + chemo (n = 789)	Chemo (n = 792)
mOS (95% CI), mo	14.4 (13.1–16.2)	11.1 (10.1–12.1)	13.8 (12.4–14.8)	11.4 (10.7–12.3)	13.7 (12.4–14.5)	11.6 (10.9–12.5)
HR (95% CI)	0.71 (0.61–0.81)		0.76 (0.67–0.85)		0.79 (0.71–0.88)	
60-mo OS rate (95% CI), %	16 (12–19)	6 (4–9)	13 (11–16)	5 (4–7)	12 (10–14)	6 (4–8)

Janjigian YY, GI ASCO 2025

KEYNOTE-859: Overall Survival Benefit with PD-1 inhibitor improves with higher PD-L1 CPS





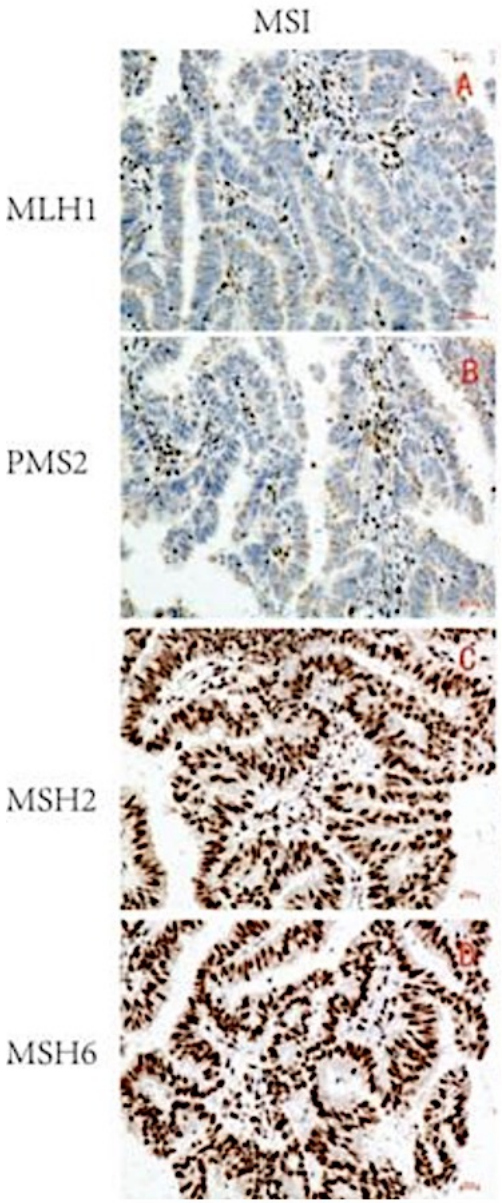
Rha SY, et al. ASCO 2024; MH Ryu et al. ESMO Asia Congress 2024

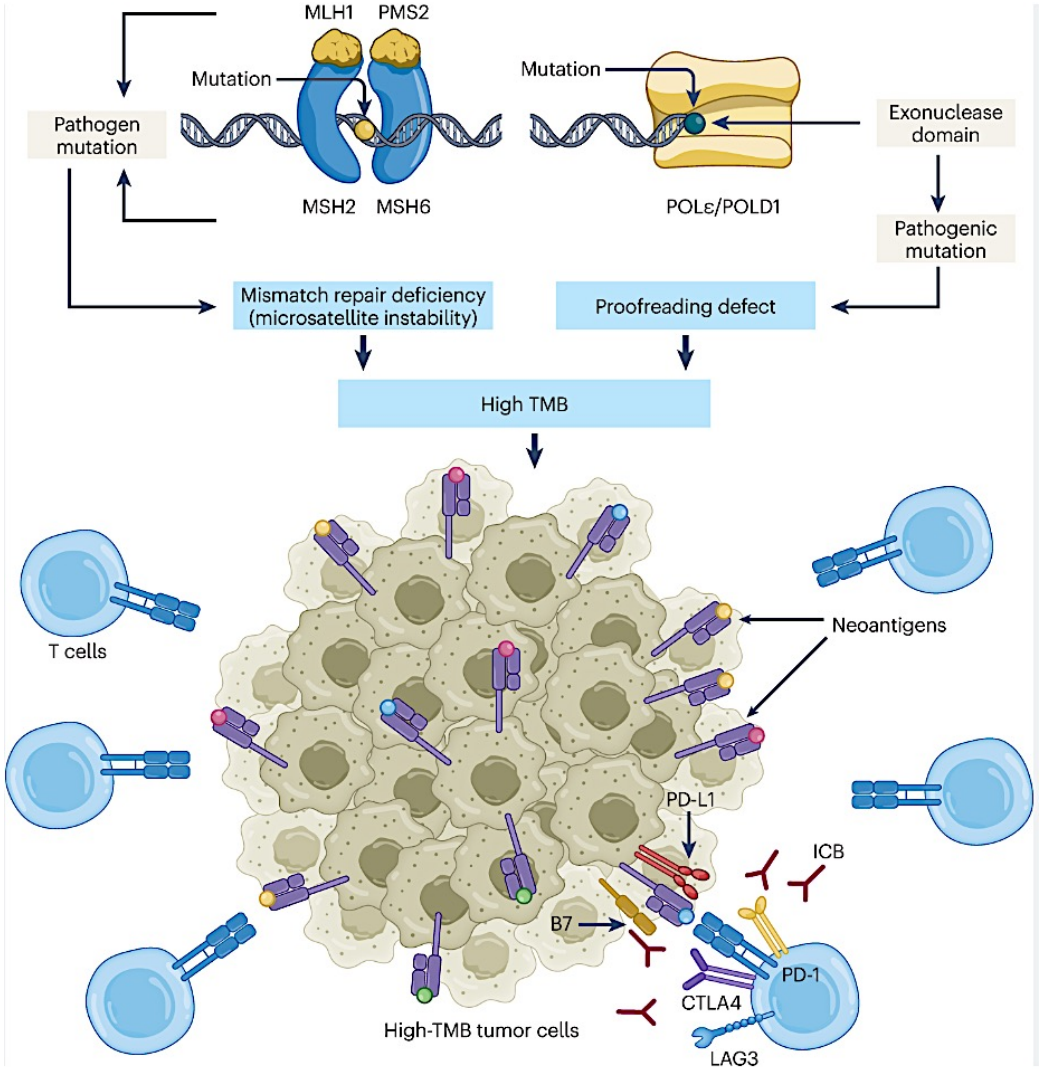
Patient Case

- 67-year-old woman with Stage 4 gastric cancer, PD-L1 CPS: 10
- Started FOLFOX+nivolumab
- At next restaging scan, liver lesions decreased in size with decreased gastric wall thickening
- Disease control for 2 years before disease progression

Management of dMMR/MSI-H Gastric/GEJ Cancers

Role of MMR Deficiency and MSI in Gastric Cancer

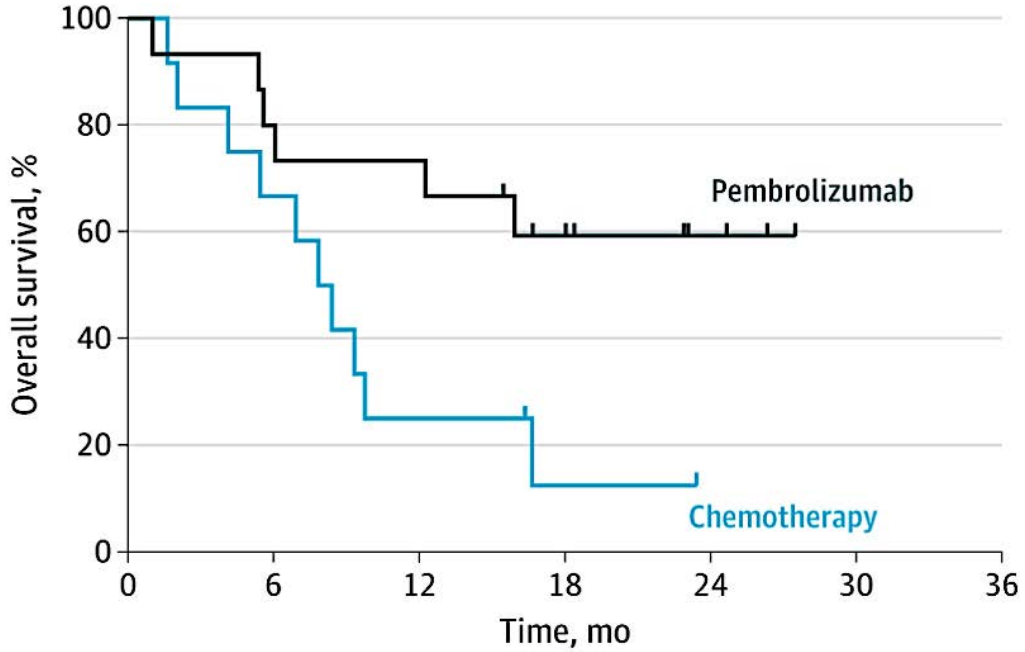




Alouani, E Nature Cancer 2022, Wang, Y J Cancer 2021

Survival benefit with PD-1 inhibitor based therapy for for MSI-H gastric cancer

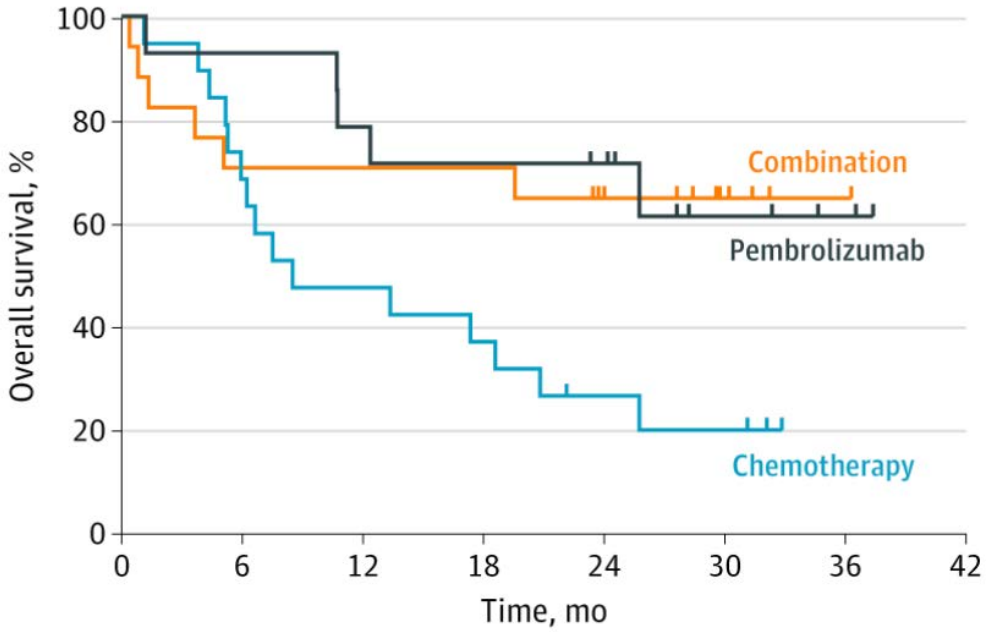
B Patients with MSI-H tumors in KEYNOTE-061



No. at risk

Pembrolizumab	15	12	11	6	3	0	0
Chemotherapy	12	8	3	1	0	0	0

D Patients with MSI-H tumors in KEYNOTE-062



No. at risk

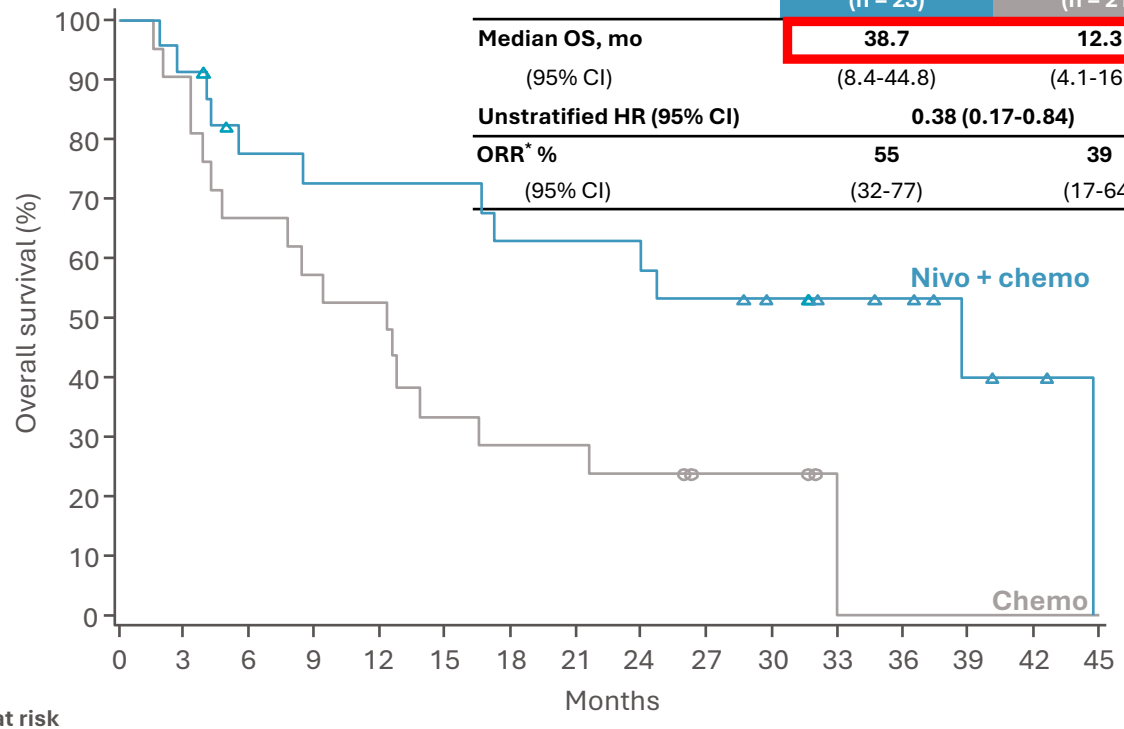
Pembrolizumab	14	13	11	10	9	4	2	0
Combination	17	12	12	12	9	4	1	0
Chemotherapy	19	13	9	7	4	3	0	0

Chao J, JAMA Oncology 2021

Significant survival benefit with PD-1 inhibitor for MSI-H gastric cancer CheckMate 649

MSI-H

	Nivo + chemo (n = 23)	Chemo (n = 21)
Median OS, mo	**38.7**	**12.3**
(95% CI)	(8.4-44.8)	(4.1-16.5)
Unstratified HR (95% CI)	**0.38 (0.17-0.84)**	
ORR* %	**55**	**39**
(95% CI)	(32-77)	(17-64)

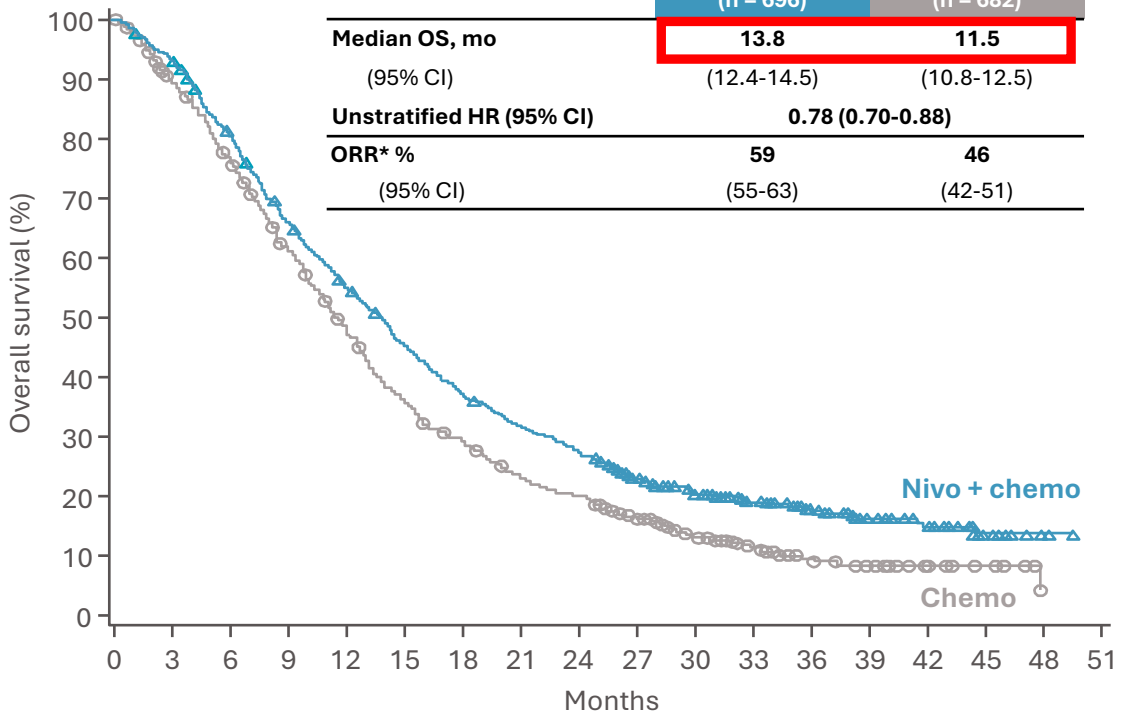


No. at risk

Nivo + chemo	23	21	16	15	15	15	13	13	12	11	9	7	6	3	2	0
Chemo	21	19	14	12	11	7	6	6	5	3	3	0	0	0	0	0

MSS

	Nivo + chemo (n = 696)	Chemo (n = 682)
Median OS, mo	**13.8**	**11.5**
(95% CI)	(12.4-14.5)	(10.8-12.5)
Unstratified HR (95% CI)	**0.78 (0.70-0.88)**	
ORR* %	**59**	**46**
(95% CI)	(55-63)	(42-51)



Nivo + chemo	696	646	554	452	375	308	251	214	184	137	103	75	50	29	22	9	2	0
Chemo	682	601	506	405	312	235	188	146	126	94	67	44	28	20	12	6	0	0

Shitara K et al. *Nature*. 2022

Recommendations for PD-1 inhibitor-based therapy for gastric cancer

- For pMMR gastric/GEJ cancer, can add PD-1 inhibitor to doublet chemo for PD-L1 CPS+ tumors
  - Increasing survival benefit with higher PD-L1 CPS
- For dMMR/MSI-H gastric cancer, a PD-1 inhibitor-based treatment (monotherapy or with chemo) has significant clinical benefit

Roundtable Discussion

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TO PRACTICE

Nursing Considerations for Patients Receiving an Anti-PD-1/PD-L1 Antibody

Brooke Parker MSN, FNP

Gastrointestinal Oncology

University of Colorado Cancer Center

Setting the Stage

The Players

- T Cells – Immune cells that help detect and destroy abnormal cells
- PD- 1 – Proteins on T cells that downregulate the immune response
- PDL-1 – Protein on cancer cells and will bind with our T cells PD-1 to “turn off” our immune system. This is called the **PD-1 Pathway**
- Immunotherapy – Anti PDL-1/PD-1 antibodies bind proteins to keep your immune system (T cells) working!

Why is it being given?

- Per NCCN guidelines, patients with GEJ cancer who have either **PDL-1 CPS > 1** or are **MSI-H/dMMR** should receive immunotherapy

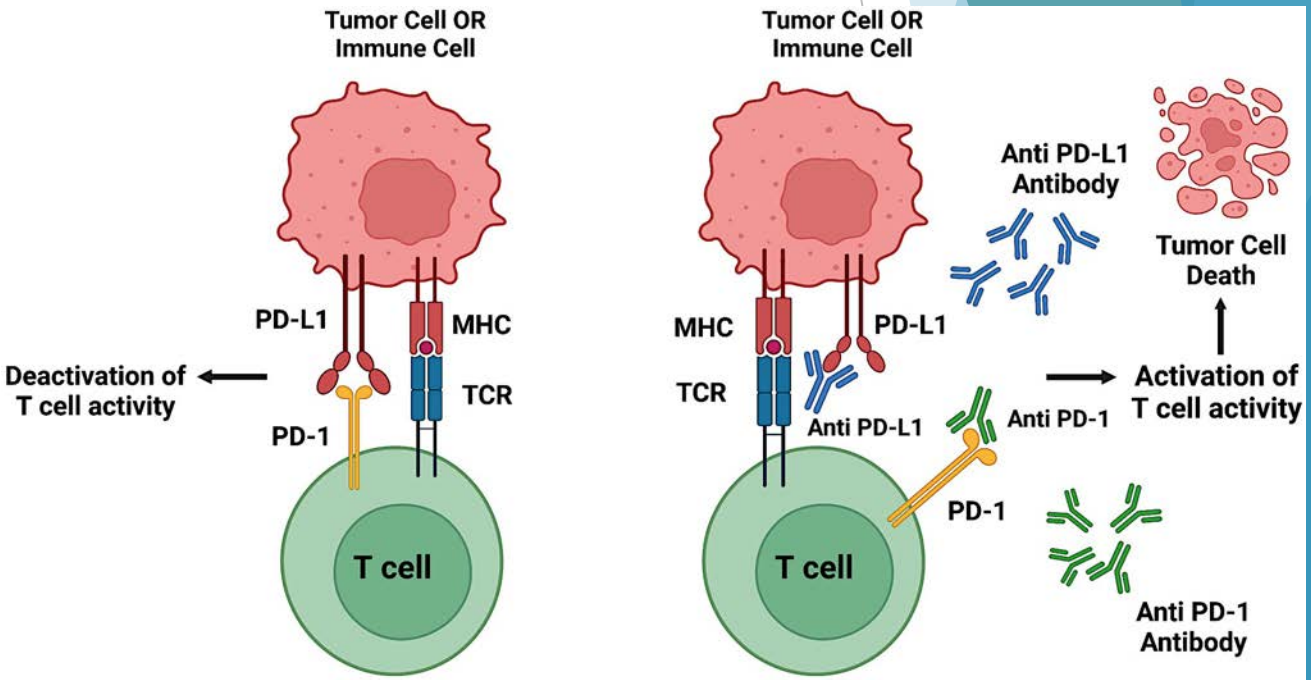


Image Parvel, 2023
NCCN GEJ Guidelines, 2025
Jeddo, 2024

Adverse Events of Anti PD-1/PDL-1 Antibodies

- Onset - typically 3-6 months
- Prevalence – Any AEs 66%, severe/life threatening ~6%

Fatigue (16-25%)

Cutaneous (20%)

Pneumonitis (<10%)

Hormone related (1-6%)

Hepatitis (5% or less)

Muscles and Joints (5% or less)

Colitis (1-3%)

Heart, Kidney, CNS (<1%)

Infusion Reaction (<1%)

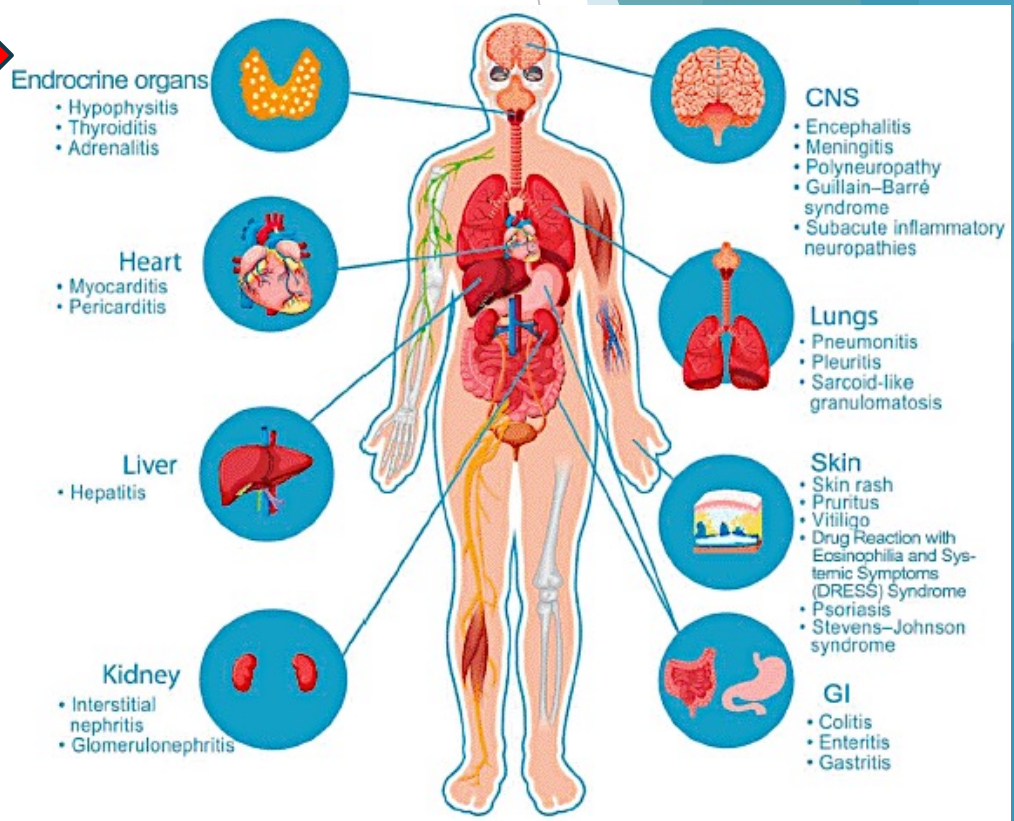
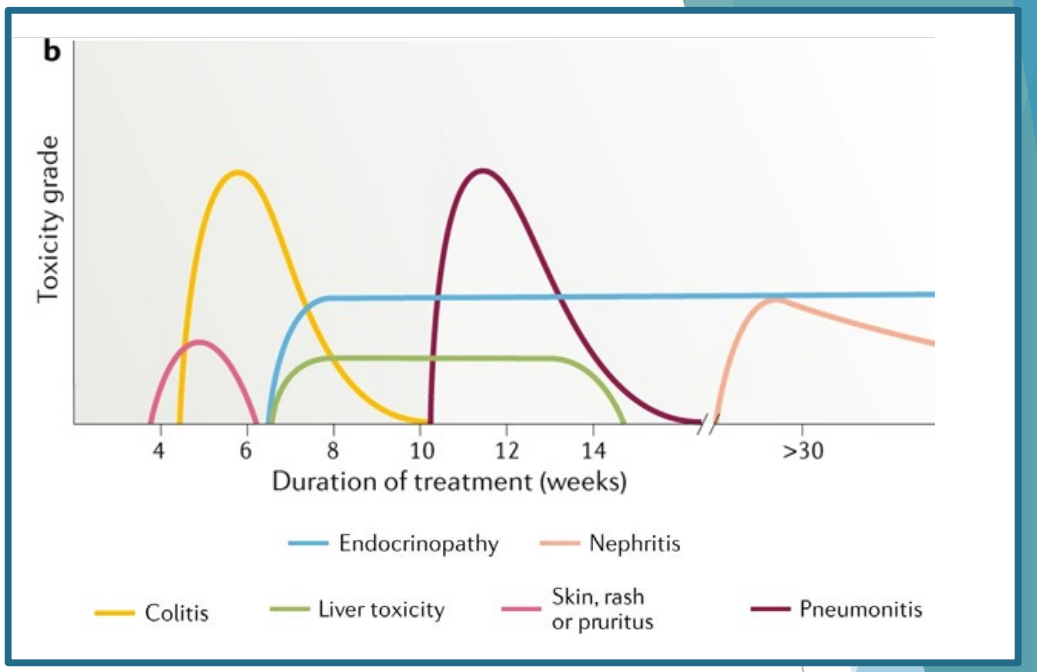


Image Abdihamid, 2021
Naidoo, 2015
NCCN Management of Immunotherapy-Related Toxicities 2024

Starting Treatment

- Does the patient have a hx of autoimmune disease?
- Communication from the patient is key!
  - Early recognition and early management
- Provide wallet card
- Educate on the importance of keeping a symptom diary



When to call

- Severe fatigue
- Rash
- Cough
- Shortness of breath
- Chest pain
- New/worsening diarrhea
- Headache
- Muscle weakness
- Vision changes
- Muscle & joint pain

Image Martins, 2019

While on Treatment

Monitor

- Physical exams
  - Skin checks
- Blood work
  - CBC, CMP every treatment
  - TSH and FT4 every 4-6 weeks
  - Consider serum cortisol every 4-6 weeks
- O2 sats
- Periodic Imaging
- Internal history

Treatment of ICI AEs

- Treatment depends on severity of AEs
- Grade 3-4
  - Discontinue treatment
  - First line - steroids
    - Prednisone 1-2 mg/kg/day for 4-8 weeks
    - Prolonged steroid taper
  - Second line – immunomodulators
- Endocrinopathies
  - Hormone replacements

NCCN Management of Immunotherapy-Related Toxicities 2024

Clinical Experience

- 54 yo male with stage IV gastric cancer. PMH of obesity and poorly controlled T2DM (no current insulin use)
- Began FOLFOX + Nivolumab on 11/3/24
- On 1/15/25 he complained of having 8 episodes of diarrhea per day with negative GI PCR
- Started on 100mg prednisone with PJP prophylaxis and a PPI
- 1 week later he returned to clinic with improvement in diarrhea but a blood glucose of 349mg/dL
- Started on insulin by PCP and successfully completed taper

NCCN Prevention and treatment of cancer-related infections. Guidelines, 2024

Roundtable Discussion

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Agenda

Introduction: Clinical Presentation of Gastroesophageal Cancer

Module 1: Management of Localized or Locally Advanced Gastroesophageal Cancers; Current and Future Role of Immune Checkpoint Inhibitors

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Module 4: Considerations in the Care of Patients with HER2-Positive Gastroesophageal Cancers

Clinical Scenario

A patient with newly diagnosed CLDN18.2-positive metastatic gastric cancer who is about to begin first-line treatment with chemotherapy in combination with zolbetuximab

Management of Metastatic Gastric/GEJ Adenocarcinoma: First Line Therapy

Manish A. Shah, MD, FASCO
Weill Cornell Medicine/NewYork-Presbyterian
mas9313@med.cornell.edu

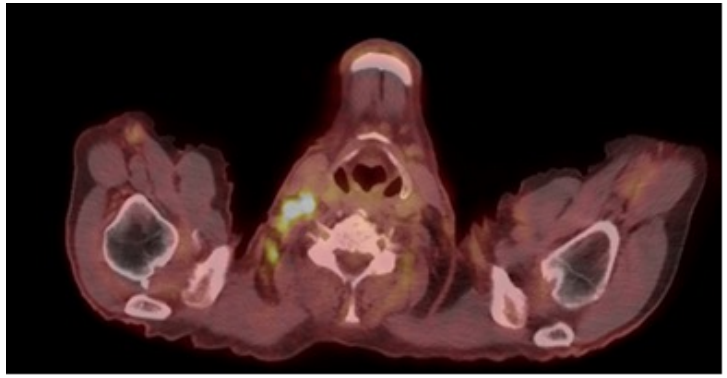
Case Study

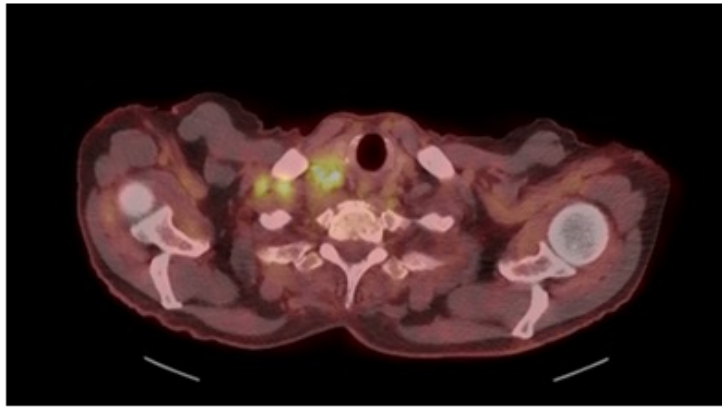
- Patient:
  - 85-year-old male
- PMH:
  - HFrecEF, HTN, HLD, IPMNs, ESRD secondary to bilateral native nephrectomies for urogenital cancer s/p DDKT 2021
- HPI:
  - 1 year history of worsening fatigue, abdominal pain, weight loss

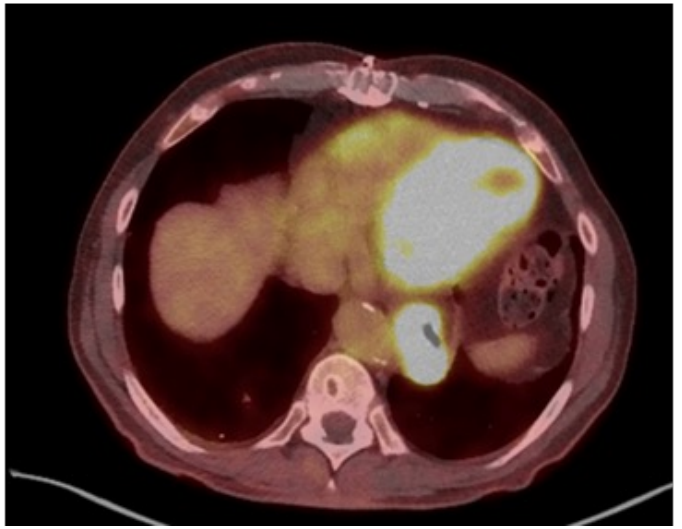
Case Study

Staging

- EGD: large, ulcerated, partially circumferential (involving one-half of the lumen circumference) mass with oozing bleeding was found in the distal esophagus.
- Biopsy: invasive poorly differentiated adenocarcinoma with signet ring cell features, MMR proficient, HER2 IHC equivocal, arising in a background of intestinal metaplasia and high-grade dysplasia
- PD-L1 CPS 20%
- CLDN18.2 IHC is 80%
- PET scan: right neck and supraclavicular adenopathy, SUV avid distal esophageal malignancy.



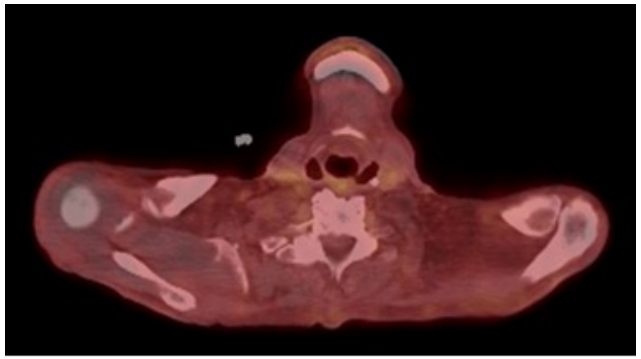


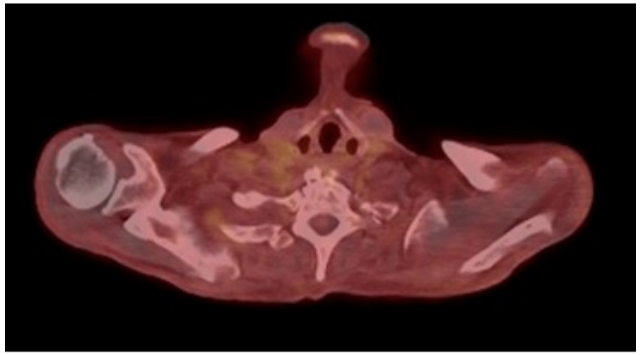


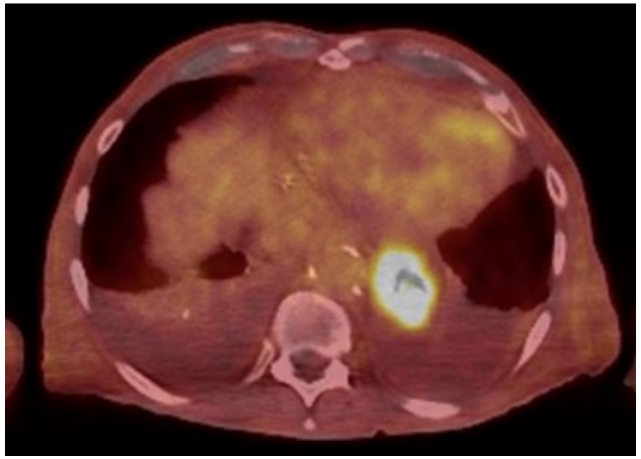
Case Study

- **Esophageal cancer treatment**
  - Option 1: Chemotherapy with immunotherapy
  - Option 2: Chemotherapy with Claudin18.2 inhibition
  - Option 3: Chemotherapy

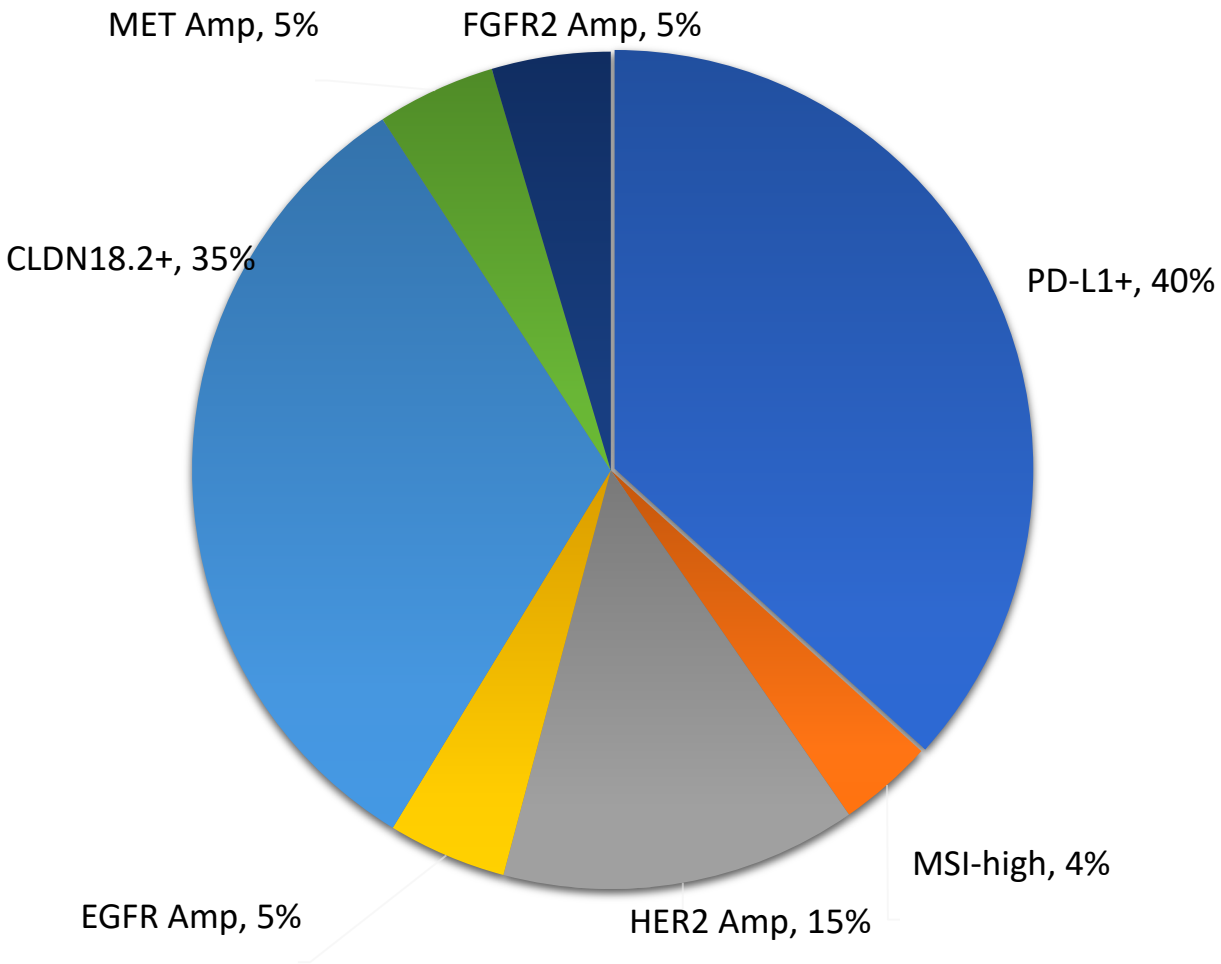
- Things to consider – patient has a transplanted kidney. There is ~30%-40% rate of graft failure.







Key Biomarkers in Gastroesophageal Cancer



Key markers in advanced disease

- **HER2** positive: 15%-20% of patients; improved survival with chemo + HER2-targeting trastuzumab
- **MSI** high: 3%-5% of patients, high response rates to immunotherapies ± chemo
- **PD-L1** positive: 30%-50% of patients; identifies those more likely to benefit from immunotherapy; likely gradation within PD-L1+ (CPS)
- **CLDN18.2** high: 30%-35% of patients; response predictor for CLDN18.2-targeting agent

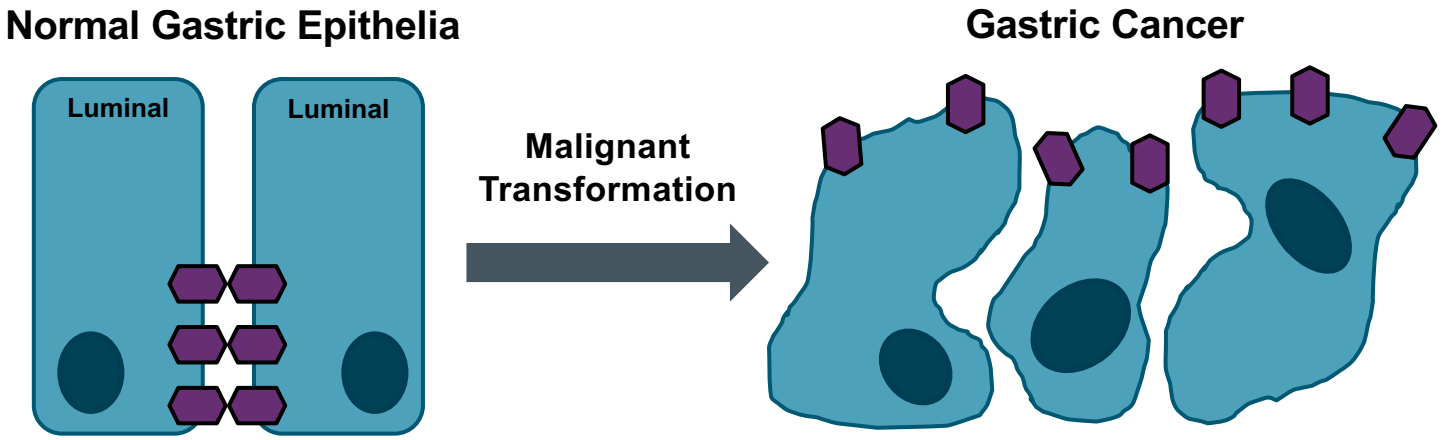
Investigational biomarkers

- **FGFR2** amp: 5%-10% of patients; multiple trials of inhibitors
- **FGFR2** high: May be up to 30% of HER2 negative
- **EGFR** amp: 5%-7%; may predict response to EGFR agents

- **Tumor agnostic**
- Mismatch repair deficiency (or MSI-H)
- Tumor mutation burden
- *NTRK* fusion

Kuwata T. *Pathol Int.* 2024;74(6):301-316.

Claudin18.2: Leveraging Biology

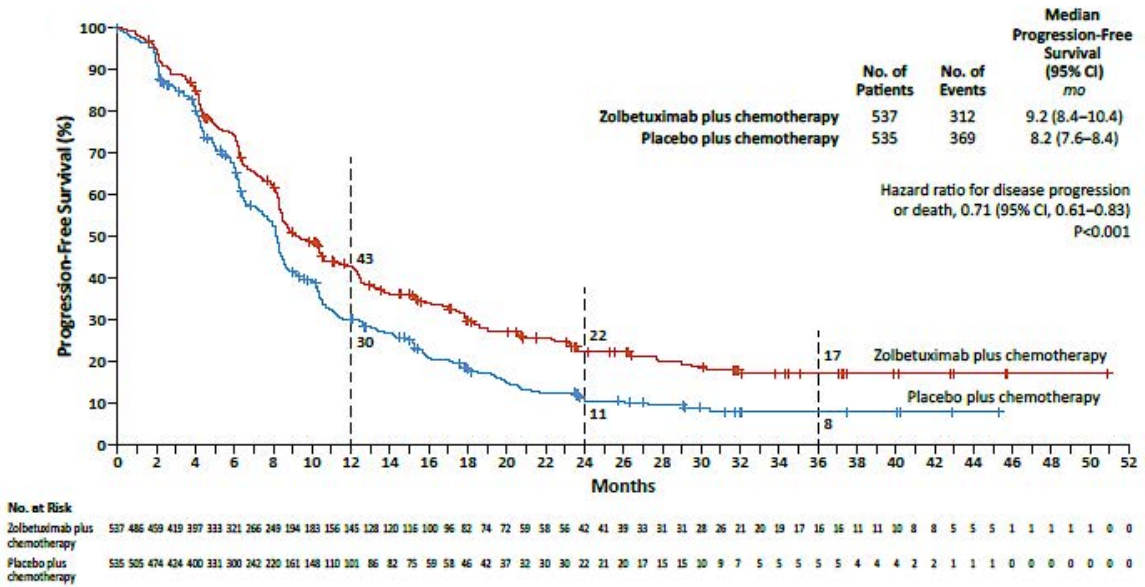


- Claudin18.2 is a major structural component of intercellular tight junctions
- Not routinely expressed in any normal tissue outside gastric mucosa (cancer-restricted antigen)
- Broadly expressed in several tumor types including gastric, GEJ, biliary, and pancreatic

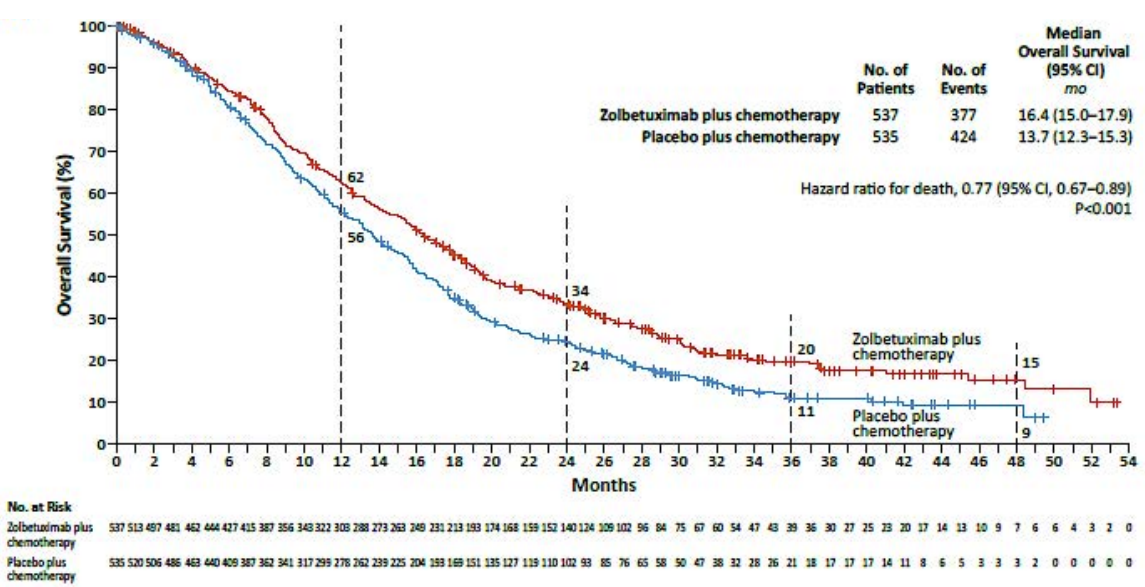
Baek JH et al. *Anticancer Res.* 2019;39(12):6973-6979.

SPOTLIGHT and GLOW – Combined Final Analysis

Progression Free Survival



Overall Survival



Total Population – 1072 (n=537 Zolbe + chemo)
PFS HR 0.71 (0.61-0.83), p < 0.001
OS HR 0.77 (0.67-0.89), p < 0.01

Measurable disease (n=820),
Complete Response - 5.2%. v. 3.1%
Partial Response - 52.2%. v. 52.2%
Overall Response Rate - 57.4%. Vs. 55.3%

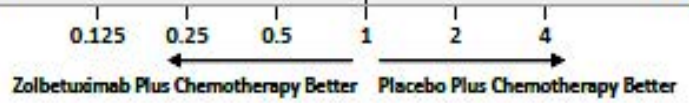
Key Toxicity

≥Grade 3 toxicity higher than control
Nausea - 12.6%. vs. 4.7%
Vomiting 14.3%. vs. 4.9%
Decreased appetite - 6.4% vs. 2.5%

Shitara K, Shah MA et al. *N Engl J Med.* 391(12):1159-1162.

SPOTLIGHT and GLOW – Combined Final Analysis

Subgroup	Zolbetuximab Plus Chemotherapy (no. events/no. patients)	Placebo Plus Chemotherapy (no. events/no. patients)	Hazard Ratio (95% CI)
All patients	377/537	424/535	0.77 (0.67–0.89)
Age			
≤65 yr	241/357	284/361	0.73 (0.62–0.87)
>65 yr	136/180	140/174	0.85 (0.67–1.07)
Sex			
Male	243/335	272/331	0.78 (0.66–0.93)
Female	134/202	152/204	0.76 (0.60–0.96)
Region			
Asia	166/245	190/247	0.71 (0.58–0.88)
Non-Asia	211/292	234/288	0.83 (0.69–1.00)
Number of metastatic sites			
0–2	274/408	312/407	0.76 (0.65–0.90)
≥3	103/129	112/128	0.78 (0.59–1.02)
Prior gastrectomy			
No	276/378	303/378	0.83 (0.71–0.98)
Yes	101/159	121/157	0.65 (0.50–0.85)
Lauren classification			
Diffuse	120/169	164/217	0.82 (0.65–1.04)
Intestinal	75/106	90/107	0.65 (0.47–0.88)
Mixed/other	96/135	85/103	0.88 (0.66–1.18)
Primary site			
Stomach	301/438	331/419	0.72 (0.62–0.84)
Gastroesophageal junction	76/99	93/116	1.02 (0.76–1.39)
Race			
White	175/234	183/224	0.89 (0.72–1.09)
Asian	171/254	196/255	0.69 (0.56–0.85)



Key Points

- Broad activity
- ? GEJ resistance?
- ? White people?

Validated Target

Shitara K, Shah MA et al. *N Engl J Med.* 391(12):1159-1162.

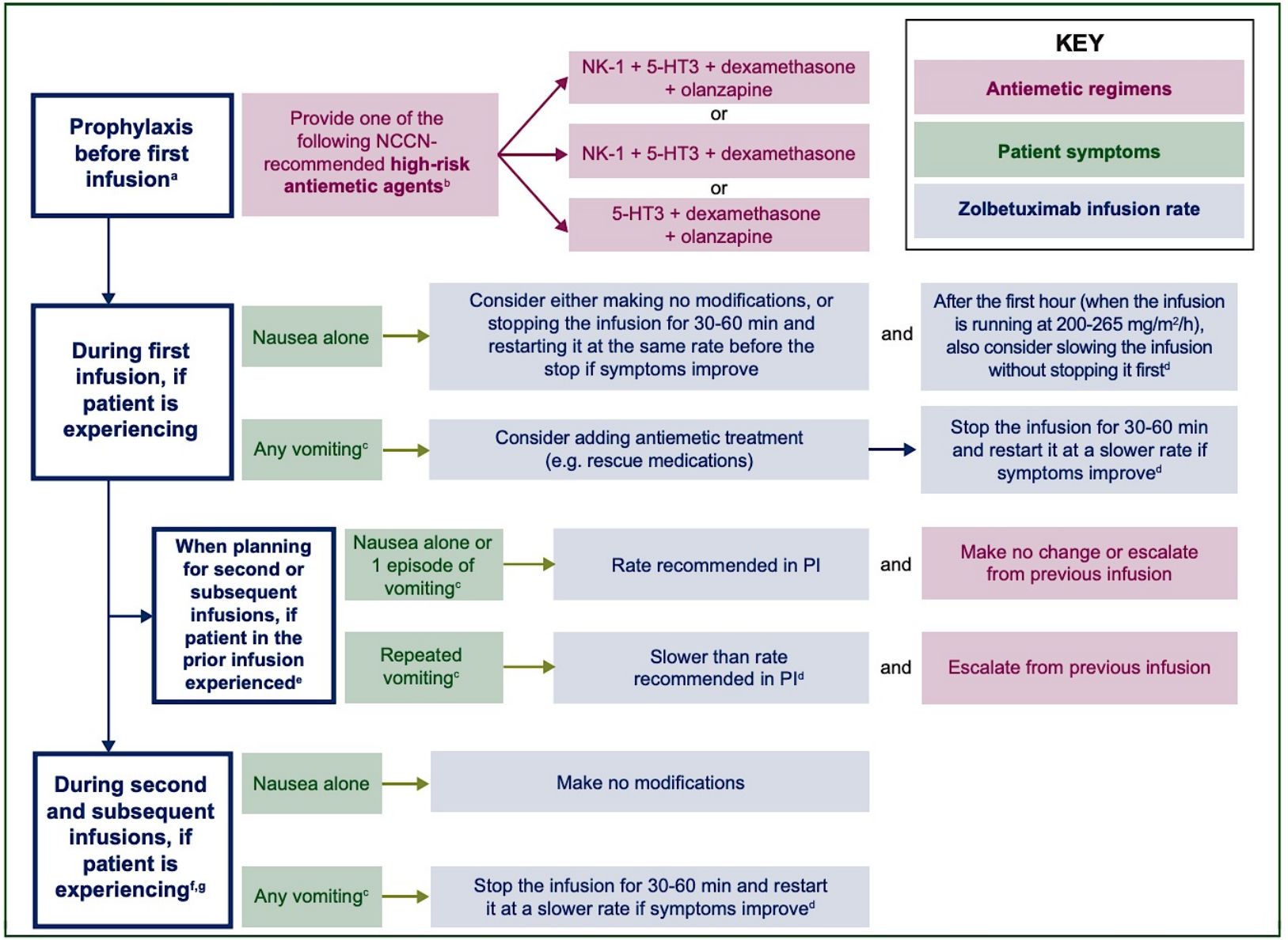


Figure 2. Consensus guidance and essential strategies on the prevention and management of nausea and vomiting in patients treated with zolbetuximab plus chemotherapy.

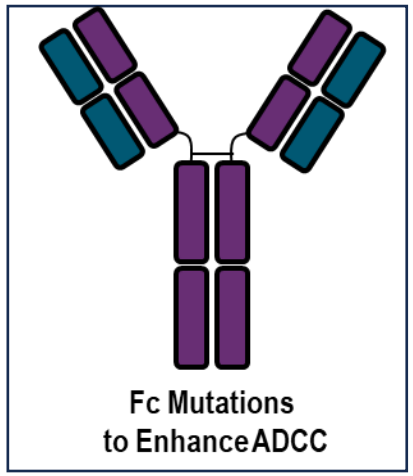
Table 3. Prophylaxis before first zolbetuximab infusion

Provide any of the NCCN-recommended treatment options for high-emetic-risk regimens[a]
NK-1 antagonist + 5-HT3 antagonist + dexamethasone + olanzapine[b]
NK-1 antagonist + 5-HT3 antagonist + dexamethasone
5-HT3 antagonist + dexamethasone + olanzapine

CLDN 18.2 Targeted Therapies

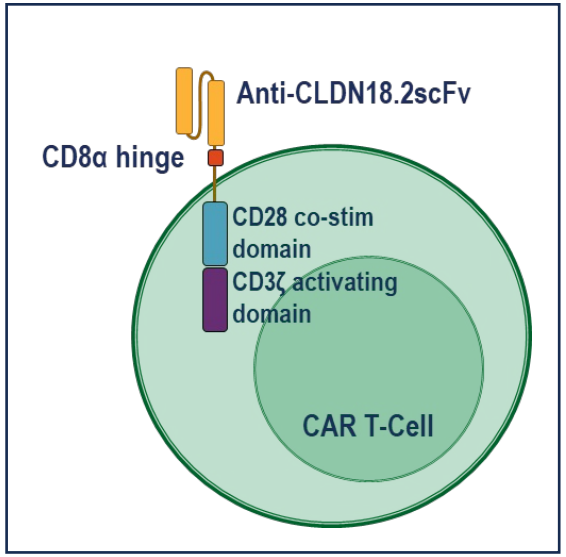
Monoclonal antibody

- Humanized mAb
- Engineered mAb



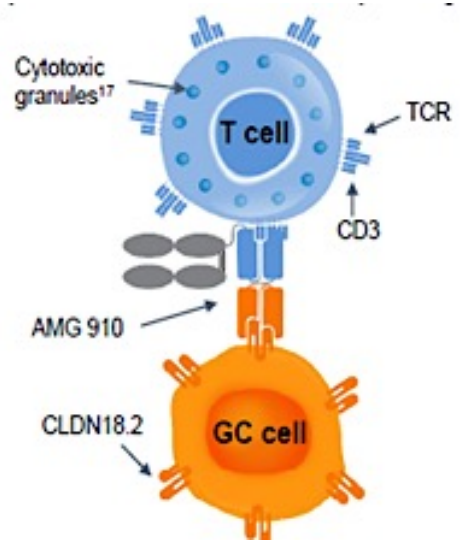
Zolbetuximab
TST-001
ABI011, MIL93,
ZL1211 etc.

CAR-T



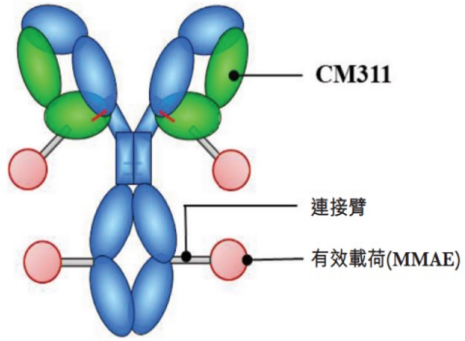
CT-041
LCAR-C18S
LY011

Bispecific



AMG910/ASP2138 (CD3)
TJ-CD4B (4-1BB)
PT886 (CD47)
Q-1802 (PD-L1)
IBI 389

ADCs

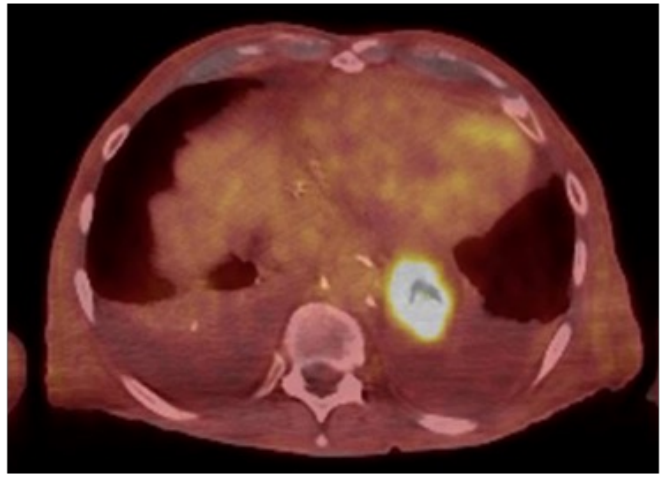


CMG901, EO-3021
TORL-2800
TPX4589
RC118
LM302
SOT102
SKB315
JS107
IBI343

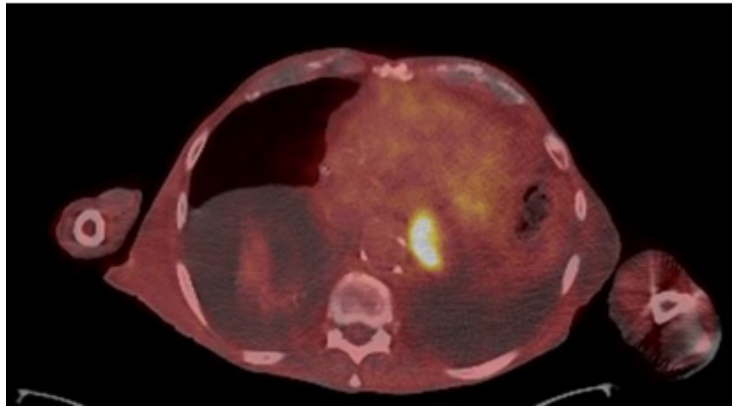
Case Study

- After counseling, patient did undergo FOLFOX plus zolbetuximab.
- The first infusion was fraught with nausea and vomiting necessitating the infusion to be held
- **PET**: Decreased SUV avidity within the distal esophageal, approximately 6 cm, SUV 13.7, previously 9.6 cm SUV 21.1 possibly reflecting residual tumor ± inflammatory process

PRE-treatment



Post-treatment



Conclusions

- Critical to obtain Biomarkers to optimally treat advanced Gastric/GEJ adenocarcinoma
  - PD-L1
  - HER2
  - MMR
  - CLDN18.2
  - FGFR2
- Immunotherapy + chemotherapy for PD-L1 positive gastric/GEJ adeno
- CLDN18.2 positive tumors – zolbetuximab
- HER2 – chemotherapy + pembrolizumab + trastuzumab

Roundtable Discussion

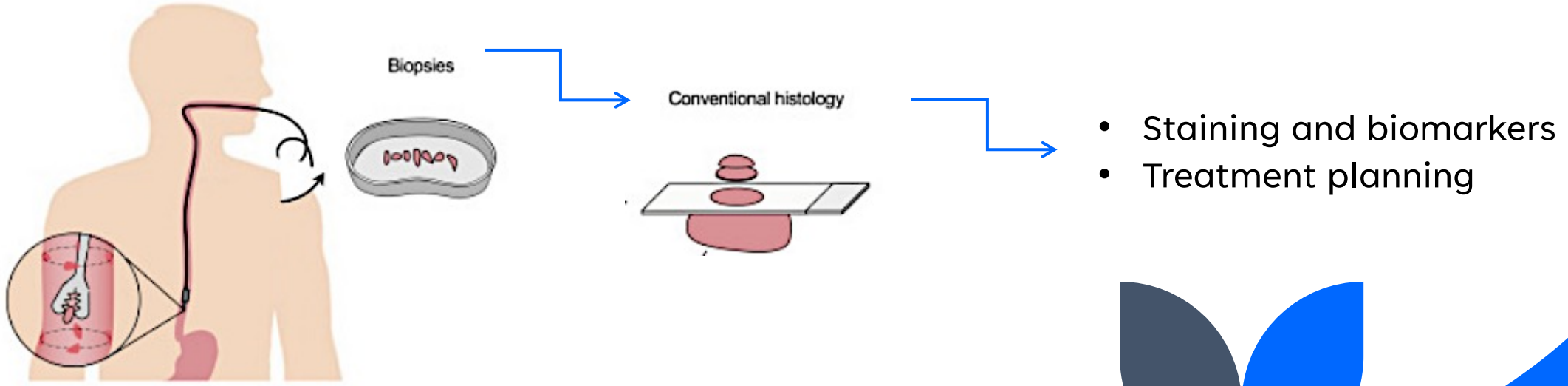
RTP
RESEARCH
TO PRACTICE

Tolerability/Toxicity Profile of Zolbetuximab

Michal F Segal, BSN, RN, OCN

Gastroesophageal Ca and Claudin 18.2

- Newly diagnosed metastatic disease
- Treatment is palliative
- Response measured with CT or MRI
- Chemotherapy backbone
- Add-ons: monoclonal antibodies and immunotherapy
- Biomarkers – PDL1, HER2, MMR, Claudin18.2

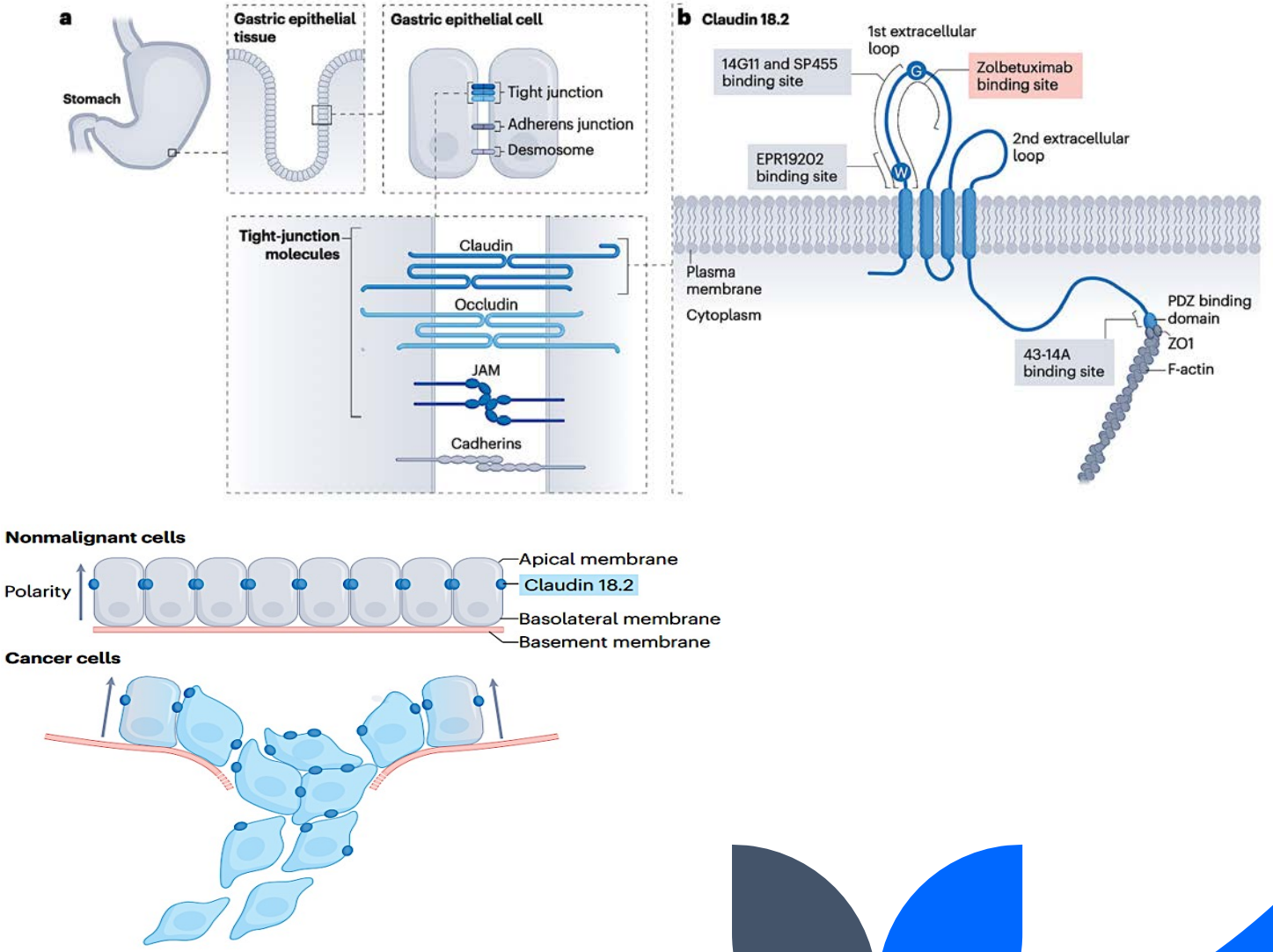


Claudin 18.2 Carcinogenesis

CLDN18.2 is a tight junction molecule on healthy tissue

Abnormal expression leads to disruption of tight junction integrity, loss of cohesion and cellular polarity, impaired differentiation, and increased invasion

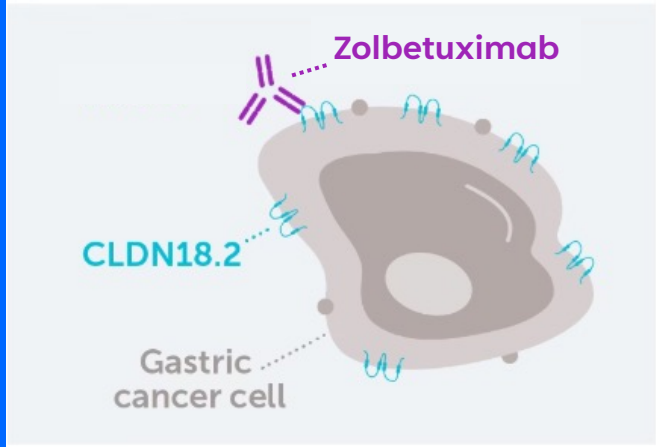
CLDN18.2 becomes expressed on surface of gastric tumor



Hewitt et al. BMC Cancer 2006; Jun et al. Int J Surg 2014; Sanada et al. J Pathol 2006; Suzuki et al. Cell Mol Gastroenterol 2019; Nakayama et al, Nat Rev Clin Oncol 2024

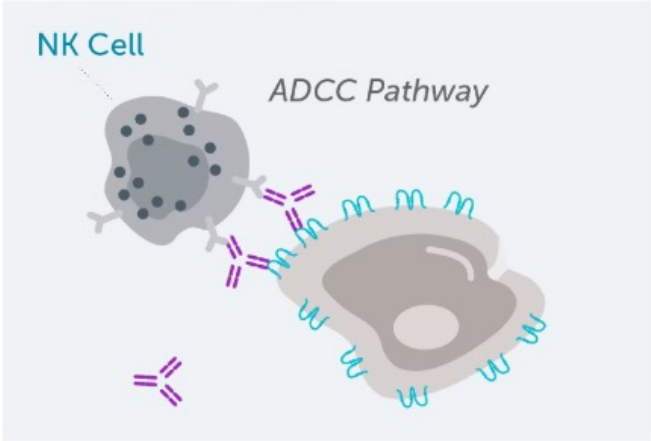
Zolbetuximab Mechanism of Action

CLDN18.2 DIRECTED



Zolbetuximab is a CLDN18.2-directed cytolytic antibody that selectively binds to cells that express CLDN18.2, where cytotoxic immune responses are activated.

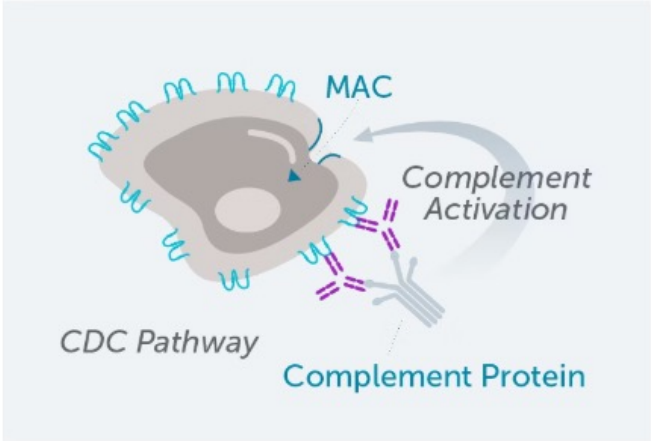
ADCC: ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY



Zolbetuximab depletes CLDN18.2+ cells via ADCC.

- ADCC: Effector cells, such as natural killer cells, recognize antibody-targeted tumor cells and release cytotoxic molecules for lysis

CDC: COMPLEMENT-DEPENDENT CYTOTOXICITY



Zolbetuximab also depletes CLDN18.2+ cells via CDC.

- CDC: In addition, complement proteins gather to assemble a membrane attack complex (MAC) which forms pores that lyse targeted tumor cells

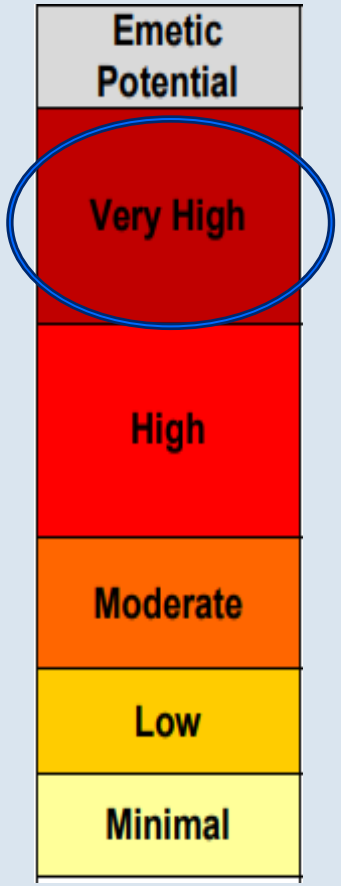
https://www.vyloyhcp.com/mechanism-of-action

Side Effects and Patient Education

- Most common side effects: nausea and vomiting
- Important safety: hypersensitivity reactions, including **infusion-related reactions**
- Potential overlapping toxicities in combination with mFOLFOX6
  - GI: nausea, vomiting, abdominal pain
  - Hematological: anemia and neutropenia
- GI adverse reactions often occur within 30–45 minutes of initiating infusion
- Reducing initial infusion rate is associated with lower severity of GI toxicity events or hypersensitivity
    - overall better subject tolerability
- Patients with prior gastrectomy – less symptoms

GI, gastrointestinal; mFOLFOX6, modified 5-fluorouracil, leucovorin and oxaliplatin.

Side Effects Management - ASCO



Drug class	Day 1	Days 2-4
5-HT_3 receptor antagonist **(select one)**	• Palonosetron 0.50 mg oral or 0.25 mg IV • Granisetron 2 mg oral or 1 mg or 0.01 mg/kg IV or 1 transdermal patch or 10 mg subcutaneous • Tropisetron 5 mg IV/PO • Ondansetron Single 24-mg dose administered by tablets, successive oral dissolving tablets, or oral dissolving film applications before the start of chemotherapy, or 8mg or 0.15 mg/kg IV • Dolasetron 100 mg oral ONLY • Tropisetron 5 mg oral or 5 mg IV • Ramosetron 0.3 mg IV	N/A
NK1-receptor antagonist **(select one)**	• Aprepitant 125 mg PO **or** 130 mg IV • Fosaprepitant 150 mg IV • Netupitant-palonosetron 300 mg netupitant/0.5 mg palonosetron oral in single capsule • Fosnetupitant-palonosetron 235 mg fosnetupitant/0.25 mg palonosetron IV Rolapitant 180 mg PO	Aprepitant 80 mg PO once daily on Days 2-3 (if oral aprepitant on Day 1)
Dexamethasone	12 mg or 20 mg IV/PO	8 mg IV/PO once daily
Olanzapine	5 mg or 10 mg, PO, once	5 mg or 10 mg PO daily

Day 1: recommend having an anti-emetic ordered ahead of infusion if needed (PRN)

5-HT3, 5-hydroxytryptamine 3 receptor antagonist; ASCO, American Society of Clinical Oncology; IV, intravenous; N/A, not applicable; NK-1, Neurokinin 1; PO, by mouth; PRN, when required.

Hesketh PJ, et al. *J Clin Oncol* 2020;38(24):2782–2797.

Monitoring and Support

- Stress importance of delayed emesis regimen (dexamethasone and olanzapine days 2-4)
- Stress to take PRNs
- Stress to call office if not managing at home
- Eat, hydrate, maintain weight
- IV hydration
- Dose reductions
- Check in calls
- Antacids as needed and daily mucosal protectant (PPI)
- Sleep elevated, on pillows or a wedge
- Try eating dry foods
- Hard candy, such as mints, ginger, or tart candies
- Avoid hot or strong-smelling foods when nauseous

Diet Review

- Liberalize diet
- Small, frequent meals; eat slowly; chew food well
- Avoid eating foods that are fried, greasy, creamy, rich or spicy; avoid alcohol
- Eat calorie-dense foods
- High-protein foods
- High-protein supplemental drinks and powders
- In case of dysphagia, stick to soft, puréed, blended food
- Avoid chewy or tough foods
- Treat food like medicine

https://www.cvs.com/shop/boost-original-nutritional
https://kaynutrition.com/calorie-dense-foods/

Self-Care Measures

- Oral hygiene
- Infection precautions – Manage constipation or diarrhea
- Take pain medication for pain
- Moisturize skin and wear sun protection (SPF 30)
  - Safety precautions – wear comfortable, protective footwear; wear thick, supportive socks; wear slippers at home; use night lights/clear path to bathroom
- Rest when needed – keep naps to a minimum; plan events and activities for time points when energy will be highest
- Use relaxation methods to manage stress
- Listening to music
- Deep breathing exercises
- Yoga, Meditation
- Applying a damp washcloth with or without peppermint oil to the back of your neck
- Progressive muscle relaxation (PMR)
- Exercising at home
- Using acupressure and other complementary therapies
- Support groups
- Advocacy groups

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Clinical Presentation of Gastroesophageal Cancer

Module 1: Management of Localized or Locally Advanced Gastroesophageal Cancers; Current and Future Role of Immune Checkpoint Inhibitors

Module 2: Incorporation of Immunotherapeutic Strategies for HER2-Negative Metastatic Gastroesophageal Tumors

Module 3: Role of Therapy Targeting CLDN18.2 in Advanced Gastric/Gastroesophageal Junction Adenocarcinoma

Module 4: Considerations in the Care of Patients with HER2-Positive Gastroesophageal Cancers

Clinical Scenario

A patient with HER2-positive metastatic gastric cancer who has experienced disease progression on first-line pembrolizumab/ chemotherapy/trastuzumab and is about to begin treatment with trastuzumab deruxtecan

Considerations in the Care of Patients with HER2-Positive Gastroesophageal Cancers

Sunnie Kim, MD

Patient Case

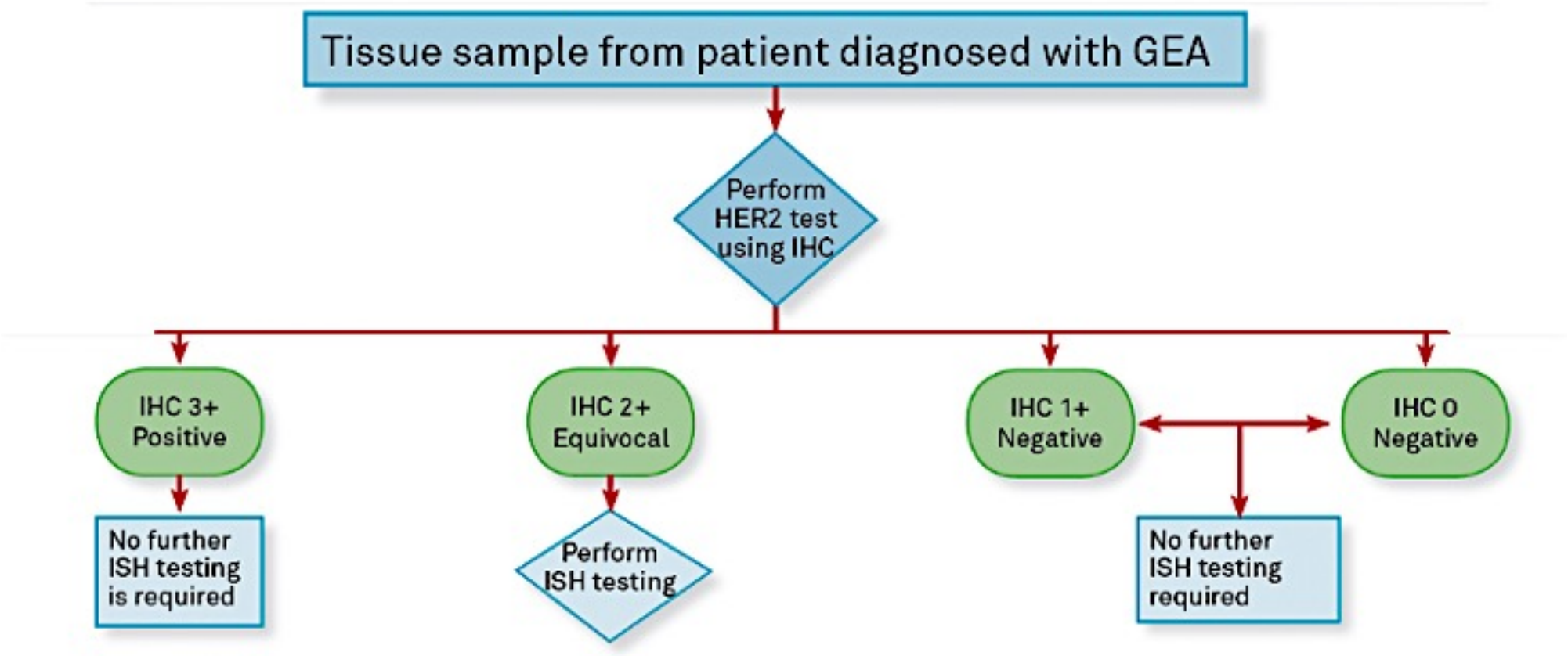
- 59-year-old man presents with dysphagia, weight loss, heartburn
- EGD reveals fungating mass in GEJ
- Pathology shows poorly differentiated adenocarcinoma
- CT CAP shows multiple liver lesions concerning for metastases
- Biomarker testing shows intact MMR proteins, PD-L1 CPS: 1, HER2 IHC 2+, Claudin 18.2 negative

Next steps?

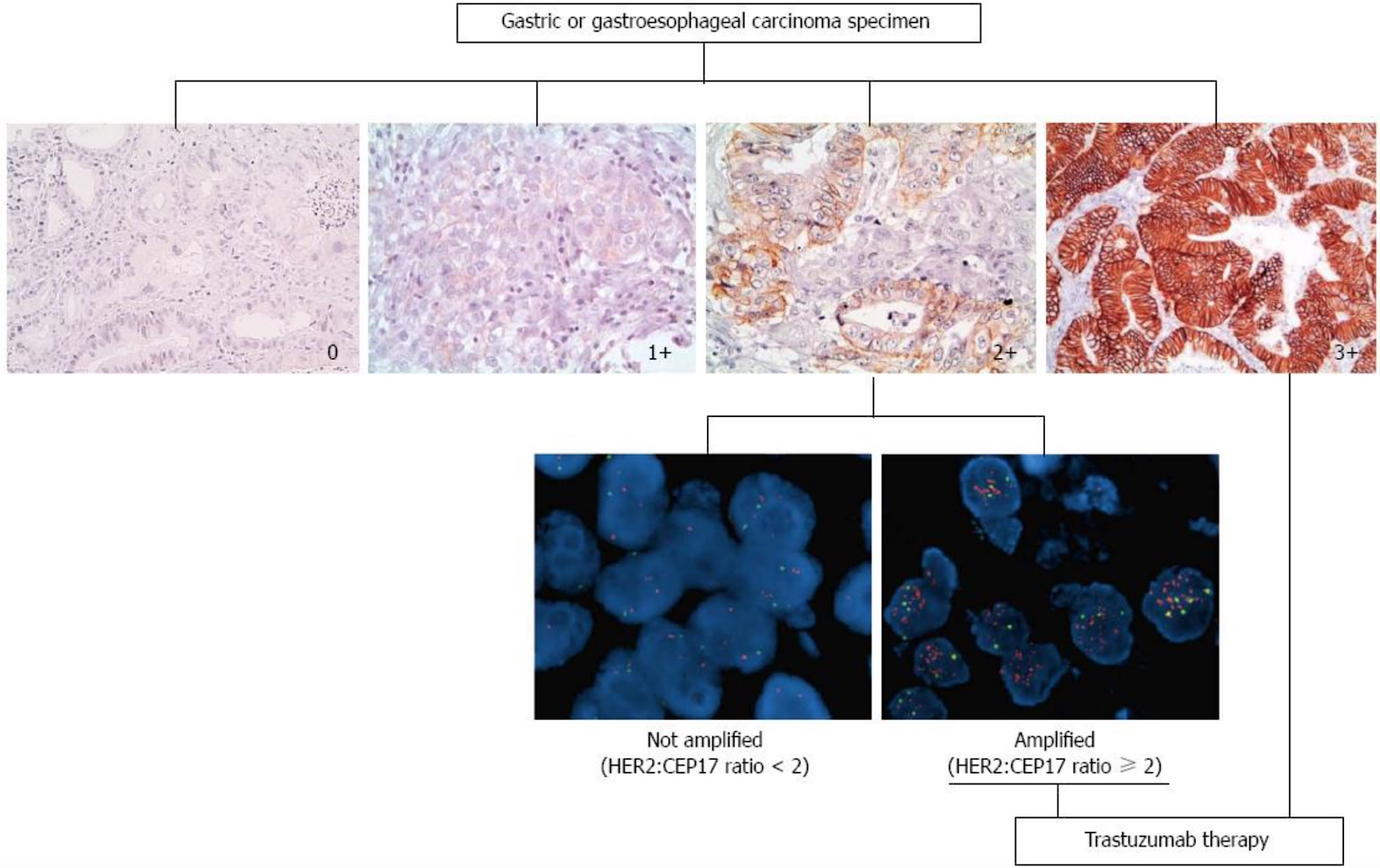
Biomarker Testing in Advanced GE Cancer

- Mismatch Repair Proteins/Microsatellite Instability
- HER2
- Claudin 18.2
- PD-L1 CPS
- Rarer biomarkers: NTRK, BRAF V600E, RET, EBV, EGFR

HER2 Testing Algorithm



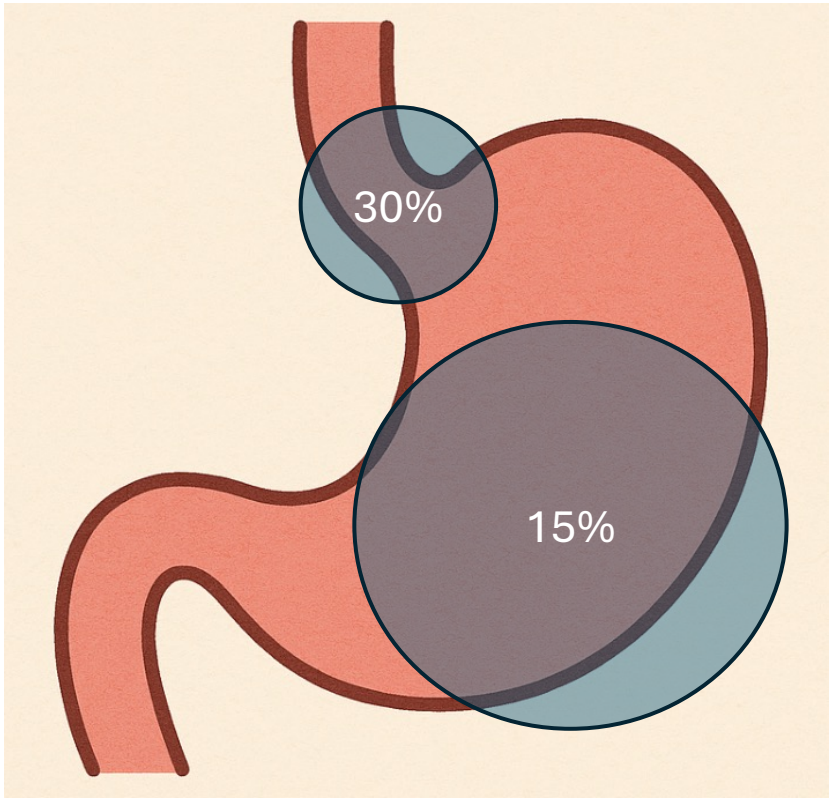
Adapted from American College of Pathologists, 2016



Grillo F, *World J Gastroenterol* 2016

HER2 overexpression differs based on location and histology

By Location



By Histology

- 30% of intestinal type gastric cancers
- 15% of mixed type tumors
- 5% of diffuse type

Signet ring type is typically HER2 negative.

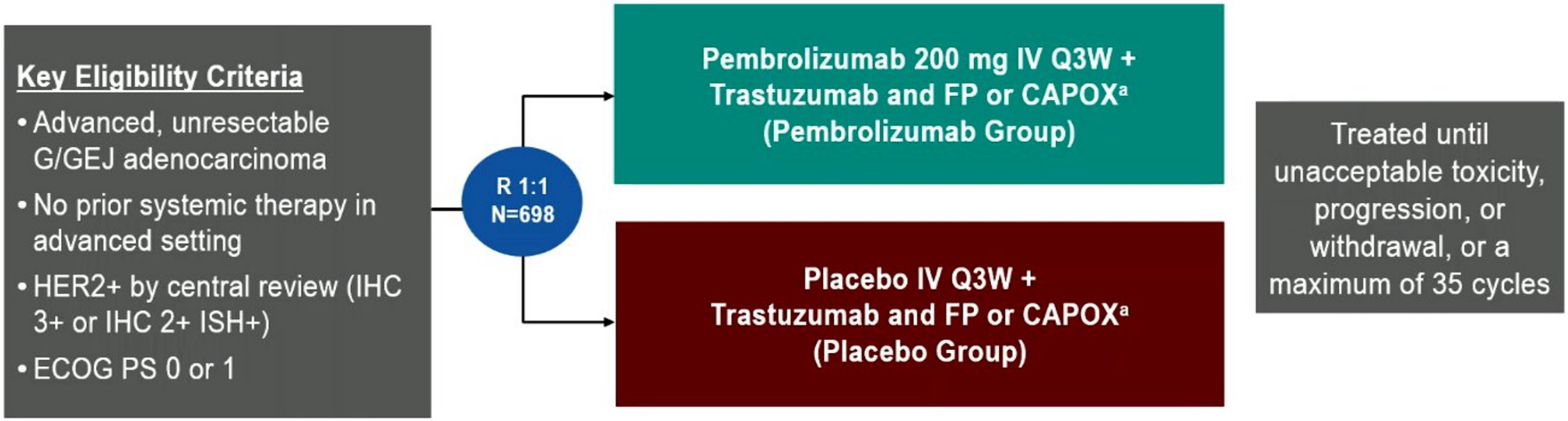
Van Cutsem, Gastric Cancer 2015

Patient Case continued

- 59-year-old man with Stage IV GEJ adenoca to liver
- Biomarker testing shows intact MMR proteins, PD-L1 CPS: 1, HER2 IHC 2+, Claudin 18.2 negative

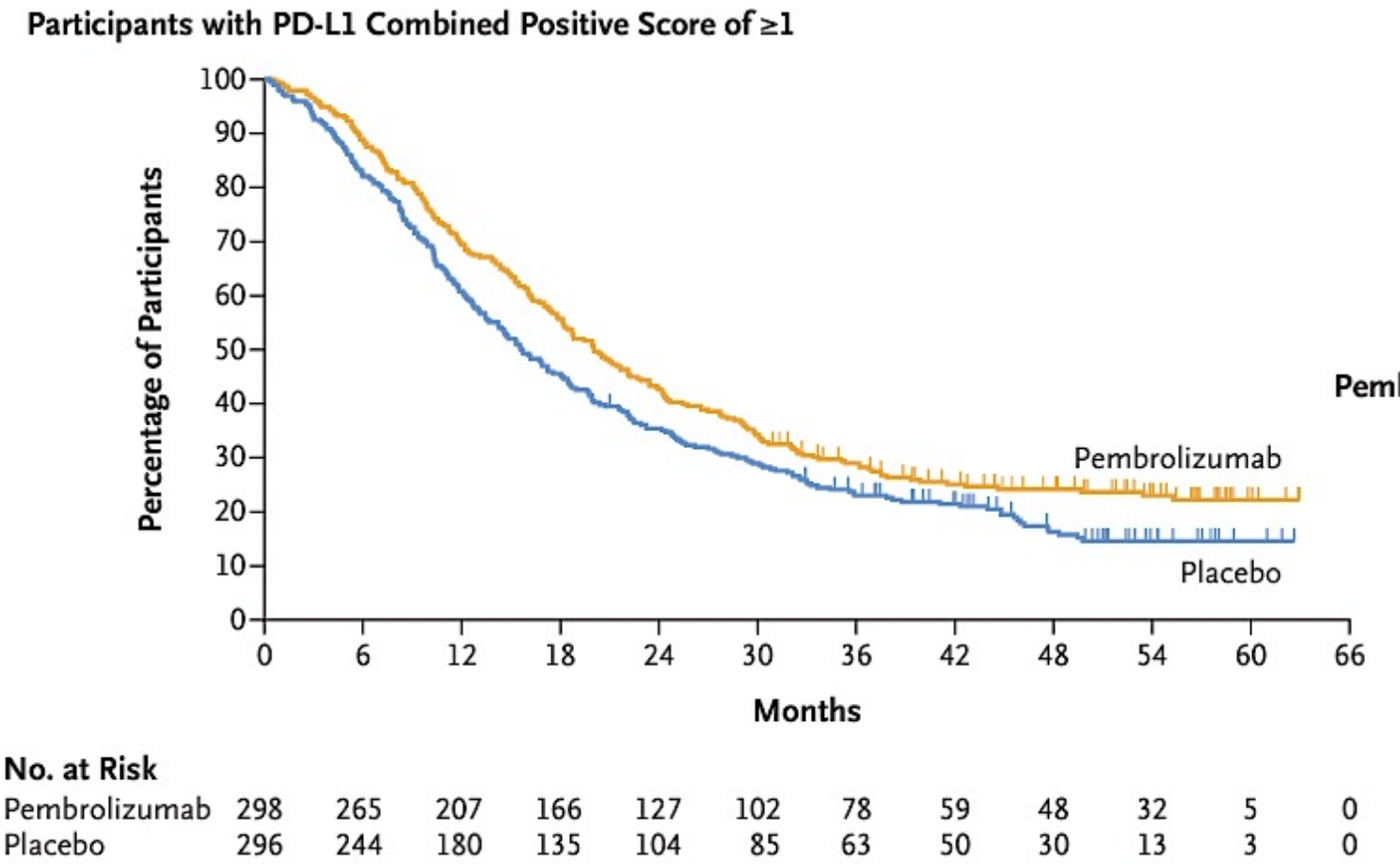
- HER2 FISH positive
- Started on FOLFOX, trastuzumab, pembrolizumab

KEYNOTE-811 Study Design



Janjigian, ESMO 2024

Chemo+Trastuzumab+Pembro shows OS benefit



	No. of Events (%)	Median Overall Survival (95% CI)
		mo
Pembrolizumab	226 (76)	20.1 (17.9–22.9)
Placebo	244 (82)	15.7 (13.5–18.5)

Hazard ratio for death, 0.79
(95% CI, 0.66–0.95)

Current FDA approval is to use quadruplet in PD-L1 CPS>/=1

Janjigian, NEJM 2024

No clinical benefit with PD-L1 CPS<1

	PD-L1 CPS ≥1		PD-L1 CPS <1	
	Pembrolizumab Group N = 298	Placebo Group N = 296	Pembrolizumab Group N = 52	Placebo Group N = 52
PFS, median (95% CI), mo	10.9 (8.5-12.5)	7.3 (6.8-8.4)	9.5 (8.3-12.6)	9.5 (7.9-13.0)
HR (95% CI)	0.72 (0.60-0.87)		0.99 (0.62-1.56)	
OS, median (95% CI), mo	20.1 (17.9-22.9)	15.7 (13.5-18.5)	18.2 (13.9-22.9)	20.4 (16.4-24.7)
HR (95% CI)	0.79 (0.66-0.95)		1.10 (0.72-1.68)	

Janjigian, ESMO 2024

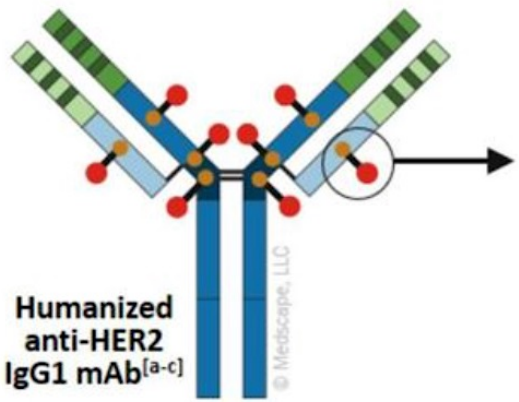
Trastuzumab Deruxtecan

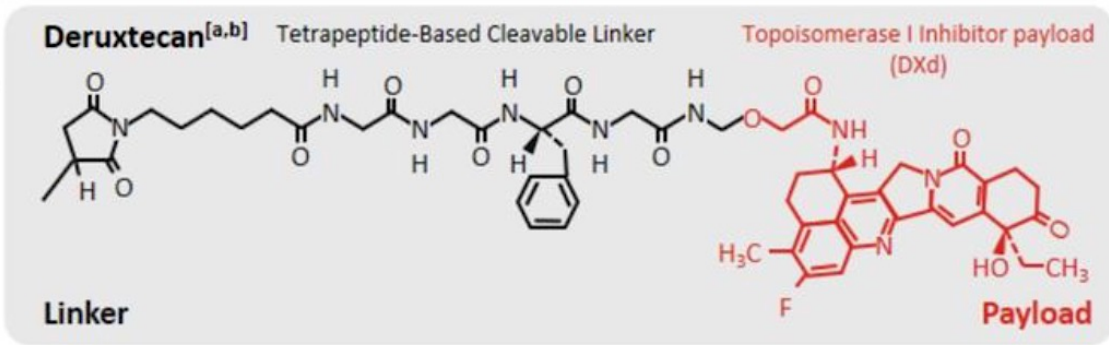
Novel ADC Designed to Deliver an Optimal Antitumor Effect

Trastuzumab deruxtecan is an ADC composed of 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker

Payload MOA: topoisomerase I inhibitor
High potency of payload
High drug to antibody ratio ≈ 8
Payload with short systemic half-life
Stable linker-payload
Tumor-selective cleavable linker
Membrane-permeable payload



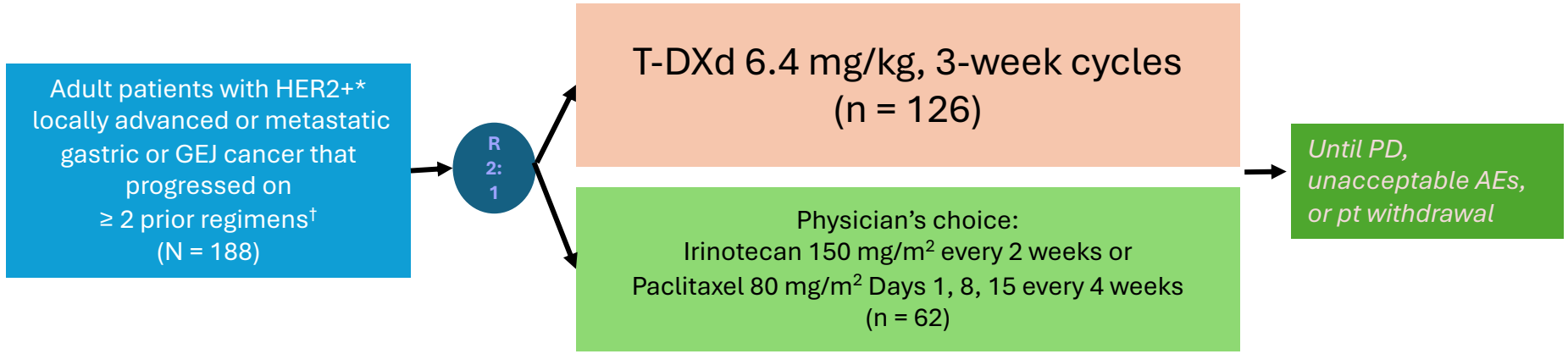


The clinical relevance of these features is under investigation.

a. Nakada T, et al. *Chem Pharm Bull* (Tokyo). 2019;67:173-185; b. Ogitani Y, et al. *Clin Cancer Res*. 2016;22):5097-5108; c. Trail PA, et al. *Pharmacol Ther*. 2018;181:126-142; d. Ogitani Y, et al. *Cancer Sci*. 2016;107:1039-1046.

DESTINY-Gastric01: 2L treatment option for HER2+ gastric/GEJ adenoca

- Multicenter, open-label, randomized phase II study



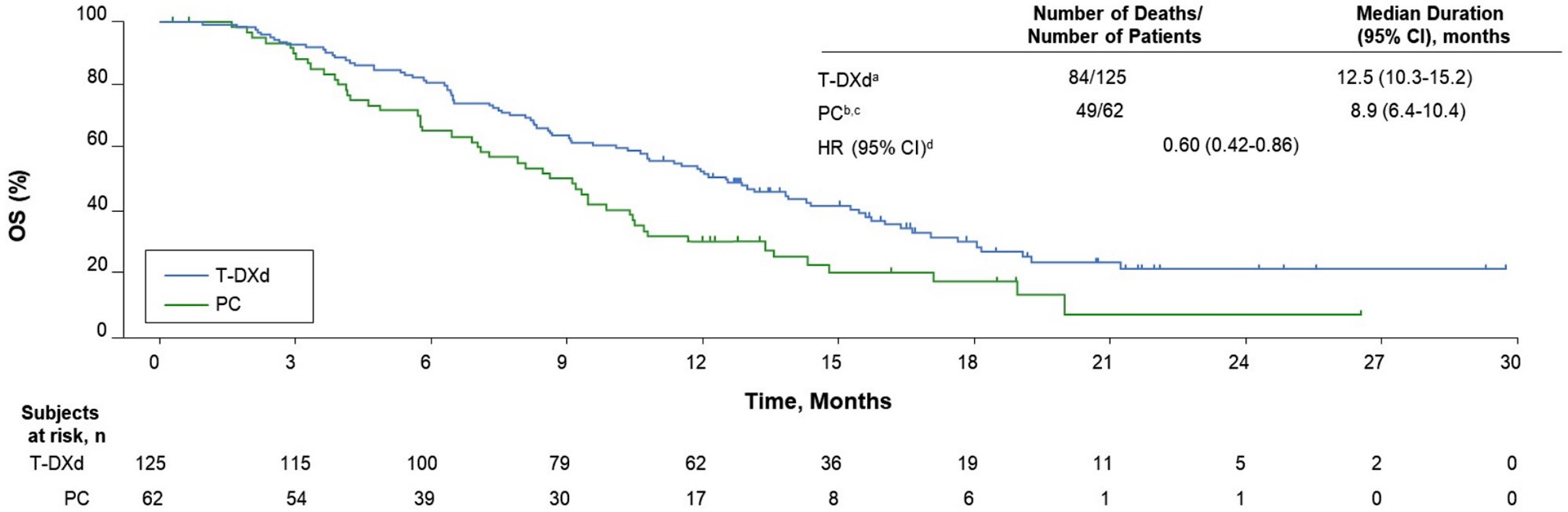
Primary endpoint: ORR by ICR (RECIST v1.1)
Secondary endpoints: OS (key), DoR, PFS, DCR, confirmed ORR, safety

Stratified by region (Japan vs Korea), ECOG PS (0 vs 1), HER2 status (IHC 3+ vs IHC 2+/ISH+)

*HER2+ based on IHC 3+ or IHC 2+/ISH+ according to ASCO/CAP guidelines.
†Prior regimens included fluoropyrimidine, a platinum agent, and trastuzumab or approved biosimilar.

Shitara. ASCO 2020. Abstr 4513. Shitara. N Engl J Med 2020; 382:2419-2430

OS Improvement Noted in T-DXd Group



	Number of Deaths/ Number of Patients	Median Duration (95% CI), months
T-DXd[a]	84/125	12.5 (10.3-15.2)
PC[b,c]	49/62	8.9 (6.4-10.4)
HR (95% CI)[d]	0.60 (0.42-0.86)	

Subjects at risk, n											
T-DXd	125	115	100	79	62	36	19	11	5	2	0
PC	62	54	39	30	17	8	6	1	1	0	0

Yamaguchi, GI ASCO 2022

What is the optimal 2L treatment for HER2+ GC?

Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial

Lancet Oncol 2014; 15: 1224–35

DESTINY-GASTRIC04

Advanced HER2+ gastric/GEJ cancer

After disease progression with trastuzumab regimen

→ T-DXd 6.4mg/kg

→ Ramucirumab Paclitaxel

Press Release (March 3, 2025): Overall survival benefit of T-DXd over ram/paclitaxel


MED
ONCS
TREATING
HER2+ GC
RAM/
PACLITAXEL
Humanized
anti-HER2
IgG1 mAb
Deruxtecan
Linker
Payload
T-DXD

Patient Case continued

- 59-year-old man with Stage IV GEJ adenoca to liver
- Biomarker testing shows intact MMR proteins, PD-L1 CPS: 1, HER2 IHC 2+, Claudin 18.2 negative
- HER2 FISH positive
- Started on FOLFOX, trastuzumab, pembrolizumab

- Disease progression after 9 months
- Retested tumor HER2→2+/FISH positive
- Started T-DXd, disease response for 6 months

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

NURSING CONSIDERATIONS FOR TRASTUZUMAB DERUXTECAN

Brooke Parker MSN, FNP

Gastrointestinal Oncology

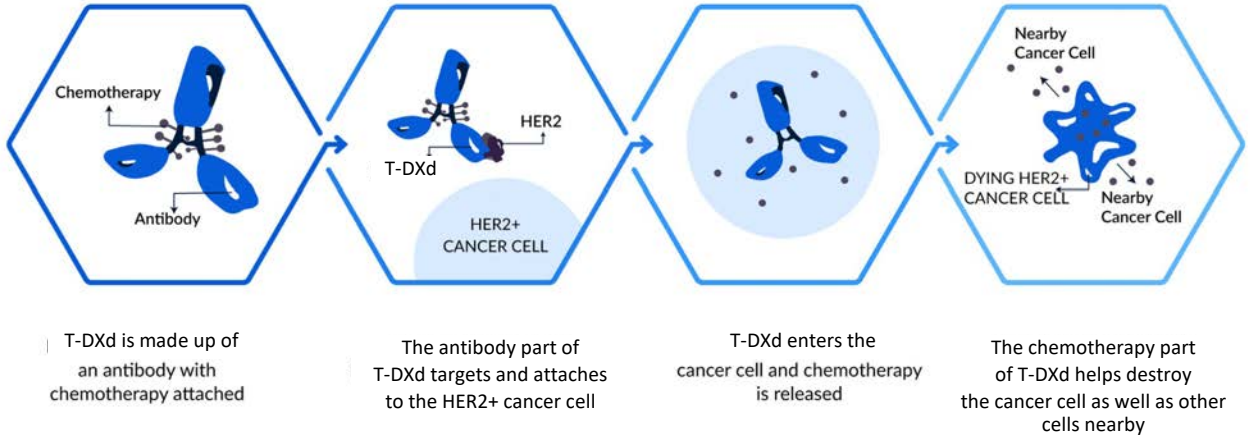
University of Colorado Cancer Center

WHY TRASTUZUMAB DERUXTECAN

How does it work?

- HER2 gene can malfunction and cause an excess of HER2 receptors, which leads to uncontrolled cell growth.
  - Occurs in 10-30% of gastric/gastroesophageal cancers
- Trastuzumab is a type of antibody that targets these HER2 receptors.
  - This blocks the receptor to help prevent cell growth
- Deruxtecan is a topoisomerase I inhibitor (like irinotecan) and is combined with trastuzumab.
  - The trastuzumab is a homing beacon and the deruxtecan acts like a chemo-bomb directly to the tumor cell.

Mechanism of Action of T-DXd



Why we give it

- Second line therapy for gastric/esophageal cancers for patients with HER2 overexpression

Media Delveinsight, 2023
Iqbal, 2014
NCCN Guidelines (Gastric and Gastroesophageal), 2025

COMMON ADVERSE EVENTS SEEN
(DESTINY-GASTRIC01 STUDY)

	Any Grade	Grade ≥3
Nausea	63%	5%
Neutrophil count decreased	63%	38%
Decreased appetite	60%	17%
Anemia	58%	38%
Platelet count decreased	39%	10%
Diarrhea	32%	2%
Vomiting	26%	--
Alopecia	22%	--
Fatigue	22%	7%
Interstitial Lung Disease	10%	2%

When to call

- Coughing, chest tightness, wheezing
- Trouble breathing or shortness of breath
- Feeling tired
- Swelling of your ankles or legs
- Irregular heartbeat
- Sudden weight gain
- Dizziness or feeling light-headed
- Loss of consciousness
- Fever

*No decreased left ejection fraction seen with this study. However, thought to be anywhere between 3-8%

Shitara, 2020

MANAGEMENT OF ADVERSE EFFECTS

Common AEs – Fatigue, nausea, vomiting, diarrhea, neutropenia etc.

- Manage as you would with any typical chemotherapy
  - Anti-emetics
  - Anti-diarrheals
  - GCSF
  - Hold treatment and consider dose reduction

Left ventricular dysfunction

- Need baseline TTE prior to initiating treatment. Repeat every 3 months while on treatment
- Holds, discontinuations and dose reductions are based off of severity of LVEF decrease

Dose Reductions in GE
Dose level -1 = 5.4 mg/kg
Dose level -2 = 4.4 mg/kg

T-DXd package insert.

MANAGEMENT OF INTERSTITIAL LUNG DISEASE

Asymptomatic gr 1 ILD

- Consider corticosteroid treatment (eg, ≥0.5 mg/kg per day prednisolone or equivalent)
- Interrupt T-DXd until resolved to Grade 0, then:
  - If resolved in ≤28 days from date of onset, maintain dose
  - If resolved in >28 days from date of onset, reduce dose 1 level

Gr ≥ 2 symptomatic ILD

- Promptly initiate systemic corticosteroid treatment (eg, ≥1 mg/kg per day prednisolone or equivalent)
- Continue for ≥14 days followed by gradual taper for ≥4 weeks
- Permanently discontinue T-DXd in patients who are diagnosed with any symptomatic ILD/pneumonitis

Chiu et al., 2023

CLINICAL EXPERIENCE

- 64 yo old male with stage IV esophageal cancer
- Treated with T-DXd from 10/18/24-1/08/25. Discontinued treatment due to clinical progression and switched to paclitaxel + ramucirumab
- 1/30/25 complained of increased SOB. CTA chest for PE showed no evidence of PE, but diffuse bilateral ground glass opacities and septal thickening
- Started on 80mg of prednisone
- Attempted taper, but unable to complete due to worsening symptoms. Admitted to hospice following disease progression

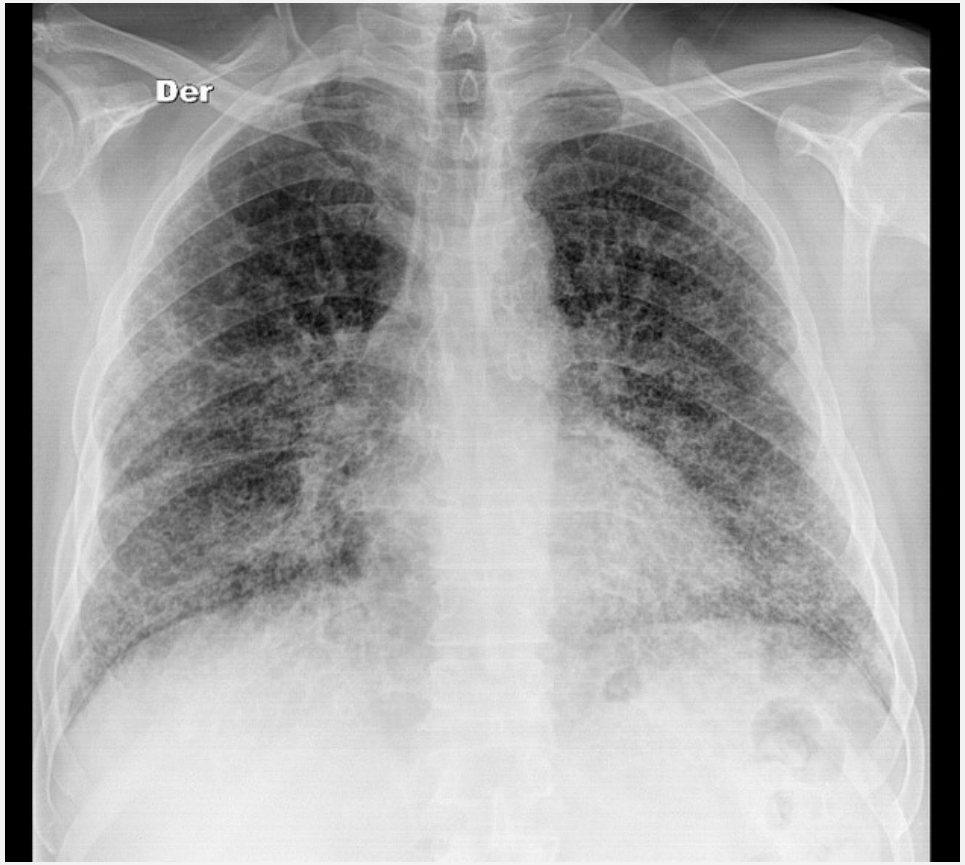


Image Cuete, n.d.

Roundtable Discussion

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TO PRACTICE

Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Non-Hodgkin Lymphoma

Saturday, April 12, 2025

6:00 PM – 7:30 PM

Faculty

Christopher Flowers, MD, MS
Manali Kamdar, MD, MBBS
Robin Klebig, MSN, APRN, CNP, AOCNP
Caitlin Murphy, DNP, FNP-BC, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

To Claim NCPD Credit

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Virtual attendees: The NCPD credit link is posted in the chat room.

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