Meet The Professor
Optimizing the Management of Gastroesophageal Cancers

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

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

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, the parent company of GHI, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mersana Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

RTP
RESEARCH
TO PRACTICE

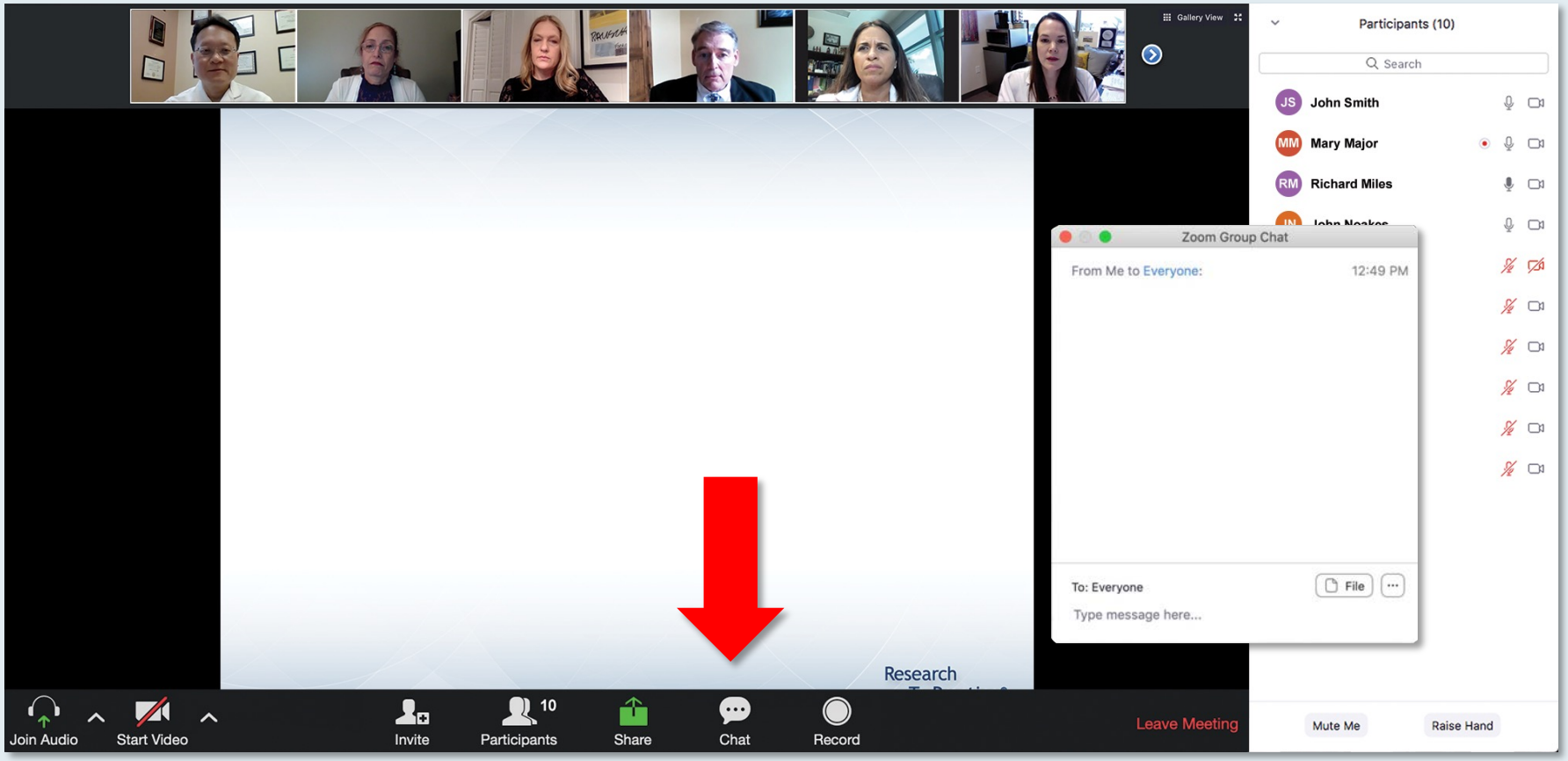
Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Prof Van Cutsem — Disclosures

Advisory Committee	AbbVie Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Biocartis, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, GlaxoSmithKline, Halozyme Inc, Helsinn Healthcare SA, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Lilly, Merck KGaA, Merck Sharp & Dohme LLC, Mirati Therapeutics, Novartis, Pierre Fabre, Roche Laboratories Inc, Seagen Inc, Servier Pharmaceuticals LLC, Sirtex Medical Ltd, Taiho Oncology Inc, Terumo Medical Corporation, TRIGR (trial), Zymeworks Inc
Research Grants to Institution	Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Ipsen Biopharmaceuticals Inc, Lilly, Merck KGaA, Merck Sharp & Dohme LLC, Novartis, Roche Laboratories Inc, Servier Pharmaceuticals LLC

We Encourage Clinicians in Practice to Submit Questions

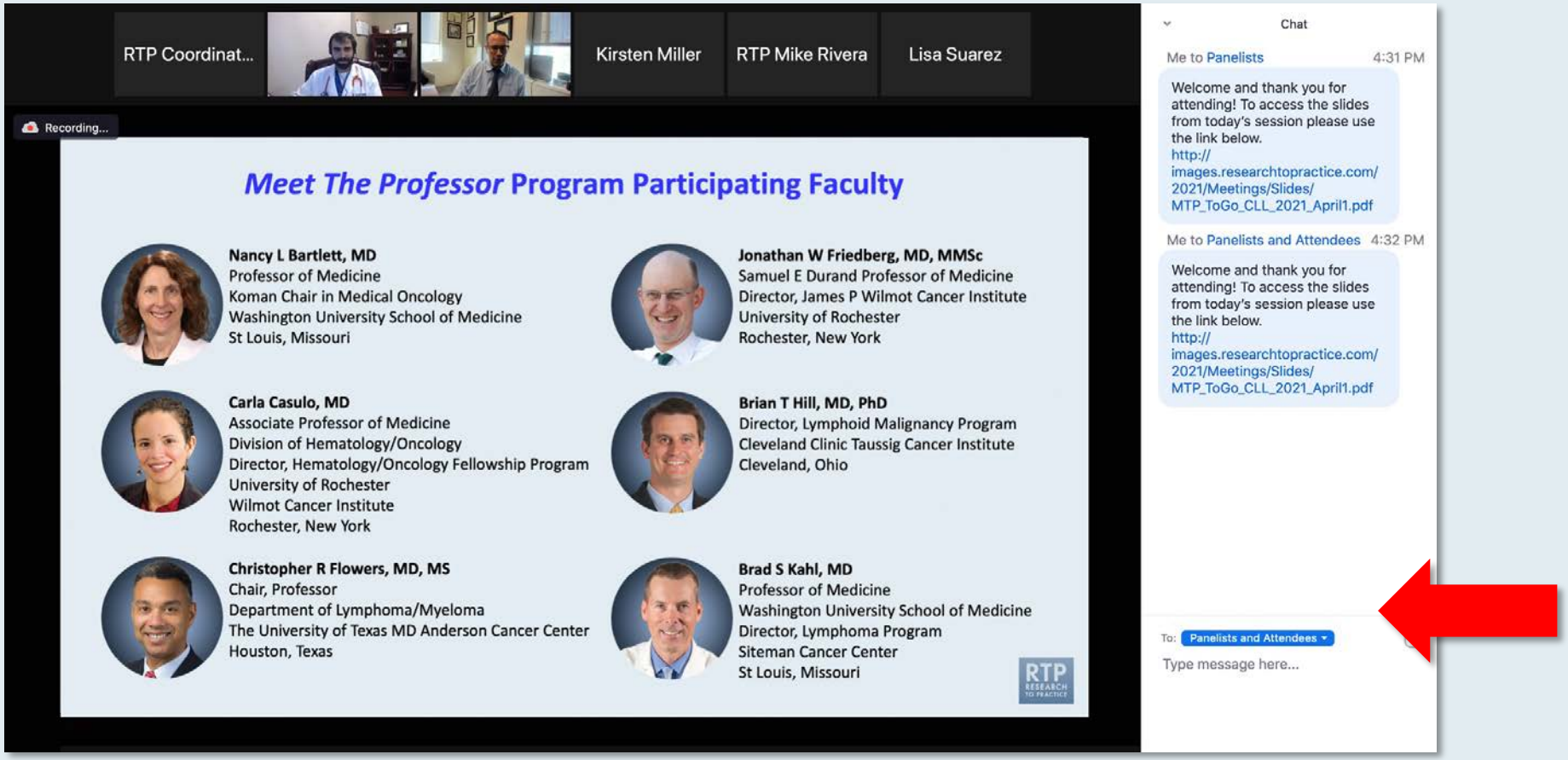


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

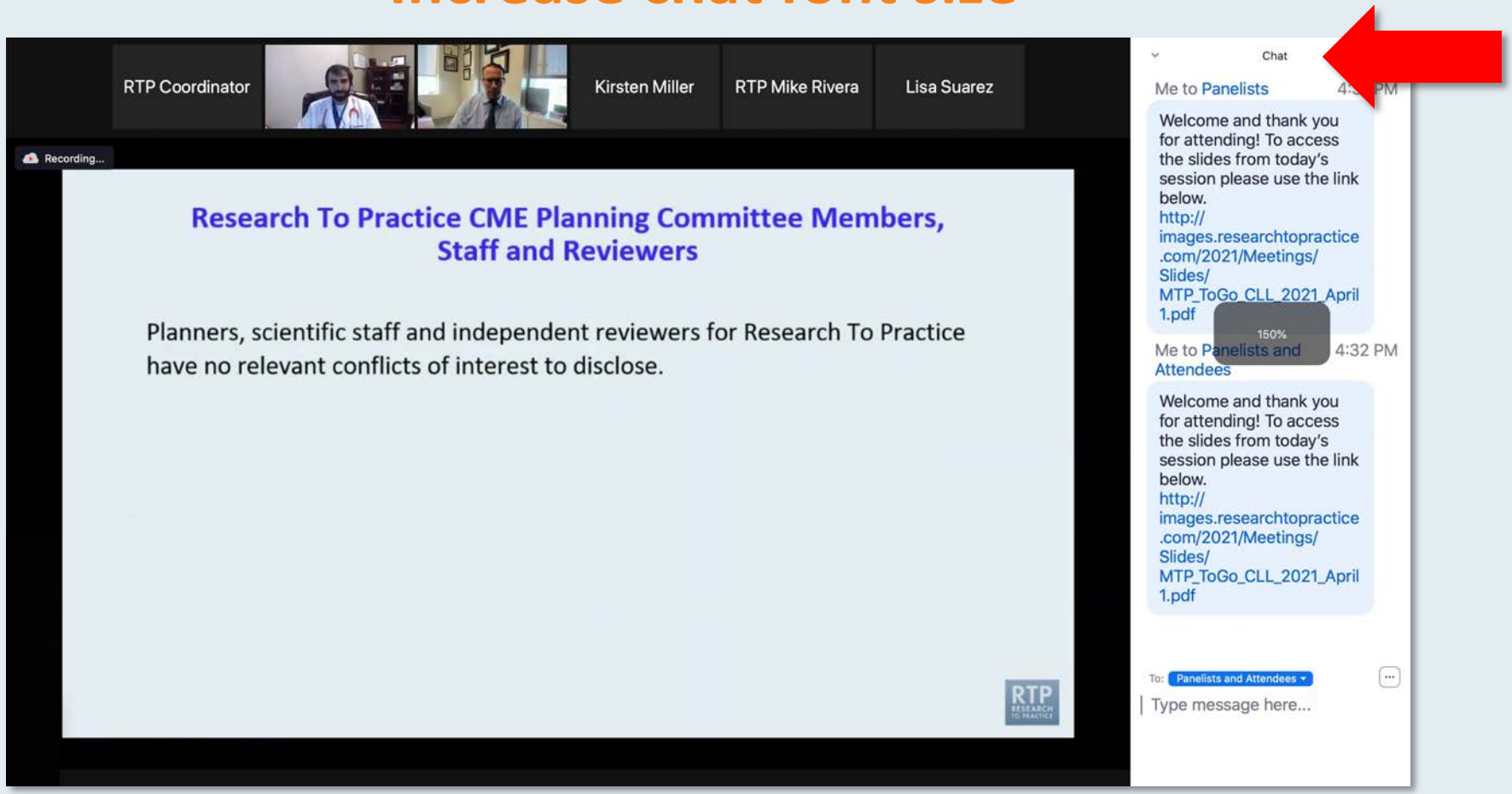


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

ONCOLOGY TODAY

WITH DR NEIL LOVE

Gastroesophageal Cancers

DR SAMUEL KLEMPNER

MASSACHUSETTS GENERAL HOSPITAL

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

PARP Inhibition in the Management of Prostate Cancer — Where We Are and Where We're Headed

Thursday, June 23, 2022
5:00 PM – 6:00 PM ET

Faculty

Johann S de Bono, MB ChB, MSc, PhD, FMedSci
Fred Saad, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Chronic Myeloid Leukemia

Tuesday, June 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Jorge E Cortes, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

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

Thursday, June 30, 2022
5:00 PM – 6:00 PM ET

Faculty

Joel W Neal, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Ovarian Cancer

Wednesday, July 6, 2022
5:00 PM – 6:00 PM ET

Faculty

Ursula Matulonis, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 7, 2022
5:00 PM – 6:00 PM ET

Faculty

Ghassan Abou-Alfa, MD, MBA

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Tuesday, July 12, 2022
5:00 PM – 6:00 PM ET

Faculty

Samuel J Klempner, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE

Meet The Professor
Optimizing the Management of Gastroesophageal Cancers

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

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

Samuel J Klempner, MD
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
New York, New York

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

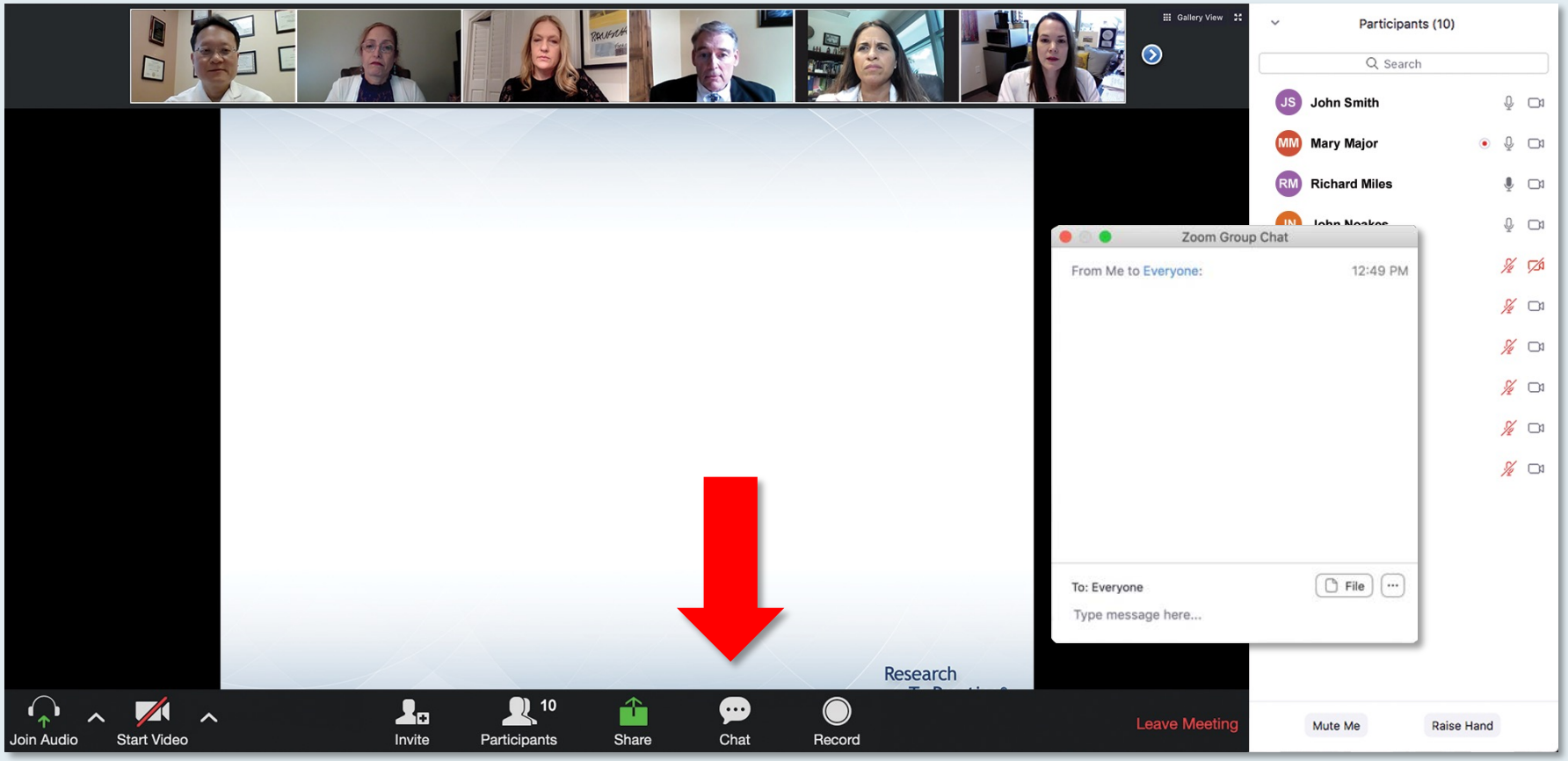
Eric Van Cutsem, MD, PhD
Professor of Medicine
Digestive Oncology
University Hospitals Leuven
Leuven, Belgium

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
Research To Practice

RTP
RESEARCH TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions



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

RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

Gastroesophageal Cancers

DR SAMUEL KLEMPNER

MASSACHUSETTS GENERAL HOSPITAL

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

PARP Inhibition in the Management of Prostate Cancer — Where We Are and Where We're Headed

Thursday, June 23, 2022
5:00 PM – 6:00 PM ET

Faculty

Johann S de Bono, MB ChB, MSc, PhD, FMedSci
Fred Saad, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Chronic Myeloid Leukemia

Tuesday, June 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Jorge E Cortes, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

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

Thursday, June 30, 2022
5:00 PM – 6:00 PM ET

Faculty

Joel W Neal, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Ovarian Cancer

Wednesday, July 6, 2022
5:00 PM – 6:00 PM ET

Faculty

Ursula Matulonis, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 7, 2022
5:00 PM – 6:00 PM ET

Faculty

Ghassan Abou-Alfa, MD, MBA

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Tuesday, July 12, 2022
5:00 PM – 6:00 PM ET

Faculty

Samuel J Klempner, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor
Optimizing the Management of Gastroesophageal Cancers

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

Commercial Support

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

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Prof Van Cutsem — Disclosures

Advisory Committee	AbbVie Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Biocartis, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, GlaxoSmithKline, Halozyme Inc, Helsinn Healthcare SA, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Lilly, Merck KGaA, Merck Sharp & Dohme LLC, Mirati Therapeutics, Novartis, Pierre Fabre, Roche Laboratories Inc, Seagen Inc, Servier Pharmaceuticals LLC, Sirtex Medical Ltd, Taiho Oncology Inc, Terumo Medical Corporation, TRIGR (trial), Zymeworks Inc
Research Grants to Institution	Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Ipsen Biopharmaceuticals Inc, Lilly, Merck KGaA, Merck Sharp & Dohme LLC, Novartis, Roche Laboratories Inc, Servier Pharmaceuticals LLC

Philip L Brooks, MD
Northern Light Eastern Maine Medical Center
Brewer, Maine

Lionel A Kankeu Fonkoua, MD
Mayo Clinic
Rochester, Minnesota

Shaachi Gupta, MD, MPH
Florida Cancer Specialists
Lake Worth, Florida

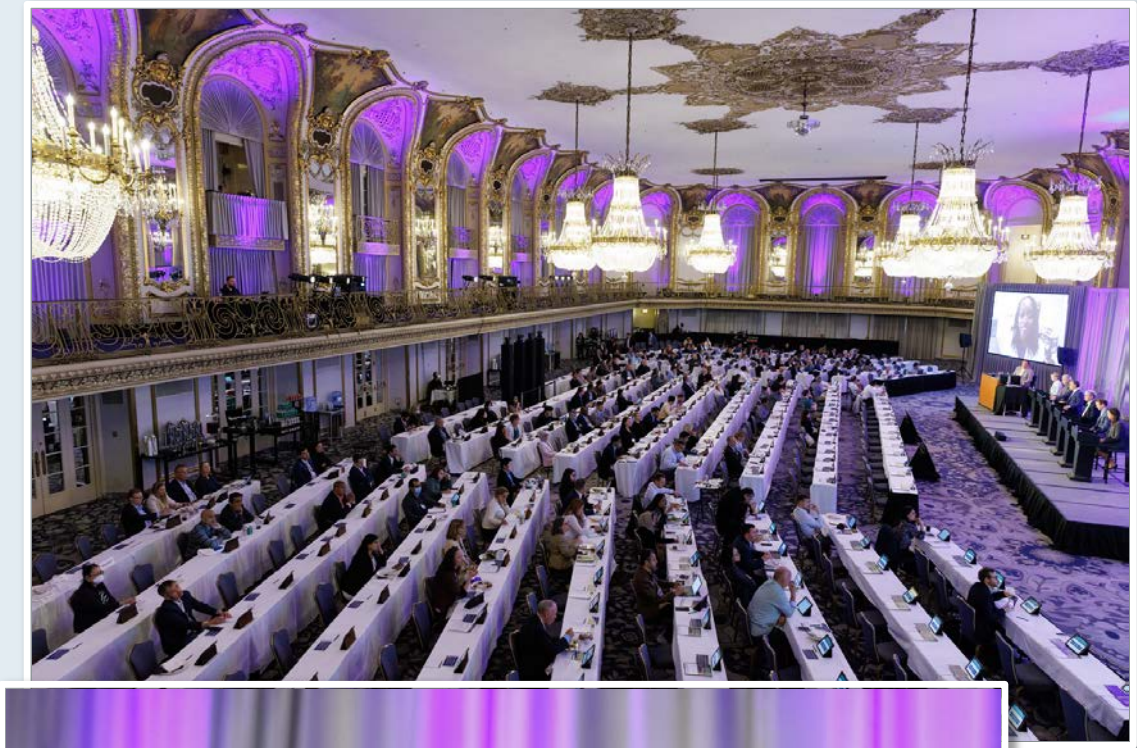
Vignesh Narayanan, MD
Colorado Permanente Medical Group
Lone Tree, Colorado

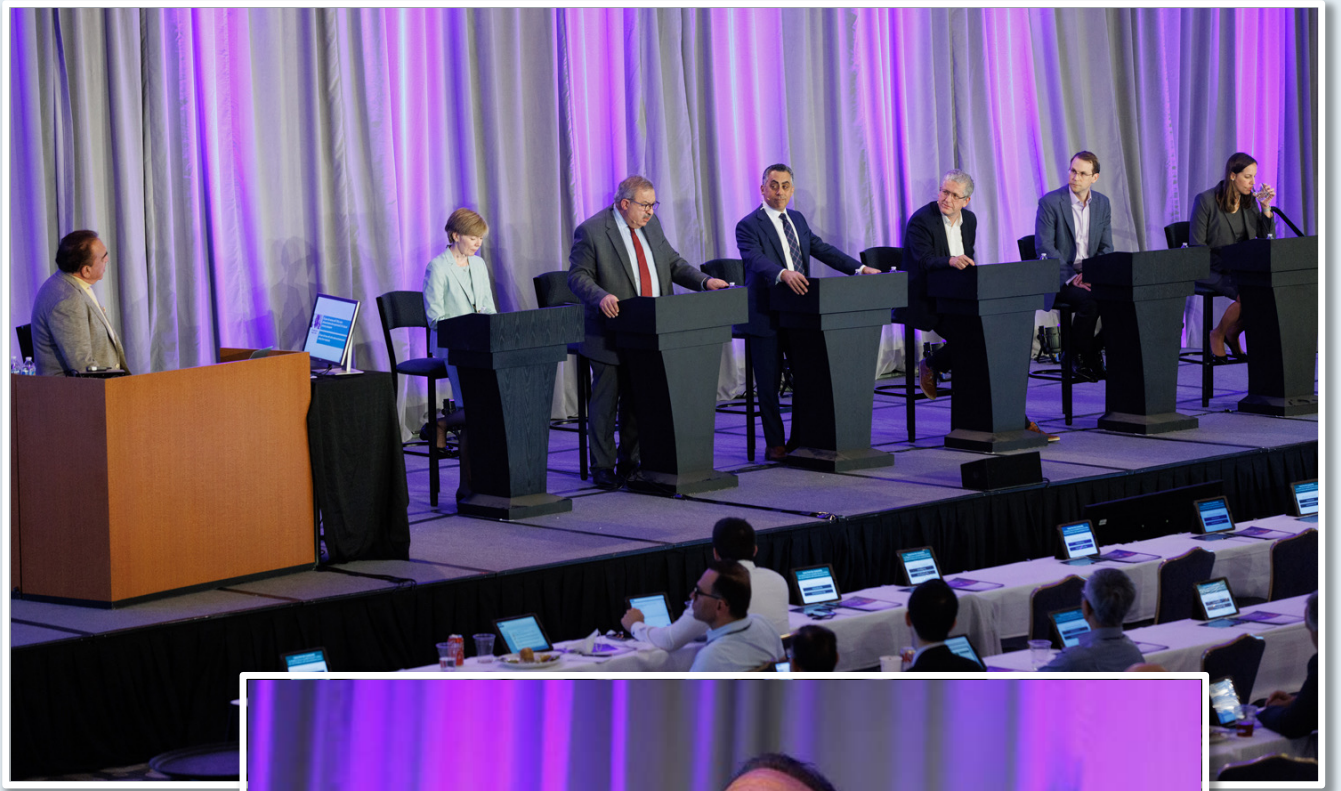
Namrata I Peswani, MD
Harold C Simmons Comprehensive Cancer Center
Richardson, Texas

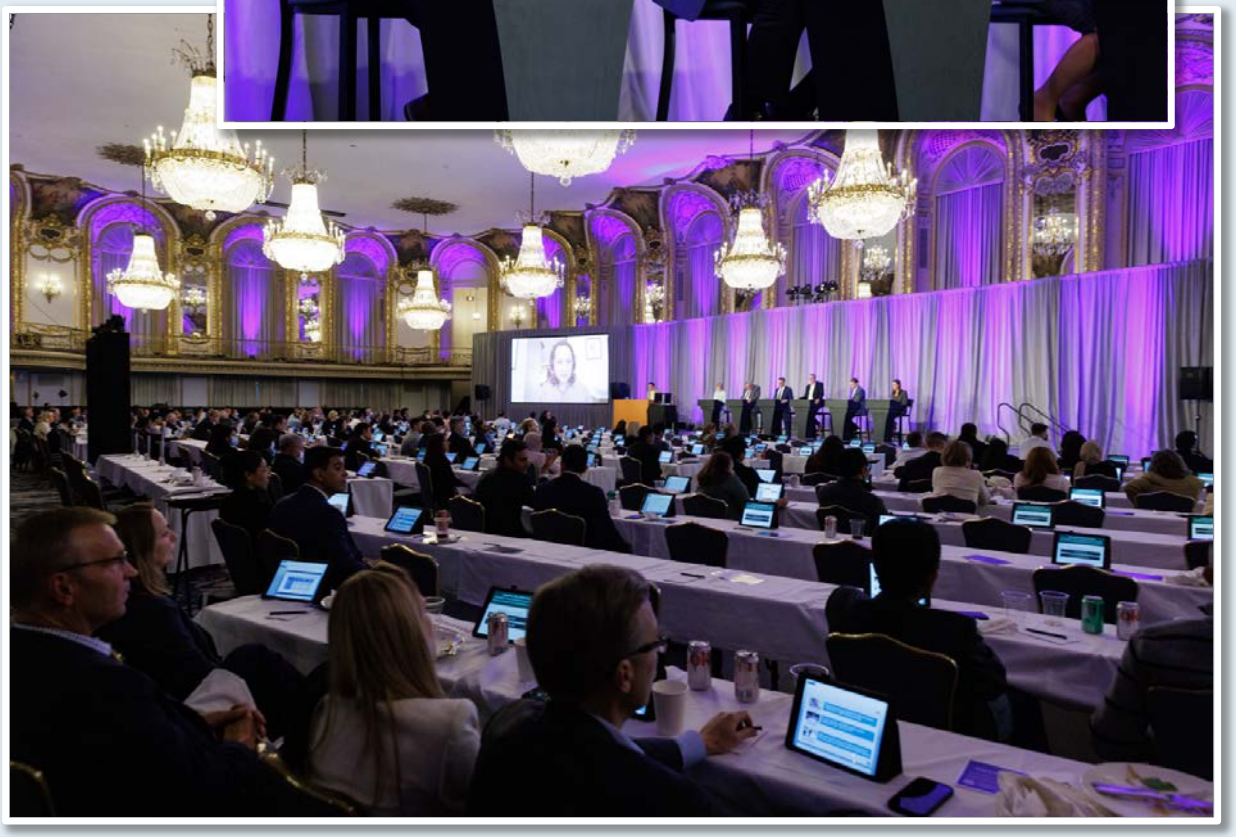
Erik Rupard, MD
The Reading Hospital
West Reading, Pennsylvania

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

RTP
RESEARCH TO PRACTICE







Who is this?

1. The Rolling Stones
2. The Beatles
3. Crosby, Stills, Nash & Young
4. Coldplay
5. Foo Fighters
6. I don’t know

Case Presentation: A 51-year-old woman with metastatic hepatoid carcinoma of the ovary with an FGFR fusion

Dr Syed Ahmed (Libertyville, Illinois)

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Prof Van Cutsem

Introduction: Journal Club with Prof Van Cutsem – Part 1

MODULE 1: Case Presentations

- Dr Peswani: A 76-year-old woman with HER2-negative metastatic gastric cancer – MSI high, PD-L1 >20%
- Dr Gupta: A 74-year-old man with multiple comorbidities and HER2-negative metastatic gastroesophageal junction (GEJ) adenocarcinoma – MSS, PD-L1-positive
- Dr Narayanan: A 55-year-old man with HER2-positive metastatic GEJ adenocarcinoma – PD-L1 low
- Dr Fonkoua: A 65-year-old woman with HER2-equivocal metastatic GEJ adenocarcinoma – pMMR, PD-L1 CPS 10
- Dr Brooks: A 64-year-old woman with HER2-negative metastatic esophageal adenocarcinoma with COPD and vascular disease – pMMR, PD-L1 CPS 5
- Dr Strickland: A 65-year-old man with HER2-negative localized esophageal adenocarcinoma and history of GERD and Barrett's esophagus – pMMR, PD-L1 CPS 1
- Dr Rupard: A 63-year-old man with squamous cell carcinoma of the esophagus who has local and oligometastatic nodal recurrence

MODULE 2: Journal Club with Prof Van Cutsem – Part 2

MODULE 3: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Prof Van Cutsem

Introduction: Journal Club with Prof Van Cutsem – Part 1

- RAINBOW – Ramucirumab/paclitaxel
- Trials in progress

MODULE 1: Case Presentations

- Dr Peswani: A 76-year-old woman with HER2-negative metastatic gastric cancer – MSI high, PD-L1 >20%
- Dr Gupta: A 74-year-old man with multiple comorbidities and HER2-negative metastatic gastroesophageal junction (GEJ) adenocarcinoma – MSS, PD-L1-positive
- Dr Narayanan: A 55-year-old man with HER2-positive metastatic GEJ adenocarcinoma – PD-L1 low
- Dr Fonkoua: A 65-year-old woman with HER2-equivocal metastatic GEJ adenocarcinoma – pMMR, PD-L1 CPS 10
- Dr Brooks: A 64-year-old woman with HER2-negative metastatic esophageal adenocarcinoma with COPD and vascular disease – pMMR, PD-L1 CPS 5
- Dr Strickland: A 65-year-old man with HER2-negative localized esophageal adenocarcinoma and history of GERD and Barrett's esophagus – pMMR, PD-L1 CPS 1
- Dr Rupard: A 63-year-old man with squamous cell carcinoma of the esophagus who has local and oligometastatic nodal recurrence

MODULE 2: Journal Club with Prof Van Cutsem – Part 2

MODULE 3: Appendix of Key Publications

RTP
RESEARCH TO PRACTICE

Oncologist 2021;26(3):e414-24.

The Oncologist®

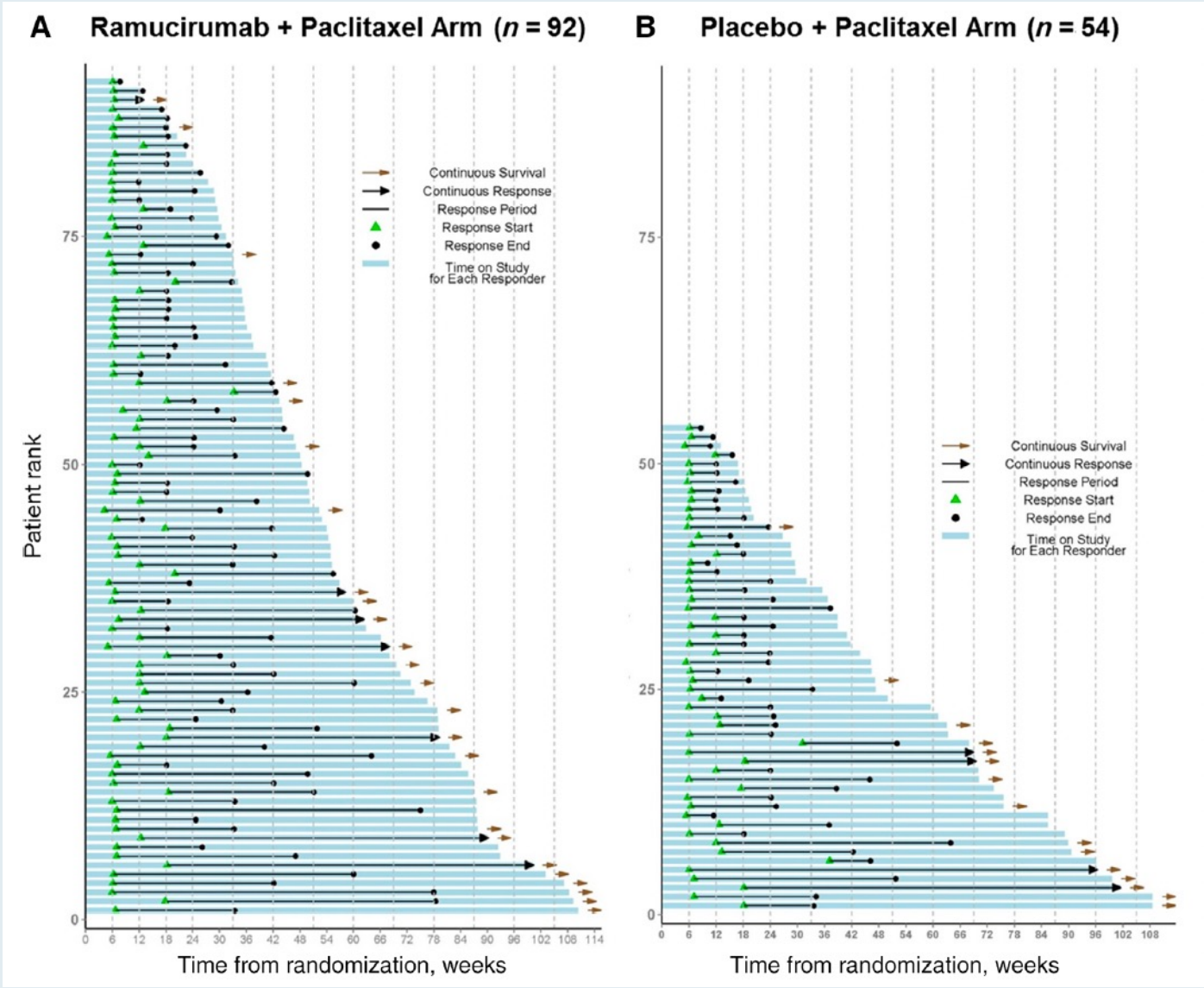
Gastrointestinal Cancer

Tumor Response and Symptom Palliation from RAINBOW, a Phase III Trial of Ramucirumab Plus Paclitaxel in Previously Treated Advanced Gastric Cancer

Stefano Cascinu,[a] György Bodoky,[b] Kei Muro,[c] Eric Van Cutsem,[d] Sang Cheul Oh,[e] Gunnar Folprecht,[f] Sumitra Ananda,[g] Gustavo Girotto,[h] Zev A. Wainberg,[i] Maria Luisa Limon Miron,[j] Jaffer Ajani,[k] Ran Wei,[l] Astra M. Liepa,[m] Roberto Carlesi,[m] Michael Emig,[m] Atsushi Ohtsu[n]

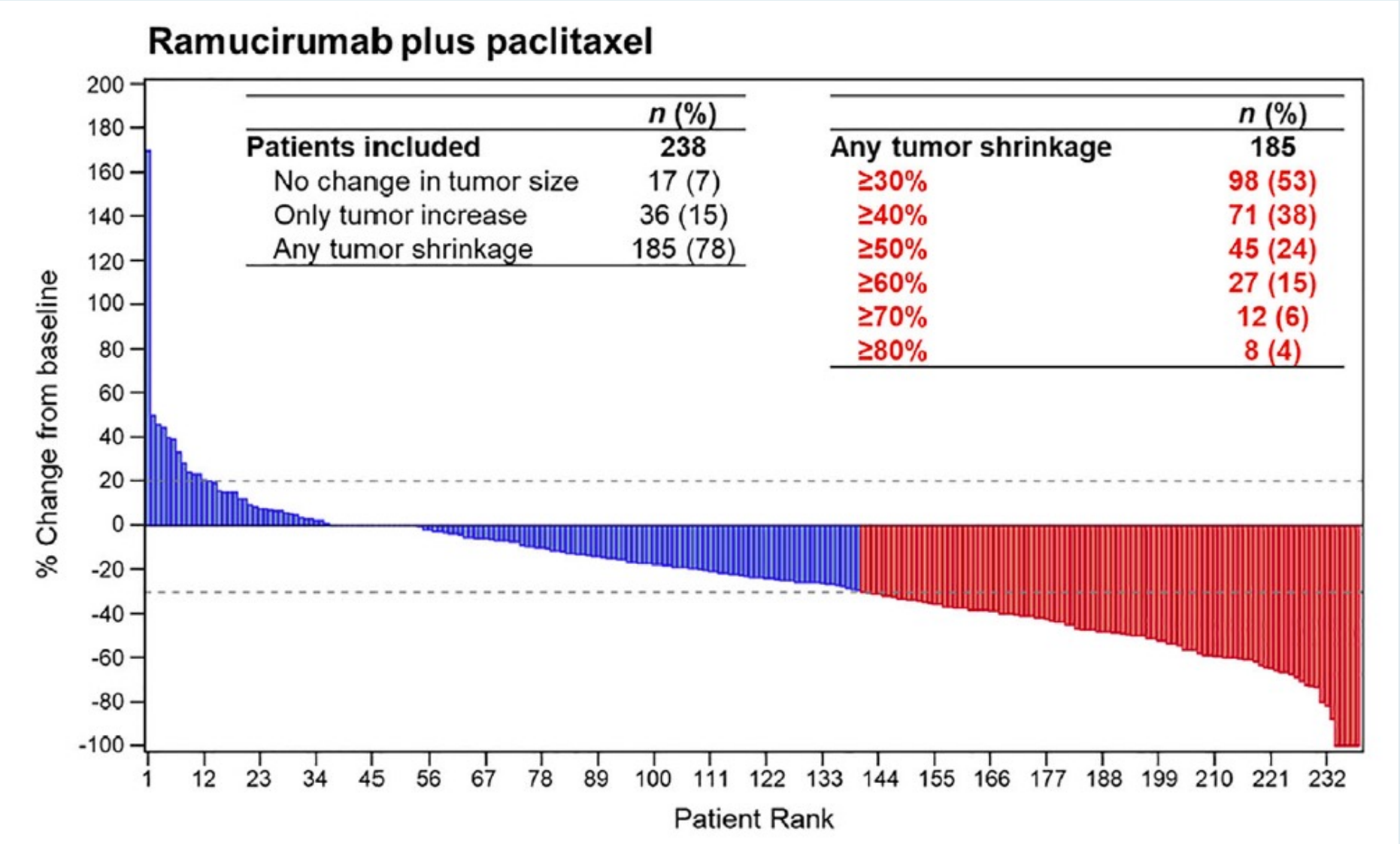
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Time to and Duration of Tumor Responses for Patients with an Objective Response



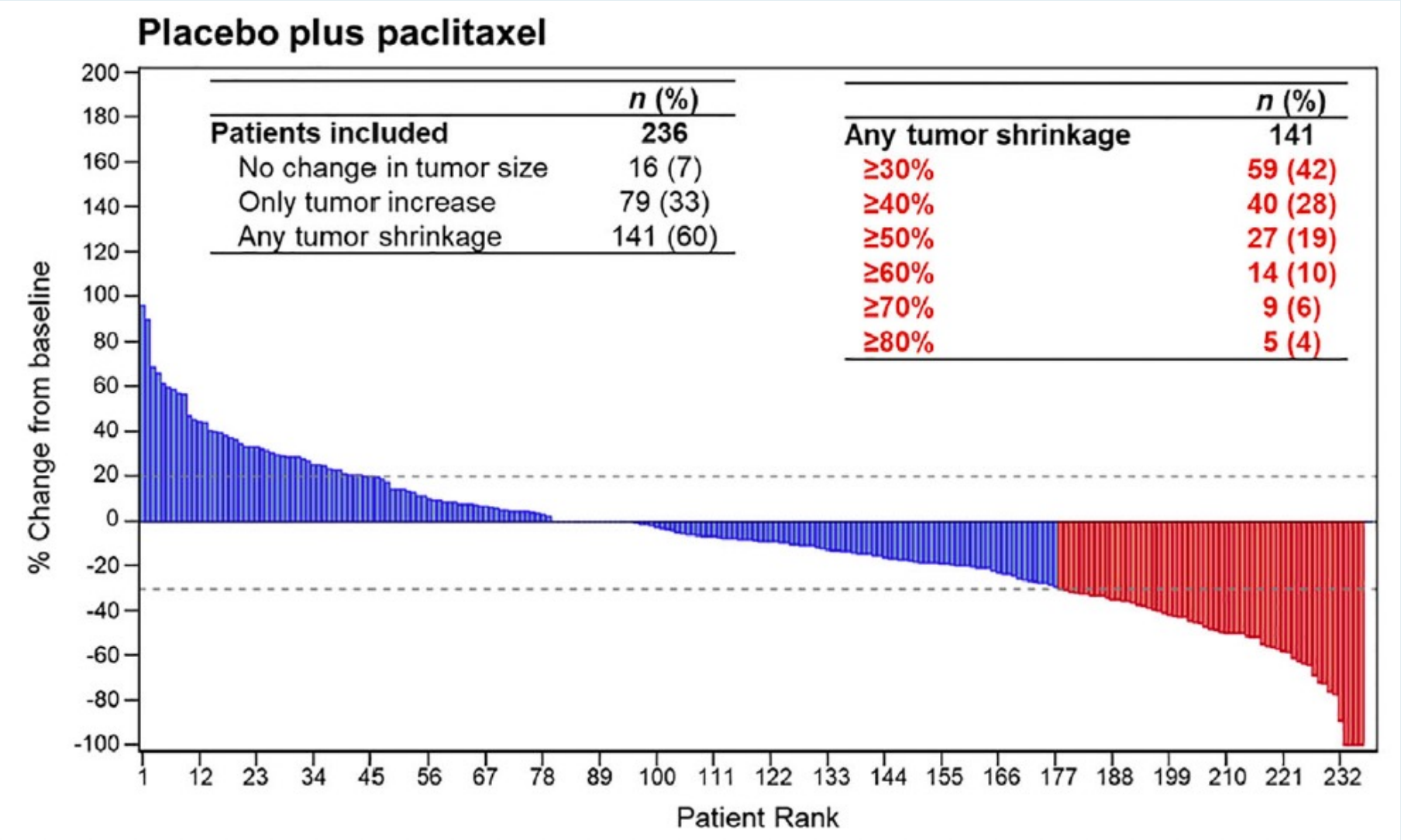
Cascinu S et al. *Oncologist* 2021;26(3):e414-24.

Best Percent Change in Tumor Size from Baseline



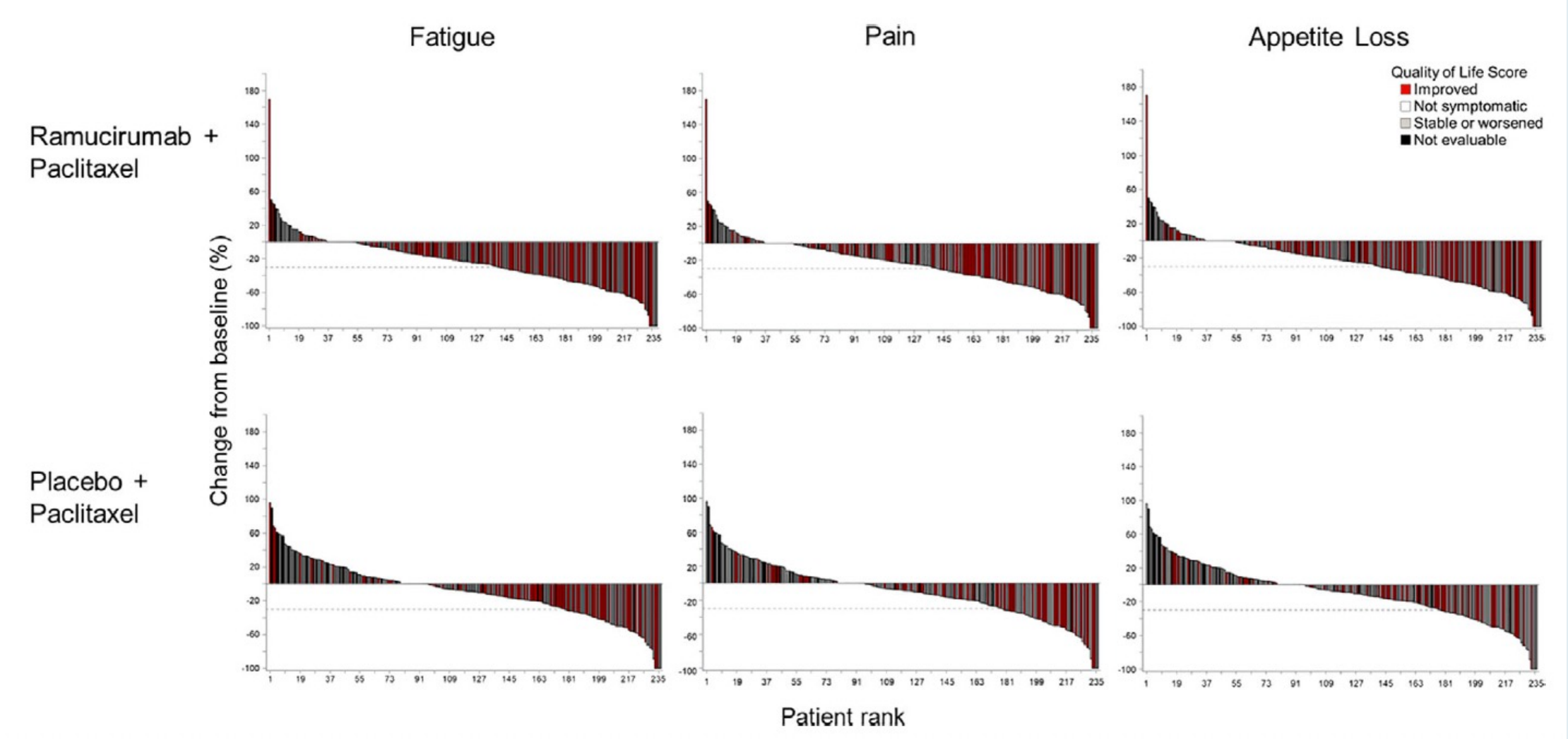
Cascinu S et al. *Oncologist* 2021;26(3):e414-24.

Best Percent Change in Tumor Size from Baseline



Cascinu S et al. *Oncologist* 2021;26(3):e414-24.

Association of Best Percent Change in Tumor Size with Best Improvement in Selected Symptoms



Cascinu S et al. *Oncologist* 2021;26(3):e414-24.

Meet The Professor with Prof Van Cutsem

Introduction: Journal Club with Prof Van Cutsem – Part 1

- RAINBOW – Ramucirumab/paclitaxel
- Trials in progress

MODULE 1: Case Presentations

- Dr Peswani: A 76-year-old woman with HER2-negative metastatic gastric cancer – MSI high, PD-L1 >20%
- Dr Gupta: A 74-year-old man with multiple comorbidities and HER2-negative metastatic gastroesophageal junction (GEJ) adenocarcinoma – MSS, PD-L1-positive
- Dr Narayanan: A 55-year-old man with HER2-positive metastatic GEJ adenocarcinoma – PD-L1 low
- Dr Fonkoua: A 65-year-old woman with HER2-equivocal metastatic GEJ adenocarcinoma – pMMR, PD-L1 CPS 10
- Dr Brooks: A 64-year-old woman with HER2-negative metastatic esophageal adenocarcinoma with COPD and vascular disease – pMMR, PD-L1 CPS 5
- Dr Strickland: A 65-year-old man with HER2-negative localized esophageal adenocarcinoma and history of GERD and Barrett's esophagus – pMMR, PD-L1 CPS 1
- Dr Rupard: A 63-year-old man with squamous cell carcinoma of the esophagus who has local and oligometastatic nodal recurrence

MODULE 2: Journal Club with Prof Van Cutsem – Part 2

MODULE 3: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

MATTERHORN: Efficacy and Safety of Neoadjuvant-Adjuvant Durvalumab and FLOT Chemotherapy in Resectable Gastric and Gastroesophageal Junction Cancer — A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study

Janjigian YY et al.

ASCO 2021;Abstract TPS4151.

A Randomized Phase 3 Study Evaluating the Efficacy and Safety of First-Line Pembrolizumab plus Lenvatinib plus Chemotherapy versus Chemotherapy in Patients with Advanced/Metastatic Gastroesophageal Adenocarcinoma: LEAP-015

Cohen DJ et al.

Gastrointestinal Cancers Symposium 2022;Abstract TPS369.

TPS4173

ASCO 2022

Phase 2 Open-Label Study of Pembrolizumab Plus Lenvatinib and Belzutifan in Patients With Advanced Solid Tumors

R.K. Kelley[1]; E. Van Cutsem[2]; M.S. Lee[3]; I. Wolf[4]; M. Fakih[5]; J. de Vos-Geelen[6]; V. Lee[7]; A. Vogel[8]; X.L. Wu[9]; F. Jin[9]; G.S. Naik[9]; E.M. O'Reilly[10]

Trial in progress: Phase 1b/3 study of bemarituzumab + mFOLFOX6 + nivolumab versus placebo + mFOLFOX6 + nivolumab in previously untreated advanced gastric and gastroesophageal junction (GEJ) cancer with FGFR2b overexpression (FORTITUDE-102)

Zev Wainberg[1], Eric Van Cutsem[2], Markus Moehler[3], Yoon-Koo Kang[4], Priscilla Yen[5], Elizabeth Finger[6], Alissa Keegan[5], Kohei Shitara[7]

ASCO 2022 | Abstract TPS4165

Meet The Professor with Prof Van Cutsem

Introduction: Journal Club with Prof Van Cutsem – Part 1

MODULE 1: Case Presentations

- Dr Peswani: A 76-year-old woman with HER2-negative metastatic gastric cancer – MSI high, PD-L1 >20%
- Dr Gupta: A 74-year-old man with multiple comorbidities and HER2-negative metastatic gastroesophageal junction (GEJ) adenocarcinoma – MSS, PD-L1-positive
- Dr Narayanan: A 55-year-old man with HER2-positive metastatic GEJ adenocarcinoma – PD-L1 low
- Dr Fonkoua: A 65-year-old woman with HER2-equivocal metastatic GEJ adenocarcinoma – pMMR, PD-L1 CPS 10
- Dr Brooks: A 64-year-old woman with HER2-negative metastatic esophageal adenocarcinoma with COPD and vascular disease – pMMR, PD-L1 CPS 5
- Dr Strickland: A 65-year-old man with HER2-negative localized esophageal adenocarcinoma and history of GERD and Barrett's esophagus – pMMR, PD-L1 CPS 1
- Dr Rupard: A 63-year-old man with squamous cell carcinoma of the esophagus who has local and oligometastatic nodal recurrence

MODULE 2: Journal Club with Prof Van Cutsem – Part 2

MODULE 3: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 76-year-old woman with HER2-negative metastatic gastric cancer, multiple mutations and Lynch syndrome – MSI high, PD-L1 >20%

Dr Namrata Peswani (Richardson, Texas)

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, MSI-high gastric adenocarcinoma?

1. Chemotherapy
2. Pembrolizumab + chemotherapy
3. Nivolumab + chemotherapy
4. Nivolumab + ipilimumab
5. Pembrolizumab
6. Nivolumab
7. Other

MSI = microsatellite instability

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, MSI-high gastric adenocarcinoma?

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

RTP RESEARCH TO PRACTICE

JAMA Oncology
JAMA Oncol 2021;7(6):895-902.
View Article

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

Joseph Chao, MD,[1] Charles S. Fuchs, MD,[2] Kohei Shitara, MD,[3] Josep Tabernero, MD,[4] Kei Muro, MD,[5] Eric Van Cutsem, MD,[6] Yung-Jue Bang, MD,[7] Ferdinando De Vita, MD,[8] Gregory Landers, MD,[9] Chia-Jui Yen, MD,[10] Ian Chau, MD,[11] Anneli Elme, MD,[12] Jeeyun Lee, MD,[13] Mustafa Özgüroğlu, MD,[14] Daniel Catenacci, MD,[15] Harry H. Yoon, MD,[16] Erluo Chen, MPH,[17] David Adelberg, MD,[17] Chie-Schin Shih, MD,[17] Sukrut Shah, PhD,[17] Pooja Bhagia, MD,[17] and Zev A. Wainberg, MD[18]

Case Presentation: A 74-year-old man with multiple comorbidities and HER2-negative metastatic GEJ adenocarcinoma – MSS, PD-L1-positive

Dr Shaachi Gupta (Lake Worth, Florida)

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

MSS = microsatellite stable; CPS = combined positive score

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 1?

 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

RTP RESEARCH TO PRACTICE

Case Presentation: A 55-year-old man with HER2-positive metastatic GEJ adenocarcinoma – PD-L1 low

Dr Vignesh Narayanan (Lone Tree, Colorado)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 65-year-old woman with HER2-equivocal metastatic GEJ adenocarcinoma – pMMR (mismatch repair proficient), PD-L1 CPS 10

Dr Lionel Fonkoua (Rochester, Minnesota)

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-negative, MSS adenocarcinoma of the GEJ (PD-L1 CPS ≥5) who has experienced disease progression on first-line FOLFOX/nivolumab or FOLFOX/pembrolizumab?

 Dr Enzinger	Ramucirumab/ paclitaxel	 Dr Shah	Ramucirumab/ paclitaxel
 Dr Janjigian	Ramucirumab/ paclitaxel	 Dr Strickler	Ramucirumab/ paclitaxel
 Dr Klempner	Ramucirumab/ paclitaxel	 Dr Yoon	Ramucirumab/ paclitaxel

RTP RESEARCH 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/pembrolizumab?

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

RTP RESEARCH TO PRACTICE

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;600:727-30. 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

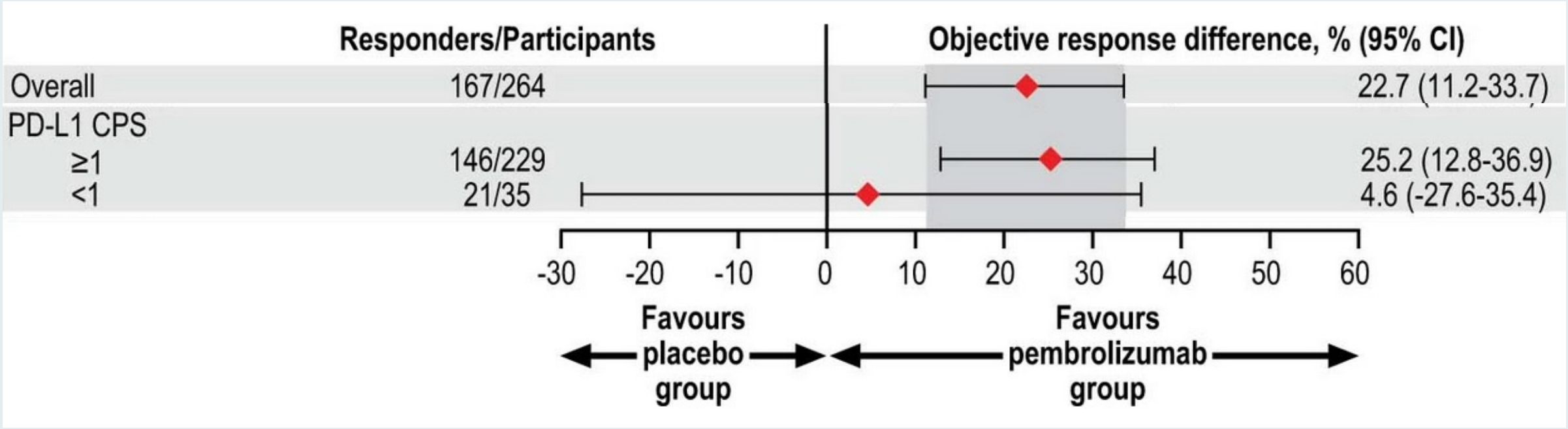
Received: 25 May 2021

Accepted: 30 September 2021

Published online: 15 December 2021

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: Treatment Difference in Objective Response for PD-L1 CPS Subgroups in the Efficacy Population



CPS = combined positive score

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

Pembrolizumab Plus Trastuzumab and Chemotherapy for HER2+ Metastatic Gastric or Gastroesophageal Junction Cancer: Initial Findings of the Global Phase 3 KEYNOTE-811 Study

Yelena Y. Janjigian,[1] Akihito Kawazoe,[2] Patricio Yañez,[3] Suxia Luo,[4] Sara Lonardi,[5] Oleksii Kolesnik,[6] Olga Barajas,[7] Yuxian Bai,[8] Lin Shen,[9] Yong Tang,[10] Lucjan S. Wyrwicz,[11] Kohei Shitara,[2] Shukui Qin,[12] Eric Van Cutsem,[13] Josep Tabernero,[14] Lie Li,[15] Chie-Schin Shih,[15] Pooja Bhagia,[15] Hyun Cheol Chung,[16] on behalf of the KEYNOTE-811 Investigators

ASCO 2021;Abstract 4013.

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

DESTINY-Gastric02 Study Design

An open-label, multicenter phase 2 study in Western patients with HER2+ gastric or GEJ cancer (NCT04014075)

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)

[a]Enrollment of 80 patients was planned; actual enrollment was 79 patients.
[b]Other secondary endpoints were ORR, PFS, and DOR by investigator assessment, pharmacokinetics, anti-drug antibodies, and patient-reported outcomes.

1. Shitara K et al. *N Engl J Med*. 2020;382:2419-30.

DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; ICR, independent central review; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; Q3W, every 3 weeks.

2021 ESMO congress

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

Efficacy Endpoints

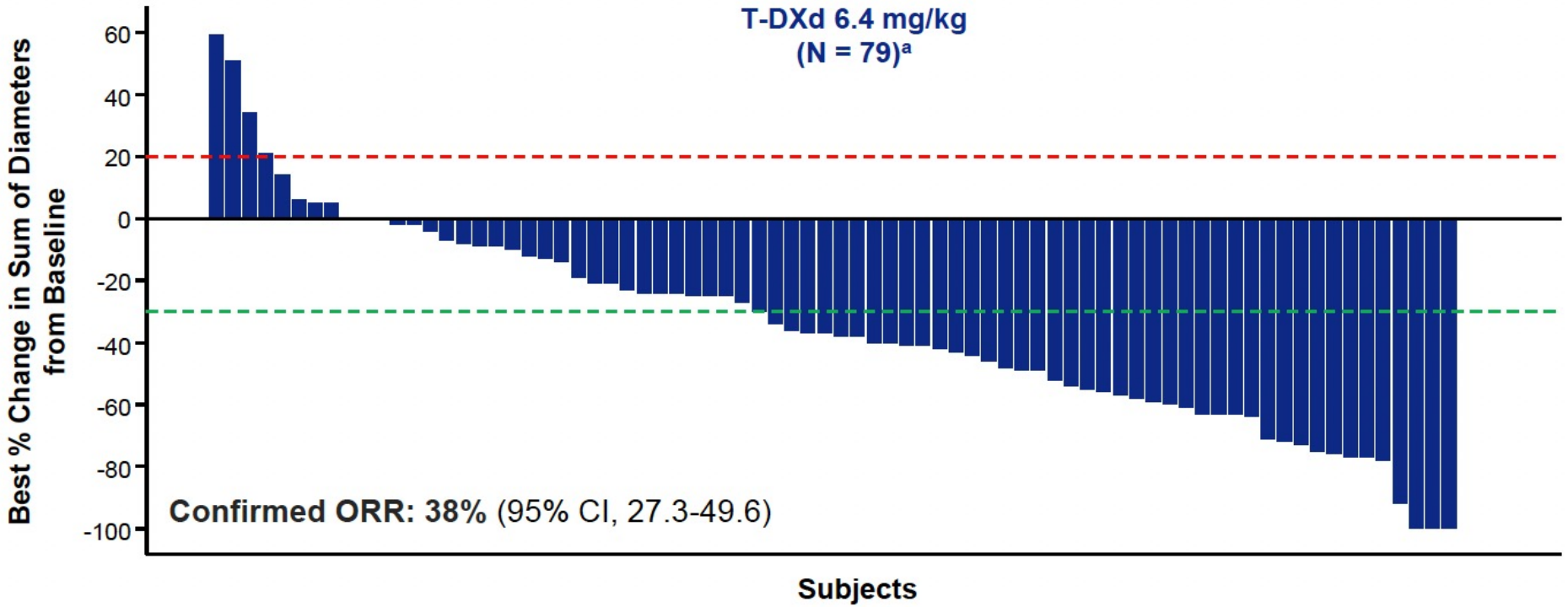
	Patients (N = 79)
Confirmed ORR[a], n (%)	**30 (38)** (95% CI, 27.3-49.6)
Confirmed best overall response, n (%)	
CR	**3 (3.8)**
PR	**27 (34.2)**
SD	**34 (43.0)**
PD	**13 (16.5)**
Not evaluable	**2 (2.5)**
Median DOR,[b] months	8.1 (95% CI, 4.1-NE)
Confirmed DCR[c], n (%)	64 (81.0) (95% CI, 70.6-89.0)
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.

2021 ESMO congress

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

Best Percentage Change of Tumor Size from Baseline



2021 ESMO congress

[a]3 patients were missing baseline or post-baseline target lesion assessment.
Red line at 20% indicates progressive disease; green line at -30% indicates partial response.
Analysis conducted in the full analysis set.

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

Overall 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%)

2021 ESMO congress

Data are shown as number (%) of patients unless stated otherwise.
ILD, interstitial lung disease; TEAE, treatment-emergent adverse event.

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

Drug-related TEAEs in ≥15% of Patients

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.

Adjudicated Drug-Related 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.

Case Presentation: A 64-year-old woman with HER2-negative metastatic esophageal adenocarcinoma with COPD and vascular disease – pMMR, PD-L1 CPS 5

Dr Philip Brooks (Brewer, Maine)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 65-year-old man with HER2-negative localized esophageal adendocarcinoma and history of GERD and Barrett's esophagus – pMMR, PD-L1 CPS 1

Dr Matthew Strickland (Boston, Massachusetts)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 63-year-old man with squamous cell carcinoma of the esophagus who has local and oligometastatic nodal recurrence

Dr Erik Rupard (West Reading, Pennsylvania)

RTP
RESEARCH
TO PRACTICE

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

Challenges in enrolling patients on clinical trials

Dr Erik Rupard (West Reading, Pennsylvania)

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Prof Van Cutsem

Introduction: Journal Club with Prof Van Cutsem – Part 1

MODULE 1: Case Presentations

- Dr Peswani: A 76-year-old woman with HER2-negative metastatic gastric cancer – MSI high, PD-L1 >20%
- Dr Gupta: A 74-year-old man with multiple comorbidities and HER2-negative metastatic gastroesophageal junction (GEJ) adenocarcinoma – MSS, PD-L1-positive
- Dr Narayanan: A 55-year-old man with HER2-positive metastatic GEJ adenocarcinoma – PD-L1 low
- Dr Fonkoua: A 65-year-old woman with HER2-equivocal metastatic GEJ adenocarcinoma – pMMR, PD-L1 CPS 10
- Dr Brooks: A 64-year-old woman with HER2-negative metastatic esophageal adenocarcinoma with COPD and vascular disease – pMMR, PD-L1 CPS 5
- Dr Strickland: A 65-year-old man with HER2-negative localized esophageal adenocarcinoma and history of GERD and Barrett's esophagus – pMMR, PD-L1 CPS 1
- Dr Rupard: A 63-year-old man with squamous cell carcinoma of the esophagus who has local and oligometastatic nodal recurrence

MODULE 2: Journal Club with Prof Van Cutsem – Part 2

MODULE 3: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

European Journal of Cancer 166 (2022) 254–269

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Review

Definition of oligometastatic esophagogastric cancer and impact of local oligometastasis-directed treatment: A systematic review and meta-analysis

Tiuri E. Kroese [a,b,*], Hanneke W.M. van Laarhoven [c], Magnus Nilsson [d], Florian Lordick [e], Matthias Guckenberger [f], Jelle P. Ruurda [a], Domenico D'Ugo [g], Karin Haustermans [h], Eric van Cutsem [i], Richard van Hillegersberg [a], Peter S.N. van Rossum [b]

Clin Cancer Res 2022;[Online ahead of print].

Association of Tumor Mutational Burden with Efficacy of Pembrolizumab± Chemotherapy as First-Line Therapy for Gastric Cancer in the Phase III KEYNOTE-062 Study

Keun-Wook Lee,[1*] Eric Van Cutsem,[2] Yung-Jue Bang,[3] Charles S. Fuchs,[4] Iveta Kudaba,[5] Marcelo Garrido,[6] Hyun Cheol Chung,[7] Jeeyun Lee,[8] Hugo R. Castro,[9] Joseph Chao,[10] Zev A. Wainberg,[11] Z. Alexander Cao,[12] Deepti Aurora-Garg,[12] Julie Kobie,[12] Razvan Cristescu,[12] Pooja Bhagia,[12] Sukrut Shah,[12] Josep Tabernero,[13] Kohei Shitara,[14] Lucjan Wyrwicz[15]

Gastric Cancer (2021) 24:970–977

SHORT COMMUNICATION

Trifluridine/tipiracil in patients with metastatic gastroesophageal junction cancer: a subgroup analysis from the phase 3 TAGS study

Wasat Mansoor[1] · Hendrik-Tobias Arkenau[2] · Maria Alsina[3] · Kohei Shitara[4] · Peter Thuss-Patience[5] · Sinead Cuffe[6] · Mikhail Dvorkin[7] · David Park[8] · Takayuki Ando[9] · Marc Van Den Eynde[10] · Giordano D. Beretta[11] · Alberto Zaniboni[12] · Toshihiko Doi[4] · Josep Tabernero[13] · David H. Ilson[14] · Lukas Makris[15] · Karim A. Benhadji[16] · Eric Van Cutsem[17]

Phase II Study of Zolbetuximab plus Pembrolizumab in Claudin 18.2-Positive Locally Advanced or Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma (G/GEJ) — ILUSTRO Cohort 3

Klempner SJ et al.

Gastrointestinal Cancers Symposium 2021;Abstract TPS260.

Zolbetuximab + CAPOX versus CAPOX in First-Line Treatment of Claudin18.2^{+}/HER2^{-} Advanced/Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma: GLOW Phase 3 Study

Shah MA et al.

Gastrointestinal Cancers Symposium 2022;Abstract TPS365.

Meet The Professor with Prof Van Cutsem

Introduction: Journal Club with Prof Van Cutsem – Part 1

MODULE 1: Case Presentations

- Dr Peswani: A 76-year-old woman with HER2-negative metastatic gastric cancer – MSI high, PD-L1 >20%
- Dr Gupta: A 74-year-old man with multiple comorbidities and HER2-negative metastatic gastroesophageal junction (GEJ) adenocarcinoma – MSS, PD-L1-positive
- Dr Narayanan: A 55-year-old man with HER2-positive metastatic GEJ adenocarcinoma – PD-L1 low
- Dr Fonkoua: A 65-year-old woman with HER2-equivocal metastatic GEJ adenocarcinoma – pMMR, PD-L1 CPS 10
- Dr Brooks: A 64-year-old woman with HER2-negative metastatic esophageal adenocarcinoma with COPD and vascular disease – pMMR, PD-L1 CPS 5
- Dr Strickland: A 65-year-old man with HER2-negative localized esophageal adenocarcinoma and history of GERD and Barrett's esophagus – pMMR, PD-L1 CPS 1
- Dr Rupard: A 63-year-old man with squamous cell carcinoma of the esophagus who has local and oligometastatic nodal recurrence

MODULE 2: Journal Club with Prof Van Cutsem – Part 2

MODULE 3: 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.

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

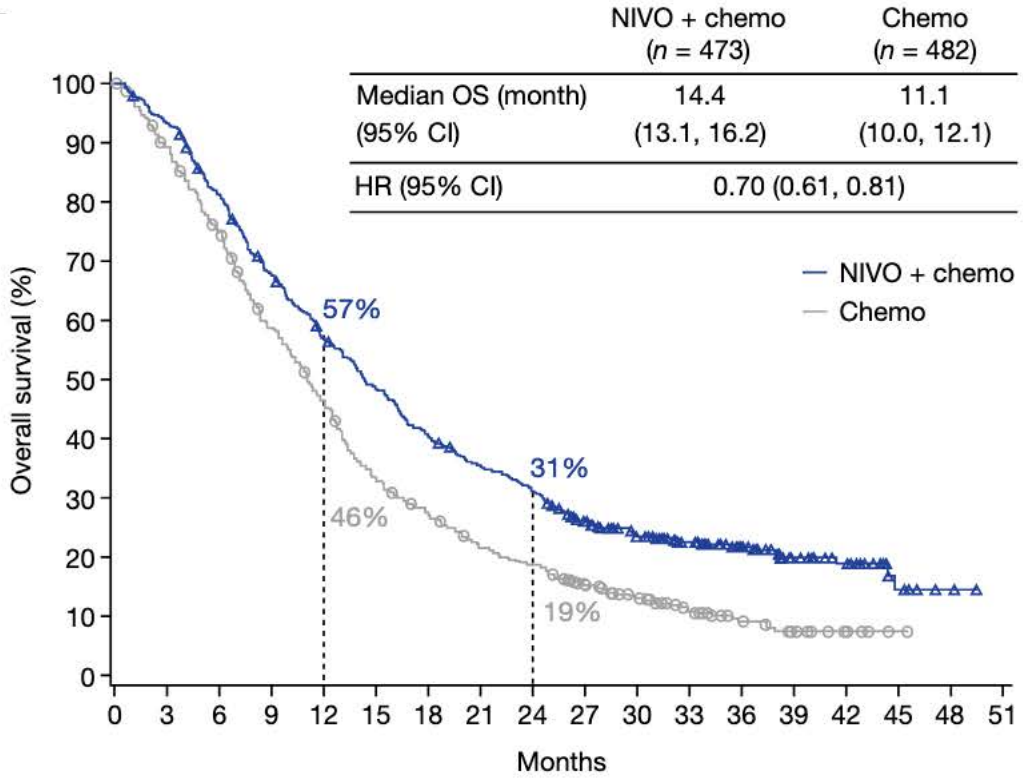
Published online: 23 March 2022

Open access

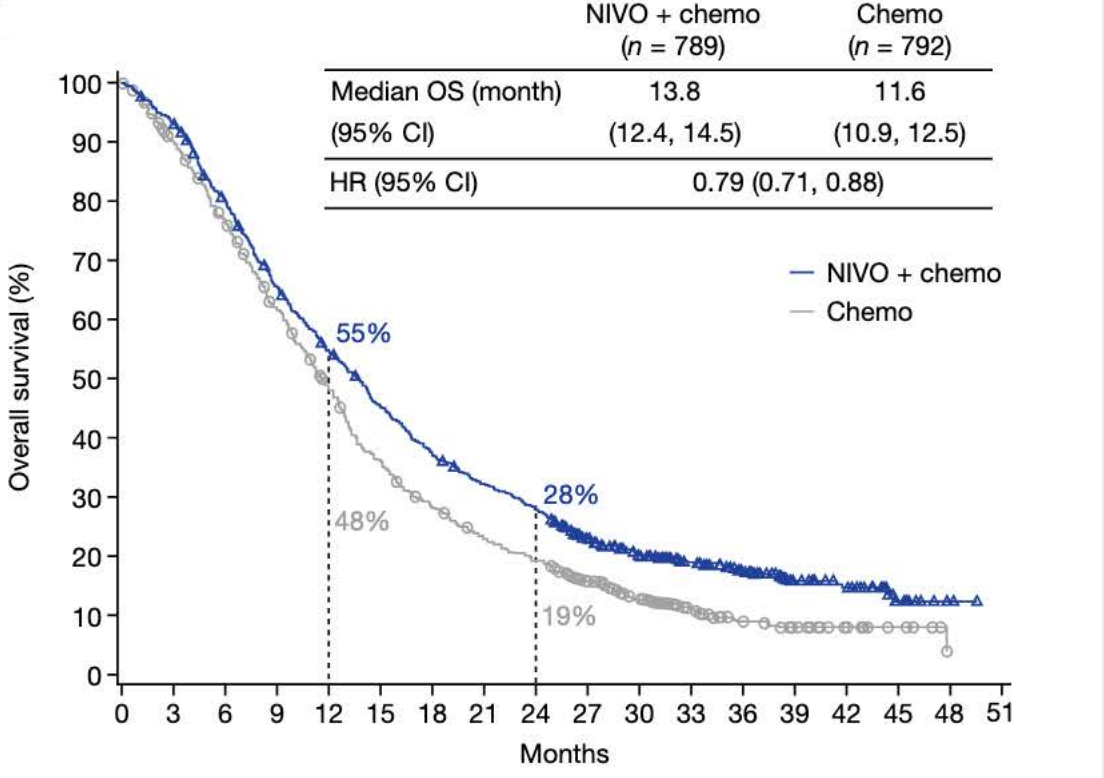
Kohei Shitara[1], Jaffer A. Ajani[2], Markus Moehler[3], Marcelo Garrido[4], Carlos Gallardo[5], Lin Shen[6], Kensei Yamaguchi[7], Lucjan Wyrwicz[8], Tomasz Skoczylas[9], Arinilda Campos Bragagnoli[10], Tianshu Liu[11], Mustapha Tehfe[12], Elena Elimova[13], Ricardo Bruges[14], Thomas Zander[15], Sergio 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

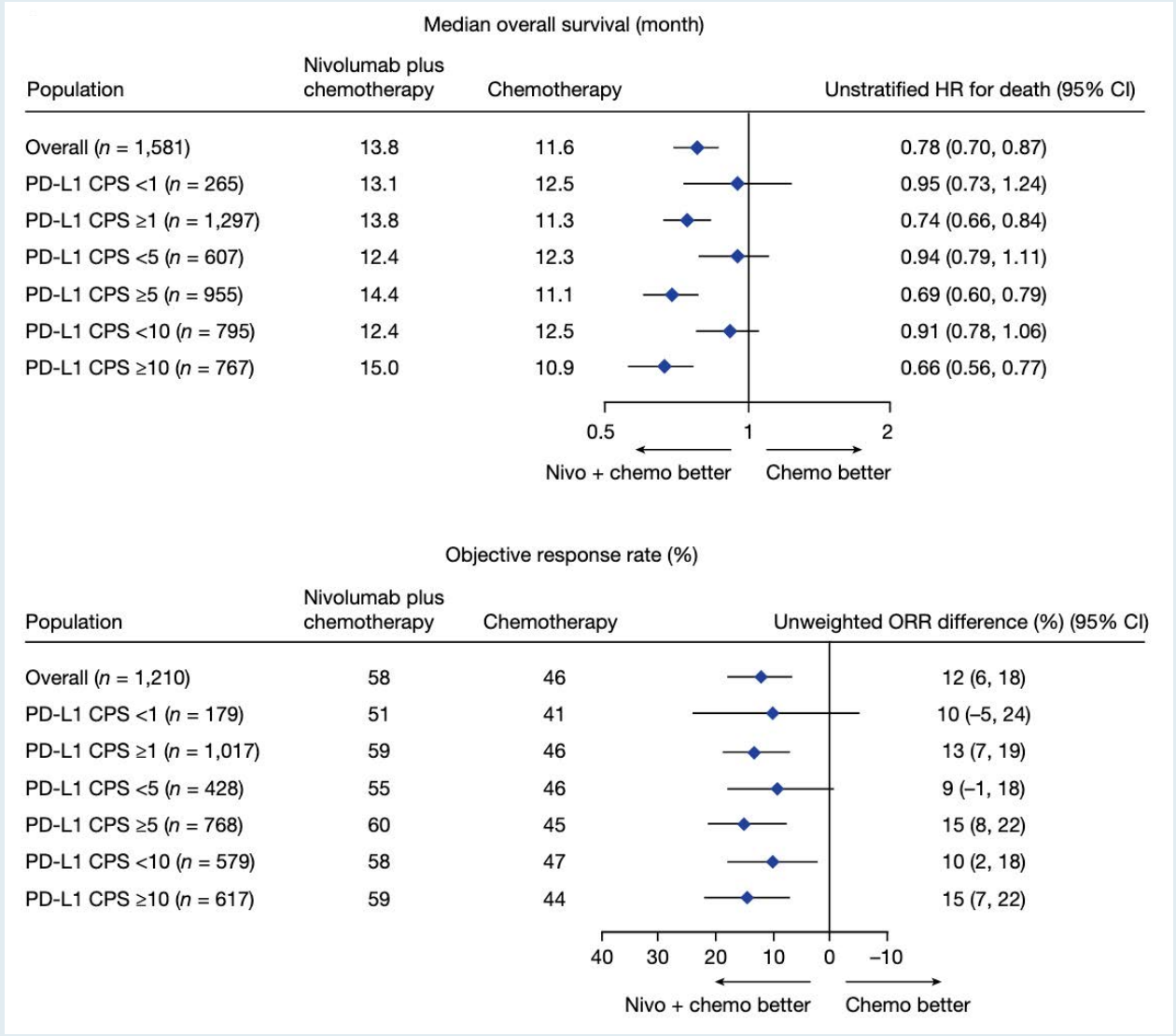


CPS = combined positive score

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



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

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

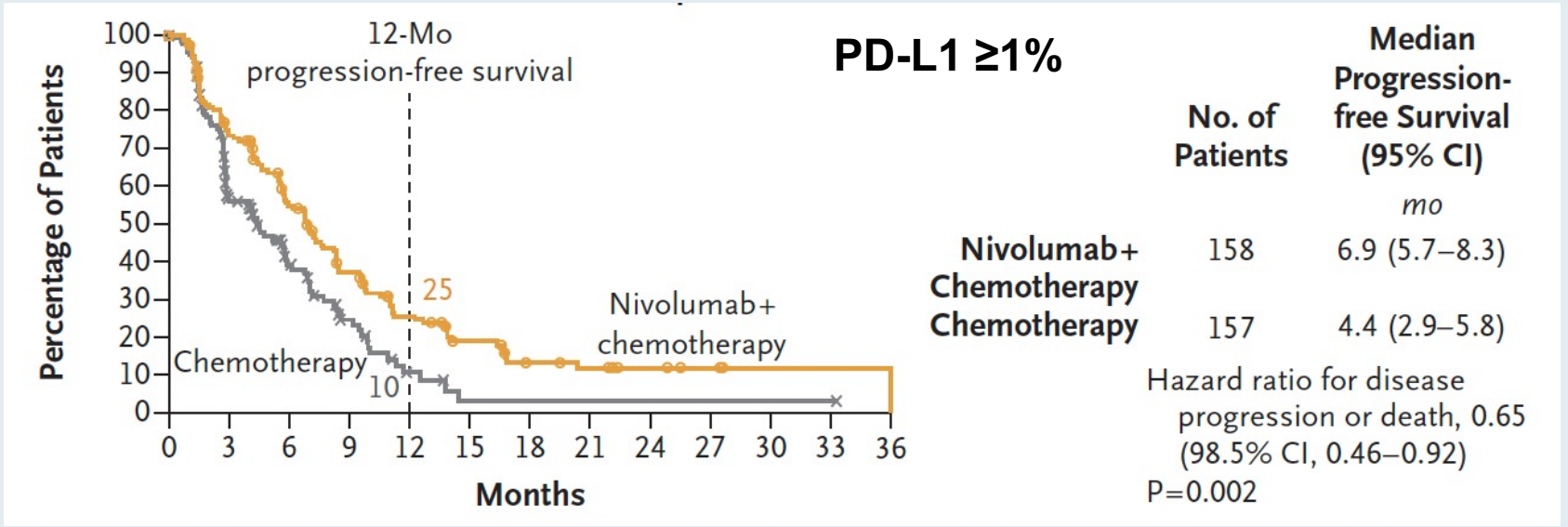
ORIGINAL ARTICLE

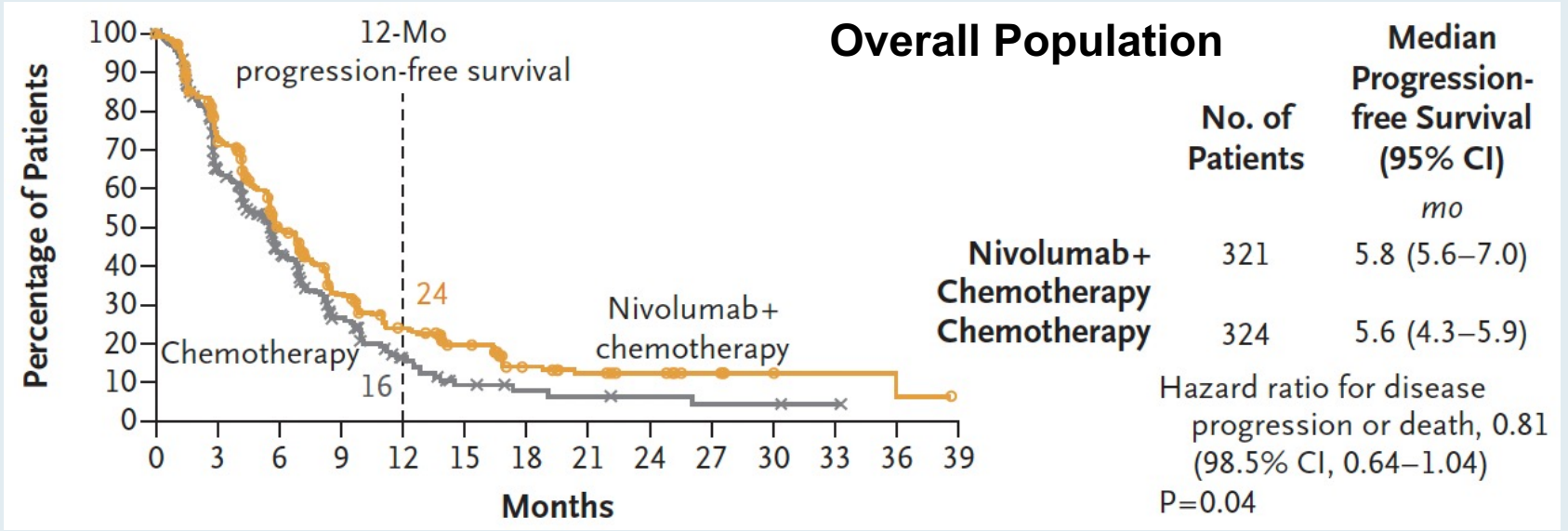
Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma

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.

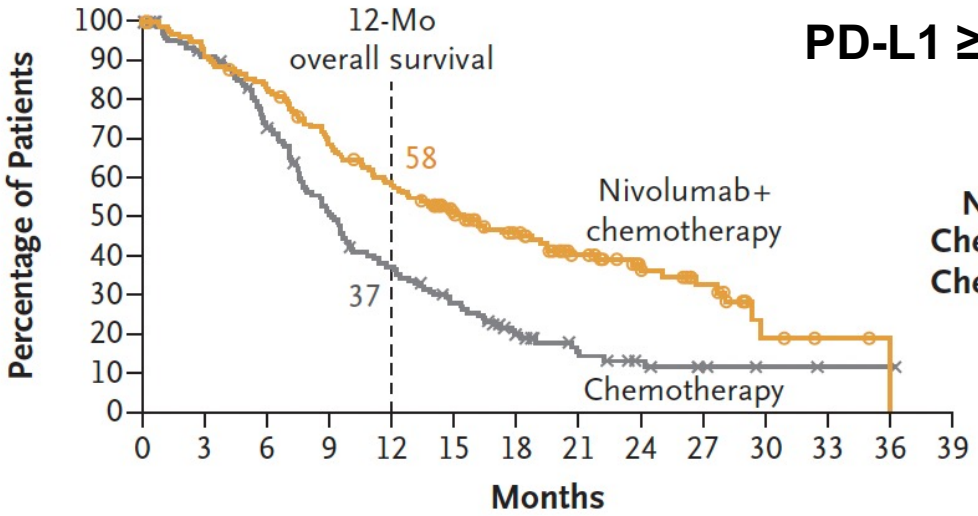
CheckMate 648: Progression-Free Survival for PD-L1 ≥1% and in the Overall Population – Nivolumab + Chemotherapy





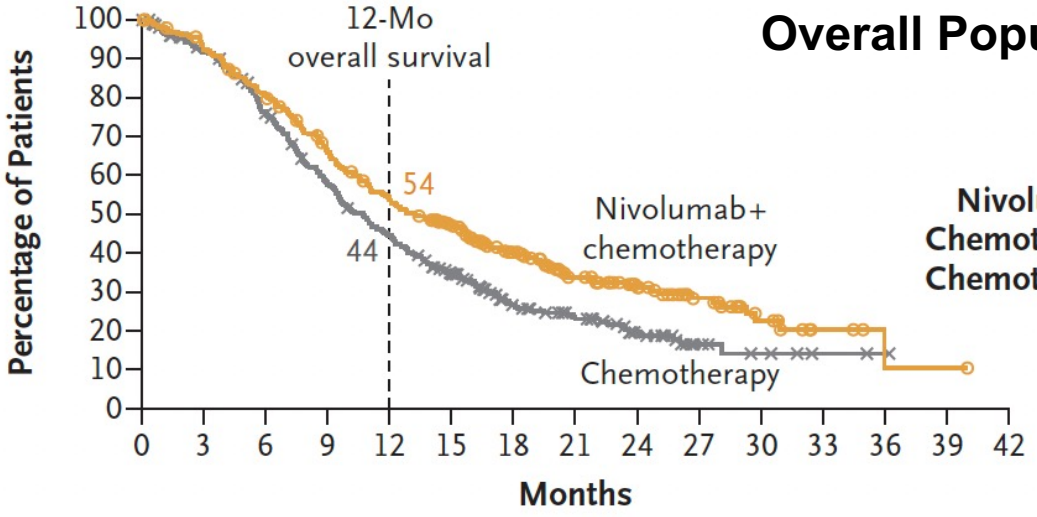
Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

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



	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



	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)

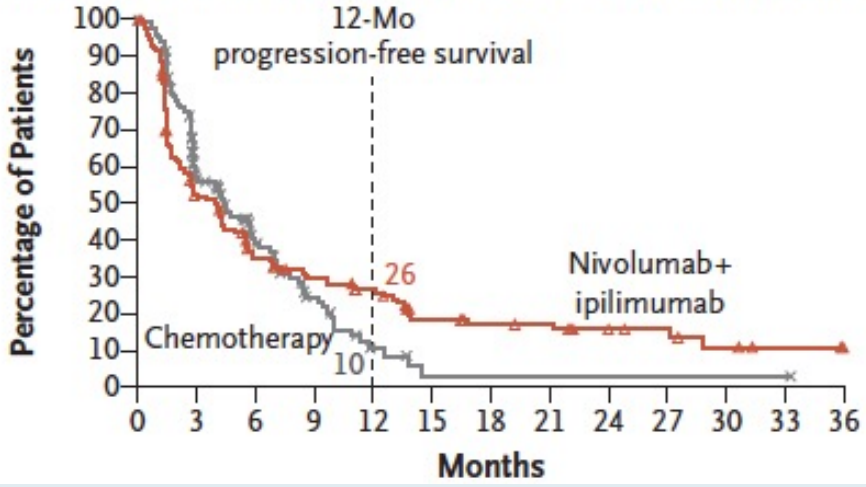
Hazard ratio for death, 0.74 (99.1% CI, 0.58–0.96)
P=0.002

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

RTP RESEARCH TO PRACTICE

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

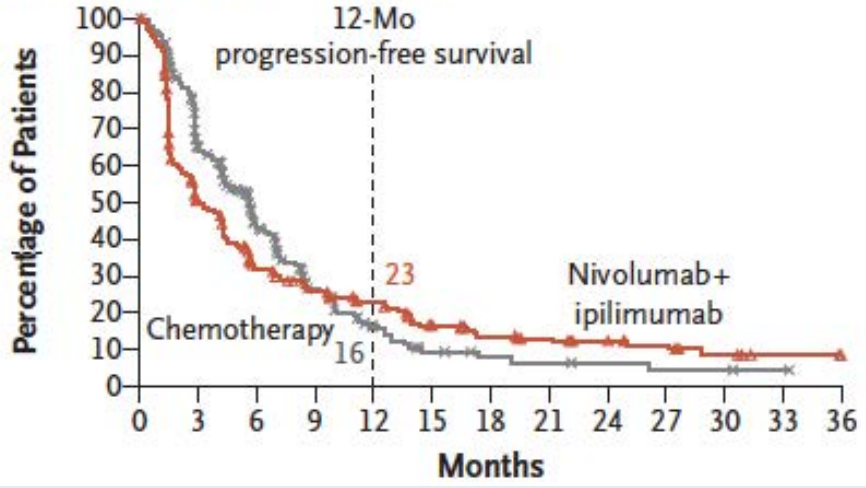
Progression-free Survival in Patients with Tumor-Cell PD-L1 Expression of ≥1%



	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



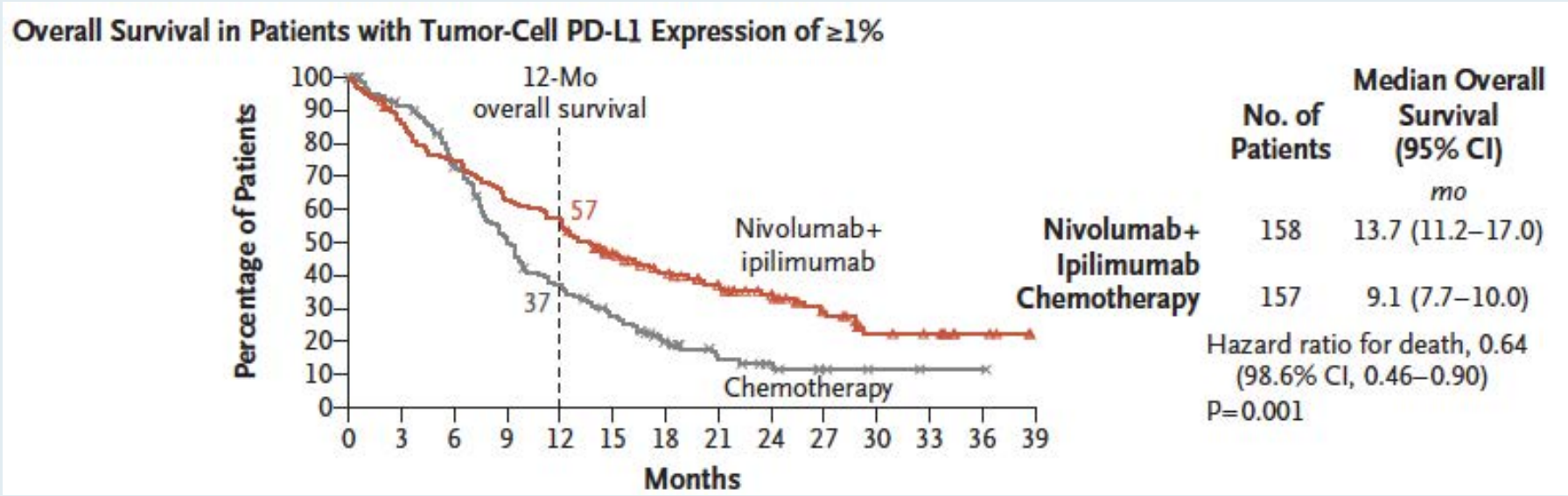
	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Nivolumab+ Ipilimumab	325	2.9 (2.7–4.2)
Chemotherapy	324	5.6 (4.3–5.9)

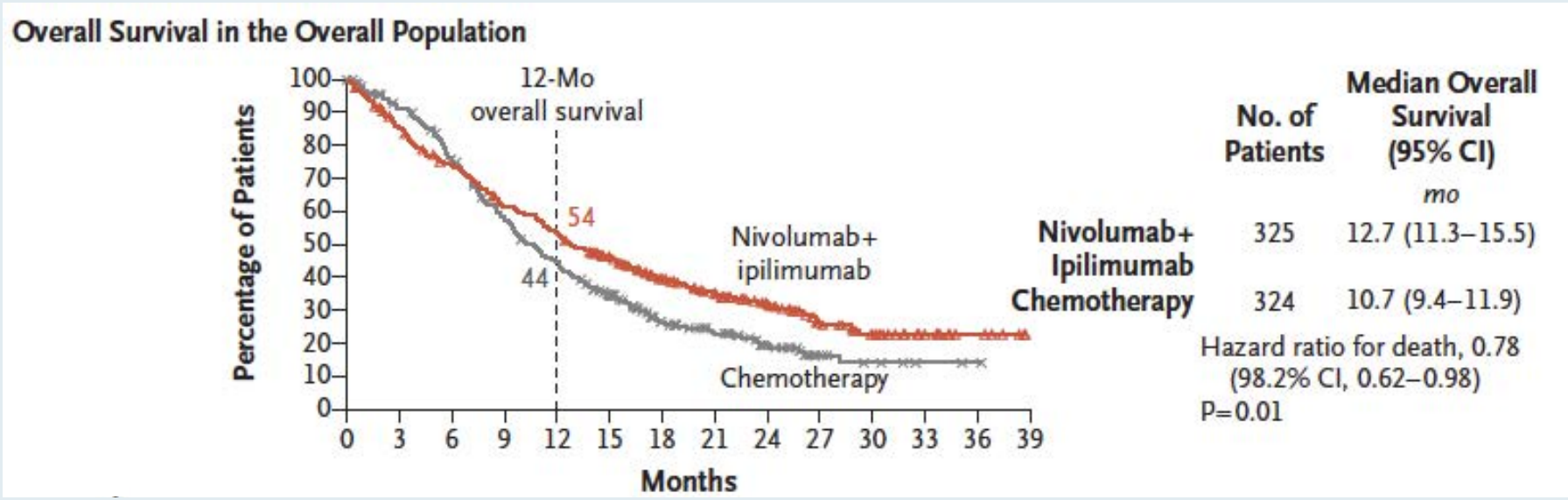
Hazard ratio for disease progression or death, 1.26 (95% CI, 1.04–1.52)
P value not tested

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

RTP RESEARCH TO PRACTICE

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.

Nivolumab (NIVO) plus Chemotherapy (Chemo) or Ipilimumab (IPI) vs Chemo as First-Line Treatment for Advanced Esophageal Squamous Cell Carcinoma (ESCC): Expanded Efficacy and Safety Analyses from CheckMate 648

Chau I et al.

ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-3.

2021 ASCO ANNUAL MEETING

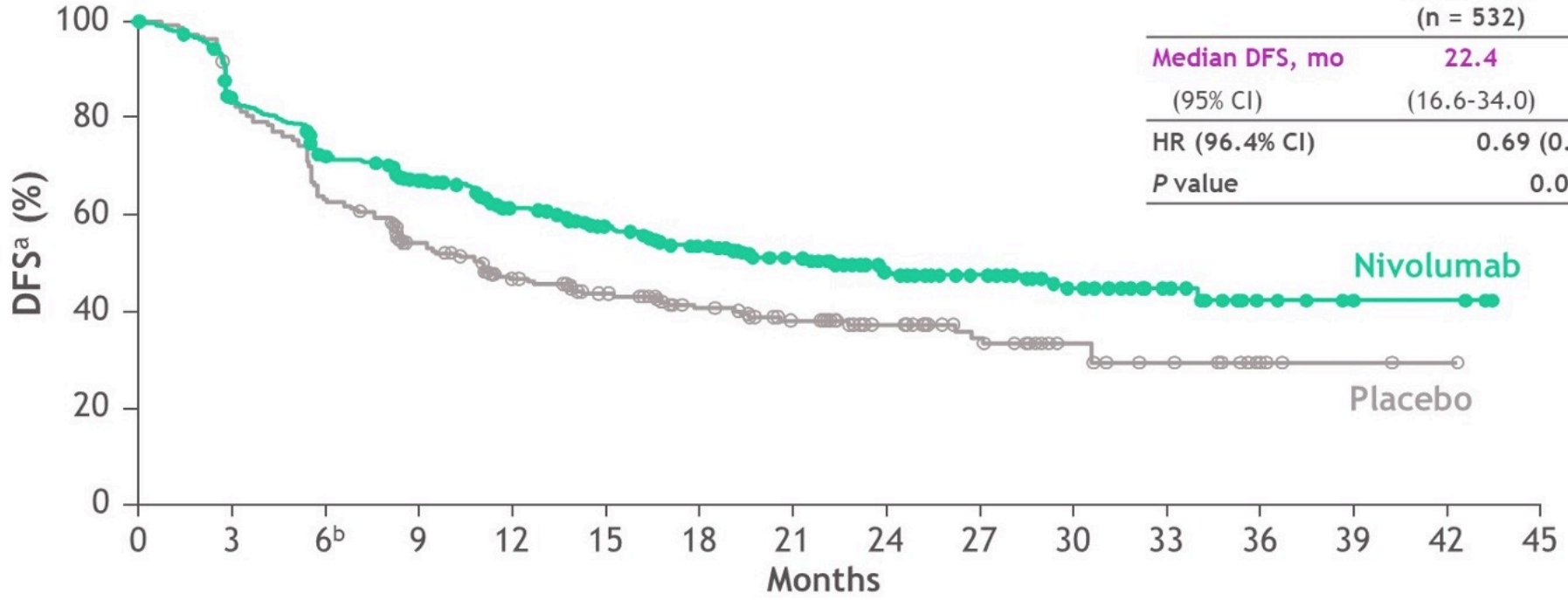
Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

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.

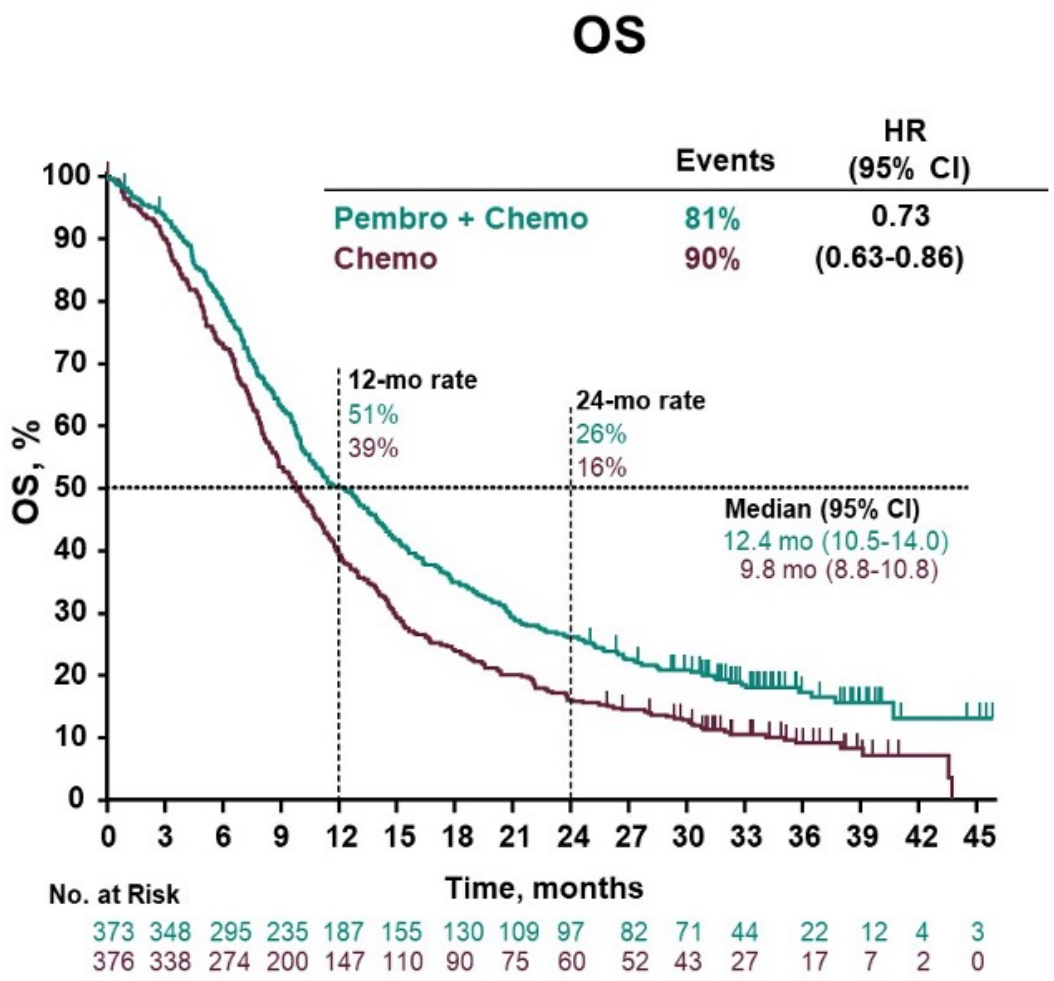
First-line Pembrolizumab Plus Chemotherapy Versus Chemotherapy in Advanced Esophageal Cancer: Longer-term Efficacy, Safety, and Quality-of-life Results From the Phase 3 KEYNOTE-590 Study

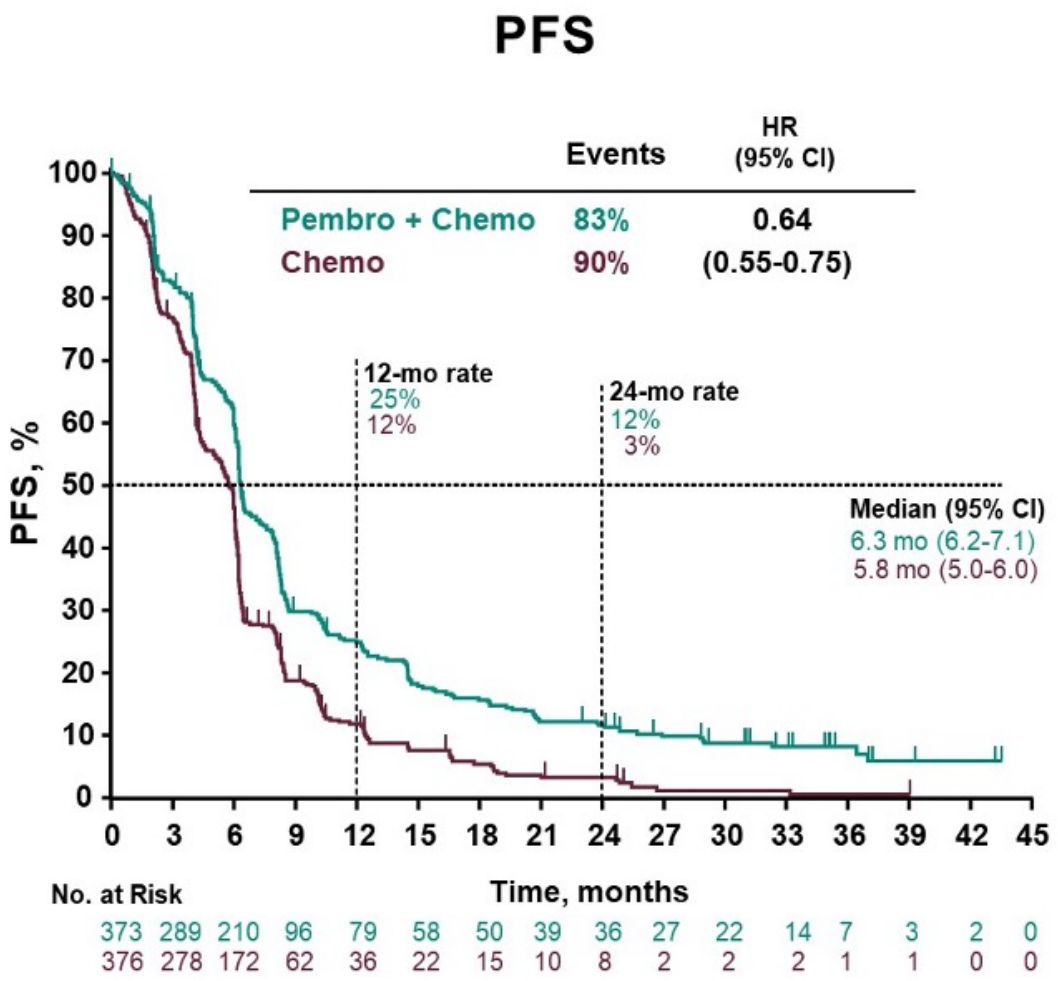
Jean-Philippe Metges,[1] Ken Kato,[2] Jong-Mu Sun,[3] Manish A. Shah,[4] Peter Enzinger,[5] Antoine Adenis,[6] Toshihiko Doi,[7] Takashi Kojima,[7] Zhigang Li,[8] Sung-Bae Kim,[9] Byoung Chul Cho,[10] Wasat Mansoor,[11] Shau-Hsuan Li,[12] Patrapim Sunpaweravong,[13] Maria Alsina Maqueda,[14] Gary L.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



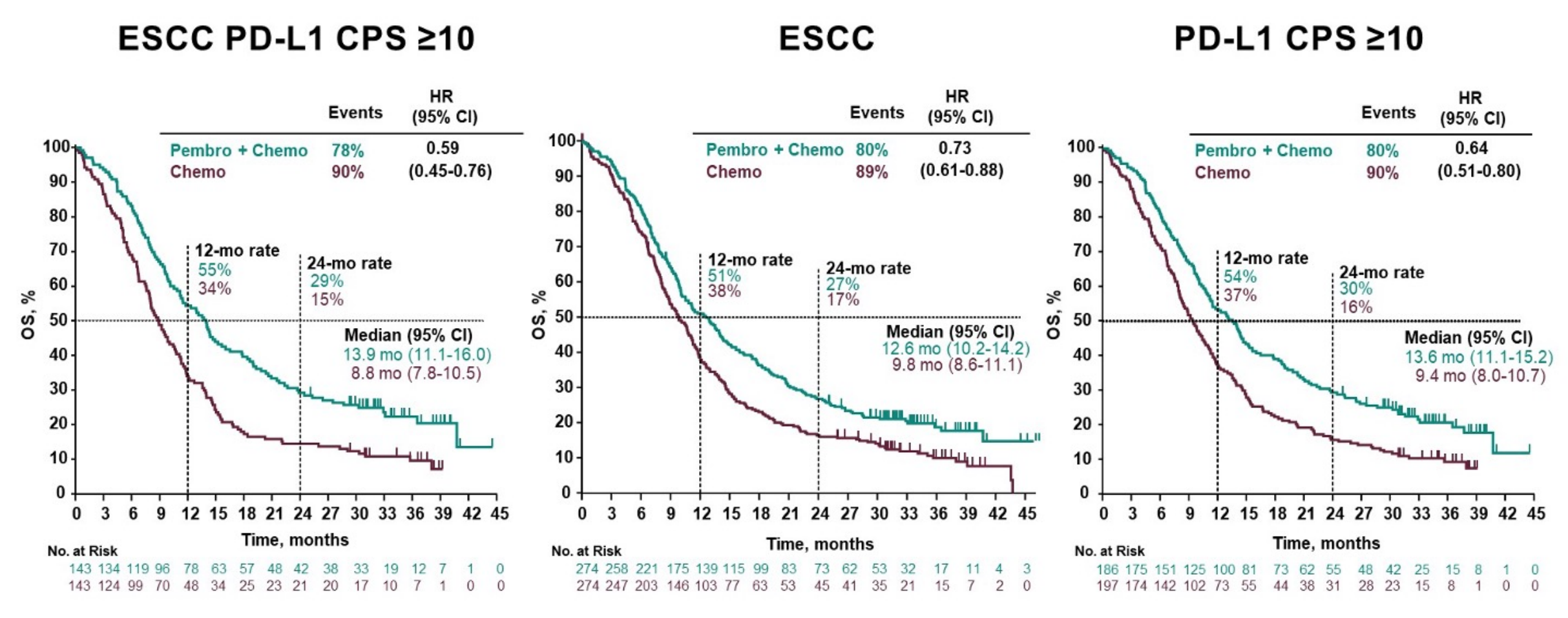


OS = overall survival; PFS = progression-free survival

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

RTP RESEARCH TO PRACTICE

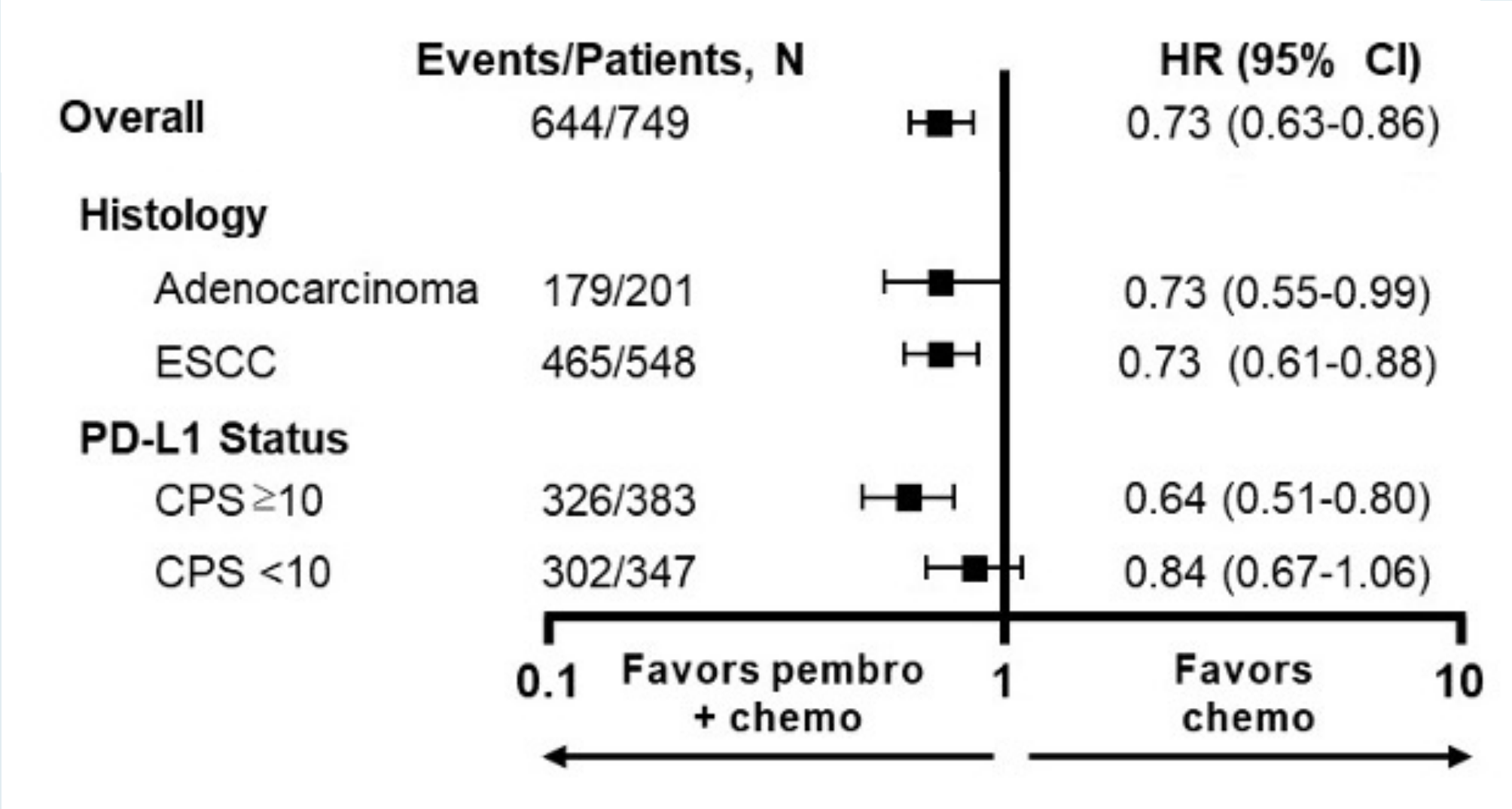
KEYNOTE-590: Overall Survival (OS) in Prespecified Subgroups



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.

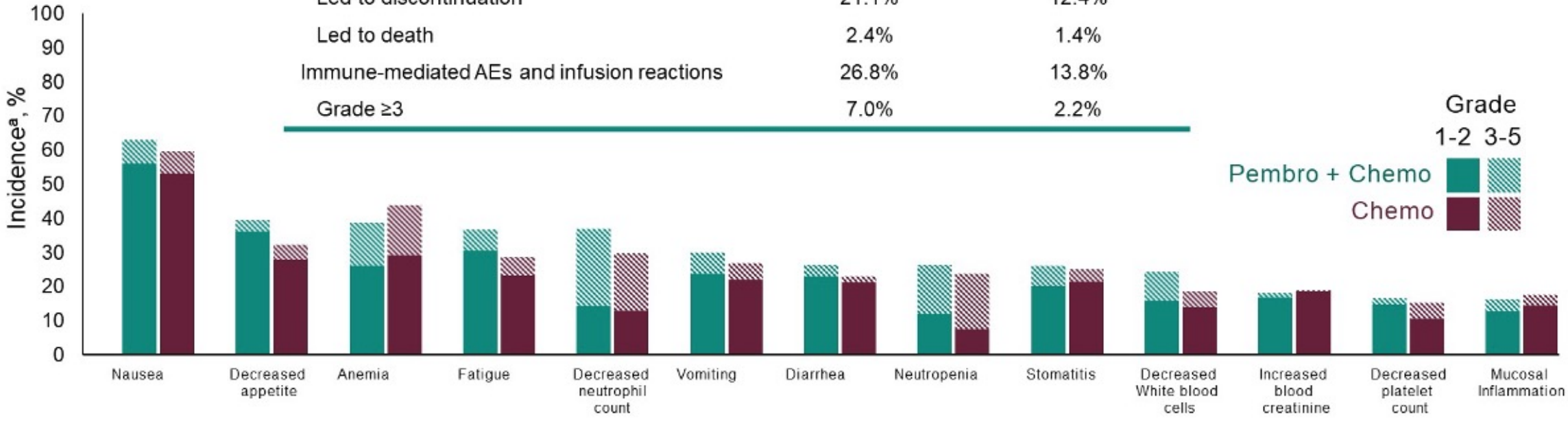
KEYNOTE-590: Antitumor Response

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%



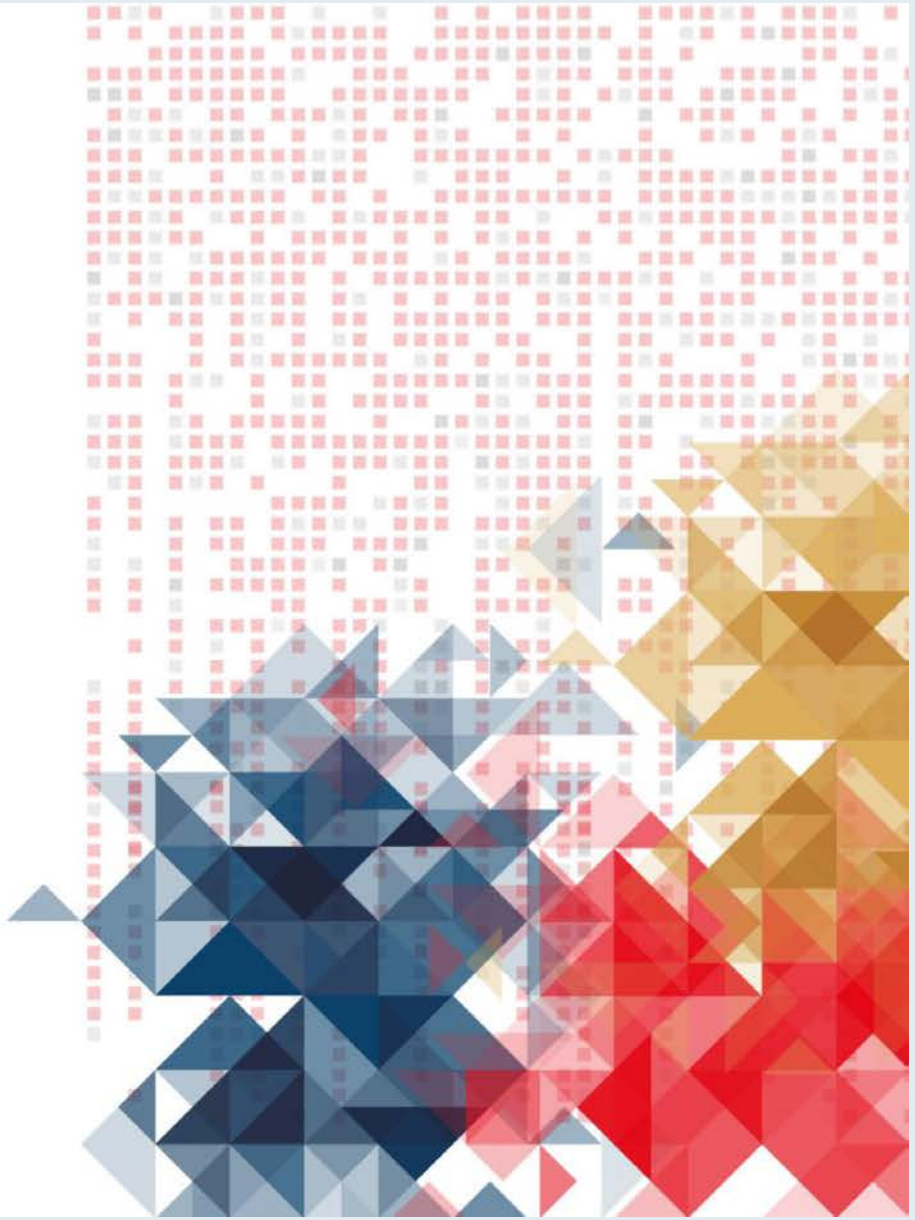
Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

2021 ESMO congress

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



Abstract LBA53

RTP RESEARCH TO PRACTICE

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).

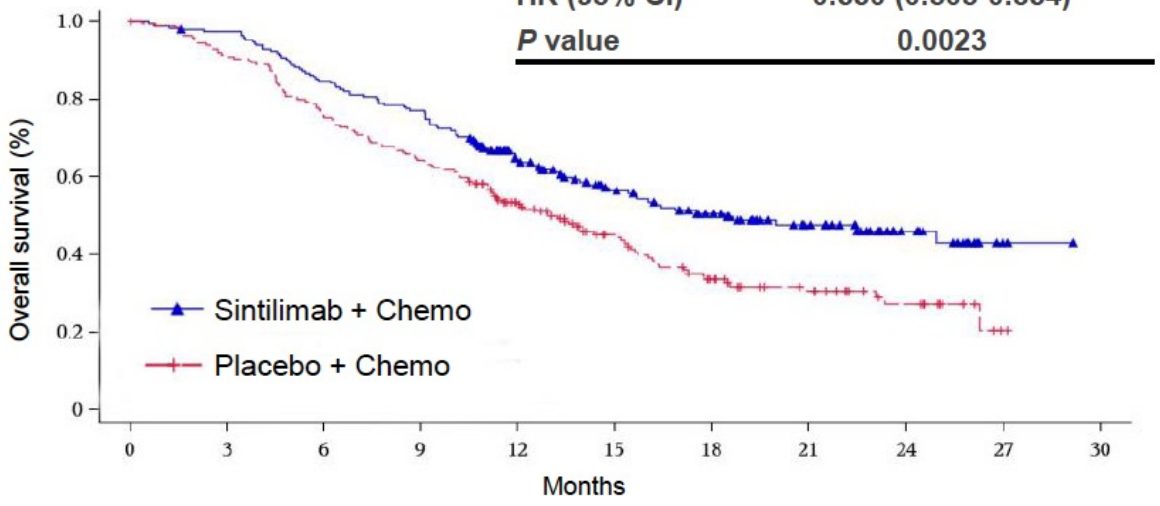
[a] ClinicalTrial.gov number, NCT03745170; [b] Sintilimab 3 mg/kg for body weight <60 kg, 200 mg for ≥60 kg; Oxaliplatin 130 mg/m^2 IV; Capecitabine 1000 mg/m^2 PO Bid d1-14;
[c] Until progressive disease, intolerable toxicity, withdrawal of consent. Treatment is given for a maximum of 2 years.

Xu J et al. ESMO 2021;Abstract LBA53.

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

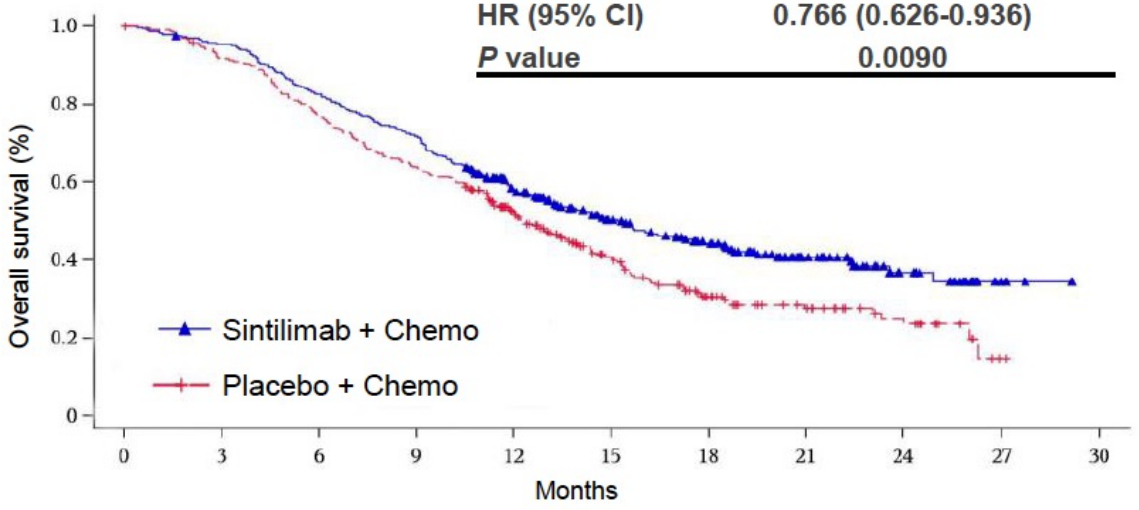
PD-L1 CPS ≥5

	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

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]

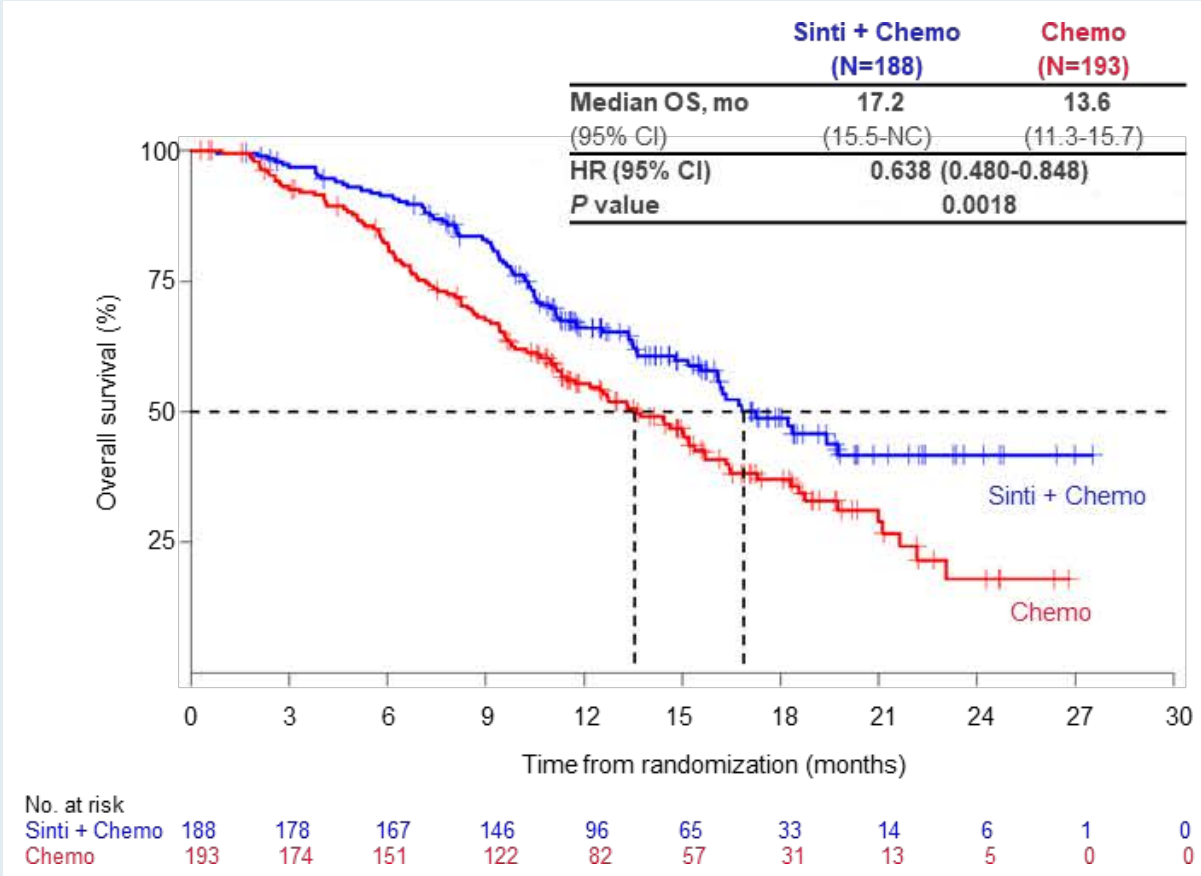
[1]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China, [2]Department of Gastrointestinal Oncology, Peking University Cancer Hospital & Institute, Beijing, China, [3]Department of Oncology, The Affiliated 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

ESMO 2021;Abstract LBA52.

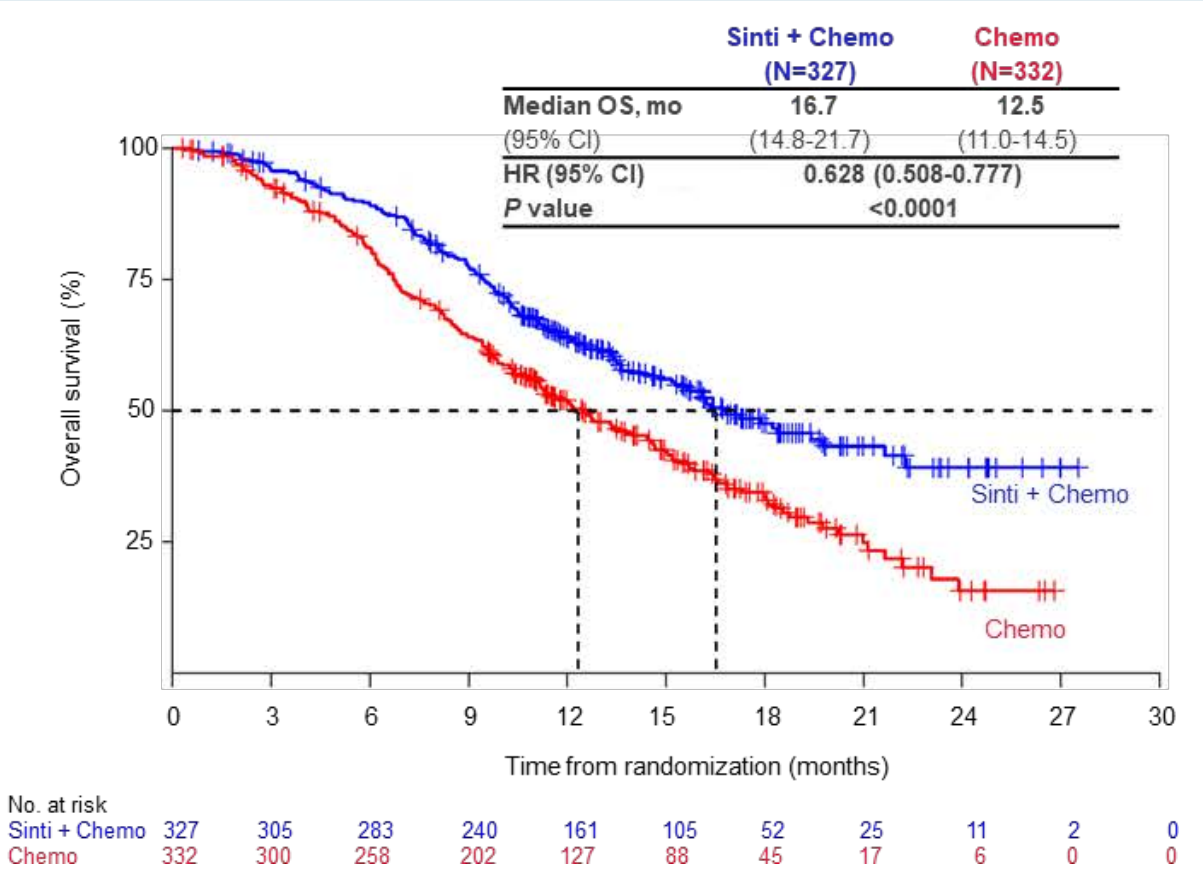
RTP RESEARCH TO PRACTICE

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

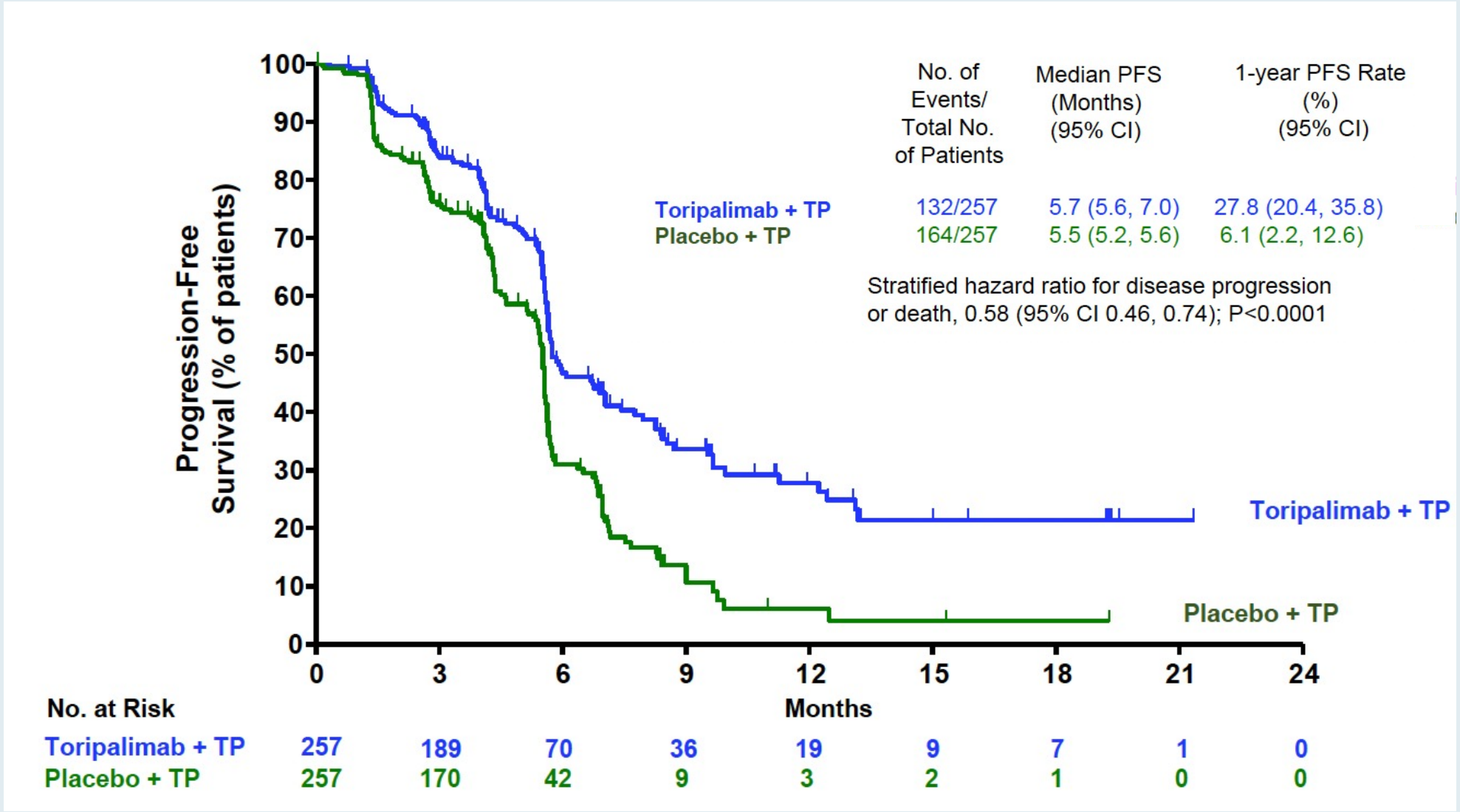
CellPress

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**

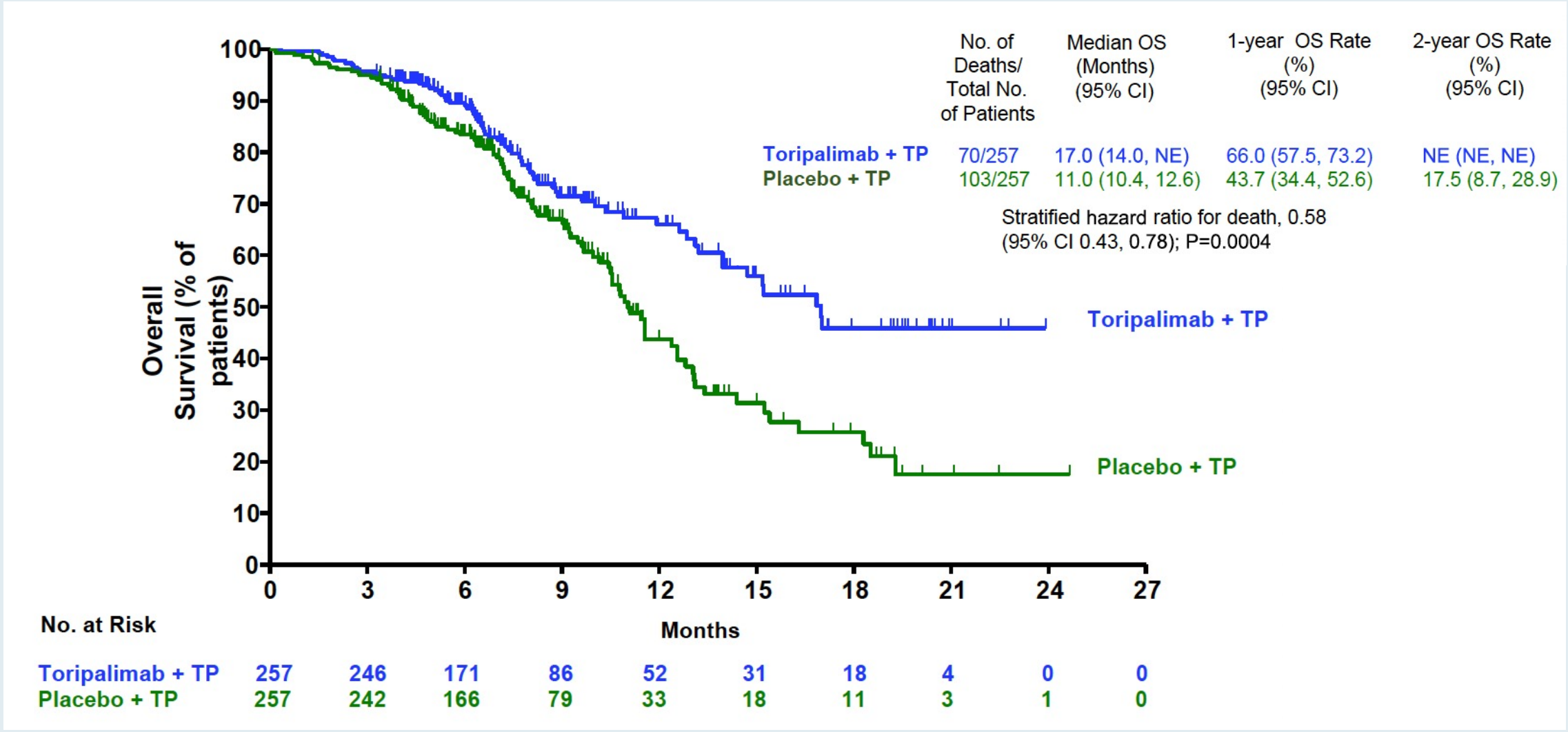
JUPITER-06: Progression-Free Survival (BICR, ITT Population)



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)

Adverse event, no. of patients (%)	Toripalimab + TP (n = 257) no. (%)		Placebo + TP (n = 257) no. (%)	
	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.

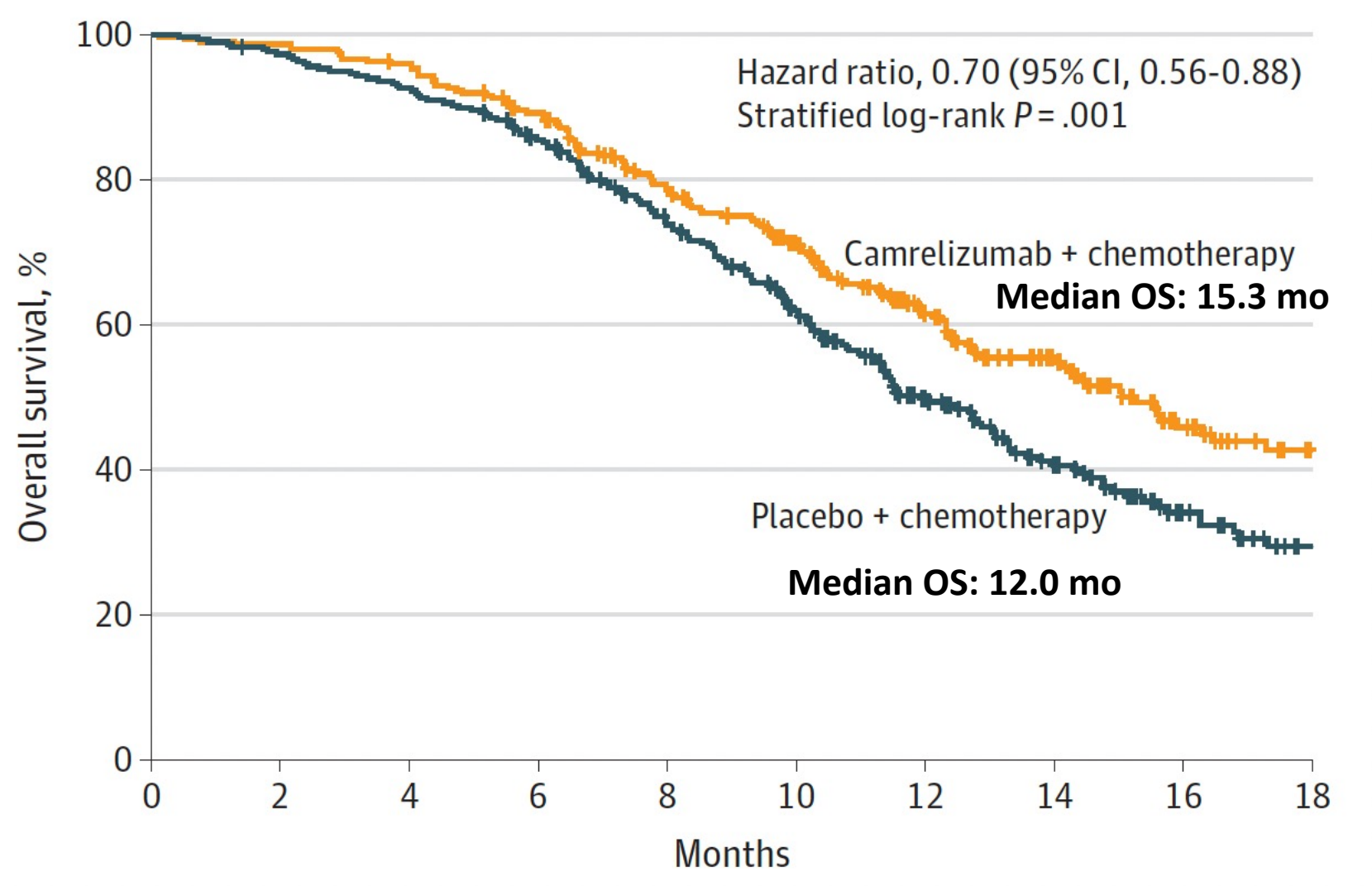
JAMA | Original Investigation

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

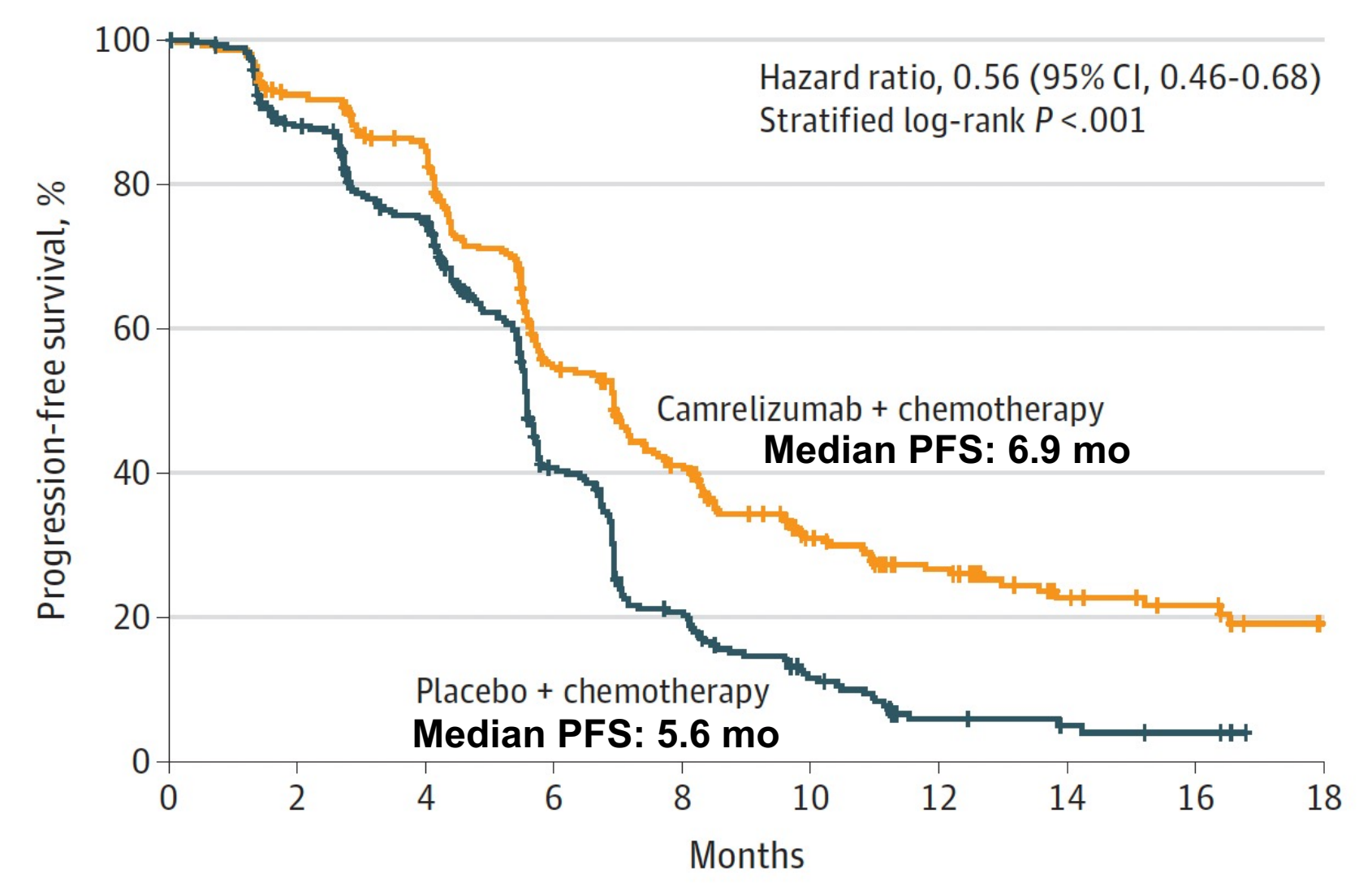
ESCORT-1st: Overall Survival (Coprimary Endpoint)



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

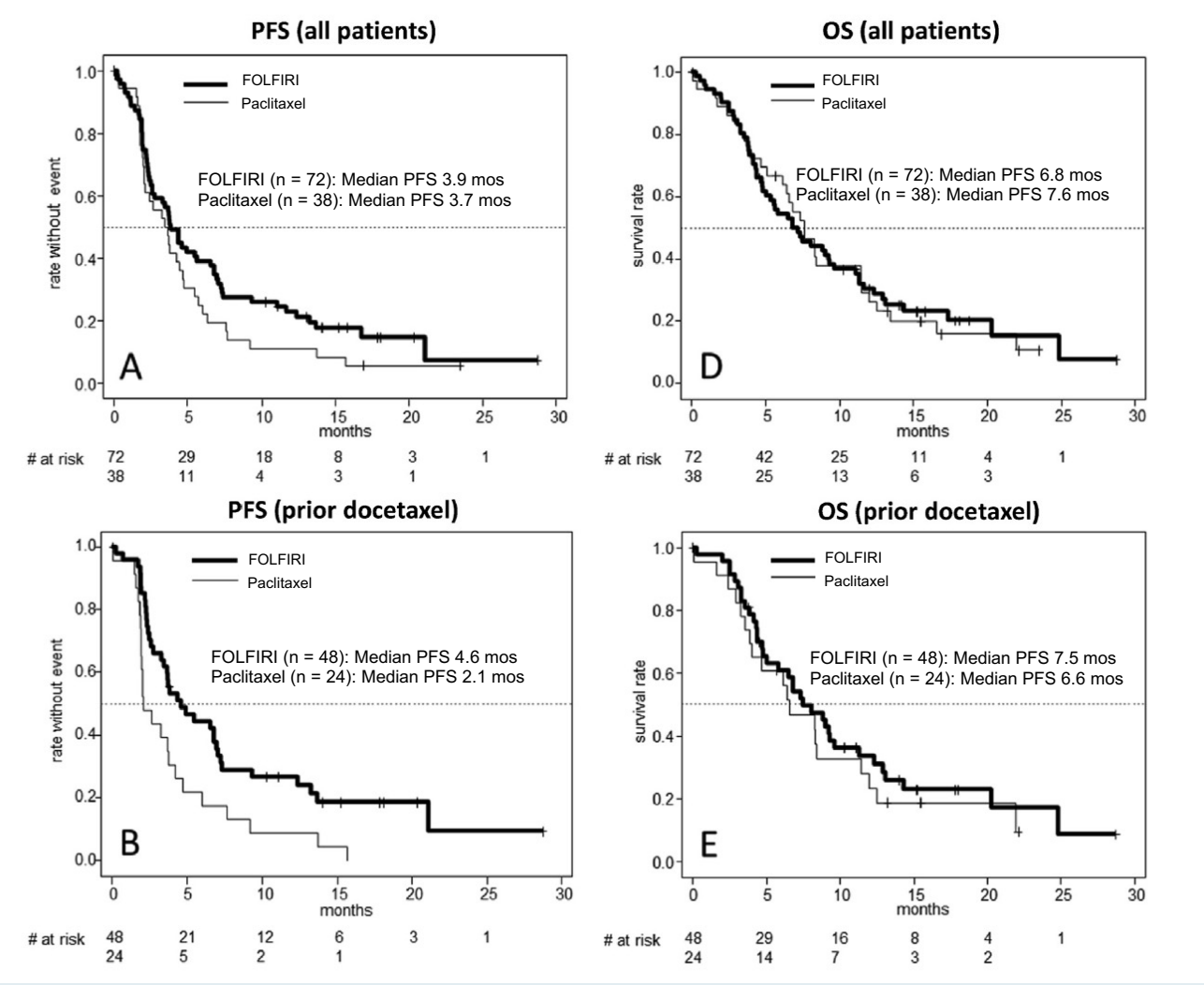
journal homepage: www.ejcancer.com

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



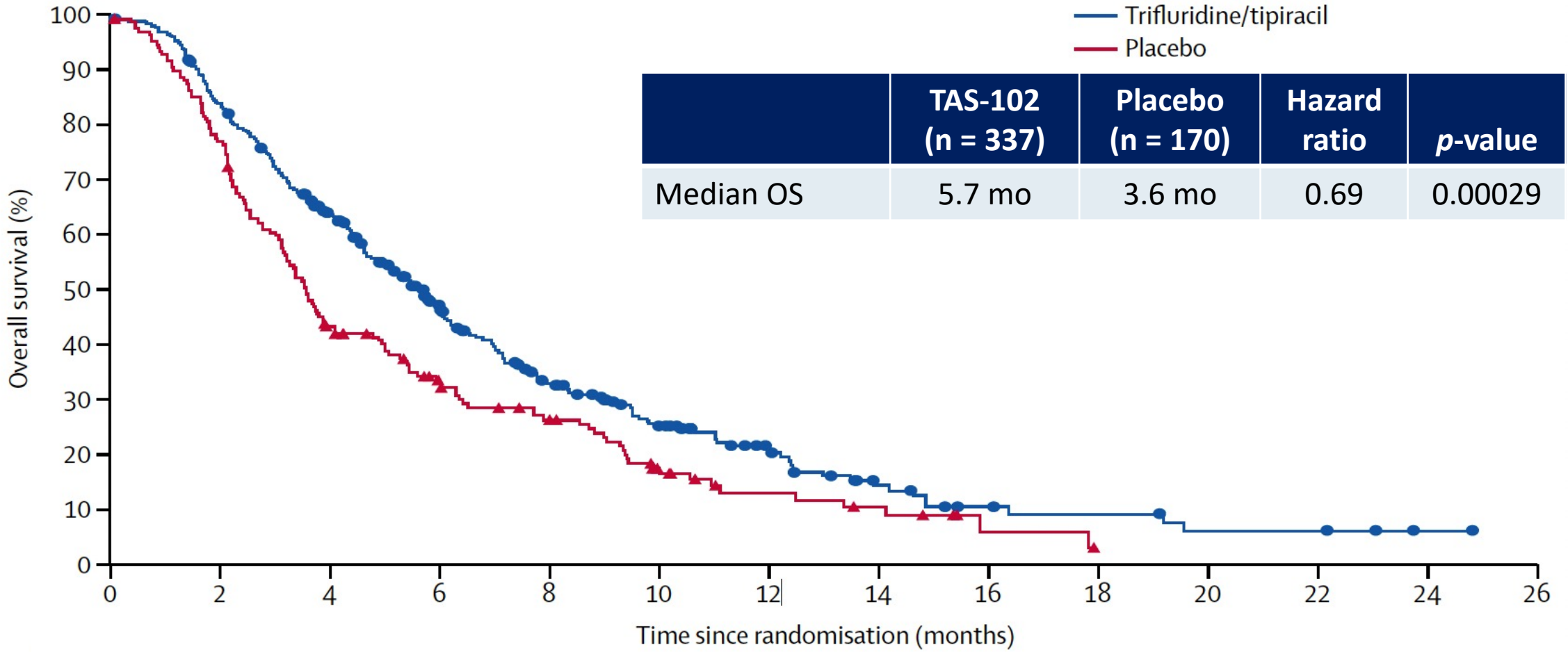
Lorenzen S et al. *Eur J Cancer* 2022;165:48-57.

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.

Phase III RATIONALE 306 Trial of First-Line Tislelizumab with Chemotherapy for Advanced Esophageal Cancer Meets Its Primary Overall Survival Endpoint

Press Release – April 27, 2022

"[Positive topline results were announced] from an interim analysis of the Phase III RATIONALE 306 study, which showed anti-PD-1 immune checkpoint inhibitor tislelizumab plus chemotherapy significantly improved overall survival (OS) compared to chemotherapy in patients with previously untreated unresectable, locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC), regardless of PD-L1 expression. These data will be submitted to regulatory authorities, and will be presented at an upcoming medical meeting.

RATIONALE 306 (NCT03783442) is a multi-regional Phase III, randomized, placebo-controlled, double-blind study of tislelizumab in combination with chemotherapy versus chemotherapy alone in patients with unresectable, locally advanced recurrent or metastatic ESCC. Approximately 649 study participants were randomized 1:1 to receive either tislelizumab plus chemotherapy or chemotherapy alone. The primary endpoint is OS. Secondary endpoints include progression-free survival, objective response rate, duration of response, health-related quality of life measures and safety."

https://www.novartis.com/news/media-releases/novartis-tislelizumab-plus-chemotherapy-significantly-improved-overall-survival-first-line-treatment-advanced-esophageal-cancer-phase-iii-study

RATIONALE-306: Randomized, Global, Phase 3 Study of Tislelizumab plus Chemotherapy versus Chemotherapy as First-Line Treatment for Locally Advanced Unresectable or Metastatic Esophageal Squamous Cell Carcinoma (ESCC)

Yoon H et al.

ESMO World Congress on Gastrointestinal Cancer 2022;Abstract LBA-1.

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

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 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

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, MSI-high squamous cell carcinoma of the esophagus?

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

RTP RESEARCH TO PRACTICE

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

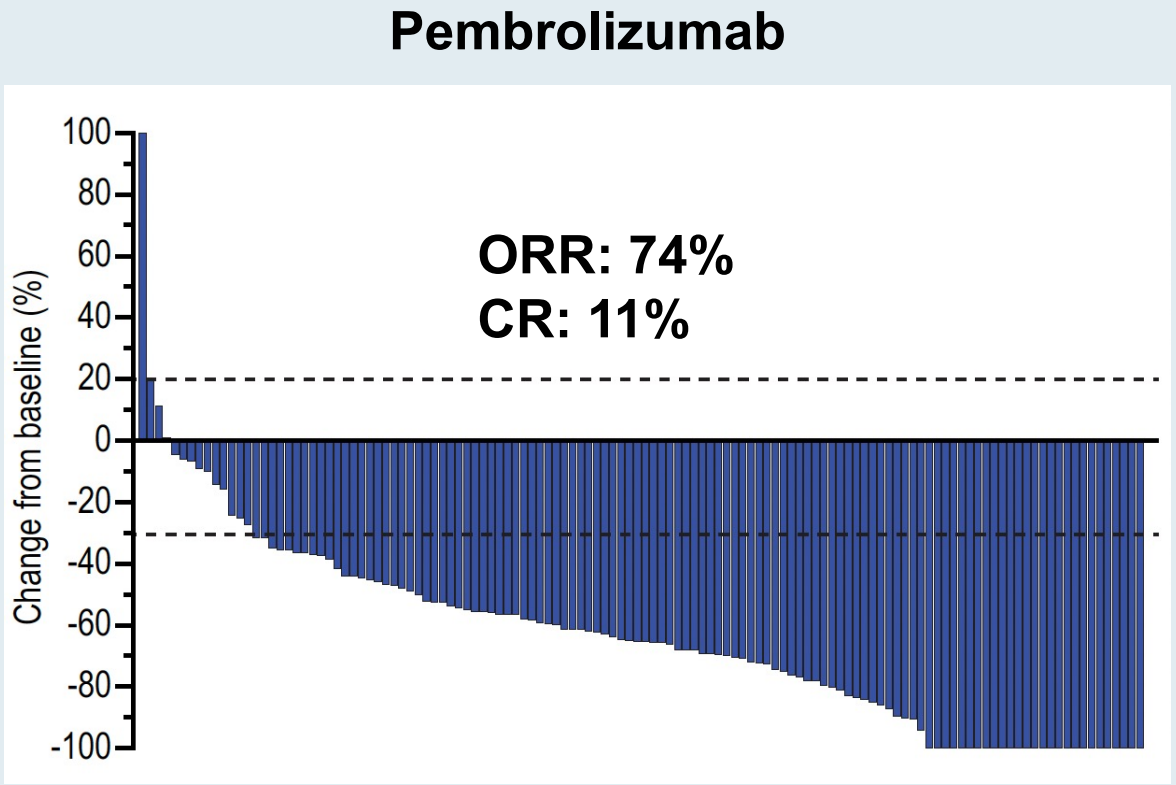
Received: 25 May 2021

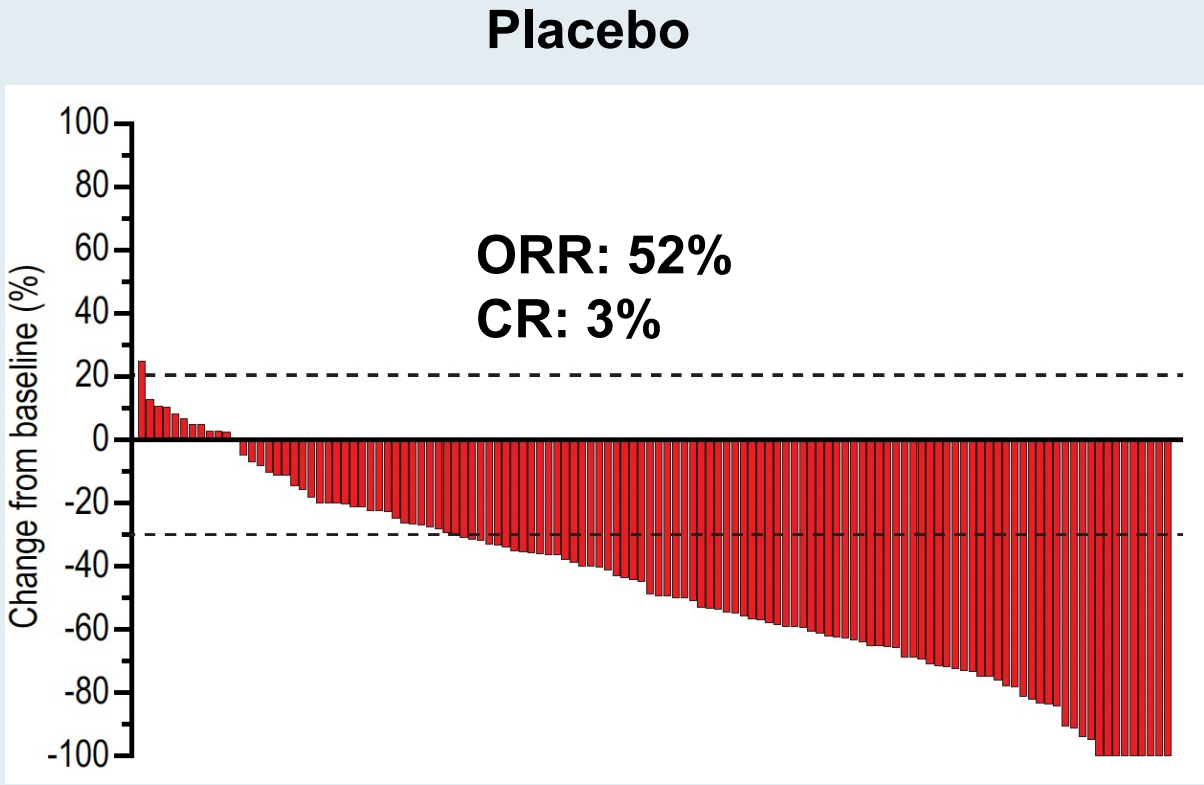
Accepted: 30 September 2021

Published online: 15 December 2021

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.

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.

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)

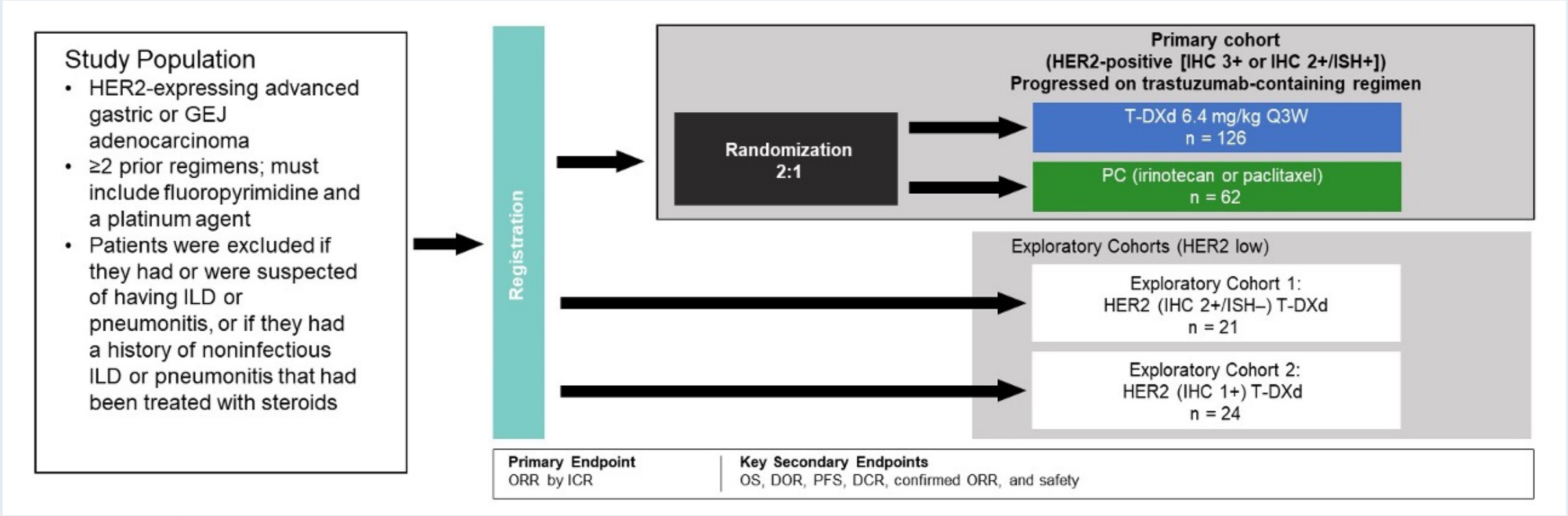
Kensei Yamaguchi

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

DESTINY-Gastric01 Randomized, Phase II Study Design

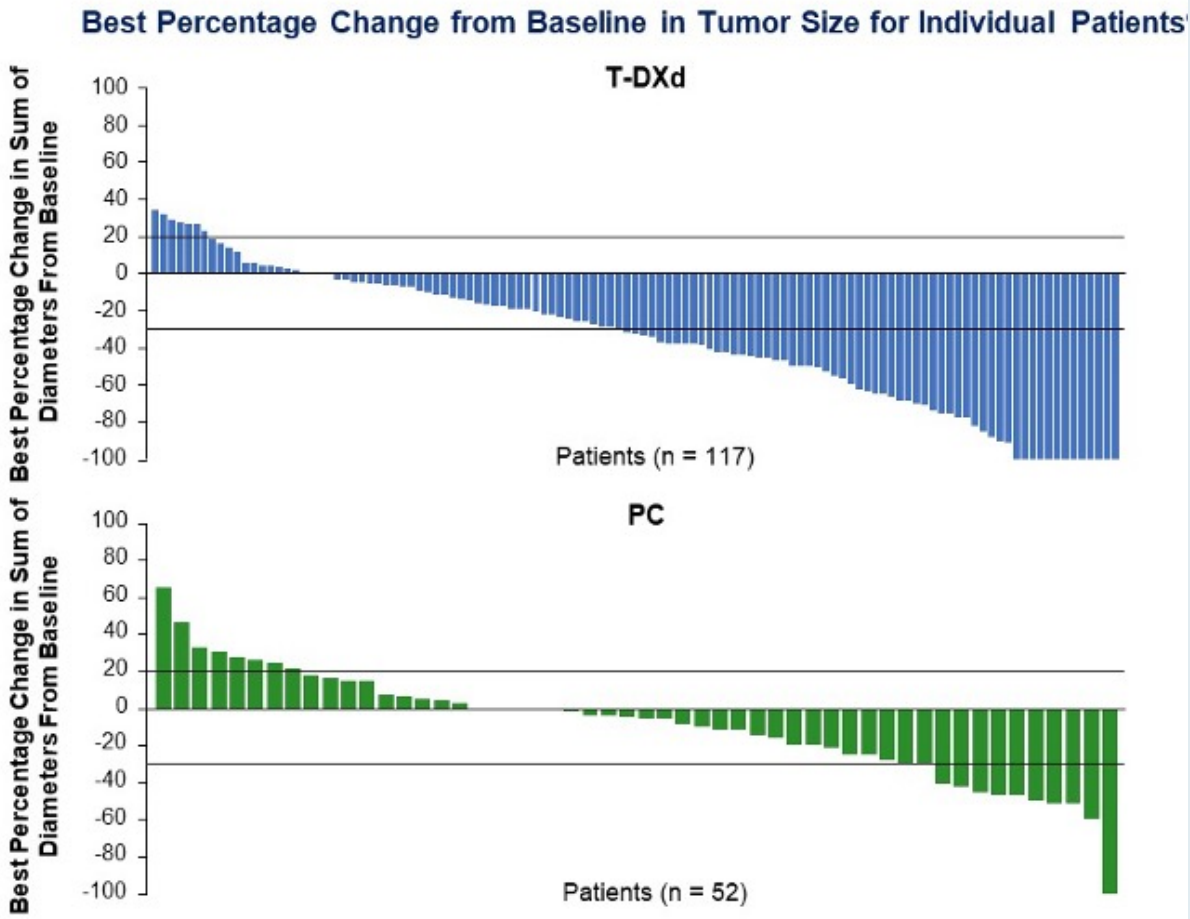


PC = physician's choice

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

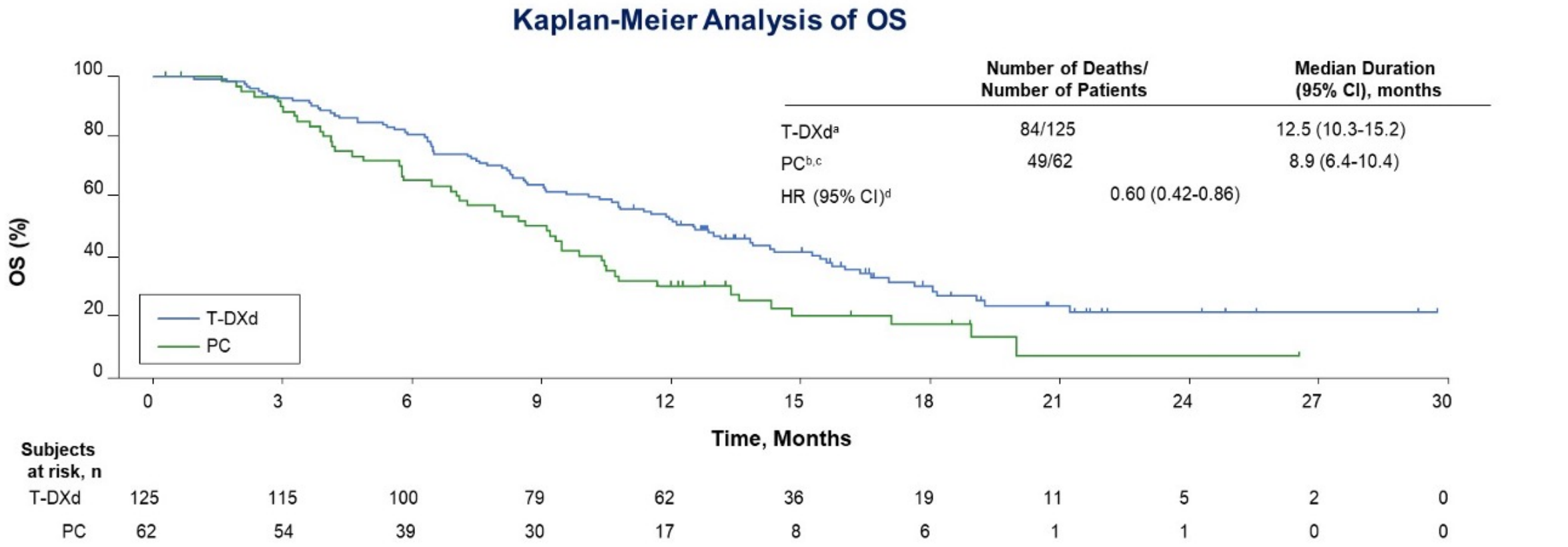
DESTINY-Gastric01: Antitumor Activity

	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.

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.

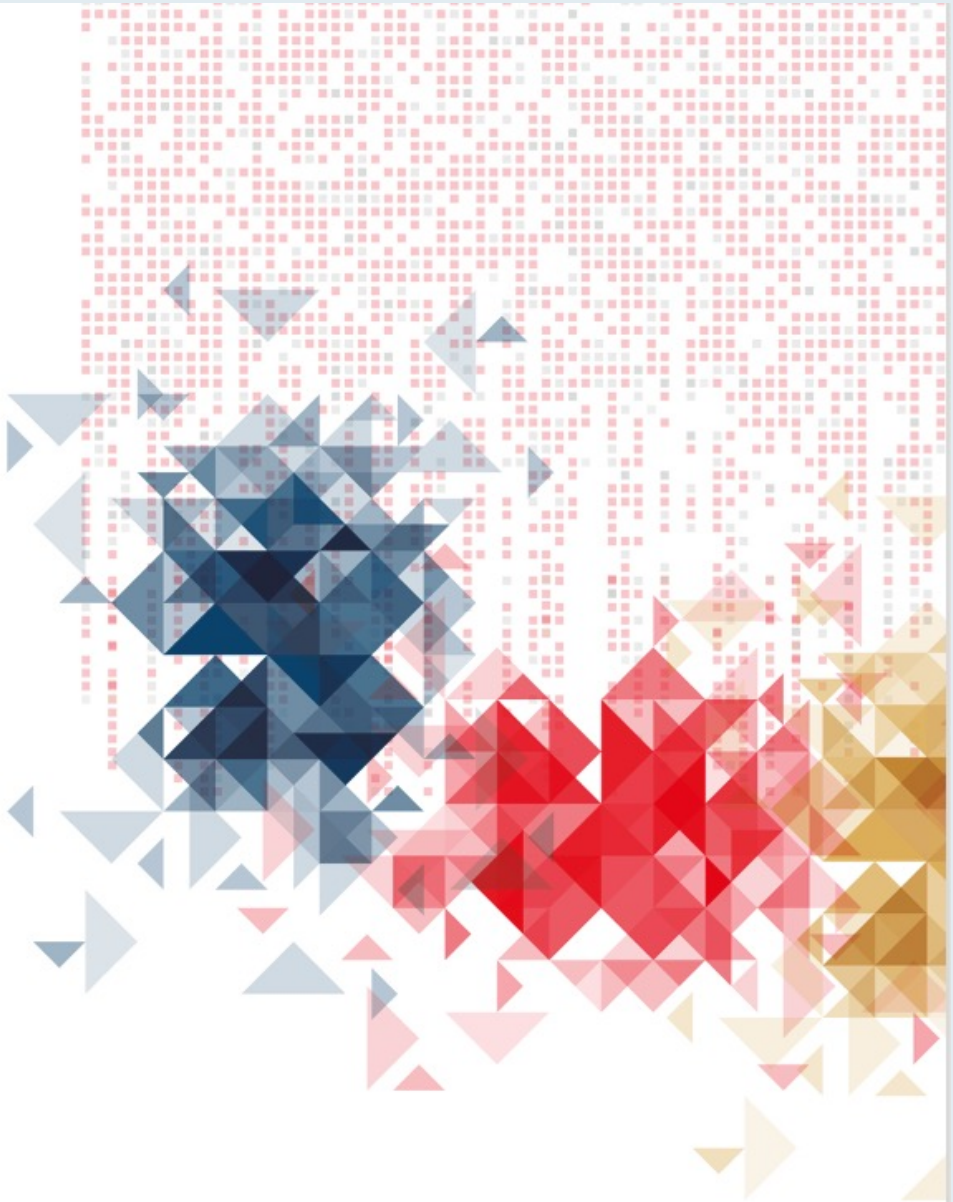
2021 ESMO congress

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



Abstract LBA55

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

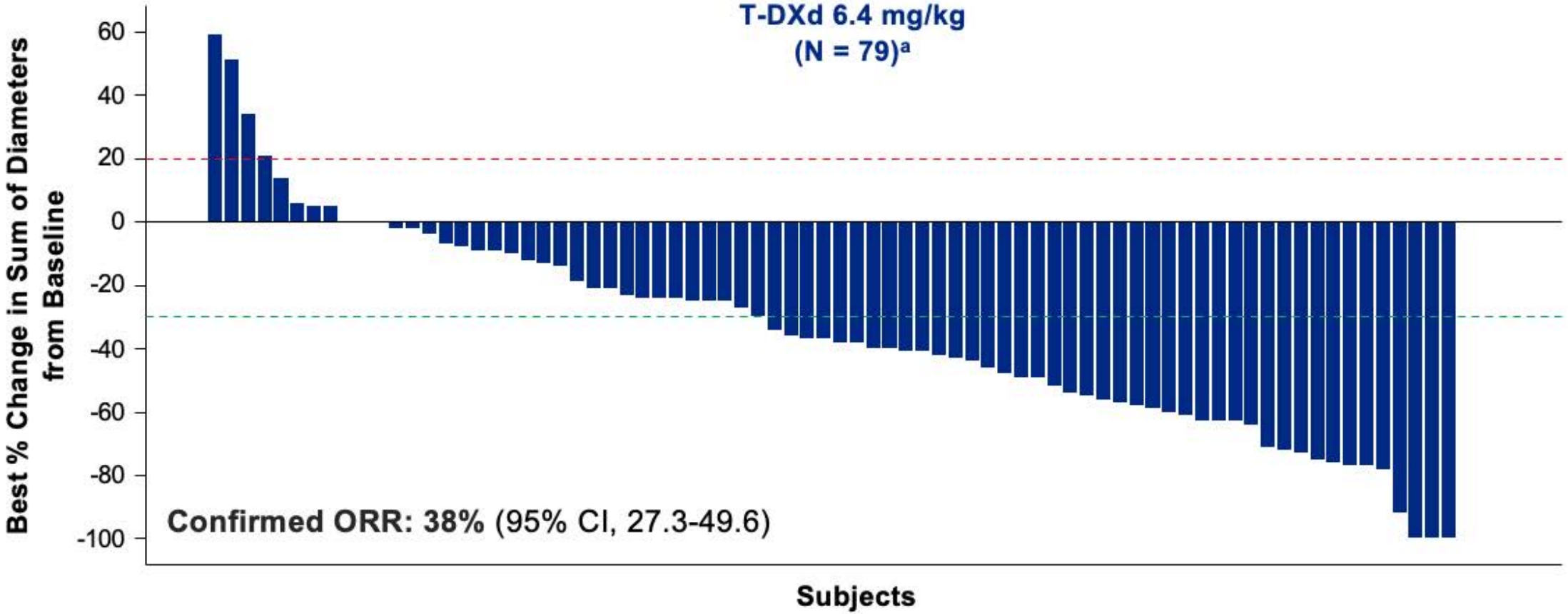
Secondary endpoints[b]

- 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.

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.

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

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)

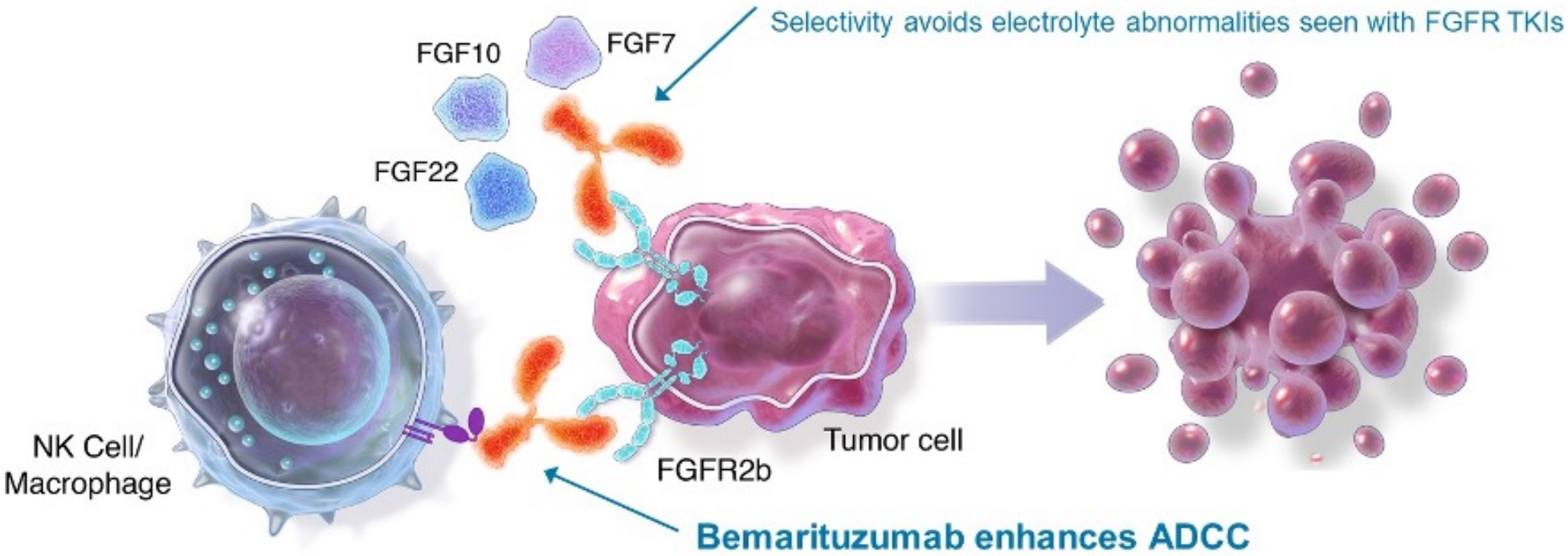
Presenter: Daniel Catenacci, MD
University of Chicago

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.

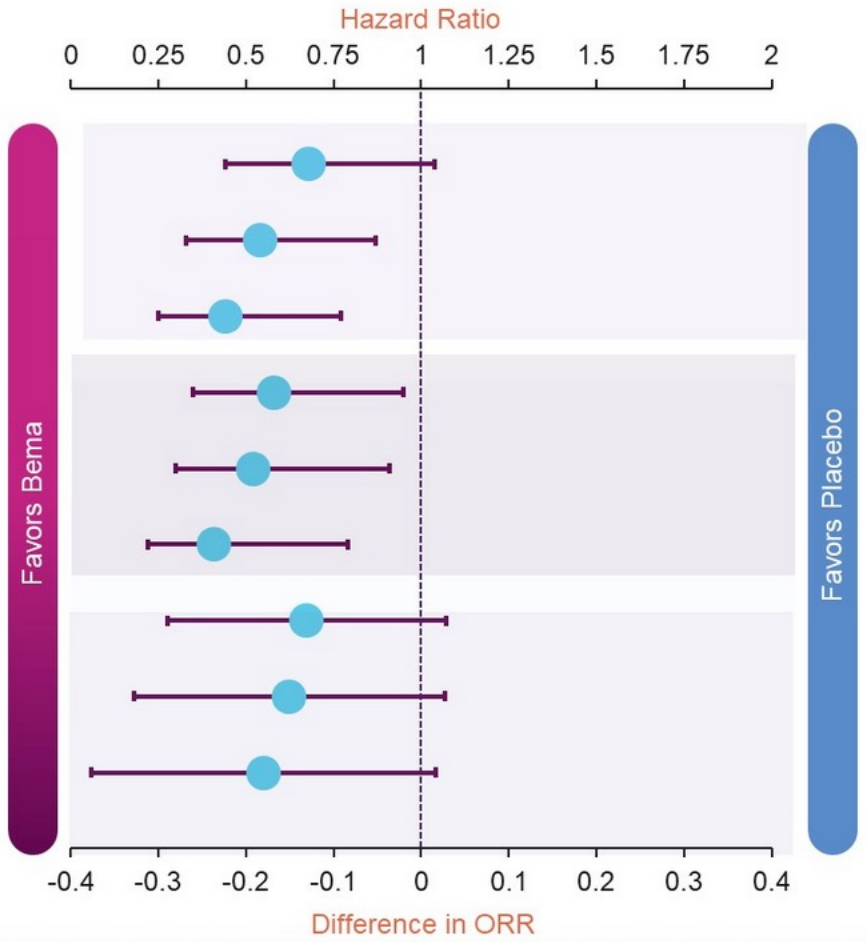
1. Catenacci D, et al. *J Clin Oncol*. 2020.

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

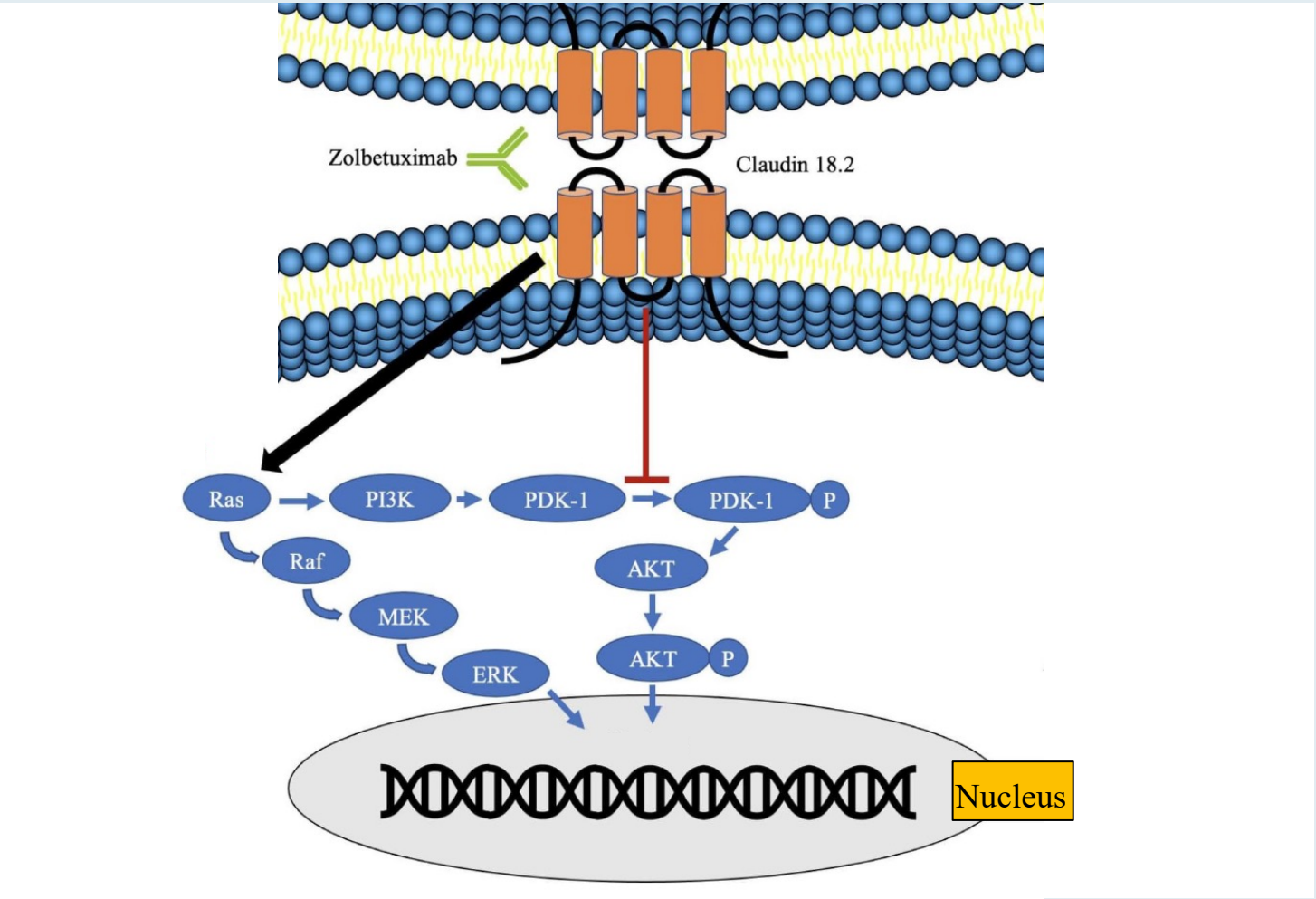
Selected AE (Preferred term)	Any Grade		Grade ≥3	
	Bema (N = 76)	Placebo (N = 77)	Bema (N = 76)	Placebo (N = 77)
Total Events	**76 (100.0%)**	**76 (98.7%)**	**63 (82.9%)**	**57 (74.0%)**
Nausea	36 (47.4%)	41 (53.2%)	0	3 (3.9%)
Vomiting	22 (28.9%)	24 (31.2%)	2 (2.6%)	2 (2.6%)
Diarrhea	31 (40.8%)	24 (31.2%)	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

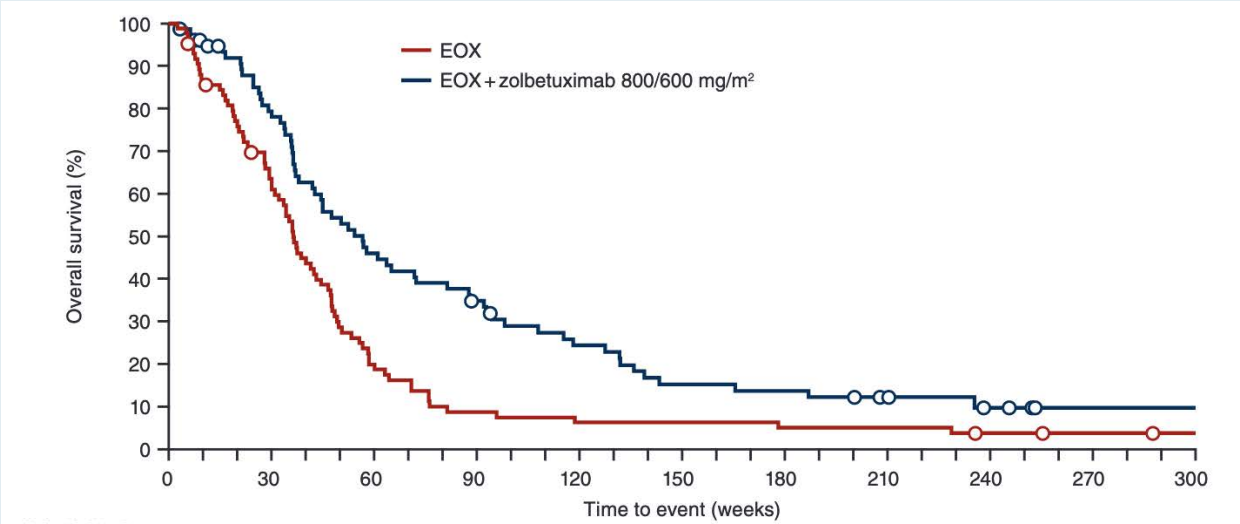
FAST: a randomised phase II study of zolbetuximab (IMAB362) plus EOX versus EOX alone for first-line treatment of advanced CLDN18.2-positive gastric and gastro-oesophageal adenocarcinoma

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

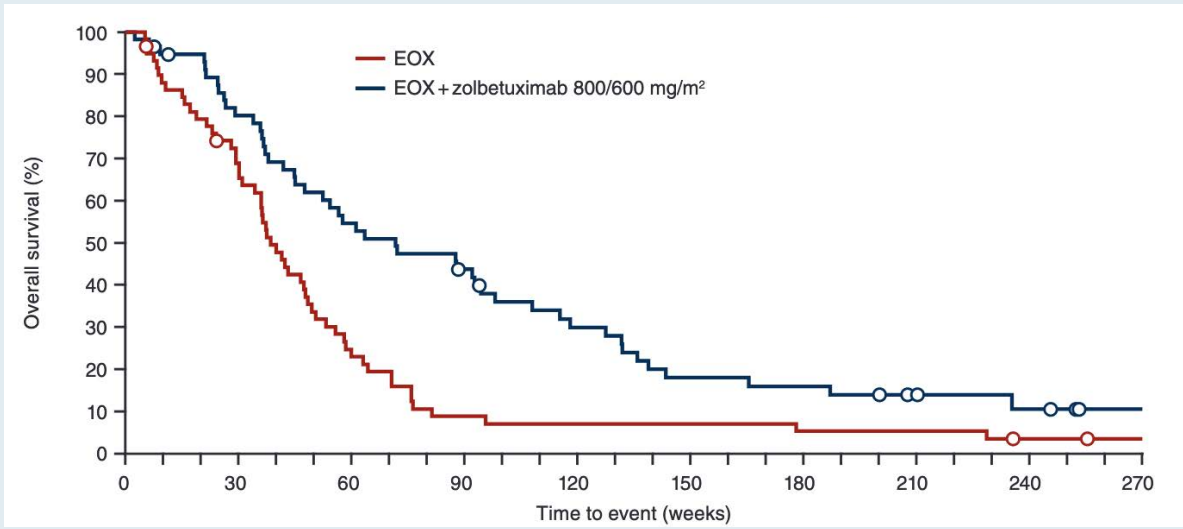
FAST: Overall Survival with Zolbetuximab in Combination with Chemotherapy for Advanced CLDN18.2-Positive Gastric and Gastroesophageal Adenocarcinoma

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

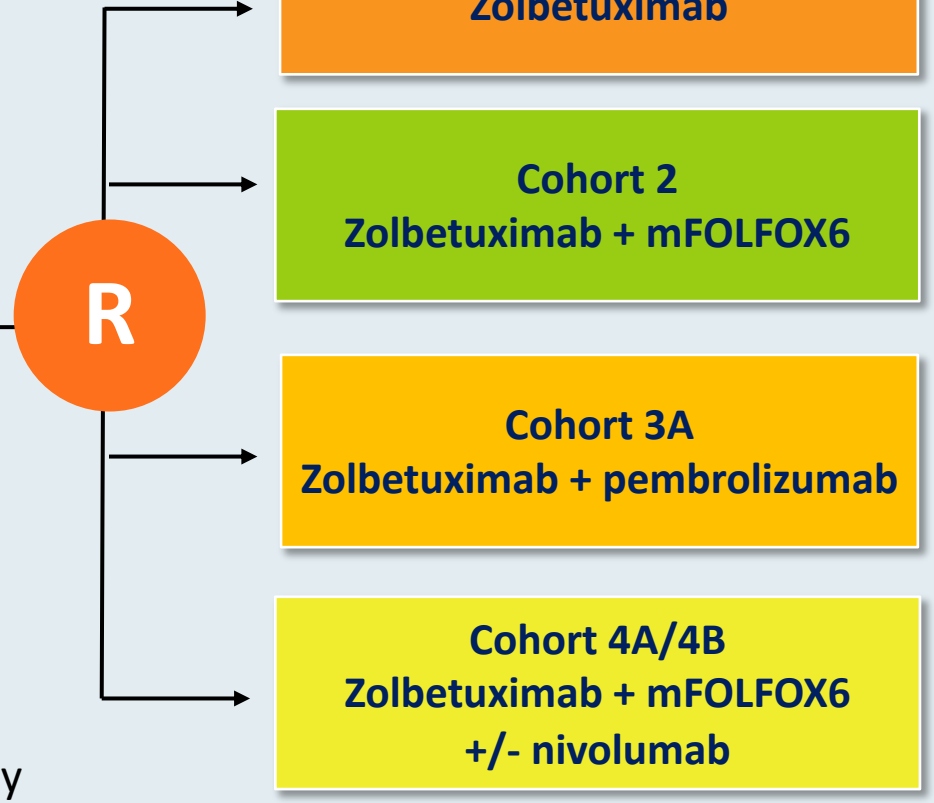
www.clinicaltrials.gov. Accessed March 2022.

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



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

www.clinicaltrials.gov. Accessed March 2022.

RTP RESEARCH TO PRACTICE

PARP Inhibition in the Management of Prostate Cancer — Where We Are and Where We're Headed

Thursday, June 23, 2022
5:00 PM – 6:00 PM ET

Faculty

Johann S de Bono, MB ChB, MSc, PhD, FMedSci
Fred Saad, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE