Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, August 17, 2022
5:00 PM – 6:00 PM ET

Faculty

John Strickler, MD

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Lilly, and Merck.

Dr Love — Disclosures

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Dr Strickler — Disclosures

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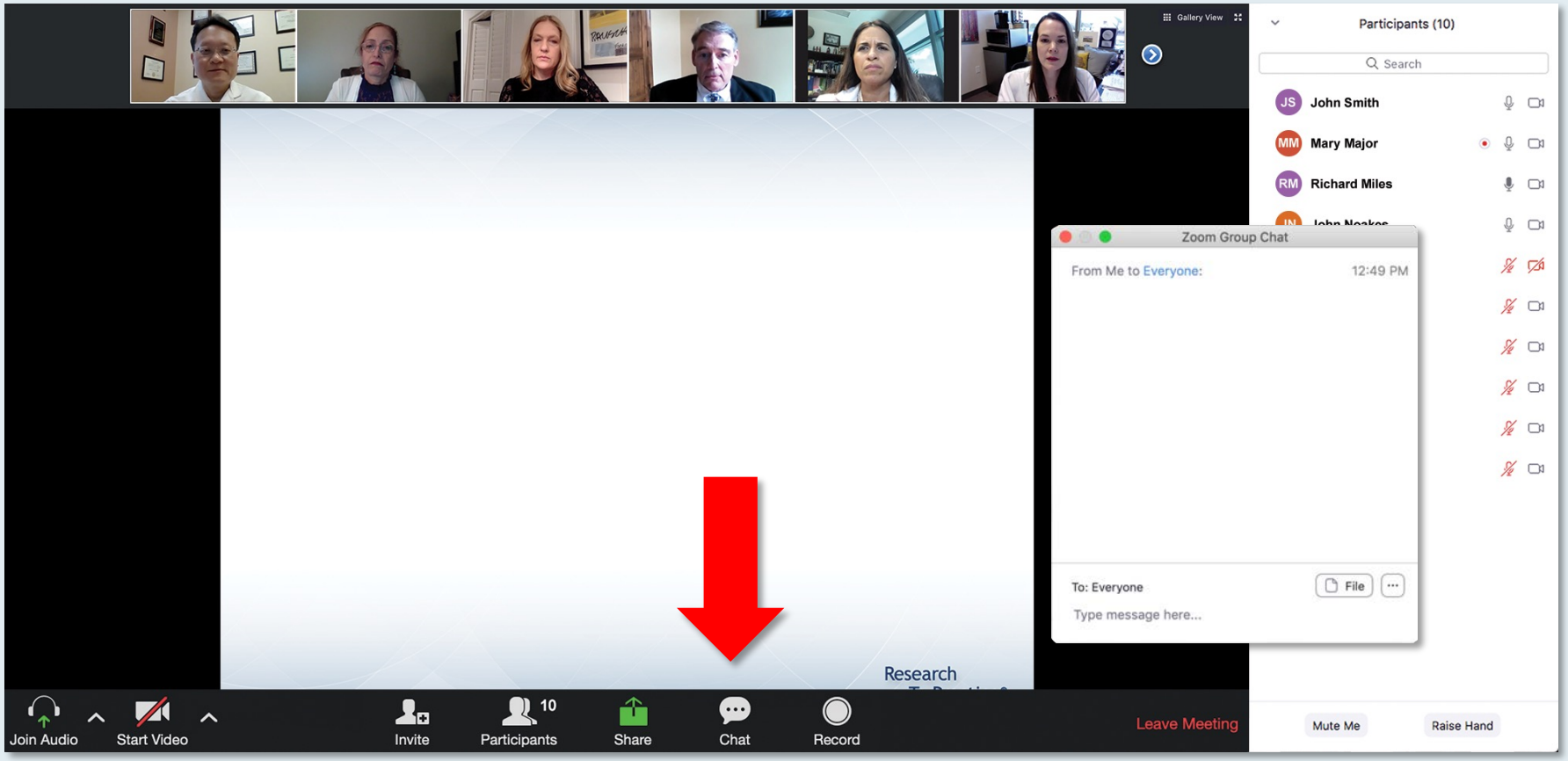
We Encourage Clinicians in Practice to Submit Questions



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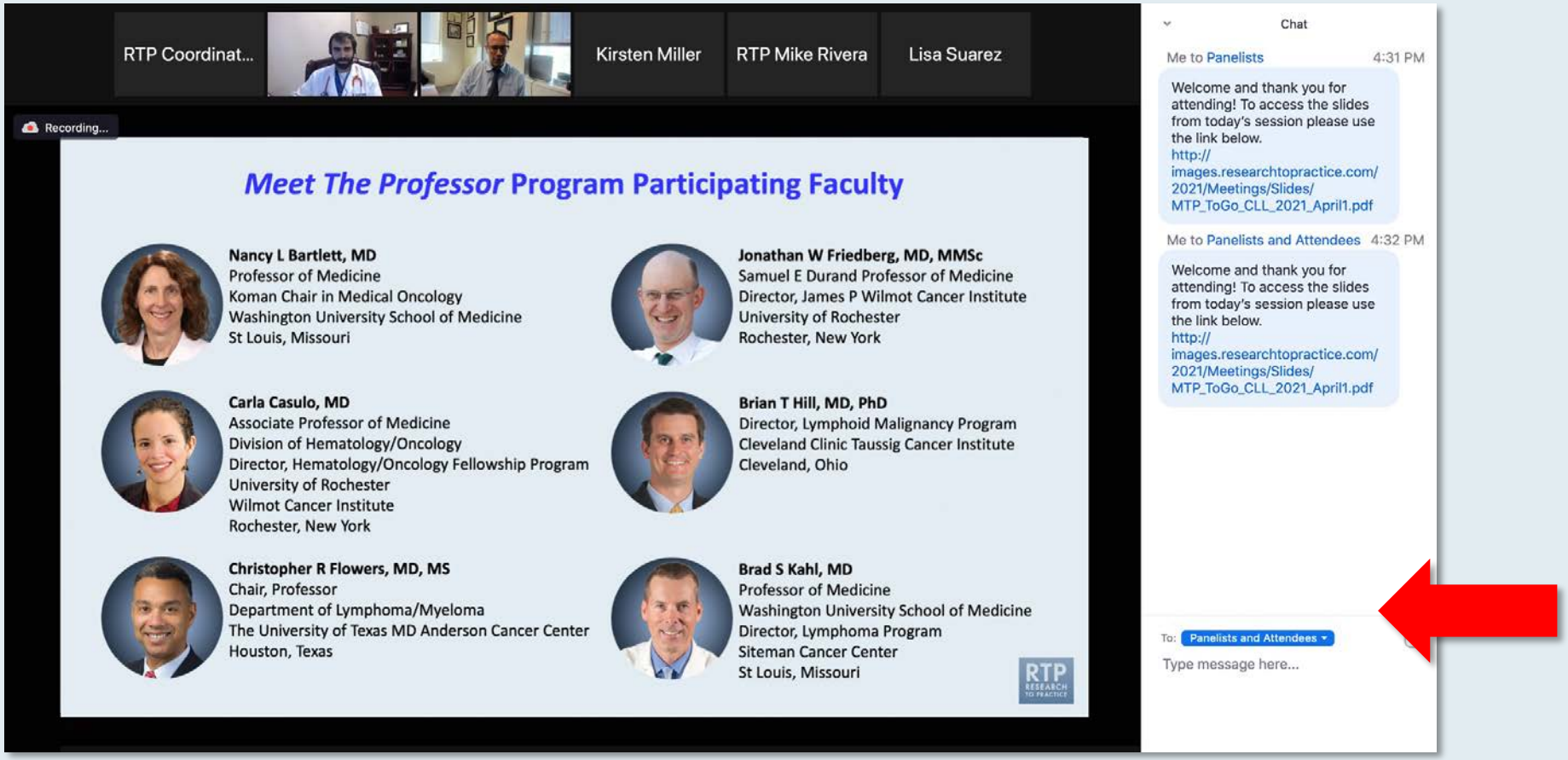
Expand chat submission box



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

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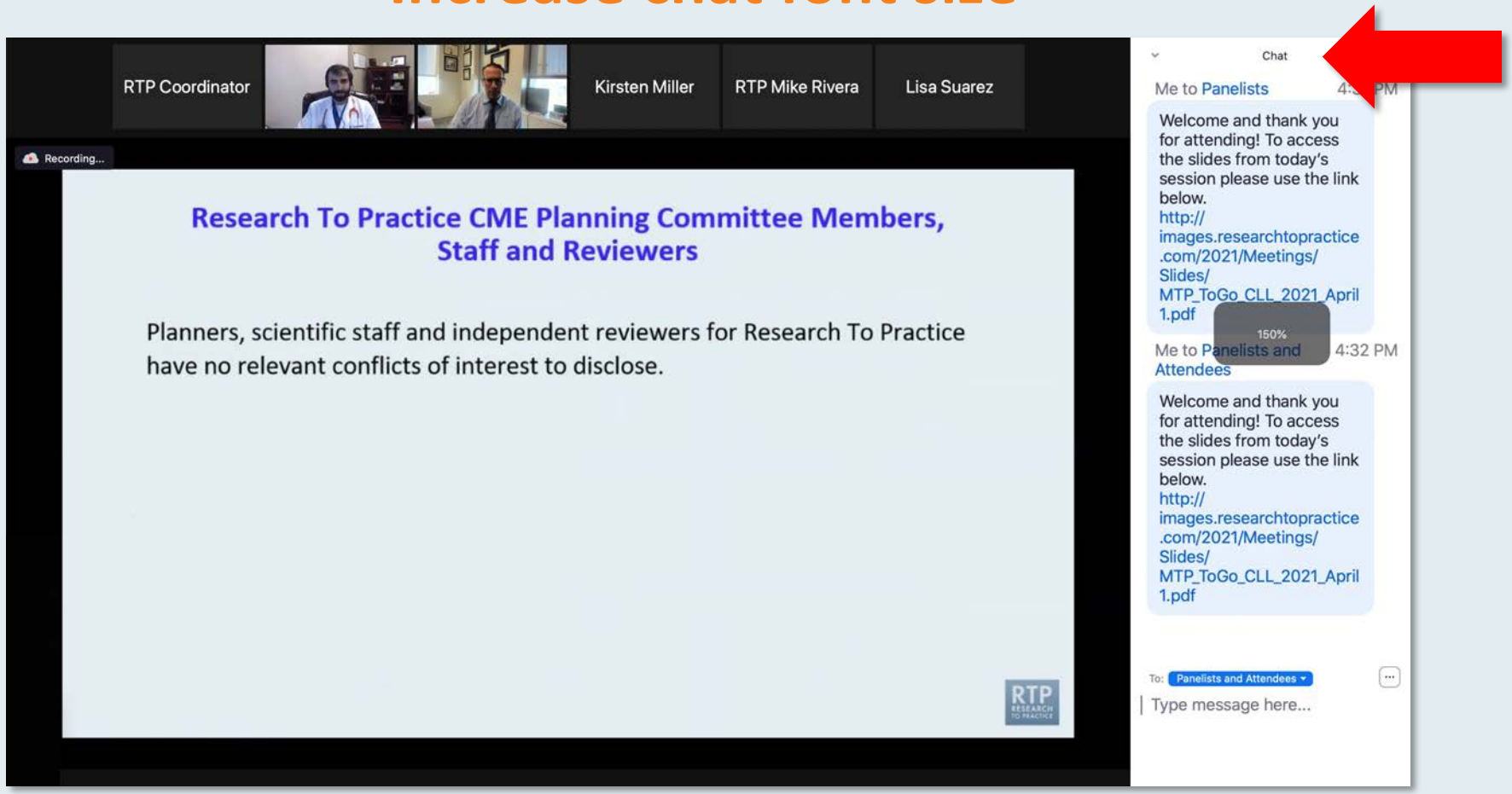

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Gastroesophageal Cancers

DR SAMUEL KLEMPNER

MASSACHUSETTS GENERAL HOSPITAL

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Meet The Professor

Optimizing the Management of Ovarian Cancer

Thursday, August 25, 2022
5:00 PM – 6:00 PM ET

Faculty

Richard T Penson, MD, MRCP

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Wednesday, August 31, 2022
5:00 PM – 6:00 PM ET

Faculty

Lecia V Sequist, MD, MPH

Moderator

Neil Love, MD

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TO PRACTICE

Meet The Professor

Optimizing the Management of HER2-Positive Breast Cancer

Thursday, September 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Mark D Pegram, MD

Moderator

Neil Love, MD

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RESEARCH
TO PRACTICE

Exploring Current Considerations and Promising Investigational Approaches for Patients with Myelodysplastic Syndromes

A CME/MOC-Accredited Virtual Event

Thursday, September 8, 2022

5:00 PM – 6:00 PM ET

Faculty

Guillermo Garcia-Manero, MD
Gail J Roboz, MD
David Sallman, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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Meet The Professor
Optimizing the Management of Gastroesophageal Cancers

John Strickler, MD
Associate Professor
Duke University
Durham, North Carolina

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Meet The Professor Program Participating Faculty

Peter C Enzinger, MD
Director, Center for Esophageal and Gastric Cancer
Dana-Farber/Brigham and Women's Cancer Center
Institute Physician, Dana-Farber Cancer Institute
Associate Professor, Harvard Medical School
Boston, Massachusetts

Yelena Y Janjigian, MD
Associate Professor
Chief of Gastrointestinal Oncology Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, New York

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Associate Professor
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

Manish A Shah, MD
Chief, Solid Tumor Oncology Service
Director, Gastrointestinal Oncology Program
Co-Director, Center for Advanced Digestive Care
Bartlett Family Professor of Gastrointestinal Oncology
Weill Cornell Medicine/NewYork-Presbyterian Hospital
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John Strickler, MD
Associate Professor
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Durham, North Carolina

Eric Van Cutsem, MD, PhD
Professor of Medicine
Digestive Oncology
University Hospitals Leuven
Leuven, Belgium

Harry H Yoon, MD, MHS
Associate Professor of Oncology
Chair, Gastroesophageal Cancer
Disease Group
Mayo Clinic Comprehensive
Cancer Center
Rochester, Minnesota

MODERATOR
Neil Love, MD
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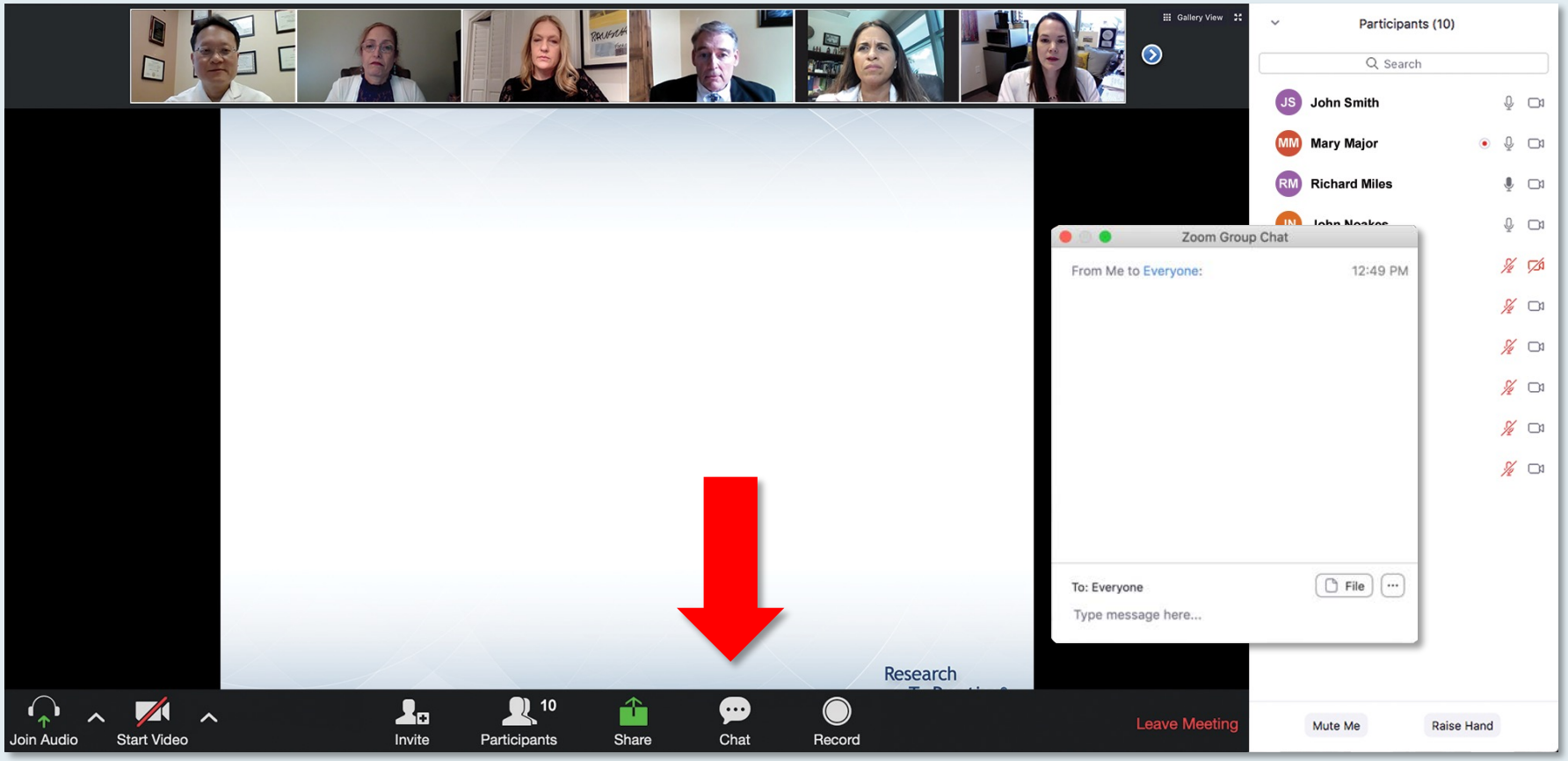

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ONCOLOGY TODAY

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Gastroesophageal Cancers

DR SAMUEL KLEMPNER

MASSACHUSETTS GENERAL HOSPITAL

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Meet The Professor

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Meet The Professor
Optimizing the Management of Gastroesophageal Cancers

John Strickler, MD
Associate Professor
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Durham, North Carolina

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Dr Strickler — Disclosures

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

Priya Rudolph, MD, PhD
Georgia Cancer Specialists
Northside Hospital Cancer Institute
Athens, Georgia

Ranju Gupta, MD
Lehigh Valley Health Network
Bethlehem, Pennsylvania

Matthew R Strickland, MD
Massachusetts General
Hospital Cancer Center
Boston, Massachusetts

Minesh Dinubhai Patel, MD
Piedmont Cancer Institute
Peachtree City, Georgia

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Meet The Professor with Dr Strickler: Management of Upper GI Cancers

Introduction

Case Presentations

Appendix of Key Publications

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Meet The Professor with Dr Strickler: Management of Upper GI Cancers

Introduction

Case Presentations

Appendix of Key Publications

RTP RESEARCH TO PRACTICE

JCO Precis Oncol 2021;September 16;5:PO.21.00030.

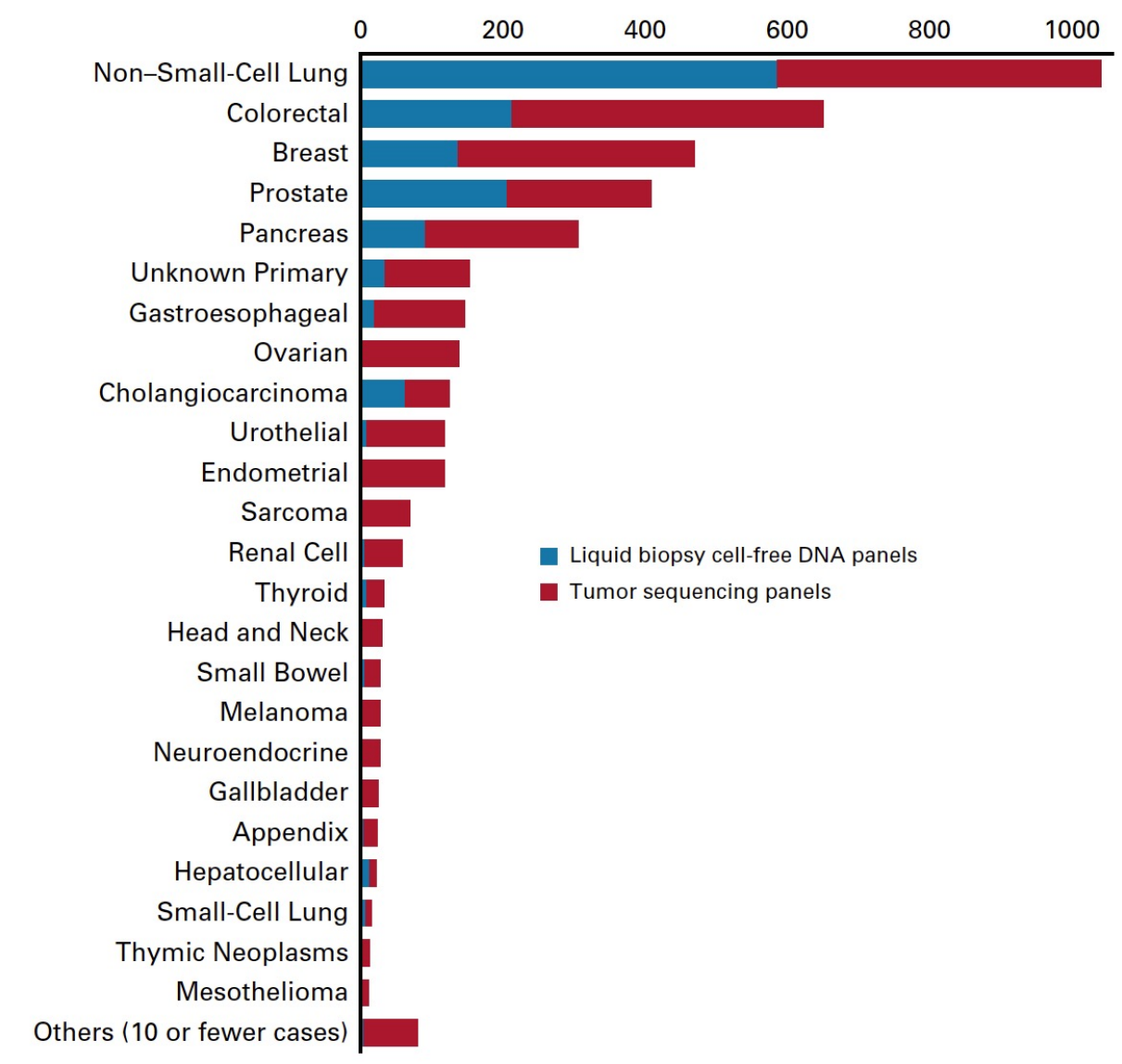
PRECISION MEDICINE

original reports

Implementation of a Molecular Tumor Registry to Support the Adoption of Precision Oncology Within an Academic Medical Center: The Duke University Experience

Michelle F. Green, PhD[1]; Jonathan L. Bell, MD[1]; Christopher B. Hubbard, BS[1]; Shannon J. McCall, MD[1]; Matthew S. McKinney, MD[2]; Jinny E. Riedel, MS[3]; Carolyn S. Menendez, MD[3,4]; James L. Abbruzzese, MD[3,5]; John H. Strickler, MD[3,5]; and Michael B. Datto, MD, PhD[1]

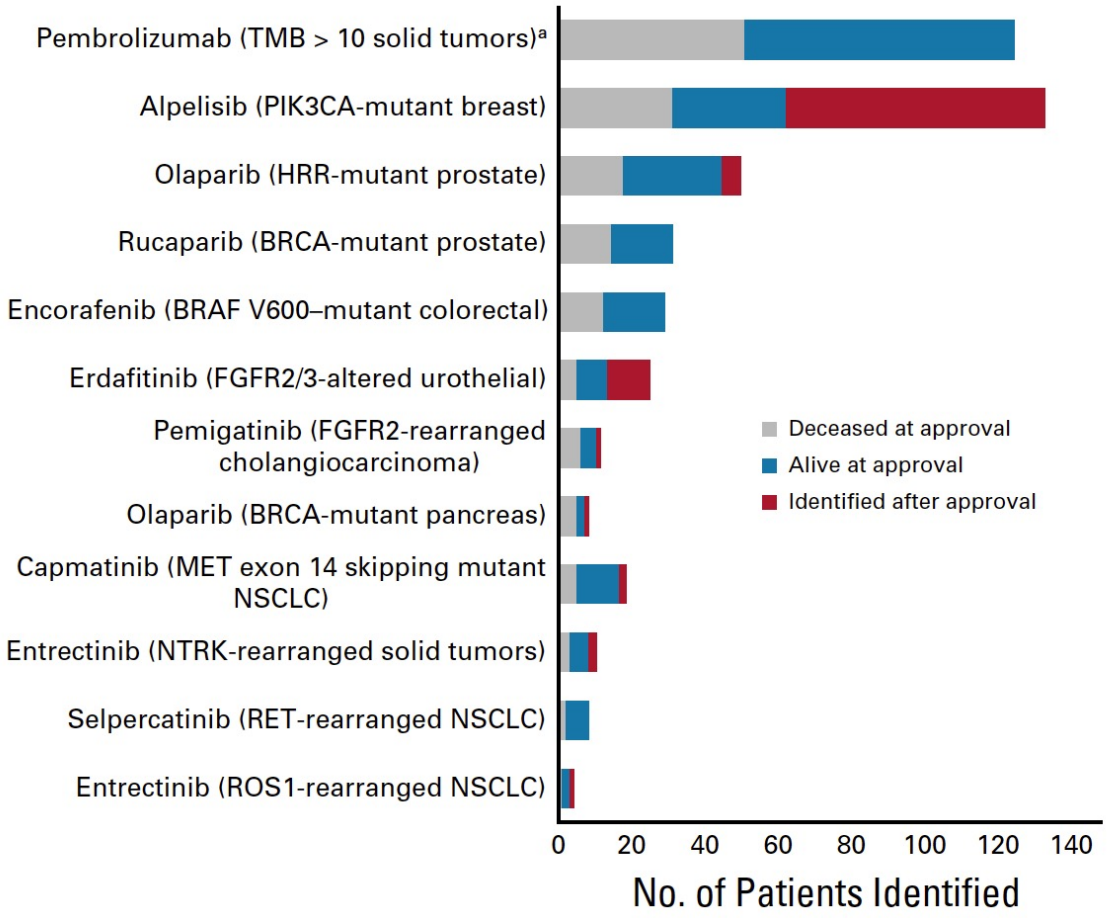
Total Number of Liquid Biopsy-Based and Tumor Sequencing Profiles by Cancer Type



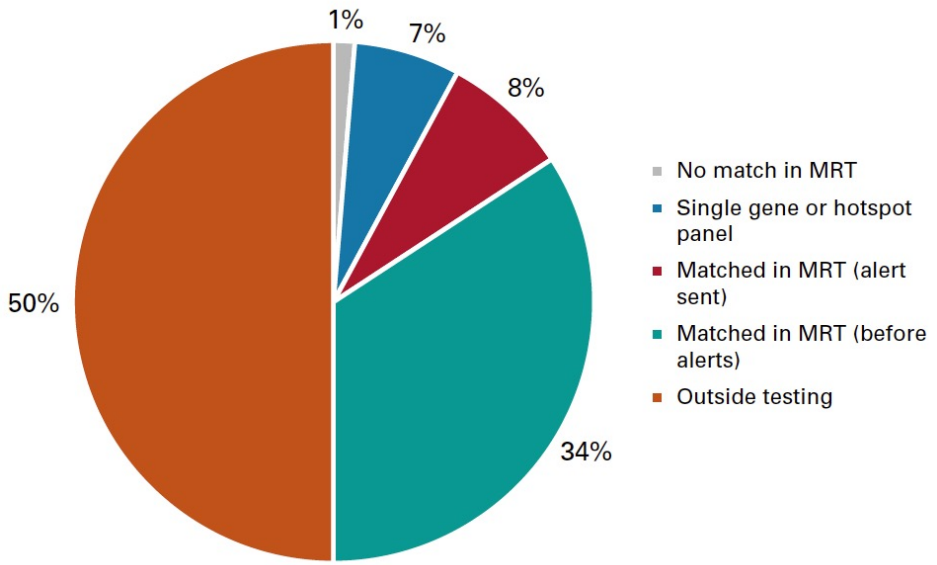
Green MF et al. *JCO Precis Oncol* 2021;September 16;5:PO.21.00030.

Newly Approved Therapy Alerts and Clinical Trial Matching

Newly Approved Therapies Stratified by Vital Status and Detection of Alteration Relative to Approval

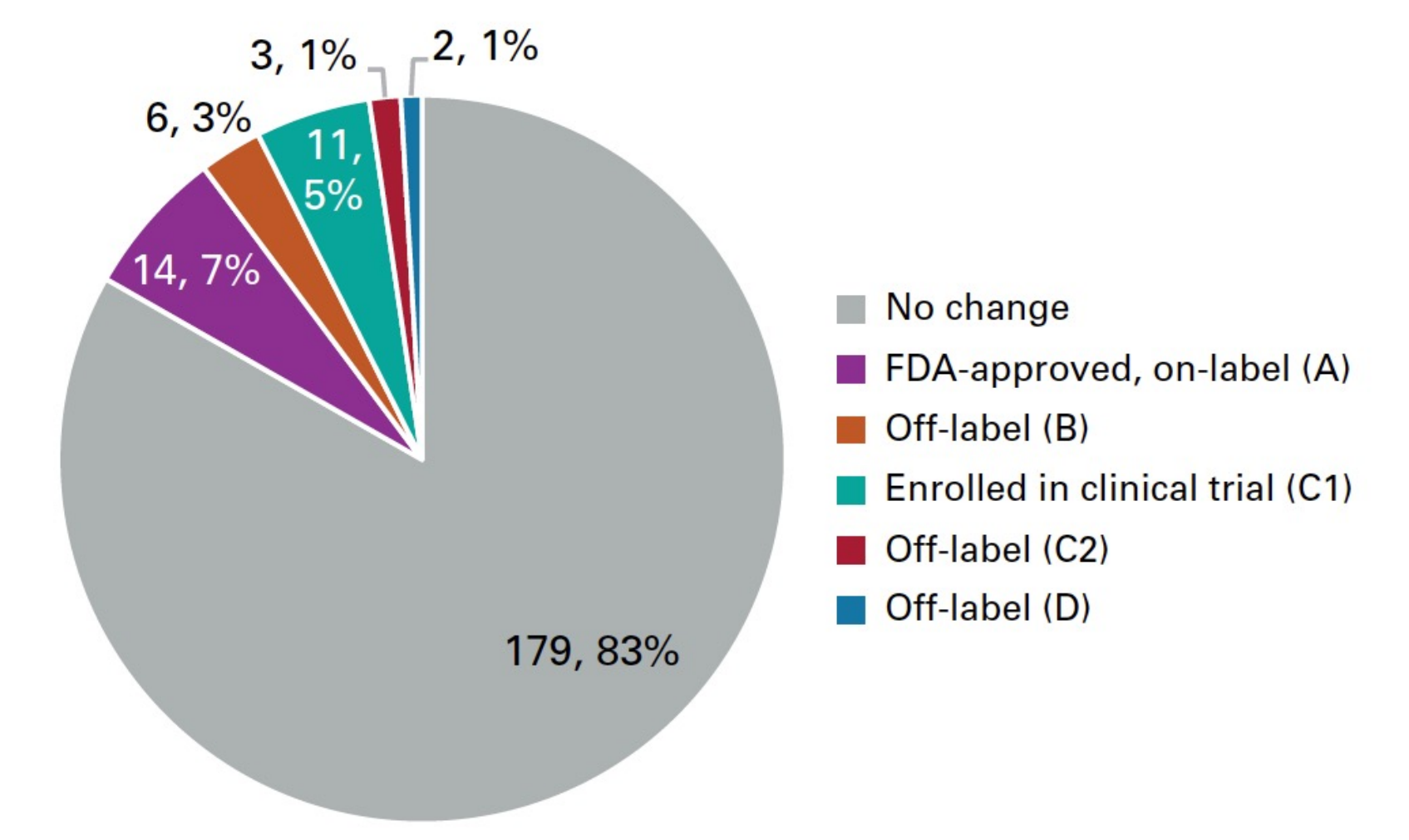


Sources of Genomic Profiling Results



Green MF et al. *JCO Precis Oncol* 2021;September 16;5:PO.21.00030.

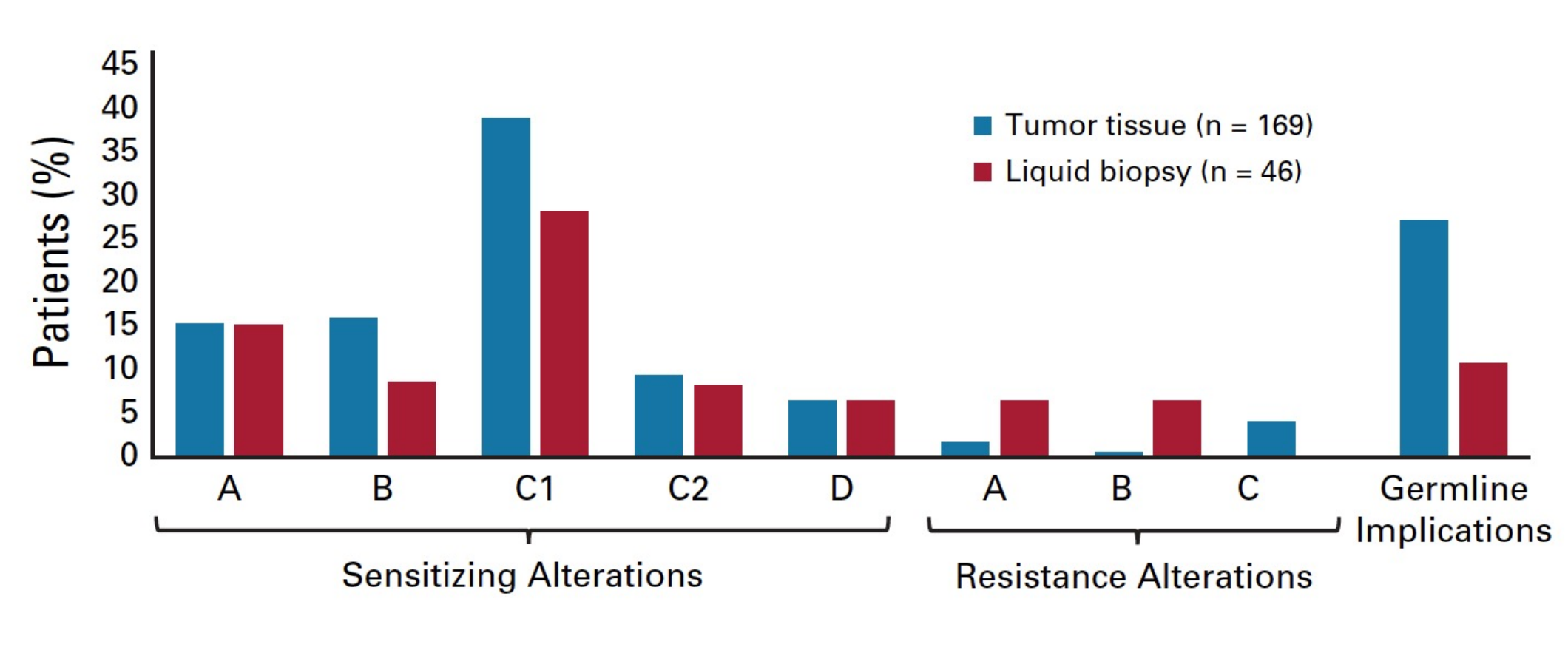
MTB Patient Outcomes: Change in Therapy Based on NGS Results and Stratified by Clinical Evidence Level



MTB = molecular tumor board; NGS = next-generation sequencing

Green MF et al. *JCO Precis Oncol* 2021;September 16;5:PO.21.00030.

MTB Patient Outcomes: Proportion of Patients Receiving Tumor Tissue or Liquid Biopsy Tests Who Harbor Actionable Mutations



Green MF et al. *JCO Precis Oncol* 2021;September 16;5:PO.21.00030.

Meet The Professor with Dr Strickler: Management of Upper GI Cancers

Case Presentations

- Dr Patel: A 60-year-old man with GEJ adenocarcinoma who responds to neoadjuvant CRT but declines surgery and develops PD (HER2 1+, PD-L1 2%)
- Dr Strickland: A frail 87-year-old woman with unresectable gastric cancer who chooses to receive systemic therapy (PD-L1 0%, HER2 negative, MSS)
- Dr Gupta: A 65-year-old man with T3N1M0 mixed gastric adenocarcinoma who responds well to neoadjuvant FLOT and has minimal residual disease at surgery
- Dr Strickland: A 62-year-old man with PMH of prostate cancer who is now diagnosed with T2N1M0, HER2-positive GEJ adenocarcinoma
- Dr Rudolph: A 33-year-old man with metastatic HER2-positive gastric adenocarcinoma who is responding well to FOLFOX, trastuzumab and nivolumab
- Dr Brenner: A 61-year-old man with metastatic HER2-positive esophageal cancer and germline CHEK2 mutation with PD on chemotherapy, pembrolizumab, trastuzumab and later T-DXd (PD-L1 12%)
- Dr Strickland: A 75-year-old man with symptomatic anemia who is diagnosed with metastatic esophageal adenocarcinoma (PD-L1 8%, MSS, HER2 1+)
- Dr Strickland: A 62-year-old woman with squamous cell esophageal carcinoma metastatic to bone (PD-L1 TPS 10%)

RTP RESEARCH TO PRACTICE

Case Presentation: A 60-year-old man with GEJ adenocarcinoma who responds to neoadjuvant CRT but declines surgery and develops PD (HER2 1+, PD-L1 2%)

Dr Minesh Patel (Peachtree City, Georgia)

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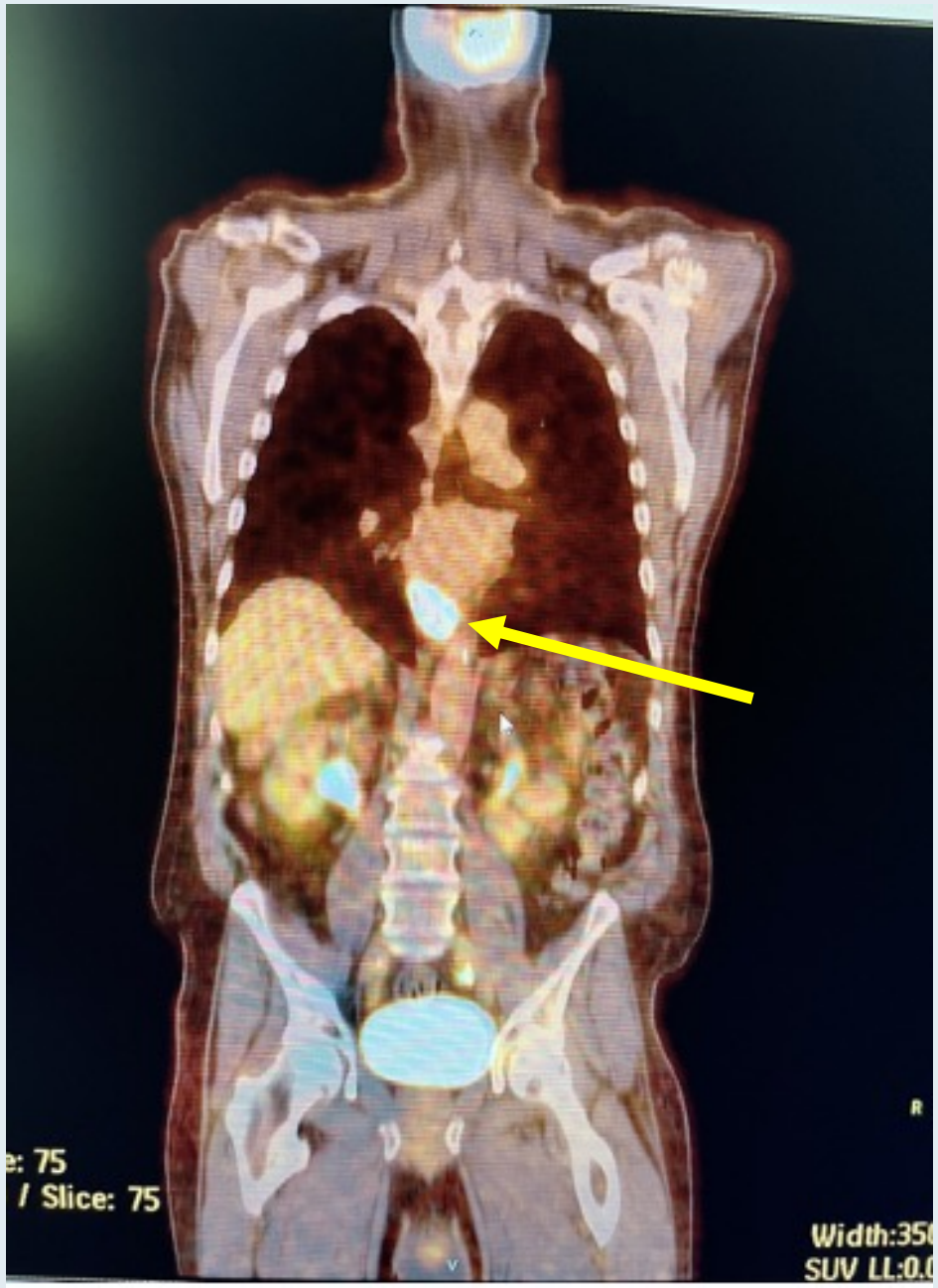

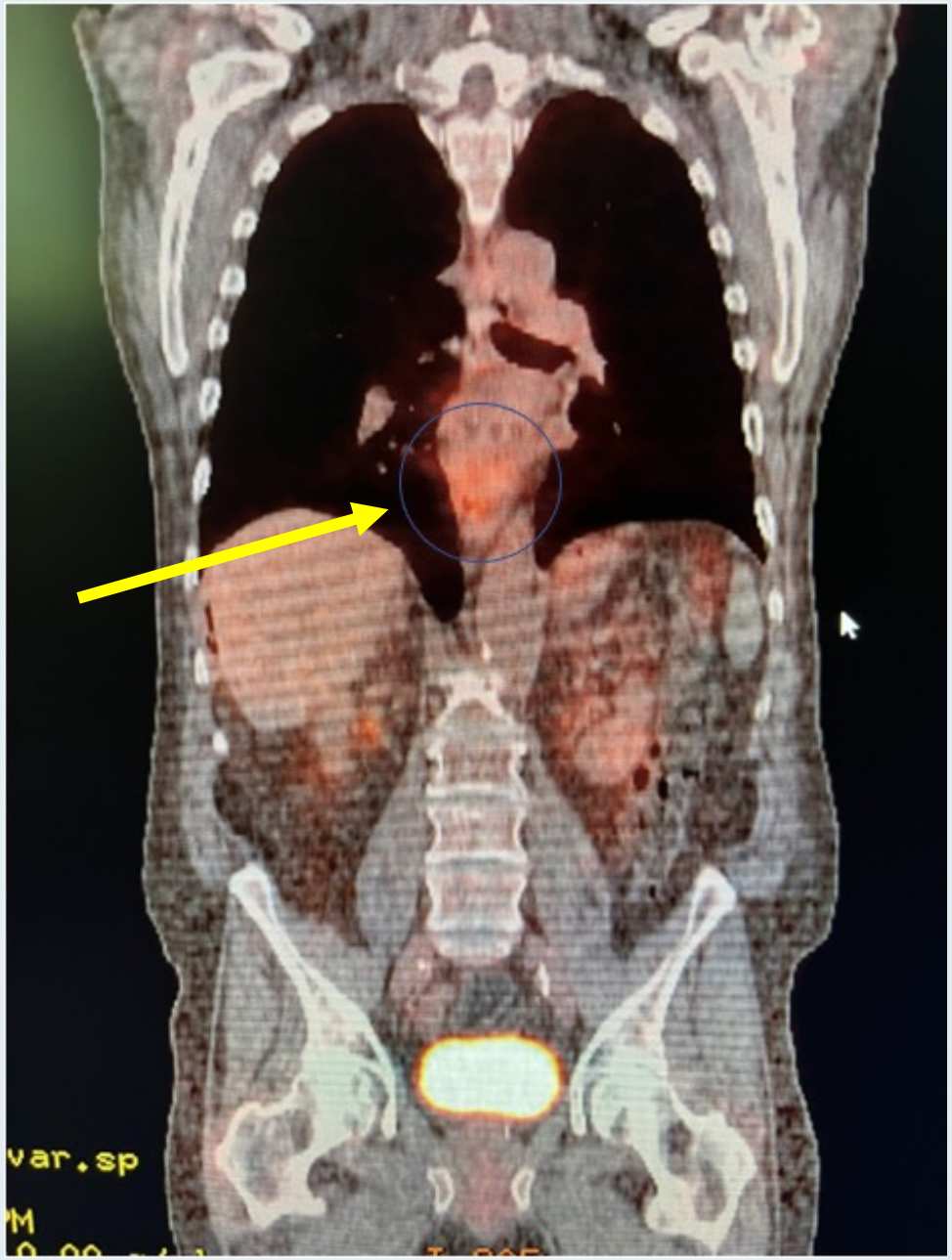

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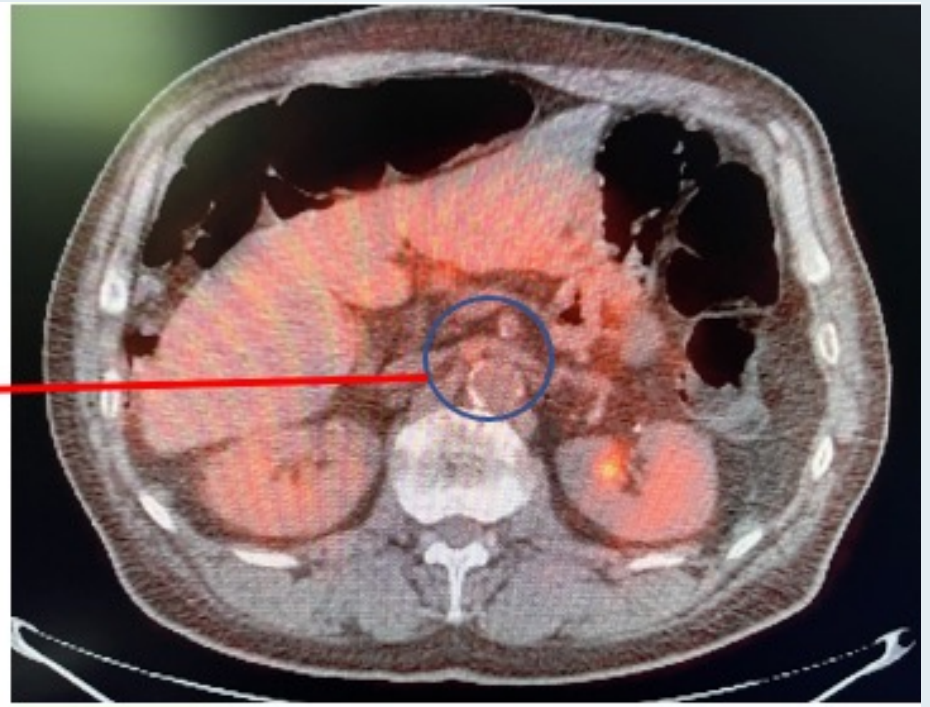
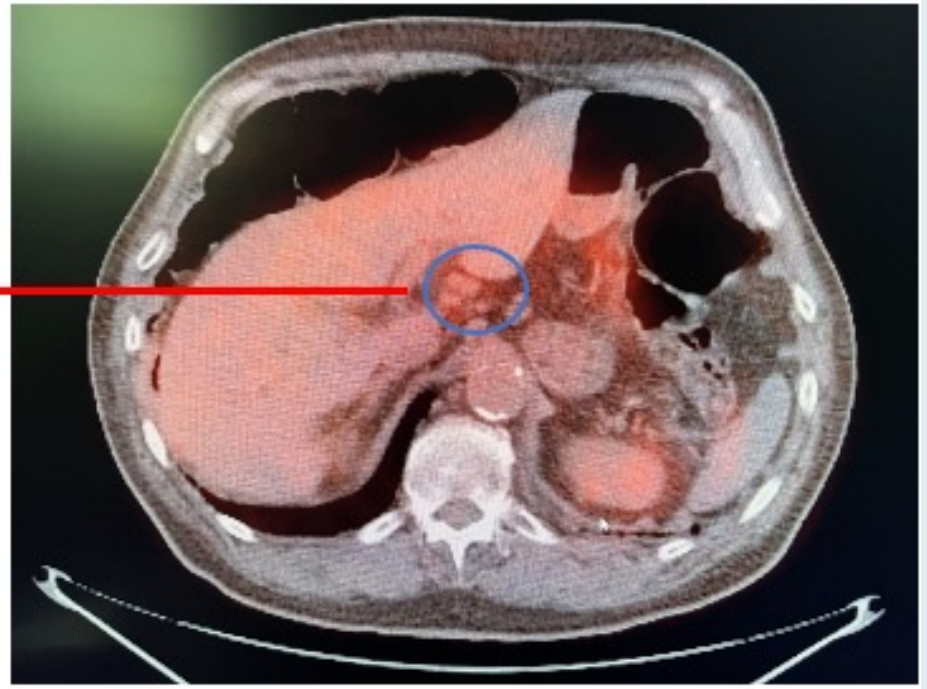
Periportal FDG avid node



Gastrohepatic ligament
FDG avid node



Case Presentation: A frail 87-year-old woman with unresectable gastric cancer who chooses to receive systemic therapy (PD-L1 0%, HER2 negative, MSS)

Dr Matthew Strickland (Boston, Massachusetts)

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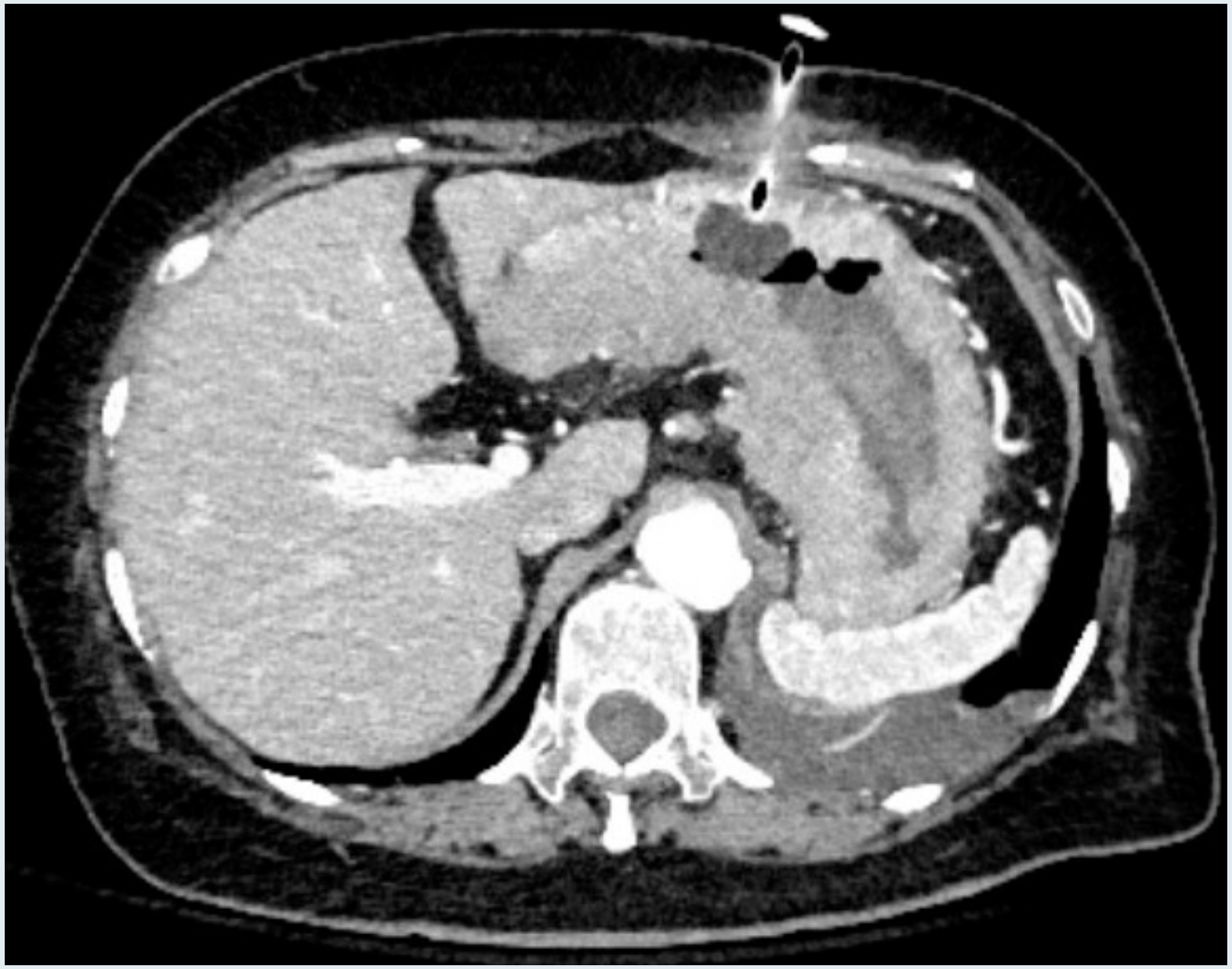
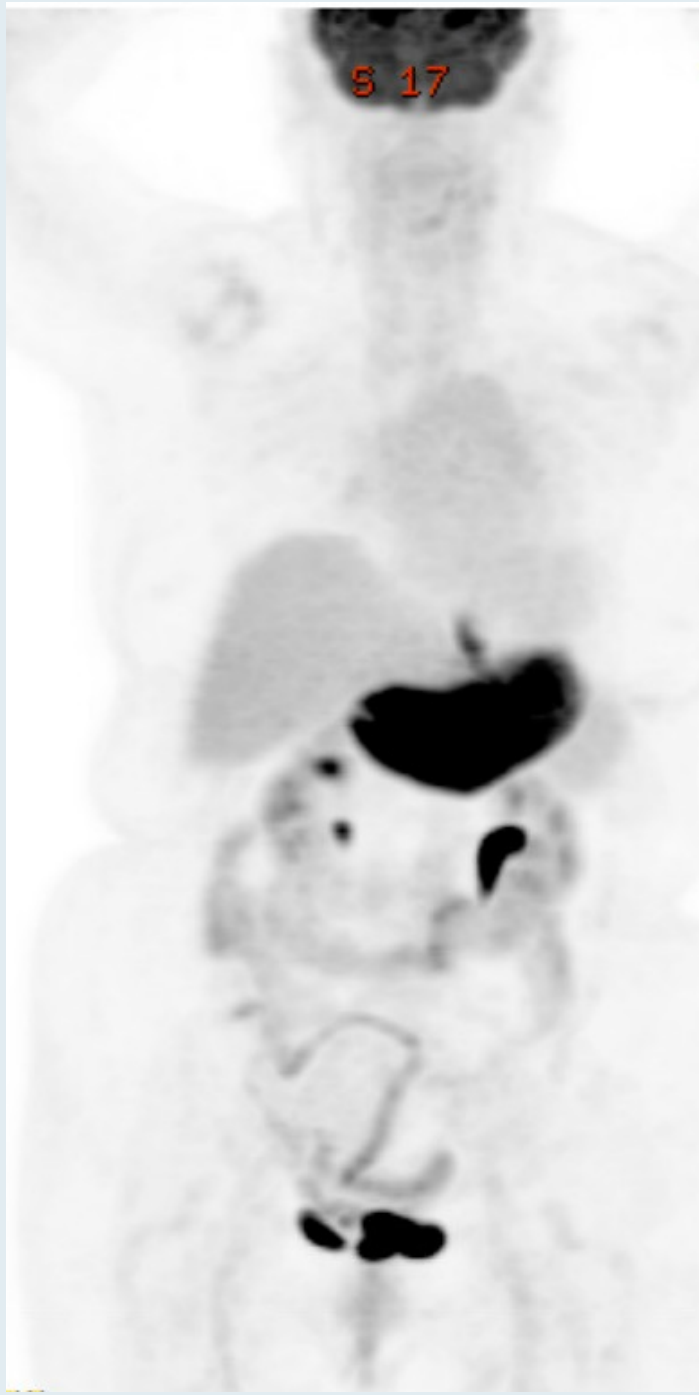
Diffuse thickening of stomach wall

Associated with FDG uptake





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Case Presentation: A 65-year-old man with T3N1M0 mixed gastric adenocarcinoma who responds well to neoadjuvant FLOT and has minimal residual disease at surgery

Dr Ranju Gupta (Bethlehem, Pennsylvania)

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Outside of a clinical trial, would you attempt to access an anti-PD-1/PD-L1 antibody as part of neoadjuvant therapy for a patient with MSI-high gastroesophageal cancer?

 Dr Enzinger	No	 Dr Shah	Yes
 Dr Janjigian	Yes	 Dr Strickler	Yes
 Dr Klempner	Yes	 Dr Yoon	Yes

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A patient with HER2-negative, MSS gastric adenocarcinoma receives preoperative FLOT, undergoes resection and has significant residual disease at surgery (PD-L1 CPS = 0). Regulatory and reimbursement issues aside, what would you generally recommend?

 Dr Enzinger	Continue FLOT postoperatively	 Dr Shah	Continue FLOT postoperatively
 Dr Janjigian	Continue FLOT postoperatively	 Dr Strickler	Continue FLOT postoperatively
 Dr Klempner	Continue FLOT postoperatively	 Dr Yoon	Continue FLOT postoperatively

FLOT = fluorouracil/leucovorin/oxaliplatin/docetaxel

RTP RESEARCH TO PRACTICE

A patient with HER2-negative, MSS gastric adenocarcinoma receives preoperative FLOT, undergoes resection and has significant residual disease at surgery (PD-L1 CPS = 10). Regulatory and reimbursement issues aside, what would you generally recommend?

 Dr Enzinger	Switch to FOLFOX + nivolumab postoperatively	 Dr Shah	Continue FLOT postoperatively
 Dr Janjigian	Continue FLOT postoperatively + PD-1/PD-L1 antibody	 Dr Strickler	Continue FLOT postoperatively
 Dr Klempner	Continue FLOT postoperatively	 Dr Yoon	Continue FLOT postoperatively

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS gastric adenocarcinoma with a PD-L1 CPS of 0?

 Dr Enzinger	FOLFOX	 Dr Shah	FOLFOX
 Dr Janjigian	FOLFOX + nivolumab	 Dr Strickler	FOLFOX
 Dr Klempner	FOLFOX	 Dr Yoon	FOLFOX

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS gastric adenocarcinoma with a PD-L1 CPS of 5?

 Dr Enzinger	FOLFOX + nivolumab	 Dr Shah	FOLFOX + nivolumab
 Dr Janjigian	FOLFOX + nivolumab	 Dr Strickler	FOLFOX + nivolumab
 Dr Klempner	FOLFOX + nivolumab	 Dr Yoon	FOLFOX or FOLFOX + pembro

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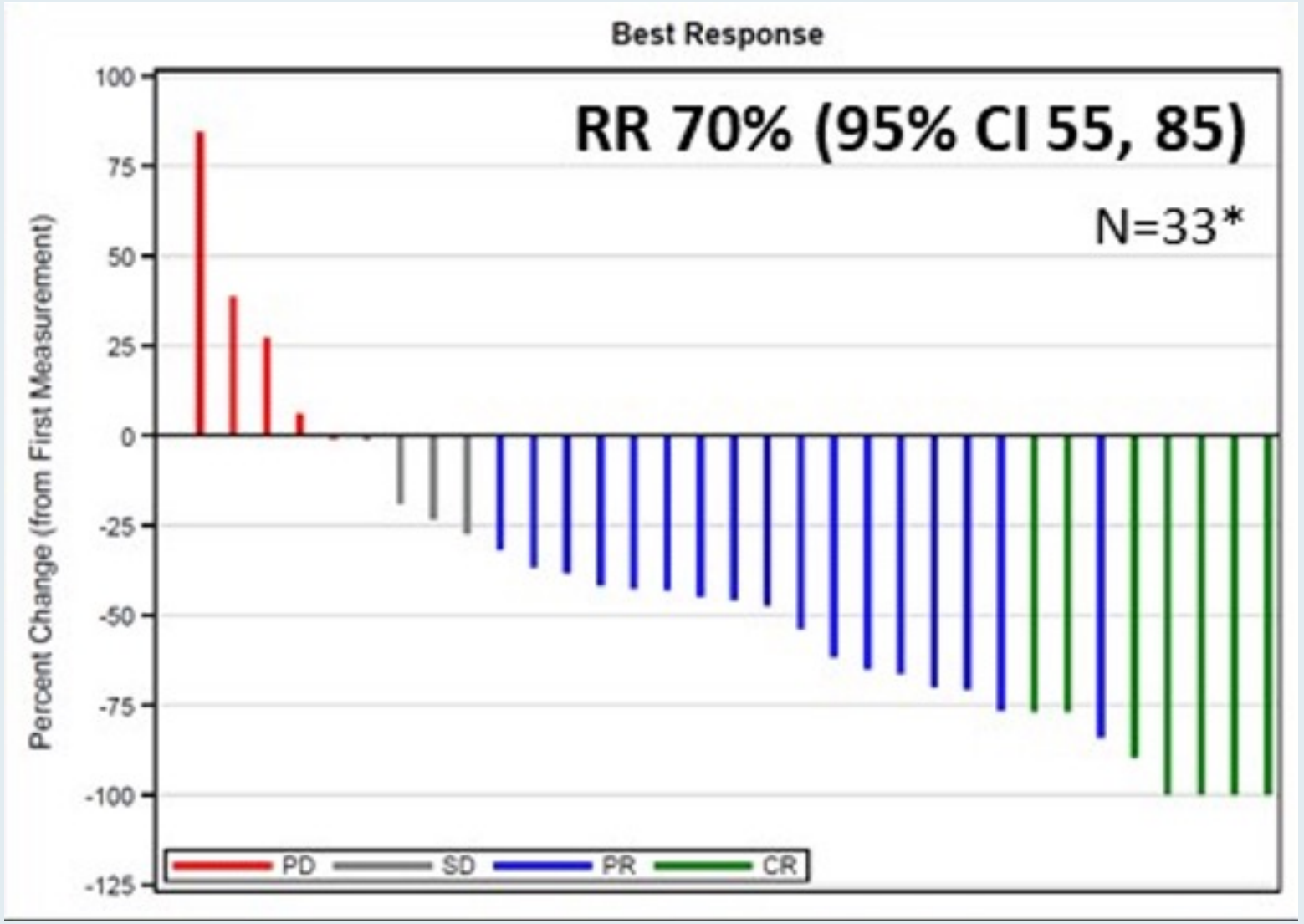
KEYlargo: A Phase II Study of First-Line Pembrolizumab (P), Capecitabine (C), and Oxaliplatin (O) in HER2-Negative Gastroesophageal (GE) Adenocarcinoma

Uronis HE et al.

Gastrointestinal Cancers Symposium 2021;Abstract 228.

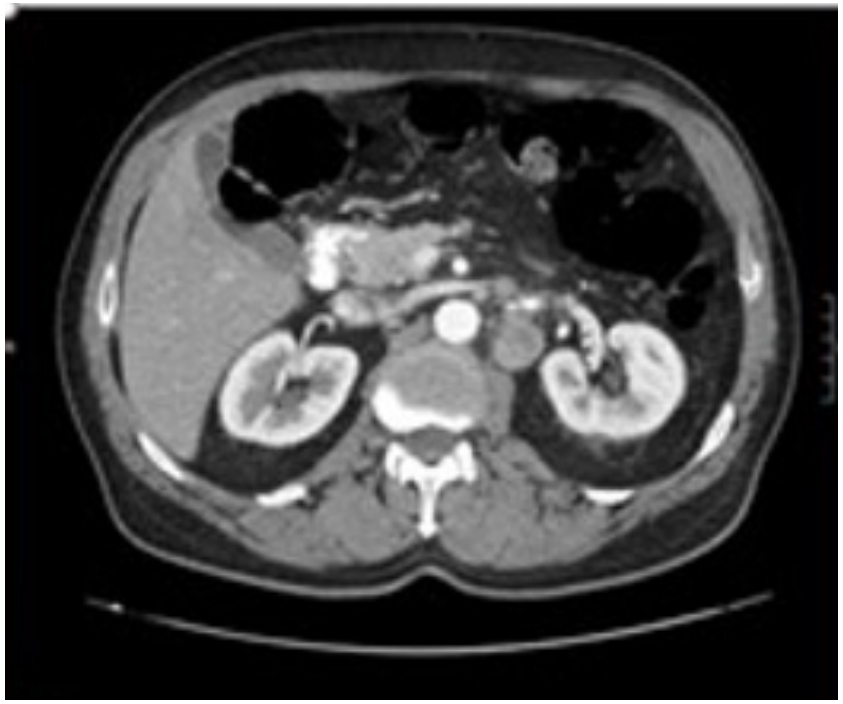
KEYlargo: Best Response



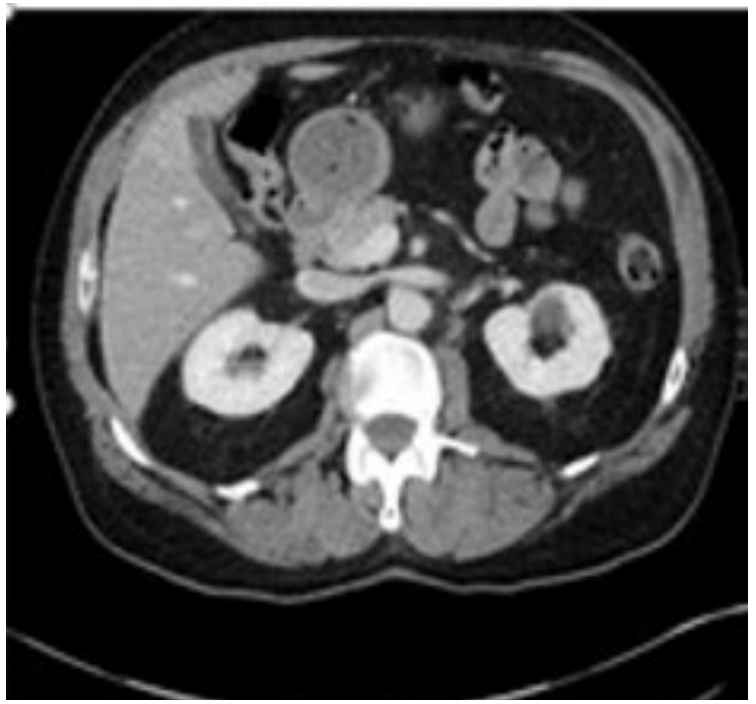
Uronis HE et al. Gastrointestinal Cancers Symposium 2021;Abstract 228.

KEYlargo: Baseline and After 3 Cycles of Pembrolizumab, Capecitabine and Oxaliplatin

Baseline



After cycle 3



Uronis HE et al. Gastrointestinal Cancers Symposium 2021;Abstract 228.

DKN-01 in Combination with Pembrolizumab in Patients with Advanced Gastroesophageal Adenocarcinoma (GEA): Tumoral DKK1 Expression as a Predictor of Response and Survival

Klempner SJ et al.

Gastrointestinal Cancers Symposium 2020;Abstract 357.

Blood-Based Genomic Profiling of Cell Free DNA (cfDNA) to Identify Microsatellite Instability (MSI-H), Tumor Mutational Burden (TMB) and WNT/B-Catenin Pathway Alterations in Patients with Gastrointestinal (GI) Tract Cancers

Isaacs J et al.

ASCO 2019;Abstract 3552.

Clin Cancer Res 2021 March 1;27(5):1236-41.

CLINICAL CANCER RESEARCH | PERSPECTIVES

Tumor Mutational Burden as a Predictor of Immunotherapy Response: Is More Always Better?

John H. Strickler[1], Brent A. Hanks[1,2,3], and Mustafa Khasraw[1,2]

Case Presentation: A 62-year-old man with PMH of prostate cancer who is now diagnosed with T2N1M0, HER2-positive GEJ adenocarcinoma

Dr Matthew Strickland (Boston, Massachusetts)

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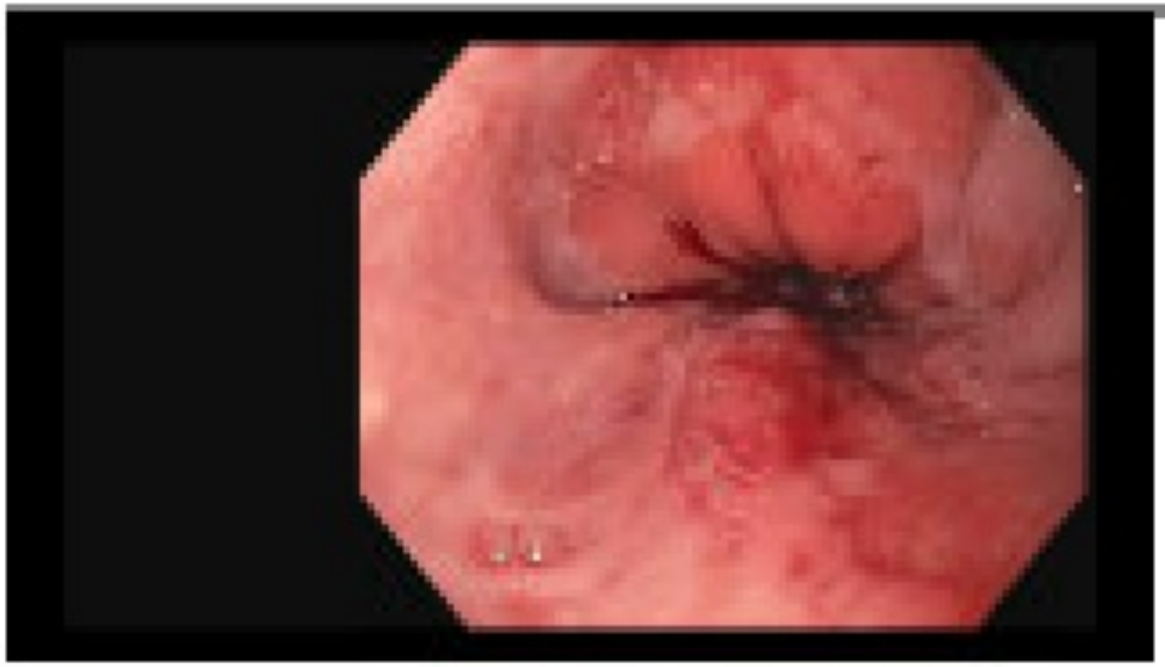
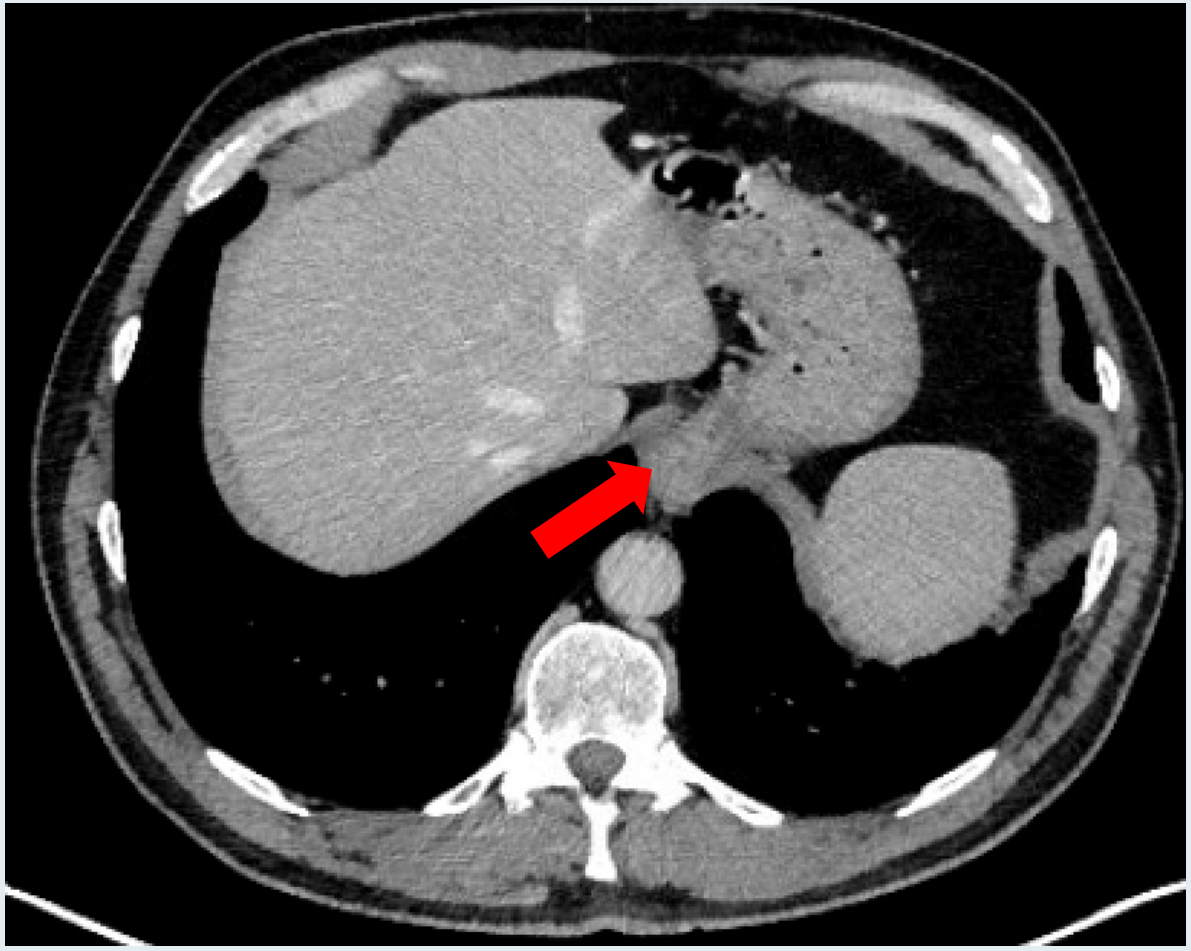
EGD – Malignant-appearing stenosis at distal esophagus/GEJ

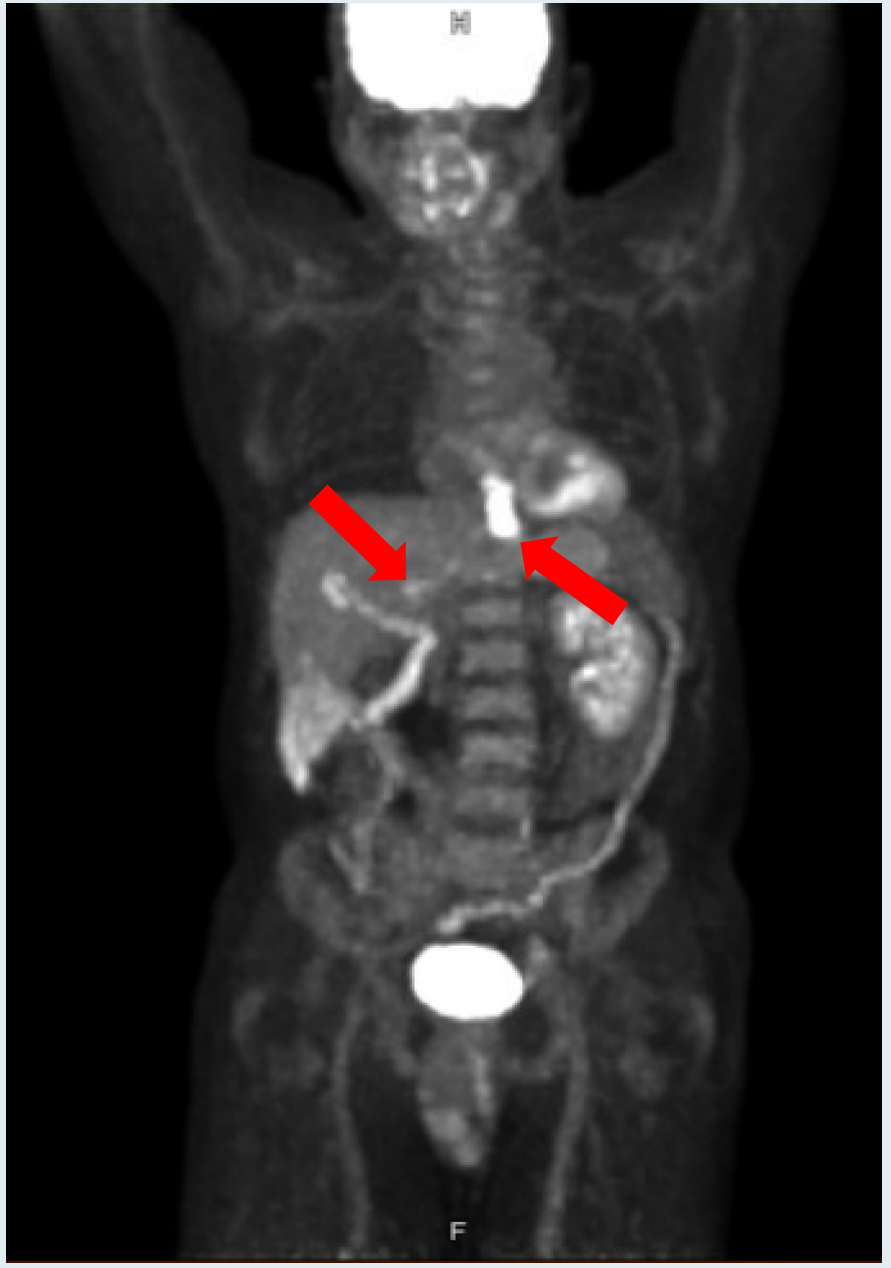


T2 (submucosal involvement by endosonographic criteria)

PET CT

Shows FDG-avid primary at distal esophagus/GEJ
Intense FDG uptake in gastrohepatic node





Case Presentation: A 33-year-old man with metastatic HER2-positive gastric adenocarcinoma who is responding well to FOLFOX, trastuzumab and nivolumab

Dr Priya Rudolph (Athens, Georgia)

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TO PRACTICE

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment for a patient with newly diagnosed metastatic HER2-positive, MSS gastric adenocarcinoma with a PD-L1 CPS of 0?

 Dr Enzinger	FOLFOX/trastuzumab	 Dr Shah	Trastuzumab/FOLFOX/ pembro
 Dr Janjigian	Trastuzumab/CAPOX/ pembro	 Dr Strickler	FOLFOX/trastuzumab
 Dr Klempner	Trastuzumab/chemo*/ pembro	 Dr Yoon	Trastuzumab/FOLFOX/ pembro

* FOLFOX or CAPOX

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment for a patient with newly diagnosed metastatic HER2-positive, MSS gastric adenocarcinoma with a PD-L1 CPS ≥1?

 Dr Enzinger	Trastuzumab/FOLFOX/ pembro	 Dr Shah	Trastuzumab/FOLFOX/ pembro
 Dr Janjigian	Trastuzumab/CAPOX/ pembro	 Dr Strickler	FOLFOX/trastuzumab
 Dr Klempner	Trastuzumab/CAPOX/ pembro	 Dr Yoon	Trastuzumab/FOLFOX/ pembro

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-positive, MSS gastric adenocarcinoma (PD-L1 CPS ≥1) with disease progression on FOLFOX/trastuzumab?

 Dr Enzinger	Trastuzumab deruxtecan if HER2+ on rebiopsy	 Dr Shah	Ramucirumab/ paclitaxel
 Dr Janjigian	CAPOX + pembrolizumab	 Dr Strickler	Trastuzumab deruxtecan
 Dr Klempner	Ramucirumab/ paclitaxel	 Dr Yoon	Ramucirumab/ paclitaxel

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-positive, MSS gastric adenocarcinoma (PD-L1 CPS ≥1) with disease progression on FOLFOX/trastuzumab/pembrolizumab?

 Dr Enzinger	Trastuzumab deruxtecan if HER2+ on rebiopsy	 Dr Shah	Ramucirumab/ paclitaxel
 Dr Janjigian	Trastuzumab deruxtecan	 Dr Strickler	Trastuzumab deruxtecan
 Dr Klempner	Ramucirumab/ paclitaxel	 Dr Yoon	Ramucirumab/ paclitaxel

RTP RESEARCH TO PRACTICE

What have you observed in terms of the tolerability of trastuzumab deruxtecan?

 Dr Enzinger	Nausea often, ILD sometimes	 Dr Shah	Toxic
 Dr Janjigian	Fine	 Dr Strickler	No significant toxicity
 Dr Klempner	Similar to chemo, cytopenias and GI symptoms	 Dr Yoon	Significant fatigue

ILD = interstitial lung disease

At what grade of ILD would you permanently discontinue therapy with trastuzumab deruxtecan for a patient with HER2-positive gastric/GEJ adenocarcinoma?

 Dr Enzinger	Grade 3	 Dr Shah	Grade 2
 Dr Janjigian	Grade 2	 Dr Strickler	Grade 2
 Dr Klempner	Grade 2	 Dr Yoon	Grade 2

RTP RESEARCH TO PRACTICE

Have you or would you offer trastuzumab deruxtecan to a patient with HER2-low gastric/GEJ adenocarcinoma outside of a clinical trial?

 Dr Enzinger	I have not but would for the right patient	 Dr Shah	I have not but would for the right patient
 Dr Janjigian	I have	 Dr Strickler	I have not and would not
 Dr Klempner	I have not and would not	 Dr Yoon	I have not and would not

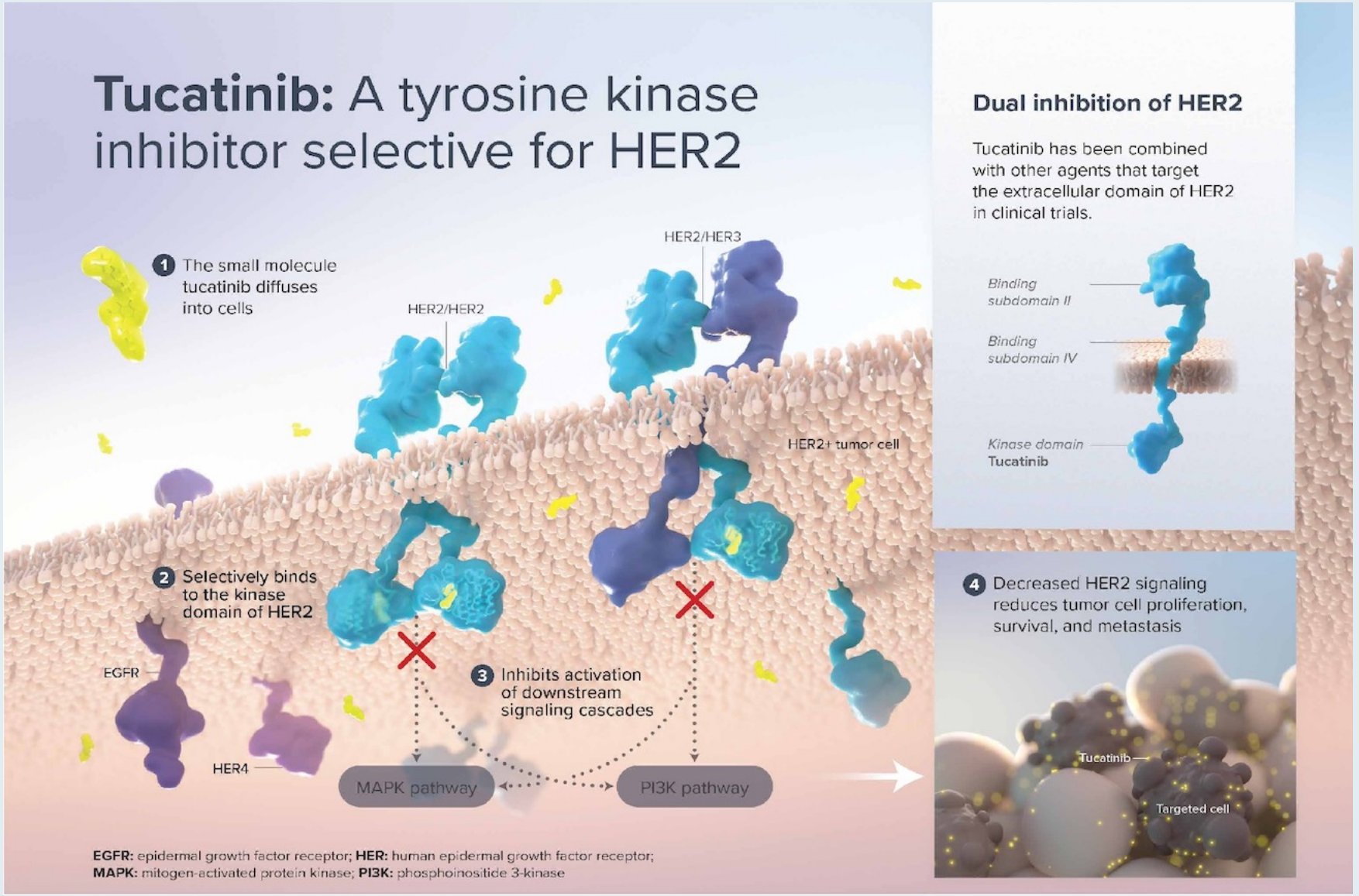
RTP RESEARCH TO PRACTICE

MOUNTAINEER-02: Phase 2/3 Study of Tucatinib, Trastuzumab, Ramucirumab, and Paclitaxel in Previously Treated HER2+ Gastric or Gastroesophageal Junction Adenocarcinoma (Trial in Progress)

Catenacci DV et al.

Gastrointestinal Cancers Symposium 2022;Abstract TPS371.

Tucatinib Proposed Mechanism of Action



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

RTP RESEARCH TO PRACTICE

Phase 1b/2, Open-Label, Dose-Escalation and Expansion Trial of Tucatinib in Combination with Trastuzumab with and without Oxaliplatin-Based Chemotherapy or Pembrolizumab in Patients with Unresectable or Metastatic HER2+ Gastrointestinal Cancers (Trial in Progress)

Park H et al.

Gastrointestinal Cancers Symposium 2022;Abstract TPS376.

Clinical Review & Education

JAMA Oncology | Review

Diagnosis and Treatment of ERBB2-Positive Metastatic Colorectal Cancer
A Review

John H. Strickler, MD; Takayuki Yoshino, MD, PhD; Rondell P. Graham, MBBS; Salvatore Siena, MD; Tanios Bekaii-Saab, MD

JAMA Oncol 2022 May 1;8(5):760-9.

ASCO 2022 Educational Book

GASTROINTESTINAL CANCER—GASTROESOPHAGEAL, PANCREATIC, AND HEPATOBILIARY

Overcoming Resistance to Targeted Therapies in Gastrointestinal Cancers: Progress to Date and Progress to Come

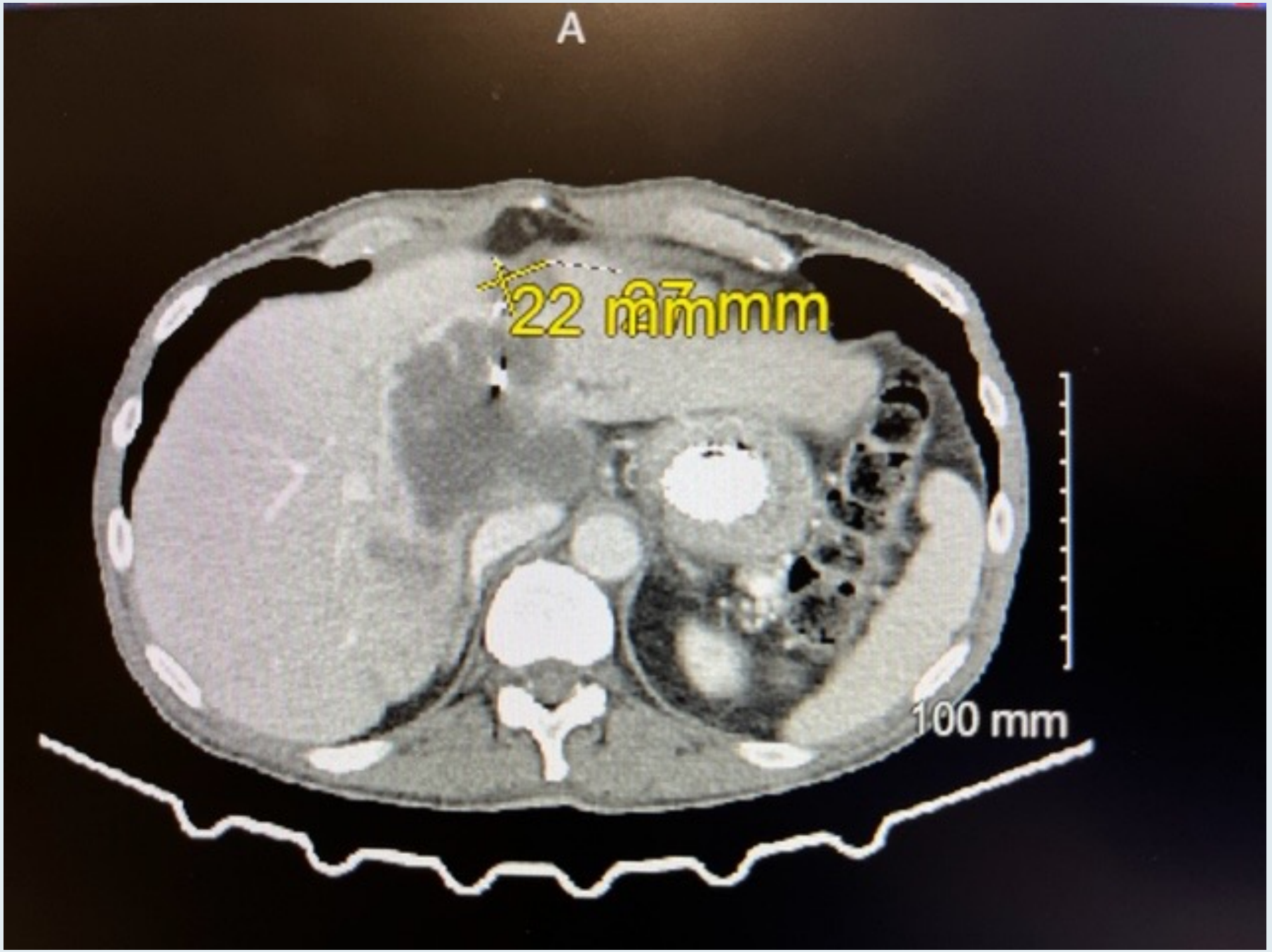
Christopher Chen, MD[1]; Maria Di Bartolomeo, MD[2]; Salvatore Corallo, MD[2]; John H. Strickler, MD[3]; and Lipika Goyal, MD, DPhil[1]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Case Presentation: A 61-year-old man with metastatic HER2-positive esophageal cancer and germline CHEK2 mutation with PD on chemotherapy, pembrolizumab, trastuzumab and later T-DXd (PD-L1 12%)

Dr Warren Brenner (Boca Raton, Florida)

RTP
RESEARCH
TO PRACTICE


A
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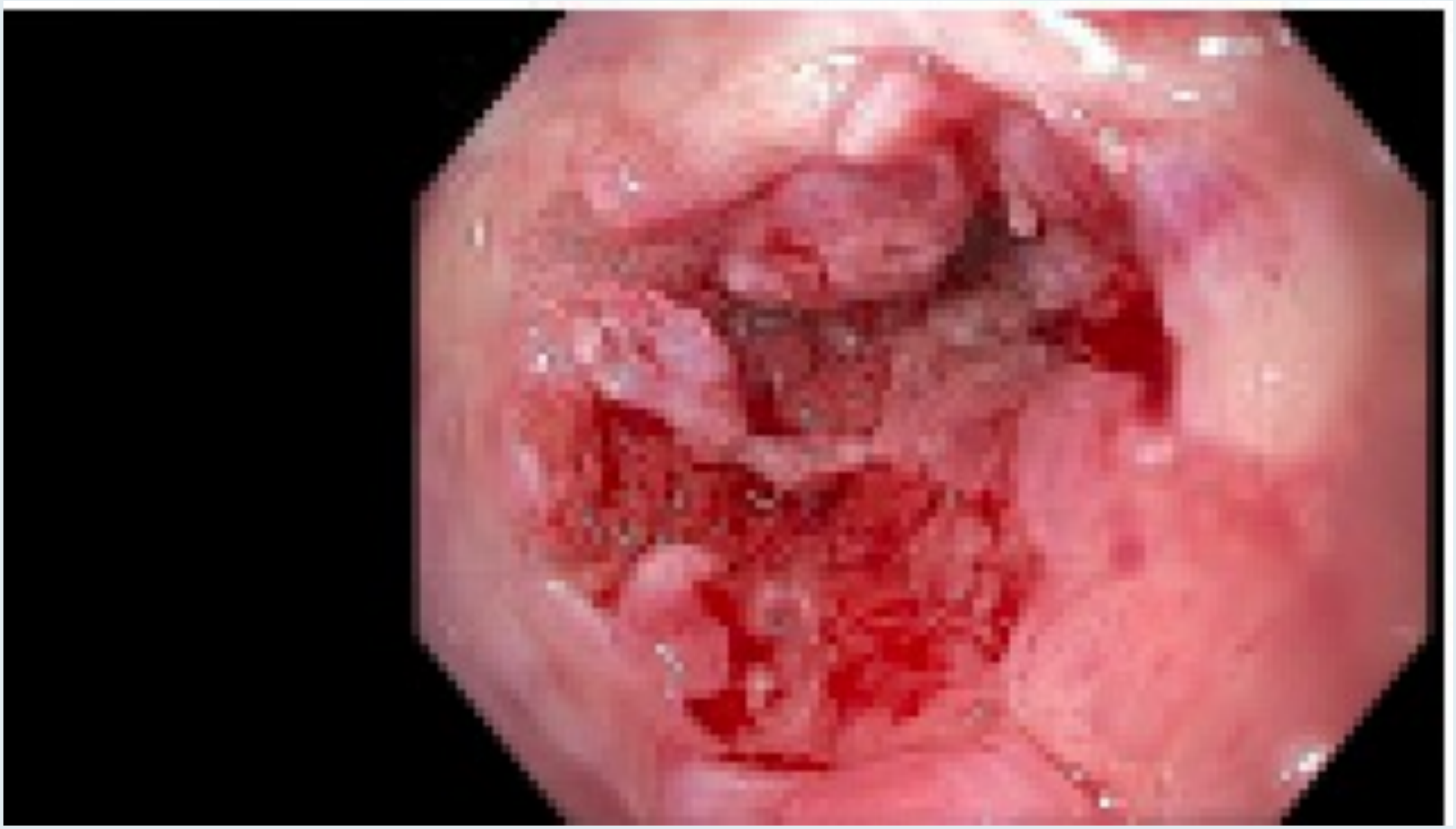
Case Presentation: A 75-year-old man with symptomatic anemia who is diagnosed with metastatic esophageal adenocarcinoma (PD-L1 8%, MSS, HER2 1+)

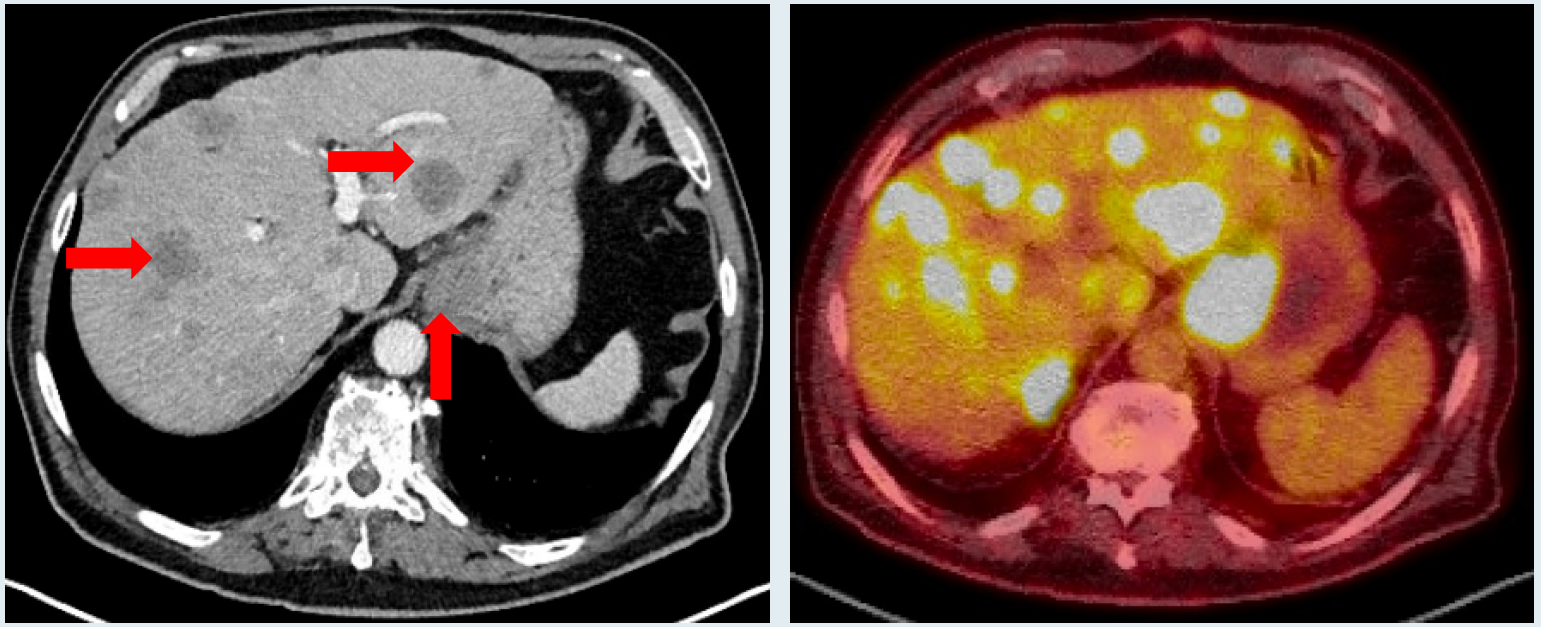
Dr Matthew Strickland (Boston, Massachusetts)

RTP
RESEARCH
TO PRACTICE

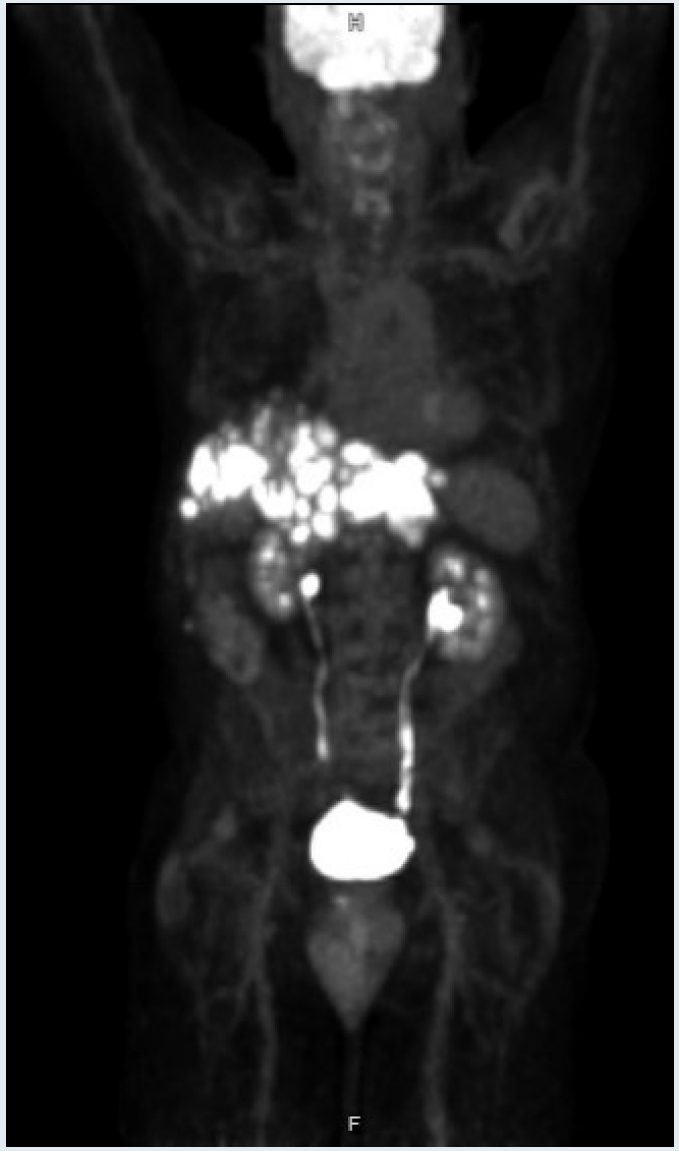
Malignant-appearing stenosis at distal esophagus/GEJ



Multifocal Hepatic Metastases



FDG-Avid Primary at Distal Esophagus Extending into Gastric Cardia

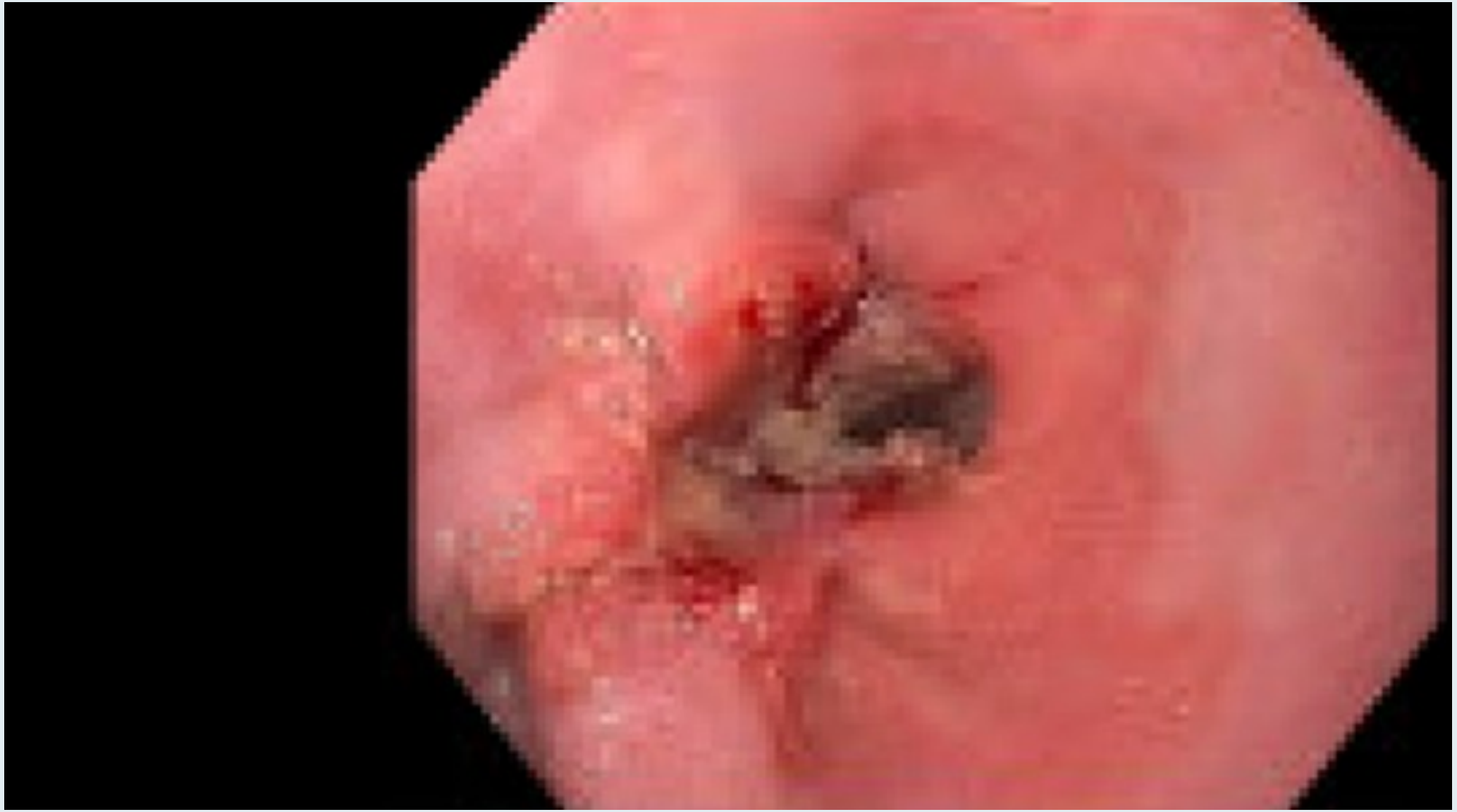


Case Presentation: A 62-year-old woman with squamous cell esophageal carcinoma metastatic to bone (PD-L1 TPS 10%)

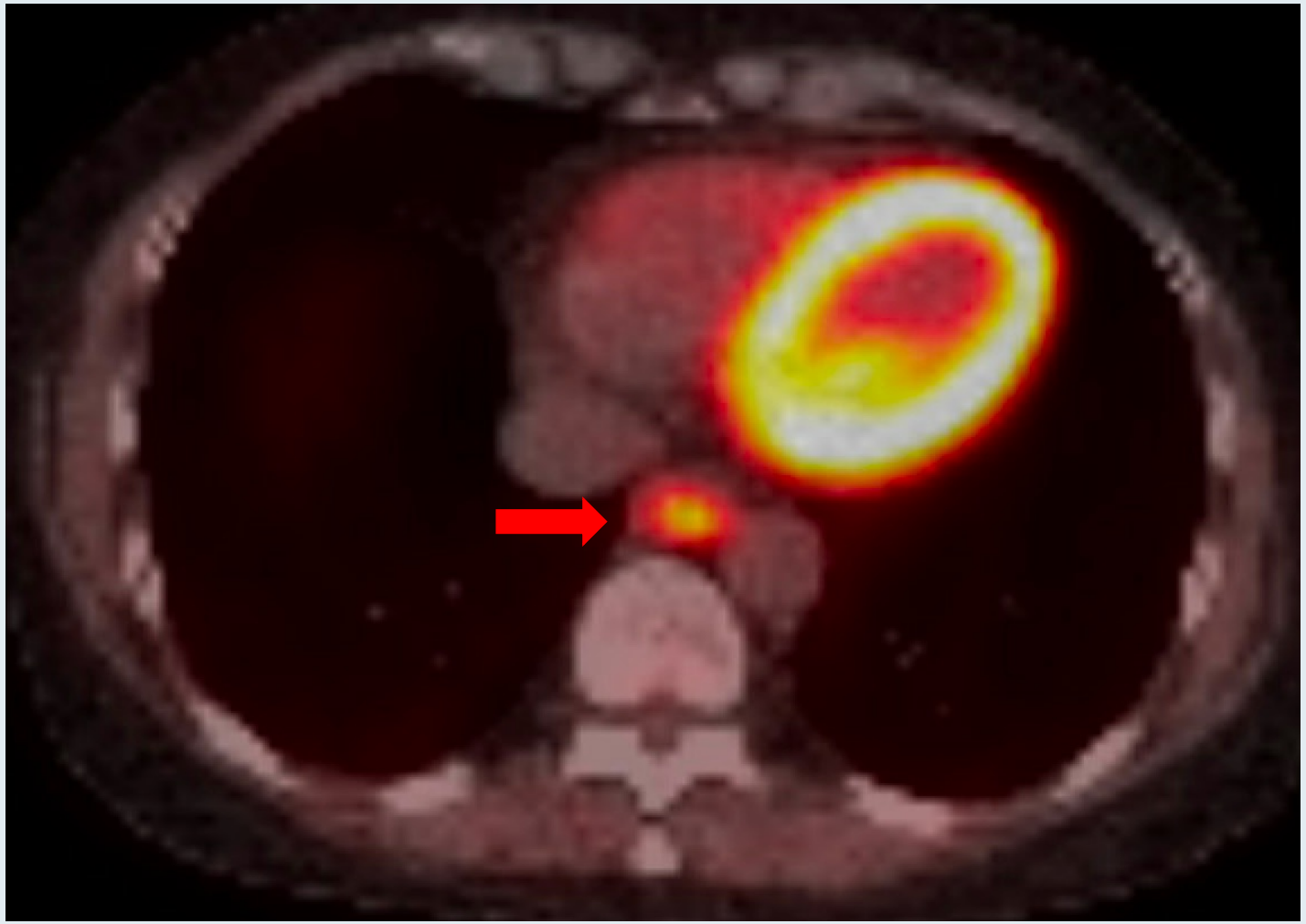
Dr Matthew Strickland (Boston, Massachusetts)

RTP
RESEARCH
TO PRACTICE

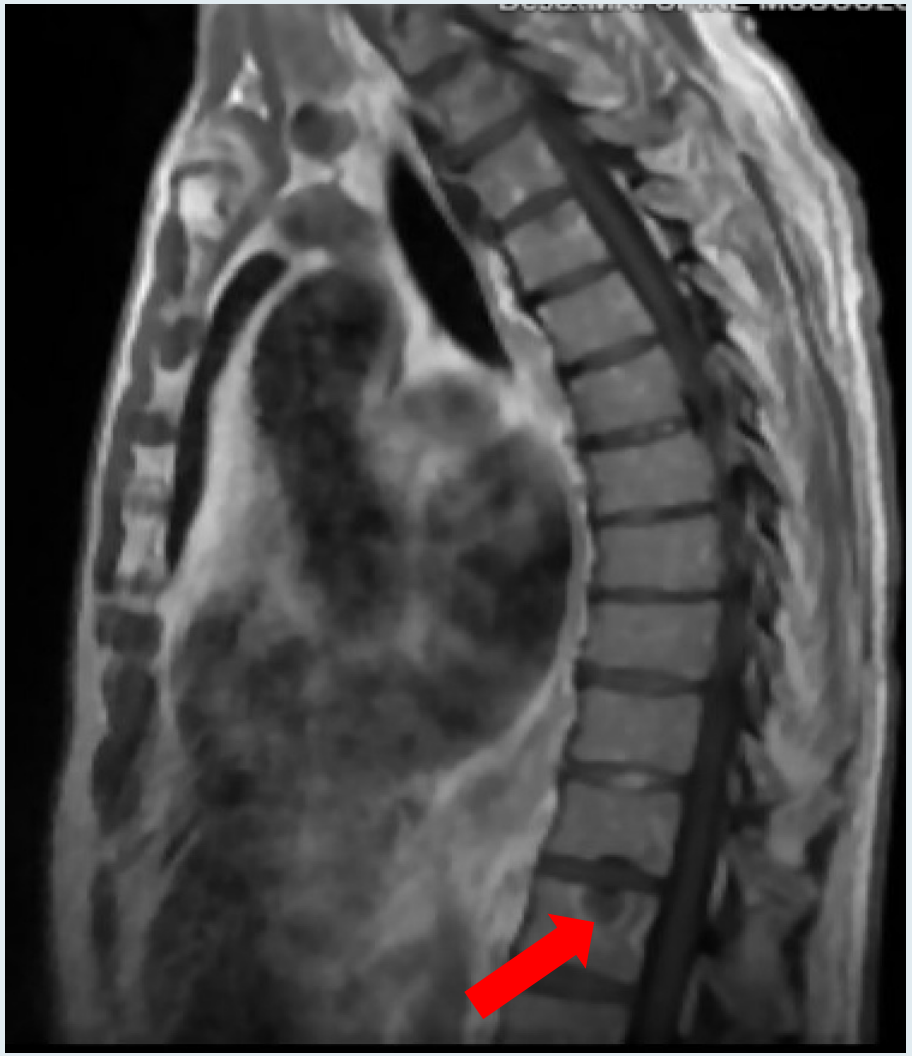
Mass: Lower Third of the Esophagus



FDG-Avid Primary at Distal Esophagus



MRI Spine – T5 Lytic Lesion



Management of stent placement; approach to clinically significant neuropathy

Dr Matthew Strickland (Boston, Massachusetts)

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 0?

 Dr Enzinger	FOLFOX	 Dr Shah	FOLFOX
 Dr Janjigian	FOLFOX + nivolumab	 Dr Strickler	FOLFOX
 Dr Klempner	FOLFOX	 Dr Yoon	FOLFOX

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 1?

 Dr Enzinger	FOLFOX	 Dr Shah	FOLFOX
 Dr Janjigian	FOLFOX + nivolumab	 Dr Strickler	FOLFOX
 Dr Klempner	FOLFOX + nivolumab	 Dr Yoon	FOLFOX

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 5?

 Dr Enzinger	FOLFOX + nivolumab	 Dr Shah	FOLFOX
 Dr Janjigian	FOLFOX + nivolumab	 Dr Strickler	FOLFOX + pembrolizumab
 Dr Klempner	FOLFOX + nivolumab	 Dr Yoon	FOLFOX

Regulatory and reimbursement issues aside, which first-line therapy would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 10?

 Dr Enzinger	FOLFOX + nivolumab	 Dr Shah	FOLFOX + pembrolizumab
 Dr Janjigian	FOLFOX + nivolumab	 Dr Strickler	FOLFOX + pembrolizumab
 Dr Klempner	FOLFOX + nivolumab	 Dr Yoon	FOLFOX + nivolumab

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Strickler: Management of Upper GI Cancers

Introduction

Case Presentations

Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

HER2-Negative Gastroesophageal Cancers

Checkpoint Inhibitor Approvals for HER2-Negative Gastric, GEJ and Esophageal Cancers

Regimen/FDA approval date/Pivotal trial	Location	Histology	Setting	PD-L1
Nivolumab 5/20/21 (CM-577)	Esophageal, GEJ	Adenocarcinoma and squamous	• Completed resected, with residual pathologic disease after neoadjuvant chemoradiation	Not required
Pembrolizumab + cisplatin/5-FU 3/22/2021 (KN-590)	Esophageal, GEJ	Adenocarcinoma and squamous	• Recurrent locally advanced or metastatic • Not amenable to surgical resection or definitive chemoradiation	Not required
Nivolumab + mFOLFOX6 or CAPOX 4/16/2021 (CM-649)	Gastric, GEJ, esophageal	Adenocarcinoma	• Advanced or metastatic gastric, GEJ or esophageal adenocarcinoma	Not required
Pembrolizumab 7/30/2019 (KN-181)	Esophageal, GEJ	Squamous	• Recurrent locally advanced or metastatic • Not amenable to surgical resection or definitive chemoradiation • After ≥1 prior lines of systemic therapy	CPS ≥10
Nivolumab 6/10/2020 (ATTRACTION-3)	Esophageal	Squamous	• Unresectable advanced, recurrent or metastatic • After prior fluoropyrimidine- and platinum-based • chemotherapy	Not required

Kelly RJ et al. *New Engl J Med* 2021;384(13):1191-203. Sun J et al. *Lancet* 2021;398(10302):759-71. Janjigian YY et al. *Lancet* 2021;398(10294):27-40. Kojima T et al. *J Clin Oncol* 2020;38(35):4138-48. Kato K et al. *Lancet Oncol* 2019;20(11):1506-17.

ASCO Gastrointestinal Cancers Symposium

GERCOR

Neo-adjuvant nivolumab plus ipilimumab and adjuvant nivolumab in patients (pts) with localized MSI/dMMR gastric or oeso-gastric junction (G-OGJ) adenocarcinoma NEONIPIGA phase II GERCOR study

T André,[1] D Tougeron, G Piessen, C de la Fouchardière, C Louvet, A Adenis, M Jary, C Tournigand, T Aparicio, J Desrame, A Lièvre, ML Garcia-Larnicol, T Pudlarz, J Henriques, R Cohen, J Lefèvre, M Svrcek

[1]Sorbonne University, Saint-Antoine Hospital, Department of Medical Oncology, Paris, France

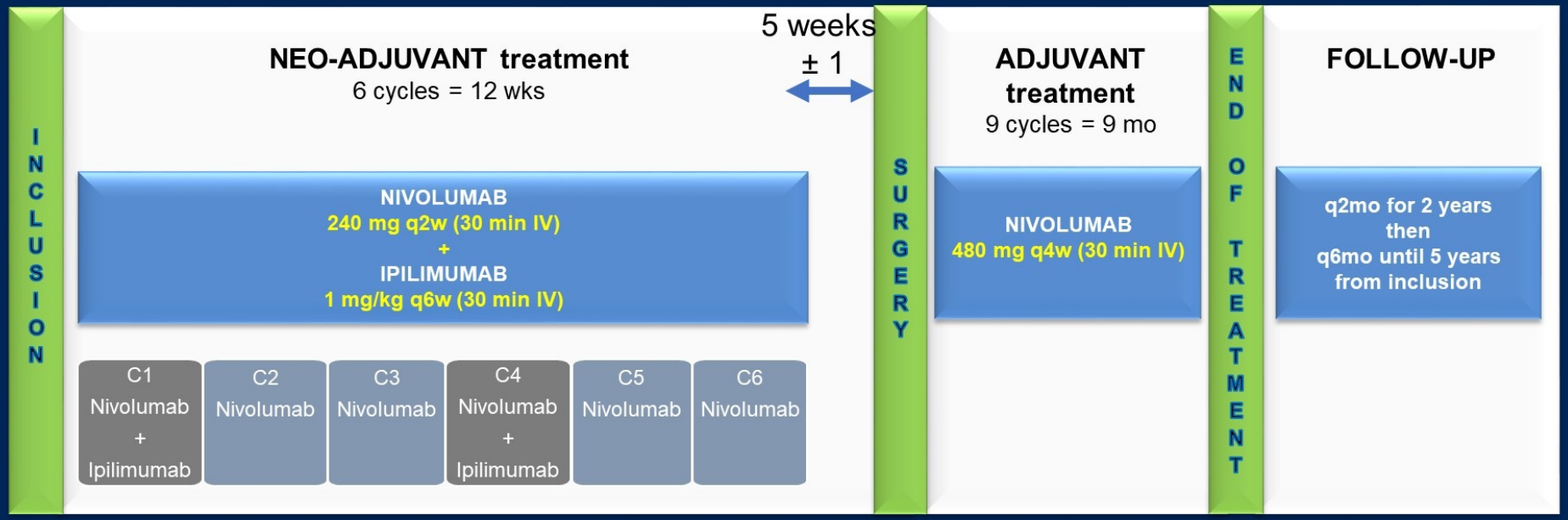
Gastrointestinal Cancers Symposium 2022;Abstract 244.

RTP RESEARCH TO PRACTICE

NEONIPIGA Design

NEONIPIGA: Study design/methods

- Phase II study evaluating efficacy of neo-adjuvant nivolumab and ipilimumab followed by adjuvant nivolumab in pts with resectable OGA MSI/dMMR, T2-T4 NxM0
- The primary objective was pathological complete response rate (pCRR).



ClinicalTrials.gov: NCT04006262

OGA = oeso-gastric adenocarcinoma

Andre T et al. Gastrointestinal Cancers Symposium 2022;Abstract 244.

NEONIPIGA Conclusions

Conclusions

- The primary objective with **59% pathological complete Response Rate was met (17/29 pts evaluable for** pCRR**)**
- Neo-adjuvant nivolumab & ipilimumab is feasible in pts with MSI/dMMR resectable OGJ/gastric adenocarcinoma
- No new safety concerns: with 25% of grade 3-4 TRAE (max/pts)
- Surgical complications are as expected with this type of surgeries
- 94% of pts included are free of events with 12 months follow-up
- Neonipiga raises the question whether the surgery can be delayed or avoided for some pts with localized MSI/dMMR G-OGJ adenocarcinoma if immune-check point inhibitors are effective.

Andre T et al. Gastrointestinal Cancers Symposium 2022;Abstract 244.

Surgical and pathological outcome, and pathological regression, in patients receiving perioperative atezolizumab in combination with FLOT chemotherapy versus FLOT alone for resectable esophagogastric adenocarcinoma: Interim results from DANTE, a randomized, multicenter, phase IIb trial of the FLOT-AIO German Gastric Cancer Group and Swiss SAKK.

Presented by Dr. S-E Al-Batran, Oral Abstract Session

2022 ASCO ANNUAL MEETING

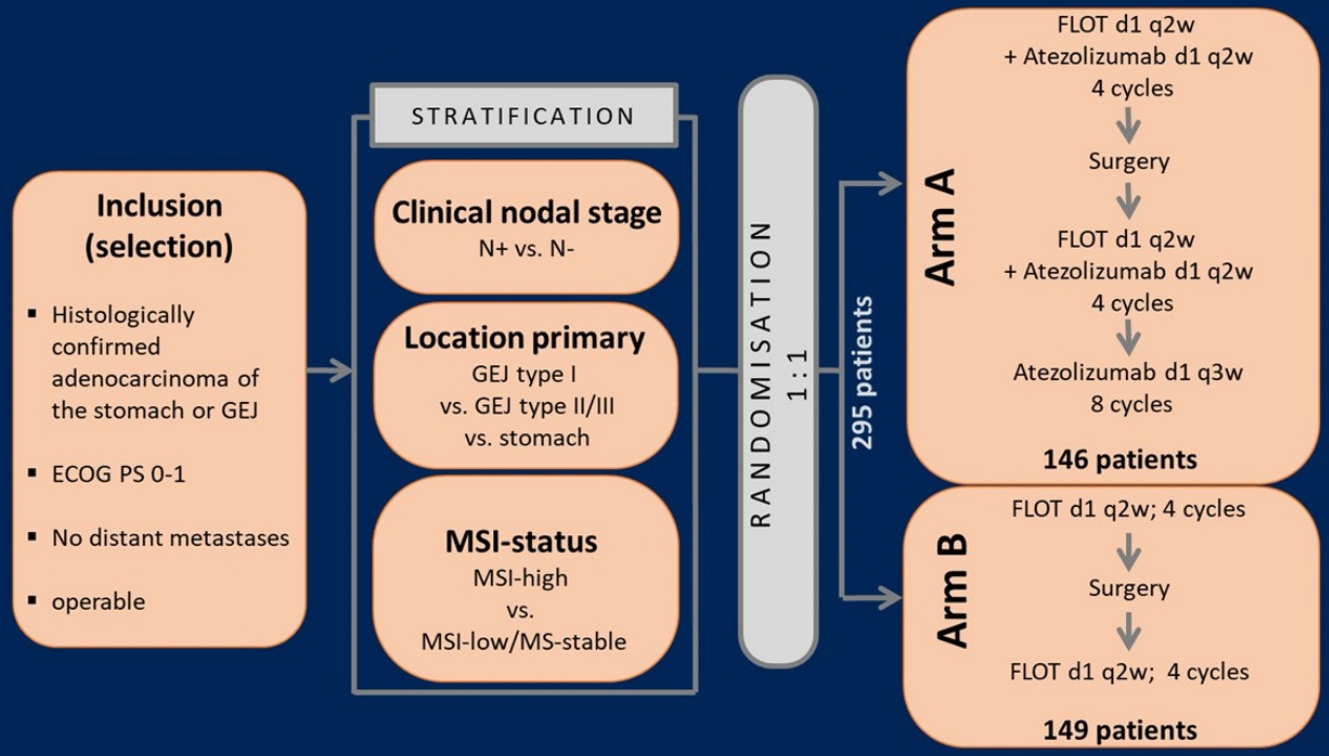
#ASCO22

PRESENTED BY:
Katrina Pedersen, MD, MS

Al-Batran SE et al. ASCO 2022;Abstract 4003. | Discussant, Katrina Pedersen, MD, MS

Study Flow Chart

DANTE is an investigator-initiated phase-II trial with the potential to transition into a phase-III trial



Al-Batran SE et al. ASCO 2022;Abstract 4003. | Discussant, Katrina Pedersen, MD, MS

Histopathology (pTNM)

	FLOT + Atezolizumab (N=146)		FLOT (N=149)	
pT0-stage	34	23%	22	15%
pN0-stage	100	69%	81	54%
pT0/N0	34	23%	21	14%
pT-stage				
≤T1	62	43%	55	37%
T2	27	19%	16	11%
T3	47	32%	61	41%
T4	4	3%	10	7%
pT0-T2	89	61%	71	48%
pT3-T4	51	35%	71	48%
pM1-stage	2	1%	4	3%

Al-Batran SE et al. ASCO 2022;Abstract 4003. | Discussant, Katrina Pedersen, MD, MS

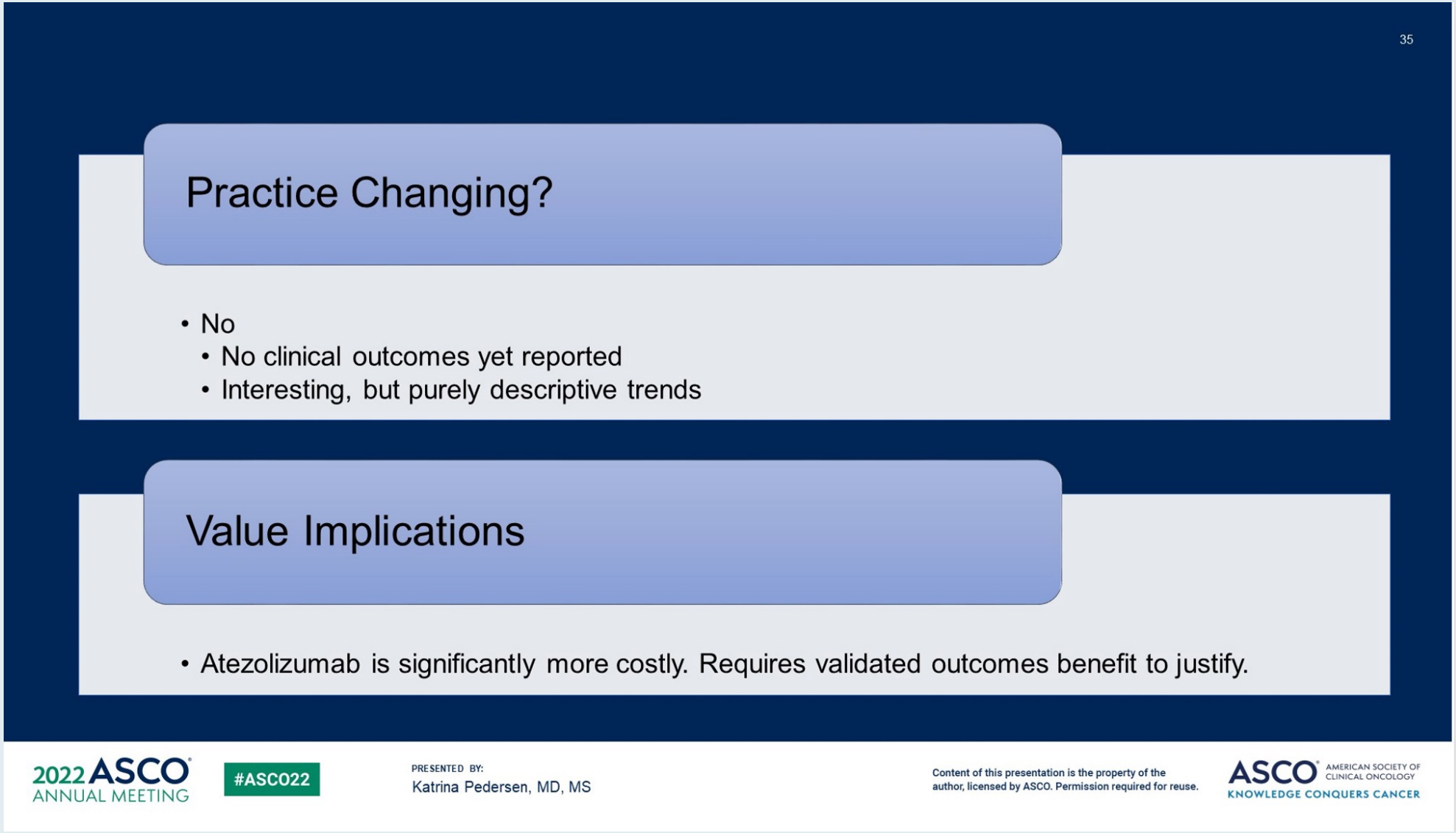
Pathological response (local vs. central assessment)

Pathological Regression **FLOT + Atezolizumab (arm A) vs. FLOT (arm B)**	Local assessment				Central assessment[1]			
	TRG1a[2]		TRG1a/b[3]		TRG1a[2]		TRG1a/b[3]	
	A	B	A	B	A	B	A	B
All patients (N= 295; 146|149)	35 (24%)	23 (15%)	71 (49%)	58 (39%)	37 (25%)	36 (24%)	72 (49%)	66 (44%)
PD-L1 CPS ≥1 (N=170; 82|88)	20 (24%)	13 (15%)	42 (51%)	40 (46%)	21 (26%)	20 (23%)	43 (52%)	41 (47%)
PD-L1 CPS ≥5 (N=81; 40|41)	11 (28%)	8 (20%)	22 (55%)	18 (44%)	13 (33%)	9 (22%)	21 (53%)	19 (46%)
PD-L1 CPS ≥10 (N=53; 27|26)	9 (33%)	3 (12%)	18 (67%)	10 (39%)	11 (41%)	5 (19%)	19 (70%)	13 (50%)
MSI high (N=23; 8|15)	5 (63%)	4 (27%)	6 (75%)	7 (47%)	5 (63%)	4 (27%)	6 (75%)	7 (47%)

[1]central assessment by one pathologist based on a representative tumor sample
[2]pathological complete regression acc. to Becker
[3]pathological subtotal regression acc. to Becker

Al-Batran SE et al. ASCO 2022;Abstract 4003. | Discussant, Katrina Pedersen, MD, MS

Discussant Conclusions



Katrina Pedersen, MD, MS, Discussant

RTP RESEARCH TO PRACTICE

Article

Nature 2022;[Online ahead of print].

Nivolumab plus chemotherapy or ipilimumab in gastro-oesophageal cancer

https://doi.org/10.1038/s41586-022-04508-4

Received: 22 October 2021

Accepted: 3 February 2022

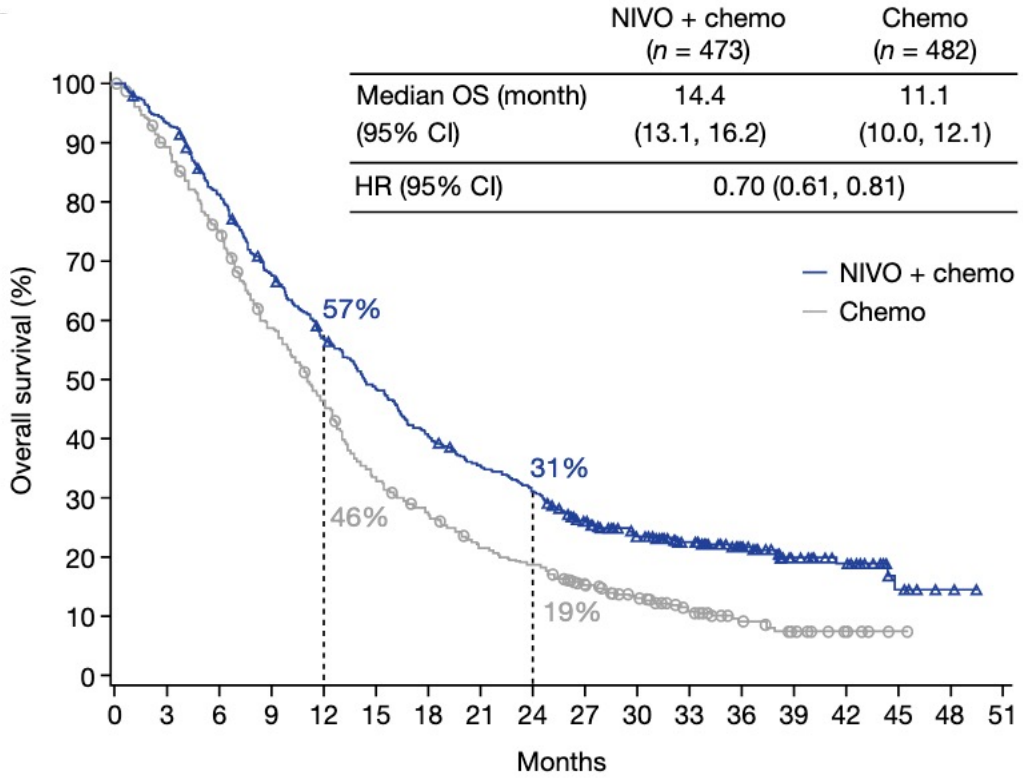
Published online: 23 March 2022

Open access

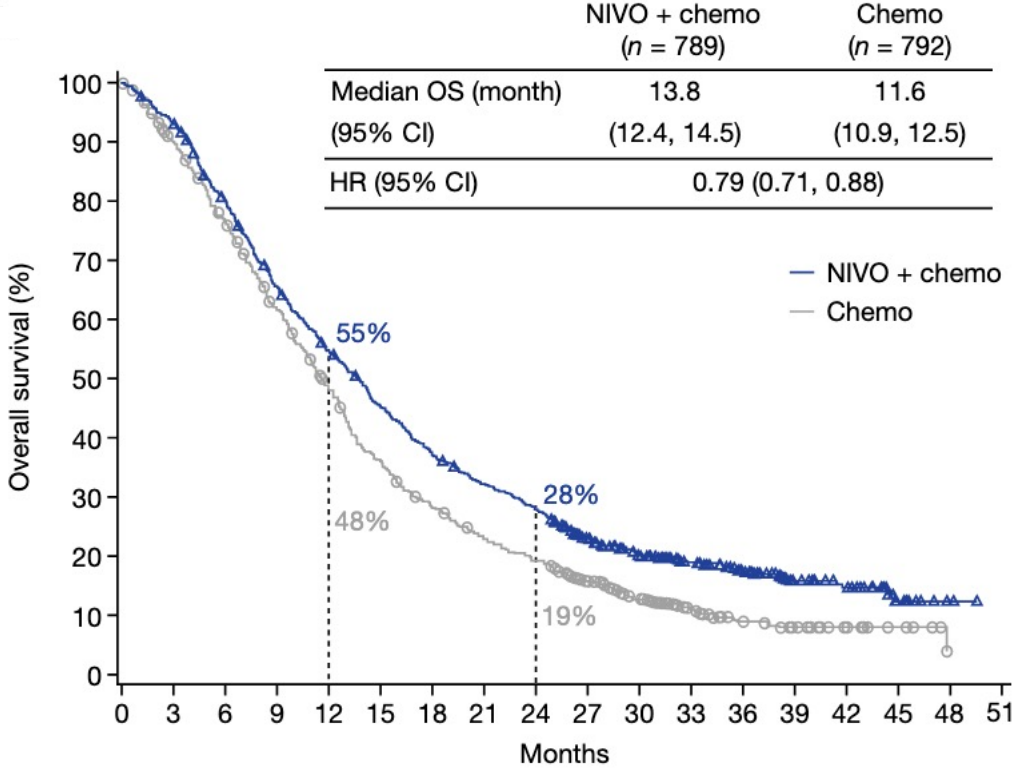
Kohei Shitara[1], Jaffer A. Ajani[2], Markus Moehler[3], Marcelo Garrido[4], Carlos Gallardo[5], Lin Shen[6], Kensei Yamaguchi[7], Lucjan Wyrwicz[8], Tomasz Skoczylas[9], Arinilda Campos Bragagnoli[10], Tianshu Liu[11], Mustapha Tehfe[12], Elena Elimova[13], Ricardo Bruges[14], Thomas Zander[15], Sergio de Azevedo[16], Ruben Kowalyszyn[17], Roberto Pazo-Cid[18], Michael Schenker[19], James M. Cleary[20], Patricio Yanez[21], Kynan Feeney[22], Michalis V. Karamouzis[23], Valerie Poulart[24], Ming Lei[24], Hong Xiao[24], Kaoru Kondo[24], Mingshun Li[24] & Yelena Y. Janjigian[25]✉

CheckMate 649: Overall Survival

PD-L1 CPS ≥5



All randomly assigned patients



CPS = combined positive score

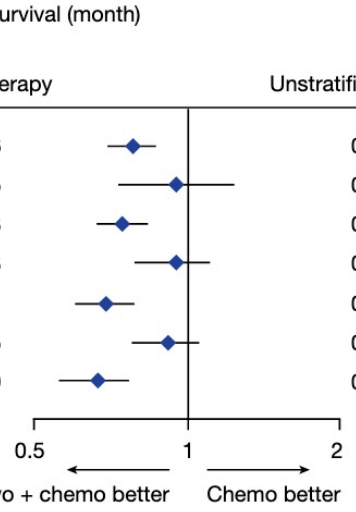
Shitara K et al. *Nature* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

CheckMate 649: Efficacy Subgroup Analysis by PD-L1 CPS Excluding Patients with MSI-High Tumors

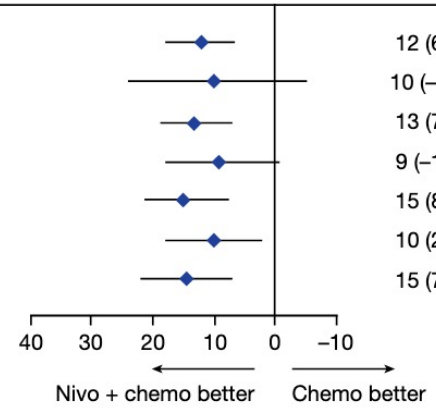
Median overall survival (month)

Population	Nivolumab plus chemotherapy	Chemotherapy	Unstratified HR for death (95% CI)
Overall (*n* = 1,581)	13.8	11.6	0.78 (0.70, 0.87)
PD-L1 CPS <1 (*n* = 265)	13.1	12.5	0.95 (0.73, 1.24)
PD-L1 CPS ≥1 (*n* = 1,297)	13.8	11.3	0.74 (0.66, 0.84)
PD-L1 CPS <5 (*n* = 607)	12.4	12.3	0.94 (0.79, 1.11)
PD-L1 CPS ≥5 (*n* = 955)	14.4	11.1	0.69 (0.60, 0.79)
PD-L1 CPS <10 (*n* = 795)	12.4	12.5	0.91 (0.78, 1.06)
PD-L1 CPS ≥10 (*n* = 767)	15.0	10.9	0.66 (0.56, 0.77)



Objective response rate (%)

Population	Nivolumab plus chemotherapy	Chemotherapy	Unweighted ORR difference (%) (95% CI)
Overall (*n* = 1,210)	58	46	12 (6, 18)
PD-L1 CPS <1 (*n* = 179)	51	41	10 (–5, 24)
PD-L1 CPS ≥1 (*n* = 1,017)	59	46	13 (7, 19)
PD-L1 CPS <5 (*n* = 428)	55	46	9 (–1, 18)
PD-L1 CPS ≥5 (*n* = 768)	60	45	15 (8, 22)
PD-L1 CPS <10 (*n* = 579)	58	47	10 (2, 18)
PD-L1 CPS ≥10 (*n* = 617)	59	44	15 (7, 22)



Shitara K et al. *Nature* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

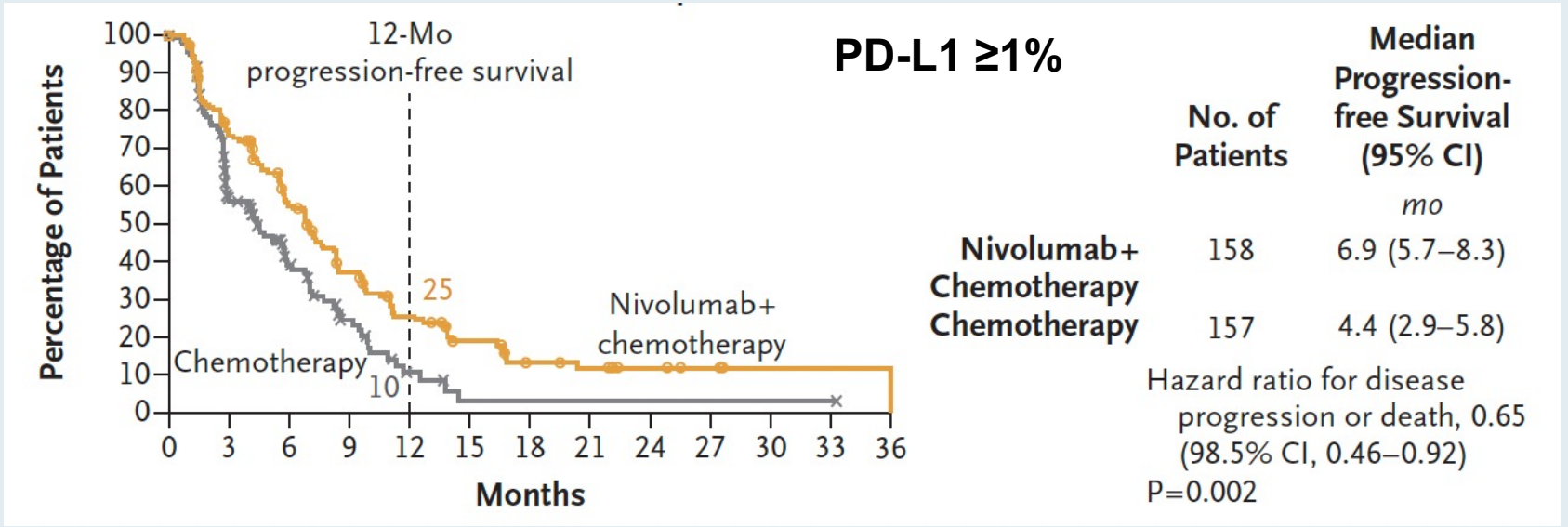
ORIGINAL ARTICLE

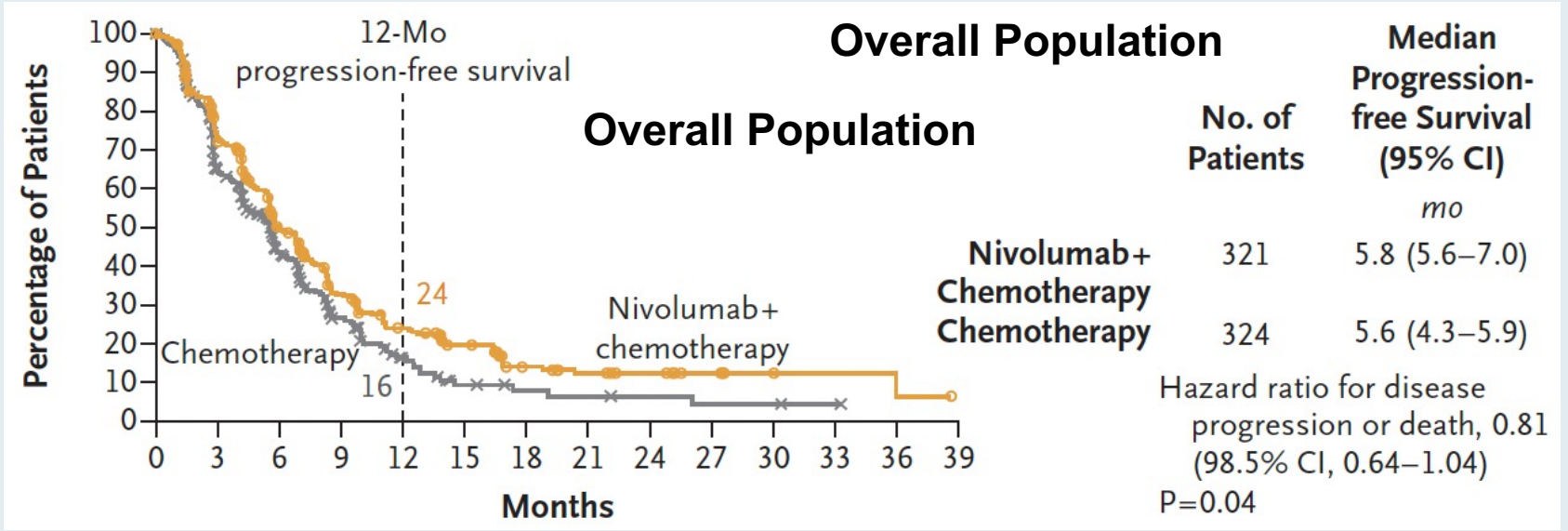
Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma

Y. Doki, J.A. Ajani, K. Kato, J. Xu, L. Wyrwicz, S. Motoyama, T. Ogata, H. Kawakami, C.-H. Hsu, A. Adenis, F. El Hajbi, M. Di Bartolomeo, M.I. Braghiroli, E. Holtved, S.A. Ostoich, H.R. Kim, M. Ueno, W. Mansoor, W.-C. Yang, T. Liu, J. Bridgewater, T. Makino, I. Xynos, X. Liu, M. Lei, K. Kondo, A. Patel, J. Gricar, I. Chau, and Y. Kitagawa, for the CheckMate 648 Trial Investigators*

New Engl J Med 2022;386(5):449-62.

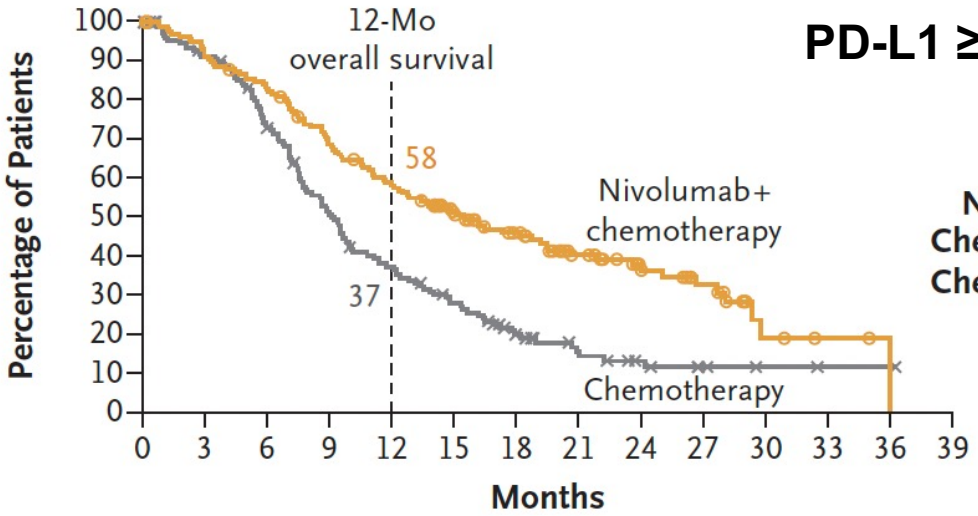
CheckMate 648: Progression-Free Survival for PD-L1 ≥1% and in the Overall Population – Nivolumab + Chemotherapy





Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

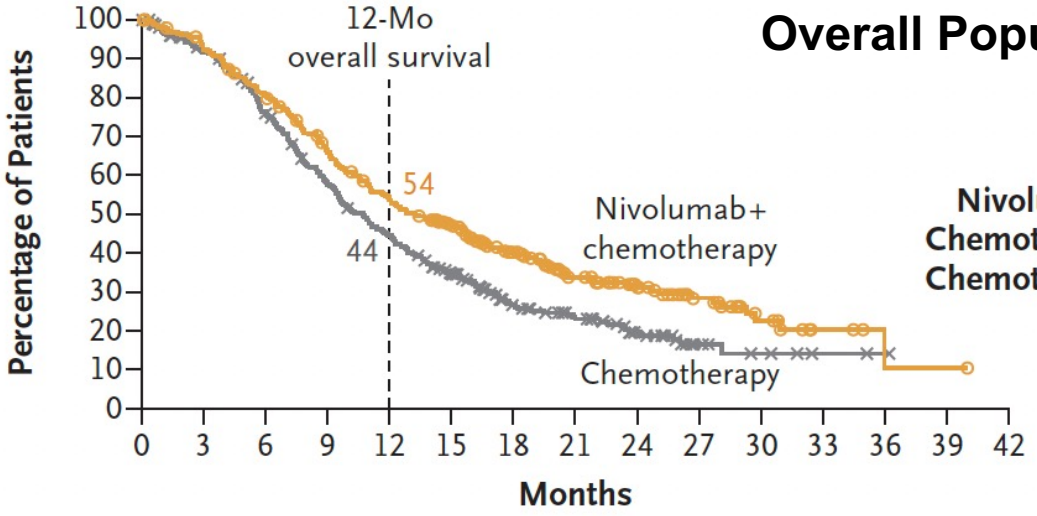
CheckMate 648: Overall Survival for PD-L1 ≥1% and in the Overall Population – Nivolumab + Chemotherapy



PD-L1 ≥1%

	No. of Patients	Median Overall Survival (95% CI)
		mo
Nivolumab+ Chemotherapy	158	15.4 (11.9–19.5)
Chemotherapy	157	9.1 (7.7–10.0)

Hazard ratio for death, 0.54
(99.5% CI, 0.37–0.80)
P<0.001



Overall Population

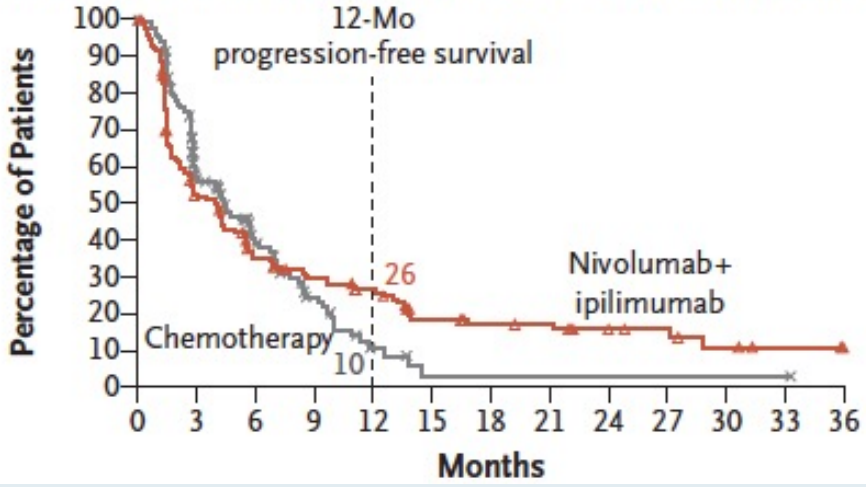
	No. of Patients	Median Overall Survival (95% CI)
		mo
Nivolumab+ Chemotherapy	321	13.2 (11.1–15.7)
Chemotherapy	324	10.7 (9.4–11.9)

Hazard ratio for death, 0.74
(99.1% CI, 0.58–0.96)
P=0.002

Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

CheckMate 648: Progression-Free Survival for PD-L1 ≥1% and in the Overall Population – Nivolumab + Ipilimumab

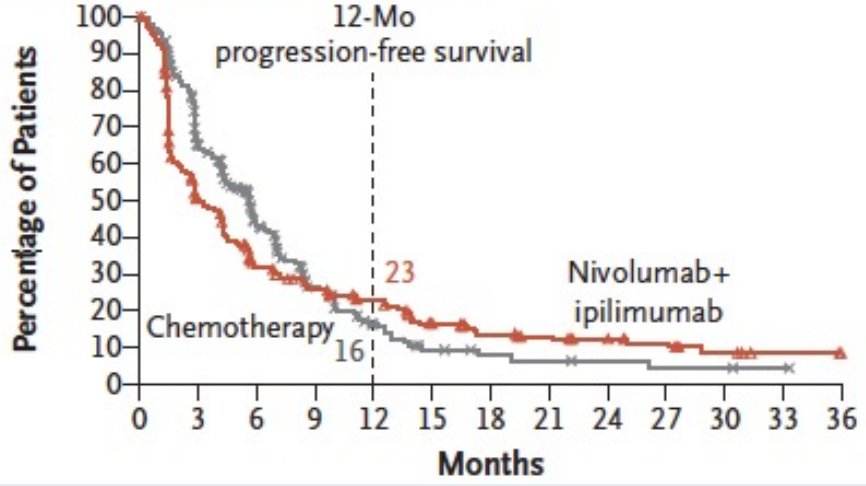
Progression-free Survival in Patients with Tumor-Cell PD-L1 Expression of ≥1%



	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Nivolumab+ Ipilimumab	158	4.0 (2.4–4.9)
Chemotherapy	157	4.4 (2.9–5.8)

Hazard ratio for disease progression or death, 1.02 (98.5% CI, 0.73–1.43)
P=0.90

Progression-free Survival in the Overall Population

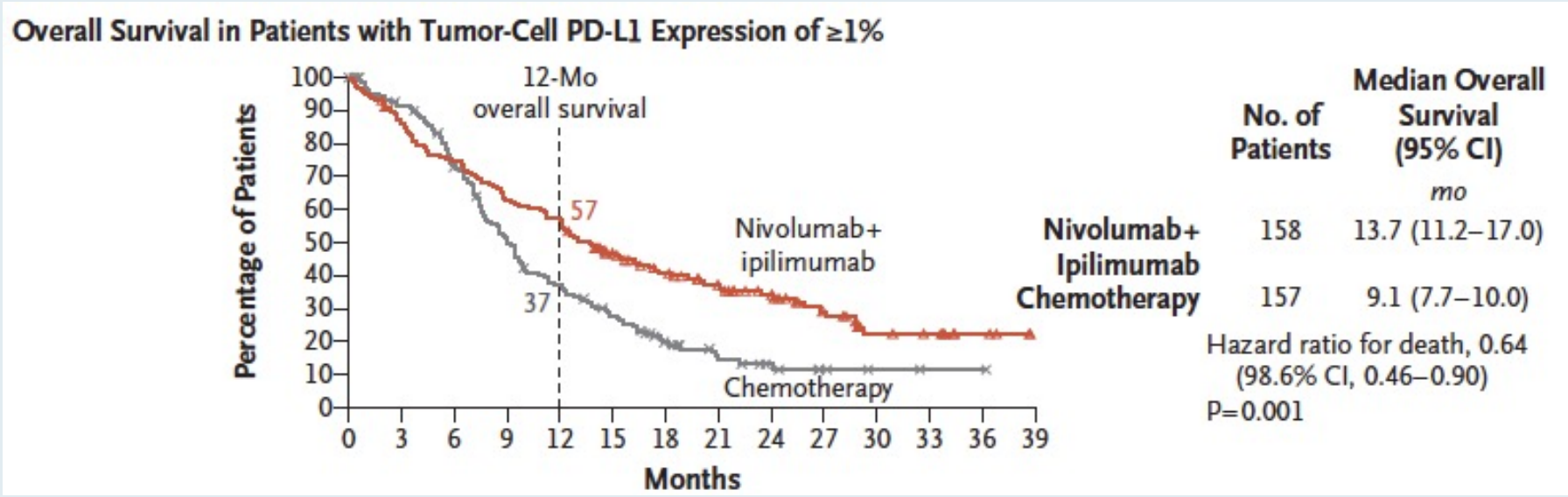


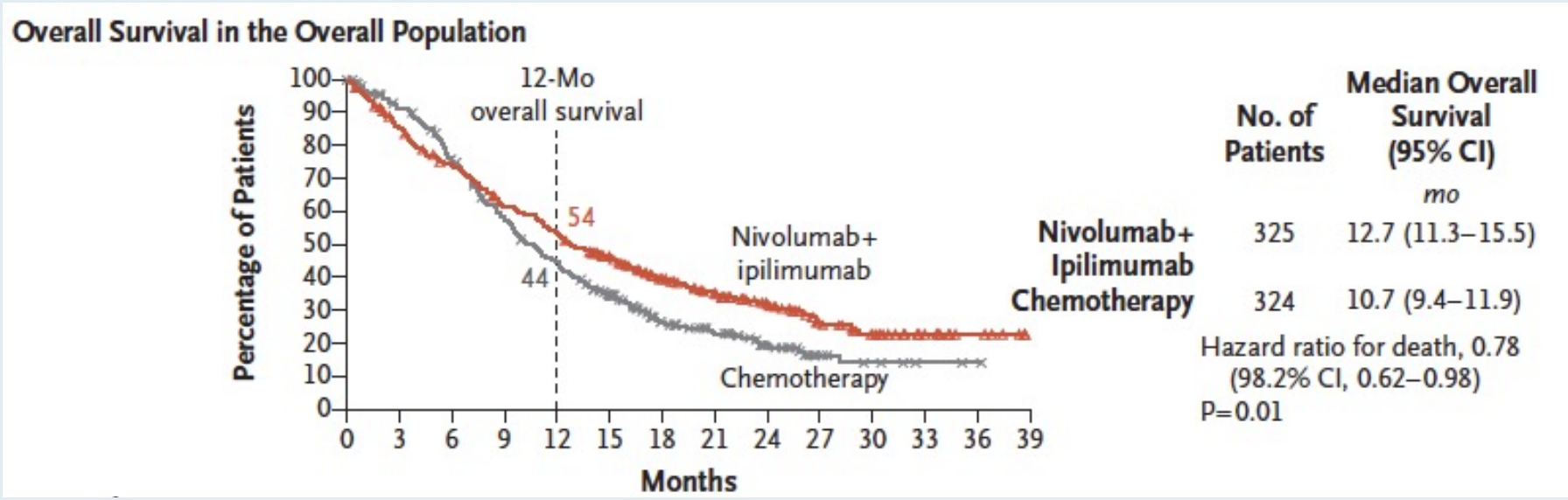
	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Nivolumab+ Ipilimumab	325	2.9 (2.7–4.2)
Chemotherapy	324	5.6 (4.3–5.9)

Hazard ratio for disease progression or death, 1.26 (95% CI, 1.04–1.52)
P value not tested

Doki Y et al. *New Engl J Med* 2022;386(5):449-62.

CheckMate 648: Overall Survival for PD-L1 ≥1% and in the Overall Population – Nivolumab + Ipilimumab





Doki Y et al. *New Engl J Med* 2022;386(5):449-62.

CheckMate 648: Antitumor Activity (BICR)

Endpoint	PD-L1 ≥1%			Overall population		
	Nivo/chemo (n = 158)	Nivo/ipi (n = 158)	Chemotherapy (n = 157)	Nivo/chemo (n = 321)	Nivo/ipi (n = 325)	Chemotherapy (n = 324)
ORR	53%	35%	20%	47%	28%	27%
Best overall response						
CR	16%	18%	5%	13%	11%	6%
PR	37%	18%	15%	34%	17%	21%
SD	25%	27%	46%	32%	32%	46%
PD	14%	30%	15%	13%	32%	12%
Median DoR	8.4 mo	11.8 mo	5.7 mo	8.2 mo	11.1 mo	7.1 mo
Pts with ongoing response	13%	25%	3%	17%	22%	6%

BICR = blinded independent central review

Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

CheckMate 648: Select Treatment-Related Adverse Events

Endpoint	Nivolumab/chemotherapy (N = 310)		Nivolumab/ipilimumab (N = 322)		Chemotherapy (N = 304)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Serious AEs	53%	35%	20%	47%	28%	27%
AEs leading to discontinuation	16%	18%	5%	13%	11%	6%
Nausea	59%	4%	8%	<1%	52%	3%
Stomatitis	32%	6%	4%	0	23%	2%
Anemia	30%	10%	4%	1%	22%	6%
Decreased neutrophils	21%	8%	1%	0	17%	8%
Decreased white cells	14%	4%	1%	0	9%	2%

Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

Checkmate-649 versus Checkmate-648

CM-649 - Gastric cancer

NIVO (1 mg/kg) + IPI (3 mg/kg) Q3W × 4 then NIVO 240 mg Q2W[e]

Different schedules!

CM-648 - Esophageal cancer

NIVO (3 mg/kg) Q2W + IPI (1 mg/kg) Q6W

CM-649: Treatment-related Adverse Events

All treated,[a] n (%)	NIVO + chemo (n = 782)[b]		Chemo (n = 767)[b]		NIVO + IPI (n = 403)[c]		Chemo (n = 389)[c]	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAEs[d]	739 (95)	471 (60)	682 (89)	344 (45)	323 (80)	155 (38)	356 (92)	180 (46)
Serious TRAEs[d]	175 (22)	133 (17)	94 (12)	77 (10)	122 (30)	93 (23)	54 (14)	45 (12)
TRAEs leading to discontinuation[d,e]	300 (38)	141 (18)	188 (25)	70 (9)	88 (22)	68 (17)	101 (26)	37 (10)
Treatment-related deaths[f]	16 (2)[g]		4 (< 1)[h]		10 (2)[i]		3 (< 1)[j]	

Lordick F. ESMO 2021;Discussant.

WORLD CONGRESS ON Gastrointestinal Cancer

O-3

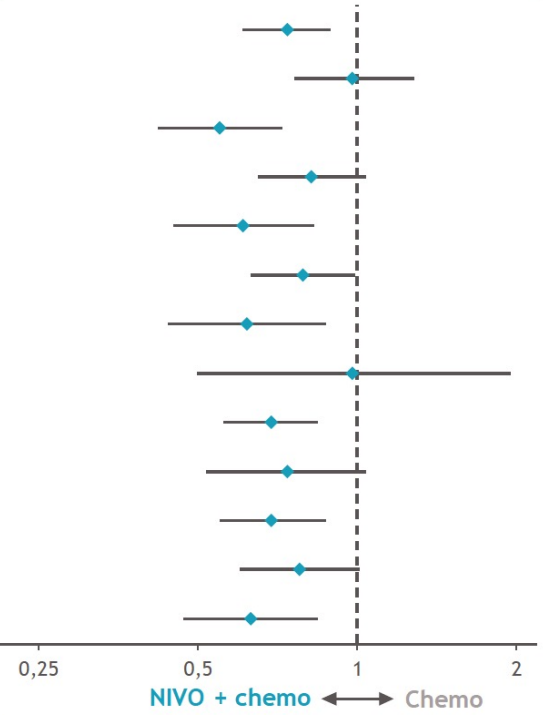
Nivolumab plus chemotherapy or ipilimumab vs chemotherapy as first-line treatment for advanced esophageal squamous cell carcinoma: expanded efficacy and safety analyses from CheckMate 648

Ian Chau,[1] Jaffer A. Ajani,[2] Yuichiro Doki,[3] Jianming Xu,[4] Lucjan Wyrwicz,[5] Satoru Motoyama,[6] Takashi Ogata,[7] Hisato Kawakami,[8] Chih-Hung Hsu,[9] Antoine Adenis,[10] Farid El Hajbi,[11] Maria Di Bartolomeo,[12] Maria Ignez Braghiroli,[13] Eva Holtved,[14] Mariela Blum Murphy,[2] Sandzhar Abdullaev,[15] Samira Soleymani,[15] Ming Lei,[15] Ken Kato,[16] Yuko Kitagawa[17]

[1]Royal Marsden Hospital, London & Surrey, UK; [2]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Osaka University Graduate School of Medicine, Osaka, Japan; [4]Affiliated Hospital Cancer Center, Academy of Military Medical Sciences, Beijing, China; [5]Klinika Onkologii i Radioterapii, Narodowy Instytut Onkologii, Warszawa, Poland; [6]Akita University Hospital, Akita, Japan; [7]Kanagawa Cancer Center, Kanagawa, Japan; [8]Kindai University Faculty of Medicine, Osakasayama, Japan; [9]National Taiwan University Hospital, Taipei, Taiwan; [10]Institut du Cancer de Montpellier, Montpellier, France; [11]Centre Oscar Lambret, Lille, France; [12]Fondazione IRCCS Instituto Nazionale dei Tumori, Milan, Italy; [13]Institute of Cancer of São Paulo, University of São Paulo, São Paulo, Brazil; [14]Odense University Hospital, Odense, Denmark; [15]Bristol Myers Squibb, Princeton, NJ, USA; [16]National Cancer Center Hospital, Tokyo, Japan; [17]Keio University School of Medicine, Tokyo, Japan

CheckMate 648: Overall Survival by Baseline PD-L1 Status – Nivolumab with Chemotherapy versus Chemotherapy

Category (all randomized)	Subgroup	Median OS, months		Unstratified HR for death	Unstratified HR (95% CI)
		NIVO + chemo	Chemo		
Overall (N = 645)		13.2	10.7	0.74	
Tumor cell PD-L1 expression[a]	< 1% (n = 329)	12.0	12.2	0.98	
	≥ 1% (n = 314)	15.4	9.2	0.55	
	< 5% (n = 408)	12.8	11.1	0.82	
	≥ 5% (n = 235)	13.7	9.5	0.61	
	< 10% (n = 444)	12.3	10.8	0.79	
	≥ 10% (n = 199)	14.7	9.5	0.62	
PD-L1 CPS[b,c]	< 1 (n = 51)	9.9	12.1	0.98	
	≥ 1 (n = 558)	13.8	9.8	0.69	
	< 5 (n = 188)	12.0	9.4	0.74	
	≥ 5 (n = 421)	15.2	11.1	0.69	
	< 10 (n = 329)	12.1	9.7	0.78	
	≥ 10 (n = 280)	16.1	11.6	0.63	



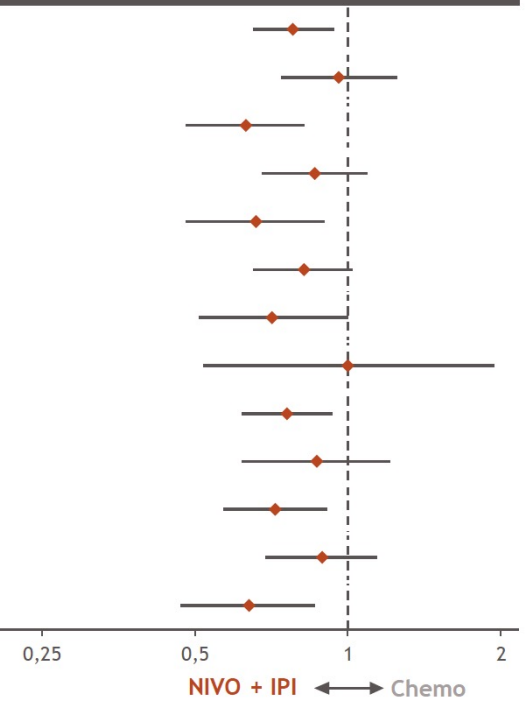
- HRs were below 1 favoring NIVO + chemo vs chemo across all PD-L1 expression subgroups
- Largest magnitude of benefit was observed in patients with tumor cell PD-L1 ≥ 1%, with no further enrichment in higher tumor cell PD-L1 expression subgroups

[a]Indeterminate, not evaluable, or missing (n = 2); [b]Indeterminate, not evaluable, or missing (n = 36); [c]Analysis by CPS was exploratory. Adapted from Doki Y, et al. *N Engl J Med* 2022;386:449-462.

Chau I et al. World Congress on Gastrointestinal Cancer 2022;Abstract O-3.

CheckMate 648: Overall Survival by Baseline PD-L1 Status – Nivolumab with Ipilimumab versus Chemotherapy Alone

Category (all randomized)	Subgroup	Median OS, months		Unstratified HR for death
		NIVO + IPI	Chemo	
Overall (N = 649)		12.7	10.7	0.78
Tumor cell PD-L1 expression[a]	< 1% (n = 330)	12.0	12.2	0.96
	≥ 1% (n = 314)	13.7	9.2	0.63
	< 5% (n = 409)	12.4	11.1	0.86
	≥ 5% (n = 235)	13.0	9.5	0.66
	< 10% (n = 444)	12.5	10.8	0.82
	≥ 10% (n = 200)	13.0	9.5	0.71
PD-L1 CPS[b,c]	< 1 (n = 55)	11.5	12.1	1.00
	≥ 1 (n = 546)	12.7	9.8	0.76
	< 5 (n = 197)	11.4	9.4	0.87
	≥ 5 (n = 404)	14.5	11.1	0.72
	< 10 (n = 330)	11.2	9.7	0.89
	≥ 10 (n = 271)	16.7	11.6	0.64



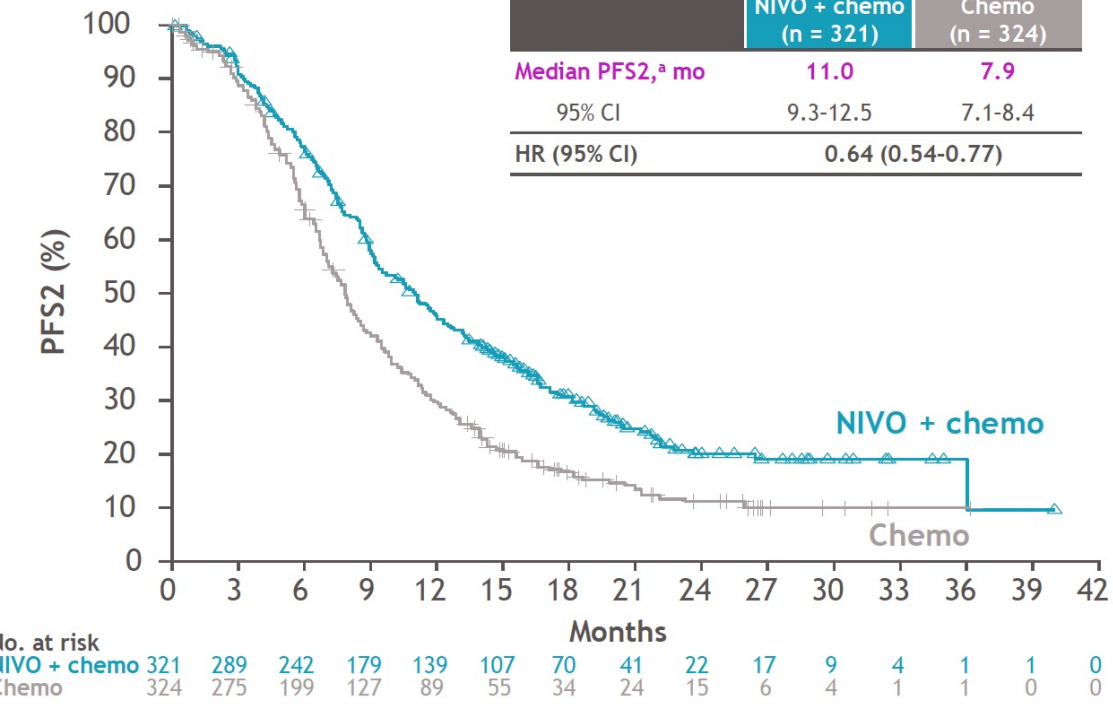
- HRs were below 1 favoring NIVO + IPI vs chemo across all PD-L1 expression subgroups, except for CPS < 1 (n = 55; HR = 1)
- Largest magnitude of benefit was observed in patients with tumor cell PD-L1 ≥ 1%, with no further enrichment in higher tumor cell PD-L1 expression subgroups

[a]Indeterminate, not evaluable, or missing (n = 5); [b]Indeterminate, not evaluable, or missing (n = 48); [c]Analysis by CPS was exploratory. Adapted from Doki Y, et al. *N Engl J Med* 2022;386:449-462.

Chau I et al. World Congress on Gastrointestinal Cancer 2022;Abstract O-3.

CheckMate 648: PFS2 Analysis with Nivolumab and Chemotherapy versus Chemotherapy

All randomized patients



	NIVO + chemo (n = 321)	Chemo (n = 324)
Median PFS2,[a] mo	11.0	7.9
95% CI	9.3-12.5	7.1-8.4
HR (95% CI)	0.64 (0.54-0.77)	

First subsequent therapy,[b] n (%)	NIVO + chemo (n = 321)	Chemo (n = 324)
Any subsequent therapy	163 (51)	203 (63)
Radiotherapy	70 (22)	91 (28)
Surgery	9 (3)	9 (3)
Systemic anticancer therapy[c]	149 (46)	181 (56)
Immunotherapy	4 (1)	28 (9)
Other systemic anticancer therapy	146 (45)	157 (48)

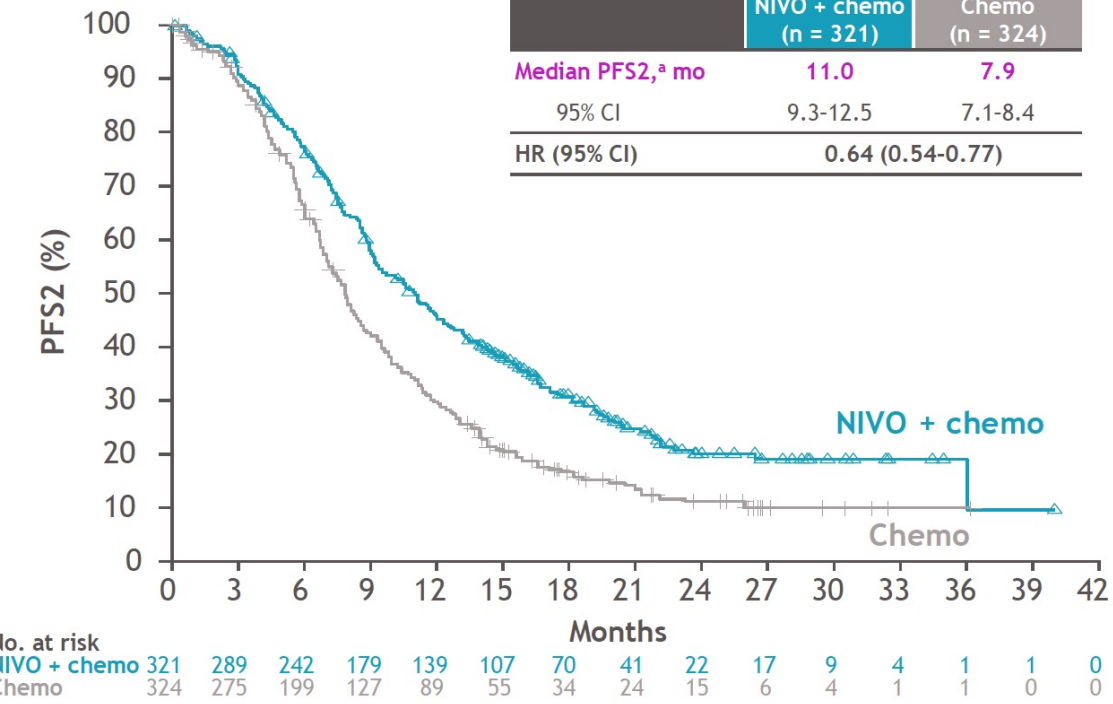
- PFS2 favored NIVO + chemo vs chemo with a 36% reduction in the risk of death, initiation of second subsequent systemic therapy, or disease progression on subsequent therapy

[a]Per investigator; [b]Patients may have received more than 1 type of subsequent therapy; [c]Patients may have received multiple subsequent systemic therapies; the first subsequent systemic therapies patients received are summarized in the table, regardless of their timing relative to the subsequent radiotherapy and surgery. PFS2, progression-free survival on subsequent therapy (time from randomization to progression after subsequent systemic therapy, initiation of second subsequent systemic therapy, or death, whichever was earlier).

Chau I et al. World Congress on Gastrointestinal Cancer 2022;Abstract O-3.

CheckMate 648: PFS2 Analysis with Nivolumab and Chemotherapy versus Chemotherapy

All randomized patients



	NIVO + chemo (n = 321)	Chemo (n = 324)
Median PFS2,[a] mo	11.0	7.9
95% CI	9.3-12.5	7.1-8.4
HR (95% CI)	0.64 (0.54-0.77)	

First subsequent therapy,[b] n (%)	NIVO + chemo (n = 321)	Chemo (n = 324)
Any subsequent therapy	163 (51)	203 (63)
Radiotherapy	70 (22)	91 (28)
Surgery	9 (3)	9 (3)
Systemic anticancer therapy[c]	149 (46)	181 (56)
Immunotherapy	4 (1)	28 (9)
Other systemic anticancer therapy	146 (45)	157 (48)

- PFS2 favored NIVO + chemo vs chemo with a 36% reduction in the risk of death, initiation of second subsequent systemic therapy, or disease progression on subsequent therapy

[a]Per investigator; [b]Patients may have received more than 1 type of subsequent therapy; [c]Patients may have received multiple subsequent systemic therapies; the first subsequent systemic therapies patients received are summarized in the table, regardless of their timing relative to the subsequent radiotherapy and surgery. PFS2, progression-free survival on subsequent therapy (time from randomization to progression after subsequent systemic therapy, initiation of second subsequent systemic therapy, or death, whichever was earlier).

Chau I et al. World Congress on Gastrointestinal Cancer 2022;Abstract O-3.

2021 ASCO ANNUAL MEETING

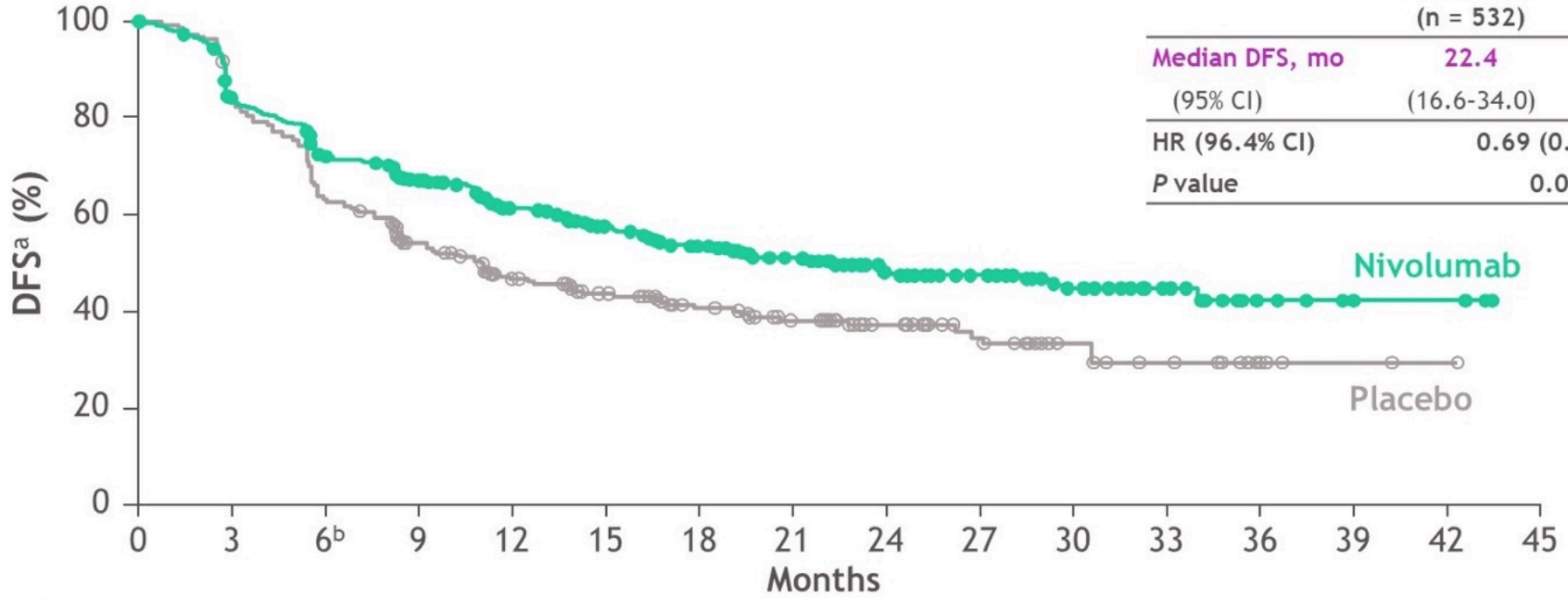
Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

Ronan J. Kelly,[1] Jaffer A. Ajani,[2] Jaroslaw Kuzdzal,[3] Thomas Zander,[4] Eric Van Cutsem,[5] Guillaume Piessen,[6] Guillermo Mendez,[7] Josephine Feliciano,[8] Satoru Motoyama,[9] Astrid Lièvre,[10] Hope Uronis,[11] Elena Elimova,[12] Cecile Grootscholten,[13] Karen Geboes,[14] Jenny Zhang,[15] Samira Soleymani,[15] Ming Lei,[15] Prianka Singh,[15] James M. Cleary,[16] Markus Moehler[17]

[1]The Charles A. Sammons Cancer Center at Baylor University Medical Center, Dallas, TX; [2]The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Jagiellonian University, John Paul II Hospital, Cracow, Poland; [4]University Hospital of Cologne, Cologne, Germany; [5]University Hospitals Gasthuisberg, Leuven and KULeuven, Leuven, Belgium; [6]University of Lille, Claude Huriez University Hospital, Lille, France; [7]Fundacion Favaloro, Buenos Aires, Argentina; [8]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; [9]Akita University Hospital, Akita, Japan; [10]CHU Pontchaillou, Rennes 1 University, Rennes, France; [11]Duke Cancer Institute, Durham, NC; [12]Princess Margaret Cancer Centre, Toronto, ON, Canada; [13]Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [14]UZ Gent, Gent, Belgium; [15]Bristol Myers Squibb, Princeton, NJ; [16]Dana Farber Cancer Institute, Boston, MA; [17]Johannes-Gutenberg University Clinic, Mainz, Germany

Abstract number 4003

CheckMate 577: Disease-Free Survival (DFS)



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

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

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

Kelly RJ et al. ASCO 2021;Abstract 4003.

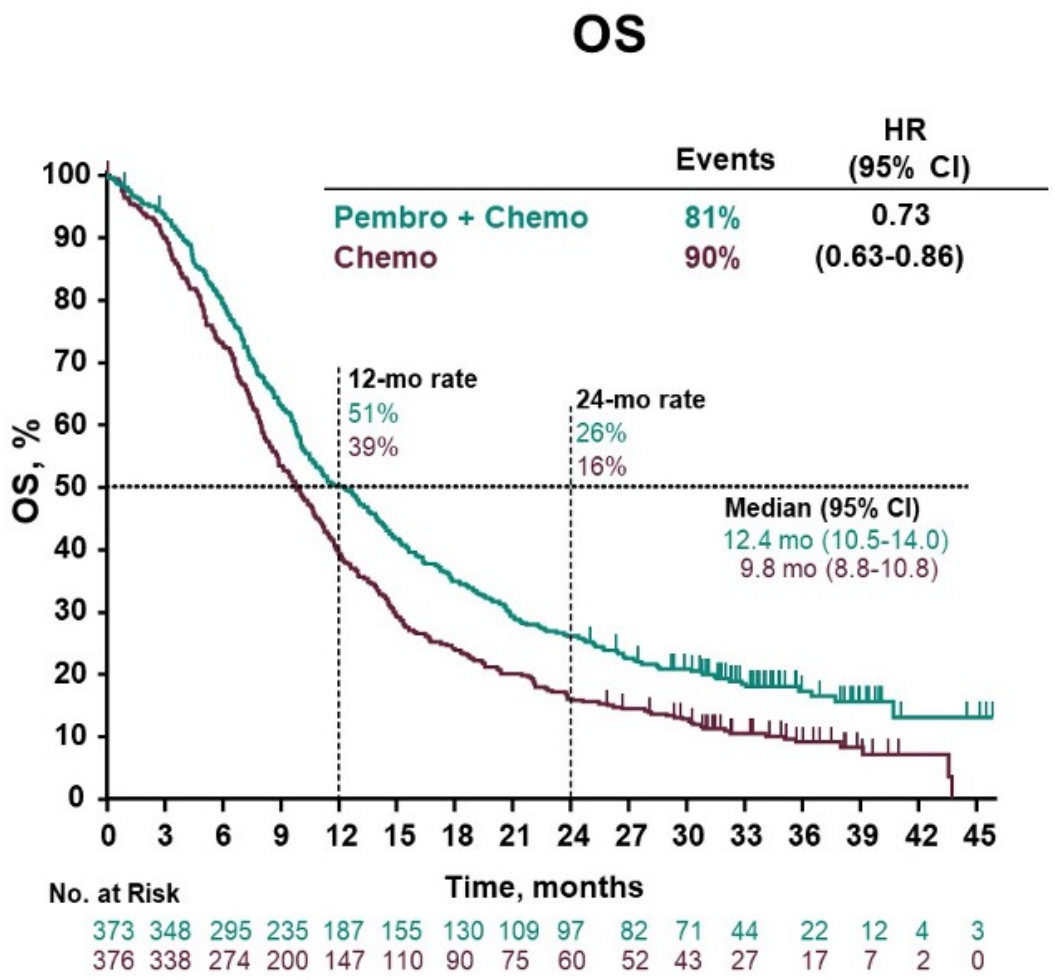
First-line Pembrolizumab Plus Chemotherapy Versus Chemotherapy in Advanced Esophageal Cancer: Longer-term Efficacy, Safety, and Quality-of-life Results From the Phase 3 KEYNOTE-590 Study

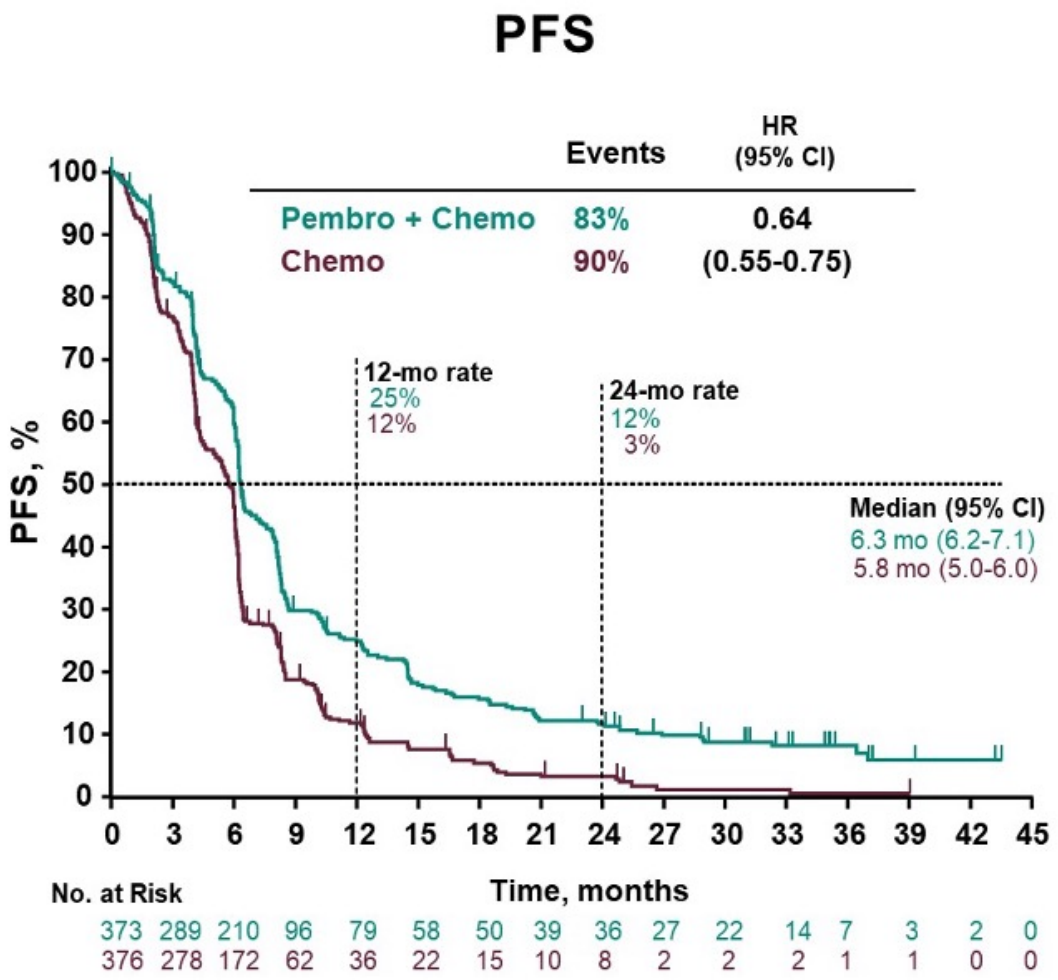
Jean-Philippe Metges,[1] Ken Kato,[2] Jong-Mu Sun,[3] Manish A. Shah,[4] Peter Enzinger,[5] Antoine Adenis,[6] Toshihiko Doi,[7] Takashi Kojima,[7] Zhigang Li,[8] Sung-Bae Kim,[9] Byoung Chul Cho,[10] Wasat Mansoor,[11] Shau-Hsuan Li,[12] Patrapim Sunpaweravong,[13] Maria Alsina Maqueda,[14] Gary L. Buchschacher, Jr,[15] Wu Jimin,[16] Sukrut Shah,[16] Pooja Bhagia,[16] Lin Shen[17]

[1]CHU Brest – Institut de Cancerologie et d'Hematologie ARPEGO Network, Brest, France; [2]National Cancer Center Hospital, Tokyo, Japan; [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [4]Weill Cornell Medical College, New York, NY, USA; [5]Dana Farber Cancer Institute, Boston, MA, USA; [6]IRCM, Inserm, Université Montpellier, ICM, Montpellier, France; [7]National Cancer Center Hospital East, Kashiwa, Japan; [8]Shanghai Chest Hospital Esophageal Disease Center, Shanghai, China; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [10]Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea; [11]Christie Hospital NHS Trust, Manchester, United Kingdom; [12]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan; [13]Prince of Songkla University Hospital, Songkhla, Thailand; [14]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [15]Kaiser Permanente Southern California, Los Angeles Medical Center, Los Angeles, CA, USA; [16]Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; [17]Peking University Cancer Hospital & Institute; Beijing, China

Gastrointestinal Cancers Symposium 2022;Abstract 241.

KEYNOTE-590: Survival Analyses (All Patients)



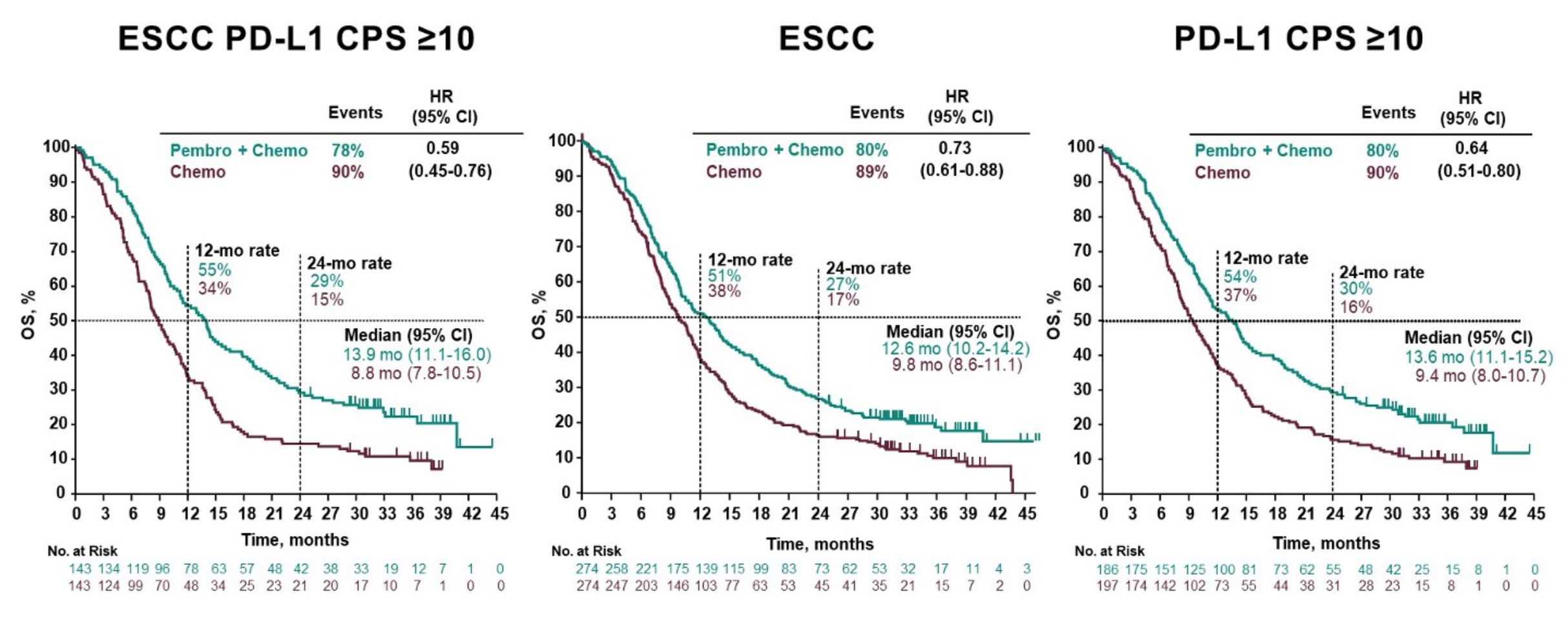


OS = overall survival; PFS = progression-free survival

Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

RTP RESEARCH TO PRACTICE

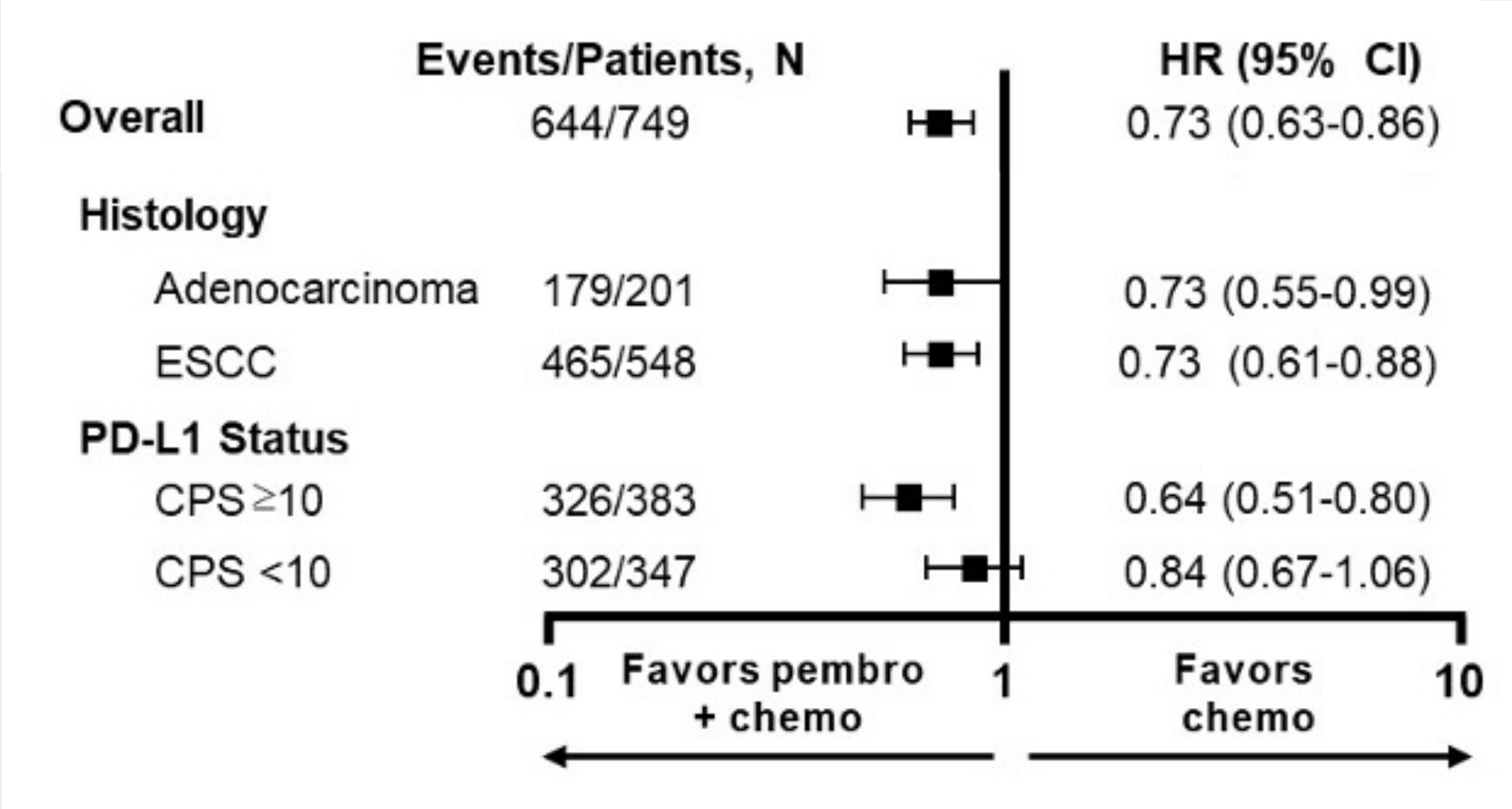
KEYNOTE-590: Overall Survival (OS) in Prespecified Subgroups



ESCC = esophageal squamous cell carcinoma

Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

KEYNOTE-590: Overall Survival in Select Subgroups



Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

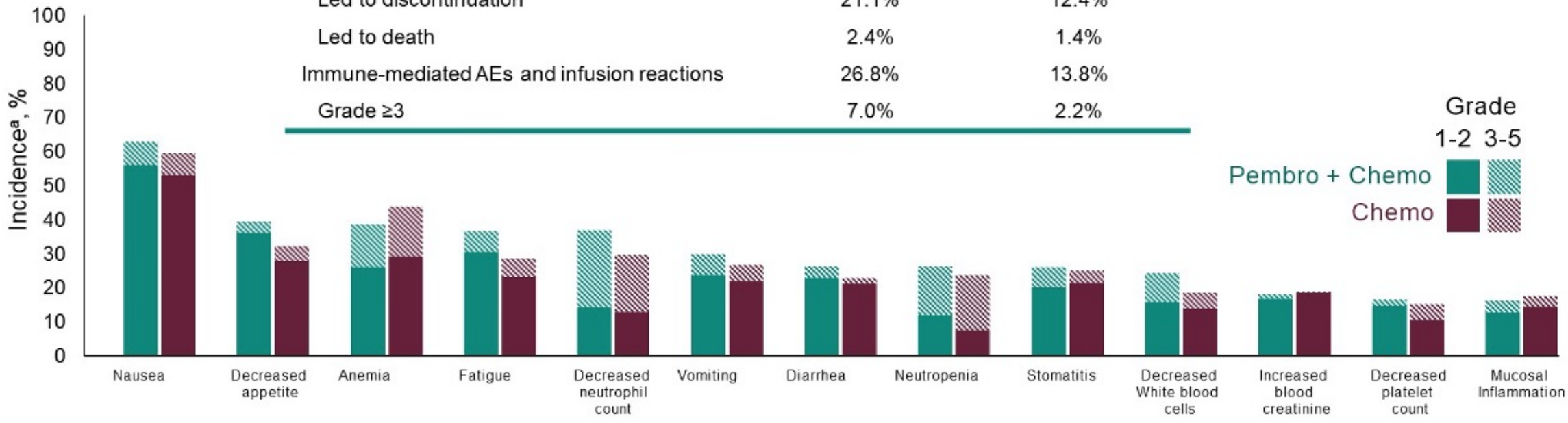
KEYNOTE-590: Antitumor Response

Best response, n (%)	Pembro + Chemo N = 373	Chemo N = 376
ORR, n (%)	**168 (45.0)**	**110 (29.3)**
Complete response	25 (6.7)	9 (2.4)
Partial response	143 (38.3)	101 (26.9)
Stable disease	126 (33.8)	174 (46.3)
Disease control rate	294 (78.8)	284 (75.5)
Progressive disease	43 (11.5)	59 (15.7)
Not evaluable/no assessment	36 (9.6)	33 (8.7)
Median DOR (range), mo	8.3 (1.2+ to 41.7+)	6.0 (1.5+ to 34.9+)
≥ 24 months response duration, %	**20.4**	**6.2**

Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

KEYNOTE-590: Adverse Events Summary

Events, n (%)	Pembro + Chemo N = 373	Chemo N = 376
Any	100%	99.5%
Treatment-related	98.4%	97.3%
Grade ≥3	71.9%	67.6%
Led to discontinuation	21.1%	12.4%
Led to death	2.4%	1.4%
Immune-mediated AEs and infusion reactions	26.8%	13.8%
Grade ≥3	7.0%	2.2%



Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

RTP RESEARCH TO PRACTICE

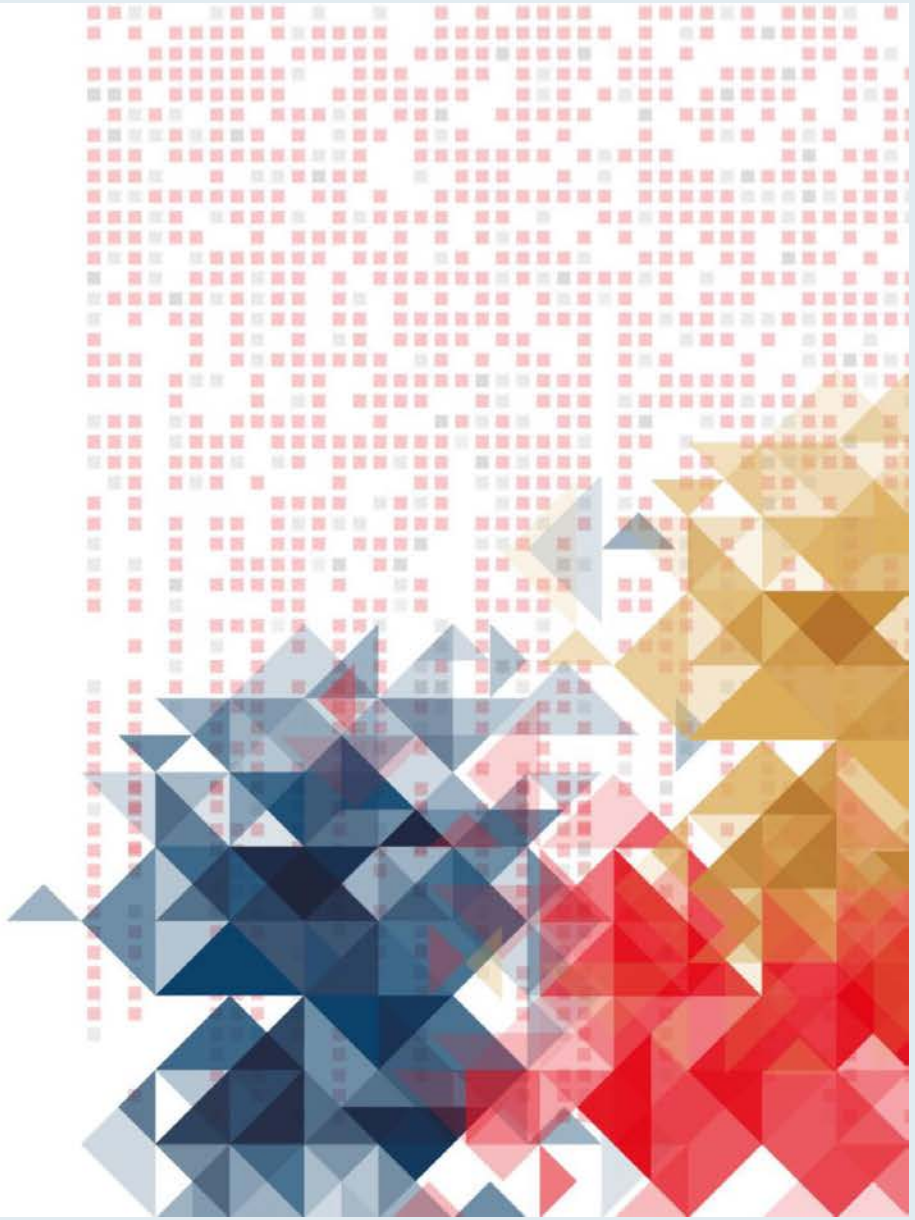
2021 ESMO congress

Abstract LBA53

Sintilimab plus chemotherapy (chemo) versus chemo as the first-line treatment for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma (ORIENT-16)

Jianming Xu*, Haiping Jiang, Yueyin Pan, Kangsheng Gu, Sundong Cang, Lei Han, Yongqian Shu, Jiayi Li, Junhui Zhao, Hongming Pan, Suxia Luo, Yanru Qin, Qunyi Guo, Yuxian Bai, Yang Ling, Yingmei Guo, Ziran Li, Ying Liu, Yan Wang, Hui Zhou

*, presenting author, MD, The Fifth Medical Center, Chinese PLA General Hospital



ORIENT-16: Phase III Trial Design

Sintilimab is a recombinant fully humanized anti-PD-1 monoclonal antibody.

Previous study has shown encouraging anti-tumor activities of Sintilimab plus chemotherapy in 1L G/GEJ cancer.

ORIENT-16[a] is a randomized, double-blind, phase 3 study

Key eligibility criteria
- Previously untreated, unresectable advanced, recurrent or metastatic G/GEJ adenocarcinoma
- ECOG PS 0 or 1
- No known Her2 positive

R 1:1

N=327 → **Sintilimab + XELOX[a] Q3W × 6 cycles, then Sintilimab + Capecitabine[a] Q3W[b]**

N=323 → **Placebo + XELOX[a] Q3W × 6 cycles, then Placebo + Capecitabine[a] Q3W[b]**

Primary endpoints:
- OS in the patients with CPS ≥5
- OS in all randomized patients

Secondary endpoints:
- PFS, ORR, DCR, and DoR
- Safety profile

Stratification factors
- ECOG PS (0 or 1)
- Liver metastasis (yes or no)
- PD-L1 (CPS <10 or ≥10)

- Data cut-off date for interim analysis was June 20, 2021
- Median follow-up: 18.8 months

Statistical considerations
- Type I error is strictly controlled using fixed sequence test. OS in CPS≥5 and all randomized are tested hierarchically
- One interim analysis is planned, and O'Brien-Fleming is used for the alpha boundary (alpha=0.0148).

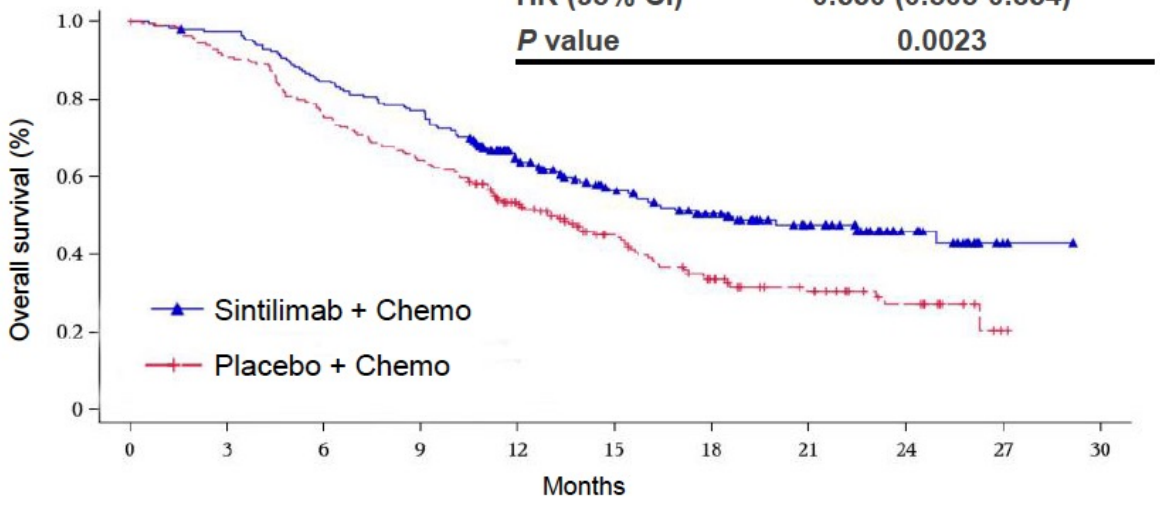
[a] ClinicalTrial.gov number, NCT03745170; [b] Sintilimab 3 mg/kg for body weight <60 kg, 200 mg for ≥60 kg; Oxaliplatin 130 mg/m^2 IV; Capecitabine 1000 mg/m^2 PO Bid d1-14;
[c] Until progressive disease, intolerable toxicity, withdrawal of consent. Treatment is given for a maximum of 2 years.

Xu J et al. ESMO 2021;Abstract LBA53.

ORIENT-16: Overall Survival (OS) with Sintilimab and Chemotherapy for Advanced Gastric or GEJ Adenocarcinoma

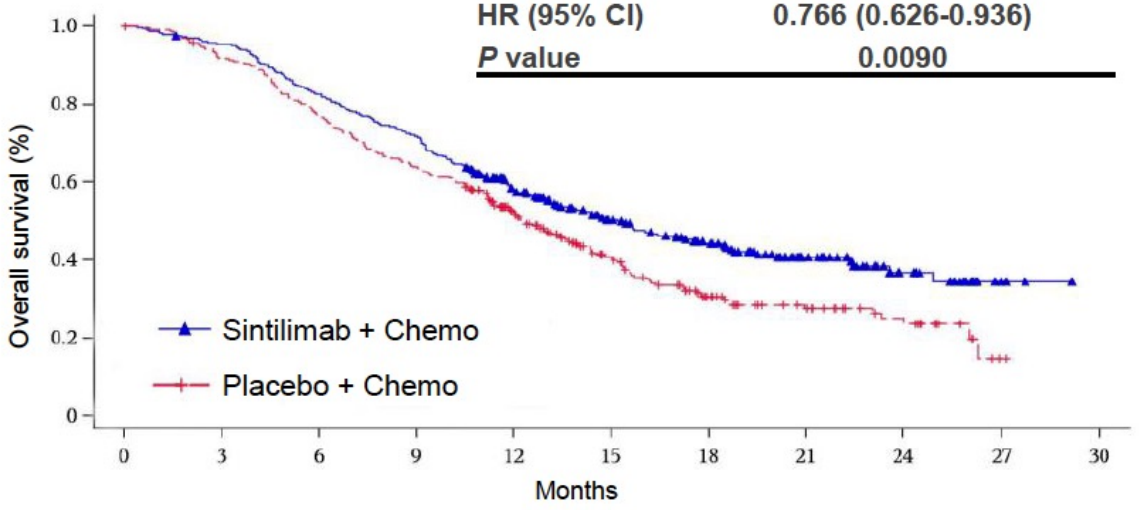
PD-L1 CPS ≥5

	Sin + Chemo (N=197)	Chemo (N=200)
Median OS, mo (95% CI)	18.4 (14.6-NC)	12.9 (11.1-.15.4)
HR (95% CI)	0.660 (0.505-0.864)	
P value	0.0023	



All patients

	Sin + Chemo (N=327)	Chemo (N=323)
Median OS, mo (95% CI)	15.2 (12.9-18.4)	12.3 (11.3-.13.8)
HR (95% CI)	0.766 (0.626-0.936)	
P value	0.0090	



Xu J et al. ESMO 2021;Abstract LBA53.

2021 ESMO congress

Abstract LBA52

Sintilimab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced or metastatic esophageal squamous cell cancer: First Results of the Phase 3 ORIENT-15 study

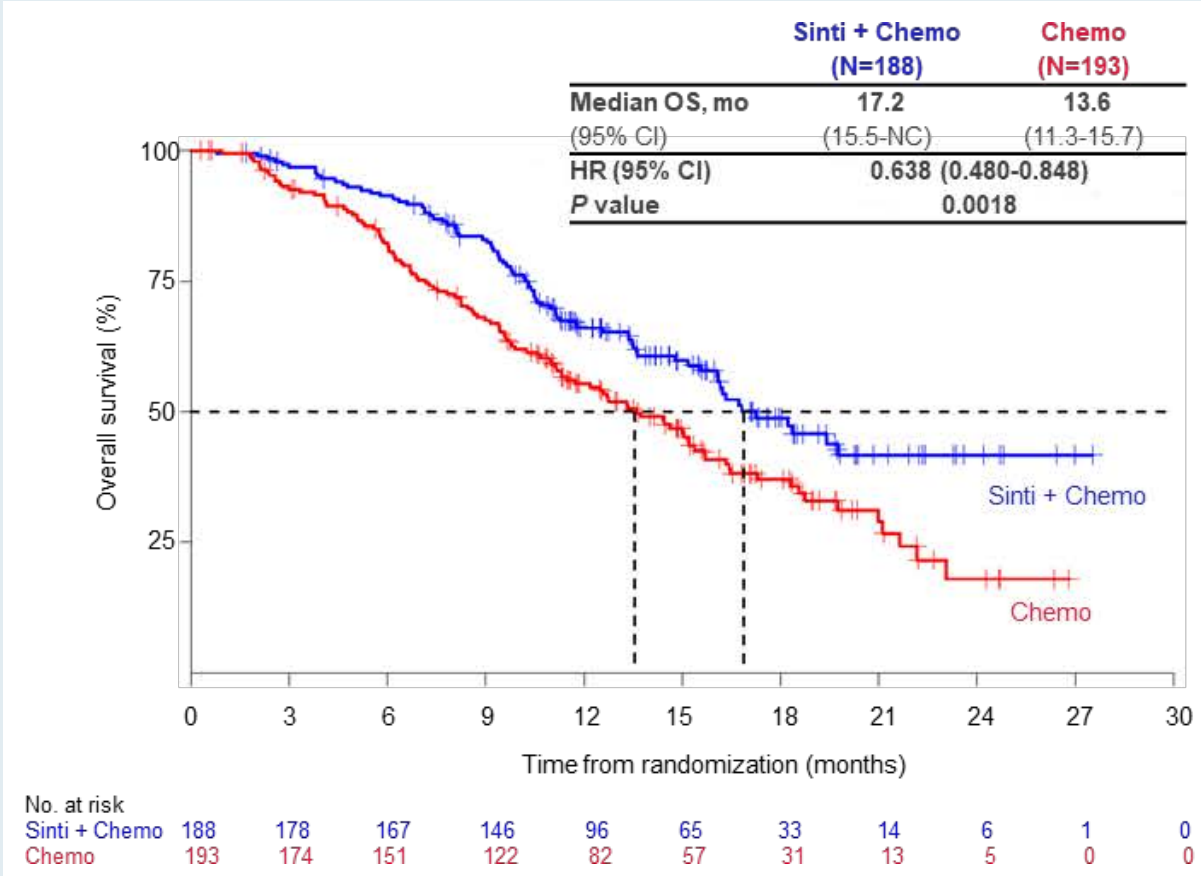
Lin Shen[1], Zhihao Lu[2], Junye Wang[3], Yongqian Shu[4], Li Kong[5], Lei Yang[6], Buhai Wang[7], Zhiwu Wang[8], Yinghua Ji[9], Guochun Cao[10], Hu Liu[11], Tongjian Cui[12], Na Li[13], Wensheng Qiu[14], Zhuo Ma[15], Yuling Chen[15], Haoyu Li[15], Xing Sun[15], Yan Wang[15], Hui Zhou[15]

[1]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China, [2]Department of Gastrointestinal Oncology, Peking University Cancer Hospital & Institute, Beijing, China, [3]Department of Oncology, The Affiliated Hospital of Jining Medical College, Jining, China, [4]Department of Medical Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China, [5]Special Needs Ward, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China, [6]Department of Medical Oncology, Nantong Cancer Hospital, Nantong, China, [7]Department of Medical Oncology, Northern Jiangsu People's Hospital, Affiliated Hospital to Yangzhou University, Yangzhou, China, [8]Department of Radiotherapy and Chemotherapy, Tangshan People Hospital, Tangshan, China, [9]Department of Medical Oncology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, China, [10]Department of Oncology, Jiangsu Cancer Hospital, Nanjing Medical University, Nanjing, China, [11]Department of Medical Oncology, Anhui provincial Cancer Hospital, University of Science and Technology of China, Hefei, China, [12]Department of Oncology, Fujian Provincial Hospital, Fuzhou, China, [13]Department of Medical Oncology, Suining Central Hospital, Suining, China, [14]Department of Medical Oncology, The Affiliated Hospital of Qingdao University, Qingdao, China, [15]Medical Oncology, Innovent Biologics, Inc., Suzhou, China, [16]Biostatistics, Innovent Biologics, Inc., Suzhou, China

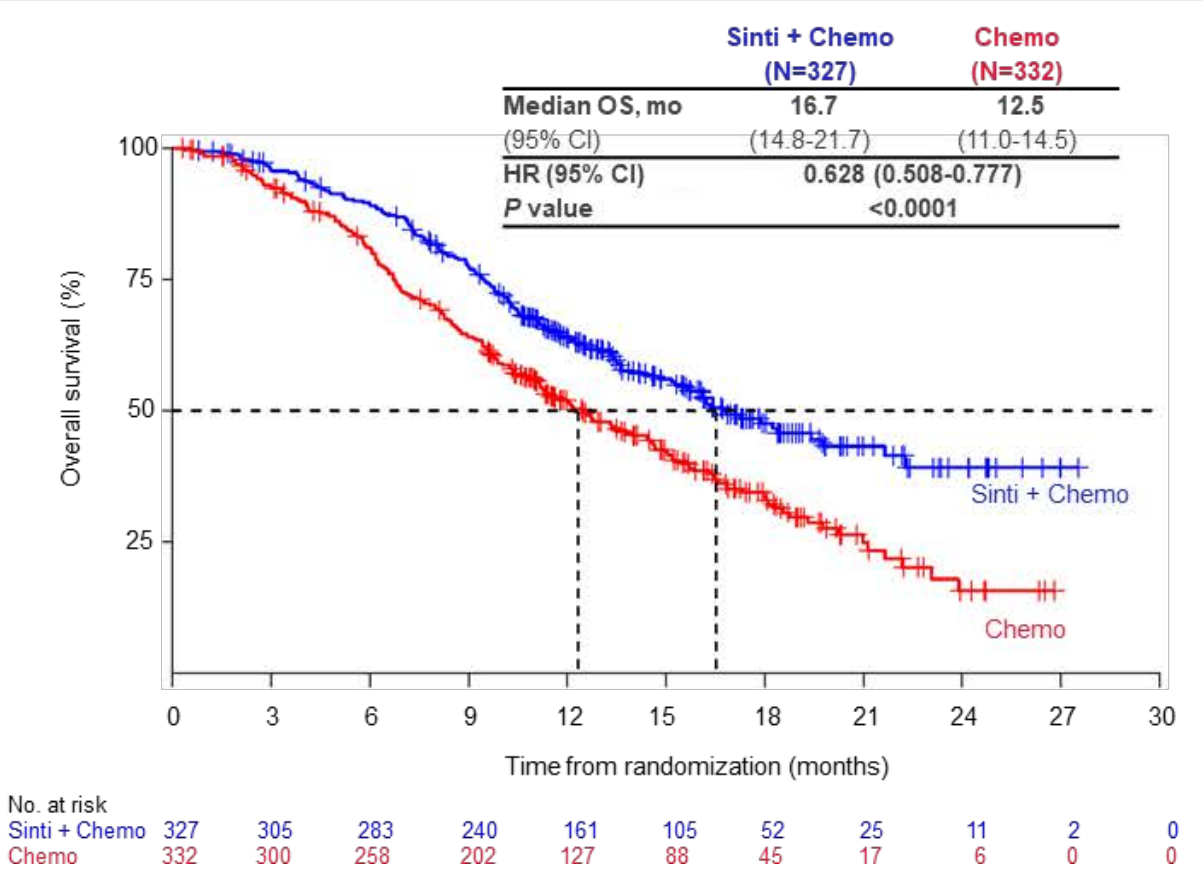
RTP RESEARCH TO PRACTICE

ORIENT-15: Overall Survival with Sintilimab and Chemotherapy for Advanced or Metastatic Esophageal Squamous Cell Carcinoma

PD-L1 CPS ≥10



All patients



Shen L et al. ESMO 2021;Abstract LBA52.

RTP RESEARCH TO PRACTICE

Cancer Cell 2022;40(3):277-88.e3

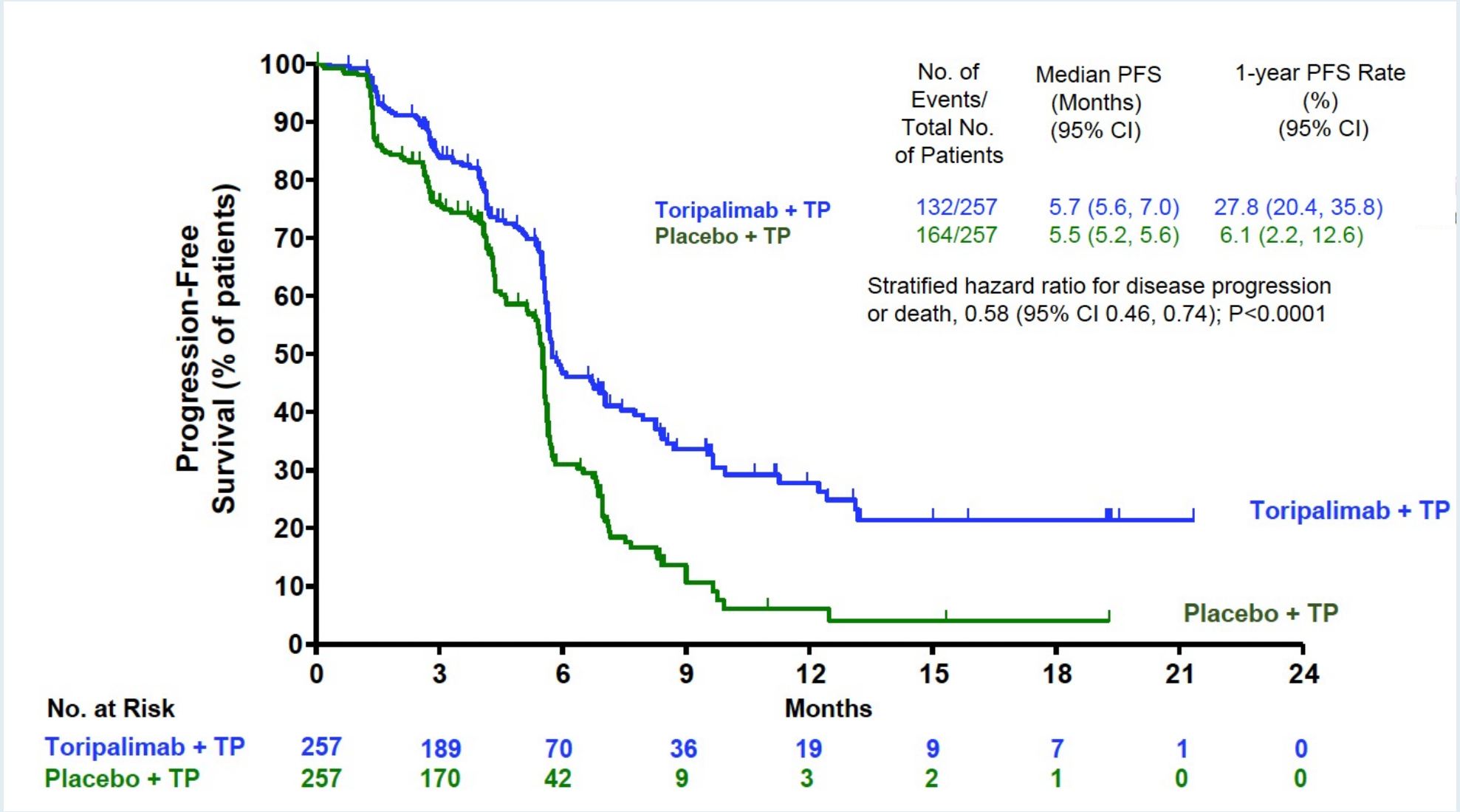
CellPress

Article

Toripalimab plus chemotherapy in treatment-naïve, advanced esophageal squamous cell carcinoma (JUPITER-06): A multi-center phase 3 trial

Zi-Xian Wang,[1,2,76] Chengxu Cui,[3,76] Jun Yao,[4,76] Yanqiao Zhang,[5,76] Mengxia Li,[6] Jifeng Feng,[7] Shujun Yang,[8] Yun Fan,[9] Jianhua Shi,[10] Xizhi Zhang,[11] Lin Shen,[12] Yongqian Shu,[13] Cailian Wang,[14] Tianyang Dai,[15] Teng Mao,[16] Long Chen,[17] Zengqing Guo,[18] Bo Liu,[19] Hongming Pan,[20] Shundong Cang,[21] Yi Jiang,[22] Junye Wang,[23] Min Ye,[24] Zhendong Chen,[25] Da Jiang,[26] Qin Lin,[27] Wei Ren,[28] Junsheng Wang,[29] Lin Wu,[30] Yong Xu,[31] Zhanhui Miao,[32] Meili Sun,[33] Conghua Xie,[34] et al

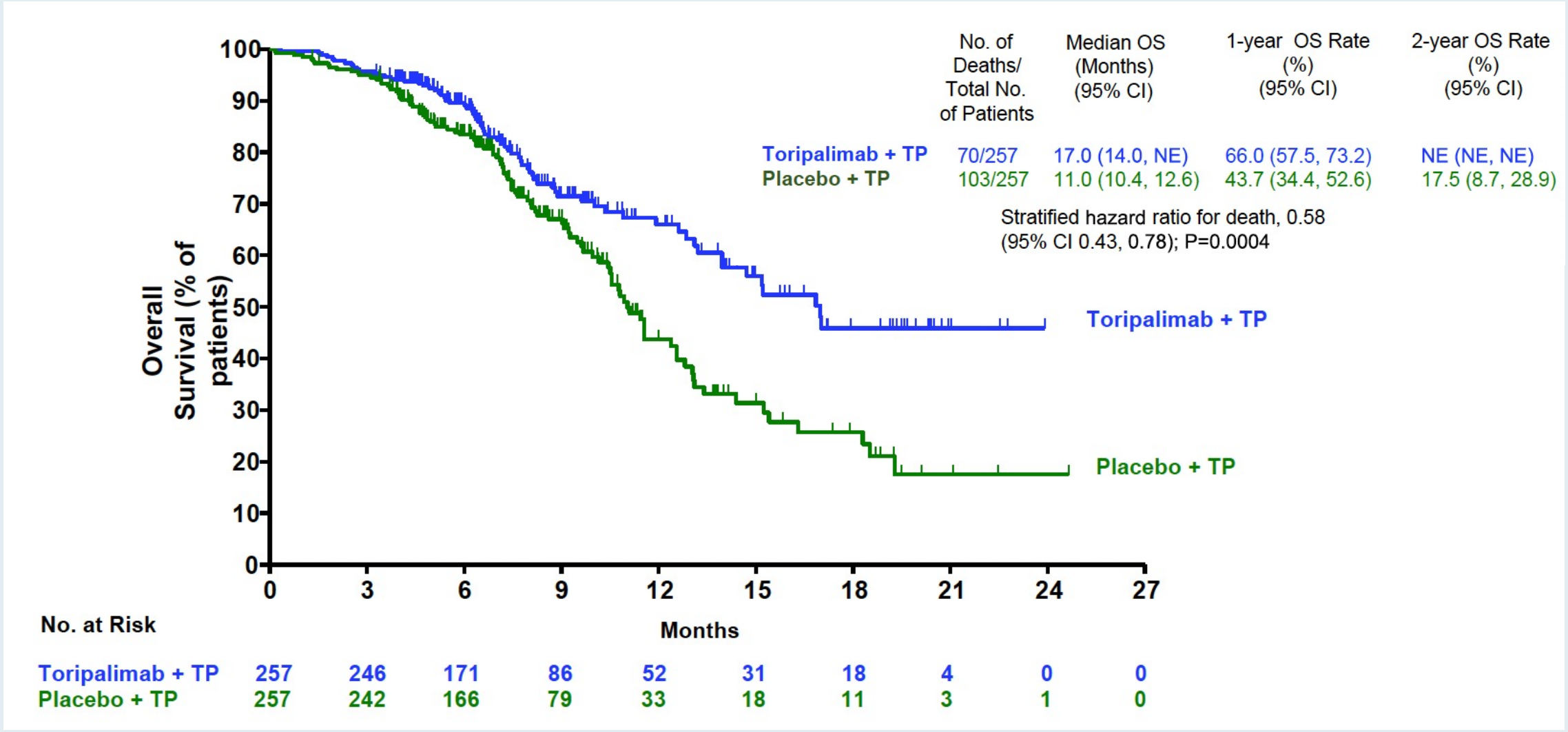
JUPITER-06: Progression-Free Survival (BICR, ITT Population)



Wang ZX et al. *Cancer Cell* 2022;40(3):277-88.e3

RTP RESEARCH TO PRACTICE

JUPITER-06: Overall Survival (ITT Population)



Wang ZX et al. *Cancer Cell* 2022;40(3):277-88.e3

RTP RESEARCH TO PRACTICE

JUPITER-06: Tumor Response

Variable	Toripalimab + TP (n = 257)	Placebo + TP (n = 257)
Best overall response, no. (%)		
Complete response	30 (11.7)	18 (7.0)
Partial response	148 (57.6)	116 (45.1)
Stable disease	51 (19.8)	77 (30.0)
Progressive disease	18 (7.0)	35 (13.6)
Non-CR/non-PD[a]	1 (0.4)	2 (0.8)
Not evaluable[b]	9 (3.5)	9 (3.5)
Objective response rate (ORR)		
ORR % (95% CI)	69.3 (63.2–74.8)	52.1 (45.8–58.4)
Difference in ORR % (95% CI)	17.2 (9.0–25.4)	
p value[c]	<0.0001	
Disease control rate (DCR)		
DCR % (95% CI)	89.1 (84.6–92.6)	82.1 (76.9–86.6)
Difference in DCR % (95% CI)	7.1 (1.1–13.1)	
p value[c]	0.0206	

Wang ZX et al. *Cancer Cell* 2022;40(3):277-88.e3

JUPITER-06: Select Treatment-Emergent Adverse Events (TEAEs)

	Toripalimab + TP (n = 257) no. (%)		Placebo + TP (n = 257) no. (%)	
Adverse event, no. of patients (%)	All grades	grade ≥3	all grades	grade ≥3
Any TEAE	255 (99.2)	188 (73.2)	255 (99.2)	180 (70.0)
Anemia	201 (78.2)	28 (10.9)	207 (80.5)	38 (14.8)
Leukopenia	174 (67.7)	52 (20.2)	138 (53.7)	34 (13.2)
Neutropenia	173 (67.3)	109 (42.4)	139 (54.1)	85 (33.1)
Nausea	111 (43.2)	0 (0)	118 (45.9)	5 (1.9)
Fatigue	110 (42.8)	11 (4.3)	101 (39.3)	5 (1.9)
Neuropathy peripheral	104 (40.5)	3 (1.2)	111 (43.2)	10 (3.9)
Vomiting	103 (40.1)	5 (1.9)	94 (36.6)	5 (1.9)
Decreased appetite	101 (39.3)	3 (1.2)	118 (45.9)	5 (1.9)

Wang ZX et al. *Cancer Cell* 2022;40(3):277-88.e3

Research

JAMA 2021;326(10):916-25.

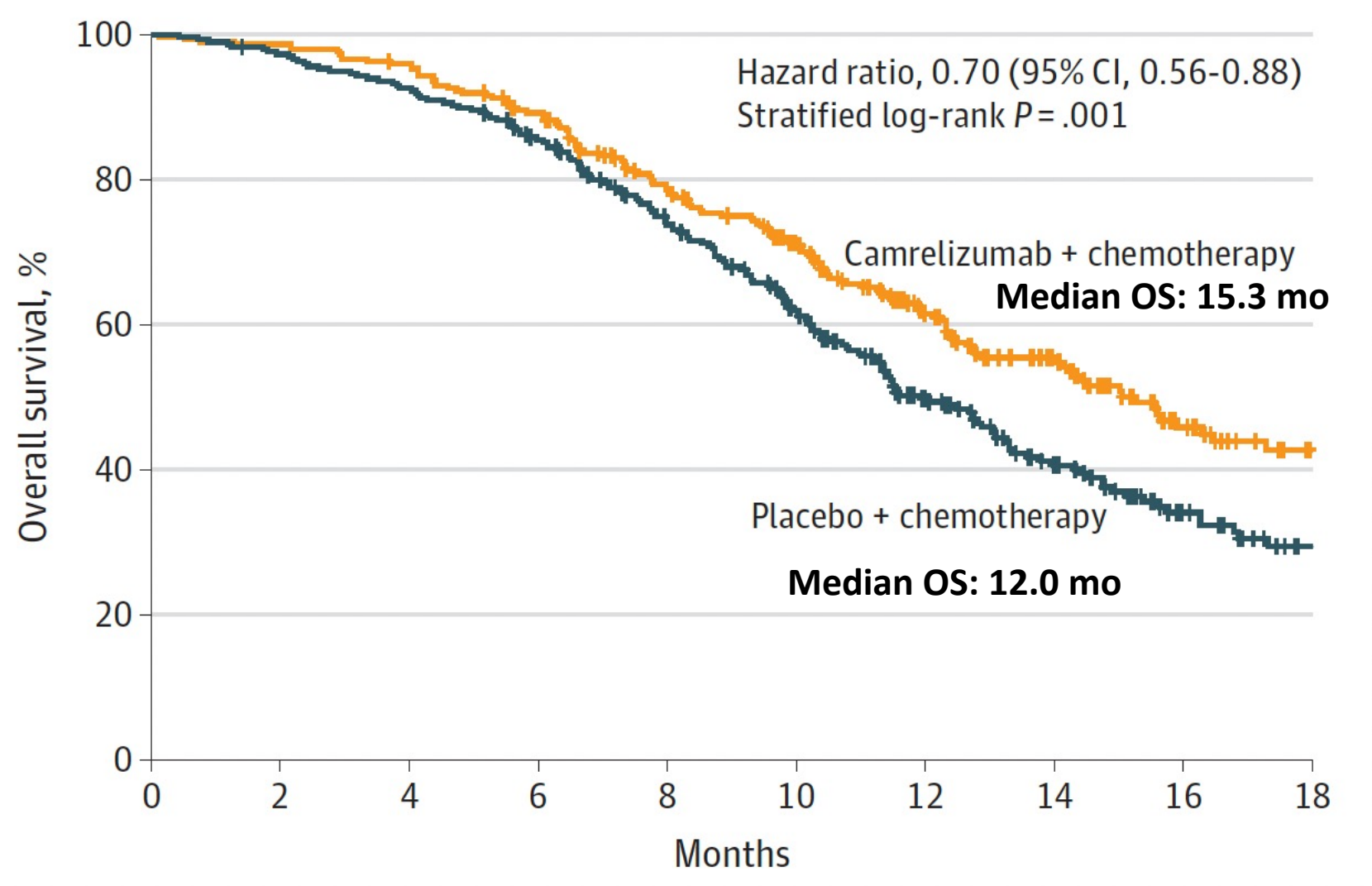
JAMA | Original Investigation

Effect of Camrelizumab vs Placebo Added to Chemotherapy on Survival and Progression-Free Survival in Patients With Advanced or Metastatic Esophageal Squamous Cell Carcinoma

The ESCORT-1st Randomized Clinical Trial

Huiyan Luo, MD, PhD; Jin Lu, BS; Yuxian Bai, MD; Teng Mao, MM; Jun Wang, MD; Qingxia Fan, BS; Yiping Zhang, MB; Kuaile Zhao, MD; Zhendong Chen, MB; Shegan Gao, MD; Jiancheng Li, MD; Zhichao Fu, MD; Kangsheng Gu, MD; Zhihua Liu, MD; Lin Wu, MD; Xiaodong Zhang, MD; Jifeng Feng, PhD; Zuoxing Niu, MM; Yi Ba, MD; Helong Zhang, MD; Ying Liu, MD; Li Zhang, MB; Xuhong Min, BS; Jing Huang, MD; Ying Cheng, MD; Dong Wang, MD; Yu Shen, PhD; Qing Yang, MD; Jianjun Zou, MD; Rui-Hua Xu, MD, PhD; for the ESCORT-1st Investigators

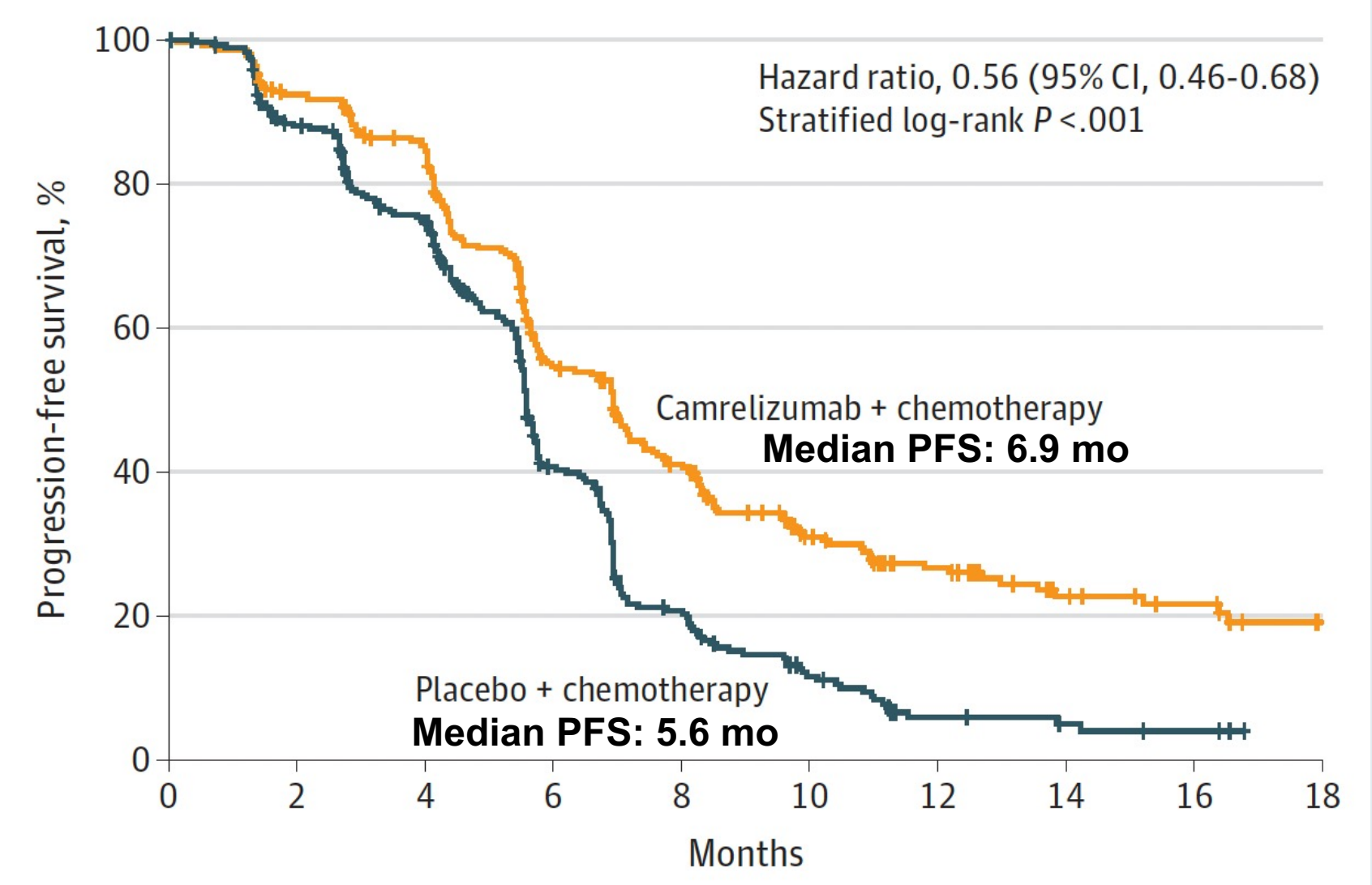
ESCORT-1st: Overall Survival (Coprimary Endpoint)



Luo H et al. *JAMA* 2021;326(10):916-25.

RTP RESEARCH TO PRACTICE

ESCORT-1st: Progression-Free Survival (Coprimary Endpoint)



Luo H et al. *JAMA* 2021;326(10):916-25.

RTP RESEARCH TO PRACTICE

ESCORT-1st: Select Adverse Events

	No. (%) of patients			
	Camrelizumab + chemotherapy (n = 298)		Placebo + chemotherapy (n = 297)	
	Any grade[a]	≥Grade 3	Any grade	≥Grade 3
Treatment-related adverse events[b]	296 (99.3)[c]	189 (63.4)	288 (97.0)	201 (67.7)
Reactive cutaneous capillary endothelial proliferation	238 (79.9)	3 (1.0)	32 (10.8)	0
Anemia	229 (76.8)	52 (17.4)	217 (73.1)	40 (13.5)
White blood cell count decreased	202 (67.8)	72 (24.2)	194 (65.3)	79 (26.6)
Neutrophil count decreased	201 (67.4)	119 (39.9)	186 (62.6)	129 (43.4)
Nausea	150 (50.3)	4 (1.3)	154 (51.9)	5 (1.7)
Asthenia	141 (47.3)	6 (2.0)	129 (43.4)	8 (2.7)
Alopecia	135 (45.3)	1 (0.3)	147 (49.5)	0
Decreased appetite	129 (43.3)	2 (0.7)	134 (45.1)	5 (1.7)
Vomiting	117 (39.3)	10 (3.4)	106 (35.7)	6 (2.0)
Platelet count decreased	77 (25.8)	8 (2.7)	73 (24.6)	6 (2.0)

Luo H et al. *JAMA* 2021;326(10):916-25.

ESCORT-1st: Immune-Related Adverse Events

	No. (%) of patients			
	Camrelizumab + chemotherapy (n = 298)		Placebo + chemotherapy (n = 297)	
	Any grade[a]	≥Grade 3	Any grade	≥Grade 3
Immune-related adverse events[d]	252 (84.6)		98 (33.0)	
Reactive capillary endothelial proliferation	238 (79.9)		32 (10.8)	
Hypothyroidism	34 (11.4)		13 (4.4)	
Pruritus	20 (6.7)		7 (2.4)	
Hyperthyroidism	16 (5.4)		3 (1.0)	
Rash	16 (5.4)		6 (2.0)	
Pneumonitis	15 (5.0)		9 (3.0)	
Blood thyroid stimulating hormone decreased	10 (3.4)		1 (0.3)	

Luo H et al. *JAMA* 2021;326(10):916-25.

Lancet 2014;383(9911):31-9.

Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial

*Charles S Fuchs, Jiri Tomasek, Cho Jae Yong, Filip Dumitru, Rodolfo Passalacqua, Chanchal Goswami, Howard Safran, Lucas Vieira dos Santos, Giuseppe Aprile, David R Ferry, Bohuslav Melichar, Mustapha Tehfe, Eldar Topuzov, John Raymond Zalcberg, Ian Chau, William Campbell, Choondal Sivanandan, Joanna Pikiel, Minori Koshiji, Yanzhi Hsu, Astra M Liepa, Ling Gao, Jonathan D Schwartz, Josep Tabernero, for the REGARD Trial Investigators**

Lancet Oncol 2014;15(11):1224-35.

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

*Hansjochen Wilke, Kei Muro, Eric Van Cutsem, Sang-Cheul Oh, György Bodoky, Yasuhiro Shimada, Shuichi Hironaka, Naotoshi Sugimoto, Oleg Lipatov, Tae-You Kim, David Cunningham, Philippe Rougier, Yoshito Komatsu, Jaffer Ajani, Michael Emig, Roberto Carlesi, David Ferry†, Kumari Chandrawansa, Jonathan D Schwartz, Atsushi Ohtsu, for the RAINBOW Study Group**

Pivotal Phase III Studies of Ramucirumab for Advanced Gastric or GEJ Adenocarcinoma

Study	N	Setting	Treatment	Median OS	Hazard ratio (*p*-value)
REGARD	355	PD after first-line therapy	Ramucirumab Placebo	5.2 mo 3.8 mo	HR: 0.776 (*p* = 0.047)
RAINBOW	665	PD after first-line therapy	Ramucirumab/paclitaxel Placebo/paclitaxel	9.6 mo 7.4 mo	HR: 0.807 (*p* = 0.017)

Fuchs CS et al. *Lancet* 2014;383(9911):31-9. Wilke H et al. *Lancet Oncol* 2014;15(11):1224-35.

European Journal of Cancer 165 (2022) 48–57

Available online at www.sciencedirect.com

ScienceDirect

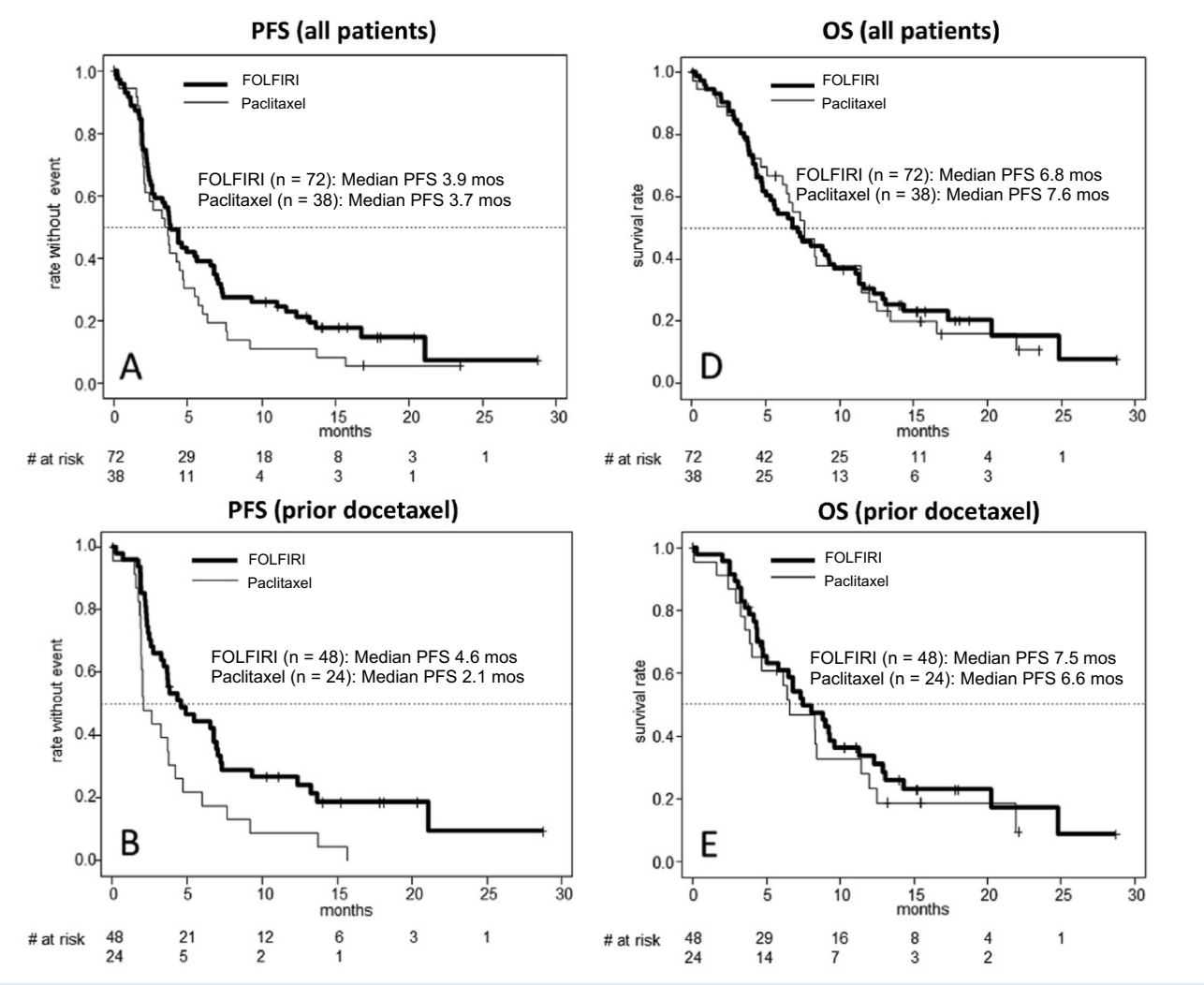
journal homepage: www.ejcancer.com

Original Research

FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for patients with advanced or metastatic gastroesophageal adenocarcinoma with or without prior docetaxel – results from the phase II RAMIRIS Study of the German Gastric Cancer Study Group at AIO

Sylvie Lorenzen [a,*], Peter Thuss-Patience [b], Claudia Pauligk [c], Eray Gökkurt [d], Thomas Ettrich [e], Florian Lordick [f], Michael Stahl [g], Peter Reichardt [h], Martin Sökler [i], Daniel Pink [j,k], Stefan Probst [l], Axel Hinke [m], Thorsten O. Goetze [c,n,1], Salah E. Al-Batran [c,n,1]

Phase II RAMIRIS Trial of Second-Line Ramucirumab with FOLFIRI: Patients with Advanced or Metastatic Gastroesophageal Adenocarcinoma with or without Prior Docetaxel



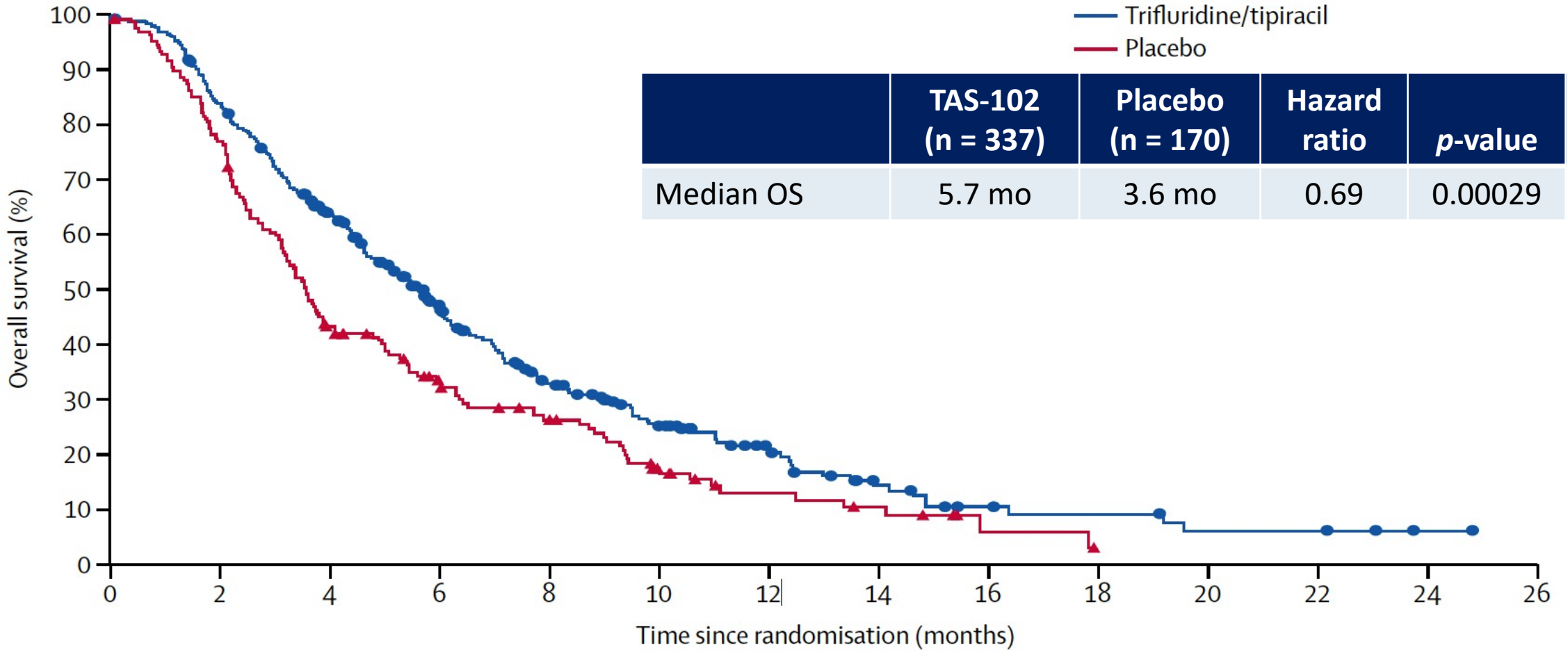
Lorenzen S et al. *Eur J Cancer* 2022;165:48-57.

Lancet Oncol 2018;19(11):1437-48.

Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial

Kohei Shitara, Toshihiko Doi, Mikhail Dvorkin, Wasat Mansoor, Hendrik-Tobias Arkenau, Aliaksandr Prokharau, Maria Alsina, Michele Ghidini, Catia Faustino, Vera Gorbunova, Edvard Zhavrid, Kazuhiro Nishikawa, Ayumu Hosokawa, Şuayib Yalçın, Kazumasa Fujitani, Giordano D Beretta, Eric Van Cutsem, Robert E Winkler, Lukas Makris, David H Ilson, Josep Tabernero

TAGS: Overall Survival (Intent-to-Treat Population)



	TAS-102 (n = 337)	Placebo (n = 170)	Hazard ratio	*p*-value
Median OS	5.7 mo	3.6 mo	0.69	0.00029

Shitara K et al. *Lancet Oncol* 2018;19(11):1437-48.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

WORLD CONGRESS ON Gastrointestinal Cancer

Abstract LBA-1

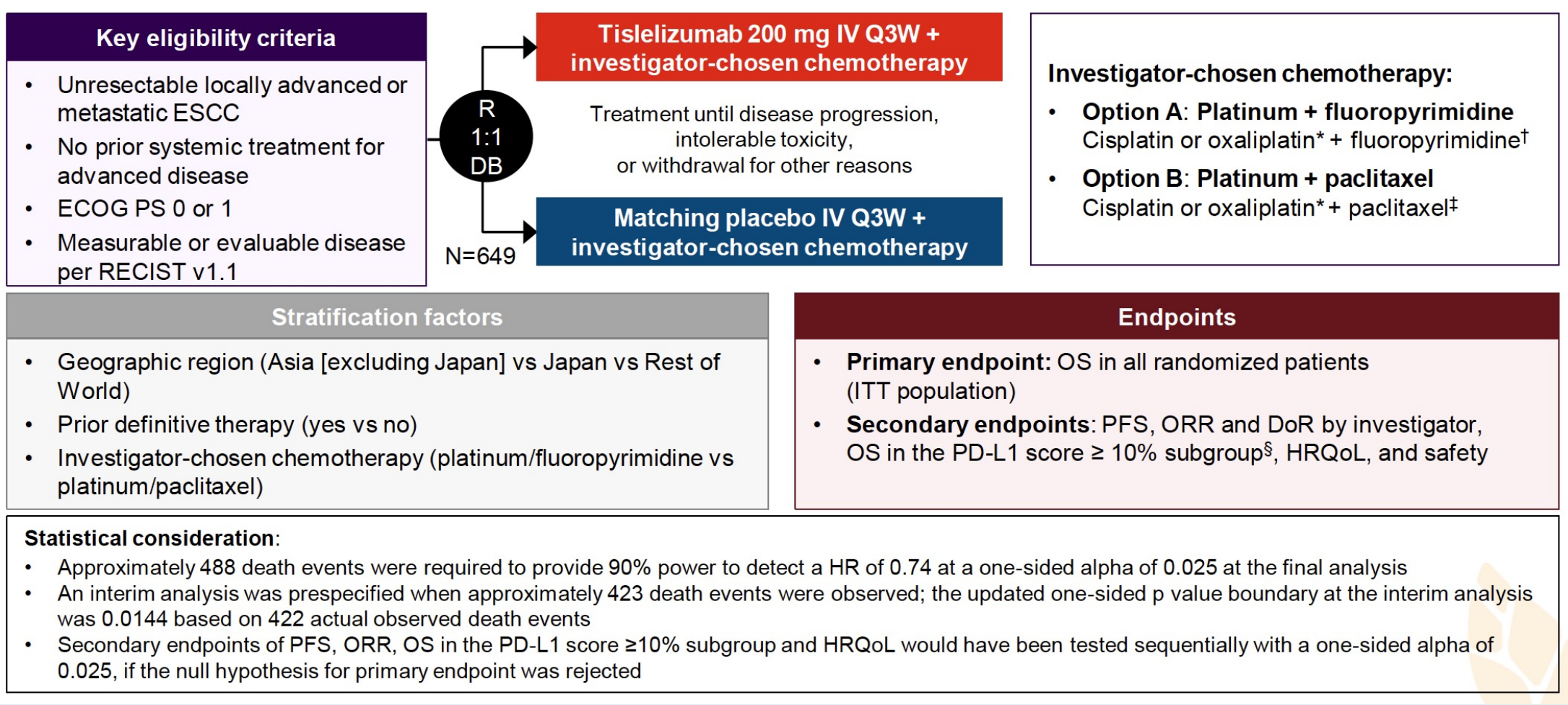
RATIONALE-306: Randomized, global, placebo-controlled, double-blind Phase 3 study of tislelizumab plus chemotherapy versus chemotherapy as first-line treatment for advanced or metastatic esophageal squamous cell carcinoma

Harry H. Yoon MD,[1] Ken Kato MD,[2] Eric Raymond MD,[3] Richard Hubner MD,[4] Yongqian Shu MD,[5] Yueyin Pan MD,[6] Yi Jiang MD,[7] Jingdong Zhang MD,[8] Sook Ryun Park MD,[9] Takashi Kojima MD,[10] Chen-Yuan Lin MD,[11] Eugeny Gotovkin MD,[12] Lucjan Wyrwicz MD,[12] Ryu Ishihara MD,[13] Liyun Li MD,[14] Aiyang Tao PhD,[15] Jingwen Shi PhD,[14] Lei Wang MD,[14] Jianming Xu MD[16]

[1]Mayo Clinic, Rochester, MN, USA; [2]National Cancer Center Hospital, Tokyo, Japan; [3]Centre Hospitalier Paris Saint-Joseph, Paris, France; [4]Christie NHS Foundation Trust, Manchester, UK; [5]Jiangsu Province Hospital, Nanjing, China; [6]Anhui Provincial Hospital, Hefei, China; [7]Cancer Hospital of Shantou University Medical College, Shantou, China; [8]Liaoning Cancer Hospital, Shenyang, China; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [10]National Cancer Center Hospital East, Tokyo, Japan; [11]China Medical University Hospital, Taichung, Taiwan; [12]Ivanovo Regional Oncology Dispensary, Ivanovo, Russia; [13]Osaka International Cancer Institute, Osaka, Japan; [14]BeiGene (Beijing) Co., Ltd., Beijing, China; [15]BeiGene (Ridgefield Park) Co., Ltd., Ridgefield Park, NJ, USA; [16]Chinese PLA General Hospital, Beijing, China

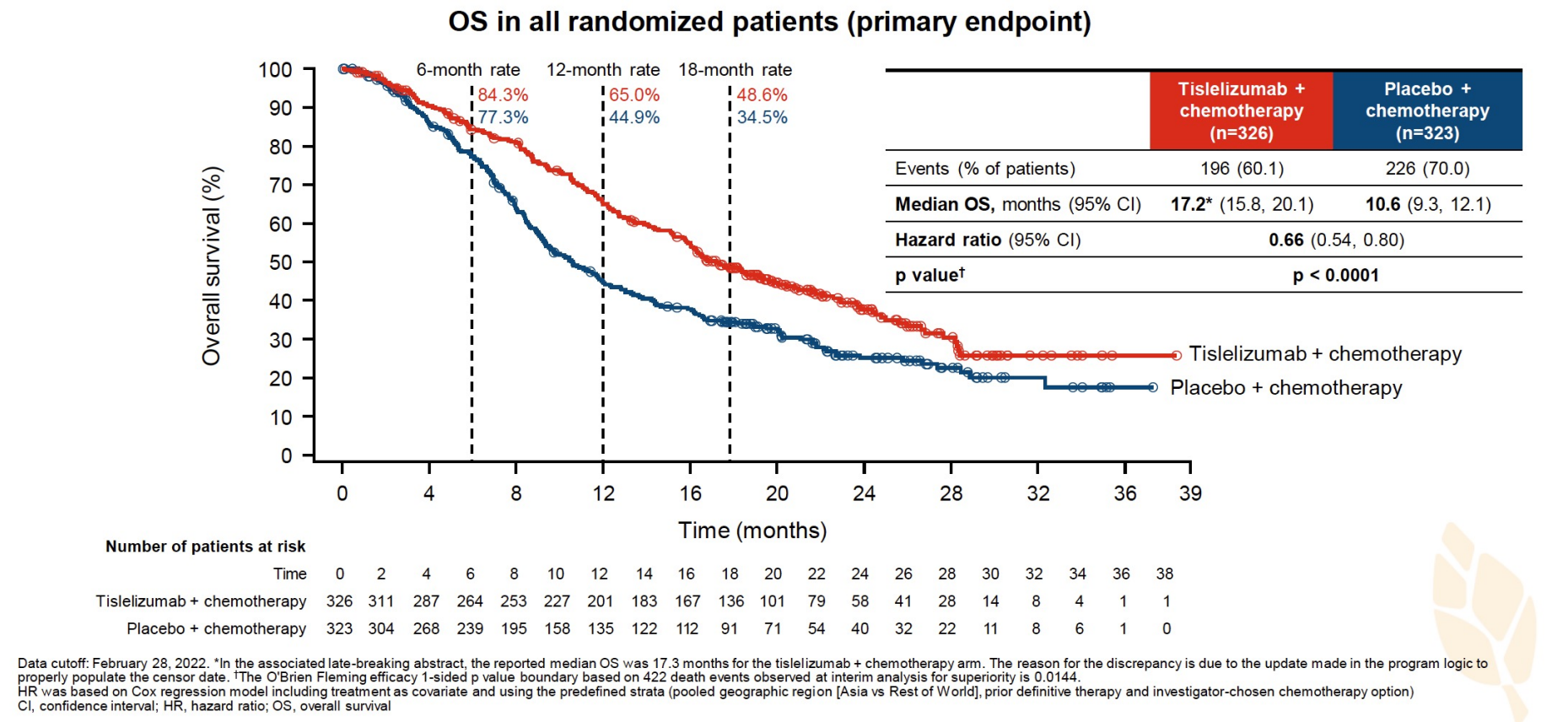
RTP RESEARCH TO PRACTICE

RATIONALE-306: Phase III Trial Design



Yoon HH et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract LBA-1.

RATIONALE-306 Primary Endpoint: OS with First-Line Tislelizumab and Chemotherapy for Advanced or Metastatic Esophageal Squamous Cell Carcinoma



	Tislelizumab + chemotherapy (n=326)	Placebo + chemotherapy (n=323)
Events (% of patients)	196 (60.1)	226 (70.0)
Median OS, months (95% CI)	**17.2*** (15.8, 20.1)	**10.6** (9.3, 12.1)
Hazard ratio (95% CI)	**0.66** (0.54, 0.80)	
p value†	**p < 0.0001**	

Data cutoff: February 28, 2022. *In the associated late-breaking abstract, the reported median OS was 17.3 months for the tislelizumab + chemotherapy arm. The reason for the discrepancy is due to the update made in the program logic to properly populate the censor date. †The O'Brien Fleming efficacy 1-sided p value boundary based on 422 death events observed at interim analysis for superiority is 0.0144.
HR was based on Cox regression model including treatment as covariate and using the predefined strata (pooled geographic region [Asia vs Rest of World], prior definitive therapy and investigator-chosen chemotherapy option)
CI, confidence interval; HR, hazard ratio; OS, overall survival

OS benefit with tislelizumab and chemotherapy was observed regardless of baseline PD-L1 expression and across prespecified subgroups.

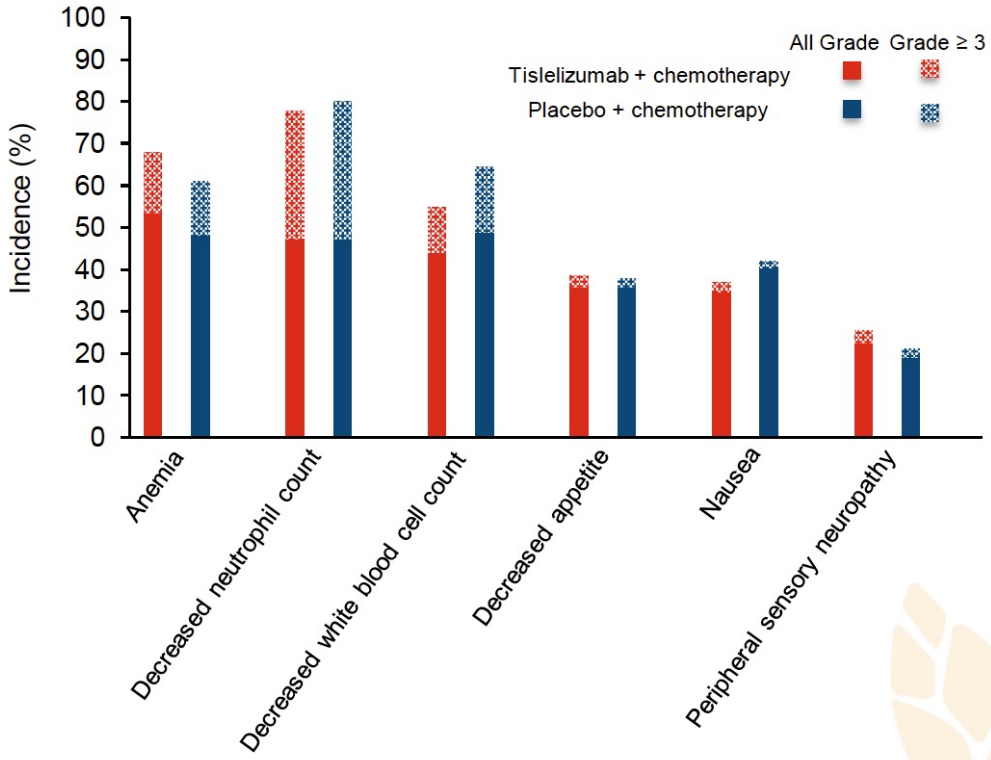
Yoon HH et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract LBA-1.

RATIONALE-306: Safety Summary with First-Line Tislelizumab and Chemotherapy for Advanced or Metastatic Esophageal Squamous Cell Carcinoma

Summary of safety and tolerability

n (%)	Tislelizumab + chemotherapy (n=324)	Placebo + chemotherapy (n=321)
Patients with ≥ 1 treatment-related TEAE*	313 (96.6)	309 (96.3)
≥ Grade 3	216 (66.7)	207 (64.5)
Serious AE	93 (28.7)	62 (19.3)
Leading to death†	6 (1.9)	4 (1.2)
Patients with ≥ 1 TEAE leading to discontinuation	103 (31.8)	72 (22.4)
Patients with ≥ 1 immune-mediated AE	70 (21.6)	19 (5.9)
≥ Grade 3	28 (8.6)	5 (1.6)

Most common treatment-related TEAEs (incidence ≥ 20%)



Data cutoff: February 28, 2022. For each row category, a patient with two or more adverse events in that category was counted only once. AEs grades were evaluated based on National Cancer Institute–Common Terminology Criteria for Adverse Events (version 4.03). AE terms were coded using Medical Dictionary for Drug Regulatory Affairs version 24.0.
*Treatment-related TEAEs included TEAEs that were considered by the investigator to be related to study drug or TEAEs with a missing causality. †Deaths due to disease progression are not included as treatment-related TEAEs leading to death. AE, adverse event; TEAE, treatment-emergent adverse event

Yoon HH et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract LBA-1.

HER2-Positive Gastroesophageal Cancers

Recent FDA Approvals in HER2-Positive Gastric, GEJ and Esophageal Cancer

Regimen/FDA approval date/Pivotal trial	Location	Histology	Setting	PD-L1
Pembrolizumab + trastuzumab + chemotherapy 5/5/2021 (KN-811)	Gastric, GEJ	Adenocarcinoma	• First-line treatment for locally advanced, unresectable or metastatic HER2-positive gastric or GEJ adenocarcinoma	Not required
Trastuzumab deruxtecan 1/15/2021 (DESTINY-Gastric01)	Gastric, GEJ	Adenocarcinoma	• Patients who have received a prior trastuzumab-based regimen	Not required

Janjigian YY et al. *Nature* 2021; 600: 727–730. www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-fam-trastuzumab-deruxtecan-nxki-her2-positive-gastric-adenocarcinomas

Nature 2021;600(7890):727-30.

Article

The KEYNOTE-811 trial of dual PD-1 and HER2 blockade in HER2-positive gastric cancer

https://doi.org/10.1038/s41586-021-04161-3

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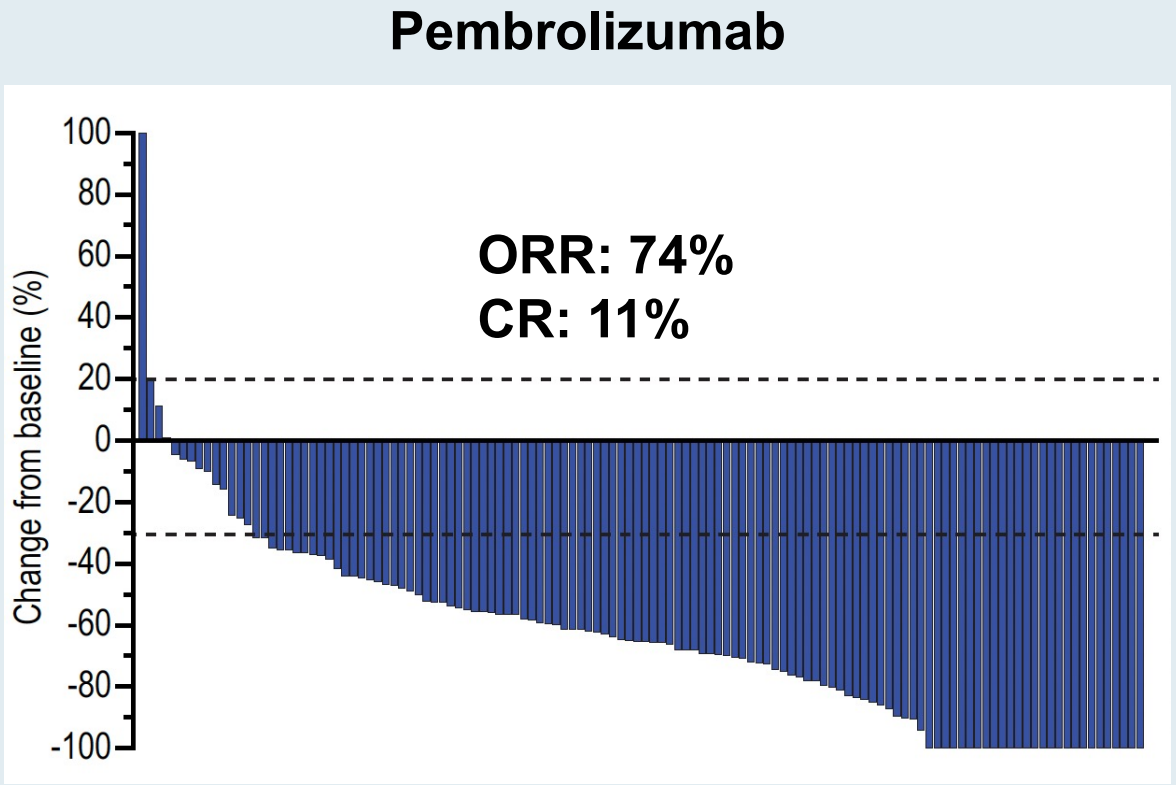
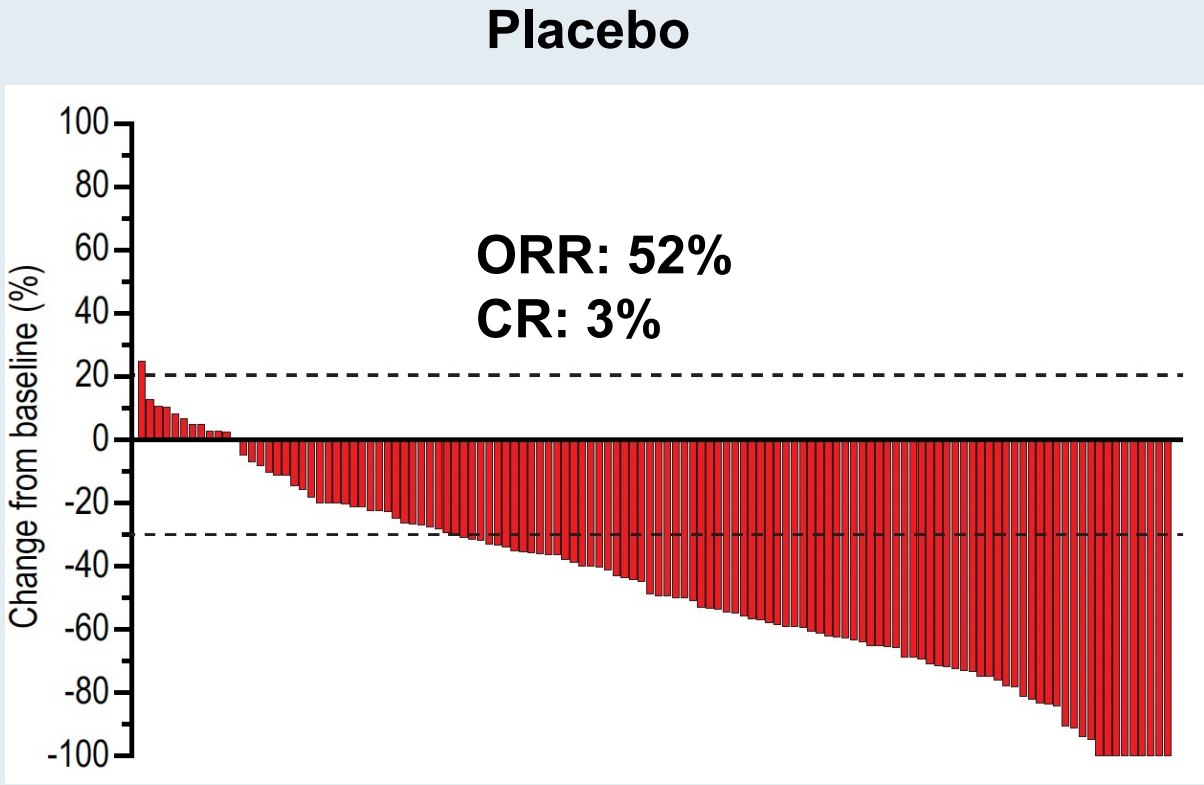
Yelena Y. Janjigian[1]✉, Akihito Kawazoe[2], Patricio Yañez[3], Ning Li[4], Sara Lonardi[5], Oleksii Kolesnik[6], Olga Barajas[7], Yuxian Bai[8], Lin Shen[9], Yong Tang[10], Lucjan S. Wyrwicz[11], Jianming Xu[12], Kohei Shitara[2], Shukui Qin[13], Eric Van Cutsem[14], Josep Tabernero[15], Lie Li[16], Sukrut Shah[16], Pooja Bhagia[16] & Hyun Cheol Chung[17]

KEYNOTE-811: Overall Response Rate (ORR)





Janjigian YY et al. *Nature* 2021;600(7890):727-30.

RTP RESEARCH TO PRACTICE

KEYNOTE-811: Summary of Adverse Events

Number of events (%)	Any cause		Immune-mediated events and infusion reactions[a]	
	Pembrolizumab group (*n* = 217)	Placebo group (*n* = 216)	Pembrolizumab group (*n* = 217)	Placebo group (*n* = 216)
Any grade	211 (97.2)	212 (98.1)	73 (33.6)	45 (20.8)
Grade 3–5	124 (57.1)	124 (57.4)	21 (9.7)	7 (3.2)
Serious	68 (31.3)	83 (38.4)	19 (8.8)	7 (3.2)
Led to death	7 (3.2)	10 (4.6)	3 (1.4)	1 (0.5)
Led to discontinuation of any drug	53 (24.4)	56 (25.9)	12 (5.5)	5 (2.3)
Pembrolizumab or placebo	12 (5.5)	15 (6.9)	7 (3.2)	2 (0.9)
Trastuzumab	12 (5.5)	16 (7.4)	7 (3.2)	2 (0.9)
Any chemotherapy	50 (23.0)	52 (24.1)	12 (5.5)	5 (2.3)
All drugs	8 (3.7)	12 (5.6)	6 (2.8)	2 (0.9)

The treatment regimen included trastuzumab and chemotherapy in both groups.

[a]Events with a possible immune-mediated cause and infusion reactions were considered regardless of attribution to study treatment or immune relatedness by the investigator and are based on a list of terms provided by the sponsor.

Janjigian YY et al. *Nature* 2021;600(7890):727-30.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

WORLD CONGRESS ON Gastrointestinal Cancer

SO-7

Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial

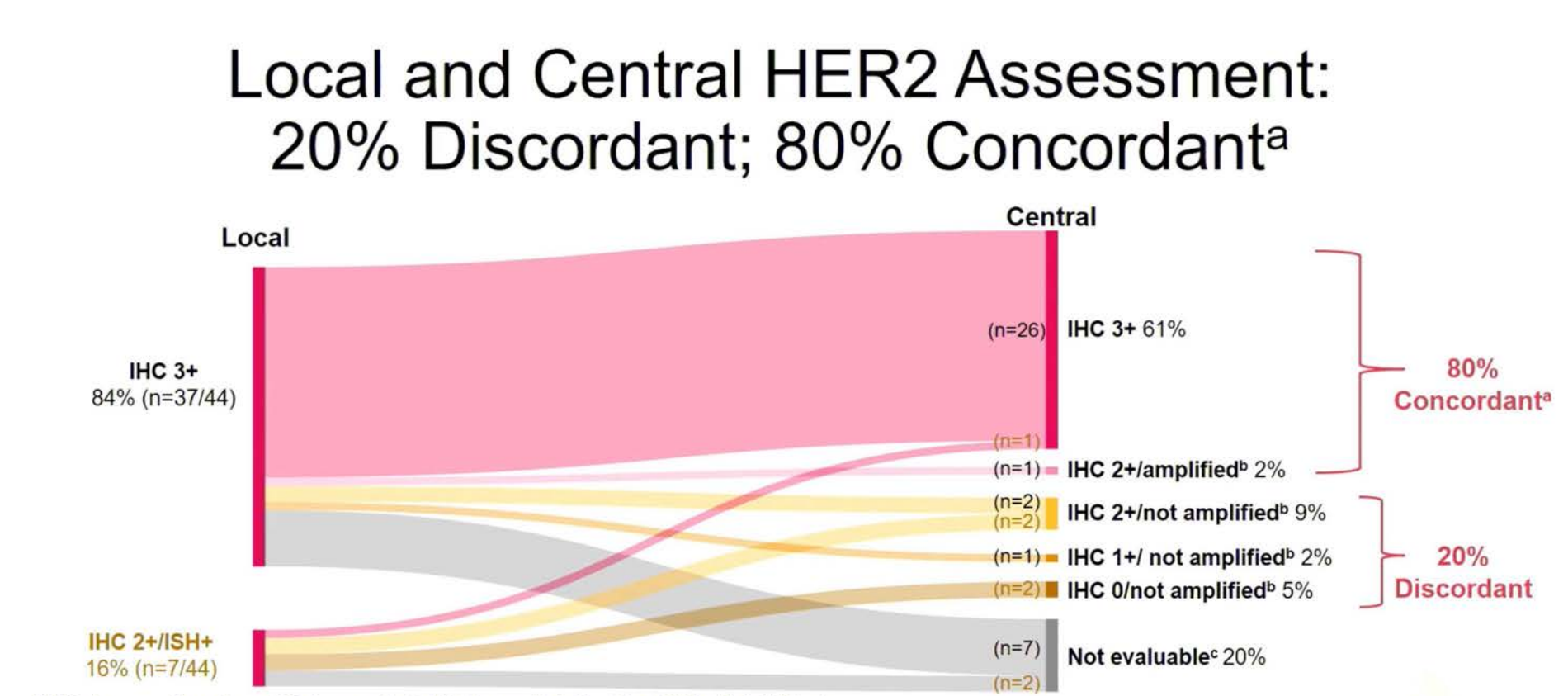
Yelena Y. Janjigian, MD[1]; Sun Young Rha, MD, PhD[2]; Do-Youn Oh, MD, PhD[3]; Marc Díez García, MD[4]; Hanneke van Laarhoven, MD, PhD[5]; Yee Chao, MD, PhD[6]; Maria Di Bartolomeo, MD[7]; Nadia Haj Mohammad, MD, PhD[8]; Wenyan Zhong, PhD[9]; Elizabeth Croydon, MD[10]; Fabiola Cecchi, PhD, PharmD[9]; Jeeyun Lee, MD[11]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Yonsei Cancer Center, Yonsei University College of Medicine, Seodaemun-gu, Seoul, Korea; [3]Seoul National University Hospital, Seoul National University College of Medicine, Jongno-gu, Seoul, Korea; [4]Vall d'Hebron University Hospital-VHIO, Barcelona, Spain; [5]Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands; [6]Taipei Veterans General Hospital, National Yang Ming Chiao Tung University, Taipei, Taiwan; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [8]University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands; [9]AstraZeneca Pharmaceuticals LP, Gaithersburg, MD, USA; [10]AstraZeneca Pharmaceuticals LP, Cambridge, UK; [11]Samsung Medical Center, Sungkyunkwan University School of Medicine, Gangnam-gu, Seoul, Korea

ESMO World Congress on Gastrointestinal Cancer 2022, June 29-July 2, 2022, Barcelona, Spain

RTP RESEARCH TO PRACTICE

Discordant HER2 Assessment



HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization.

[a] Concordance rate was defined as the percentage of samples classified as HER2 positive by both local and central assessment.

[b] HER2 amplification using FoundationOne® (F1CDx).

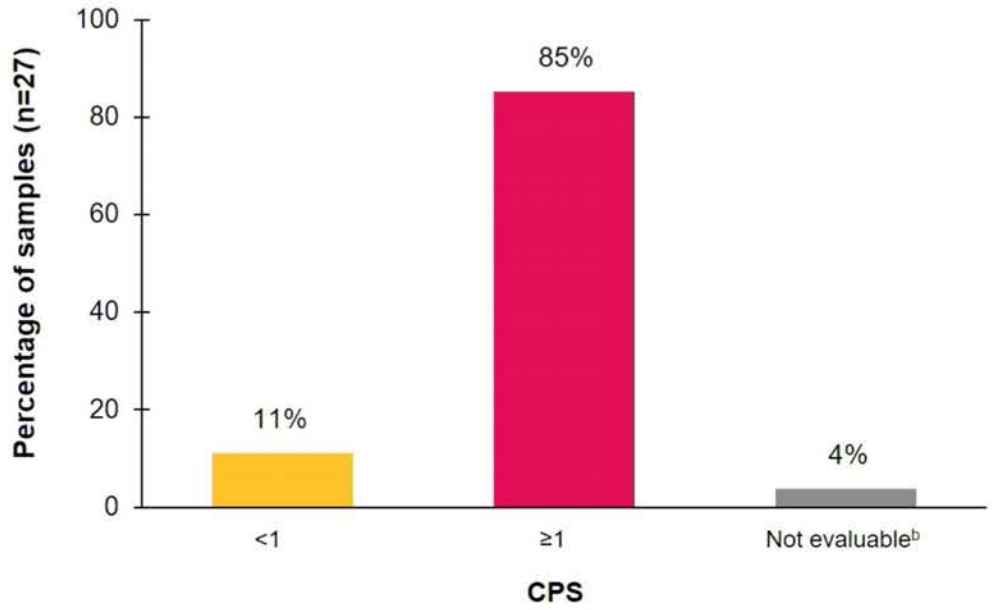
[c] Samples with missing IHC/amplification data due to an insufficient number of tumor cells (<100) on the tissue section for HER2 IHC assessment or insufficient tumor content collected for next-generation sequencing.

Janjigian YY, et al. Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial. Presented at ESMO World Congress on Gastrointestinal Cancer; June 29-July 2, 2022; Barcelona, Spain. Abstract SO-7.

Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract SO-7.

PD-L1 Expression and HER2 Coexpression

PD-L1 Expression by Central Assessment[a]: 85% PD-L1 Positive



CPS	% (n/N)
CPS <1	11 (3/27)
CPS ≥1	85 (23/27)
CPS ≥1 to <5	37 (10/27)
CPS ≥5	48 (13/27)
Not evaluable[b]	4 (1/27)

CPS, combined positive score; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; PD-L1, programmed death ligand 1.

[a] PD-L1 expression was centrally assessed using a verified IHC assay (PD-L1 IHC 22C3 pharmDx; Agilent Technologies).

[b] There was an insufficient number of viable tumor cells (<100) present for PD-L1 testing.

Janjigian YY, et al. Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial. Presented at ESMO World Congress on Gastrointestinal Cancer; June 29-July 2, 2022; Barcelona, Spain. Abstract SO-7.

Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract SO-7.

Support for Dual Anti-HER2 and Anti-PD-L1 Therapy

Conclusions

- In a subset of patients with GC/GEJA in the ongoing DESTINY-Gastric03 trial, 20% discordance was observed between local and central HER2 testing, consistent with previously reported data in GC[1]
  - Discordance may be attributed to tissue heterogeneity
- Substantial overlap (85%) was observed between HER2 and PD-L1 positivity in this GC/GEJA population, consistent with earlier studies[2]
- These data support dual anti-HER2 and anti–PD-L1 therapy in HER2-positive GC/GEJA

GC, gastric cancer; GEJA, gastroesophageal junction adenocarcinoma; HER2, human epidermal growth factor receptor 2; PD-L1, programmed death ligand 1.

1. Huemer F, et al. *J Clin Med*. 2020;9(4):935. 2. Janjigian YY, et al. *Nature*. 2021;600:727-730.

Janjigian YY, et al. Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial. Presented at ESMO World Congress on Gastrointestinal Cancer; June 29-July 2, 2022; Barcelona, Spain. Abstract SO-7.

Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract SO-7.

Poster 242

ASCO Gastrointestinal Cancers Symposium 2022

Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients With HER2–Positive Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma: Final Overall Survival (OS) Results From a Randomized, Multicenter, Open-Label, Phase 2 Study (DESTINY-Gastric01)

Kensei Yamaguchi

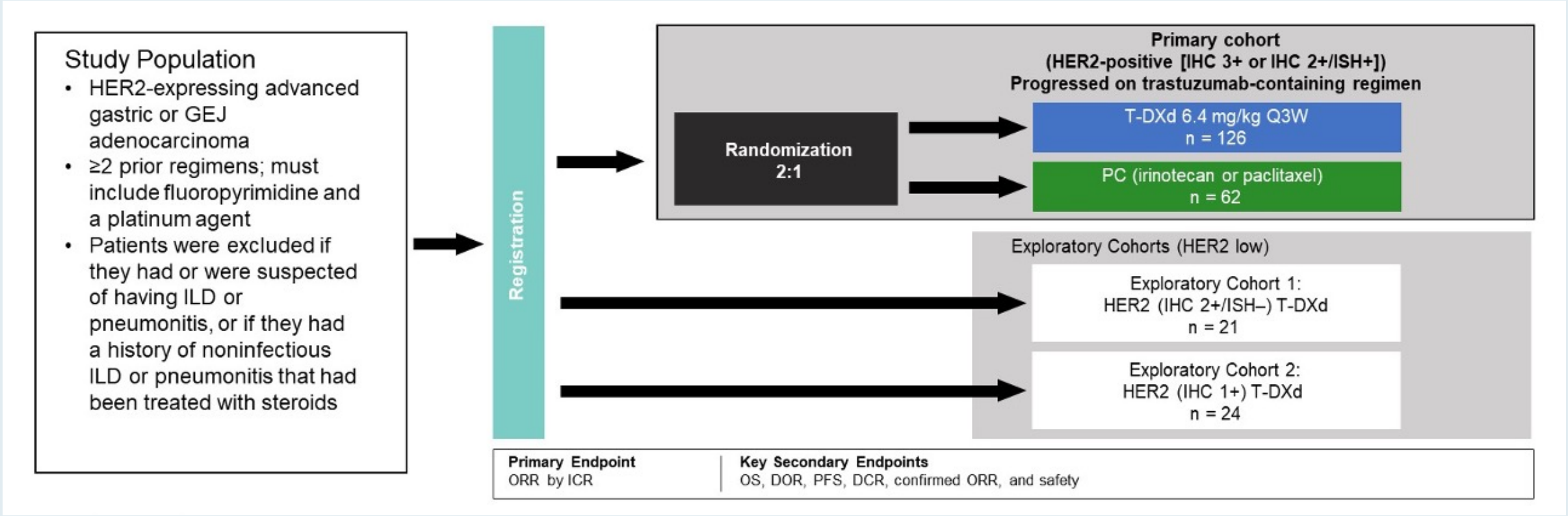
The Cancer Institute Hospital of JFCR, Tokyo, Japan

ON BEHALF OF THE DESTINY-GASTRIC01 INVESTIGATORS

Additional authors: Yung-Jue Bang, Satoru Iwasa, Naotoshi Sugimoto, Min-Hee Ryu, Daisuke Sakai, Hyun Cheol Chung, Hisato Kawakami, Hiroshi Yabusaki, Jeeyun Lee, Kaku Saito, Yoshinori Kawaguchi, Takahiro Kamio, Akihito Kojima, Masahiro Sugihara, Kohei Shitara

PRESENTED BY: Kensei Yamaguchi, MD

DESTINY-Gastric01 Randomized, Phase II Study Design

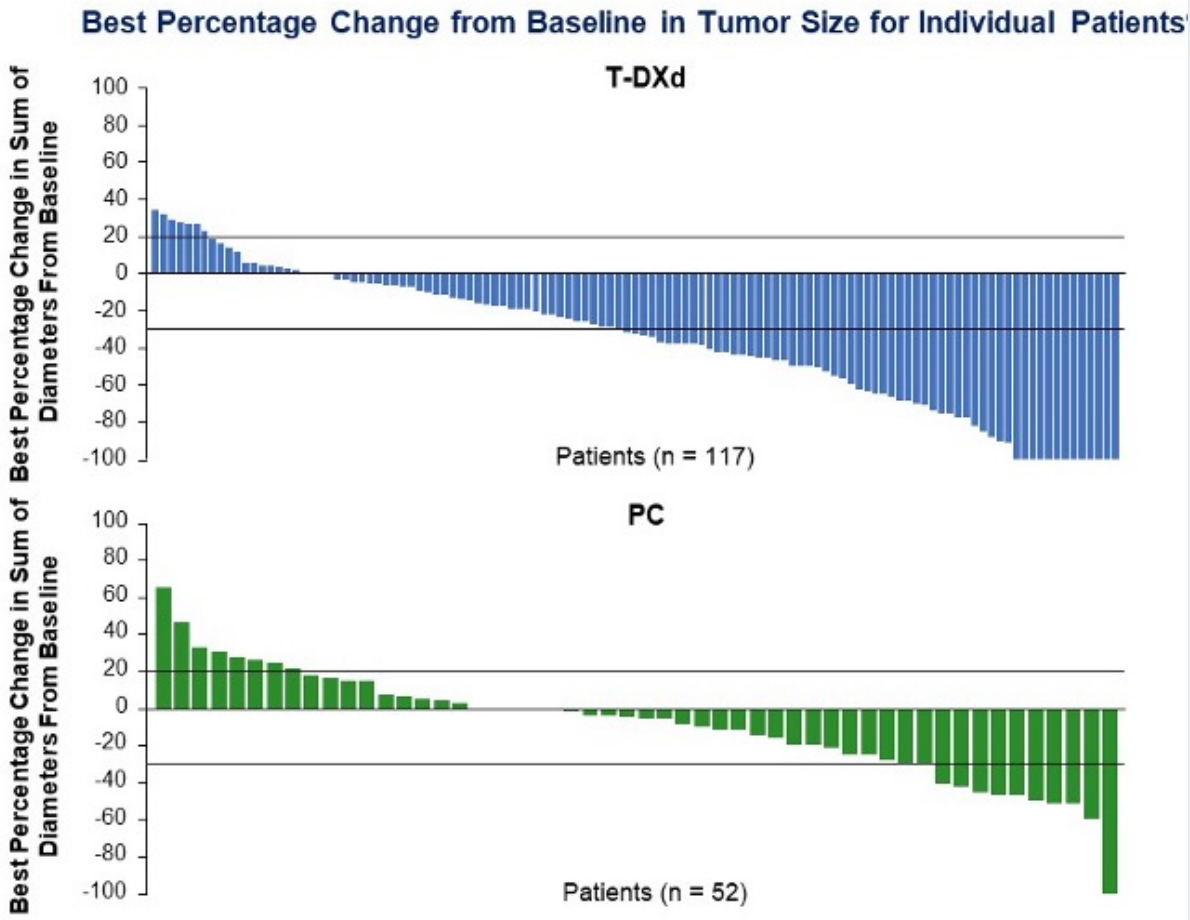


PC = physician's choice

Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

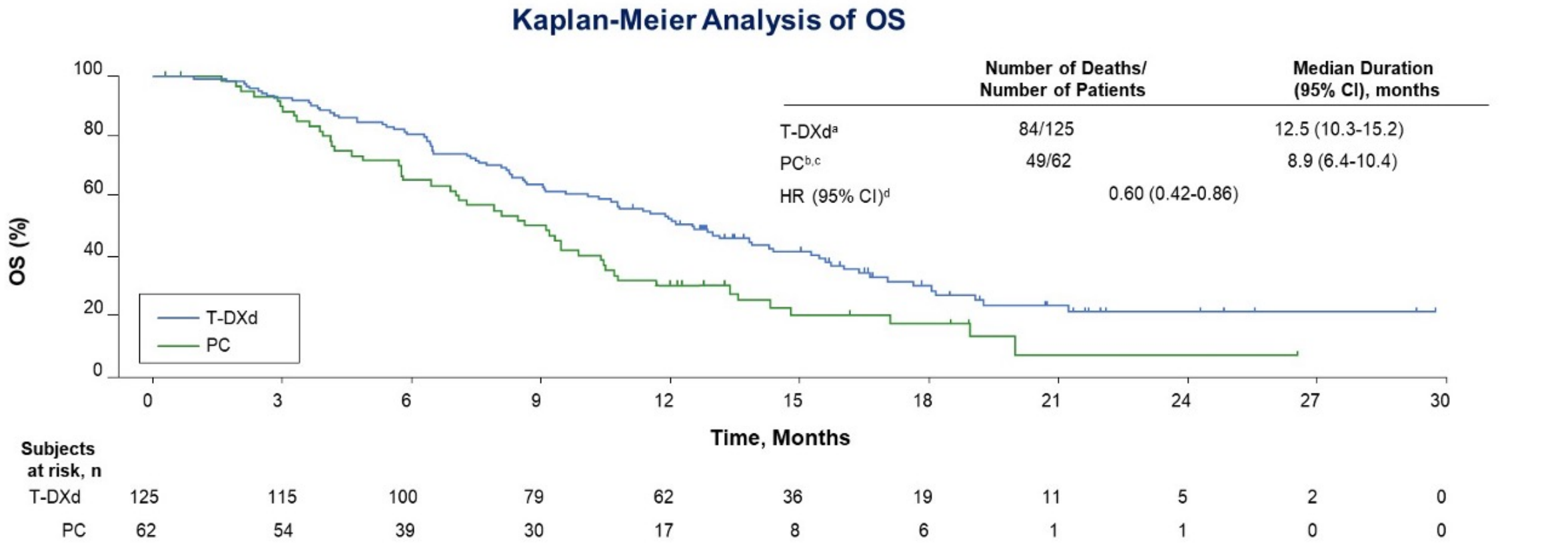
DESTINY-Gastric01: Antitumor Activity

	T-DXd n = 119	PC Overall n = 56
ORR (CR + PR) by ICR, n (%)[a]	**61 (51.3) 95% CI, 41.9-60.5**	**8 (14.3) 95% CI, 6.4-26.2**
	P < 0.0001[b]	
CR	11 (9.2)	0
PR	50 (42.0)	8 (14.3)
SD	42 (35.3)	27 (48.2)
PD	14 (11.8)	17 (30.4)
Not evaluable	2 (1.7)	4 (7.1)
Confirmed ORR (CR + PR) by ICR, n (%)[a]	50 (42.0) 95% CI, 33.0-51.4	7 (12.5) 95% CI, 5.2-24.1
CR	10 (8.4)	0
PR	40[c] (33.6)	7 (12.5)
SD	52 (43.7)	28 (50.0)
PD	14 (11.8)	17 (30.4)
Not evaluable	3 (2.5)	4 (7.1)
Confirmed DCR (CR + PR + SD), n (%)[a]	102 (85.7) 95% CI, 78.1-91.5	35 (62.5) 95% CI, 48.5-75.1
Confirmed DOR, median, months	12.5 95% CI, 5.6-NE	3.9 95% CI, 3.0-4.9
TTR, median, months	1.5 95% CI, 1.4-1.7	1.6 95% CI, 1.3-1.7



Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

DESTINY-Gastric01: Final Overall Survival (OS)



As in the primary analysis (101 OS events; 54.0% maturity), in this updated analysis (133 OS events; 71.1% maturity), T-DXd showed superior antitumor activity compared to PC

Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

RTP RESEARCH TO PRACTICE

DESTINY-Gastric01: Select Adverse Events

Adverse event	T-DXd (n = 125)		PC overall (n = 62)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Neutrophil count decrease	65%	51%	36%	24%
Nausea	63%	6%	47%	2%
Decreased appetite	61%	17%	45%	13%
Anemia	58%	38%	31%	23%
Platelet count decrease	40%	11%	7%	3%
WBC count decrease	38%	21%	36%	11%
Lymphocyte count decrease	23%	12%	3%	2%

16 patients (13%) had T-DXd-related interstitial lung disease/pneumonitis

- 13/16 were Grade 1 or 2
- Median time to first onset: 102.5 days

Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

DESTINY-Gastric01: Exploratory Biomarker Analysis of OS in HER2-Positive or HER2-Low Advanced Gastric or GEJ Cancer

Exploratory biomarker in primary HER2-positive cohort	Median OS
Plasma HER2 amplification	
Not amplified	12.1 mo
Amplified	13.0 mo
Plasma HER2 copy number*	
Above 6.0	21.2 mo
Below 6.0	12.0 mo
Exploratory biomarker in exploratory HER2-low cohort	
Plasma HER2 extracellular domain†	
Above 11.6 ng/mL	10.1 mo
Below 11.6 ng/mL	4.3 mo

*An exploratory cutoff (copy number = 6.0) value was determined, which minimized *p*-value, estimated by log-rank test. Below 6.0 includes patients without amplification; † An exploratory cutoff value of 11.6 ng/mL in exploratory cohorts was determined, which minimized *p*-value, estimated by log-rank test.

Shitari K et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-14.

2021 ESMO congress

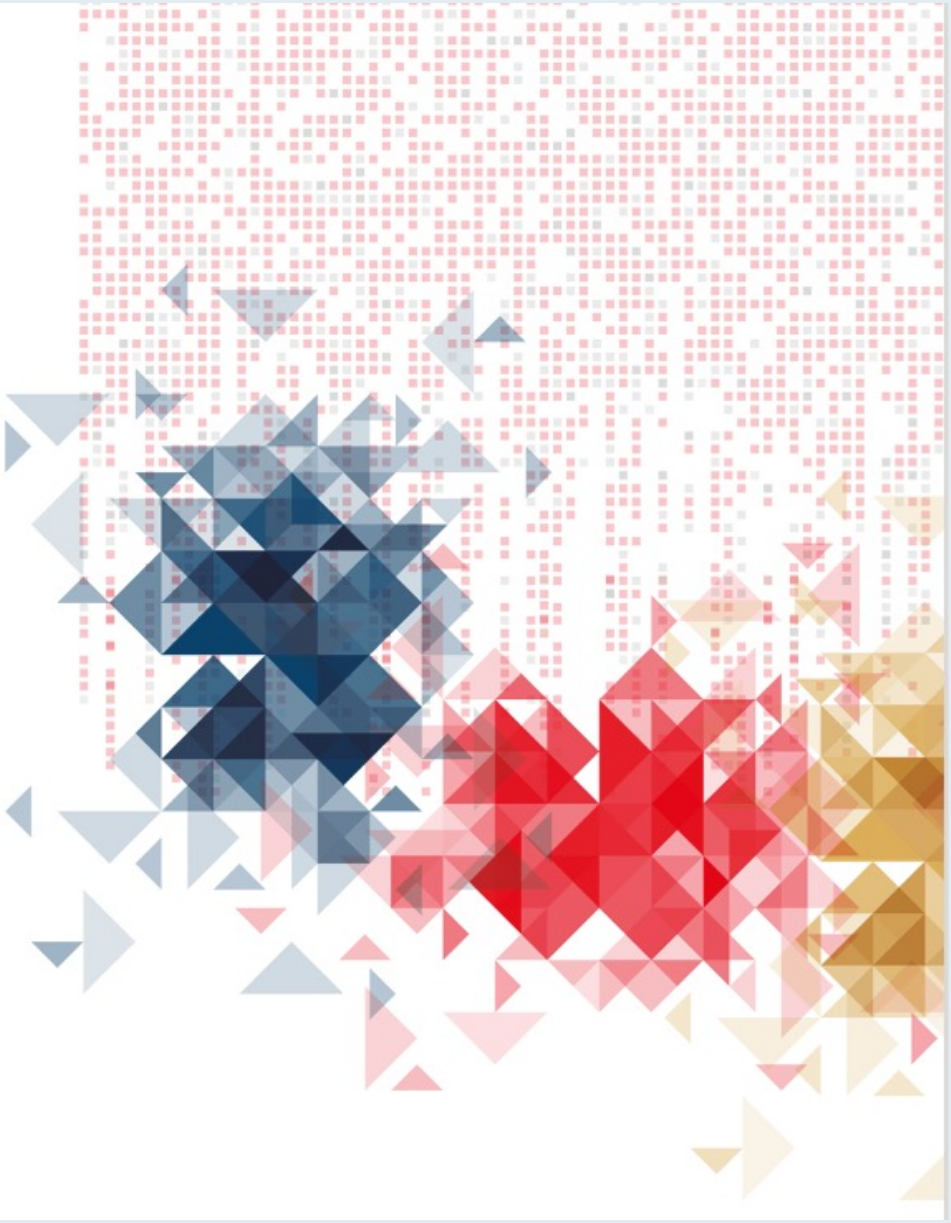
Abstract LBA55

Primary Analysis of a Phase 2 Single-Arm Trial of Trastuzumab Deruxtecan (T-DXd) in Western Patients With HER2-Positive (HER2+) Unresectable or Metastatic Gastric or Gastroesophageal Junction (GEJ) Cancer Who Progressed on or After a Trastuzumab-containing Regimen

Eric Van Cutsem, MD[a], Maria di Bartolomeo, Elizabeth Smyth, Ian Chau, Haeseong Park, Salvatore Siena, Sara Lonardi, Zev A. Wainberg, Jaffer Ajani, Joseph Chao, Jabed Seraj, Yoshinori Kawaguchi, Amy Qin, Jasmeet Singh, Gerold Meinhardt, Geoffrey Ku

On behalf of the DESTINY-Gastric02 investigators

[a]University Hospital Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium



RTP RESEARCH TO PRACTICE

DESTINY-Gastric02 Phase II Study Design

Key eligibility criteria

- Pathologically documented, unresectable or metastatic gastric or GEJ cancer
- Centrally confirmed HER2 positive disease (defined as IHC 3+ or IHC 2+/ISH+) on biopsy after progression on first-line trastuzumab-containing regimen
- ECOG PS 0 or 1

T-DXd
6.4 mg/kg Q3W
N = 79[a]

Primary endpoint

- Confirmed ORR by ICR

Secondary endpoints[b]

- PFS by ICR
- OS
- DOR by ICR
- Safety and tolerability

- DESTINY-Gastric02 is the first study focused only on second-line T-DXd monotherapy in Western patients with HER2+ gastric/GEJ cancer who have progressed on a trastuzumab-containing regimen
  - It is the follow-on study to DESTINY-Gastric01, which evaluated T-DXd third-line or later in Asian patients[1]
- Patients were enrolled in Europe (Belgium, Great Britain, Italy, Spain) and the United States (data cutoff: April 9, 2021)

Van Cutsem E et al. ESMO 2021;Abstract LBA55.

Efficacy Endpoints

	Patients (N = 79)
Confirmed ORR[a], n (%)	**30 (38)** (95% CI, 27.3-49.6)
Confirmed best overall response, n (%)	
CR	**3 (3.8)**
PR	**27 (34.2)**
SD	**34 (43.0)**
PD	**13 (16.5)**
Not evaluable	**2 (2.5)**
Median DOR,[b] months	8.1 (95% CI, 4.1-NE)
Confirmed DCR[c], n (%)	64 (81.0) (95% CI, 70.6-89.0)
Median TTR, months	1.4 (95% CI, 1.4-2.6)
Median PFS,[d] months	5.5 (95% CI, 4.2-7.3)
Median follow up, months	5.7 (range, 0.7-15.2)

Cutoff date: April 9, 2021.
[a]Primary endpoint. [b]Secondary endpoint analysis based on responders (n=30); 21 patients were censored (reasons: initiating new anticancer therapy, adequate tumor assessment no longer available, and ongoing without occurrence of progressive disease or death). [c]Exploratory endpoint. [d]Secondary endpoint analysis in the full analysis set based on 42 events (36 PD, 6 deaths).
BOR, best overall response; CR, complete response; DCR, disease control rate; mo, months; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease; TTR, time to response.

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Van Cutsem E et al. ESMO 2021;Abstract LBA55.

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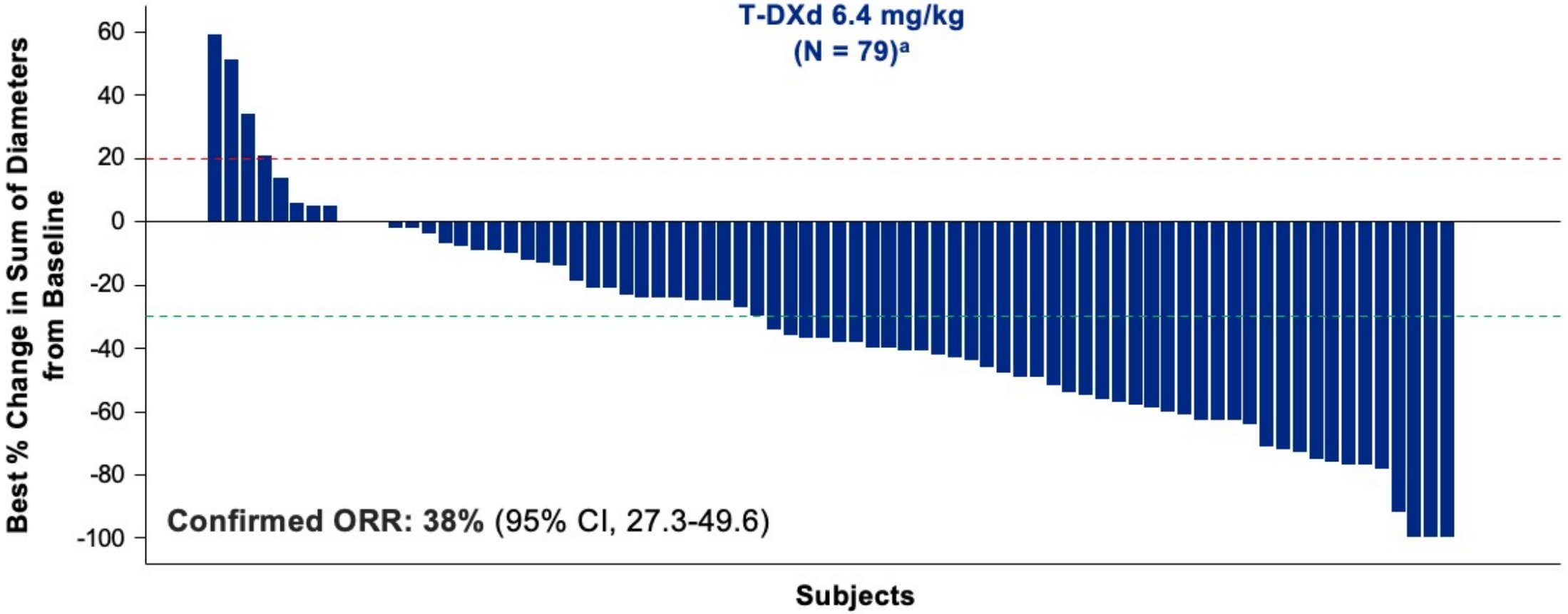
DESTINY-Gastric02: Best Percent Change in Tumor Size from Baseline



Van Cutsem E et al. ESMO 2021;Abstract LBA55.

DESTINY-Gastric02: Safety Summary

n (%)	Patients (N = 79)
Any drug-related TEAE	74 (93.7)
Drug-related TEAE Grade ≥3	21 (26.6)
Serious drug-related TEAE	8 (10.1)
Drug-related TEAE associated with discontinuation	7 (8.9)
Drug-related TEAE associated with dose reduction	15 (19.0)
Drug-related TEAE associated with an outcome of death	1 (1.3)

- Median treatment duration was 4.3 months (range, 0.7-15.9 months)
- The most common drug-related TEAEs associated with treatment discontinuation were investigator-reported pneumonitis (3.8%) and ILD (2.5%)
- The most common drug-related TEAEs associated with dose reduction were nausea (7.6%) and decreased neutrophil count (5.1%)

Van Cutsem E et al. ESMO 2021;Abstract LBA55.

DESTINY-Gastric02: Treatment-Emergent Adverse Events (TEAEs)

n (%)	Patients (N = 79)	
	Any Grade	Grade ≥3
Patients with ≥1 drug-related TEAEs	74 (93.7)	21 (26.6)
Drug-related TEAEs with ≥15% incidence in all patients		
Nausea	46 (58.2)	3 (3.8)
Fatigue	29 (36.7)	3 (3.8)
Vomiting	26 (32.9)	1 (1.3)
Diarrhea	22 (27.8)	1 (1.3)
Decreased appetite	18 (22.8)	1 (1.3)
Alopecia	17 (21.5)	0
Anemia	15 (19.0)	6 (7.6)
Decreased platelet count	13 (16.5)	1 (1.3)
Decreased neutrophil count	12 (15.2)	6 (7.6)

Van Cutsem E et al. ESMO 2021;Abstract LBA55.

DESTINY-Gastric02: Adjudicated Drug-Related Interstitial Lung Disease (ILD)/Pneumonitis

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
n (%)	2 (2.5)	3 (3.8)	0	0	1 (1.3)	6 (7.6)

- Median time to onset of adjudicated drug-related ILD/pneumonitis was 80.5 days (range, 53-85 days), with a median duration of 38.0 days (range, 15-142 days)
- 83% of adjudicated drug-related ILD/pneumonitis cases were low grade (Grade 1-2)

Van Cutsem E et al. ESMO 2021;Abstract LBA55.

Conclusions

- DESTINY-Gastric02 is the first study focused only on 2L T-DXd monotherapy in Western HER2+ patients with gastric/GEJ cancer who progressed on a trastuzumab-containing regimen
- Efficacy results demonstrate clinically meaningful and durable responses
- Safety profile was generally consistent with the established safety profile of T-DXd
- DESTINY-Gastric02 provides clinical evidence for T-DXd as a valuable 2L HER2-targeted treatment option and supports the ongoing randomized phase 3 trial, DESTINY-Gastric04 (NCT04704934)

Van Cutsem E et al. ESMO 2021;Abstract LBA55.

Novel Targeted Agents

FDA Grants Bemarituzumab Breakthrough Therapy Designation as First-Line Treatment for Gastric and Gastroesophageal Cancers that Overexpress FGFR2b

Press Release – April 19, 2021

"The US Food and Drug Administration (FDA) granted Breakthrough Therapy Designation for investigational bemarituzumab as first-line treatment for patients with fibroblast growth factor receptor 2b (FGFR2b) overexpressing and human epidermal growth factor receptor 2 (HER2)-negative metastatic and locally advanced gastric and gastroesophageal (GEJ) adenocarcinoma in combination with modified FOLFOX6 (fluoropyrimidine, leucovorin, and oxaliplatin), based on an FDA-approved companion diagnostic assay showing at least 10% of tumor cells overexpressing FGFR2b."

This designation is supported by results from the Phase 2 FIGHT trial.

https://www.amgen.com/newsroom/press-releases/2021/04/amgens-investigational-targeted-treatment-bemarituzumab-granted-breakthrough-therapy-designation

RTP RESEARCH TO PRACTICE

2021 ASCO ANNUAL MEETING

Abstract 4010

FIGHT: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF BEMARITUZUMAB (BEMA) COMBINED WITH MODIFIED FOLFOX6 IN 1L FGFR2B+ ADVANCED GASTRIC/GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA (GC) (NCT03694522)

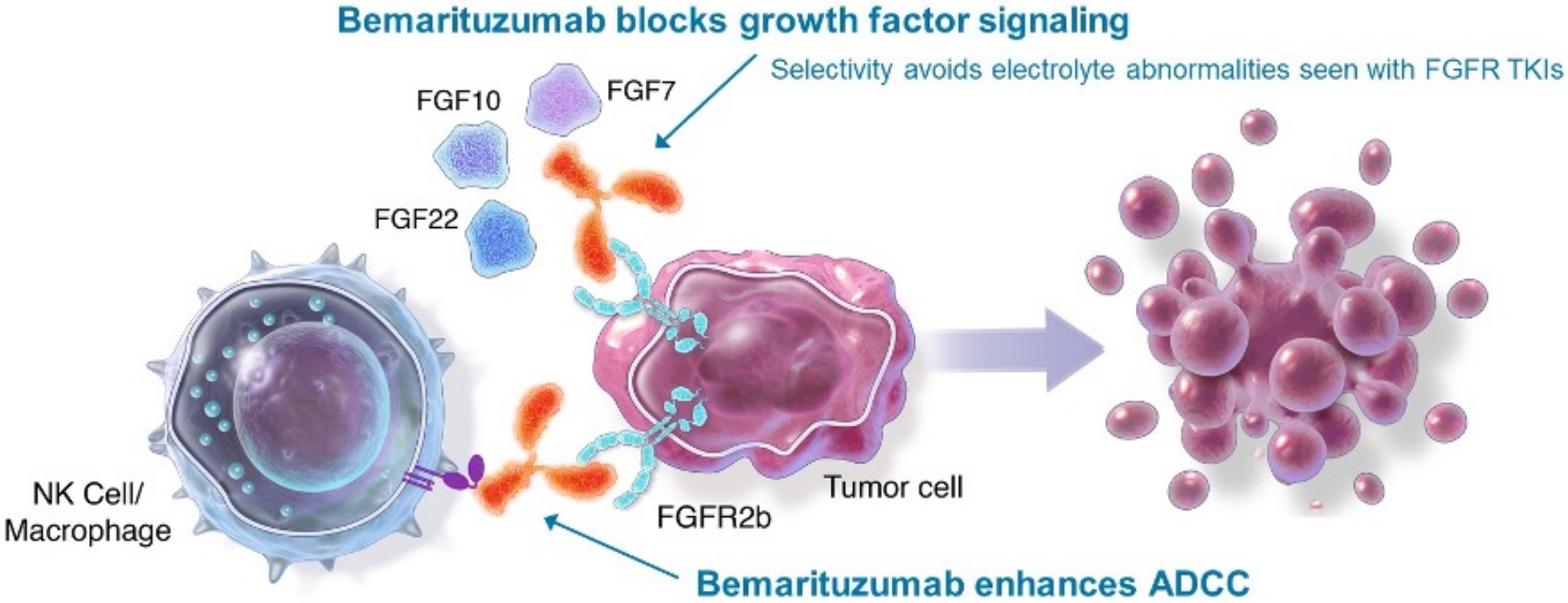
Presenter: Daniel Catenacci, MD
University of Chicago

Authors: Catenacci DV[1], Kang YK[2], Saeed A[3], Yamaguchi K[4], Qin S[5], Lee KW[6], Kim IH[7], Oh SC[8], Li J[9], Turk HM[10], Teixeira AC[11], Borg C[12], Hitre E[13], Udrea AA[14], Cardellino GG[15], Guardeño Sanchez R[16], Mitra S[17], Yang Y[17], Enzinger PC[18], Wainberg ZA[19]

[1]University of Chicago, Chicago, USA; [2]Asan Medical Center, Seoul, South Korea; [3]Kansas University Cancer Center, Westwood, KS, USA; [4]The Cancer Institute Hospital of JFCR, Koto-Ku , Tokyo, Japan; [5]81 Hospital Nanjing University of Chinese Medicine, Nanjing, China; [6]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Gyeonggi-do, South Korea; [7]The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, South Korea; [8]Korea University Guro Hospital, Seoul, South Korea; [9]Shanghai East Hospital, Shanghai, China; [10]Department of Medical Oncology, Bezmialem Vakif University, School of Medicine, Istanbul, Turkey; [11]Hospital Senhora Da Oliveira, Guimarães, Portugal; [12]Centre Hospitalier Régional Universitaire de Besançon, Besançon France; [13]National Institute of Oncology, Budapest, Hungary; [14]SC Medisprof SRL, Cluj-Napoca, Romania; [15]Department of Oncology, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy; [16]Institut Català d'Oncologia, Girona, Spain; [17]FivePrime Therapeutics, Inc., South San Francisco, USA; [18]Dana Farber Cancer Institute, Boston, USA; [19]University of California, Los Angeles, USA

RTP RESEARCH TO PRACTICE

Bemarituzumab Mechanism of Action



18% overall response rate in late-line FGFR2b+ gastroesophageal cancer[1]

ADCC, antibody-dependent cell-mediated cytotoxicity; FGF, fibroblast growth factor; IgG1, immunoglobulin G1; NK, natural killer; TKIs, tyrosine kinase inhibitors.

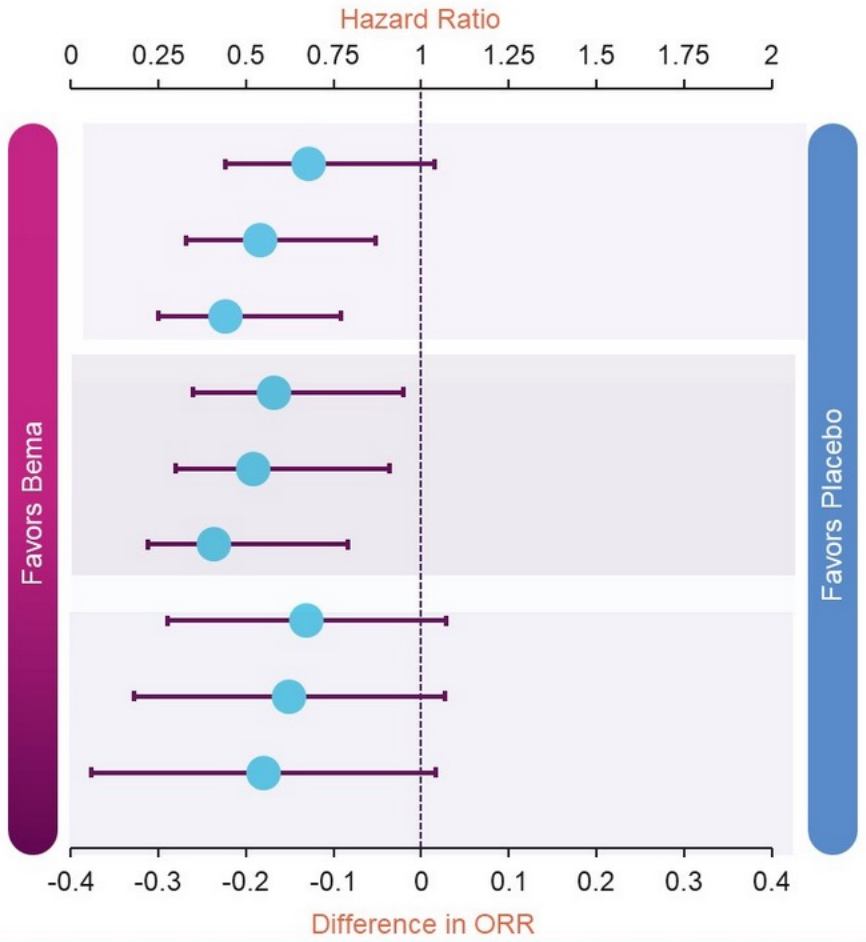
1. Catenacci D, et al. *J Clin Oncol*. 2020.

Catenacci DV et al. ASCO 2021;Abstract 4010.

FIGHT: Efficacy of First-Line Bemarituzumab with Modified FOLFOX6 for Gastric/GEJ Adenocarcinoma

Endpoint	Subgroup	Median PFS/OS (months) Response rate	HR (95% CI) Difference in ORR (95% CI)
PFS	Overall*	Bema: 9.5 Placebo: 7.4	0.68 (0.44, 1.04)
	IHC 2+ or 3+ ≥5%†	Bema: 10.2 Placebo: 7.3	0.54 (0.33, 0.87)
	IHC 2+ or 3+ ≥10%‡	Bema: 14.1 Placebo: 7.3	0.44 (0.25, 0.77)
OS	Overall	Bema: NR Placebo: 12.9	0.58 (0.35, 0.95)
	IHC 2+ or 3+ ≥5%	Bema: NR Placebo: 12.5	0.52 (0.30, 0.91)
	IHC 2+ or 3+ ≥10%	Bema: NR Placebo: 11.1	0.41 (0.22, 0.79)
ORR	Overall	Bema: 36 (46.8%) Placebo: 26 (33.3%)	-13.1%§ (-29.0%, 2.8%)
	IHC 2+ or 3+ ≥5%	Bema: 30 (51.7%) Placebo: 22 (36.7%)	-15.1%§ (-32.8%, 2.7%)
	IHC 2+ or 3+ ≥10%	Bema: 24 (54.5%) Placebo: 19 (36.5%)	-18.0%§ (-37.7%, 1.7%)

*N = 155; †N = 118; ‡N = 96; §difference in ORR is calculated by (placebo ORR – Bema ORR).
NR, not reached.



- Median OS was reached in the overall population with longer follow-up – 5.7-mo improvement

Catenacci DV et al. ASCO 2021;Abstract 4010.

RTP RESEARCH TO PRACTICE

FIGHT: Selected Treatment-Related Adverse Event Summary

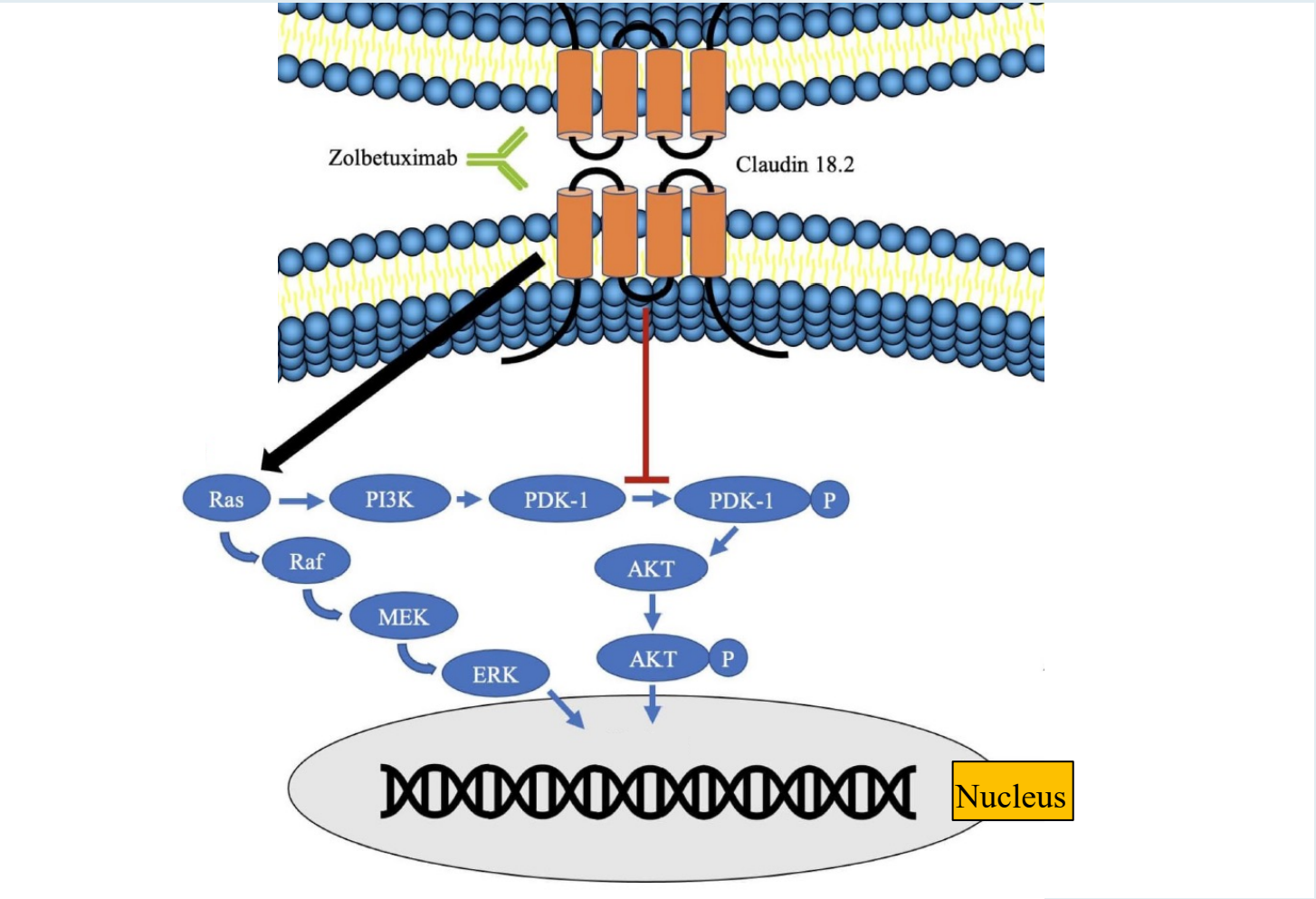
Selected AE (Preferred term)	Any Grade		Grade ≥3	
	Bema (N = 76)	Placebo (N = 77)	Bema (N = 76)	Placebo (N = 77)
Total Events	**76 (100.0%)**	**76 (98.7%)**	**63 (82.9%)**	**57 (74.0%)**
Nausea	36 (47.4%)	41 (53.2%)	0	3 (3.9%)
Vomiting	22 (28.9%)	24 (31.2%)	2 (2.6%)	2 (2.6%)
Diarrhea	31 (40.8%)	24 (31.2%)	2 (2.6%)	1 (1.3%)
Stomatitis	24 (31.6%)	10 (13.0%)	7 (9.2%)	1 (1.3%)
Peripheral sensory neuropathy	15 (19.7%)	15 (19.5%)	4 (5.3%)	3 (3.9%)
Neutrophil count decreased	31 (40.8%)	33 (42.9%)	23 (30.3%)	27 (35.1%)
Platelet count decreased	14 (18.4%)	21 (27.3%)	1 (1.3%)	0
Aspartate aminotransferase increased	23 (30.3%)	15 (19.5%)	4 (5.3%)	2 (2.6%)
Alanine aminotransferase increased	22 (28.9%)	11 (14.3%)	2 (2.6%)	1 (1.3%)
Dry eye	20 (26.3%)	5 (6.5%)	2 (2.6%)	0

AE, adverse event.

Catenacci DV et al. ASCO 2021;Abstract 4010.

RTP RESEARCH TO PRACTICE

Zolbetuximab Mechanism of Action



Adapted from Siddiqui A, Almhanna K. *Cancers* 2021;13(17):4322.

Ann Oncol 2021;32(5):609-19.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

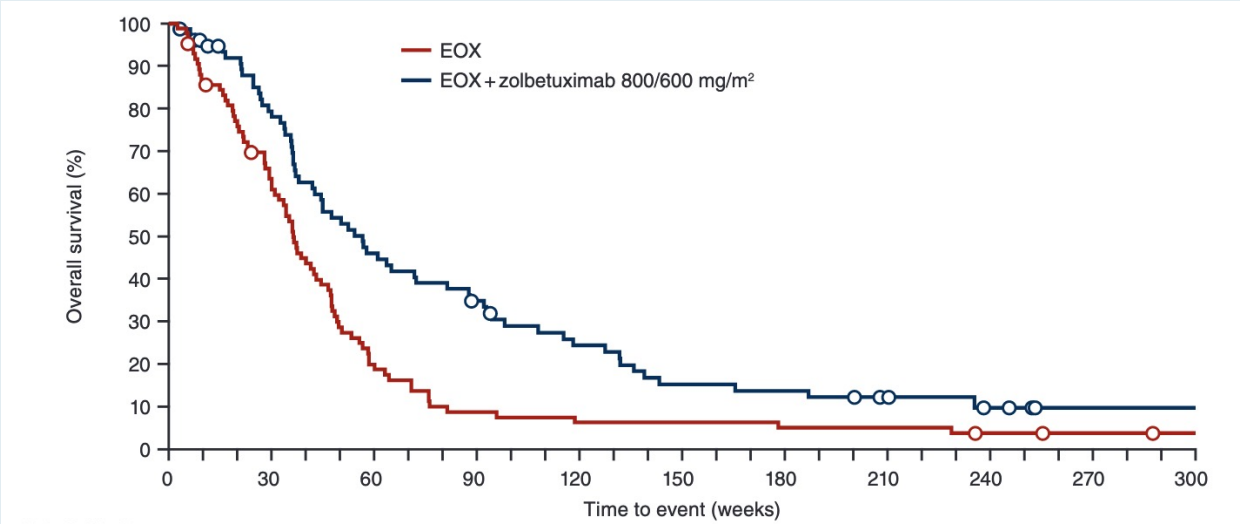
FAST: a randomised phase II study of zolbetuximab (IMAB362) plus EOX versus EOX alone for first-line treatment of advanced CLDN18.2-positive gastric and gastro-oesophageal adenocarcinoma

U. Sahin[1,2,3], Ö. Türeci[3,4], G. Manikhas[5], F. Lordick[6], A. Rusyn[7], I. Vynnychenko[8], A. Dudov[9], I. Bazin[10], I. Bondarenko[11], B. Melichar[12], K. Dhaene[13], K. Wiechen[14], C. Huber[1,3,4], D. Maurus[15], A. Arozullah[16], J. W. Park[16], M. Schuler[17†] & S.-E. Al-Batran[18*†]

RTP RESEARCH TO PRACTICE

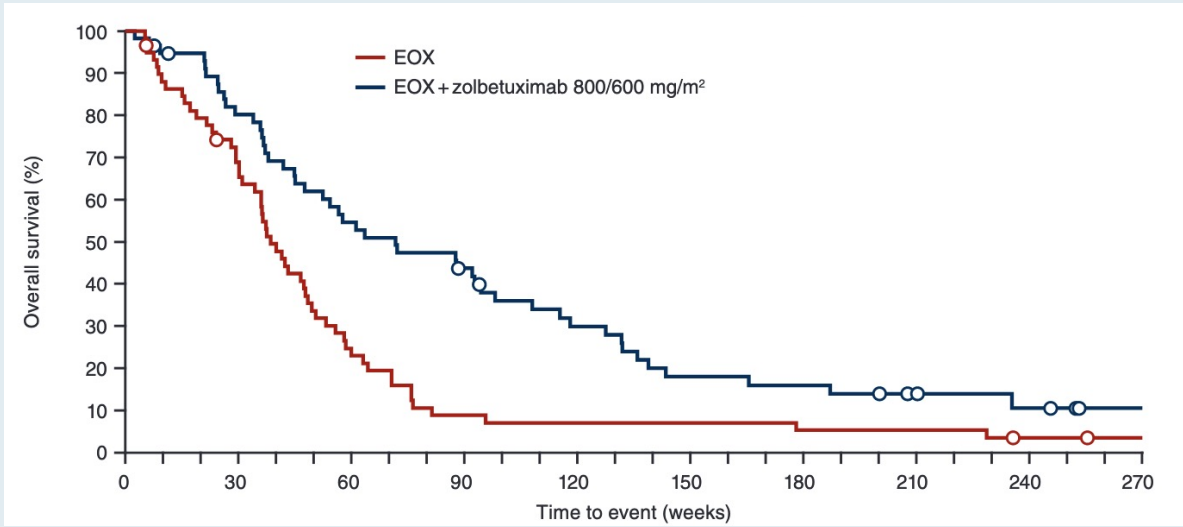
FAST: Overall Survival with Zolbetuximab in Combination with Chemotherapy for Advanced CLDN18.2-Positive Gastric and Gastroesophageal Adenocarcinoma

Overall population



Median OS
EOX (n = 84): 8.3 months
EOX + zolbetuximab (n = 77): 13.0 months
HR (*p*-value): 0.55 (<0.0005)

Patients with ≥70% CLDN18.2-positive tumor cells



Median OS
EOX (n = 59): 8.9 months
EOX + zolbetuximab (n = 57): 16.5 months
HR (*p*-value): 0.50 (<0.0005)

EOX = epirubicin/oxaliplatin/capecitabine

Sahin U et al. *Ann Oncol* 2021;32(5):609-19.

RTP RESEARCH TO PRACTICE

FAST: Select Treatment-Emergent Adverse Events

Adverse event	EOX (n = 84)		EOX + zolbetuximab (n = 77)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Nausea	76.2%	4.8%	81.8%	6.5%
Vomiting	54.8%	3.6%	67.5%	10.4%
Anemia	35.7%	7.1%	45.5%	11.7%
Neutropenia	34.5%	21.4%	44.2%	32.5%
Weight loss	31.0%	3.6%	32.5%	11.7%
Fatigue	20.2%	3.6%	31.2%	6.5%
Leukopenia	16.7%	6.0%	15.6%	7.8%

Sahin U et al. *Ann Oncol* 2021;32(5):609-19.

Ongoing Phase III Trials of Zolbetuximab in Combination with Chemotherapy as First-Line Therapy for Gastric or GEJ Adenocarcinoma

Trial identifier	N	Setting	Study arms
GLOW (NCT03653507)	507	• Locally advanced unresectable or metastatic • CLDN18.2-positive • HER2-negative	• Zolbetuximab + CAPOX • Placebo + CAPOX
SPOTLIGHT (NCT03504397)	550	• Locally advanced unresectable or metastatic • CLDN18.2-positive • HER2-negative	• Zolbetuximab + mFOLFOX6 • Placebo + mFOLFOX6

www.clinicaltrials.gov. Accessed March 2022.

ILUSTRO: Phase II Study of Zolbetuximab Alone or in Combination with Chemotherapy, Immunotherapy or Both for Metastatic or Locally Advanced Unresectable Gastric or GEJ Adenocarcinoma

Trial Identifier: NCT03505320 (Open)

Histologically confirmed gastric or GEJ adenocarcinoma
Locally advanced, unresectable or metastatic disease

Positivity for CLDN18.2 expression

- **Cohort 1A**
  Zolbetuximab
- **Cohort 2**
  Zolbetuximab + mFOLFOX6
- **Cohort 3A**
  Zolbetuximab + pembrolizumab
- **Cohort 4A/4B**
  Zolbetuximab + mFOLFOX6
  +/- nivolumab

Primary endpoint: Objective response rate with zolbetuximab monotherapy
Secondary endpoints include PFS, pharmacokinetics, safety and tolerability

www.clinicaltrials.gov. Accessed March 2022.

Meet The Professor

Optimizing the Management of Ovarian Cancer

Thursday, August 25, 2022
5:00 PM – 6:00 PM ET

Faculty

Richard T Penson, MD, MRCP

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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