Practical Perspectives: Clinical Investigators Review Actual Cases of Patients with Advanced Gastroesophageal Cancers

A CME/MOC-Accredited Live Webinar

Tuesday, November 18, 2025
5:00 PM – 6:00 PM ET

Faculty

Yelena Y Janjigian, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Faculty

Yelena Y Janjigian, MD
Professor and Chief Attending
Gastrointestinal Oncology Service
Memorial Sloan Kettering Cancer Center
New York, New York

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, and Merck.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Agendia Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeOne, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celcuity, Clovis Oncology, Coherus BioSciences, Corcept Therapeutics Inc, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Helsinn Therapeutics (US) Inc, Hologic Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Pharma America, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.

RTP
RESEARCH
TO PRACTICE

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Janjigian — Disclosures

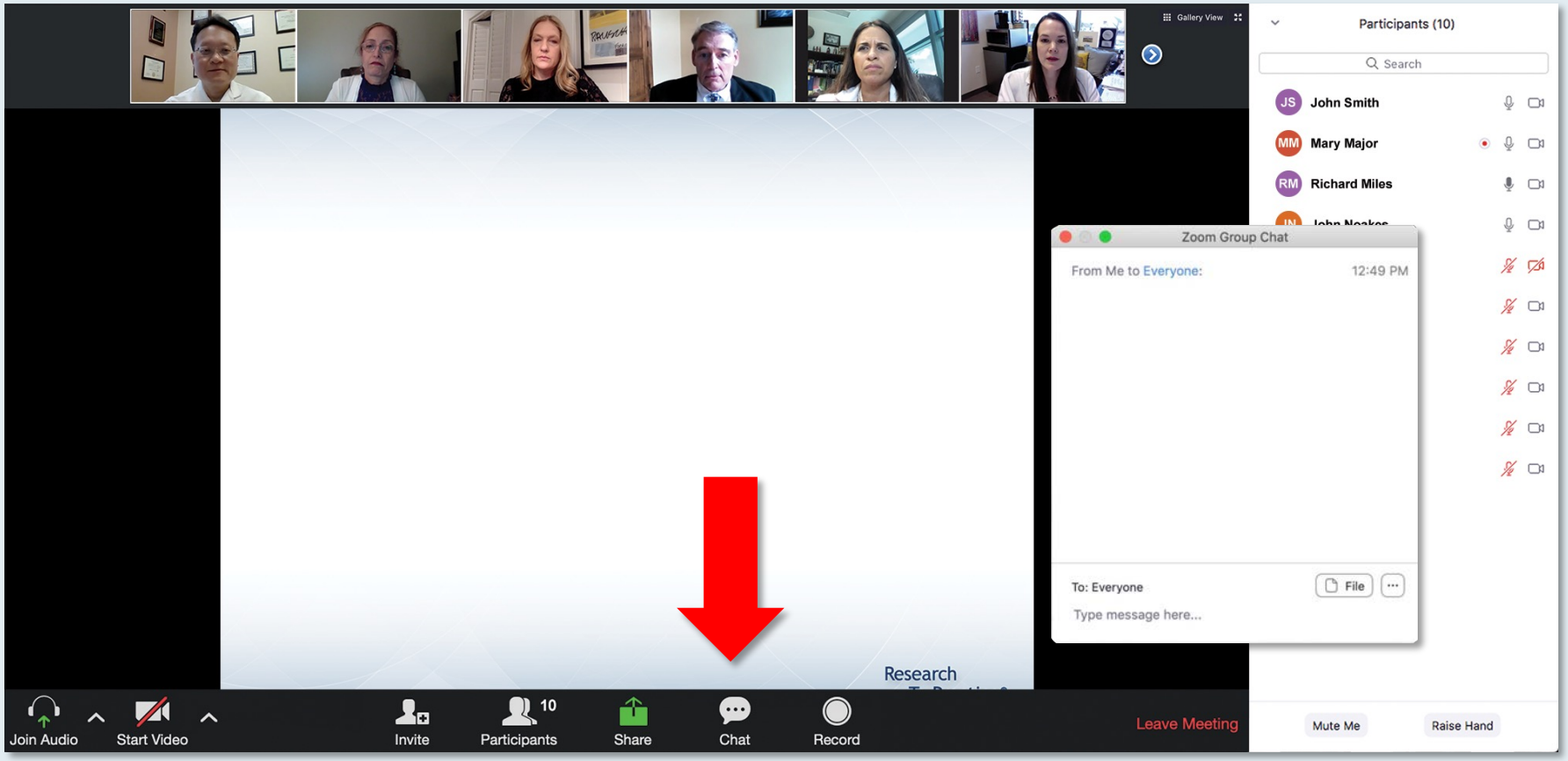
Advisory Committees	AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Daiichi Sankyo Inc
Consulting Agreements	AbbVie Inc, AlphaSights, Arcus Biosciences, ARS Pharmaceuticals, AskGene Pharma, Astellas, AstraZeneca Pharmaceuticals LP, Basilea Pharmaceutica Ltd, Bayer HealthCare Pharmaceuticals, BeOne, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Cencora, Daiichi Sankyo Inc, eChina Health, Eisai Inc, Geneos Therapeutics, Gilead Sciences Inc, GSK, Guardant Health, HC Wainwright & Co, Health Advances, Imugene, Inspirna, Lilly, Lynx Health, Merck, Merck Serono, Mersana Therapeutics Inc, PeerMD, Pfizer Inc, Sanofi, Seagen Inc, Suzhou Liangyihui Network Technology Co Ltd, Zymeworks Inc
Contracted Research	Arcus Biosciences, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Genentech, a member of the Roche Group, Inspirna, Lilly, Merck, Transcenta
Stock Options — Private Companies	Inspirna
Nonrelevant Financial Relationships	Clinical Care Options, Cycle for Survival, Debbie’s Dream Foundation, ED Medresources Inc, Fred's Team, HMP, i3Health, Imedex, Mashup Media LLC, Master Clinician Alliance, MJH Life Sciences, National Cancer Institute, OncoDaily (stock options), Paradigm Medical Communications, PeerView, Physician Education Resource (PER), Stand Up 2 Cancer, Talem Health, TotalCME, US Department of Defense, Veda Life Sciences Inc (stock options), WebMD

RTP
RESEARCH TO PRACTICE

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.

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

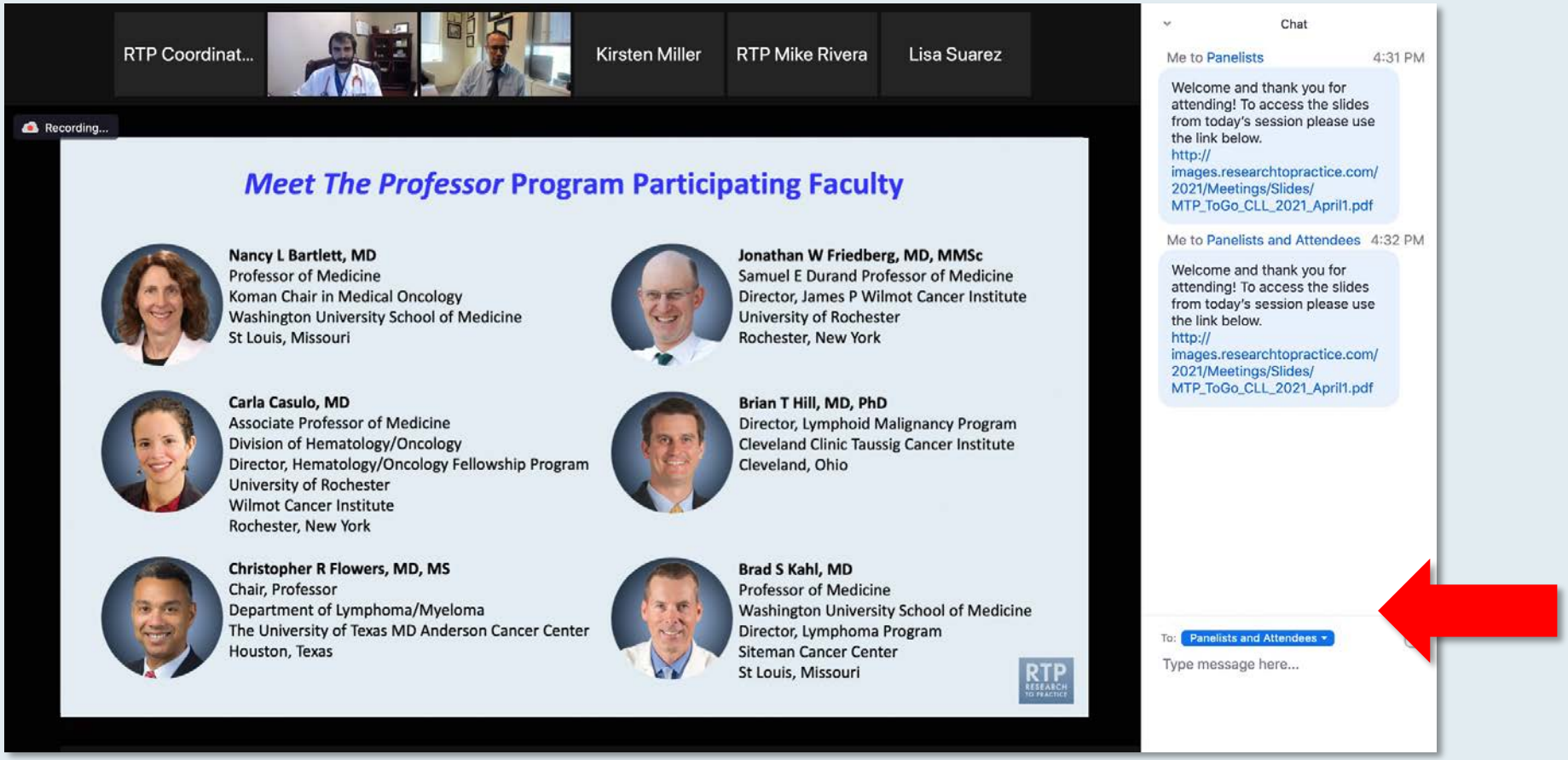


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

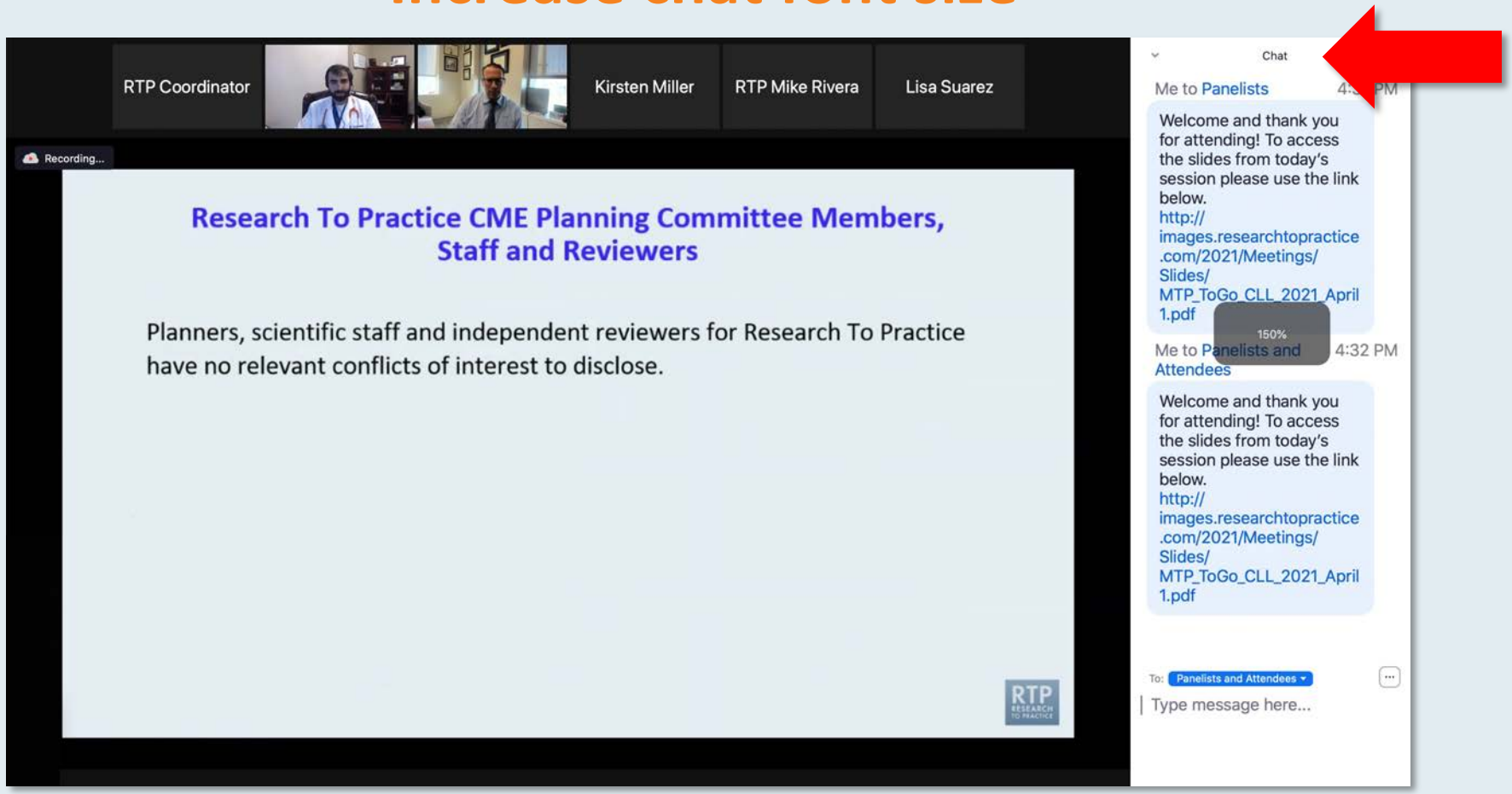


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

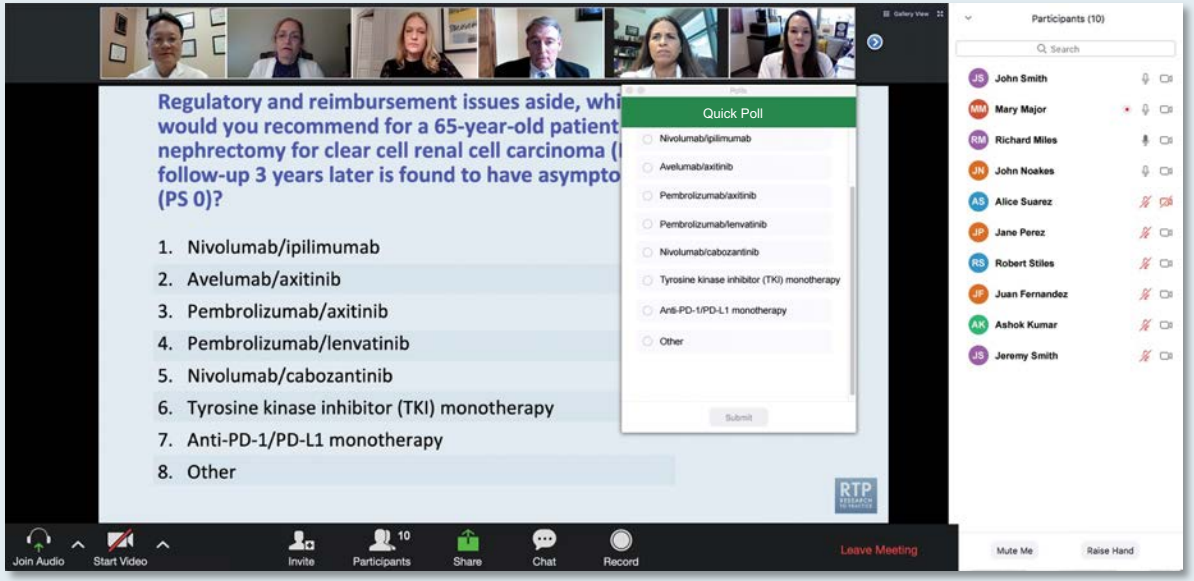
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

Advanced Gastroesophageal Cancers — Expert Perspectives on Actual Patient Cases

DR GEOFFREY Y KU
MEMORIAL SLOAN KETTERING CANCER CENTER

DR ZEV WAINBERG
UCLA SCHOOL OF MEDICINE

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Preventing and Managing Toxicities Associated with Antibody-Drug Conjugates in the Management of Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, November 19, 2025

5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO

Rita Nanda, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Cancer Conference Update: ESMO Congress 2025 — Urothelial Bladder Cancer and Prostate Cancer

A CME/MOC-Accredited Live Webinar

Thursday, November 20, 2025
5:00 PM – 6:00 PM ET

Faculty

Terence Friedlander, MD
Rana R McKay, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Exciting CME Events You Do Not Want to Miss

A Friday Satellite Symposium Series Preceding the 67th ASH Annual Meeting

Friday, December 5, 2025

Acute Myeloid Leukemia
7:30 AM – 9:30 AM ET

Myelofibrosis and Systemic Mastocytosis
3:15 PM – 5:15 PM ET

Chronic Lymphocytic Leukemia
11:30 AM – 1:30 PM ET

Follicular Lymphoma and Diffuse Large B-Cell Lymphoma
7:00 PM – 9:00 PM ET

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss the Optimal Management of Breast Cancer

A 3-Part CME Satellite Symposium Series

Antibody-Drug Conjugates for Metastatic Breast Cancer

Tuesday, December 9, 2025

7:00 PM – 8:30 PM CT

HER2-Positive Breast Cancer

Wednesday, December 10, 2025

7:00 PM – 9:00 PM CT

Endocrine-Based Therapy

Thursday, December 11, 2025

7:00 PM – 9:00 PM CT

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Grand Rounds

CME/MOC-Accredited Interactive Series

November 2025 to April 2026

Two Series

Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Host a 1-hour session at your institution:
Email Meetings@ResearchToPractice.com
or call (800) 233-6153

RTP
RESEARCH
TO PRACTICE

Save The Date

Fifth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us.

Information on how to obtain CME, ABIM MOC and ABS credit will be provided at the conclusion of the activity in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP
RESEARCH
TO PRACTICE

Practical Perspectives: Clinical Investigators Review Actual Cases of Patients with Advanced Gastroesophageal Cancers

A CME/MOC-Accredited Live Webinar

Tuesday, November 18, 2025
5:00 PM – 6:00 PM ET

Faculty

Yelena Y Janjigian, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

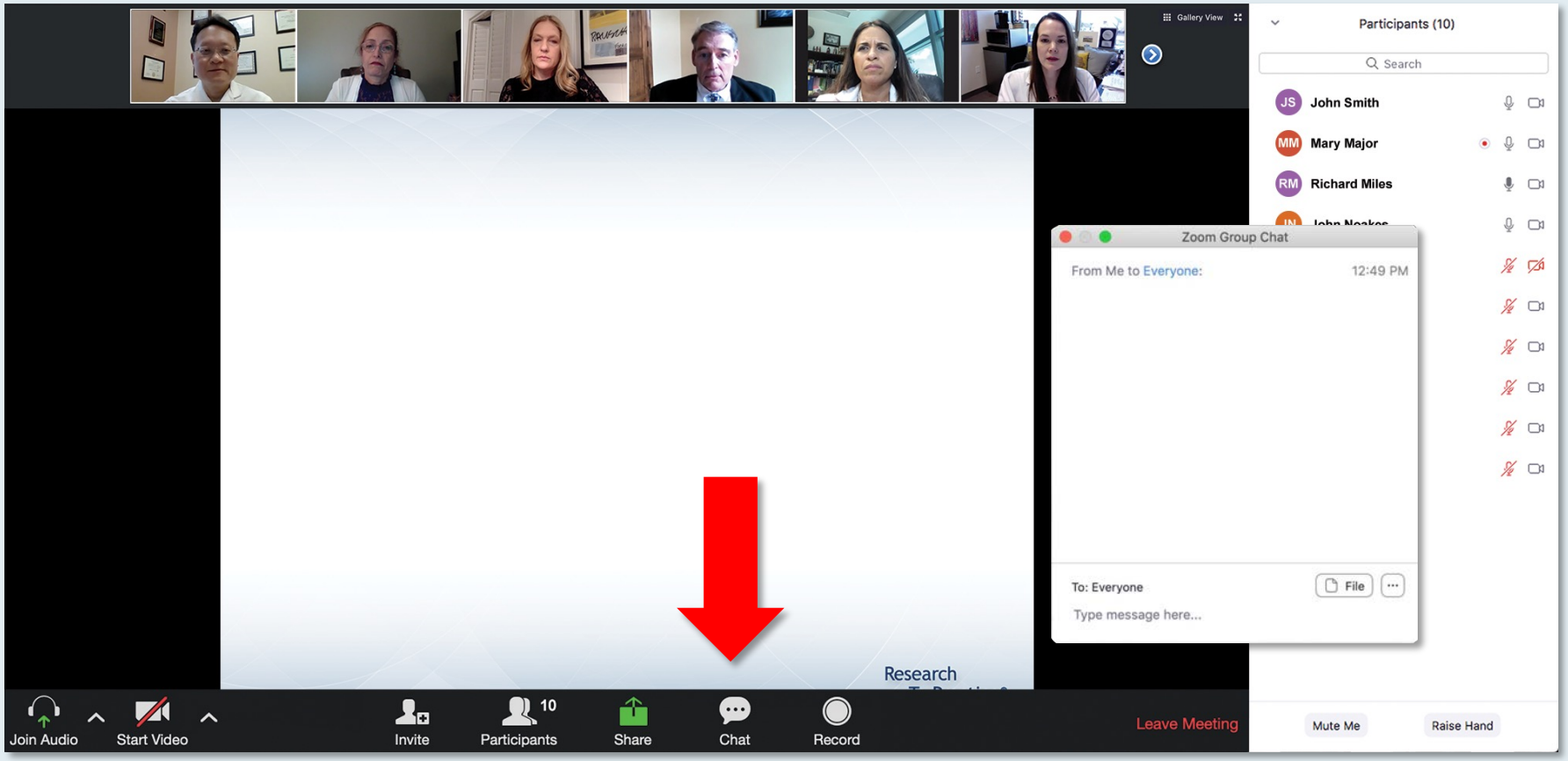
Faculty

Yelena Y Janjigian, MD
Professor and Chief Attending
Gastrointestinal Oncology Service
Memorial Sloan Kettering Cancer Center
New York, New York

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH
TO PRACTICE

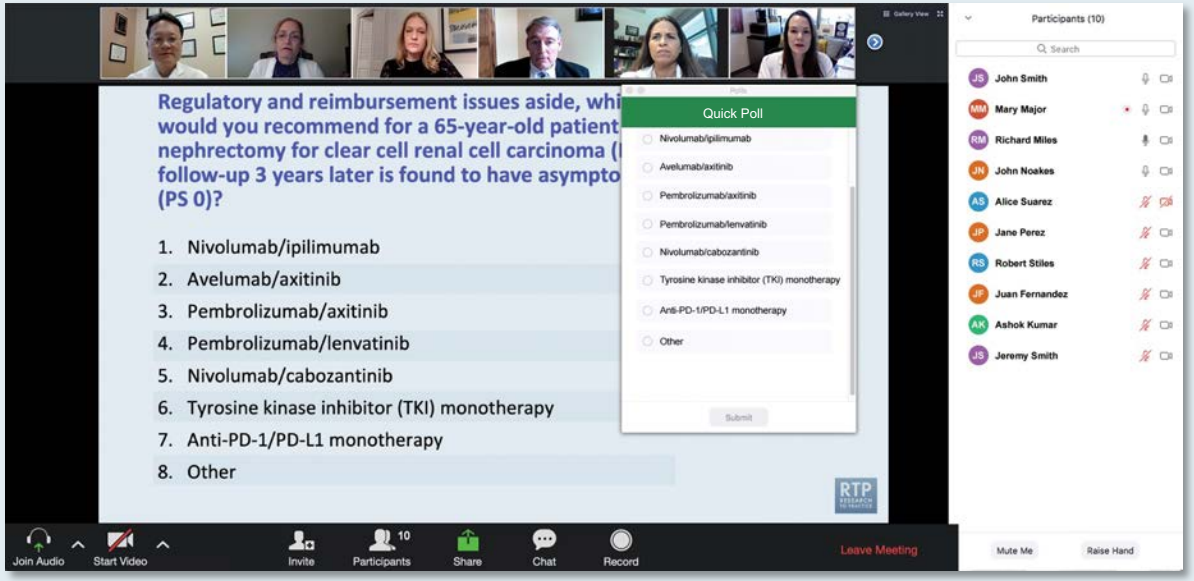
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

Advanced Gastroesophageal Cancers — Expert Perspectives on Actual Patient Cases

DR GEOFFREY Y KU
MEMORIAL SLOAN KETTERING CANCER CENTER

DR ZEV WAINBERG
UCLA SCHOOL OF MEDICINE

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Preventing and Managing Toxicities Associated with Antibody-Drug Conjugates in the Management of Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, November 19, 2025

5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO

Rita Nanda, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Cancer Conference Update: ESMO Congress 2025 — Urothelial Bladder Cancer and Prostate Cancer

A CME/MOC-Accredited Live Webinar

Thursday, November 20, 2025
5:00 PM – 6:00 PM ET

Faculty

Terence Friedlander, MD
Rana R McKay, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Exciting CME Events You Do Not Want to Miss

A Friday Satellite Symposium Series Preceding the 67th ASH Annual Meeting

Friday, December 5, 2025

Acute Myeloid Leukemia
7:30 AM – 9:30 AM ET

Myelofibrosis and Systemic Mastocytosis
3:15 PM – 5:15 PM ET

Chronic Lymphocytic Leukemia
11:30 AM – 1:30 PM ET

Follicular Lymphoma and Diffuse Large B-Cell Lymphoma
7:00 PM – 9:00 PM ET

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss the Optimal Management of Breast Cancer

A 3-Part CME Satellite Symposium Series

Antibody-Drug Conjugates for Metastatic Breast Cancer

Tuesday, December 9, 2025

7:00 PM – 8:30 PM CT

HER2-Positive Breast Cancer

Wednesday, December 10, 2025

7:00 PM – 9:00 PM CT

Endocrine-Based Therapy

Thursday, December 11, 2025

7:00 PM – 9:00 PM CT

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Grand Rounds

CME/MOC-Accredited Interactive Series

November 2025 to April 2026

Two Series

Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Host a 1-hour session at your institution:
Email Meetings@ResearchToPractice.com
or call (800) 233-6153

RTP
RESEARCH
TO PRACTICE

Save The Date

Fifth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

Practical Perspectives: Clinical Investigators Review Actual Cases of Patients with Advanced Gastroesophageal Cancers

A CME/MOC-Accredited Live Webinar

Tuesday, November 18, 2025
5:00 PM – 6:00 PM ET

Faculty

Yelena Y Janjigian, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Dr Janjigian — Disclosures

Advisory Committees	AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Daiichi Sankyo Inc
Consulting Agreements	AbbVie Inc, AlphaSights, Arcus Biosciences, ARS Pharmaceuticals, AskGene Pharma, Astellas, AstraZeneca Pharmaceuticals LP, Basilea Pharmaceutica Ltd, Bayer HealthCare Pharmaceuticals, BeOne, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Cencora, Daiichi Sankyo Inc, eChina Health, Eisai Inc, Geneos Therapeutics, Gilead Sciences Inc, GSK, Guardant Health, HC Wainwright & Co, Health Advances, Imugene, Inspirna, Lilly, Lynx Health, Merck, Merck Serono, Mersana Therapeutics Inc, PeerMD, Pfizer Inc, Sanofi, Seagen Inc, Suzhou Liangyihui Network Technology Co Ltd, Zymeworks Inc
Contracted Research	Arcus Biosciences, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Genentech, a member of the Roche Group, Inspirna, Lilly, Merck, Transcenta
Stock Options — Private Companies	Inspirna
Nonrelevant Financial Relationships	Clinical Care Options, Cycle for Survival, Debbie’s Dream Foundation, ED Medresources Inc, Fred's Team, HMP, i3Health, Imedex, Mashup Media LLC, Master Clinician Alliance, MJH Life Sciences, National Cancer Institute, OncoDaily (stock options), Paradigm Medical Communications, PeerView, Physician Education Resource (PER), Stand Up 2 Cancer, Talem Health, TotalCME, US Department of Defense, Veda Life Sciences Inc (stock options), WebMD

RTP
RESEARCH TO PRACTICE

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Agendia Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeOne, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celcuity, Clovis Oncology, Coherus BioSciences, Corcept Therapeutics Inc, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Helsinn Therapeutics (US) Inc, Hologic Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Pharma America, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, and Merck.

Research To Practice CME Planning Committee Members, Staff and Reviewers

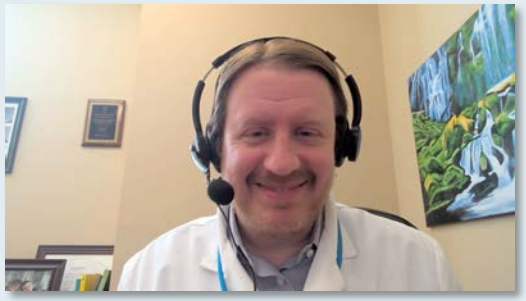
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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.

RTP
RESEARCH
TO PRACTICE

Contributing General Medical Oncologists

Susmitha Apuri, MD
Florida Cancer Specialists
Lutz, Florida



Brian P Mulherin, MD
Hematology Oncology
of Indiana
Indianapolis, Indiana

Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida

Sean Warsch, MD
Messino Cancer Centers
Asheville, North Carolina

Stephen "Fred" Divers, MD
American Oncology Network
Hot Springs, Arkansas

Jennifer Yannucci, MD
Low Country Cancer Care
Savannah, Georgia

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

RTP
RESEARCH
TO PRACTICE

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	Dr Brenner – 86-year-old man
■ Data Review: HER2-positive GE cancer	
Case 4	Dr Mulherin – 82-year-old woman
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	Dr Apuri – 82-year-old man
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	Dr Warsch – 74-year-old man
■ Data Review: CLDN18.2-positive GE cancer	

RTP
RESEARCH
TO PRACTICE

Sequence of Approvals of HER2-Targeted Agents and Regimens in Oncology: ATWT

Breast Cancer

- Trastuzumab
- Lapatinib
- Pertuzumab
- T-DM1
- Neratinib
- Tucatinib/trastuzumab/capecitabine
- Trastuzumab deruxtecan
- Margetuximab

Lung Cancer

- Trastuzumab deruxtecan
- **Zongertinib**

Colorectal Cancer

- Tucatinib/trastuzumab
- Trastuzumab deruxtecan

Gastroesophageal Cancers

- Trastuzumab
- Trastuzumab deruxtecan

Biliary Tract Cancers

- Trastuzumab deruxtecan
- Zanidatamab

RTP RESEARCH TO PRACTICE

Positive Topline Results Announced from the Phase III HERIZON-GEA-01 Trial of First-Line Zanidatamab Combinations for HER2-Positive Locally Advanced or Metastatic GE Adenocarcinoma

Press Release: November 17, 2025

Positive top-line results were announced from the Phase III HERIZON-GEA-01 trial evaluating zanidatamab-hrii in combination with chemotherapy, with or without the PD-1 inhibitor tislelizumab, as first-line treatment for HER2-positive locally advanced or metastatic GE adenocarcinoma.

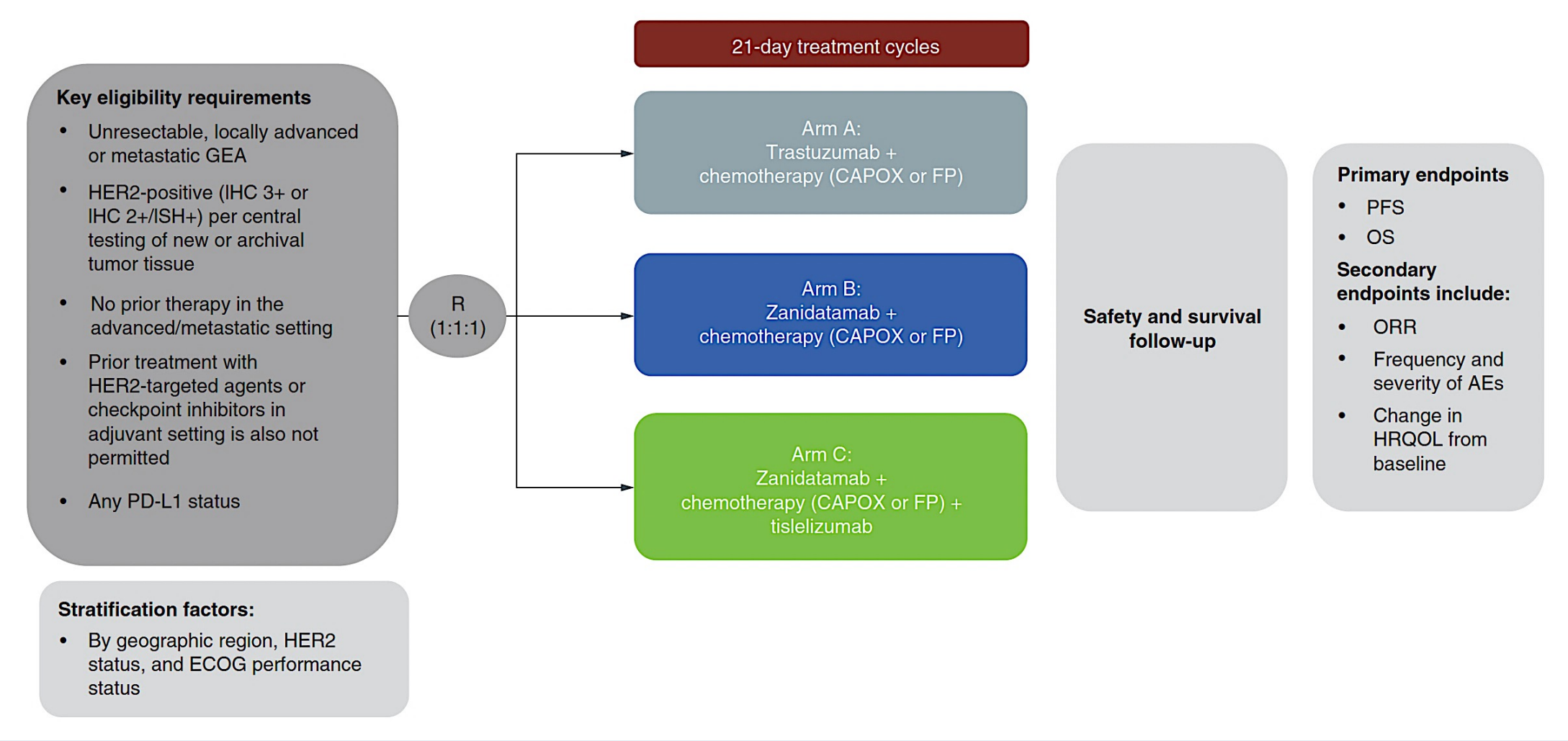
Both zanidatamab with chemotherapy and zanidatamab with tislelizumab and chemotherapy demonstrated highly statistically significant and clinically meaningful improvements in progression-free survival (PFS) compared to the control arm, trastuzumab with chemotherapy.

Zanidatamab with tislelizumab and chemotherapy also demonstrated clinically meaningful and statistically significant improvements in overall survival (OS), and zanidatamab with chemotherapy demonstrated a clinically meaningful effect with a strong trend toward statistical significance for OS. The trial is ongoing with an additional planned OS interim analysis for zanidatamab with chemotherapy currently expected in mid 2026.

Presentation at a major medical meeting in the first quarter of 2026 and for publication in a peer-reviewed journal is planned, as is rapid submission for adoption in the National Comprehensive Cancer Network® Guidelines (NCCN Guidelines®).

https://investor.jazzpharma.com/news-releases/news-release-details/positive-herizon-gea-01-phase-3-results-support-ziiherar

HERIZON-GEA-01: A Phase III Study of Zanidatamab with Chemotherapy with or without Tislelizumab for First-Line Treatment of HER2-Positive GEJ Cancer



Tabernero J et al. *Future Oncol* 2022;18(29):3255-66.

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	Dr Brenner – 86-year-old man
■ Data Review: HER2-positive GE cancer	
Case 4	Dr Mulherin – 82-year-old woman
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	Dr Apuri – 82-year-old man
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	Dr Warsch – 74-year-old man
■ Data Review: CLDN18.2-positive GE cancer	

RTP
RESEARCH
TO PRACTICE

Case Presentation: 60-year-old man with PMH of Barrett's esophagus who presents with HER2-positive metastatic esophageal adenocarcinoma (PD-L1 CPS 3)

Dr Jennifer Yannucci (Savannah, Georgia)

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	Dr Brenner – 86-year-old man
■ Data Review: HER2-positive GE cancer	
Case 4	Dr Mulherin – 82-year-old woman
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	Dr Apuri – 82-year-old man
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	Dr Warsch – 74-year-old man
■ Data Review: CLDN18.2-positive GE cancer	

RTP
RESEARCH
TO PRACTICE

Case Presentation: 62-year-old man with multiregimen-recurrent HER2-positive metastatic GEJ adenocarcinoma (CLDN18.2-positive, PD-L1 CPS 0)

Dr Neil Morganstein (Summit, New Jersey)

RTP
RESEARCH
TO PRACTICE

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	**Dr Brenner – 86-year-old man**
■ Data Review: HER2-positive GE cancer	
Case 4	Dr Mulherin – 82-year-old woman
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	Dr Apuri – 82-year-old man
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	Dr Warsch – 74-year-old man
■ Data Review: CLDN18.2-positive GE cancer	

RTP
RESEARCH
TO PRACTICE

Case Presentation: 86-year-old man with HER2-positive esophageal adenocarcinoma and brain metastases s/p first-line FOLFOX/pembrolizumab/trastuzumab

Dr Warren Brenner (Boca Raton, Florida)

RTP
RESEARCH
TO PRACTICE

FDA Amends Gastric Cancer Indication for Pembrolizumab

Press Release: November 7, 2023

"On November 7, 2023, the Food and Drug Administration revised the existing indication of pembrolizumab with trastuzumab, fluoropyrimidine, and platinum-containing chemotherapy for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.

This updated indication, which remains approved under accelerated approval regulations, **restricts its use to patients whose tumors express PD-L1 (CPS ≥ 1)** as determined by an FDA-approved test.

In a recent, prespecified interim analysis of the fully enrolled [KEYNOTE-811] trial (N=698), in a subgroup analysis conducted in patients with PD-L1 CPS <1 (N= 104), the hazard ratio (HR) for OS and PFS were 1.41 (95% CI 0.90, 2.20) and 1.03 (95% CI 0.65, 1.64), respectively."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-amends-pembrolizumabs-gastric-cancer-indication

RTP RESEARCH TO PRACTICE

FDA Approves Pembrolizumab for HER2-Positive Gastric or GE Junction Adenocarcinoma Expressing PD-L1 (CPS ≥1)

Press Release: March 19, 2025

"The Food and Drug Administration granted traditional approval to pembrolizumab with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥1).

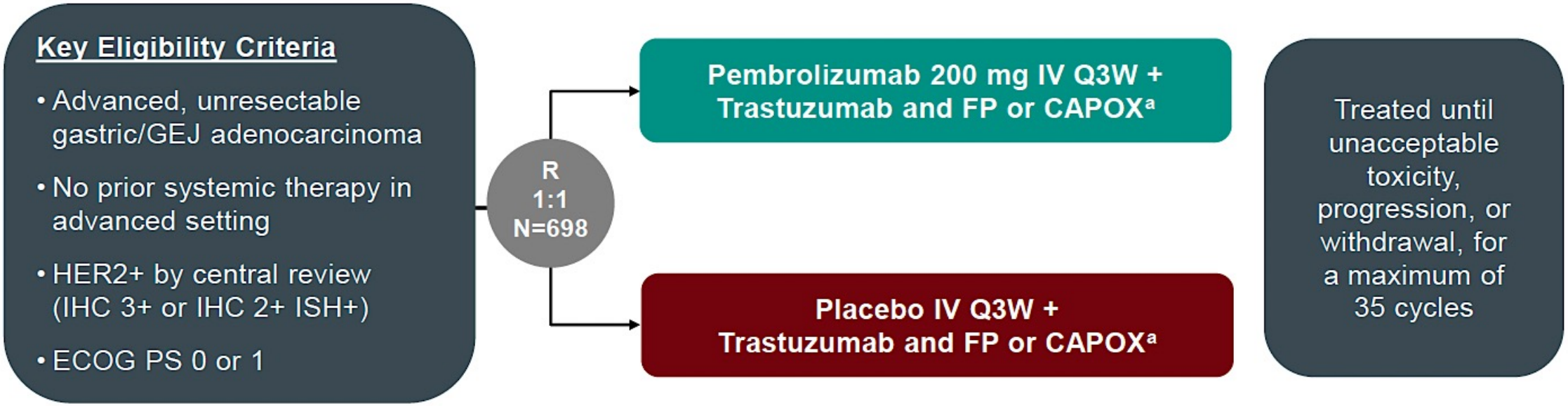
Pembrolizumab previously received accelerated approval for this indication on May 5, 2021.

Efficacy was evaluated in KEYNOTE-811 (NCT03615326), a multicenter, randomized, double-blind, placebo-controlled trial enrolling 698 patients with HER2-positive advanced gastric or GEJ adenocarcinoma not previously treated with systemic therapy for metastatic disease.

In patients with tumors that were PDL1 CPS≥1, median PFS was 10.9 months (95% CI: 8.5, 12.5) in the pembrolizumab arm and 7.3 months (95% CI: 6.8, 8.4) in the placebo arm (Hazard ratio [HR] 0.72 [95% CI: 0.60, 0.87]). Median OS was 20.1 months (95% CI: 17.9, 22.9) and 15.7 months (95% CI: 13.5, 18.5) in the respective arms (HR 0.79 [95% CI: 0.66, 0.95]."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-her2-positive-gastric-or-gastroesophageal-junction-adenocarcinoma

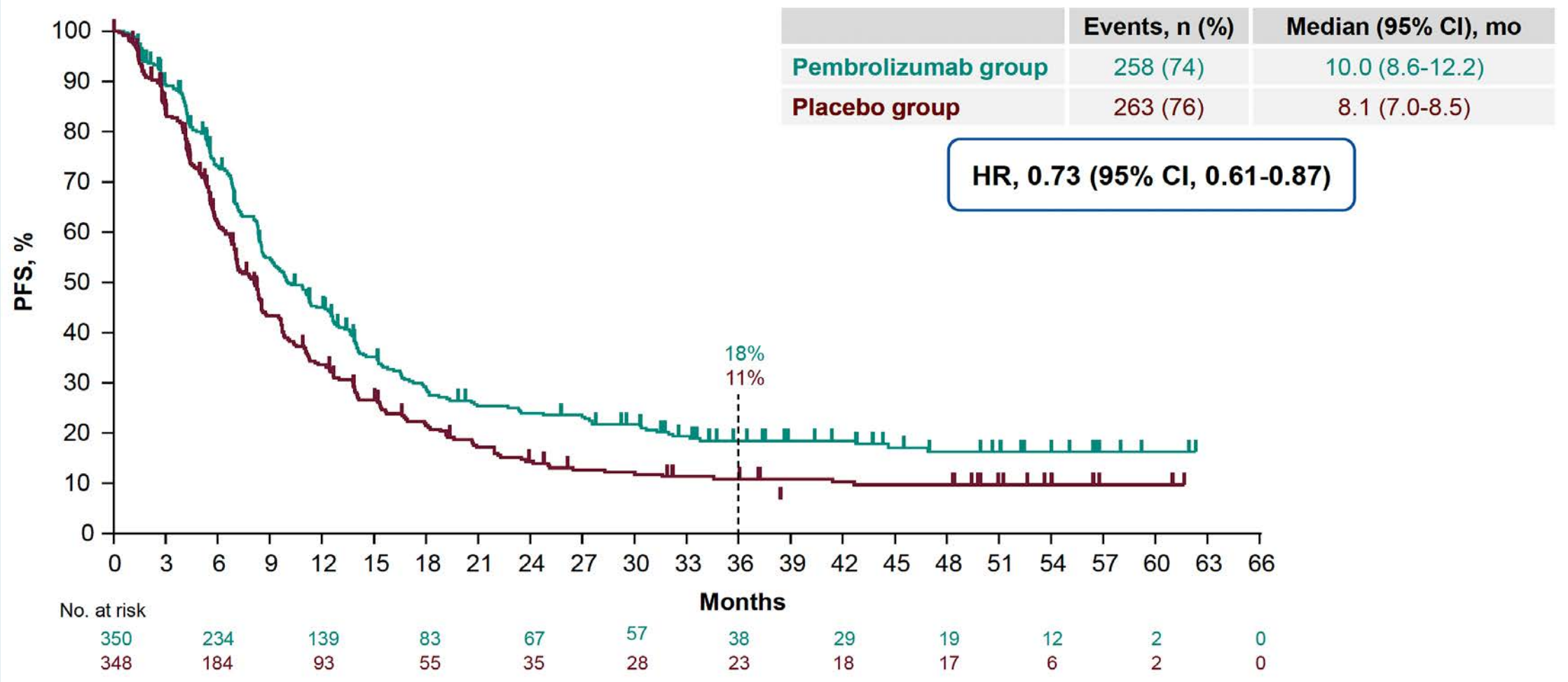
KEYNOTE-811: A Phase III Study of First-Line Pembrolizumab with Trastuzumab and Chemotherapy for HER2-Positive GE Cancers



FP = fluorouracil and cisplatin; CPS = combined positive score; OS = overall survival; PFS = progression-free survival; ORR = objective response rate; DOR = duration of response

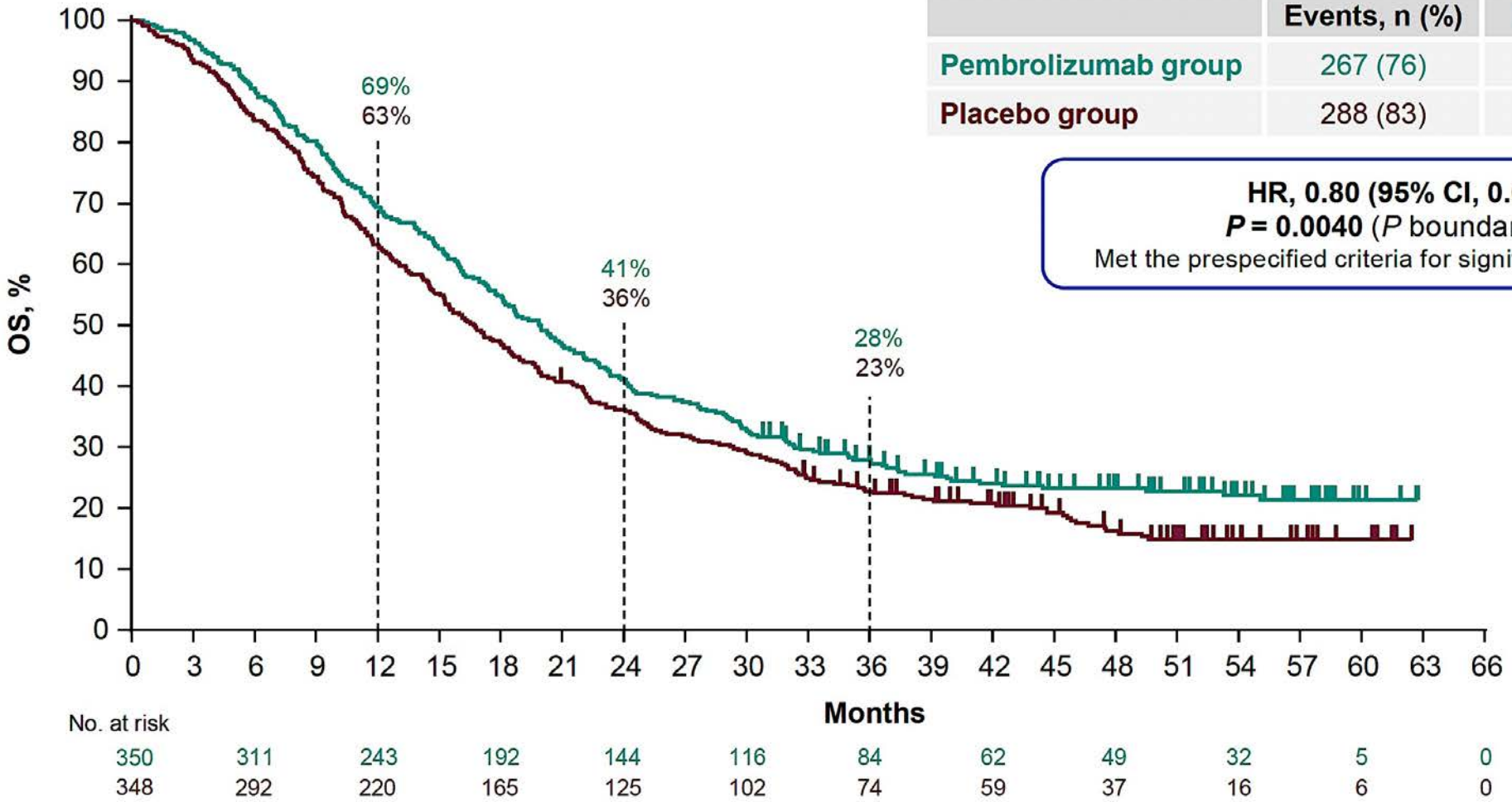
Rha S et al. ESMO Asia 2024;Abstract 128MO.

KEYNOTE-811: Progression-Free Survival (PFS)



Rha S et al. ESMO Asia 2024;Abstract 128MO.

KEYNOTE-811: Overall Survival (OS)



	Events, n (%)	Median (95% CI), mo
Pembrolizumab group	267 (76)	20.0 (17.8-22.1)
Placebo group	288 (83)	16.8 (14.9-18.7)

HR, 0.80 (95% CI, 0.67-0.94);
***P* = 0.0040** (*P* boundary, 0.0201)
Met the prespecified criteria for significance at final analysis

Rha S et al. ESMO Asia 2024;Abstract 128MO.

KEYNOTE-811: Authors' Conclusions

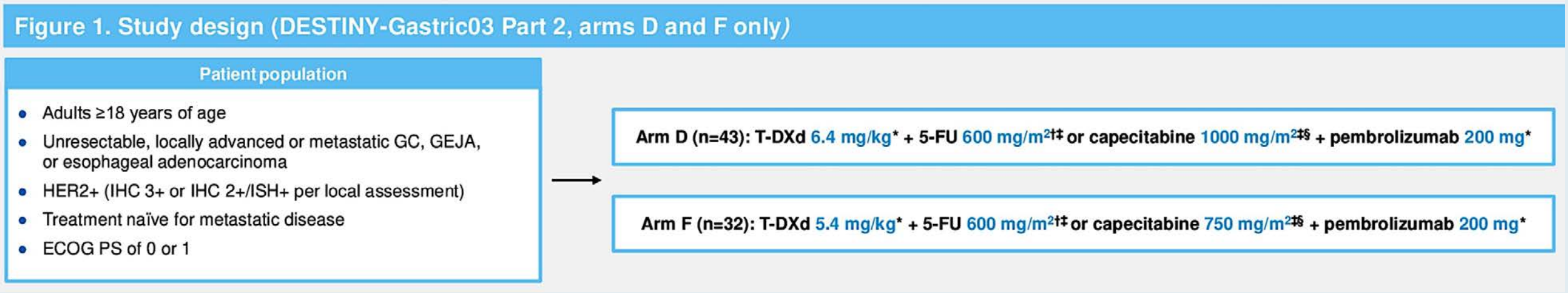
- At FA, first-line pembrolizumab plus trastuzumab and chemotherapy versus placebo plus trastuzumab and chemotherapy provided a statistically significant and clinically meaningful improvement in OS in all patients with unresectable or metastatic HER2-positive gastric/GEJ adenocarcinoma
  - Median, 20.0 versus 16.8 months; HR, 0.80; *P* = 0.004
  - OS was longer in patients with dual HER2 and PD-L1 CPS ≥1 overexpressed tumors
    - Median, 20.1 versus 15.7 months; HR, 0.79 (FA)
- KEYNOTE-811 met prespecified criteria for significance at all end points evaluated in all patients
  - ORR (IA1), PFS (IA2), OS (FA)
- No new safety concerns were identified
- These data support pembrolizumab plus trastuzumab and chemotherapy as first-line therapy in patients with unresectable or metastatic HER2-positive gastric/GEJ adenocarcinoma with PD-L1 CPS ≥1 and confirm this regimen as the standard of care in this setting

FA = final analysis; IA = interim analysis

Rha S et al. ESMO Asia 2024;Abstract 128MO.

DESTINY-Gastric03: A Phase Ib/II Study of First-Line Trastuzumab Deruxtecan (T-DXd) with Pembrolizumab and Fluoropyrimidine for HER2-Positive GEJ Cancer — Arms D and F

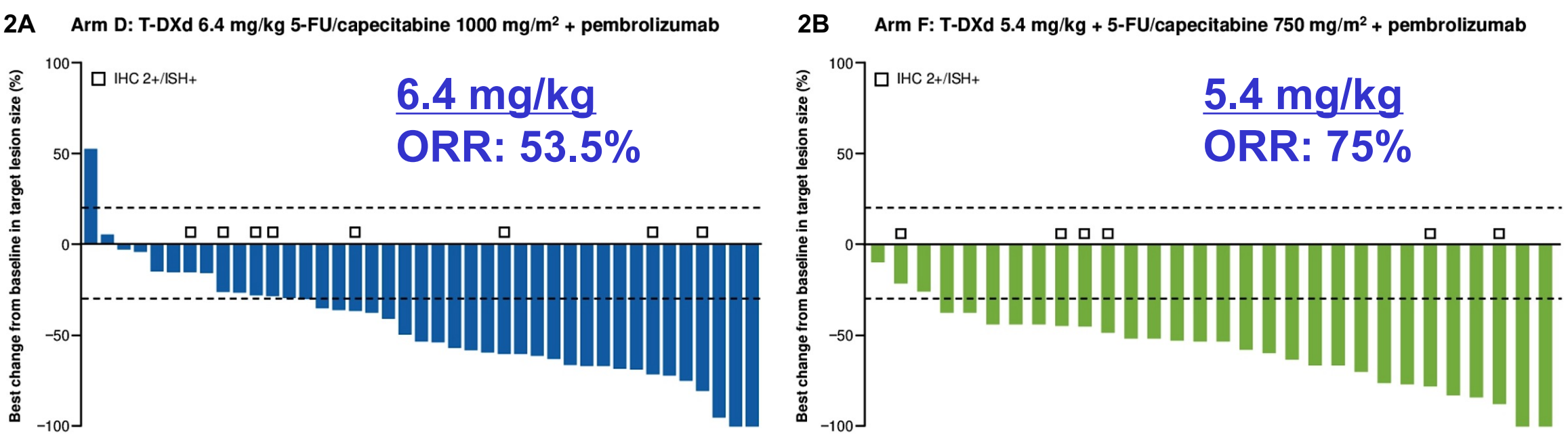
Figure 1. Study design (DESTINY-Gastric03 Part 2, arms D and F only)



GC = gastric cancer; GEJA = gastroesophageal junction adenocarcinoma; 5-FU = 5-fluorouracil

Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract 448.

DESTINY-Gastric03 Arms D and F: Response



- At similar periods of follow up, the confirmed ORR by investigator assessment was 53.5% in the T-DXd 6.4 mg/kg triplet combination arm (**Figure 2A**) and 75.0% in the 5.4 mg/kg triplet combination arm (**Figure 2B**)
  - In the T-DXd 6.4 mg/kg triplet combination arm, the ORR (n/N) was 55.9% (19/34) in patients with IHC 3+ and 44.4% (4/9) in patients with IHC 2+/ISH+
  - In the T-DXd 5.4 mg/kg triplet combination arm, the ORR (n/N) was 73.1% (19/26) in patients with IHC 3+ and 83.3% (5/6) in patients with IHC 2+/ISH+

ORR = objective response rate

Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract 448.

DESTINY-Gastric03: Authors' Conclusions

Conclusions

- T-DXd 6.4 mg/kg with fluoropyrimidine and pembrolizumab demonstrated antitumor activity (confirmed objective response rate [ORR]: 53.5%) in HER2+ GC, GEJA, or esophageal adenocarcinoma; however, it was associated with higher-than-expected toxicity
- At similar median durations of follow up, T-DXd 5.4 mg/kg and reduced-dose fluoropyrimidine with pembrolizumab showed promising early antitumor activity (confirmed ORR: 75.0%) in HER2+ GC, GEJA, or esophageal adenocarcinoma, with a manageable safety profile
- The time-matched analysis showed that lowering the dose of T-DXd to 5.4 mg/kg from 6.4 mg/kg and lowering the starting dose of capecitabine from 1000 mg/m^2 to 750 mg/m^2, improved tolerability of the triplet combination of T-DXd with fluoropyrimidine and pembrolizumab without decreasing the ORR
- These preliminary data provide encouragement for future development of T-DXd with fluoropyrimidine and pembrolizumab as a 1L treatment in HER2+ GC, GEJA, or esophageal adenocarcinoma

Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract 448.

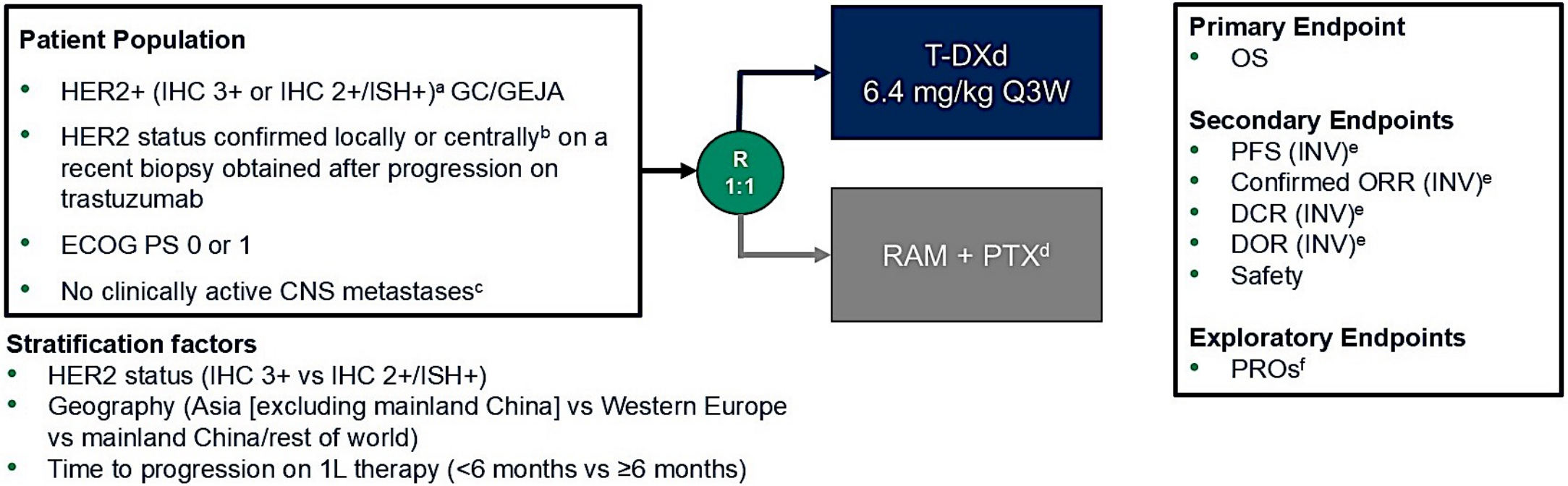
Trastuzumab Deruxtecan (T-DXd) vs Ramucirumab (RAM) + Paclitaxel (PTX) in Second-Line Treatment of Patients (Pts) with Human Epidermal Growth Factor Receptor 2-Positive (HER2+) Unresectable/Metastatic Gastric Cancer (GC) or Gastroesophageal Junction Adenocarcinoma (GEJA): Primary Analysis of the Randomized, Phase 3 DESTINY-Gastric04 Study

Shitara K et al.

ASCO 2025;Abstract LBA4002.

Phase III DESTINY-Gastric04 Study Design

DESTINY-Gastric04: A Global, Multicenter, Randomized, Phase 3 Trial (NCT04704934)

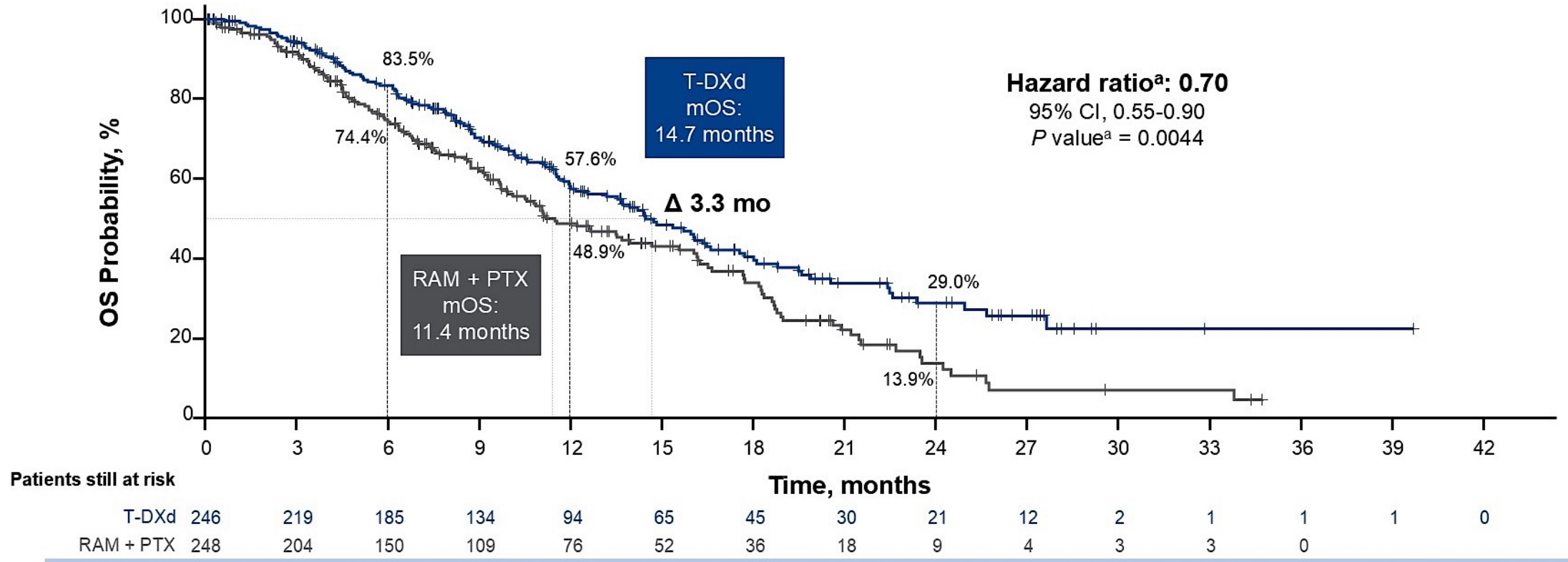


1L, first-line; ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; CNS, central nervous system; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, EuroQol 5-Dimension, 5-Level; FACT-Ga, Functional Assessment of Cancer Therapy-gastric; GC, gastric cancer; GEJA, gastroesophageal junction adenocarcinoma; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; INV, investigator; ISH, in situ hybridization; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; PTX, paclitaxel; Q3W, every 3 weeks; R, randomization; RAM, ramucirumab; RECIST v1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; T-DXd, trastuzumab deruxtecan; VAS, visual analog scale.

[a]As classified by the 2017 ASCO-CAP guidelines for HER2 testing in gastroesophageal adenocarcinoma. [b]Study protocol originally mandated HER2 status be determined centrally but was later amended to allow local determination. [c]Clinically active CNS metastases were defined as being untreated and symptomatic or requiring therapy with corticosteroids or anticonvulsants. Patients with clinically inactive CNS metastases could be enrolled. [d]RAM administered as 8 mg/kg on days 1 and 15 of each 28-day cycle and PTX administered as 80 mg/m^2 on days 1, 8, and 15 of each 28-day cycle. [e]Determined by investigator-based assessment on RECIST v1.1. [f]Based on EORTC EQ-5D-5L VAS and FACT-Ga subscales.

Shitara K et al. ASCO 2025;Abstract LBA4002, Shitara K et al. *N Engl J Med* 2025;393;336-48.

Phase III DESTINY-Gastric04: OS (Primary Endpoint)

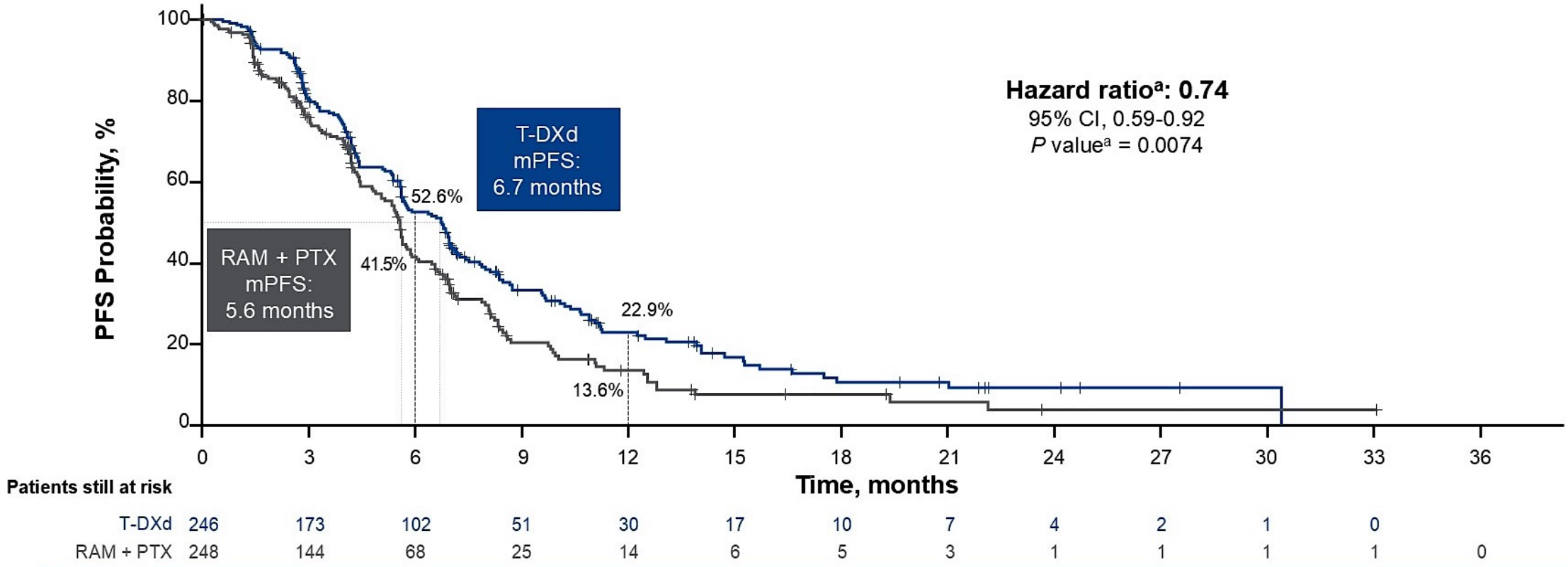


T-DXd demonstrated a statistically significant and clinically meaningful improvement in OS compared with RAM + PTX in HER2+ GC/GEJA, showing a 30% reduction in risk of death

DCO, data cutoff; GC, gastric cancer; GEJA, gastroesophageal junction adenocarcinoma; HER2, human epidermal growth factor receptor 2; mOS, median overall survival; OS, overall survival; PTX, paclitaxel; RAM, ramucirumab; T-DXd, trastuzumab deruxtecan.
At DCO (October 24, 2024), the median duration of OS follow-up was 16.8 months for T-DXd and 14.4 months for RAM + PTX. Boundary for superiority: 2-sided $P < 0.0228$.
[a]Two-sided *P* value from stratified log-rank test and stratified Cox proportional hazards model adjusted for stratification factor: HER2 status (IHC 3+ or IHC 2+/ISH+).

Shitara K et al. ASCO 2025;Abstract LBA4002, Shitara K et al. *N Engl J Med* 2025;393;336-48.

Phase III DESTINY-Gastric04: PFS by Investigator



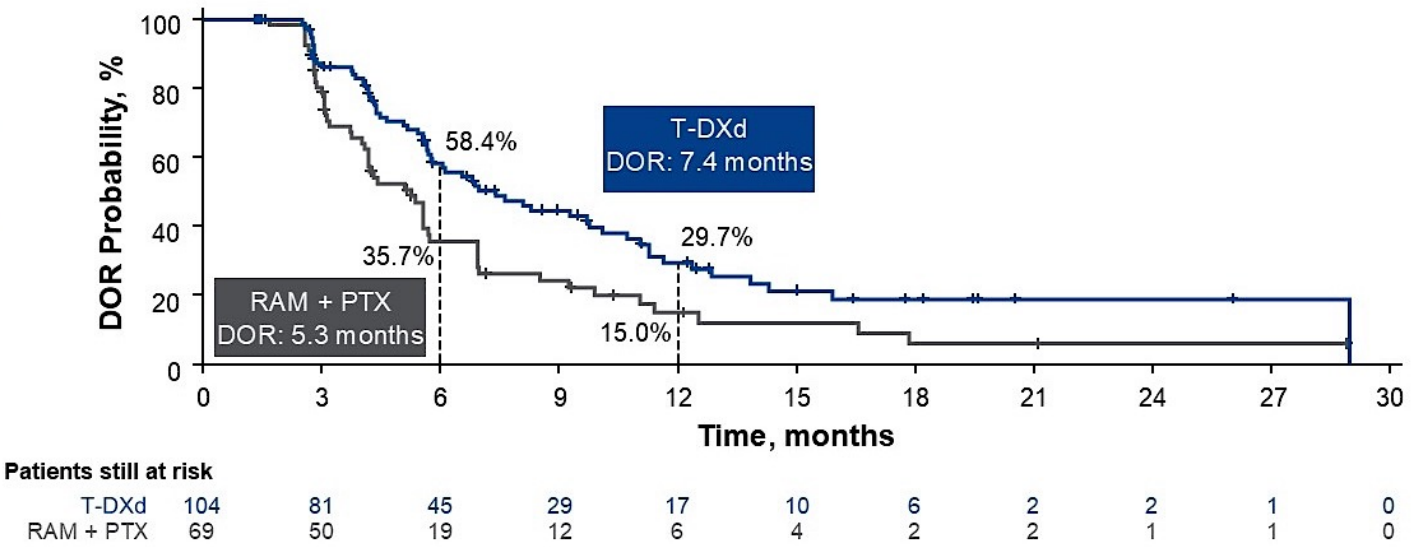
T-DXd demonstrated a statistically significant improvement in PFS compared with RAM + PTX in HER2+ GC/GEJA, showing a 26% reduction in risk of progression or death

GC, gastric cancer; GEJA, gastroesophageal junction adenocarcinoma; HER2, human epidermal growth factor receptor 2; mPFS, median progression-free survival; PFS, progression-free survival; PTX, paclitaxel; RAM, ramucirumab; T-DXd, trastuzumab deruxtecan.
Boundary for superiority: 2-sided $P < 0.0185$.
[a]Two-sided *P* value from stratified log-rank test and stratified Cox proportional hazards model adjusted for stratification factor: HER2 status (IHC 3+ or IHC 2+/ISH+).

Shitara K et al. ASCO 2025;Abstract LBA4002, Shitara K et al. *N Engl J Med* 2025;393;336-48.

Phase III DESTINY-Gastric04: Confirmed ORR, DOR

	T-DXd n = 246	RAM + PTX n = 248
Confirmed ORR (95% CI),[c] %	**44.3 (37.8-50.9)**	**29.1 (23.4-35.3)**
P value[d]	0.0006	
Difference (95% CI),[e] %	15.1 (6.1-24.2)	
DOR, median (95% CI), mo	**7.4 (5.7-10.1)**	**5.3 (4.1-5.7)**
DCR (95% CI), %	**91.9 (87.7-95.1)**	**75.9 (70.0-81.2)**
Confirmed BOR, n (%)		
CR[f]	7 (3.0)	3 (1.3)
PR	97 (41.3)	66 (27.8)
SD[g]	112 (47.7)	111 (46.8)
PD	13 (5.5)	22 (9.3)
NE	6 (2.6)	35 (14.8)



The confirmed ORR was 15.1% greater with T-DXd compared with RAM + PTX (*P* = 0.0006), with longer DOR

BOR, best overall response; CR, complete response; DCO, data cutoff; DCR, disease control rate; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; NE, not evaluable; PD, progressive disease; PR, partial response; ORR, objective response rate; PTX, paclitaxel; RAM, ramucirumab; SD, stable disease; T-DXd, trastuzumab deruxtecan.
ORR eligible patients are those who were randomly assigned at least 77 days (ie, 2 × 6 weeks − 1 week) before DCO date of interim analyses. Confirmed BOR, ORR, and DCR are calculated using the eligible patients as the denominator.
[a]Based on investigator assessment. [b]Based on ORR eligible patients. [c]Based on Clopper-Pearson method for single proportion. [d]Stratified analysis using the Cochran-Mantel-Haenszel test adjusted for stratification factor: HER2 status (IHC 3+ or IHC 2+/ISH+). [e]2-sided 95% CI for the difference in ORR is based on Wald method using continuity correction. [f]CR patients without target lesions at baseline were included. [g]Non-CR/non-PD patients without target lesions at baseline were included.

Shitara K et al. ASCO 2025;Abstract LBA4002, Shitara K et al. *N Engl J Med* 2025;393;336-48.

Phase III DESTINY-Gastric04: AEs of Special Interest

Adjudicated drug-related ILD/pneumonitis

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 244)	7 (2.9)	26 (10.7)	1 (0.4)	0	0	34 (13.9)
RAM + PTX (n = 233)	0	0	2 (0.9)	0	1 (0.4)	3 (1.3)

Left ventricular dysfunction[a]

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 244)	0	3 (1.2)	3 (1.2)	0	0	6 (2.5)
RAM + PTX (n = 233)	2 (0.9)	2 (0.9)	0	0	0	4 (1.7)

- ILD/pneumonitis events in the T-DXd arm were mainly low-grade, with no grade 4 or 5 events
  - Adjudicated drug-related ILD/pneumonitis occurred in 34 patients (13.9%) treated with T-DXd and 3 patients (1.3%) treated with RAM + PTX
- Incidence of left ventricular dysfunction was similar across both arms

AE, adverse event; ILD, interstitial lung disease; LVEF, left ventricular ejection fraction; PTX, paclitaxel; RAM, ramucirumab; T-DXd, trastuzumab deruxtecan.
[a]Includes preferred terms of ejection fraction decreased, cardiac failure, cardiac failure acute, cardiac failure congestive, and left ventricular dysfunction.

Shitara K et al. ASCO 2025;Abstract LBA4002, Shitara K et al. *N Engl J Med* 2025;393:336-48.

DESTINY-Gastric04: Authors' Conclusions

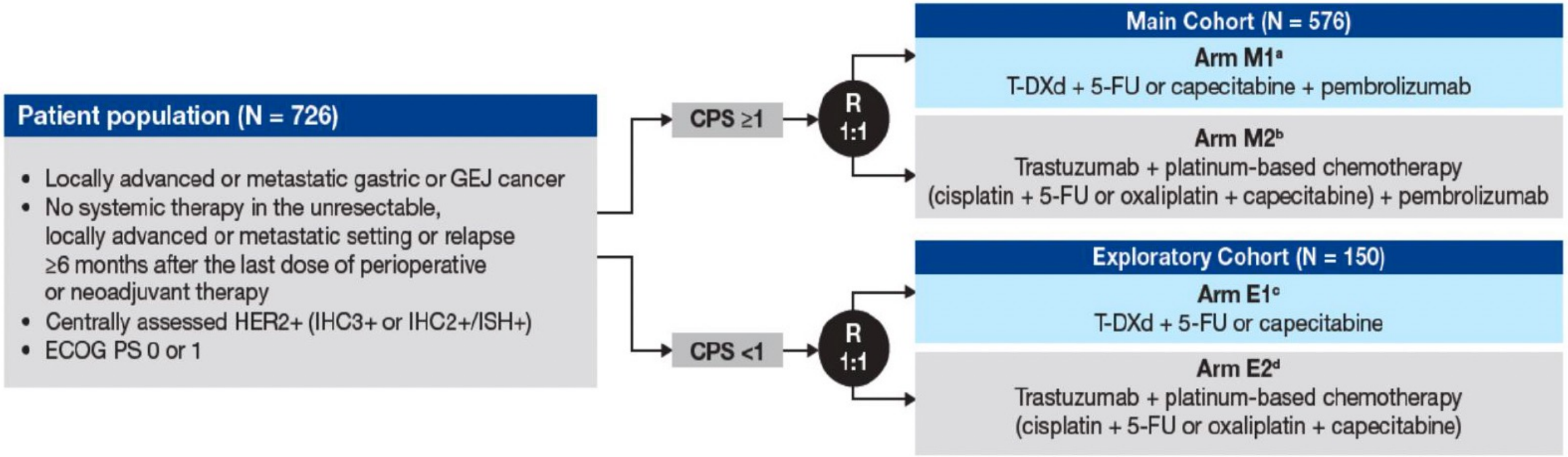
- **T-DXd demonstrated a statistically significant and clinically meaningful improvement in OS** compared with RAM + PTX in patients with HER2+ metastatic GC/GEJA in the 2L setting (median, 14.7 vs 11.4 months, respectively, with 30% reduction in risk of death: **HR, 0.70 [*P* = 0.0044]**)
- **Improvement in PFS, confirmed ORR, DCR,** and **DOR** was also observed **with T-DXd**
- The toxicity profile of T-DXd 6.4 mg/kg was generally manageable and was consistent with its known safety profile, with **no new safety signals identified**
  - Patient-reported QOL was maintained with T-DXd; scores were comparable in the T-DXd versus RAM + PTX arm
- Results support further evaluation of T-DXd in an earlier line setting

DESTINY-Gastric04 confirms T-DXd as the global 2L standard-of-care therapy for patients with HER2+ metastatic GC/GEJA

2L, second-line; DCR, disease control rate; DOR, duration of response; GC, gastric cancer; GEJA, gastroesophageal junction adenocarcinoma; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; ORR, objective response rate; OS, overall survival, PFS, progression-free survival; PTX, paclitaxel; QOL, quality of life; RAM, ramucirumab; T-DXd, trastuzumab deruxtecan.

Shitara K et al. ASCO 2025;Abstract LBA4002.

Phase III DESTINY-Gastric05



[a]T-DXd 5.4 mg/kg Q3W on day 1 plus 5-FU 600 mg/m²/day IV on days 1 to 5 or capecitabine 750 mg/m² PO BID on days 1 to 14 plus pembrolizumab 200 mg IV Q3W on day 1.

[b]Trastuzumab loading dose of 8 mg/kg IV followed by 6 mg/kg IV Q3W plus platinum-based chemotherapy (cisplatin 80 mg/m²/day IV on day 1 plus 5-FU 800 mg/m²/day IV on days 1 to 5 or oxaliplatin 130 mg/m²/day IV on day 1 plus capecitabine 1000 mg/m² PO BID on days 1 to 14) plus pembrolizumab 200 mg IV Q3W on day 1.

[c]T-DXd 5.4 mg/kg IV Q3W on day 1 plus 5-FU 600 mg/m²/day IV on days 1 to 5 or capecitabine 750 mg/m² PO BID on days 1 to 14.

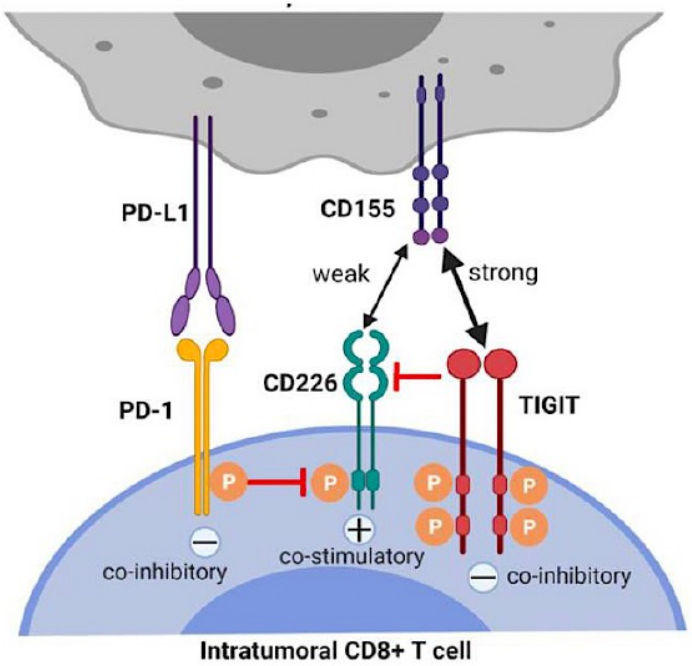
[d]Trastuzumab loading dose of 8 mg/kg IV followed by 6 mg/kg IV Q3W plus platinum-based chemotherapy (cisplatin 80 mg/m²/day IV on day 1 plus 5-FU 800 mg/m²/day IV on days 1 to 5 or oxaliplatin 130 mg/m²/day IV on day 1 plus capecitabine 1000 mg/m² PO BID on days 1 to 14).

Courtesy of Manish A Shah, MD

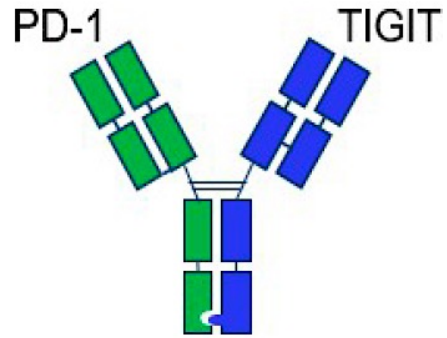
Rilvegostomig: Mechanism of Action

Rilvegostomig (AZD2936) is designed to dual blockade PD-1 and TIGIT pathway

Ligation of PD-1 & TIGIT deliver negative signals to T cells to suppress antitumour immunity



A monovalent bispecific antibody



Affinity to human TIGIT: 15 pM

Affinity to human PD-1: 0.4 nM

Fc isotype: human IgG1-TM (reduced ADCC)

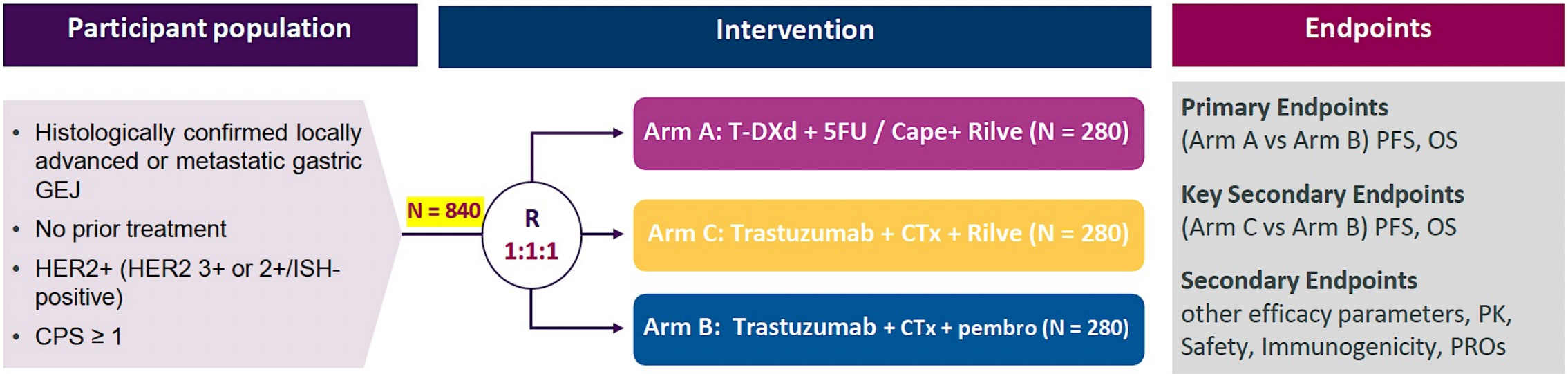
Adapted from Ge Z, et al. *Front Immunol* 2021;12:699895.

ADCC, antibody-dependent cell-mediated cytotoxicity; CD, cluster of differentiation; Fc, fragment crystallizable; IgG1, immunoglobulin G1; ITIM, immunoreceptor tyrosine-based inhibitory motif; nM, nanomolar; PD-1, programmed cell death-1; pM, picomolar; TIGIT, T cell immunoreceptor with Ig and ITIM domains.

Courtesy of Manish A Shah, MD

Phase III ARTEMIDE-Gastric01 Study

Study Design



Stratification Factors

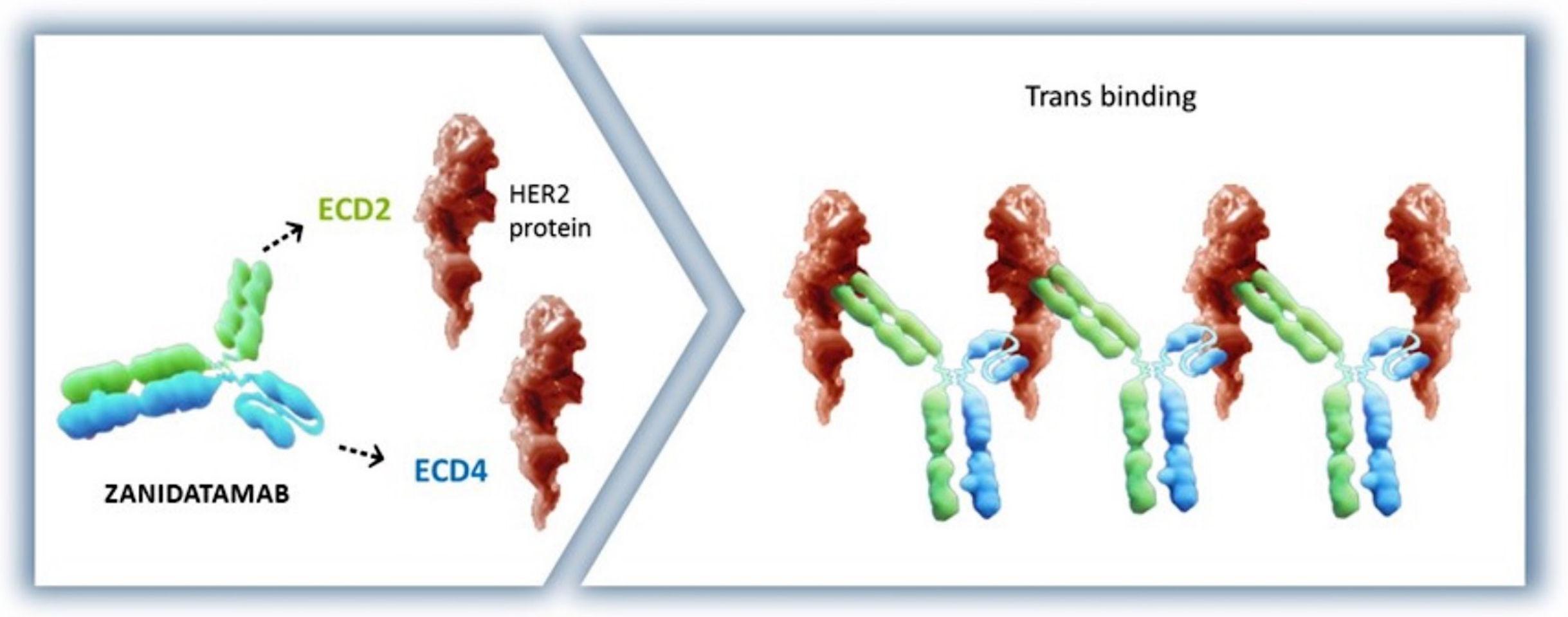
- HER2 status (IHC 3+ vs IHC 2+ plus ISH-positive)
- Geographic region (Japan/South Korea vs Rest of Asia [including China] vs North America/EU/ROW)
- PD L1 expression (CPS ≥ 10 vs CPS < 10).

Treatment arms

Arm A (treatment arm): T-DXd (dosed at 5.4 mg/kg), fluoropyrimidine (capecitabine [Investigators Choice of 750 mg/m2 twice-daily (BD) for 14 days] or 5-FU [600 mg/m2/day over 5 days]), and Rilvegostomig (dosed at 750 mg);
Arm B (control arm): Trastuzumab (8 mg/kg loading dose, followed by 6 mg/kg for subsequent cycles), with Investigators Choice of either cisplatin/5-FU (cisplatin dosed at 80 mg/m2 and 5-FU dosed at 800 mg/m2/day over 5 days) or CapeOx (capecitabine dosed at 1000 mg/m2 BD for 14 days and oxaliplatin dosed at 130 mg/m2) and pembrolizumab (dosed at 200 mg).
Arm C (CoC arm): Trastuzumab and chemotherapy the same as control arm, Rilvegostomig (dosed at 750mg)

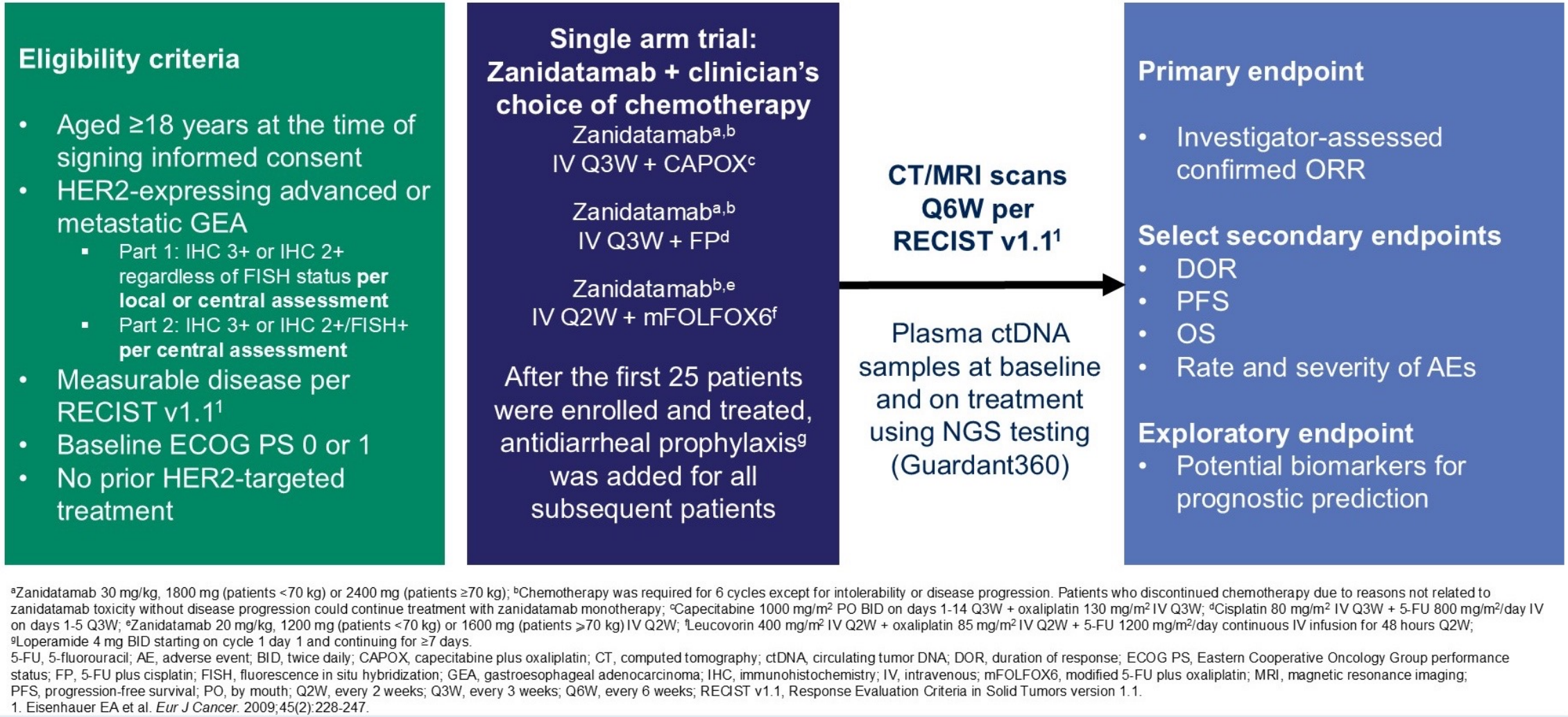
Courtesy of Manish A Shah, MD

Zanidatamab Mechanism of Action



Pant S et al. ASCO 2023;Abstract 4008.

Phase II Study of First-Line Zanidatamab and Chemotherapy for HER2-Positive Advanced GEJ Cancers



[a]Zanidatamab 30 mg/kg, 1800 mg (patients <70 kg) or 2400 mg (patients ≥70 kg); [b]Chemotherapy was required for 6 cycles except for intolerability or disease progression. Patients who discontinued chemotherapy due to reasons not related to zanidatamab toxicity without disease progression could continue treatment with zanidatamab monotherapy; [c]Capecitabine 1000 mg/m^2 PO BID on days 1-14 Q3W + oxaliplatin 130 mg/m^2 IV Q3W; [d]Cisplatin 80 mg/m^2 IV Q3W + 5-FU 800 mg/m^2/day IV on days 1-5 Q3W; [e]Zanidatamab 20 mg/kg, 1200 mg (patients <70 kg) or 1600 mg (patients ⩾70 kg) IV Q2W; [f]Leucovorin 400 mg/m^2 IV Q2W + oxaliplatin 85 mg/m^2 IV Q2W + 5-FU 1200 mg/m^2/day continuous IV infusion for 48 hours Q2W; [g]Loperamide 4 mg BID starting on cycle 1 day 1 and continuing for ≥7 days.

5-FU, 5-fluorouracil; AE, adverse event; BID, twice daily; CAPOX, capecitabine plus oxaliplatin; CT, computed tomography; ctDNA, circulating tumor DNA; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FP, 5-FU plus cisplatin; FISH, fluorescence in situ hybridization; GEA, gastroesophageal adenocarcinoma; IHC, immunohistochemistry; IV, intravenous; mFOLFOX6, modified 5-FU plus oxaliplatin; MRI, magnetic resonance imaging; PFS, progression-free survival; PO, by mouth; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

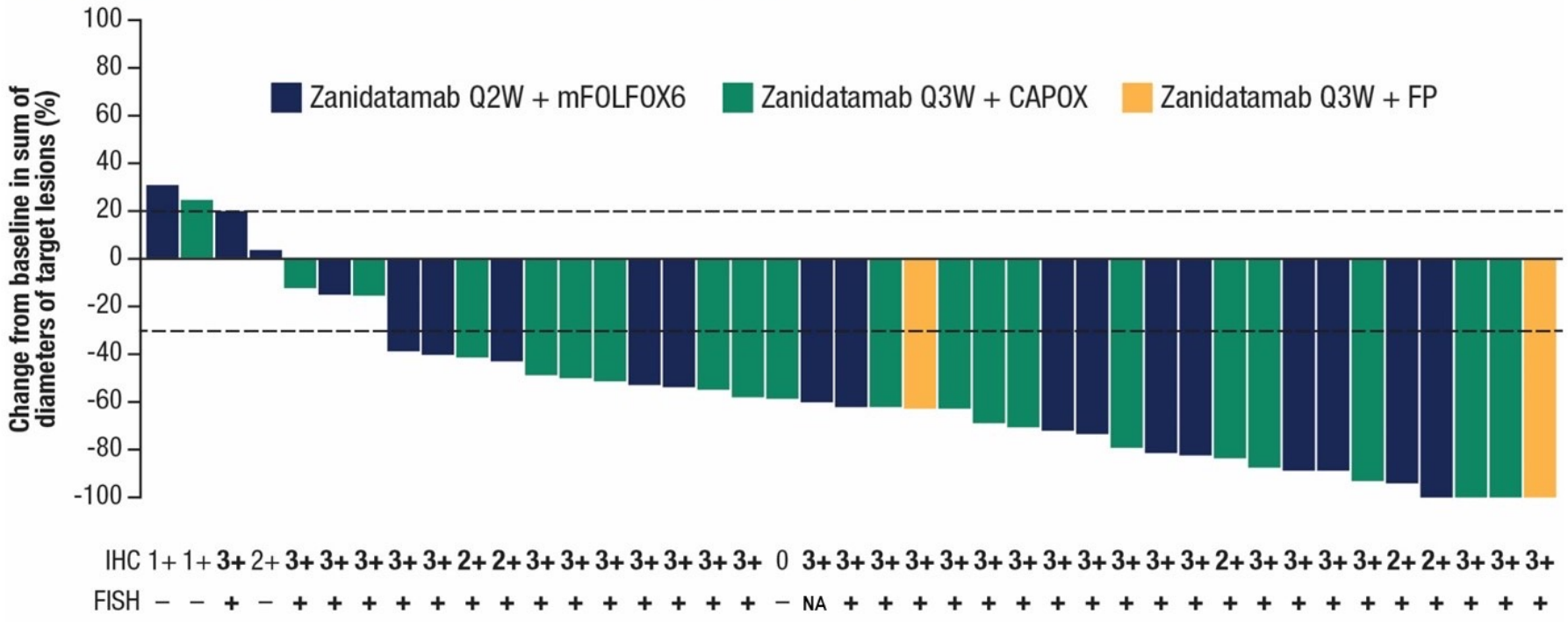
1. Eisenhauer EA et al. *Eur J Cancer*. 2009;45(2):228-247.

Elimova E et al. ASCO 2025;Abstract 4013.

Phase II Study of First-Line Zanidatamab and Chemotherapy for HER2-Positive Advanced GEJ Cancers: Antitumor Activity

- Nearly all response-evaluable patients (90%) had a decrease in target lesions from baseline

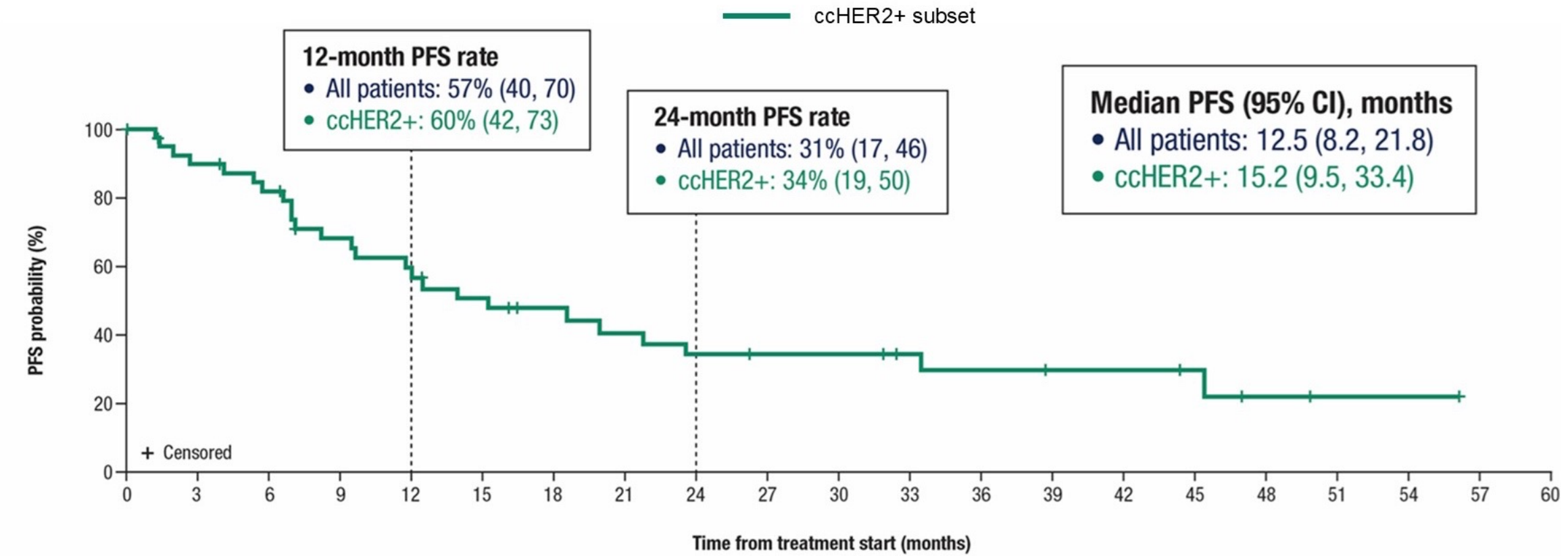
	All Patients (N = 42)	ccHER2+ Subset (n = 37)
cORR		
n (%)	32 (76)	31 (84)
95% CI	60, 88	68, 94
cBOR,[a] n (%)		
CR	3 (7)	3 (8)
PR	29 (69)	28 (76)
SD	5 (12)	4 (11)
PD	5 (12)	2 (5)
DCR[b]		
n (%)	37 (88)	35 (95)
95% CI	74, 96	82, 99
CBR[c]		
n (%)	33 (79)	32 (86)
95% CI	63, 90	72, 96



Response-evaluable patients were those who underwent at least 1 post-baseline response assessment per RECIST v1.1 or discontinued treatment due to clinical progression or death. One patient in the response-evaluable analysis set had a new lesion detected (deemed PD) on an unscheduled visit before the first scheduled tumor scan; however, measurements of this lesion were not available. Hence, this patient was not included in the waterfall plot given the missing post-baseline measurements.
[a]BOR is defined as the best response documented between the date of first dose and the date of investigator-assessed objectively documented progression, the date of subsequent anticancer therapy, any-cause death, loss to follow-up, or study discontinuation, whichever occurred first. Confirmed BOR is the BOR of a CR or PR per RECIST v1.1 confirmed ≥28 days after the first documentation; [b]Disease control was defined as a BOR of SD or confirmed CR or PR; [c]Defined as achieving a BOR of SD, non-CR, or non-PD for ≥24 weeks or confirmed CR or PR.
BOR, best overall response; cBOR, confirmed BOR; CBR, clinical benefit rate; CI, confidence interval; cORR, confirmed ORR; CR, complete response; DCR, disease control rate; PD, progressive disease; PR, partial response; NA, not available; SD, stable disease.

Elimova E et al. ASCO 2025;Abstract 4013.

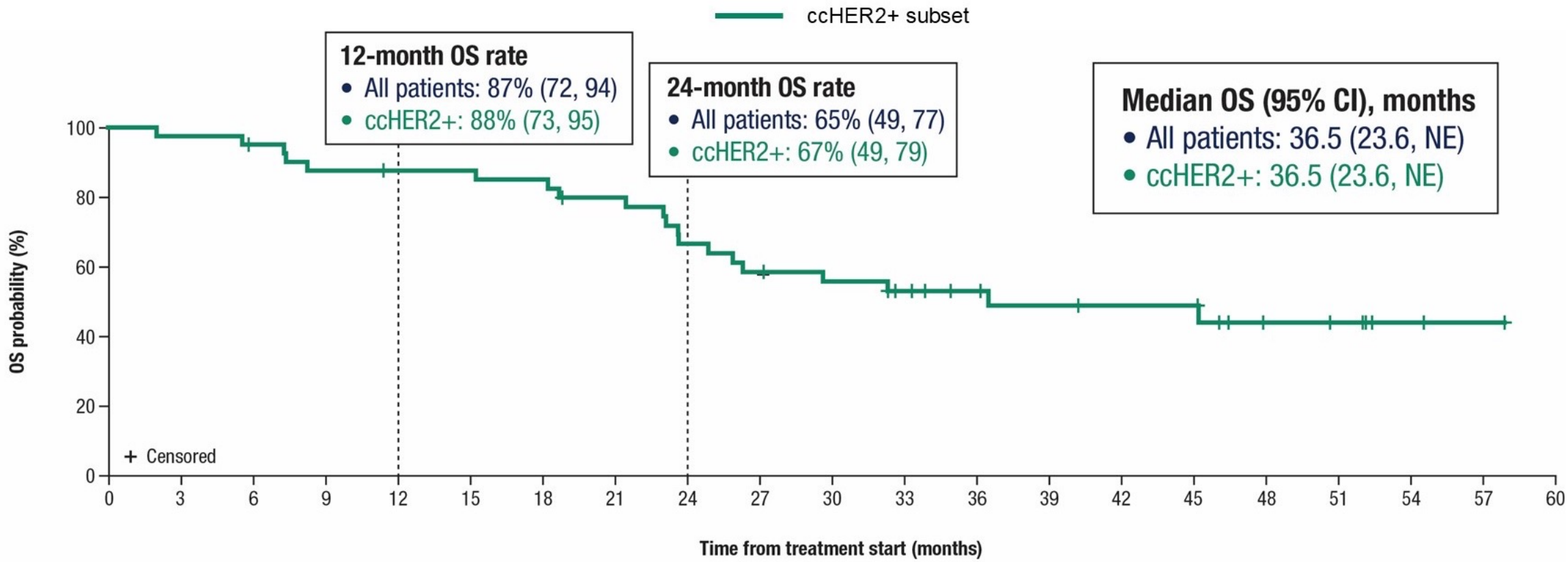
Phase II Study of First-Line Zanidatamab and Chemotherapy for HER2-Positive Advanced GEJ Cancers: PFS



Elimova E et al. ASCO 2025;Abstract 4013, Elimova E et al. Lancet Oncol 2025;26(7):847-59.

RTP RESEARCH TO PRACTICE

Phase II Study of First-Line Zanidatamab and Chemotherapy for HER2-Positive Advanced GEJ Cancers: OS



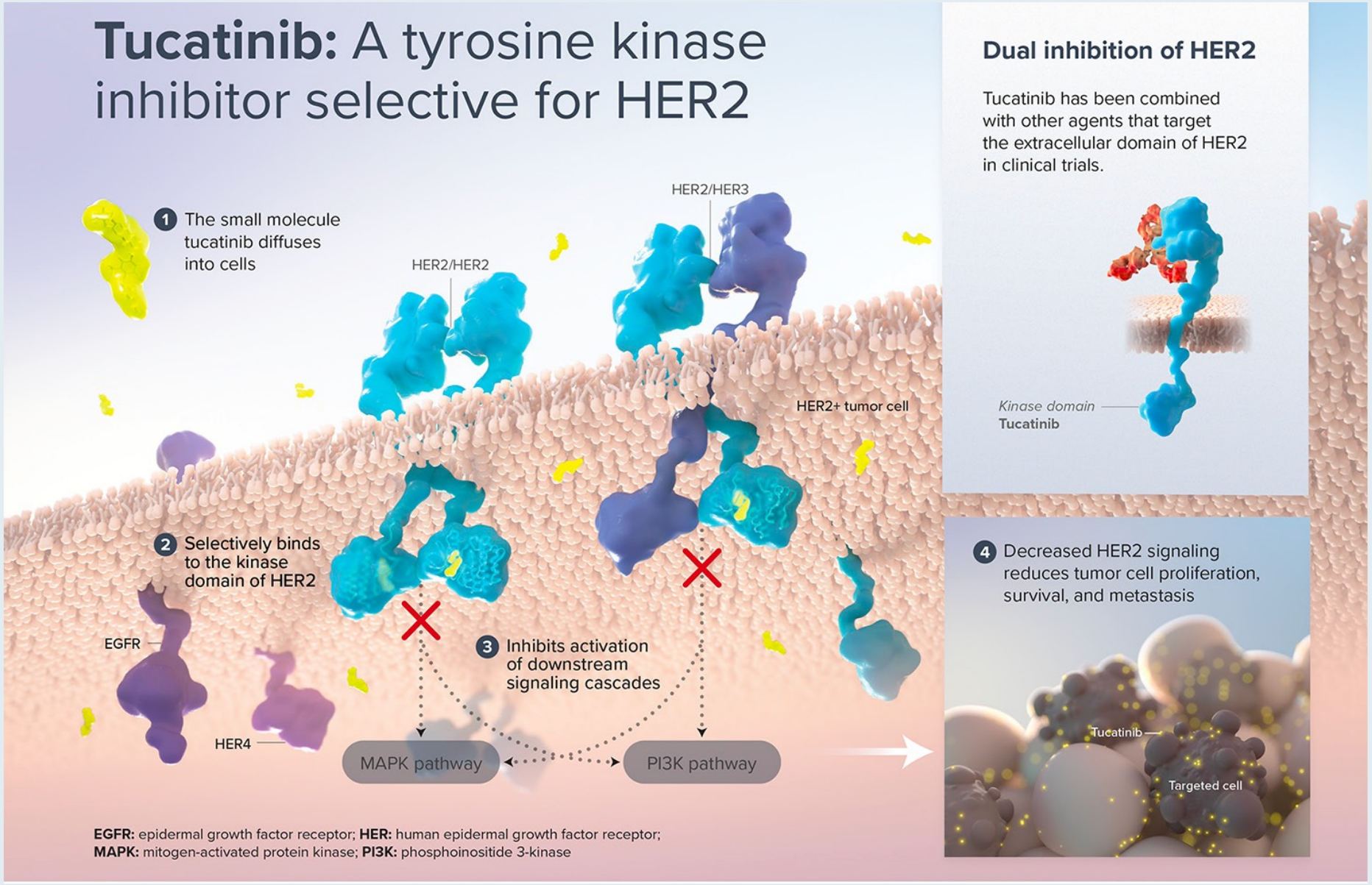
Elimova E et al. ASCO 2025;Abstract 4013, Elimova E et al. Lancet Oncol 2025;26(7):847-59.

Phase II Study of First-Line Zanidatamab and Chemotherapy: Authors' Conclusions

- In this phase 2 trial, 1L zanidatamab + chemotherapy showed clinically meaningful antitumor activity and promising survival outcomes for HER2-positive advanced GEA, especially in patients with centrally confirmed HER2-positive tumors
  - For all treated patients, 1L zanidatamab + chemotherapy was associated with a cORR of 76% (primary endpoint), median DOR of 18.7 months, median PFS of 12.5 months, and median OS of 36.5 months
- Translational data showed high *ERBB2* amplification concordance between ctDNA-based NGS and tissue-based FISH testing, and suggest that 1L zanidatamab + chemotherapy could markedly reduce total ctDNA levels early in treatment
- The safety profile of zanidatamab + chemotherapy was generally manageable with antidiarrheal prophylaxis, along with no treatment-related deaths and a low rate of treatment-related discontinuations
  - Use of antidiarrheal prophylaxis was associated with a marked reduction in grade 3 diarrhea
- Clinical development of zanidatamab + chemotherapy ± immunotherapy is ongoing with the global, randomized, phase 3 trial (HERIZON-GEA-01)

Elimova E et al. ASCO 2025;Abstract 4013.

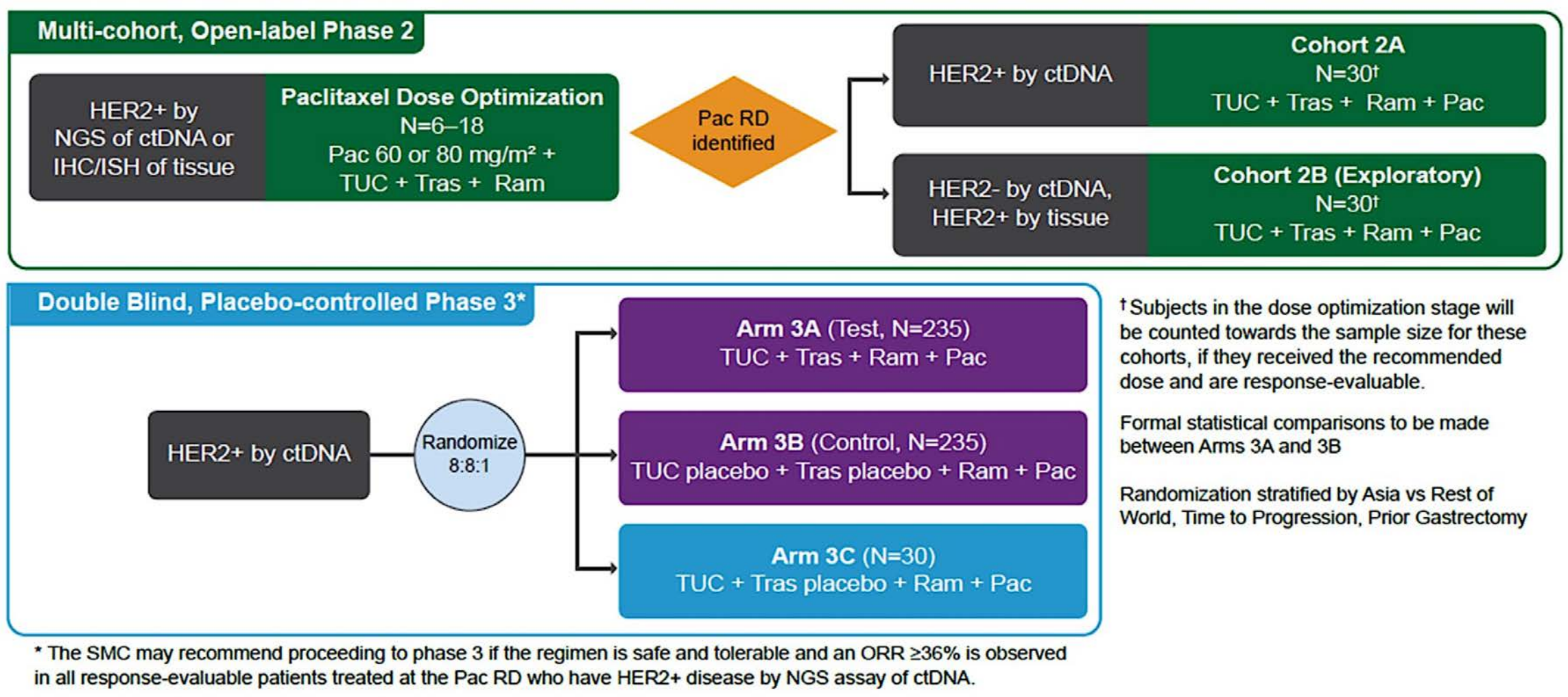
Tucatinib Proposed Mechanism of Action



Catenacci DV et al. ESMO 2021;Abstract 1434TiP.

RTP RESEARCH TO PRACTICE

MOUNTAINEER-02: A Phase II/III Study of Second-Line Tucatinib, Trastuzumab, Ramucirumab and Paclitaxel for HER2-Positive GE Cancers



ctDNA = circulating tumor DNA

Catenacci D et al. Gastrointestinal Cancers Symposium 2022;Abstract TPS371.

Abstract LBA78

BERLIN 2025 ESMO congress

Anbenitamab in combination with chemotherapy for previously treated HER2 positive gastric or gastroesophageal junction carcinomas (GC/GEJC): Interim analysis of KC-WISE

Jianming Xu
Senior Department of Oncology,
Chinese PLA general Hospital

Additional authors: Jun Zhao, Ying Liu, Yigui Chen, Suyi Li, Ying Cheng, Bo Liu, Ruixing Zhang, Haiyan Yang, Zhenyang Liu, Mingzhu Huang, Yuxian Bai, Hongyu Zhang, Yingying Du, Zhihu Li, Yanping Liu, Xiaoli Wu, Yi
On behalf of the KC-WISE investigators

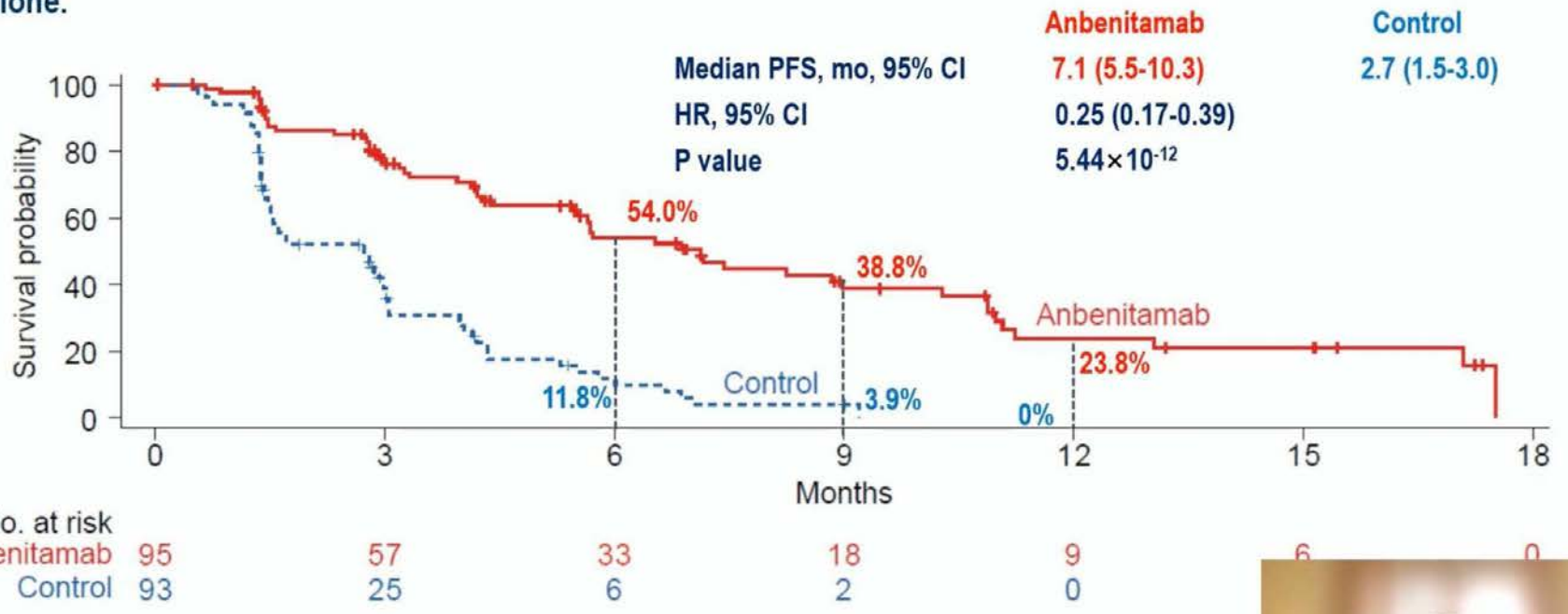
October 17 2025

RTP RESEARCH TO PRACTICE

Phase III KC-WISE Study

IRC-assessed PFS: primary endpoint

Anbenitamab plus chemotherapy significantly reduced the risk of progression or death by 75% versus chemotherapy alone.



At cutoff date of April 3, 2025, 121 PFS events occurred; The median follow-up duration was 9.7 months (95% CI, 7.2 to 11.9) in the anbenitamab group in the control group. IRC, independent review committee; HR, hazard ratio; mPFS, median progression-free survival; PFS, progression-free survival.

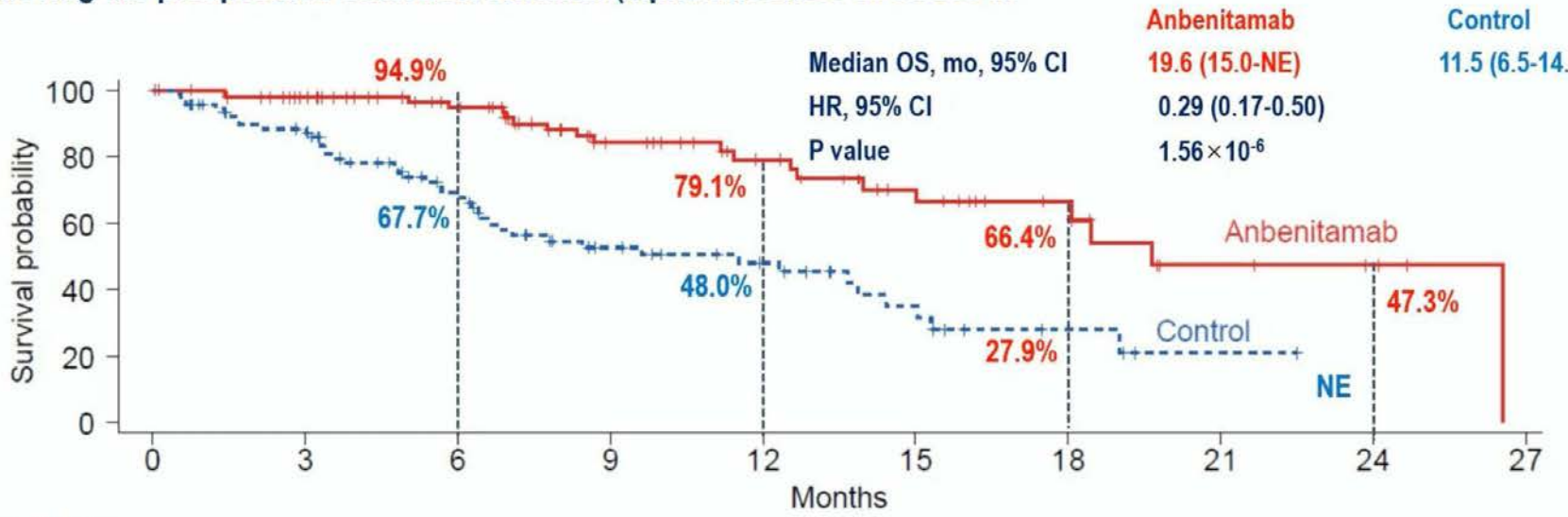
Jianming Xu

Xu J et al. ESMO 2025;Abstract LBA78.

Phase III KC-WISE Study

OS: co-primary endpoint

Compared with chemotherapy alone, anbenitamab plus chemotherapy significantly reduced the risk of death by 71%, achieving the prespecified statistical criterion (alpha threshold of 0.00001).



At cutoff date of April 3, 2025, 63 OS events occurred; The median follow-up duration was 9.7 months (95% CI, 7.2 to 11.9) in the anbenitamab group ar
in the control group. HR, hazard ratio; OS, overall survival.

Jianming Xu

Xu J et al. ESMO 2025;Abstract LBA78.

RTP RESEARCH TO PRACTICE

Phase III KC-WISE Study

Conclusions

- Anbenitamab plus chemotherapy achieved clinical meaningful and statistically significant PFS and OS benefits compared with chemotherapy alone in patients with HER2-positive GC/GEJC who progressed on trastuzumab.
  - Median PFS 7.1 vs. 2.7 months (HR=0.25; 95% CI, 0.17–0.39; $p=5.44\times10^{-12}$).
  - Median OS 19.6 vs. 11.5 months (HR=0.29; 95% CI, 0.17–0.50; $p=1.56\times10^{-6}$).
  - Similar improvement were observed in ORR, DCR and DoR.
- Anbenitamab plus chemotherapy had a favorable safety profile.
  - ≥Grade 3 TEAEs were 60.6% (anbenitamab plus chemotherapy) vs. 51.6% (chemotherapy alone)
  - The incidence of cardiotoxicity was low (3.2% vs. 3.2%), with fewer cardiac concerns.
- KC-WISE demonstrated that anbenitamab in combination with chemotherapy offer a promising treatment option for these patients.

Jianming Xu

Xu J et al. ESMO 2025;Abstract LBA78.

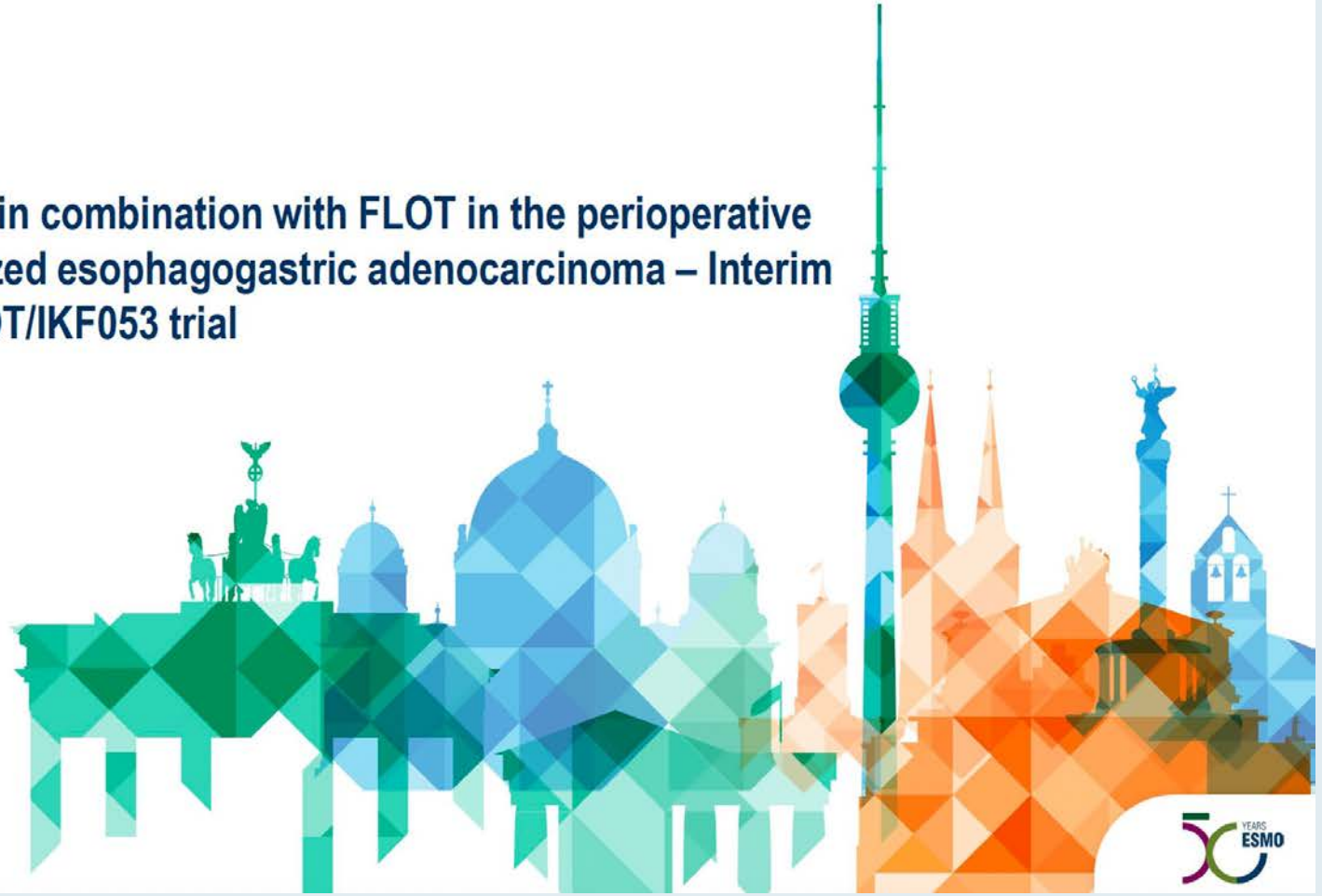
Abstract 2095MO

BERLIN 2025 ESMO congress

Pembrolizumab and trastuzumab in combination with FLOT in the perioperative treatment of HER2-positive localized esophagogastric adenocarcinoma – Interim Analysis of the phase II PHERFLOT/IKF053 trial

E. Goekkurt, **A. Stein**, S-E Al-Batran, N. Moosmann, T. J. Ettrich, T. Goetze, B. Gruen, N. Homann, S. Lorenzen, R.-D. Hofheinz, V. Rempel, G. Siegler, C. Müller, T. Broering, M. S. Cruz, C. Pauligk, M. Binder, **J. Tintelnot for the AIO study group (AIO STO 0321)**

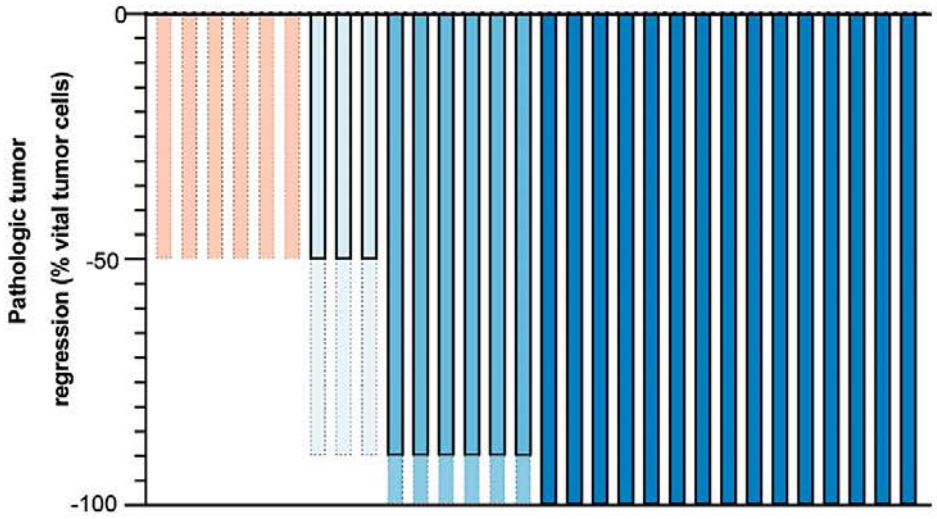
18 October 2025



Phase II PHERFLOT/IKF-053 Trial

Pathological response

All patients who consented to surgery underwent R0 resection (n=30)



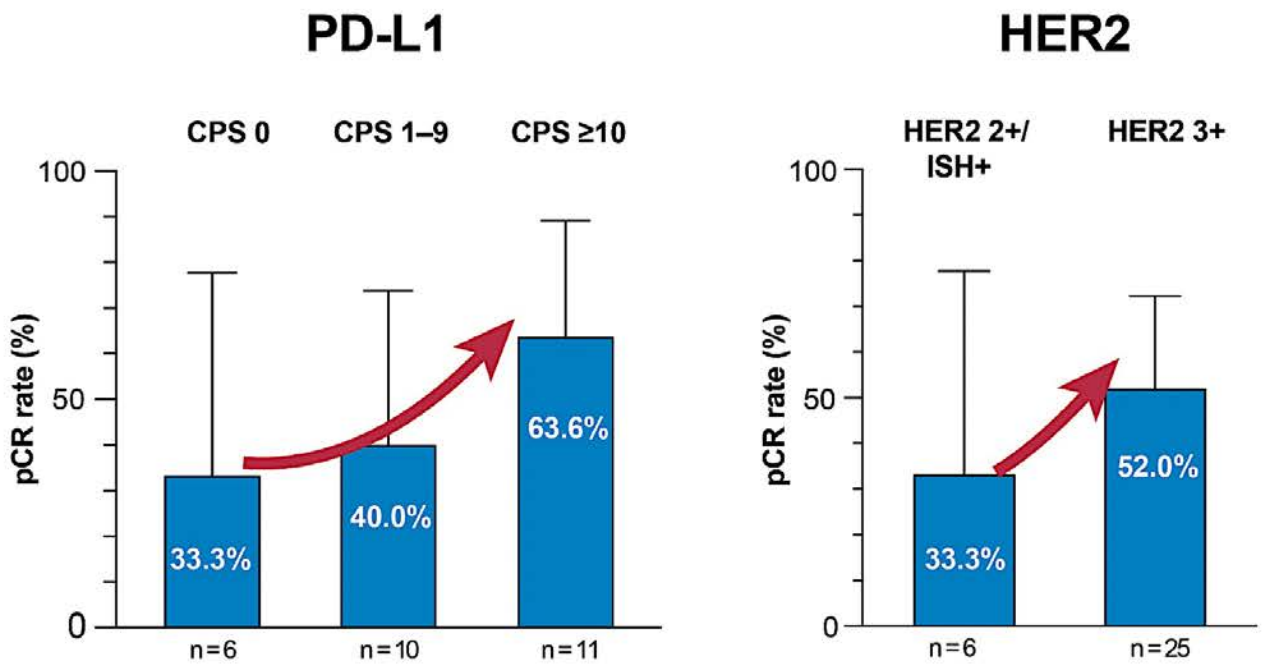
	pCR	pSR	pPR	pMR	NA
ITT, n=31	n = 15, 48.4% (30.2–66.9)	n = 6, 19.4% (7.5–37.5)	n = 3, 9.7% (2.0–25.8)	n = 6, 19.4% (7.5–37.5)	n = 1, 3.2%

Goekkurt E et al. ESMO 2025;Abstract 2095MO.

Phase II PHERFLOT/IKF-053 Trial

Pathological response

Subgroups



Goekkurt E et al. ESMO 2025;Abstract 2095MO.

Summary

- FLOT, Pembrolizumab and Trastuzumab **is feasible**
- Its safety profile is as expected, except for an increased incidence of **grade 3 diarrhea (38.7%)** and **higher re-operations**
- **pCR is 48.4%** and **pSR is 19.4%** = **67.8% major pathological response** (in the ITT)
- Higher response in CPS ≥ 10 and HER2-3+ patients

Goekkurt E et al. ESMO 2025;Abstract 2095MO.

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	Dr Brenner – 86-year-old man
■ Data Review: HER2-positive GE cancer	
Case 4	**Dr Mulherin – 82-year-old woman**
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	Dr Apuri – 82-year-old man
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	Dr Warsch – 74-year-old man
■ Data Review: CLDN18.2-positive GE cancer	

RTP
RESEARCH
TO PRACTICE

Case Presentation: 82-year-old woman with dementia and newly diagnosed dMMR metastatic GEJ adenocarcinoma (PD-L1 20%)

Dr Brian Mulherin (Indianapolis, Indiana)

RTP RESEARCH TO PRACTICE

Integrating New Advances into the Care of Patients with Cancer

A Multitumor Symposium in Partnership with the American Oncology Network

CME/MOC, NCPD and ACPE Accredited

Saturday, November 8, 2025
10:00 AM – 3:00 PM CT

RTP
RESEARCH
TO PRACTICE

Gastroesophageal Cancers Faculty

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

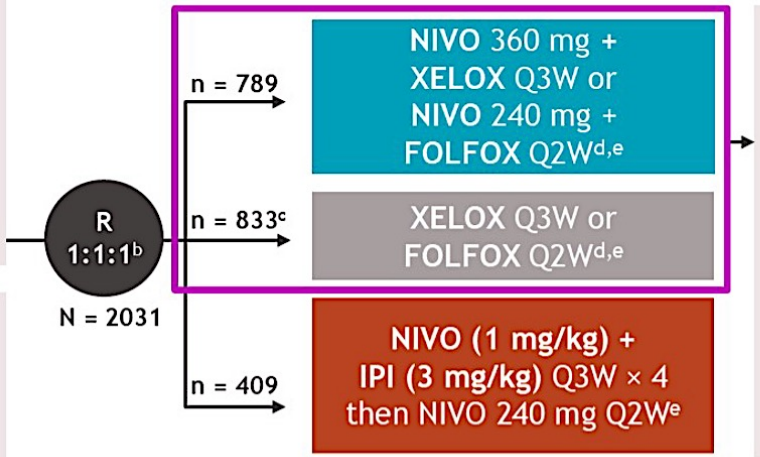
MODERATOR
Stephen "Fred" Divers, MD
Chief Medical Officer
American Oncology Network
Hot Springs, Arkansas

RTP
RESEARCH
TO PRACTICE

Nivolumab for MSI-H GE Cancers in the CheckMate 649 Trial: Overall Survival (OS) Analysis

Key eligibility criteria
- Previously untreated, unresectable, advanced or metastatic GC/GEJC/EAC
- No known HER2-positive status
- ECOG PS 0-1

Stratification factors
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[a])
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemo (XELOX vs FOLFOX)

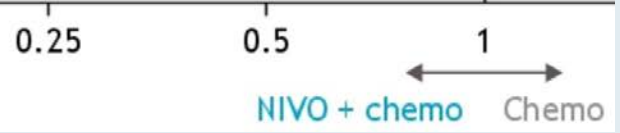


Dual primary endpoints:
- **OS** and **PFS**[f] (PD-L1 CPS ≥ 5)

Secondary endpoints:
- **OS** (PD-L1 CPS ≥ 1, all randomized)
- **OS** (PD-L1 CPS ≥ 10)
- **PFS**[f] (PD-L1 CPS ≥ 10, ≥ 1, all randomized)
- **ORR**[f]

Exploratory endpoints:
- **Safety**
- **Quality of life**

Category (all randomized)	Subgroup	Median OS, months[a]		Unstratified HR for death	Unstratified HR (95% CI)
		NIVO + chemo	Chemo		
MSI status[e]	MSS (n = 1378)	13.8	11.5	0.79	
	MSI-H (n = 44)	38.7	12.3	0.37	
Chemo regimen	FOLFOX (n = 828)	13.6	11.8	0.77	
	XELOX (n = 721)	13.9	11.8	0.80	



Elimova E et al. ASCO 2024;Abstract 4040.

MSI-H = microsatellite instability high

RTP RESEARCH TO PRACTICE

JAMA Oncology | Brief Report

Assessment of Pembrolizumab Therapy for the Treatment of Microsatellite Instability–High Gastric or Gastroesophageal Junction Cancer Among Patients in the KEYNOTE-059, KEYNOTE-061, and KEYNOTE-062 Clinical Trials

Joseph Chao, MD; Charles S. Fuchs, MD; Kohei Shitara, MD; Josep Tabernero, MD; Kei Muro, MD; Eric Van Cutsem, MD; Yung-Jue Bang, MD; Ferdinando De Vita, MD; Gregory Landers, MD; Chia-Jui Yen, MD; Ian Chau, MD; Anneli Elme, MD; Jeeyun Lee, MD; Mustafa Özgüroğlu, MD; Daniel Catenacci, MD; Harry H. Yoon, MD; Erluo Chen, MPH; David Adelberg, MD; Chie-Schin Shih, MD; Sukrut Shah, PhD; Pooja Bhagia, MD; Zev A. Wainberg, MD

2021;7(6):895-902.

Pembrolizumab for MSI-H GE Cancers in the KEYNOTE-059, KEYNOTE-061 and KEYNOTE-062 Studies

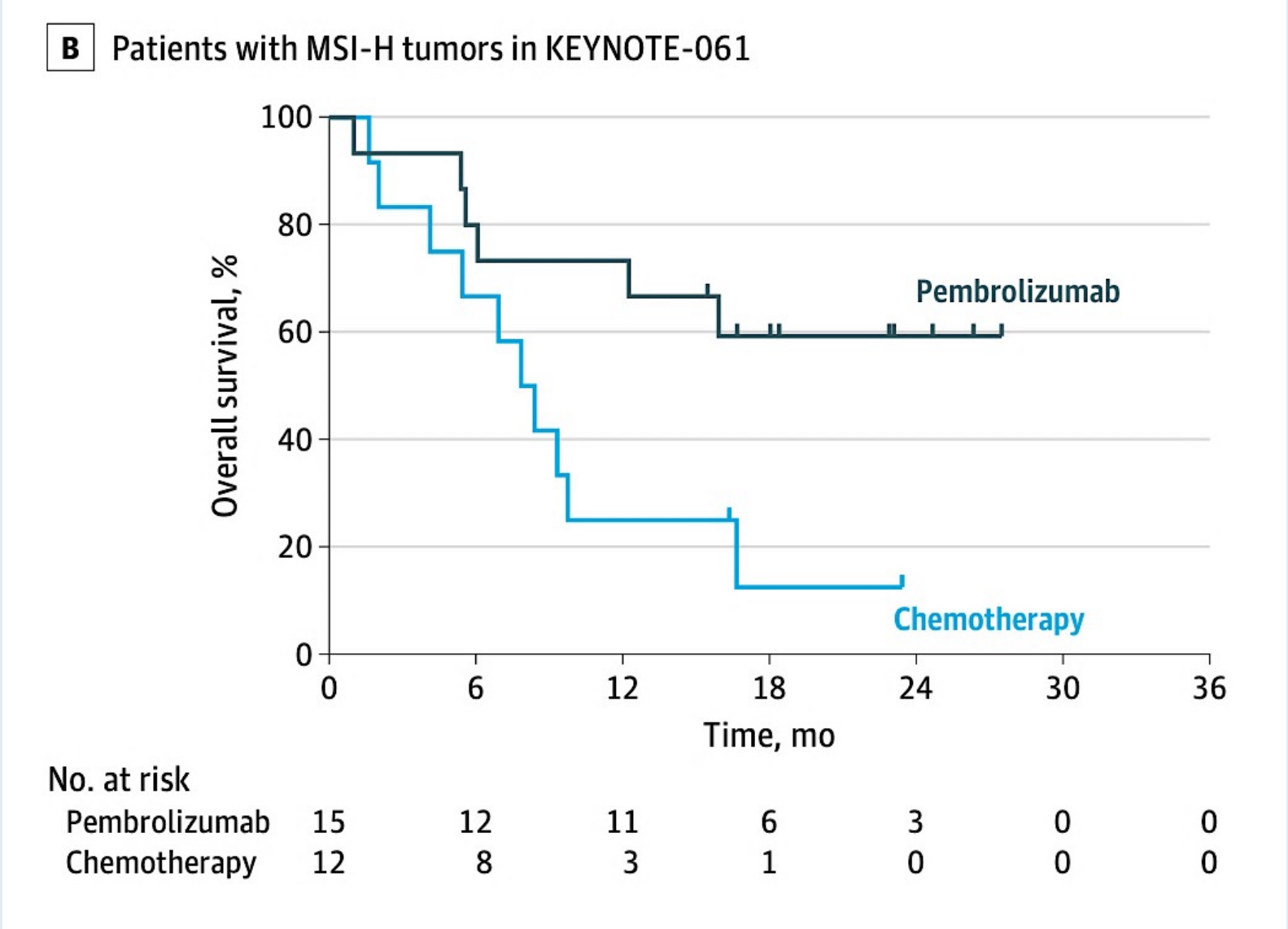
Table 2. Outcomes in Patients With Advanced Gastric or Gastroesophageal Junction Cancer by Line of Therapy

	KEYNOTE-059[a]	KEYNOTE-061[b]		KEYNOTE-062[c]		
Outcome	Pembrolizumab	Pembrolizumab	Chemotherapy	Pembrolizumab	Pembrolizumab plus chemotherapy	Chemotherapy
Patients with MSI-H tumors						
Total patients, No.	7	15	12	14	17	19
Objective response rate, % (95% CI)	57.1 (18.4-90.1)	46.7 (21.3-73.4)	16.7 (2.1-48.4)	57.1 (28.9-82.3)	64.7 (38.3-85.8)	36.8 (16.3-61.6)
Best overall response rate, %						
Complete	28.6	6.7	8.3	7.1	35.3	10.5
Partial	28.6	40.0	8.3	50.0	29.4	26.3
Stable disease	14.3	40.0	58.3	21.4	17.6	42.1
Progressive disease	0	6.7	0	14.3	0	10.5
Duration of response, median (range), mo	NR (20.0[d]-26.8[d])	NR (5.5-26.0[d])	NR (2.2[d]-12.2[d])	21.2 (1.4[d]-33.6[d])	NR (1.6[d]-34.5[d])	7.0 (2.0-30.4[d])
Survival, median (95% CI), mo						
Progression-free	NR (1.1-NR)	17.8 (2.7-NR)	3.5 (2.0-9.8)	11.2 (1.5-NR)	NR (3.6-NR)	6.6 (4.4-8.3)
Overall	NR (1.1-NR)	NR (5.6-NR)	8.1 (2.0-16.7)	NR (10.7-NR)	NR (3.6-NR)	8.5 (5.3-20.8)
Estimated overall survival rate, % (95% CI)						
12 mo	71 (NA)	73 (44-89)	25 (6-50)	79 (47-92)	71 (43-87)	47 (24-67)
24 mo	57 (NA)	59 (31-79)	NA	71 (41-88)	65 (38-82)	26 (10-57)

Chao J et al. *JAMA Oncol* 2021;7(6):895-902.

RTP RESEARCH TO PRACTICE

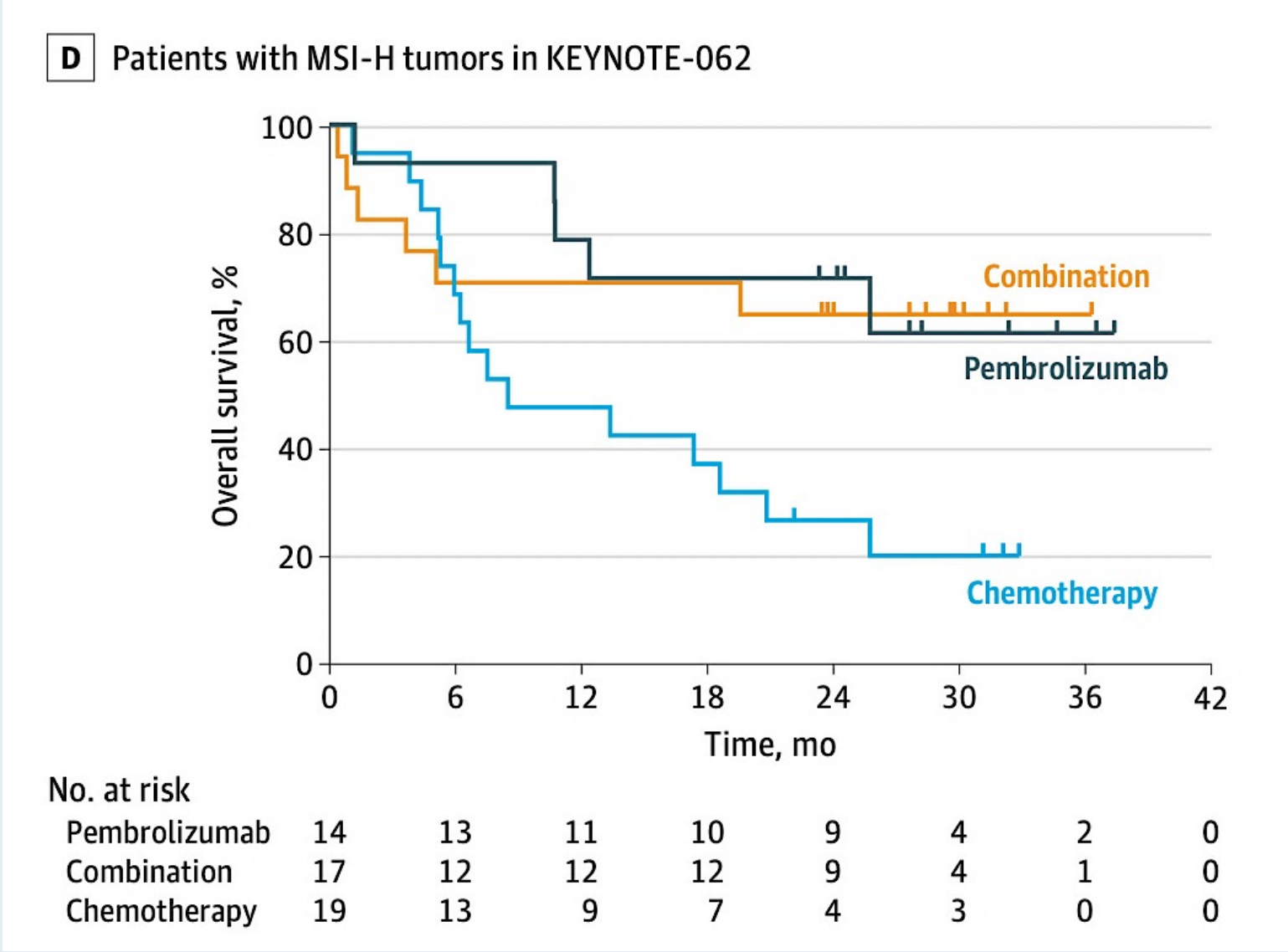
Pembrolizumab for MSI-H GE Cancers in KEYNOTE-061



Chao J et al. *JAMA Oncol* 2021;7(6):895-902.

RTP RESEARCH TO PRACTICE

Pembrolizumab for MSI-H GE Cancers in KEYNOTE-062



Chao J et al. *JAMA Oncol* 2021;7(6):895-902.

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	Dr Brenner – 86-year-old man
■ Data Review: HER2-positive GE cancer	
Case 4	Dr Mulherin – 82-year-old woman
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	Dr Apuri – 82-year-old man
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	Dr Warsch – 74-year-old man
■ Data Review: CLDN18.2-positive GE cancer	

RTP
RESEARCH
TO PRACTICE

Case Presentation: 65-year-old man with localized HER2-negative GEJ cancer (PD-L1 CPS 2, CLDN18.2-positive) and residual disease s/p neoadjuvant chemoradiation therapy and surgery

Dr Fred Divers (Hot Springs, Arkansas)

RTP RESEARCH TO PRACTICE

Abstract LBA81

BERLIN 2025 ESMO congress

Final overall survival and the association of pathological outcomes with event-free survival in MATTERHORN: a randomised, Phase 3 study of durvalumab plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel in resectable gastric / gastroesophageal junction adenocarcinoma

Josep Tabernero,[1] Salah-Eddin Al-Batran,[2] Zev A. Wainberg,[3] Kei Muro,[4] Daniela Molena,[5] Eric Van Cutsem,[6] Woo Jin Hyung,[7] Lucjan Wyrwicz,[8] Do-Youn Oh,[9] Takeshi Omori,[10] Markus Moehler,[11] Arinilda C. Bragagnoli,[12] Gabriel Garbaos,[13] Moishe Liberman,[14] María Luisa Limón Mirón,[15] Elizabeth C. Smyth,[16] Lin-Yang Cheng,[17] Nicola Valeri,[18] Ioannis Xynos,[18] Yelena Y. Janjigian[19]

[1]Medical Oncology Department, Vall d'Hebron Hospital Campus & Institute of Oncology (VHIO), UVic-UCC, Barcelona, Spain; [2]Krankenhaus Nordwest, University Cancer Center (UCT) Frankfurt, and Frankfurt Institute of Clinical Cancer Research (IKF), Frankfurt, Germany; [3]Department of Gastrointestinal Medical Oncology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [4]Department of Clinical Oncology, Aichi Cancer Center Hospital, Nagoya, Japan; [5]Division of Thoracic Surgery, Memorial Sloan Kettering Cancer Center and Weill Cornell Medicine, New York, NY, USA; [6]Department of Gastroenterology / Digestive Oncology, University Hospitals Leuven and KU Leuven, Leuven, Belgium; [7]Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea; [8]Department of Oncology and Radiotherapy, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [9]Division of Medical Oncology, Department of Internal Medicine, Seoul National University Hospital, and Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [10]Department of Gastroenterological Surgery, Osaka International Cancer Institute, Osaka, Japan; [11]Research Center for Immunotherapy (FZI), Johannes Gutenberg-University Clinic, Mainz, Germany; [12]Division of Oncology, Hospital de Câncer de Barretos-Fundação Pio XII, São Paulo, Brazil; [13]Division of Oncology, Instituto Médico de la Fundación Estudios Clínicos, Santa Fe, Argentina; [14]Division of Thoracic Surgery, Department of Surgery, Centre Hospitalier de l'Université de Montréal, Centre de Recherche du CHUM, Montréal, Quebec, Canada; [15]Department of Medical Oncology, Hospital Virgen del Rocío, Seville, Spain; [16]Oxford NIHR Biomedical Research Centre, Churchill Hospital, Oxford, UK; [17]Oncology R&D, Oncology Biometrics, AstraZeneca, Gaithersburg, MD, USA; [18]Oncology R&D, Late-Stage Development, AstraZeneca, Cambridge, UK; [19]Gastrointestinal Oncology Service, Memorial Sloan Kettering Cancer Center and Weill Cornell Medicine, New York, NY, USA

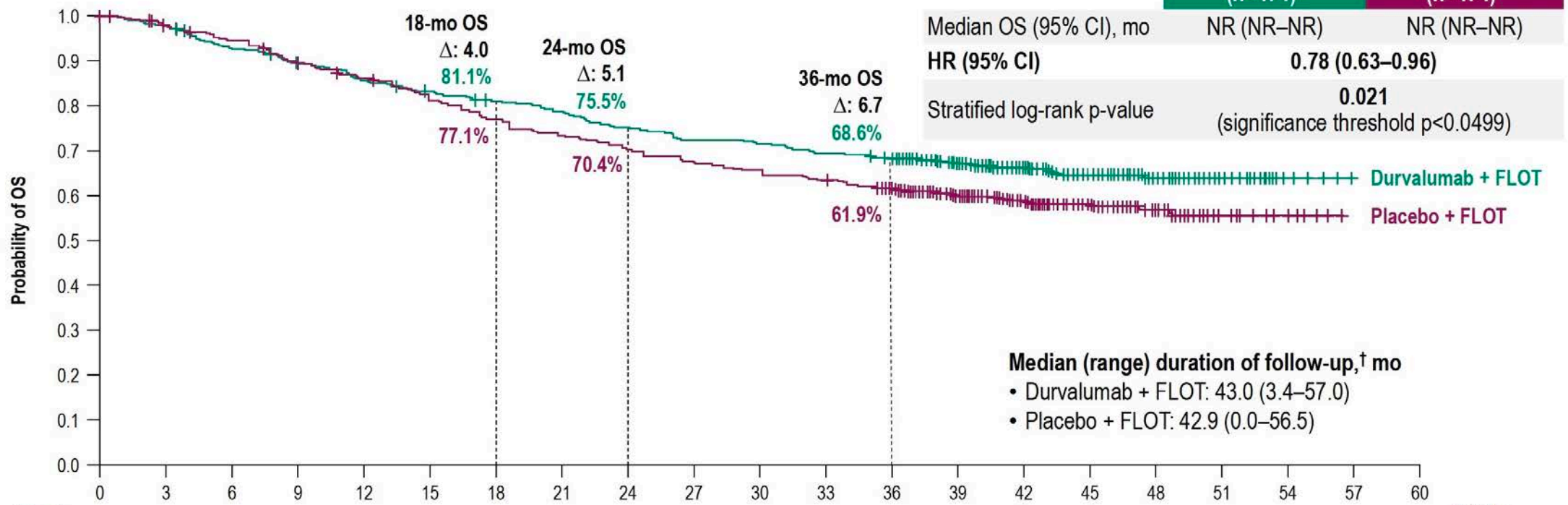
17–21 October 2025

RTP RESEARCH TO PRACTICE

Phase III MATTERHORN: Final OS

Durvalumab + FLOT demonstrated a statistically significant and clinically meaningful improvement in OS versus placebo + FLOT in the intention to treat population

	Durvalumab + FLOT (n=474)*	Placebo + FLOT (n=474)*
Median OS (95% CI), mo	NR (NR–NR)	NR (NR–NR)
HR (95% CI)	**0.78 (0.63–0.96)**	
Stratified log-rank p-value	**0.021** (significance threshold p<0.0499)	



Median (range) duration of follow-up,† mo
- Durvalumab + FLOT: 43.0 (3.4–57.0)
- Placebo + FLOT: 42.9 (0.0–56.5)

No. of participants at risk																					Total no. of events
Durvalumab + FLOT	474	464	438	422	403	389	377	367	351	338	334	323	316	255	182	112	71	29	6	1	0	160
Placebo + FLOT	474	457	439	414	395	374	355	338	324	310	298	293	278	221	167	99	61	23	7	0	0	192

*Intention to treat analysis set (all randomised participants, regardless of treatment received). †In censored participants.
Data cut-off: 01 September 2025. OS maturity: 37.1%. Events were defined as time from randomisation until the date of death due to any cause. The HR and its CI were estimated from a Cox proportional hazards model, adjusted for geographic region, clinical lymph node status, and PD-L1 expression status. The CI for the HR was calculated using a profile likelihood approach. An HR <1 favours durvalumab + FLOT. The two-sided p-value was calculated using a stratified log-rank test adjusting for geographic region, clinical lymph node status, and PD-L1 expression status.
CI, confidence interval; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; mo, month; NR, not reached; OS, overall survival; PD-L1, programmed cell death ligand-1.

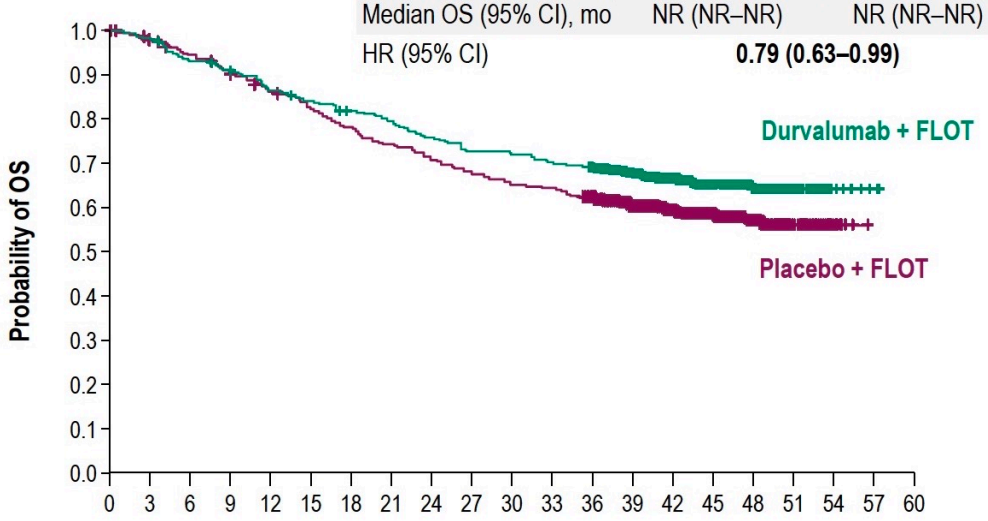
Tabernero J et al. ESMO 2025;Abstract LBA81.

Phase III MATTERHORN: OS by PD-L1 Status

OS was improved with durvalumab + FLOT versus placebo + FLOT regardless of PD-L1 status

PD-L1 TAP ≥1%*

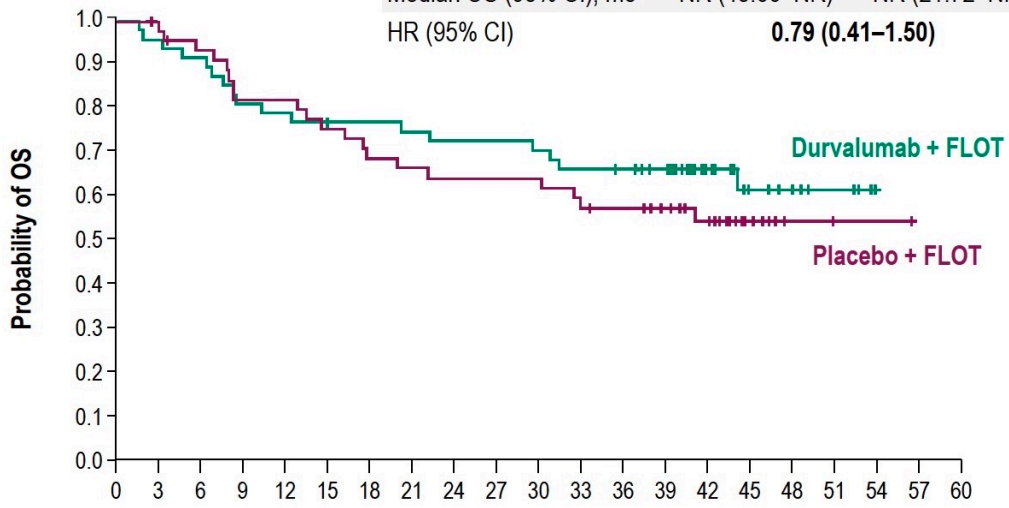
	Durvalumab + FLOT (n=426)	Placebo + FLOT (n=427)
Median OS (95% CI), mo	NR (NR–NR)	NR (NR–NR)
HR (95% CI)	**0.79 (0.63–0.99)**	



No. of participants at risk																						Total no. of events
Durvalumab + FLOT	426	418	394	383	365	353	341	332	317	304	301	292	286	229	165	101	64	25	6	1	0	143
Placebo + FLOT	427	412	397	377	358	340	324	308	295	281	270	267	253	200	152	91	59	22	6	0	0	172

PD-L1 TAP <1%*

	Durvalumab + FLOT (n=48)	Placebo + FLOT (n=47)
Median OS (95% CI), mo	NR (43.66–NR)	NR (21.72–NR)
HR (95% CI)	**0.79 (0.41–1.50)**	



No. of participants at risk																						Total no. of events
Durvalumab + FLOT	48	46	44	39	38	36	36	35	34	34	33	31	30	26	17	11	7	4	0	0	0	17
Placebo + FLOT	47	45	42	37	37	34	31	30	29	29	28	26	25	21	15	8	2	1	1	0	0	20

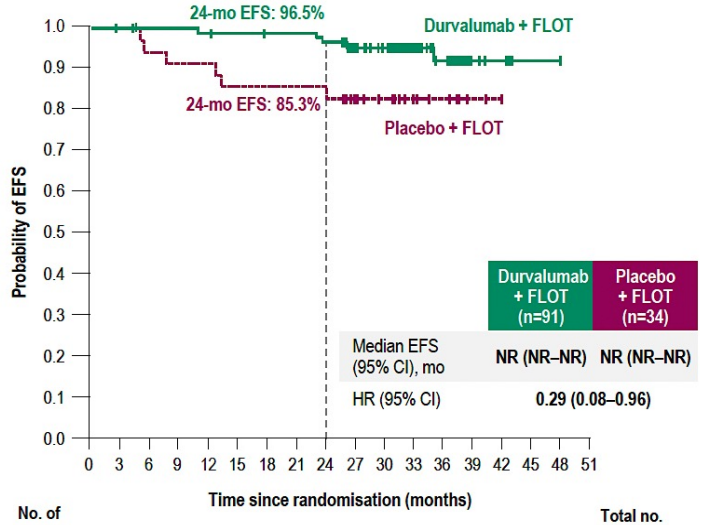
*Measured by immunohistochemistry using the investigational VENTANA PD-L1 (SP263) Assay (Roche Diagnostics) and recorded at randomisation on the Interactive Response Technology System, Randomisation and Trial Supply Management, Electronic Case Report Form or from external vendor data from samples collected on or before randomisation. Participants provided a tumour tissue sample at screening to determine PD-L1 status using the TAP scoring method.
Data cut-off: 01 September 2025. The HR and its CI were estimated from a Cox proportional hazards model. The CI for the HR was calculated using a profile likelihood approach.
CI, confidence interval; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; NR, not reached; OS, overall survival; PD-L1, programmed cell death ligand-1; TAP, Tumour Area Positivity.

Tabernero J et al. ESMO 2025;Abstract LBA81.

Phase III MATTERHORN: Pathological Response and EFS

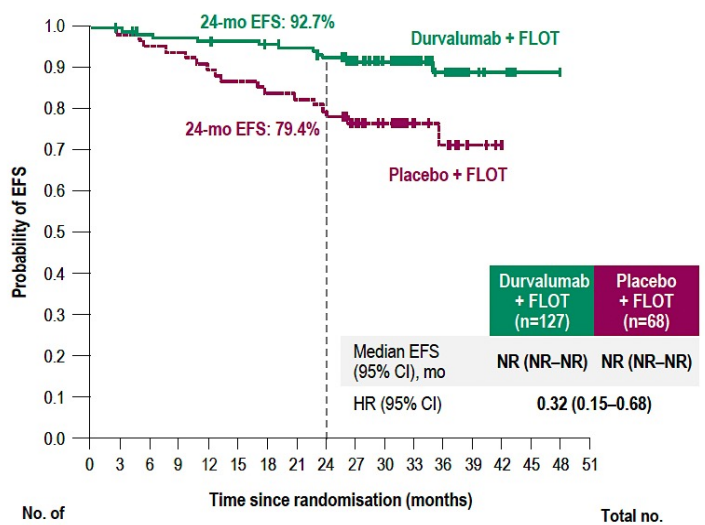
EFS was improved with durvalumab + FLOT versus placebo + FLOT among participants with any degree of pathological response

pCR



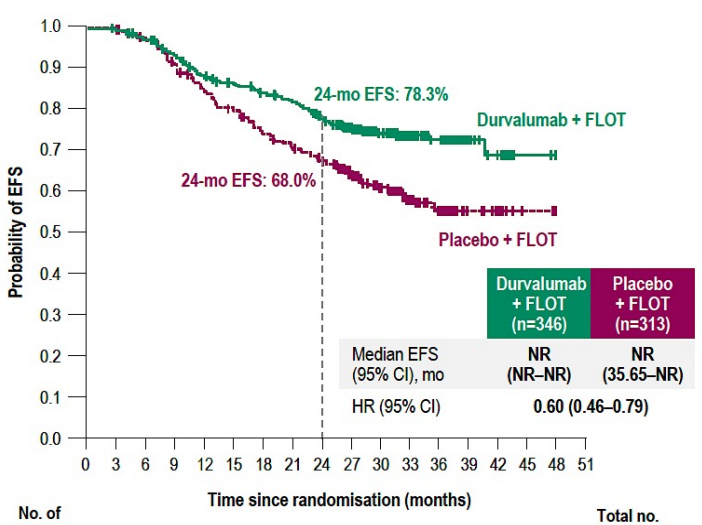
No. of participants at risk																		Total no. of events
Durvalumab + FLOT	91	90	88	88	87	86	85	85	83	68	60	38	27	7	5	1	1	0	5
Placebo + FLOT	34	34	32	31	31	29	29	29	29	23	16	11	8	2	1	0	0	0	6

MPR



No. of participants at risk																		Total no. of events
Durvalumab + FLOT	127	126	122	121	120	119	117	115	111	91	78	45	34	9	6	1	1	0	11
Placebo + FLOT	68	67	65	64	61	59	57	56	54	45	35	19	13	3	1	0	0	0	17

Any pathological response*



No. of participants at risk																		Total no. of events
Durvalumab + FLOT	346	343	330	314	295	283	273	265	248	201	162	90	75	28	17	2	1	0	87
Placebo + FLOT	313	312	300	279	257	242	224	213	200	160	129	74	54	21	17	2	1	0	123

*Among participants who completed surgery with samples that were evaluable for modified Ryan scoring by central assessment, the rate of participants who achieved any pathological response was 89.9% in the durvalumab + FLOT arm and 84.1% in the placebo + FLOT arm.
Data cut-off: 20 December 2024. pCR is defined as modified Ryan score of 0; MPR is defined as modified Ryan score of 0 and 1; any pathological response is defined as modified Ryan score 0, 1, and 2. Events were defined as the earliest of RECIST v1.1 events, non-RECIST v1.1 events or deaths due to any cause. Analysis was based on BICR assessments and / or locally by pathology testing if clinically required. The HR and its CI were estimated from a Cox proportional hazards model. The CI for the HR was calculated using a profile likelihood approach.
BICR, blinded independent central review; CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; mo, month; MPR, major pathological response; NR, not reached; pCR, pathological complete response; RECIST v1.1, Response Evaluation Criteria for Solid Tumors version 1.1.

Tabernero J et al. ESMO 2025;Abstract LBA81.

Phase III MATTERHORN: Conclusions

Conclusions

- Durvalumab + FLOT demonstrated a statistically significant and clinically meaningful improvement in OS versus FLOT alone in the intention to treat population
  - HR, 0.78 (95% CI, 0.63–0.96); p=0.021
- OS improved with durvalumab + FLOT versus placebo + FLOT, regardless of PD-L1 status
- Any degree of pathological response was associated with improved EFS for durvalumab + FLOT versus placebo + FLOT
- EFS was also improved regardless of pathological nodal status

MATTERHORN OS results strongly support perioperative durvalumab + FLOT as a new global standard of care for patients with localised G / GEJ adenocarcinoma

CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; G / GEJ, gastric / gastroesophageal junction; OS, overall survival; PD-L1, programmed cell death ligand-1.

Tabernero J et al. ESMO 2025;Abstract LBA81.

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	Dr Brenner – 86-year-old man
■ Data Review: HER2-positive GE cancer	
Case 4	Dr Mulherin – 82-year-old woman
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	**Dr Apuri – 82-year-old man**
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	Dr Warsch – 74-year-old man
■ Data Review: CLDN18.2-positive GE cancer	

RTP
RESEARCH
TO PRACTICE

Case Presentation: 82-year-old man with metastatic recurrence of esophageal adenocarcinoma (PD-L1 TPS 75%) 2 years after resection of localized disease

Dr Susmitha Apuri (Lutz, Florida)

RTP RESEARCH TO PRACTICE

FDA Amends Esophageal Cancer Indication for Nivolumab

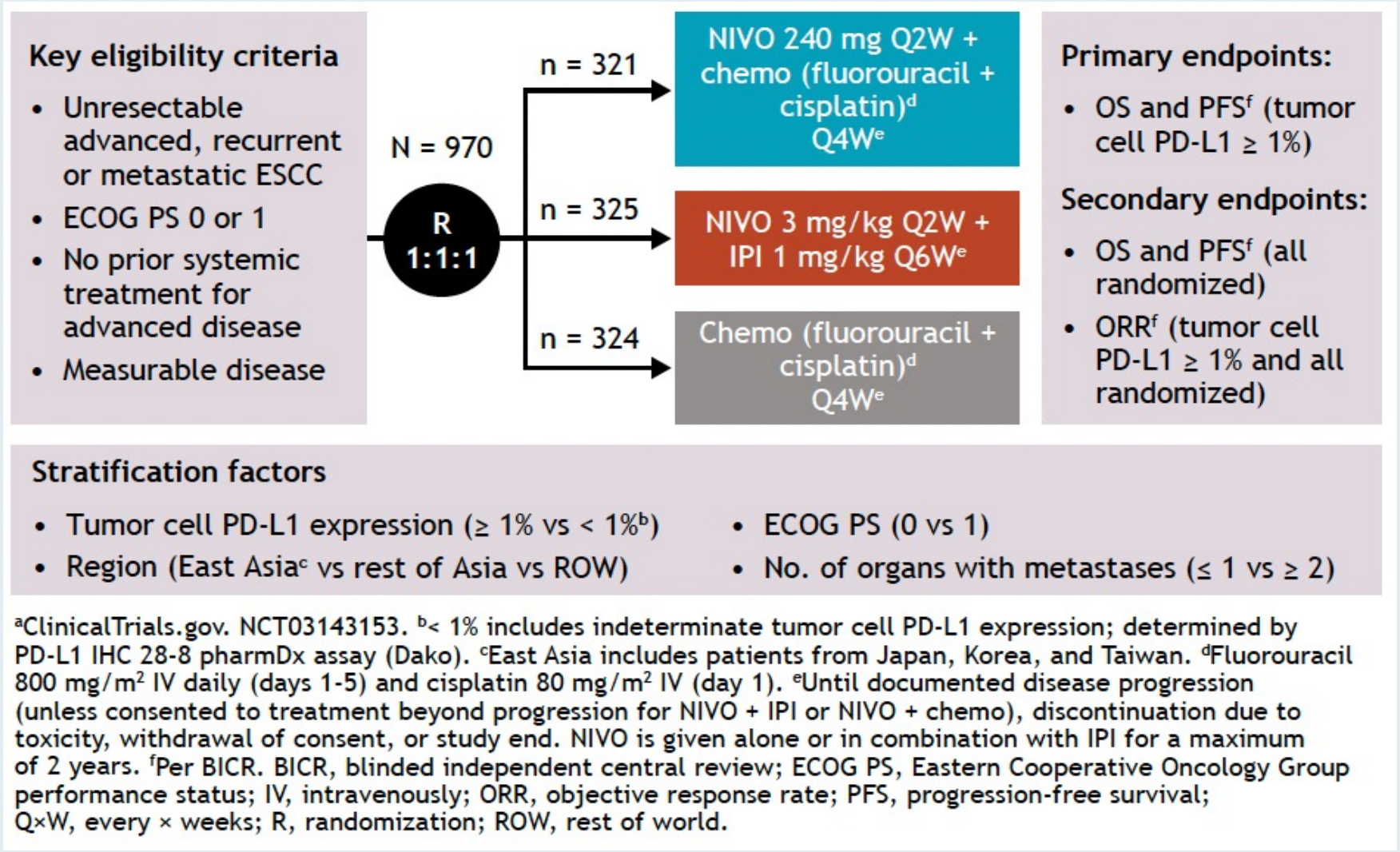
Press Release: May 23, 2025

A Prior Approval supplemental biologics license application updated the nivolumab Prescribing Information (PI) and Medication Guide (MG), revising the following indications to reflect the population (ie, PD-L1 ≥1) with a favorable risk-benefit assessment:

- Nivolumab, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) in adult patients whose tumors express PD-L1 (≥1).
- Nivolumab, in combination with ipilimumab, is indicated for the first-line treatment of unresectable advanced or metastatic ESCC in adult patients whose tumors express PD-L1 (≥1).
- Nivolumab, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the treatment of advanced or metastatic gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma in adult patients whose tumors express PD-L1 (≥1).

https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2025/125554Orig1s133ltr.pdf

CheckMate 648: A Phase III Study of First-Line Nivolumab/Chemotherapy or Nivolumab/Ipilimumab for Esophageal Squamous Cell Carcinoma (ESCC)



[a]ClinicalTrials.gov. NCT03143153. [b]< 1% includes indeterminate tumor cell PD-L1 expression; determined by PD-L1 IHC 28-8 pharmDx assay (Dako). [c]East Asia includes patients from Japan, Korea, and Taiwan. [d]Fluorouracil 800 mg/m^2 IV daily (days 1-5) and cisplatin 80 mg/m^2 IV (day 1). [e]Until documented disease progression (unless consented to treatment beyond progression for NIVO + IPI or NIVO + chemo), discontinuation due to toxicity, withdrawal of consent, or study end. NIVO is given alone or in combination with IPI for a maximum of 2 years. [f]Per BICR. BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; ORR, objective response rate; PFS, progression-free survival; Q×W, every × weeks; R, randomization; ROW, rest of world.

Chau I et al. ESMO 2025;Abstract 2106P.

Phase III CheckMate 648: Objective Response Rate (ORR) by Treatment Regimen

Response per BICR	Tumor cell PD-L1 ≥ 1%		All randomized	
	NIVO + chemo (n = 158)	Chemo (n = 157)	NIVO + chemo (n = 321)	Chemo (n = 324)
ORR (95% CI),[a,b] %	**53 (44-61)**	**20 (14-27)**	**47 (42-53)**	**27 (22-32)**
CR	17	4	15	6
PR	35	15	32	20
SD	25	46	32	46
PD	15	16	13	12
Median DOR,[c,d] months (95% CI)	8.4 (6.9-12.4)	5.7 (4.4-8.7)	8.2 (6.9-9.7)	6.9 (5.7-7.7)
DOR ≥ 60 months,[c,d] %	5	0	14	3

[a]Unable to determine best overall response in patients with tumor cell PD-L1 ≥ 1%: NIVO + chemo, n = 12; chemo, n = 29. [b]Unable to determine best overall response in all randomized patients: NIVO + chemo, n = 24; chemo, n = 50. [c]Based on Kaplan-Meier estimates. [d]No. of responders in tumor cell PD-L1 ≥ 1%, NIVO + chemo: n = 83; chemo: n = 31. No. of responders in all randomized, NIVO + chemo: n = 152; chemo: n = 87. CR, complete response; DOR, duration of response; PD, progressive disease; PR, partial response; SD, stable disease.

Response per BICR	Tumor cell PD-L1 ≥ 1%		All randomized	
	NIVO + IPI (n = 158)	Chemo (n = 157)	NIVO + IPI (n = 325)	Chemo (n = 324)
ORR (95% CI),[a,b] %	**35 (27-43)**	**20 (14-27)**	**27 (23-33)**	**27 (22-32)**
CR	18	4	12	6
PR	17	15	15	20
SD	27	46	32	46
PD	31	16	32	12
Median DOR,[c,d] months (95% CI)	11.8 (6.8-18.0)	5.7 (4.4-8.7)	11.1 (8.3-14.3)	6.9 (5.7-7.7)
DOR ≥ 60 months,[c,d] %	19	0	17	3

[a]Unable to determine best overall response in patients with tumor cell PD-L1 ≥ 1%: NIVO + IPI, n = 11; chemo, n = 29. [b]Unable to determine best overall response in all randomized patients: NIVO + IPI, n = 29; chemo, n = 50. [c]Based on Kaplan-Meier estimates. [d]No. of responders in tumor cell PD-L1 ≥ 1%, NIVO + IPI: n = 55; chemo: n = 31. No. of responders in all randomized, NIVO + IPI: n = 89; chemo: n = 87.

Chau I et al. ESMO 2025;Abstract 2106P.

Phase III CheckMate 648: Safety

All treated, n (%)[a]	NIVO + chemo (n = 310)		NIVO + IPI (n = 322)		Chemo (n = 304)	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAEs[b]	297 (96)	151 (49)	256 (80)	105 (33)	275 (90)	111 (37)
Serious TRAEs[b]	74 (24)	58 (19)	105 (33)	75 (23)	49 (16)	41 (13)
TRAEs leading to discontinuation[c]	107 (35)	30 (10)	60 (19)	44 (14)	63 (21)	18 (6)
Treatment-related deaths[d]	5 (2)[e]		7 (2)[f]		5 (2)[g]	

[a]Patients who received ≥ 1 dose of study drug. [b]Assessed in all treated patients during treatment and for up to 30 days after the last dose of study treatment. [c]TRAEs leading to discontinuation of any drug in the regimen. [d]Treatment-related deaths were reported regardless of timeframe. [e]Included 1 event each of pneumonia, pneumatosis intestinalis, acute kidney injury, pneumonitis, and pneumonitis/respiratory tract infection. [f]Included 2 events of pneumonitis; 1 event each of internal hemorrhage, immune-mediated lung disease, interstitial lung disease, and pulmonary embolism; and 1 event attributed to multiple causes, including general physical health deterioration that was assessed by the investigator as related to study treatment and malignant neoplasm progression that was assessed by the investigator as not related to study treatment. [g]Included 1 event each of septic shock, sepsis, acute kidney injury, pneumonia, and myocardial infarction.

Chau I et al. ESMO 2025;Abstract 2106P.

Phase III CheckMate 648: Authors' Conclusions

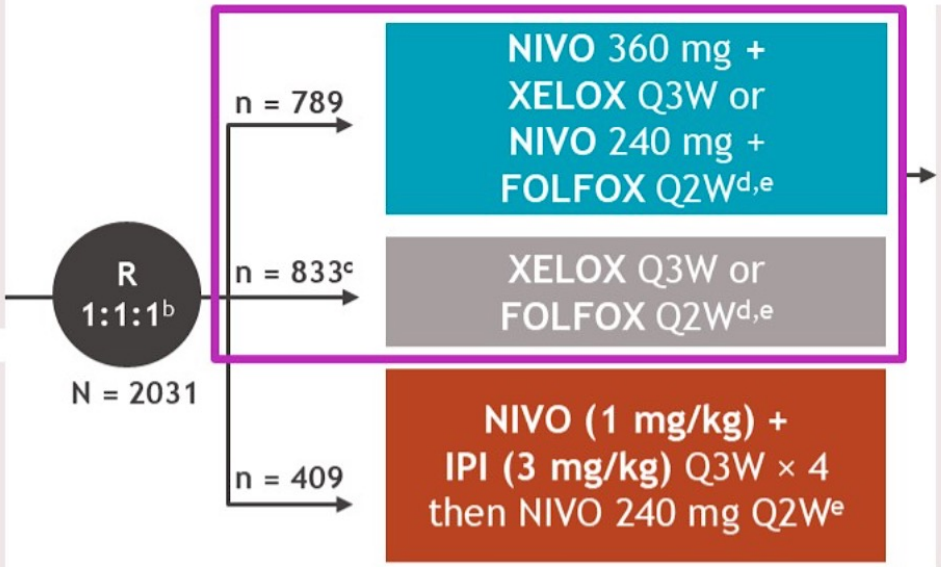
- With 5 years minimum follow-up, NIVO + chemo and NIVO + IPI continued to demonstrate clinically meaningful long-term survival benefit and more durable responses vs chemo as 1L treatment for advanced ESCC
  - OS benefits were observed with NIVO + chemo and NIVO + IPI vs chemo in patients with tumor cell PD-L1 ≥ 1% and all randomized patients
  - OS favored NIVO + chemo and NIVO + IPI across most subgroups, with the greatest magnitude of benefit seen among patients with PD-L1 ≥ 1%
  - PFS benefit with NIVO + chemo vs chemo was observed in patients with tumor cell PD-L1 ≥ 1%
  - ORR was higher with NIVO + chemo regardless of PD-L1 status and was higher with NIVO + IPI in patients with PD-L1 ≥ 1%
  - Longer DOR was observed with NIVO + chemo and NIVO + IPI vs chemo
- No new safety signals were identified with NIVO + chemo or NIVO + IPI at the 5-year follow-up
  - No additional TRAEs leading to discontinuation and no new treatment-related deaths were reported with longer follow-up
- These results further support NIVO + chemo and NIVO + IPI as 1L standard of care treatments for patients with advanced ESCC

Chau I et al. ESMO 2025;Abstract 2106P.

CheckMate 649: A Phase III Study of First-Line Nivolumab and Chemotherapy for GE Adenocarcinomas

Key eligibility criteria
- Previously untreated, unresectable, advanced or metastatic GC/GEJC/EAC
- No known HER2-positive status
- ECOG PS 0-1

Stratification factors
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[a])
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemo (XELOX vs FOLFOX)



Dual primary endpoints:
- **OS** and **PFS**[f] (PD-L1 CPS ≥ 5)

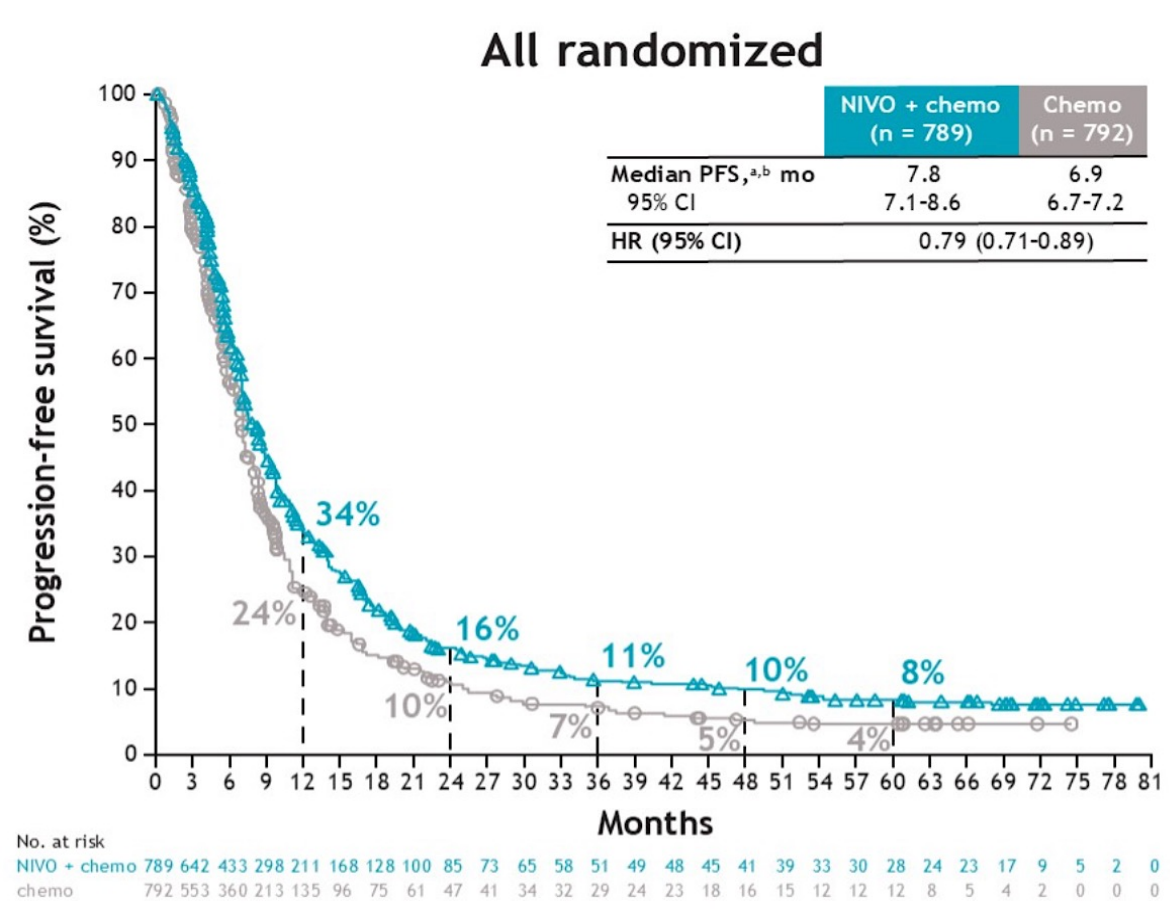
Secondary endpoints:
- **OS** (PD-L1 CPS ≥ 1, all randomized)
- **OS** (PD-L1 CPS ≥ 10)
- **PFS**[f] (PD-L1 CPS ≥ 10, ≥ 1, all randomized)
- **ORR**[f]

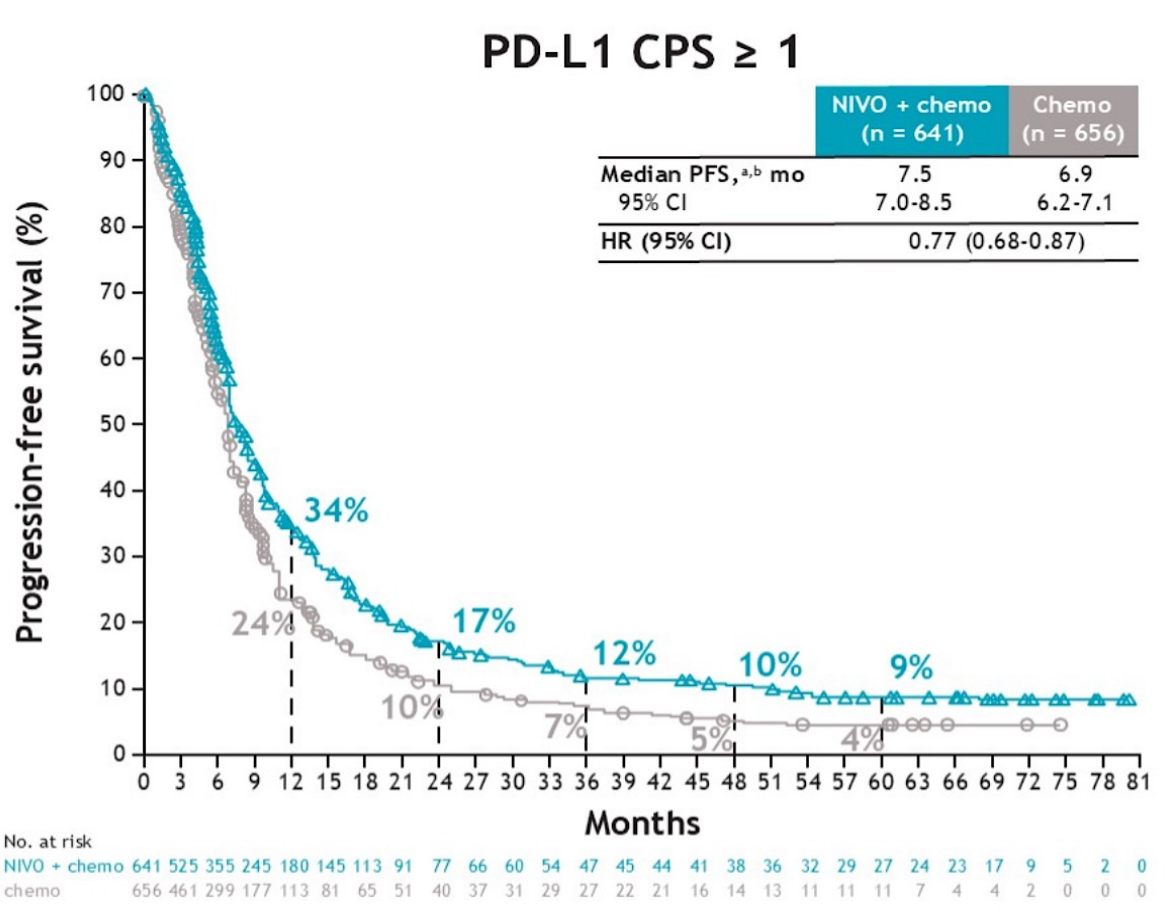
Exploratory endpoints:
- **Safety**
- **Quality of life**

- At data cutoff (May 28, 2024), the minimum follow-up (time from concurrent randomization of the last patient to clinical data cutoff) was 60.1 months
- No patients in the NIVO + chemo or chemo arms were receiving ongoing study treatment at data cutoff

Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract 398.

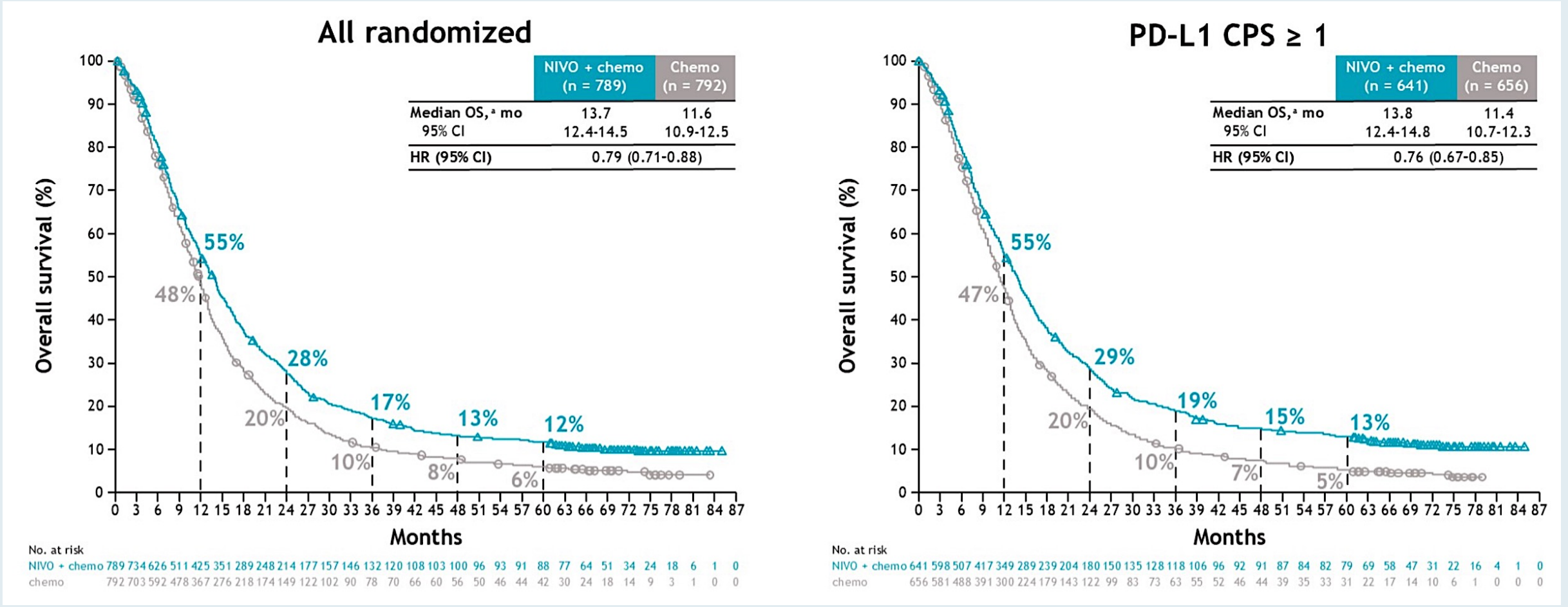
CheckMate 649: PFS





Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract 398.

CheckMate 649: OS



Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract 398.

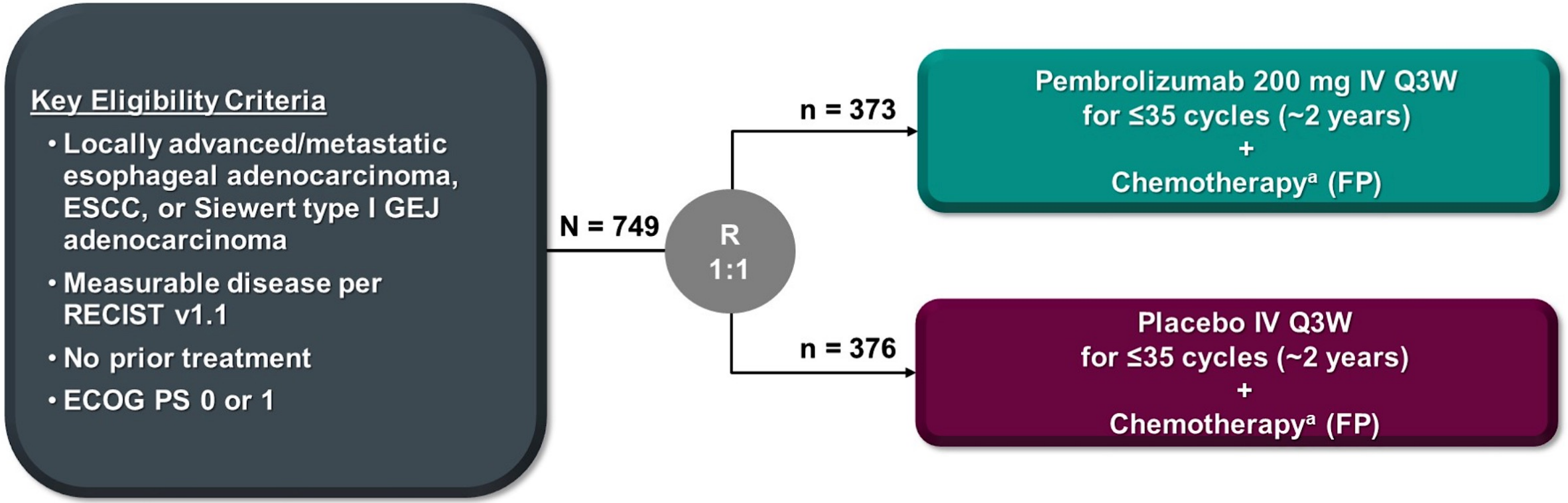
RTP RESEARCH TO PRACTICE

CheckMate 649: Authors' Conclusions

- NIVO + chemo continued to demonstrate long-term efficacy vs chemo and acceptable safety after 5 years of follow-up in previously untreated patients with advanced GC/GEJC/EAC
  - Clinically meaningful long-term OS and PFS benefits were observed in all randomized, PD-L1 CPS ≥ 1, PD-L1 CPS ≥ 5, and PD-L1 CPS ≥ 10 populations
  - OS benefit was observed across subgroups and enriched at higher PD-L1 CPS cutoffs
  - ORR was higher and DOR was longer in all randomized, PD-L1 CPS ≥ 1, PD-L1 CPS ≥ 5, and PD-L1 CPS ≥ 10 populations
- No new safety concerns were observed
- To our knowledge, these results represent the longest follow-up in a phase 3 trial of a programmed death-1 inhibitor plus chemo in advanced GC/GEJC/EAC, and continue to support NIVO + chemo as standard 1L treatment

Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract 398.

KEYNOTE-590: A Phase III Study of First-Line Pembrolizumab and Chemotherapy for GE Cancers



Stratification Factors

- Geographic region (Asia vs rest of world)
- Histology (adenocarcinoma vs squamous cell carcinoma)
- ECOG PS (0 vs 1)

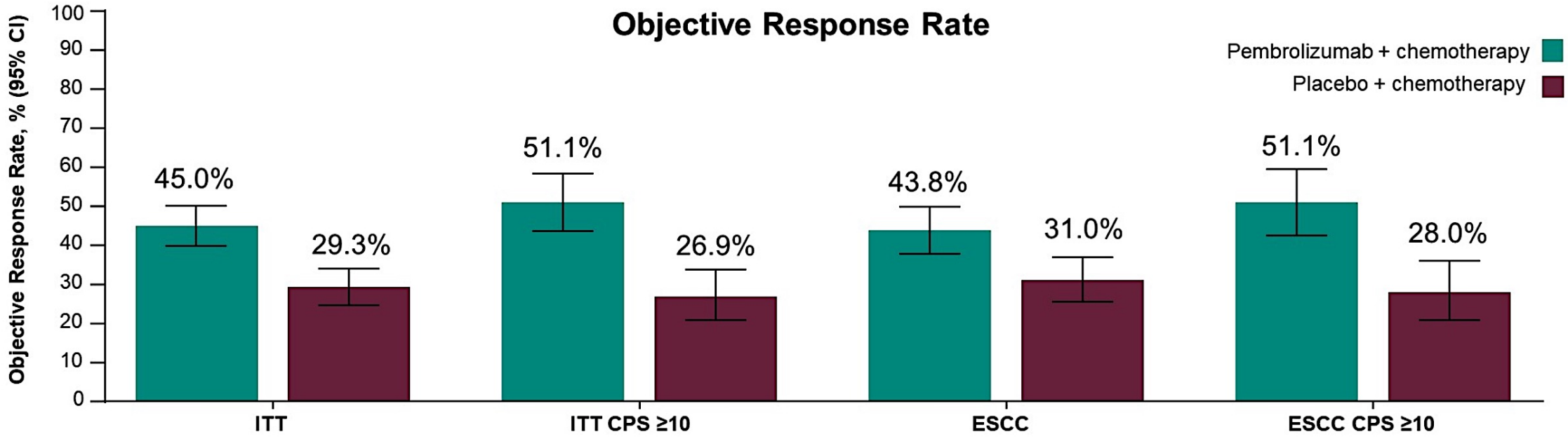
End Points

- Primary: OS,[b] PFS[c,d]
- Secondary: ORR[d], DOR[d], safety, PROs[e]

PROs = patient-reported outcomes

Shah M et al. Gastrointestinal Cancers Symposium 2024;Abstract 250.

KEYNOTE-590: Response

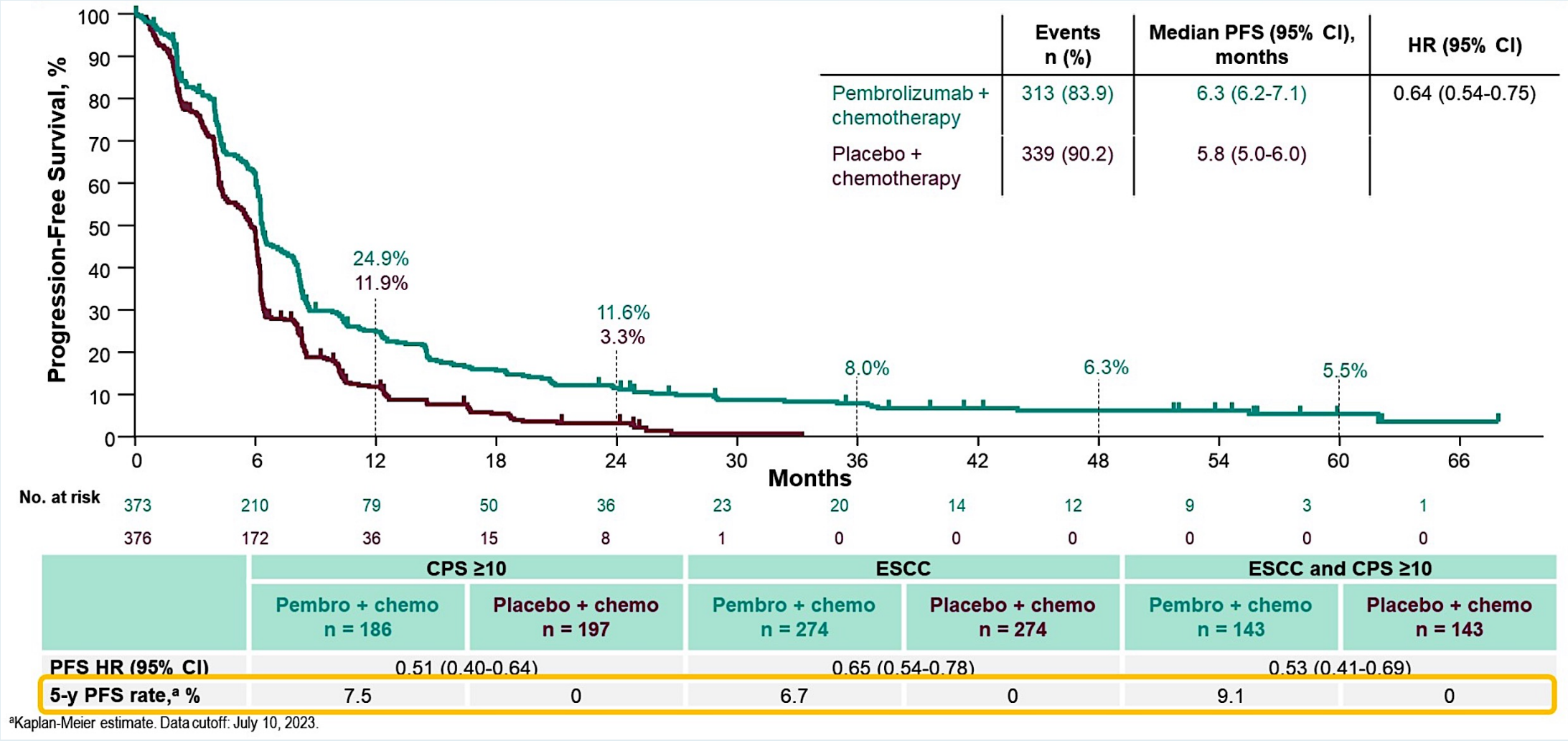


Duration of Response

	ITT		CPS ≥10		ESCC		ESCC and CPS ≥10	
	Pembro + chemo (n = 168)	Placebo + chemo (n = 110)	Pembro + chemo (n = 95)	Placebo + chemo (n = 53)	Pembro + chemo (n = 120)	Placebo + chemo (n = 85)	Pembro + chemo (n = 73)	Placebo + chemo (n = 40)
DOR,[b] median (range), months	8.3 (1.2+ to 65.9+)	6.0 (1.5+ to 31.1)	10.4 (1.9 to 65.9+)	5.6 (1.5+ to 31.1)	9.1 (1.2+ to 65.9+)	6.1 (1.5+ to 31.1)	10.4 (2.2+ to 65.9+)	4.4 (1.5+ to 31.1)

Shah M et al. Gastrointestinal Cancers Symposium 2024;Abstract 250.

KEYNOTE-590: PFS in the Intent-to-Treat Population



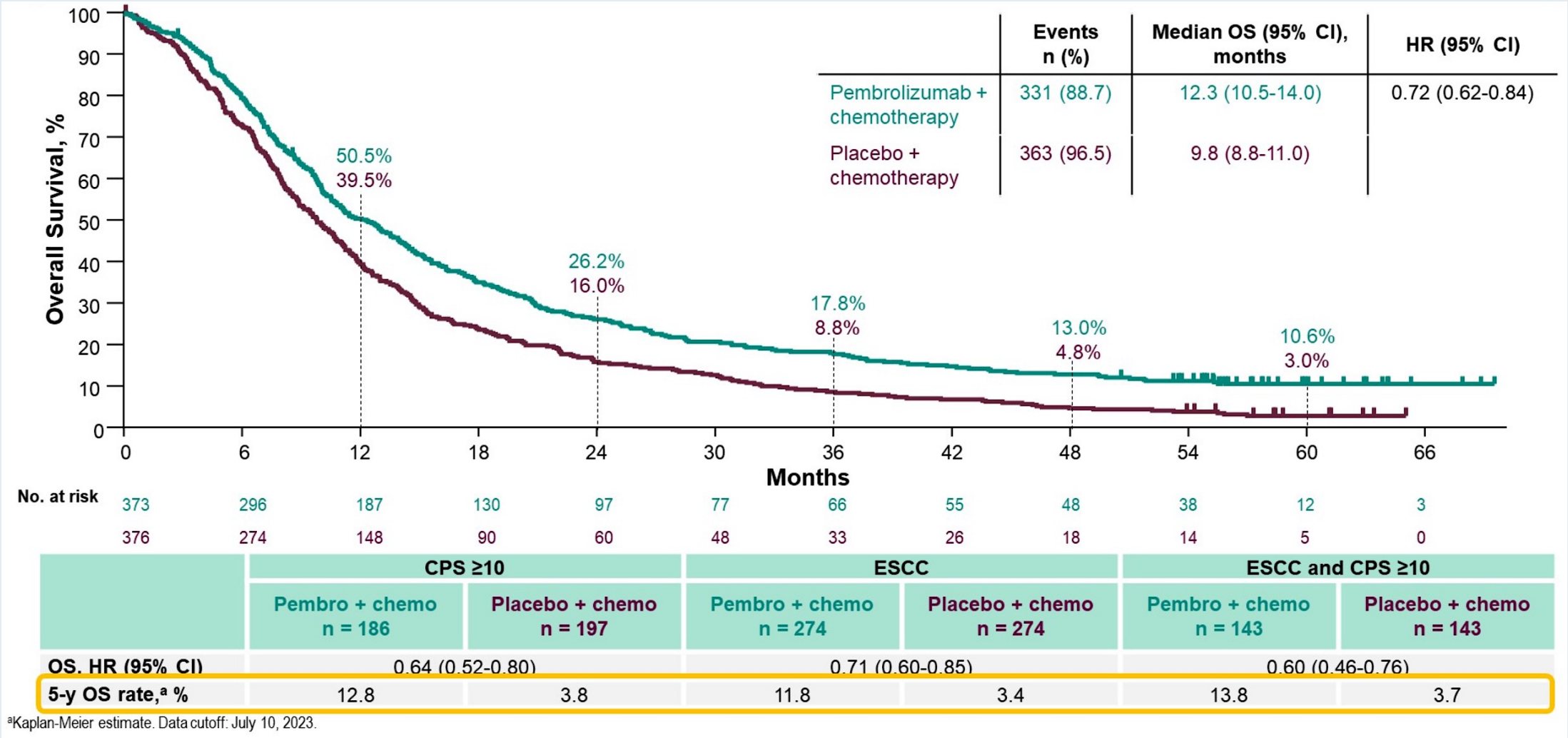
	Events n (%)	Median PFS (95% CI), months	HR (95% CI)
Pembrolizumab + chemotherapy	313 (83.9)	6.3 (6.2-7.1)	0.64 (0.54-0.75)
Placebo + chemotherapy	339 (90.2)	5.8 (5.0-6.0)	

	CPS ≥10		ESCC		ESCC and CPS ≥10	
	Pembro + chemo n = 186	Placebo + chemo n = 197	Pembro + chemo n = 274	Placebo + chemo n = 274	Pembro + chemo n = 143	Placebo + chemo n = 143
PFS HR (95% CI)	0.51 (0.40-0.64)		0.65 (0.54-0.78)		0.53 (0.41-0.69)	
5-y PFS rate,[a] %	7.5	0	6.7	0	9.1	0

[a]Kaplan-Meier estimate. Data cutoff: July 10, 2023.

Shah M et al. Gastrointestinal Cancers Symposium 2024;Abstract 250.

KEYNOTE-590: OS in the Intent-to-Treat Population



	Events n (%)	Median OS (95% CI), months	HR (95% CI)
Pembrolizumab + chemotherapy	331 (88.7)	12.3 (10.5-14.0)	0.72 (0.62-0.84)
Placebo + chemotherapy	363 (96.5)	9.8 (8.8-11.0)	

	CPS ≥10		ESCC		ESCC and CPS ≥10	
	Pembro + chemo n = 186	Placebo + chemo n = 197	Pembro + chemo n = 274	Placebo + chemo n = 274	Pembro + chemo n = 143	Placebo + chemo n = 143
OS, HR (95% CI)	0.64 (0.52-0.80)		0.71 (0.60-0.85)		0.60 (0.46-0.76)	
5-y OS rate,[a] %	12.8	3.8	11.8	3.4	13.8	3.7

[a]Kaplan-Meier estimate. Data cutoff: July 10, 2023.

Shah M et al. Gastrointestinal Cancers Symposium 2024;Abstract 250.

RTP RESEARCH TO PRACTICE

KEYNOTE-590: Authors' Conclusions

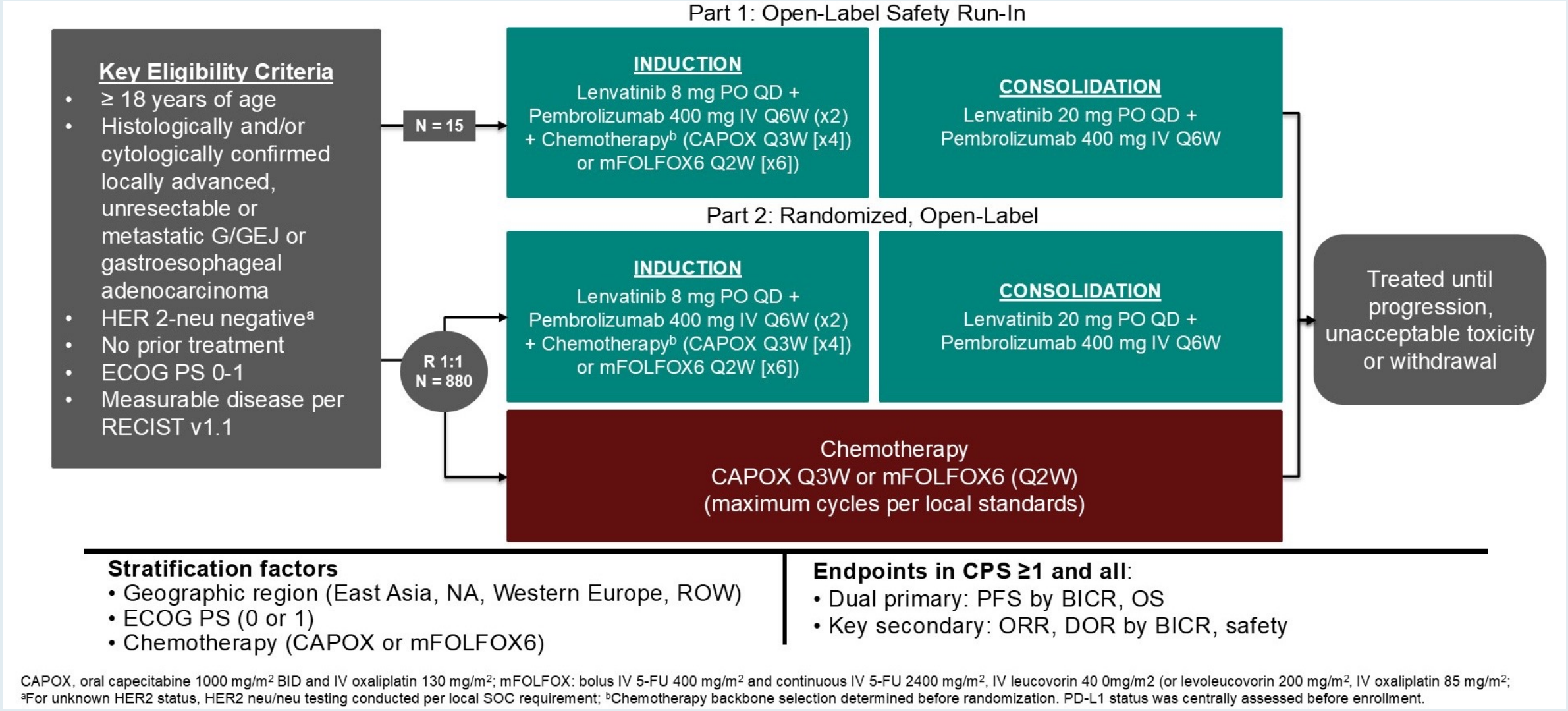
- After 5 years of follow-up, the addition of pembrolizumab to chemotherapy shows continued, durable efficacy compared with placebo + chemotherapy in advanced esophageal cancer
  - 5-year OS rates were higher with pembrolizumab + chemotherapy (10.6%) than with placebo + chemotherapy (3.0%) for the ITT population
- The addition of pembrolizumab to chemotherapy did not have a detrimental effect on health-related quality of life during treatment
- No new safety signals were observed
- These data continue to support the use of pembrolizumab + chemotherapy for advanced esophageal cancer as first-line therapy

Shah M et al. Gastrointestinal Cancers Symposium 2024;Abstract 250.

Lenvatinib plus Pembrolizumab and Chemotherapy versus Chemotherapy in Advanced, Metastatic Gastroesophageal Adenocarcinoma: The Phase 3, Randomized LEAP-015 Study

Rha S et al.
ASCO 2025;Abstract 4001.

Phase III LEAP-015 Study Design



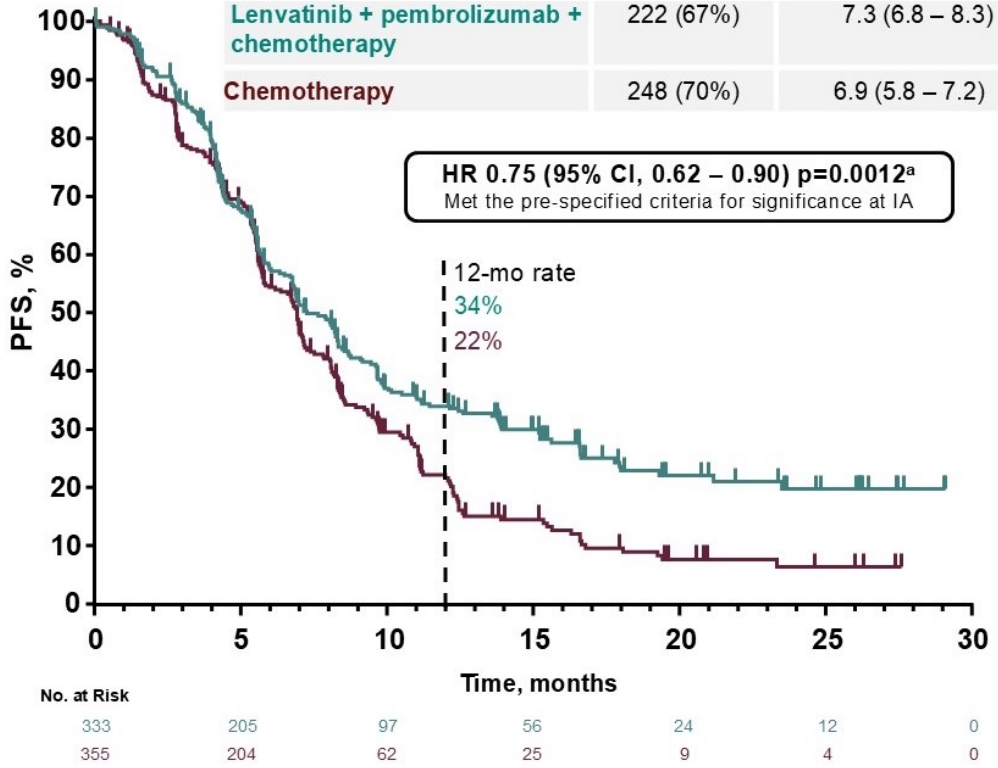
CAPOX, oral capecitabine 1000 mg/m^2 BID and IV oxaliplatin 130 mg/m^2; mFOLFOX: bolus IV 5-FU 400 mg/m^2 and continuous IV 5-FU 2400 mg/m^2, IV leucovorin 40 0mg/m2 (or levoleucovorin 200 mg/m^2, IV oxaliplatin 85 mg/m^2; [a]For unknown HER2 status, HER2 neu/neu testing conducted per local SOC requirement; [b]Chemotherapy backbone selection determined before randomization. PD-L1 status was centrally assessed before enrollment.

Shitara K et al. ASCO 2025;Abstract 4001.

Phase III LEAP-015: Interim PFS

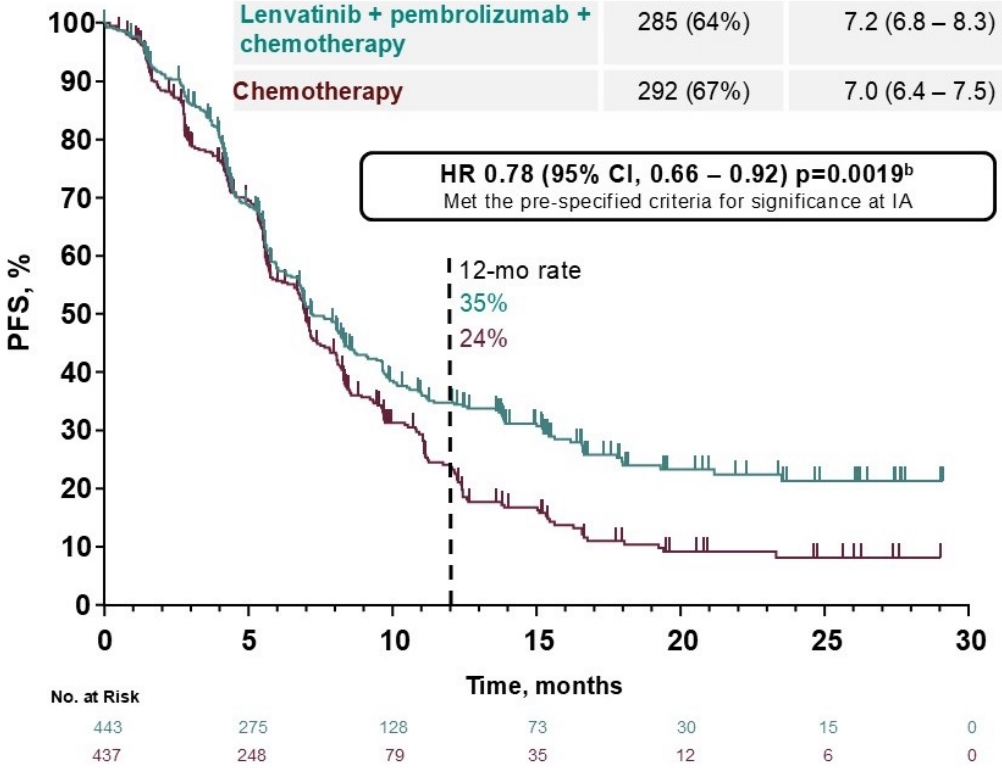
CPS ≥1

	Events, n (%)	Median (95% CI), mo
Lenvatinib + pembrolizumab + chemotherapy	222 (67%)	7.3 (6.8 – 8.3)
Chemotherapy	248 (70%)	6.9 (5.8 – 7.2)



All Randomized Participants

	Events, n (%)	Median (95% CI), mo
Lenvatinib + pembrolizumab + chemotherapy	285 (64%)	7.2 (6.8 – 8.3)
Chemotherapy	292 (67%)	7.0 (6.4 – 7.5)



Data cutoff date: 16 Nov 2023. [a]Boundary of 0.007 for significance. [b]Boundary of 0.005999 for significance.

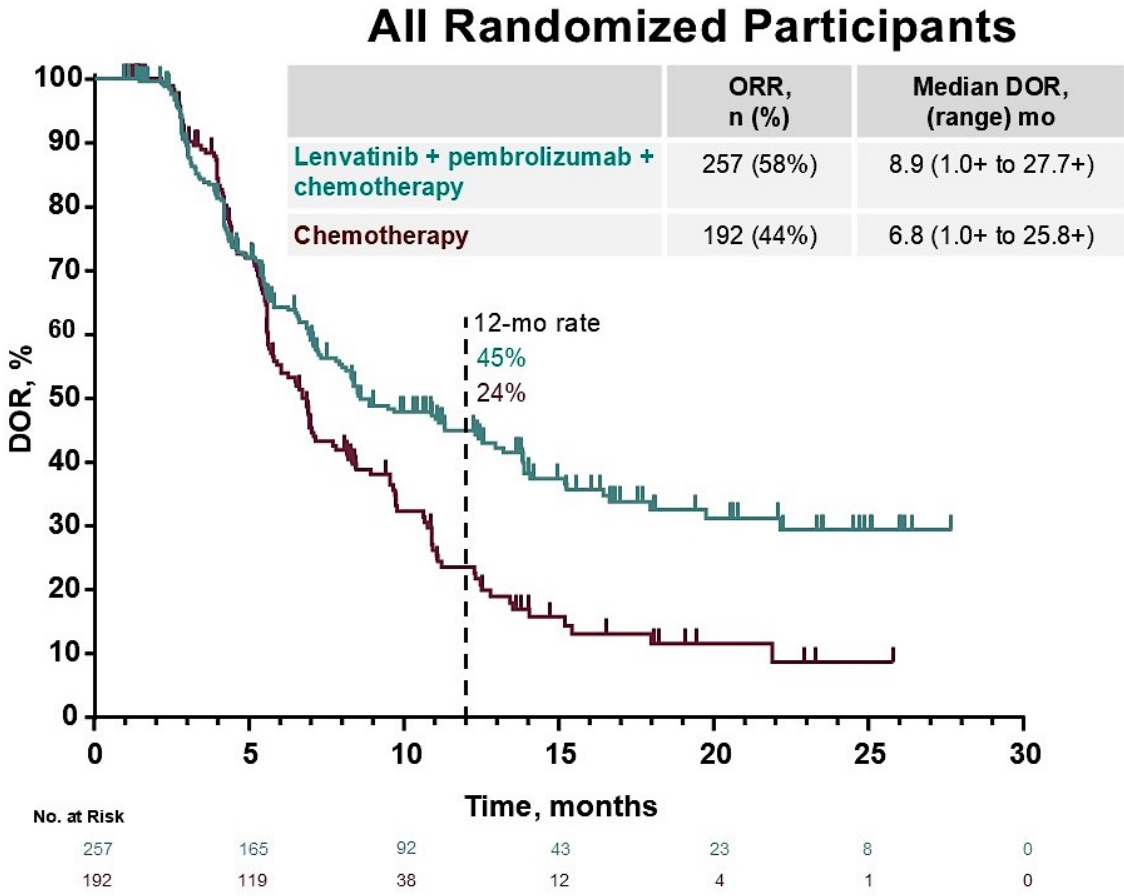
CPS = PD-L1 combined positive score

Shitara K et al. ASCO 2025;Abstract 4001, Shitara K et al. *J Clin Oncol* 2025;43(22):2502-14.

RTP RESEARCH TO PRACTICE

Phase III LEAP-015: Interim Summary of Antitumor Responses

	Lenvatinib + pembrolizumab + chemotherapy N = 443	Chemotherapy N = 437
ORR, % (95% CI)[a]	58.0 (53.3 - 62.7)	43.9 (39.2 - 48.7)
% difference (95% CI)	14.2 (7.7-20.6); P < 0.0001[b]	
Best overall response, n (%)		
Complete response	38 (8.6)	22 (5.0)
Partial response	219 (49.4)	170 (38.9)
Stable disease	140 (31.6)	168 (38.4)
Progressive disease	18 (4.1)	39 (8.9)
Not evaluable/no assessment	28 (6.3)	38 (8.7)
Median DOR (range), months	8.9 (1.0+ to 27.7+)	6.8 (1.0+ to 25.8+)
Duration ≥ 24 months	29.7%	8.7%

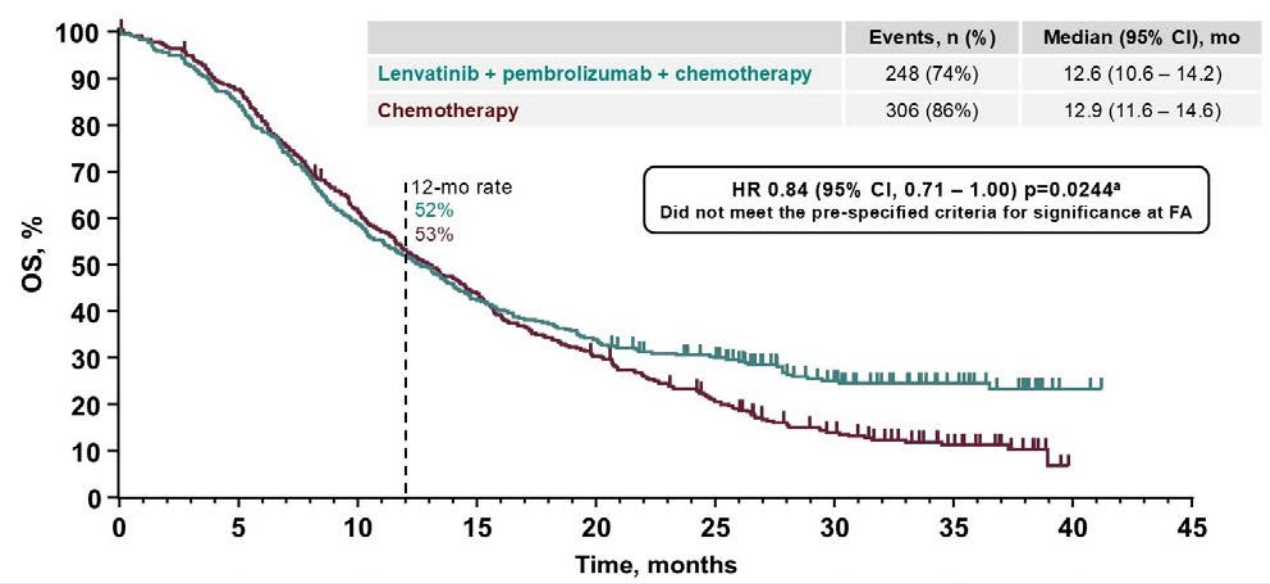


Data cutoff date: 16 Nov 2023. [a]ORR in PD-L1 CPS ≥1 was 59.5% vs 45.4% with lenvatinib + pembrolizumab + chemotherapy vs chemotherapy (% difference 14.3%). [b]Boundary of 0.001001 for significance met in in both populations.

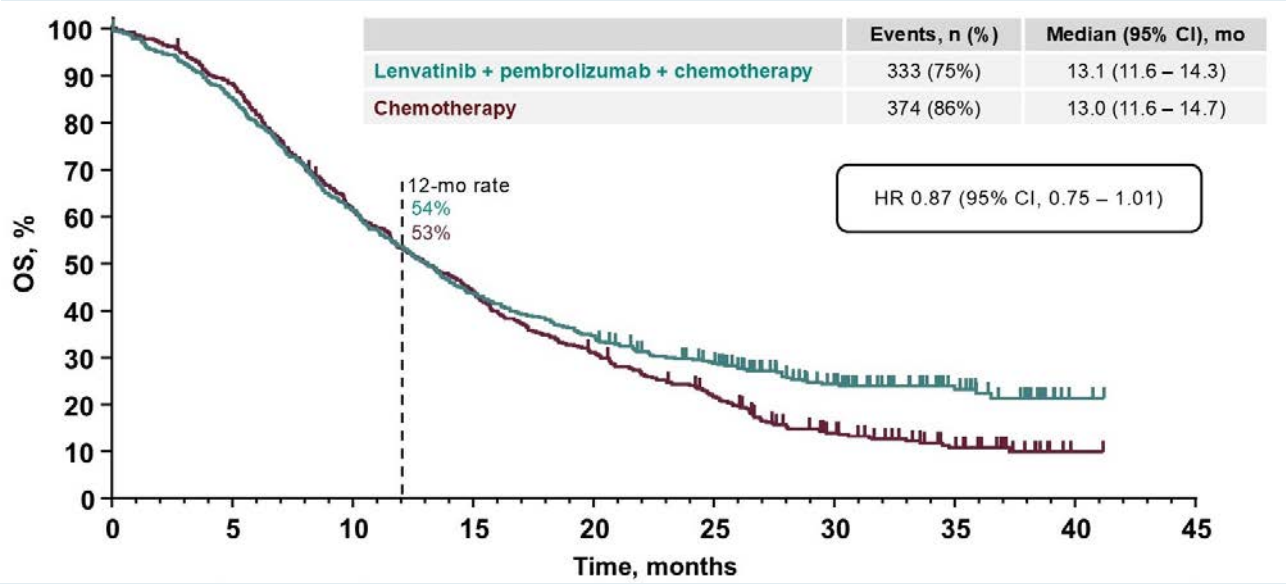
Shitara K et al. ASCO 2025;Abstract 4001, Shitara K et al. *J Clin Oncol* 2025;43(22):2502-14.

Phase III LEAP-015: OS by CPS Final Analysis

CPS ≥1



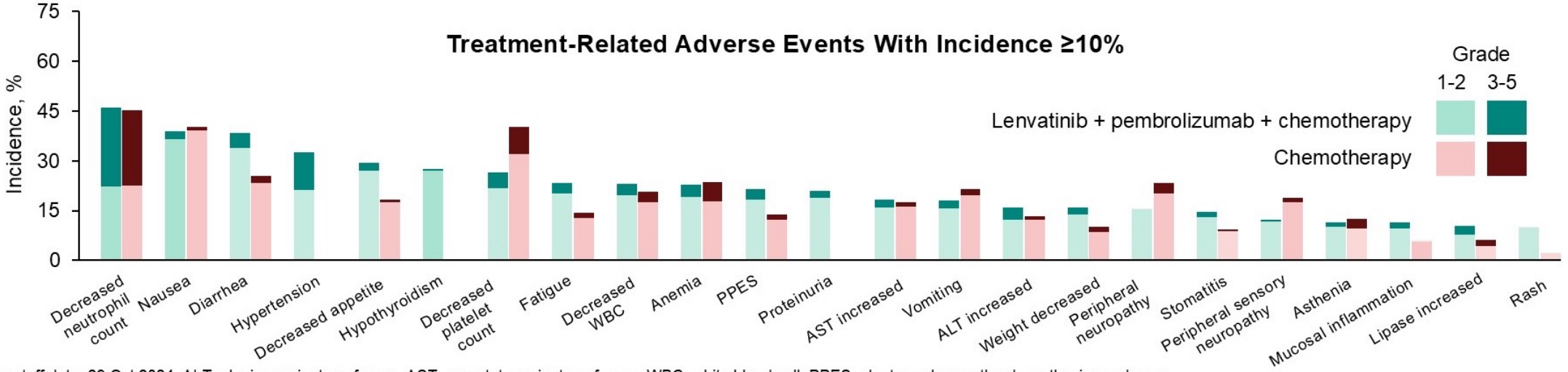
All participants



Shitara K et al. ASCO 2025;Abstract 4001, Shitara K et al. *J Clin Oncol* 2025;43(22):2502-14.

Phase III LEAP-015: Adverse Events (AEs) Summary

AEs, n (%)	Lenvatinib + pembrolizumab + chemotherapy N = 441	Chemotherapy N = 429
Median (range) duration of treatment	6.5 months (0 – 41)	5.6 months (0 – 41)
Any grade AEs	439 (99.5)	414 (96.5)
Treatment-Related AEs	430 (97.5)	394 (91.8)
Grade 3 - 4	264 (59.8)	206 (48.0)
Grade 5	24 (5.4)	2 (<1)
Led to discontinuation of any drug	119 (29.6)	99 (23.1)
Any immune-mediated adverse event	202 (45.8)	51 (11.9)



Data cutoff date: 29 Oct 2024. ALT, alanine aminotransferase, AST, aspartate aminotransferase, WBC, white blood cell, PPES, plantar-palmar erthrodysaethesia syndrome.

Shitara K et al. ASCO 2025;Abstract 4001, Shitara K et al. *J Clin Oncol* 2025;43(22):2502-14.

Phase III LEAP-015: Authors' Conclusions

- First-line lenvatinib plus pembrolizumab and chemotherapy vs chemotherapy alone provided significant improvement in PFS and ORR but not OS in PD-L1 CPS ≥1 unresectable, advanced metastatic G/GEJ adenocarcinoma
  - PFS HR 0.75 (PD-L1 CPS ≥1); HR 0.78 (all participants) at interim analysis
  - ORR 59.5% vs 45.4% (PD-L1 CPS ≥1); 58% vs 44% (all participants) at interim analysis
  - OS HR 0.84 (PD-L1 CPS ≥1); HR 0.87 (all participants) at final analysis
- Safety profiles were generally consistent with the known profiles of lenvatinib in combination with pembrolizumab or the chemotherapy regimen alone
  - Higher rate of treatment-related grade ≥3 events in the combination arm (65% vs 49%)
    - Grade 5 treatment-related events (5% vs <1%)
  - No new safety signals were identified for lenvatinib or pembrolizumab
- The feasibility of the combination requires further exploration

Shitara K et al. ASCO 2025;Abstract 4001, Shitara K et al. *J Clin Oncol* 2025;43(22):2502-14.

IDeate-Esophageal01 Phase III Trial of Ifinatamab Deruxtecan Initiated for Certain Patients with Pretreated Advanced or Metastatic ESCC

Press Release: May 19, 2025

"The first patient has been dosed in the IDeate-Esophageal01 Phase 3 trial evaluating the efficacy and safety of investigational ifinatamab deruxtecan (I-DXd) versus investigator's choice of chemotherapy in patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) with disease progression following treatment with a platinum-containing systemic therapy and an immune checkpoint inhibitor.

Ifinatamab deruxtecan is a specifically engineered, potential first-in-class B7-H3 directed DXd antibody drug conjugate."

https://www.merck.com/news/ideate-esophageal01-phase-3-trial-of-ifinatamab-deruxtecan-initiated-in-certain-patients-with-pretreated-advanced-or-metastatic-esophageal-squamous-cell-carcinoma/

Phase III TroFuse-015 Trial: Sacituzumab Tirumotecan for Metastatic GE Adenocarcinoma (GEA)

Patients with advanced unresectable or metastatic GEA, measurable disease and disease progression after 2 or more prior lines of therapy

n ≈ 450

1:1

Sacituzumab tirumotecan (4 mg/kg)
Days 1, 15, 29 (42-day cycle)

TPC (TAS-102, irinotecan, paclitaxel or docetaxel)

Primary endpoint: Overall survival
Secondary endpoints: PFS, ORR, DOR, safety

TPC = treatment of physician's choice

Shitara K et al. ESMO 2024;Abstract 263TiP. www.clinicaltrials.gov. NCT06356311. Accessed November 2025.

Management of Advanced Gastroesophageal (GE) Cancers

Case 1	Dr Yannucci – 60-year-old man
Case 2	Dr Morganstein – 62-year-old man
Case 3	Dr Brenner – 86-year-old man
■ Data Review: HER2-positive GE cancer	
Case 4	Dr Mulherin – 82-year-old woman
■ Data Review: MSI-high/dMMR GE cancer	
Case 5	Dr Divers – 65-year-old man
■ Data Review: Immunotherapy for localized GE cancer	
Case 6	Dr Apuri – 82-year-old man
■ Data Review: Immunotherapy for metastatic GE cancer	
Case 7	**Dr Warsch – 74-year-old man**
■ Data Review: CLDN18.2-positive GE cancer	

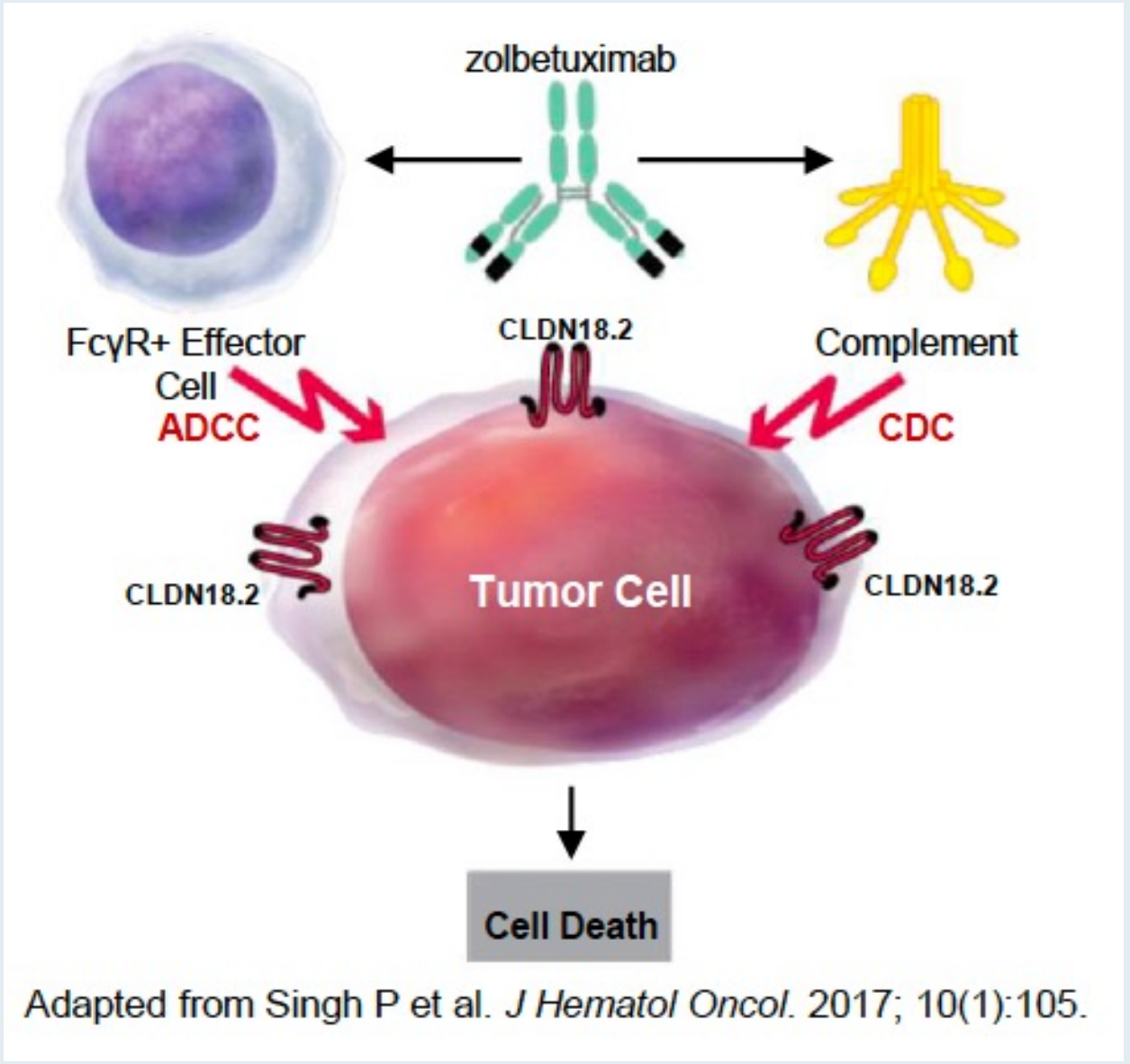
RTP
RESEARCH
TO PRACTICE

Case Presentation: 74-year-old man with CLDN18.2-positive metastatic esophageal adenocarcinoma who develops progressive toxicities with FOLFOX and zolbetuximab

Dr Sean Warsch (Asheville, North Carolina)

RTP
RESEARCH
TO PRACTICE

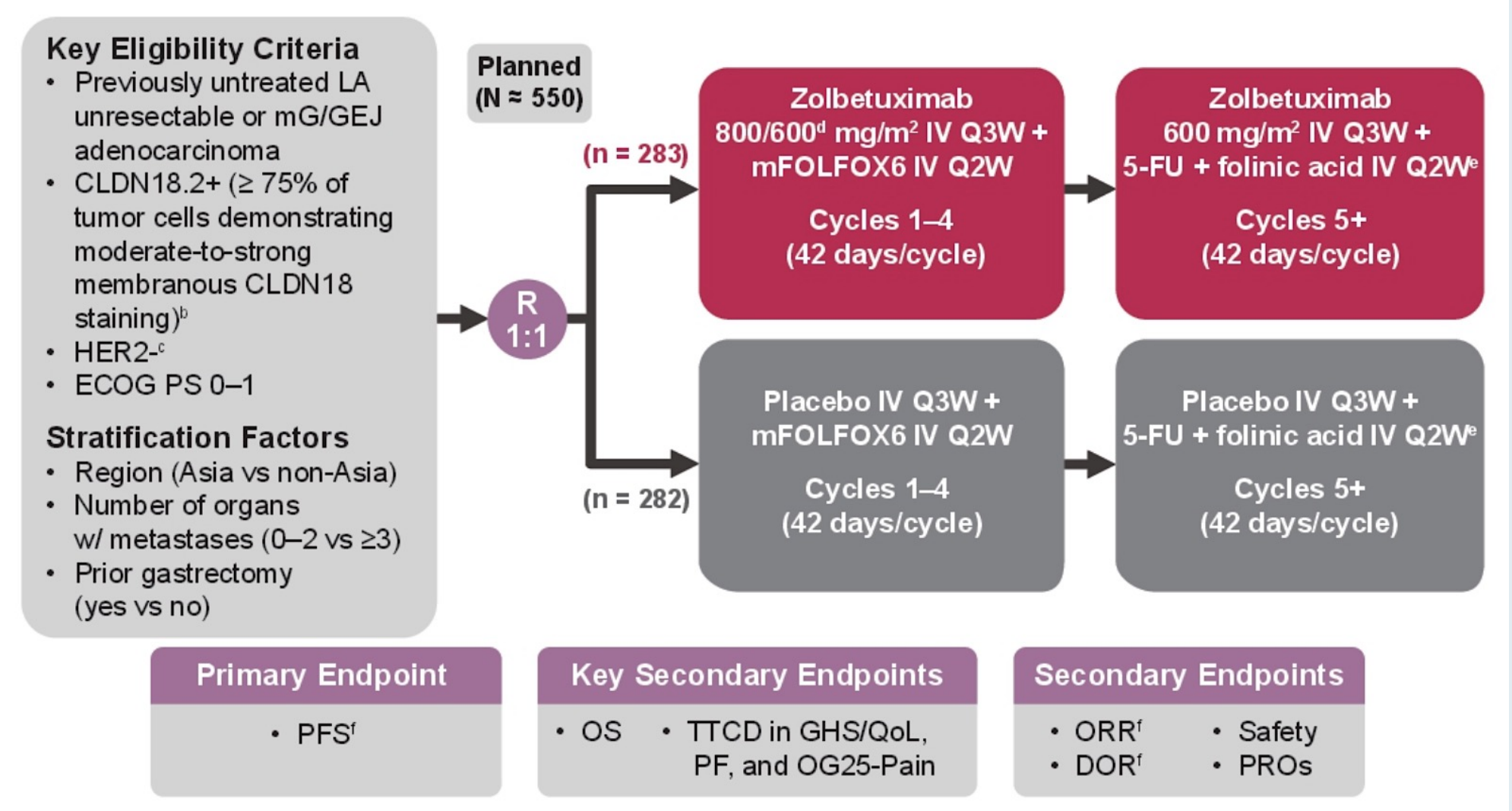
Mechanism of Action of Zolbetuximab



Adapted from Singh P et al. *J Hematol Oncol*. 2017; 10(1):105.

Lordick F et al. ESMO 2024;Abstract 134MO.

SPOTLIGHT: A Phase III Study of First-Line Zolbetuximab and mFOLFOX6 for CLDN18.2-Positive GE Adenocarcinoma



TTCD = time to confirmed deterioration; GHS/QoL = global health status/quality of life; PF = physical functioning; OG25-Pain = Oesophago-gastric Questionnaire on Abdominal Pain and Discomfort

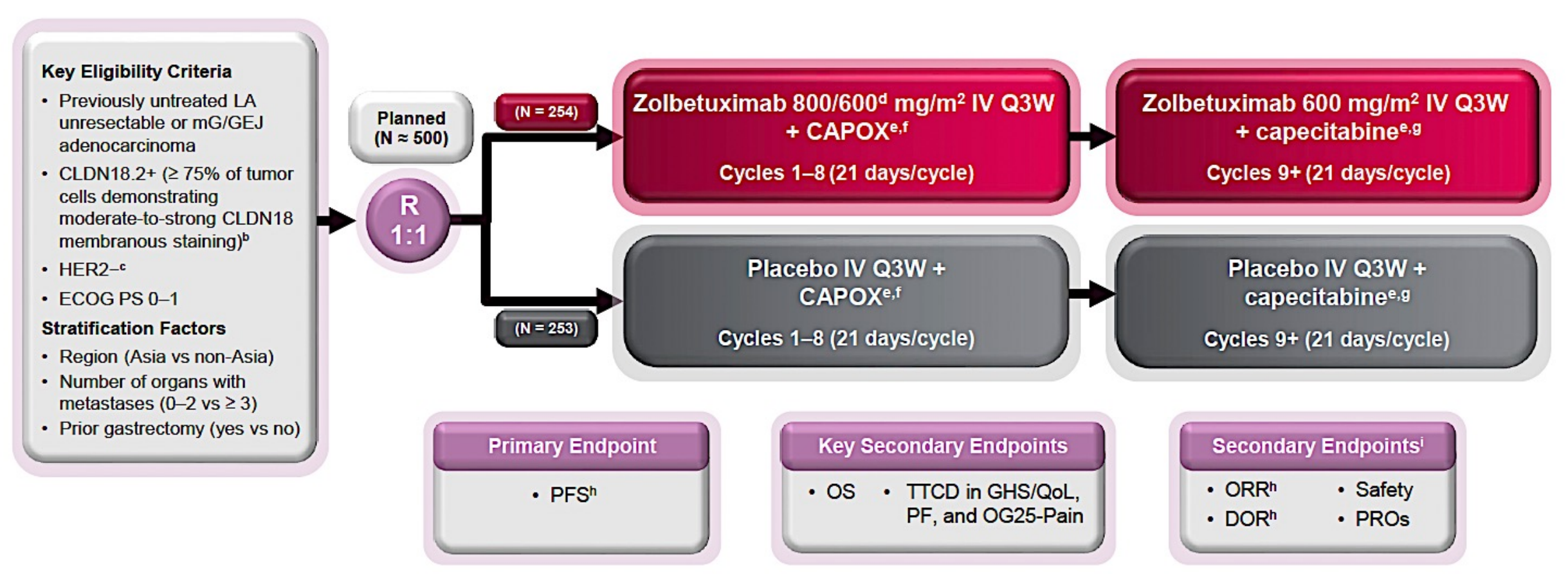
Shitara K et al. ASCO 2024;Abstract 4036.

SPOTLIGHT: Authors' Conclusions

- Zolbetuximab + mFOLFOX6 continued to demonstrate statistically significant and clinically meaningful improvement in PFS and OS versus placebo + mFOLFOX6, with no new safety signals
- Compared with the full analysis set, separation of PFS and OS curves occurred earlier in the per-protocol set population that excluded the majority of patients with early withdrawals
- These results support zolbetuximab + mFOLFOX6 as a new standard-of-care option for the first-line treatment of patients with HER2-negative, LA unresectable or mG/GEJ adenocarcinoma whose tumors are CLDN18.2-positive

Shitara K et al. ASCO 2024;Abstract 4036.

GLOW: A Phase III Study of First-Line Zolbetuximab and CAPOX for CLDN18.2-Positive GE Adenocarcinoma



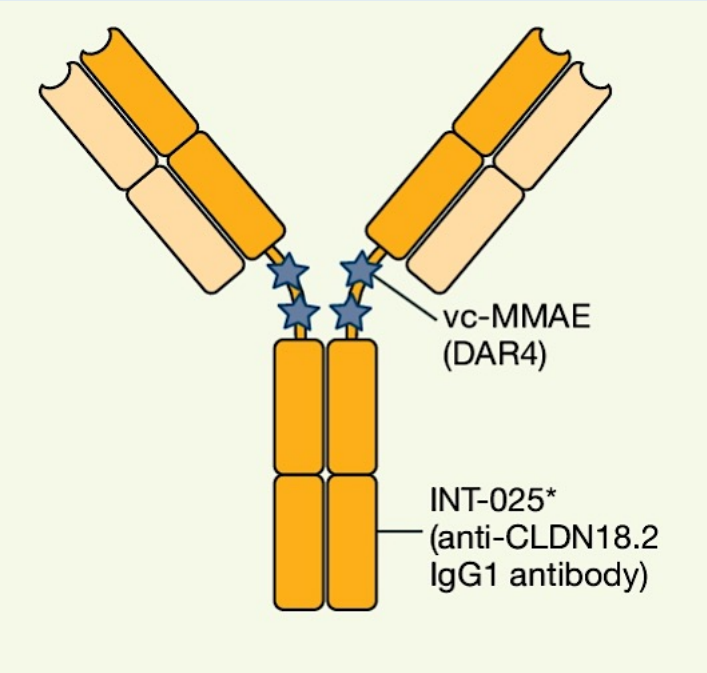
Lordick F et al. ESMO Asia 2024;Abstract 134MO.

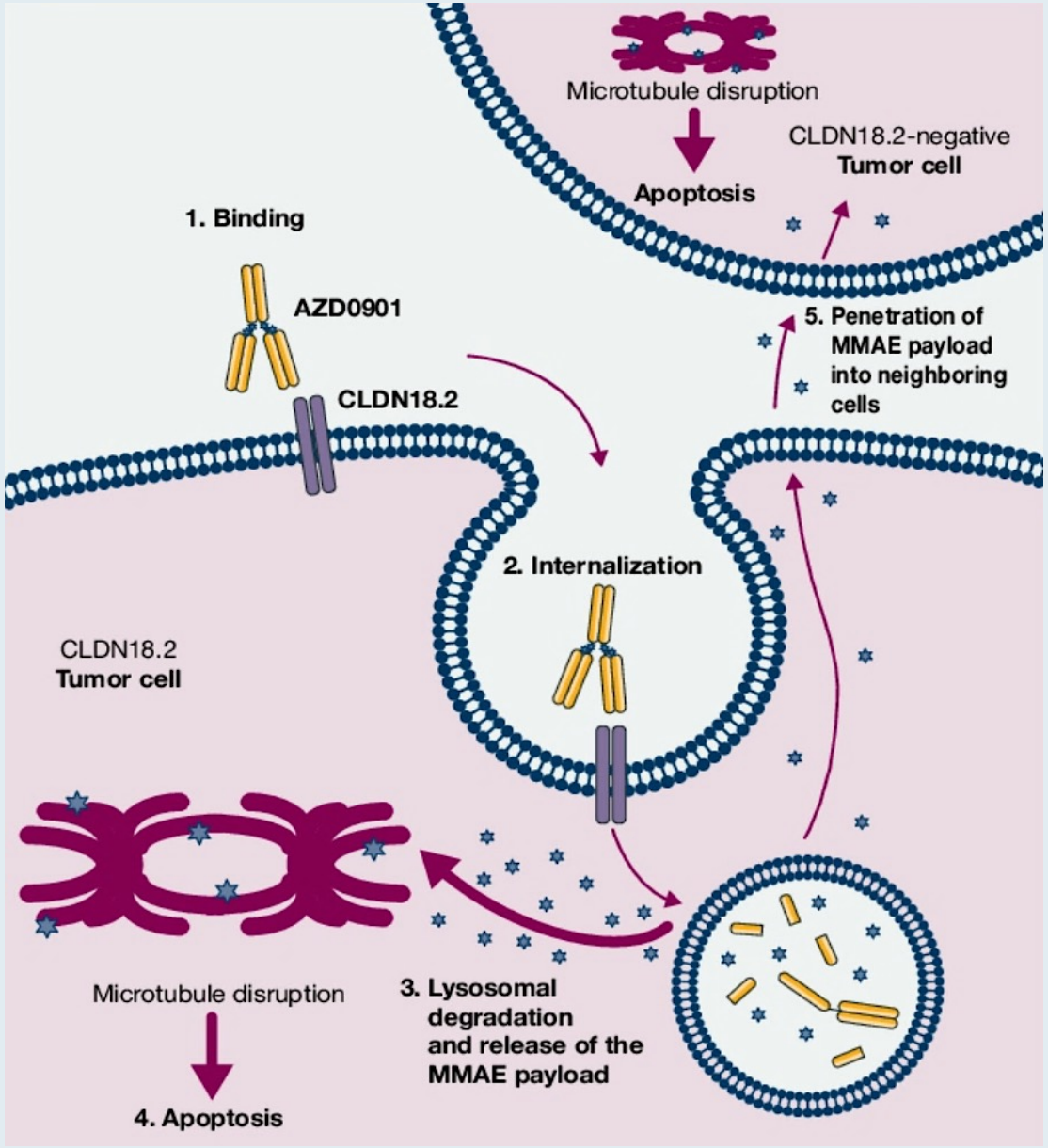
GLOW: Authors' Conclusions

- **Zolbetuximab + CAPOX continued to show a statistically significant improvement of both PFS and OS vs placebo + CAPOX**
  - mPFS: 8.28 months vs 6.80 months
  - mOS: 14.32 months vs 12.16 months
  - 24-month PFS rates: 17% vs 9%
  - 24-month OS rates: 28% vs 19%
- **Safety profile of zolbetuximab + CAPOX was consistent with prior studies of zolbetuximab, with no new safety concerns**[1–6]
  - Nausea, vomiting, and decreased appetite were the most frequent all-grade TEAEs in the zolbetuximab arm
- **These efficacy and safety results are consistent with the updated analysis of SPOTLIGHT (zolbetuximab + mFOLFOX6)**[7]
- **Based on these updated findings from GLOW, zolbetuximab + chemotherapy could be a potential 1L standard-of-care treatment option for patients with HER2−, LA unresectable or mG/GEJ adenocarcinoma whose tumors are CLDN18.2+**

Lordick F et al. ESMO Asia 2023;Abstract 134MO.

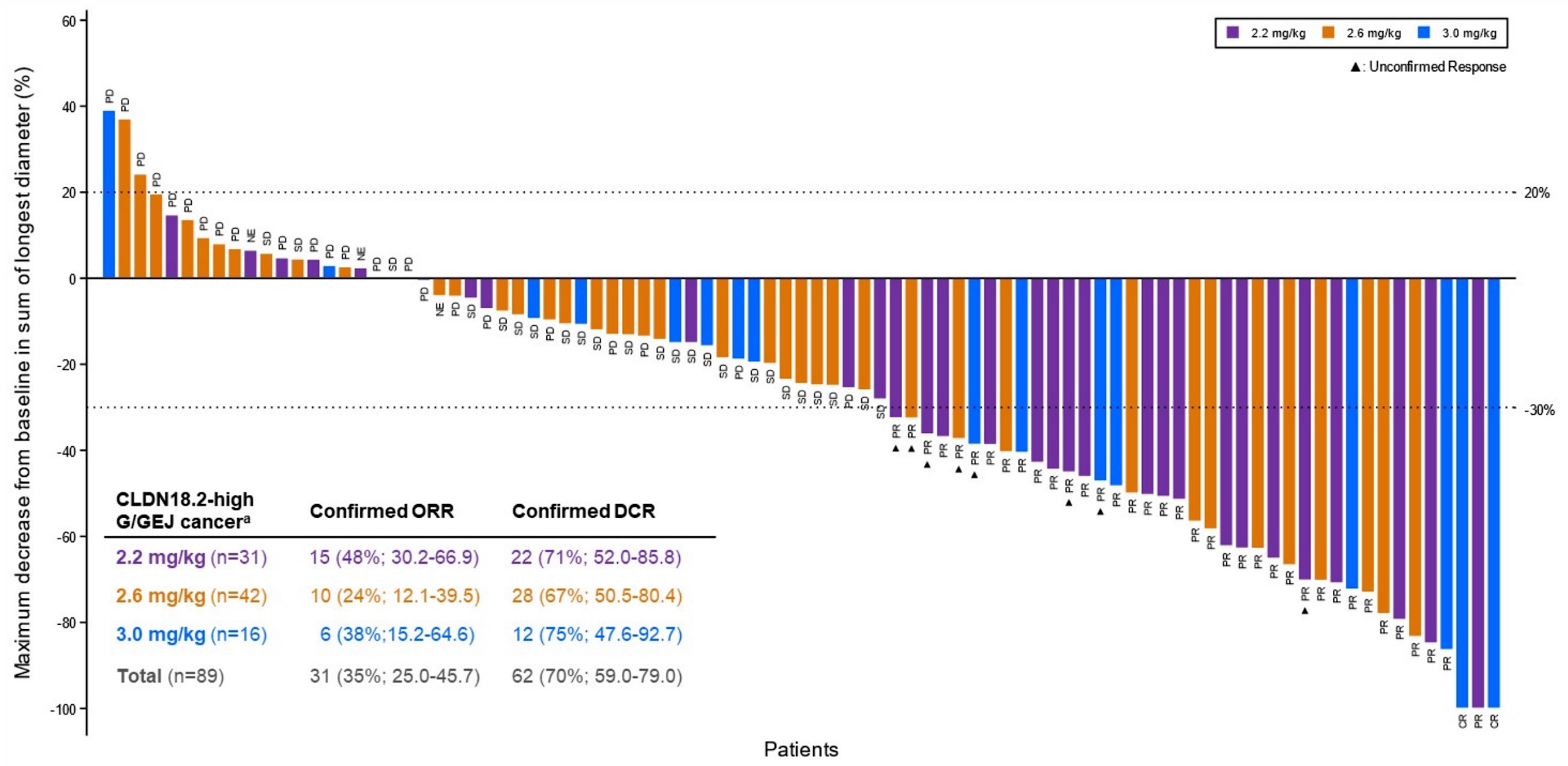
Sonesitatug Vedotin (AZD0901): An Anti-CLDN18.2 Antibody-Drug Conjugate





Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract TPS507.

Phase I Study of Sonesitatug Vedotin (AZD0901) for CLDN18.2-Positive GE Cancers: Objective Response Rate (ORR)



CLDN18.2-high G/GEJ cancer[a]	Confirmed ORR	Confirmed DCR
2.2 mg/kg (n=31)	15 (48%; 30.2-66.9)	22 (71%; 52.0-85.8)
2.6 mg/kg (n=42)	10 (24%; 12.1-39.5)	28 (67%; 50.5-80.4)
3.0 mg/kg (n=16)	6 (38%;15.2-64.6)	12 (75%; 47.6-92.7)
Total (n=89)	31 (35%; 25.0-45.7)	62 (70%; 59.0-79.0)

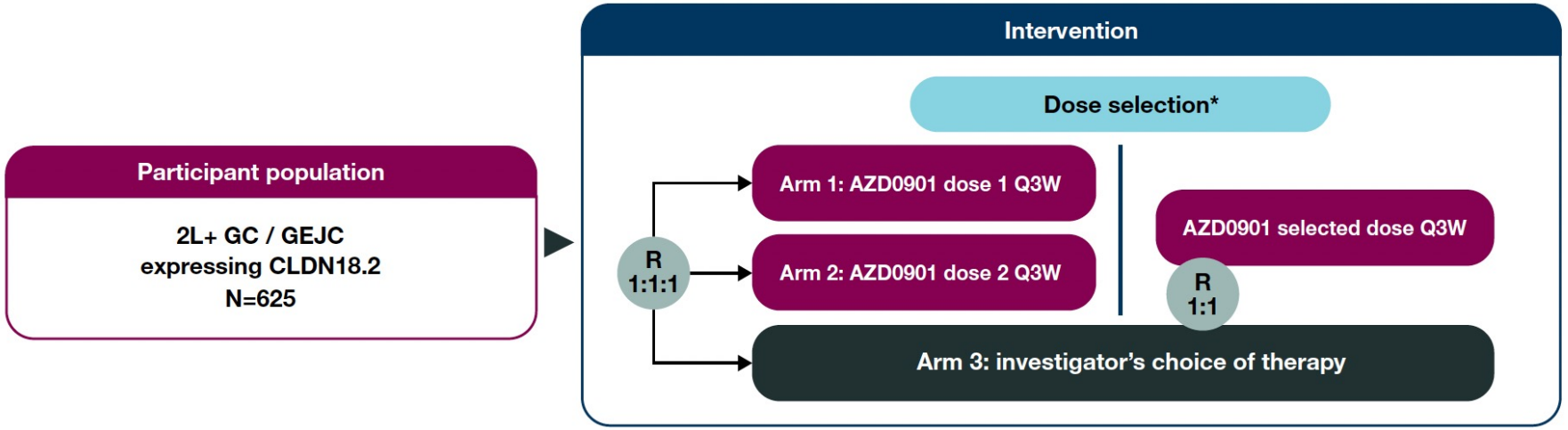
Xu R-H et al. ASCO 2024;Abstract 434420.

Phase I Study of Sonesitatug Vedotin (AZD0901): Authors' Conclusions

- **CMG901 (AZD0901) demonstrated promising clinical efficacy in pretreated patients with CLDN18.2-high G/GEJ cancer. Anti-tumor activity was observed across all the cohorts.**
  - 2.2 mg/kg cohort: confirmed ORR = 48%; mPFS = 4.8 months; mOS = 11.8 months.
- **CMG901 was generally well-tolerated, with a manageable safety profile.**
- **The current clinical program for CMG901 (AZD0901) is expanding for advanced solid tumors expressing CLDN18.2:**
  - An ongoing phase 3 registrational study in 2L+ patients (NCT06346392).
  - Additional phase 2 studies (NCT06219941; NCT05702229).

Xu R-H et al. ASCO 2024;Abstract 434420.

Phase III CLARITY Gastric 01 Trial: Sonesitatug Vedotin (AZD0901) for Advanced GE/GEJ Cancer in the Second Line or Later



Investigator's choice of therapy

- 2L: ramucirumab + paclitaxel
- 2L: paclitaxel (for participants with contraindication to ramucirumab only)
- 2L: docetaxel (for participants with contraindication to ramucirumab only)
- 3L+: irinotecan
- 3L+: TAS-102 (except China)
- 3L+: apatinib (China only)

Primary Endpoints:
PFS (all pts)
OS (third line or later participants)

*One of the AZD0901 arms (Arm 1 or Arm 2) will stop enrollment after the dose selection decision is made. Randomization will continue in a 1:1 ratio to the two remaining arms (selected AZD0901 dose arm and investigator's choice of therapy arm). AZD0901 / investigator's choice of therapy until PD, or any other discontinuation criteria are met. AZD0901 may continue beyond PD if participant continues to show clinical benefit and provides informed consent. Treatment crossover is not allowed.

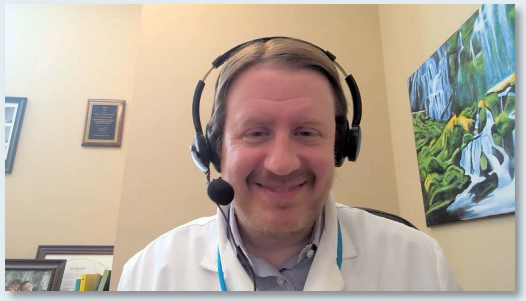
2L(+), second-line (and later); 3L(+), third-line (and later); CLDN18.2, Claudin18.2; GC, gastric cancer; GEJC, gastroesophageal junction cancer; PD, disease progression; Q3W, every 3 weeks; R, randomized.

Janjigian Y et al. Gastrointestinal Cancers Symposium 2025;Abstract TPS507.
Shitara K et al. at ESMO GI 2024;Abstract 495TiP.

RTP RESEARCH TO PRACTICE

Contributing General Medical Oncologists

Susmitha Apuri, MD
Florida Cancer Specialists
Lutz, Florida



Brian P Mulherin, MD
Hematology Oncology
of Indiana
Indianapolis, Indiana

Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida

Sean Warsch, MD
Messino Cancer Centers
Asheville, North Carolina

Stephen "Fred" Divers, MD
American Oncology Network
Hot Springs, Arkansas

Jennifer Yannucci, MD
Low Country Cancer Care
Savannah, Georgia

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

RTP
RESEARCH
TO PRACTICE

Preventing and Managing Toxicities Associated with Antibody-Drug Conjugates in the Management of Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, November 19, 2025

5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO

Rita Nanda, MD

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 for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP
RESEARCH
TO PRACTICE