Emerging Considerations for the Role of Biomarker-Driven Immunotherapy in Upper GI Cancers

SYLLABUS & COURSE GUIDE

A Free, 60-Minute Live Event
Premiere Date: Wednesday, June 25, 2025
6:30–7:30 PM ET

Register
ceconcepts.com/WC102

Faculty
Samuel J. Klempner, MD, FASCO (Moderator)
Samuel Cytryn, MD
Leslie Swanson, ARNP, AOCNP

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Call Creative Educational Concepts at 859.260.1717.

Information for Participants

Target Audience

Pathologists, medical oncologists, surgical oncologists, nurse practitioners (NPs), physician associates (PAs), nurses, and pharmacists

Overview

Upper gastrointestinal (GI) cancers are often undetected until late stages, leading to a poor prognosis. Treatment may be delayed or inappropriately assigned due to a lack of robust biomarker testing. To optimize patient outcomes, oncology clinicians must confidently possess a comprehensive understanding of predictive biomarkers, current and emerging therapies, clinical findings and implications of recent trial data, guideline updates, and the roles and responsibilities of the multidisciplinary team (MDT). It is crucial that this knowledge be applied in practice to make informed treatment decisions and reach optimal outcomes.

In this CE Concepts live webcast, expert faculty will discuss utilizing biomarker tests to select therapeutic approaches for patients with upper GI cancers, implementing current guidelines and recent clinical evidence to individualize treatment, and integrating an MDT approach to deliver high-quality disease management.

Learning Objectives

At the conclusion of this activity, participants should be able to:

- Utilize pertinent biomarker tests to select therapeutic approaches for patients diagnosed with upper GI cancers
- Implement current expert guidelines and recent clinical evidence to individualize treatment for upper GI cancers
- Integrate a multidisciplinary approach to optimize the management of upper GI cancers

Financial Support

This educational activity is supported by an independent educational grant from Bristol Myers Squibb.

Faculty

SAMUEL J. KLEMPNER, MD, FASCO (MODERATOR)
Director, Gastroesophageal Medical Oncology
Associate Professor, Harvard Medical School
Mass General Cancer Center
Boston, MA

Samuel J. Klempner, MD, FASCO, is an Associate Professor at Massachusetts General Hospital and Harvard Medical School and leads the gastric and esophageal program. His clinical and translational research is centered on cancer genomics, acquired resistance to targeted therapies, and the intersection of genomics and immune-mediated therapies to identify novel therapeutic approaches and biomarkers in gastroesophageal cancers. He serves on the NRG Non-Colorectal Cancer Core Committee, co-chairs the National Cancer Institute (NCI) Esophagogastric Task Force, and is on the National Comprehensive Cancer Network (NCCN) guideline committees for gastric and esophageal cancers. His work is supported by Stand Up 2 Cancer, NCI / National Institutes of Health (NIH), American Association for Cancer Research (AACR), the Degregorio Foundation, The Gastric Cancer Foundation, and Gateway for Cancer Research. Dr. Klempner is active in gastric and esophageal cancer outreach and patient advocacy.

SAMUEL CYTRYN, MD
Assistant Attending, Gastrointestinal Oncology Service
Memorial Sloan Kettering Cancer Center
New York, NY

Samuel Cytryn, MD, is Assistant Attending in the Gastrointestinal Oncology Service at Memorial Sloan Kettering Cancer Center. He graduated from medical school at the Icahn School of Medicine at Mount Sinai, completed his internal medicine training at New York University where he served as Chief Resident, and completed his medical oncology training at Memorial Sloan Kettering Cancer Center where he served as Chief Fellow. His clinical and research interests involve the use of immune checkpoint blockade and targeted therapy in esophageal and gastric cancer.

LESLIE SWANSON, ARNP, AOCNP
Gastrointestinal (GI) Oncology Fred Hutch Cancer Center
Seattle, WA

Leslie Swanson, ARNP, AOCNP, is a board-certified and oncology specialized nurse practitioner. She received her undergraduate degree from Seattle University and her master's degree in nursing from Duke University. Currently, she works in the gastrointestinal oncology group at Fred Hutch Cancer Center in Seattle, Washington. Ms. Swanson is also an active member of the Cholangiocarcinoma Foundation’s nursing advisory board and was just elected to serve on the Advanced Practitioner Society for Hematology and Oncology (APSHO) Foundation Board of Trustees. Outside of work, she volunteers to bring awareness to funding cancer research and spends time with her young daughter and husband.

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Consultant—Astellas Pharma US, Inc.; EcoR1; and Jazz Pharmaceuticals, Inc.
Research Support—Arcus Biosciences, Inc.

Samuel Cytryn, MD, reports the following relationships:

Advisory Board—Bristol Myers Squibb Company and Henlius USA Inc.
Consultant—Amgen Inc.; AstraZeneca; Bristol Myers Squibb Company; Gilead Sciences, Inc.; and Leerink
Research Support—Stand Up To Cancer

Leslie Swanson, ARNP, AOCNP, reports the following relationships:

Advisory Board and Consultant— Astellas Pharma US, Inc.

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EMERGING CONSIDERATIONS FOR THE ROLE OF BIOMARKER-DRIVEN IMMUNOTHERAPY IN UPPER GI CANCERS

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To Ask a Question

To submit a question, please go to the *Ask Question* tab at the bottom of the screen.

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LEARNING OBJECTIVES

1. Utilize pertinent biomarker tests to select therapeutic approaches for patients diagnosed with upper GI cancers
2. Implement current expert guidelines and recent clinical evidence to individualize treatment for upper GI cancers
3. Integrate a multidisciplinary approach to optimize the management of upper GI cancers

Biomarker Testing in GECs

Unmet Needs in Diagnosis of GECs

- Late-stage diagnosis
- Inadequate screening
- Lack of predictive biomarkers
- Diagnostic delays
- Health disparities
- Low patient health literacy and familiarity with biomarkers

GECs = gastroesophageal cancers.

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Current Biomarkers for Treatment

- HER2
- MSI/MMR
- PD-L1
- CLDN18.2
- *FGFR2*
- *EGFR*
- *MET*
- TMB-H
- *NTRK* gene fusions
- *RET* gene fusions
- *BRAF*-V600E mutations

CLDN18.2 = Claudin 18.2; EGFR = epidermal growth factor receptor; FGFR2 = fibroblast growth factor receptor 2; HER2 = human epidermal growth factor receptor 2; MMR = mismatch repair; MSI = microsatellite instability; NTRK = neurotrophic tyrosine receptor kinase; PD-L1 = programmed death ligand 1; TMB-H = high tumor mutational burden.

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Current State of Biomarker Testing

- Survey of 60 oncologists reported testing for:
  - 67% HER2
  - 62% PD-L1
  - <50% MSI/MMR, TMB, and BRAF p.V600E
  - <25% NTRK1/2/3, RET, CLDN18.2, and FGFR2
- Top challenges: limited tissue (38%), deciding whether to start treatment before receipt of results (35%), and interpreting/applying results (77%)
  - Additional challenges included turnaround time for biomarker testing and inconsistent or infrequent multidisciplinary tumor boards
  - Need to improve test ordering processes, decrease turnaround times, and standardize biomarker panels

Strickland M, et al. *J Clin Oncol*. 2025;43(4_suppl):385.

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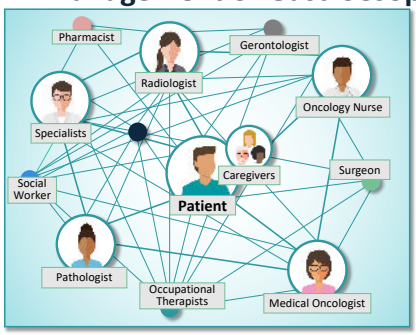
Biomarker Use by Multidisciplinary Care Teams in GEC Management

Multidisciplinary Team-Based Approach for the Management of Gastroesophageal Cancers



- Cancer care is complex, involving numerous health care professionals, which can lead to communication and coordination challenges
- MDTs are formed to improve communication, coordination, and decision-making among care professionals

Silbermann M, et al. *Ann Oncol*. 2013;24(Suppl 7):vii41.

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MDTs

- MDTs improve guideline adherence, diagnostic accuracy, clinical trial identification, outcomes, and professional relationships
- Barriers:
  - Operational: time constraints, inadequate case information, poor team dynamics, information technology issues
  - Patient: fear of treatment toxicity, personal care goals, social drivers of health
  - Health care professional: new or overlooked clinical findings not discussed, underestimating treatment feasibility

He C. Cancer Network Website. 2024. https://www.cancernetwork.com/view/multidisciplinary-team-meetings-barriers-to-implementation-in-cancer-care.

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Evolving Role of Pathologist

- Pathologist roles:
  - Initial biomarker testing and interpretation
  - Biomarker retesting during therapy and prior to switching therapies at the development of resistance
  - Determining clinical trial eligibility
- To improve pathologist participation in MDT:
  - Streamline and standardize biomarker testing process (ordering, reporting)
  - Improve tissue acquisition, handling, and management to reduce turnaround time
  - Strengthen pathology presence on MDT

Kim J, et al. Enhancing coordination around cancer biomarker and hereditary genetic testing among members of the multidisciplinary care team. American Society for Clinical Pathology (ASCP) 2022 Annual Meeting; September 7-9, 2022; Chicago, IL. Association of Community Cancer Centers Website. 2018. https://www.accc-cancer.org/docs/projects/landscape-of-pathology/pathology-summit-proceedings-final.pdf?sfvrsn=8e59b849_2&.

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Current and Emerging Therapies for Upper GI Cancers

Case 1: TR

- TR is a 55-year-old male, married, 1 child
  - No history of cancer or smoking
  - Complains of vague pain in upper abdomen and frequent indigestion
  - Has lost "a few" pounds of weight because of early satiety
  - Palpable abdomen mass and visualized by MRI and CT scan
  - Biopsy confirms stage III gastric cancer
- TR wants to receive aggressive therapy (i.e., neoadjuvant therapy, surgery, and as many lines of additional therapy as he is able to tolerate) in order to have as much time as possible with his young child

CT = computed tomography; MRI = magnetic resonance imaging.

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? Audience Response

At what stage in this patient's treatment journey should you consider sending a tumor biopsy for biomarker testing?

A. Prior to second-line therapy for metastatic disease
B. Prior to first-line therapy for metastatic disease
C. Prior to adjuvant therapy
D. Prior to neoadjuvant therapy
E. I don't know

Immunotherapy Approaches

	G	E	GEJ	Biomarker Required?	FDA-Approved Indication(s)
Durvalumab	X		X		Not approved for gastric/GEJ
Ipilimumab		X		No	Combination with nivolumab, first-line advanced/metastatic ESCC
Nivolumab	X	X	X	Yes	Adjuvant, completely resected esophageal/GEJ after neoadjuvant therapy; Combination with chemotherapy for first-line PD-L1+ advanced/metastatic ESCC/gastric/GEJ/ esophageal adenocarcinoma; Combination with ipilimumab for first-line PD-L1+ advanced/metastatic ESCC; Single-agent after chemotherapy for advanced/metastatic ESCC
Pembrolizumab	X	X	X	Yes	Second-line unresectable/metastatic MSI-H, dMMR, or TMB-high solid tumors; Combination with chemotherapy + trastuzumab for first-line HER2+/PD-L1+ advanced/metastatic gastric/GEJ adenocarcinoma; Combination with chemotherapy for first-line HER2-neg/PD-L1+ advanced/metastatic esophageal/GEJ adenocarcinoma; Combination with chemotherapy for PD-L1+ advanced/metastatic esophageal/GEJ adenocarcinoma; Single-agent strongly PD-L1+ advanced/metastatic ESCC
Tislelizumab	X	X	X	Yes	Combination with chemotherapy for first-line unresectable/metastatic PD-L1+ ESCC; Single-agent for second-line unresectable/metastatic ESCC [PD-(L)1 inhibitor naïve]; Combination with chemotherapy for first-line unresectable/metastatic HER2-neg, PD-L1+ G/GEJ adenocarcinoma
Trastuzumab	X		X	Yes	Combination with chemotherapy for first-line HER2+ metastatic gastric/GEJ adenocarcinoma
Trastuzumab deruxtecan (T-DXd)	X		X	Yes	Second-line HER2+ gastric/GEJ adenocarcinoma after prior trastuzumab
Zolbetuximab	X		X	Yes	Combination with chemotherapy, first-line HER2-neg/CLDN18.2+ gastric/GEJ adenocarcinoma

dMMR = mismatch repair deficient; ESCC = esophageal squamous carcinoma; GEJ = gastroesophageal junction; MSI-H = microsatellite instability-high; TMB = tumor mutation burden.

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NCCN Immunotherapy Recommendations

	Esophageal/GEJ		Gastric
	Adenocarcinoma	Squamous	
Neoadjuvant/ perioperative	Nivo/ipi -> nivo Pembro Tremelimumab/durvalumab*		
First-line, unresectable advanced/ metastatic	**HER2+**: chemo + trastuzumab, pembro, or trastuzumab/pembro **HER2-**: chemo + nivo, pembro, tisle, or zolbe **MSI-H/dMMR**: pembro, dostarlimab, nivo/ipi, or chemo + nivo or pembro	Nivo/ipi Chemo + nivo, pembro, or tisle **MSI-H/dMMR**: pembro, dostarlimab, nivo/ipi, or chemo + nivo or pembro	**HER2+**: chemo + trastuzumab, pembro, or trastuzumab/pembro **HER2-**: chemo + nivo, pembro, tisle, or zolbe **MSI-H/dMMR**: pembro, dostarlimab, nivo/ipi, or chemo + nivo or pembro
Second-line, unresectable advanced/ metastatic	**HER2+**: T-DXd **MSI-H/dMMR**: pembro, dostarlimab, nivo/ipi **TMB-high**: pembro	Nivo, pembro, or tisle **MSI-H/dMMR**: pembro, dostarlimab, nivo/ipi **TMB-high**: pembro	**HER2+**: T-DXd **MSI-H/dMMR**: pembro, dostarlimab, nivo/ipi **TMB-high**: pembro

*Not FDA-approved for the treatment of gastric/esophageal/GEJ cancers.
chemo = chemotherapy; ipi = ipilimumab; nivo = nivolumab; pembro = pembrolizumab; tisle = tislelizumab; zolbe = zolbetuximab.
National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Gastric Cancer, Version 2.2025. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Esophageal and Esophagogastric Junction Cancers, Version 3.2025. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf.

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Guidelines for Biomarker Testing

Esophageal/GEJ

- Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients
- PD-L1 testing if advanced/metastatic disease is documented/suspected
- HER2 testing if advanced/metastatic adenocarcinoma is documented/suspected
- CLDN18.2 testing if advanced/metastatic adenocarcinoma is document/suspected
- NGS should be considered

Gastric

- Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients
- HER2 and PD-L1 testing if advanced/metastatic disease is documented/suspected
- CLDN18.2 testing if advanced/metastatic disease is documented/suspected
- NGS should be considered

IHC = immunohistochemistry; ipi = ipilimumab; NGS = next-generation sequencing; nivo = nivolumab; PCR = polymerase chain reaction; pembro = pembrolizumab; tisle = tislelizumab; zolbe = zolbetuximab.
National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Gastric Cancer, Version 2.2025. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. NCCN. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Esophageal and Esophagogastric Junction Cancers, Version 3.2025. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf.

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Perioperative Locally Advanced Gastric/GEJ

MATTERHORN: perioperative chemotherapy ± durvalumab

NEONIPIGA: perioperative nivolumab + ipilimumab → nivolumab

INFINITY: neoadjuvant durvalumab + tremelimumab

Janjigian YY, et al. *N Engl J Med*. 2025 Jun 1. [Epub ahead of print]. André T, et al. *J Clin Oncol*. 2022;41(2):255-265. Raimondi A, et al. *Ann Oncol*. 2025;36(3):285-296.

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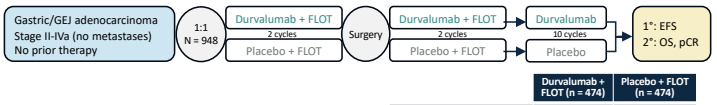
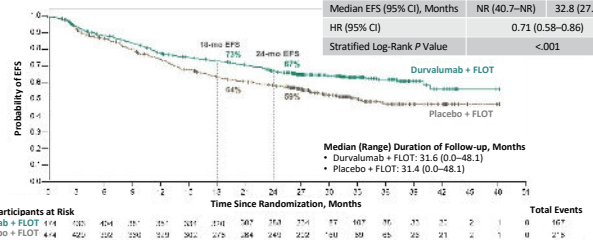
MATTERHORN: EFS



	Durvalumab + FLOT (n = 474)	Placebo + FLOT (n = 474)
Median EFS (95% CI), Months	NR (40.7–NR)	32.8 (27.9–NR)
HR (95% CI)	0.71 (0.58–0.86)	
Stratified Log-Rank *P* Value	<.001	



1° = primary endpoint; 2° = secondary endpoint; EFS = event-free survival; FLOT = 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; pCR = pathological complete response.
Janjigian YY, et al. *N Engl J Med*. 2025 Jun 1. [Epub ahead of print]. Janjigian YY, et al. *J Clin Oncol*. 2025;43(17_suppl):LBA5.

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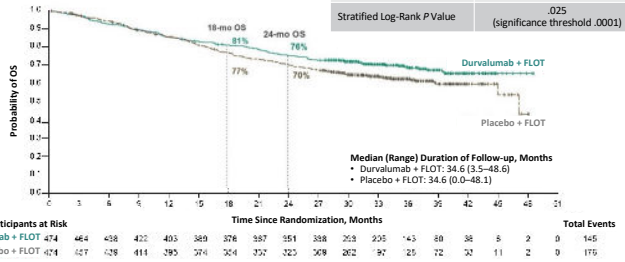
MATTERHORN: OS

	Durvalumab + FLOT (n = 474)	Placebo + FLOT (n = 474)
Median OS (95% CI), Months	NR (NR–NR)	47.2 (45.1–NR)
HR (95% CI)	0.78 (0.62–0.97)	
Stratified Log-Rank *P* Value	.025 (significance threshold .0001)	



New standard of care for perioperative treatment

OS = overall survival.
Janjigian YY, et al. *N Engl J Med*. 2025 Jun 1. [Epub ahead of print]. Janjigian YY, et al. *J Clin Oncol*. 2025;43(17_suppl):LBA5.

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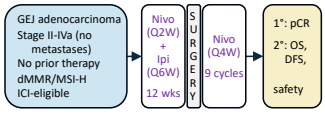
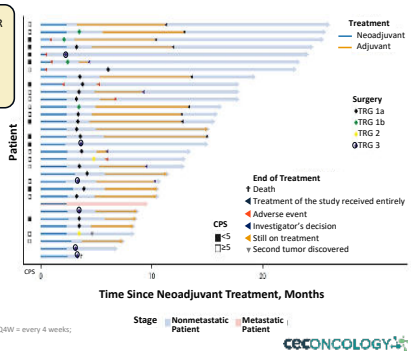
NEONIPIGA: Treatment Course



Underscores the importance of biomarker-driven, personalized immunotherapy approaches



CPS = combined positive score; ICI = immune checkpoint inhibitor; Q2W = every 2 weeks; Q4W = every 4 weeks; Q6W = every 6 weeks; TRG = tumor regression grade; wks = weeks.
André T, et al. *J Clin Oncol*. 2022;41(2):255-265.

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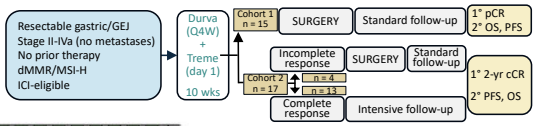
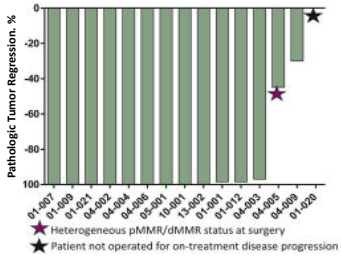
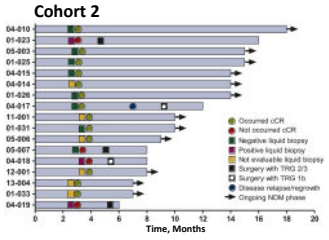
INFINITY



Cohort 1



Cohort 2



cCR = clinical complete response; Durva = durvalumab; NOM = non-operative management; PFS = progression-free survival; Treme = tremelimumab.
Raimondi A, et al. *Ann Oncol*. 2025;36(3):285-296.

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Summary of Perioperative Locally Advanced Gastric/GEJ

- Combinations of immunotherapies and targeted therapies, guided by biomarkers, are central to the management of both early and advanced gastric/GEJ cancers and improve survival and quality of life for patients
- These studies reinforce the need for biomarker testing (e.g., HER2, PD-L1, MSI, CLDN18.2) to guide therapy selection

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Case 2: ML

- ML is a 65-year-old female
  - Complains of difficulty swallowing, upper abdominal discomfort, and frequent heartburn
  - Upper endoscopy exam reveals a tumor at the GEJ, and CT scan reveals involvement of multiple regional lymph nodes
  - She is diagnosed with locally-advanced, non-resectable GEJ adenocarcinoma
  - Biopsy indicates that it is HER2-negative, PD-L1 CPS 4, CLDN18.2-negative, and proficient MMR
  - No comorbidities that would prevent treatment

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? Audience Response

Which of the following approaches is likely to provide the greatest clinical benefit?

A. Systemic fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT)
B. Systemic chemotherapy + immune checkpoint inhibitor
C. Pembrolizumab + trastuzumab + chemotherapy
D. Nivolumab + ipilimumab
E. I don't know

Overview Metastatic Gastric/GEJ

- HER2-negative
  - CheckMate-649 (chemotherapy ± nivolumab)
  - KEYNOTE-859 (chemotherapy ± pembrolizumab)
  - RATIONALE-305 (chemotherapy ± tislelizumab)
- HER2-positive
  - DESTINY-Gastric04 (T-DXd vs ramucirumab + chemotherapy)
  - KEYNOTE-811 (trastuzumab/chemotherapy ± pembrolizumab)
- CLDN+ (HER2-negative)
  - GLOW (chemotherapy ± zolbetuximab)
  - SPOTLIGHT (chemotherapy ± zolbetuximab)

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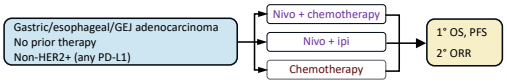
HER2-Negative Metastatic Gastric/GEJ: CheckMate-649

- HER2-negative: CheckMate-649, 5-year follow-up



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), months	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)	
mPFS (95% CI), months	8.3 (7.0-9.4)	6.1 (5.6-6.9)	7.5 (7.0-8.5)	6.9 (6.2-7.1)	7.8 (7.1-8.6)	6.9 (6.7-7.2)
HR (95% CI)	0.71 (0.61-0.82)		0.77 (0.68-0.87)		0.79 (0.71-0.89)	
ORR (95% CI), %	60 (55-65)	45 (40-50)	60 (55-64)	46 (42-51)	58 (54-62)	46 (42-50)
mDOR (95% CI), months	9.6 (8.3-12.4)	7.0 (5.7-8.0)	8.6 (7.9-10.5)	6.9 (5.8-7.6)	8.5 (7.7-9.9)	6.9 (5.9-7.6)

CI = confidence interval; HR = hazard ratio; mDOR = median duration of response; mOS = median OS; mPFS = median PFS; ORR = overall response rate.
Janjigian YY, et al. *J Clin Oncol*. 2025;43(4_suppl):398.

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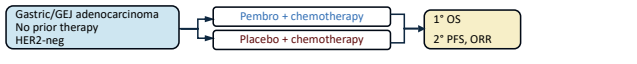
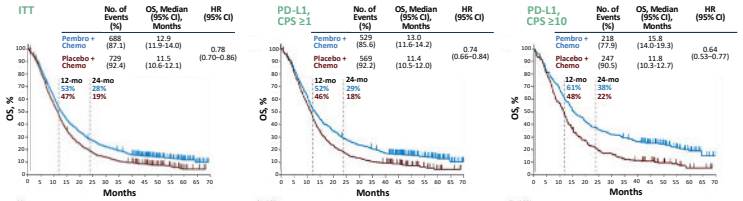
HER2-Negative Metastatic Gastric/GEJ: KEYNOTE-859





	All Patients		PD-L1 CPS ≥1		PD-L1 CPS ≥10	
	Pembro + Chemotherapy n = 790	Placebo + Chemotherapy n = 789	Pembro + Chemotherapy n = 618	Placebo + Chemotherapy n = 617	Pembro + Chemotherapy n = 280	Placebo + Chemotherapy n = 273
Median OS, Months	12.9	11.5	13.0	11.4	15.8	11.8
HR (95% CI)	0.78 (0.70–0.86)		0.74 (0.66–0.84)		0.64 (0.53–0.77)	

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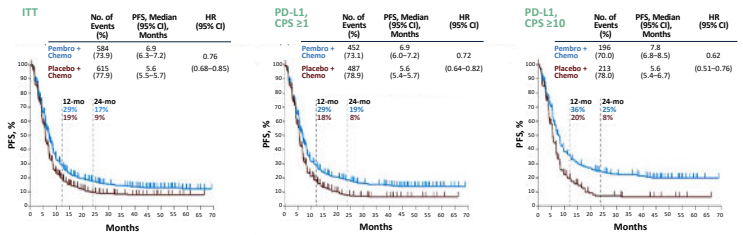
ITT = intent to treat; mo = months.
Rha SY, et al. *J Clin Oncol*. 2025;43(16_suppl):4036.

HER2-Negative Metastatic Gastric/GEJ: KEYNOTE-859



	All Patients		PD-L1 CPS ≥1		PD-L1 CPS ≥10	
	Pembro + Chemo n = 790	Placebo + Chemo n = 789	Pembro + Chemo n = 618	Placebo + Chemo n = 617	Pembro + Chemo n = 280	Placebo + Chemo n = 273
Median PFS, Months	6.9	5.6	6.9	5.6	7.8	5.6
HR (95% CI)	0.76 (0.68–0.85)		0.72 (0.64–0.82)		0.62 (0.51–0.76)	

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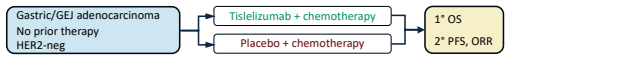
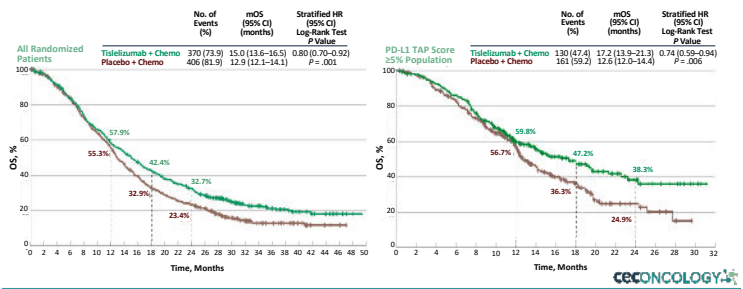
Rha SY, et al. *J Clin Oncol*. 2025;43(16_suppl):4036.

HER2-Negative Metastatic Gastric/GEJ: RATIONALE-305





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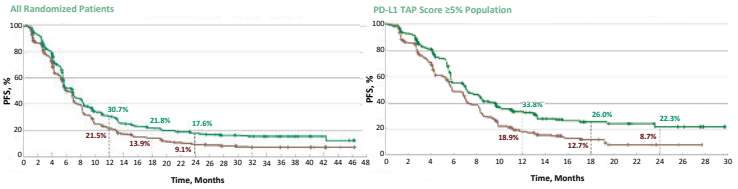
TAP = tumor area positivity.
Qiu MZ, et al. *BMJ*. 2024;385:e078876.

HER2-Negative Metastatic Gastric/GEJ: RATIONALE-305

	No. of Events (%)	mPFS (95% CI) (months)	Stratified HR (95% CI)
Tislelizumab + Chemo	361 (72.1)	6.9 (5.7–7.2)	0.80 (0.67–0.90)
Placebo + Chemo	391 (78.8)	6.2 (5.6–6.9)	

	No. of Events (%)	mPFS (95% CI) (months)	Stratified HR (95% CI) Log-Rank Test *P* Value
Tislelizumab + Chemo	169 (61.7)	7.2 (5.8–8.4)	0.67 (0.55–0.83)
Placebo + Chemo	206 (75.7)	5.9 (5.6–7.0)	*P* < 0.001



Qiu MZ, et al. *BMJ*. 2024;385:e078876.

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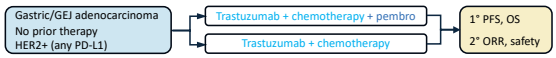
HER2+ Metastatic Gastric/GEJ: KEYNOTE-811



ITT

	No. of Events (%)	Median, Months (95% CI)
Pembro	267 (76%)	20.0 (17.8–22.1)
Placebo	288 (83%)	16.8 (14.9–18.7)

HR 0.80 (95% CI 0.67–0.94); *p* = .0040

No. at Risk												
Pembro	350	311	243	192	144	116	84	62	49	32	5	0
Placebo	348	292	220	165	125	102	74	59	37	16	6	0

PD-L1 CPS ≥1 Tumors

	No. of Events (%)	Median, Months (95% CI)
Pembro	226 (76%)	20.1 (17.9–22.9)
Placebo	244 (82%)	15.7 (13.5–18.5)

HR 0.79 (95% CI 0.66–0.95)

No. at Risk												
Pembro	298	265	207	166	127	102	78	59	48	32	5	0
Placebo	296	244	180	135	104	85	63	50	30	13	3	0

Median PFS (mo)	
Pembro	10.0
Placebo	8.4
HR 0.73 95% CI 0.61-0.87	

Janjigian YY, et al. *N Engl J Med*. 2024;391(14):1360-1362.

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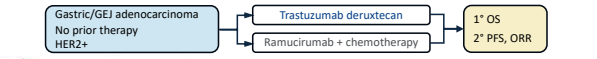
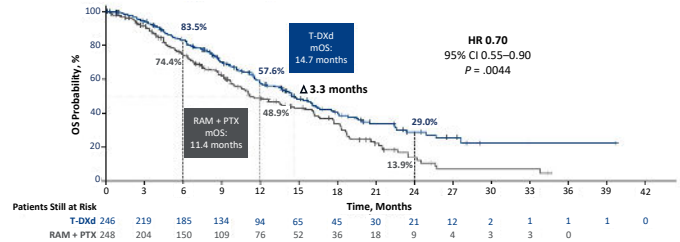
HER2+ Metastatic Gastric/GEJ: DESTINY-Gastric04





Patients Still at Risk														
T-DXd	246	219	185	134	94	65	45	30	21	12	2	1	1	1	0
RAM + PTX	248	204	150	109	76	52	36	18	9	4	3	3	0		

PTX = paclitaxel; RAM = ramucirumab.
Shitara K, et al. *J Clin Oncol*. 2025;43(17_suppl):LBA4002.

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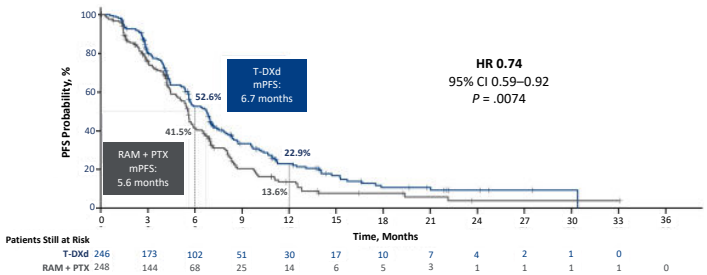
HER2+ Metastatic Gastric/GEJ: DESTINY-Gastric04



Patients Still at Risk													
T-DXd	246	173	102	51	30	17	10	7	4	2	1	0	
RAM + PTX	248	144	68	25	14	6	5	3	1	1	1	1	0

Shitara K, et al. *J Clin Oncol*. 2025;43(17_suppl):LBA4002.

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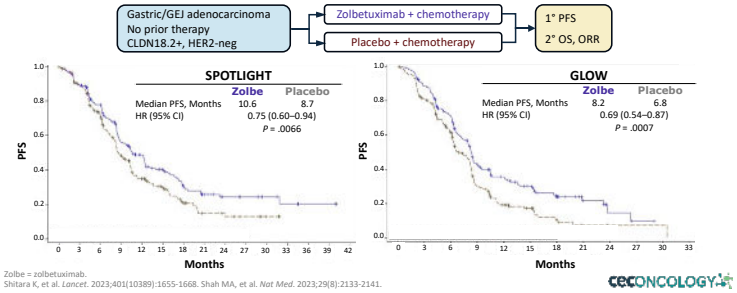
CLDN+ Metastatic Gastric/GEJ: SPOTLIGHT and GLOW

- SPOTLIGHT and GLOW



Zolbe = zolbetuximab.
Shitara K, et al. *Lancet*. 2023;401(10389):1655-1668. Shah MA, et al. *Nat Med*. 2023;29(8):2133-2141.

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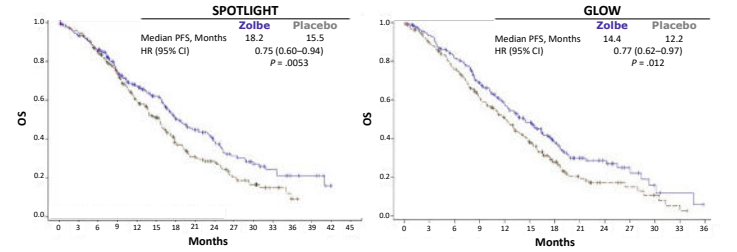
CLDN+ Metastatic Gastric/GEJ: SPOTLIGHT and GLOW

- SPOTLIGHT and GLOW



Shitara K, et al. *Lancet*. 2023;401(10389):1655-1668. Shah MA, et al. *Nat Med*. 2023;29(8):2133-2141.

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Summary of Metastatic Gastric/GEJ Studies

- Immunotherapy integration: adding immune checkpoint inhibitors to chemotherapy, especially in advanced disease, confers survival benefit
- Targeted therapy advances: expanding treatment options and improving outcomes with new agents and biomarker-driven strategies
- Personalized medicine: increasingly tailored therapies based on molecular profiling and biomarker status

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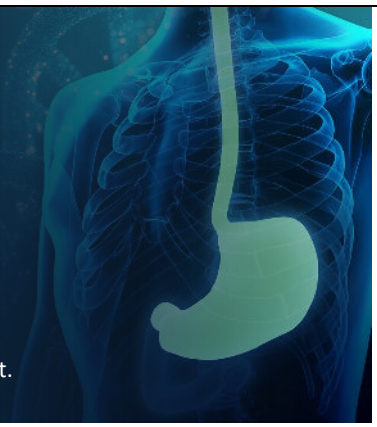
QUESTIONS & ANSWERS



Thank you for joining us.
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Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- **Biomarkers** should be assessed at the earliest opportunity and again after metastasis.
- **Guidelines** are important resources that provide state-of-the-art care and should be utilized as much as possible.
- Members of a high-functioning **MDT** support one another and utilize the unique expertise of each member to bring the highest quality of care to the patient.

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EMERGING CONSIDERATIONS FOR THE ROLE OF BIOMARKER-DRIVEN IMMUNOTHERAPY IN UPPER GI CANCERS

This educational activity is supported by an independent educational grant from Bristol Myers Squibb.