Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Wells A Messersmith, MD
Professor and Head, Division of Medical Oncology
Associate Director for Translational Research
University of Colorado Cancer Center
Aurora, Colorado

Commercial Support

This activity is supported by an educational grant from Lilly.

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, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, 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, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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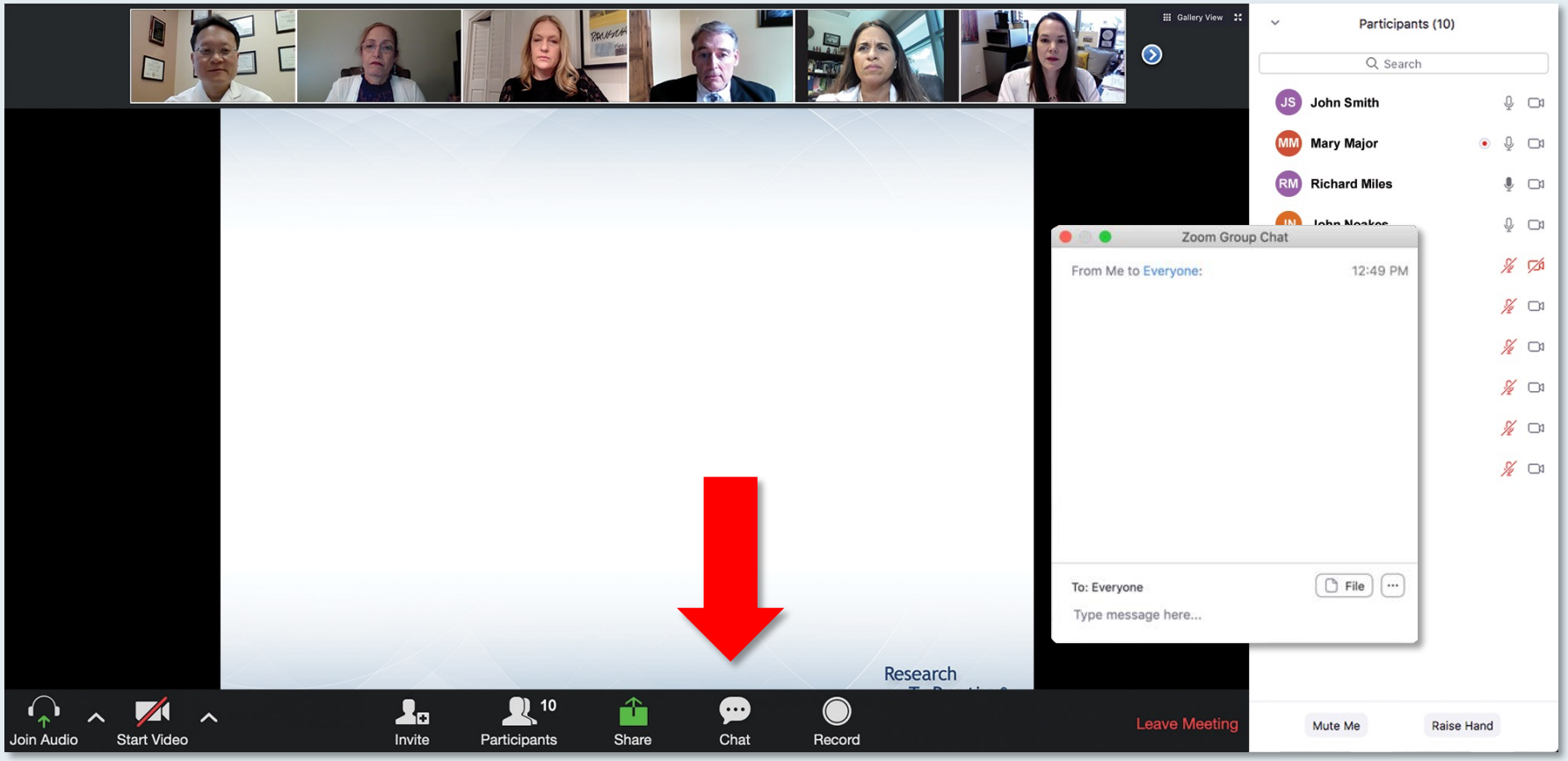
Dr Messersmith — Disclosures

Contracted Research	ALX Oncology, BeiGene Ltd, Bristol-Myers Squibb Company, Exelixis Inc, Experimental Drug Development Centre (Singapore), Immunomedics Inc, Pfizer Inc, Mitsubishi Tanabe Pharma America
Data and Safety Monitoring Board/Committee	Five Prime Therapeutics Inc, QED Therapeutics, Zymeworks

We Encourage Clinicians in Practice to Submit Questions



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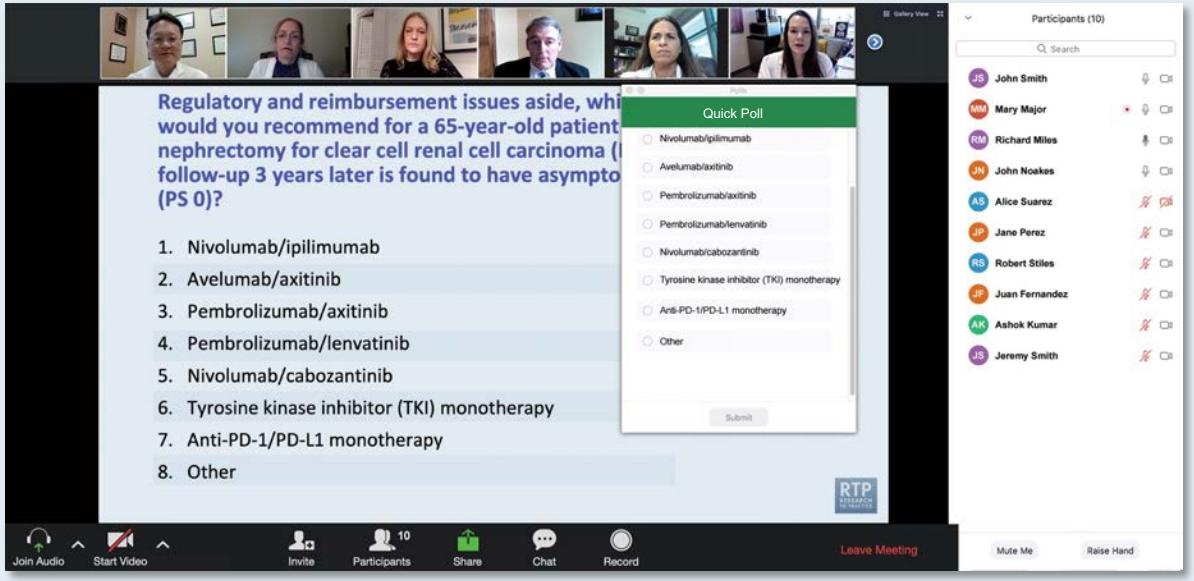

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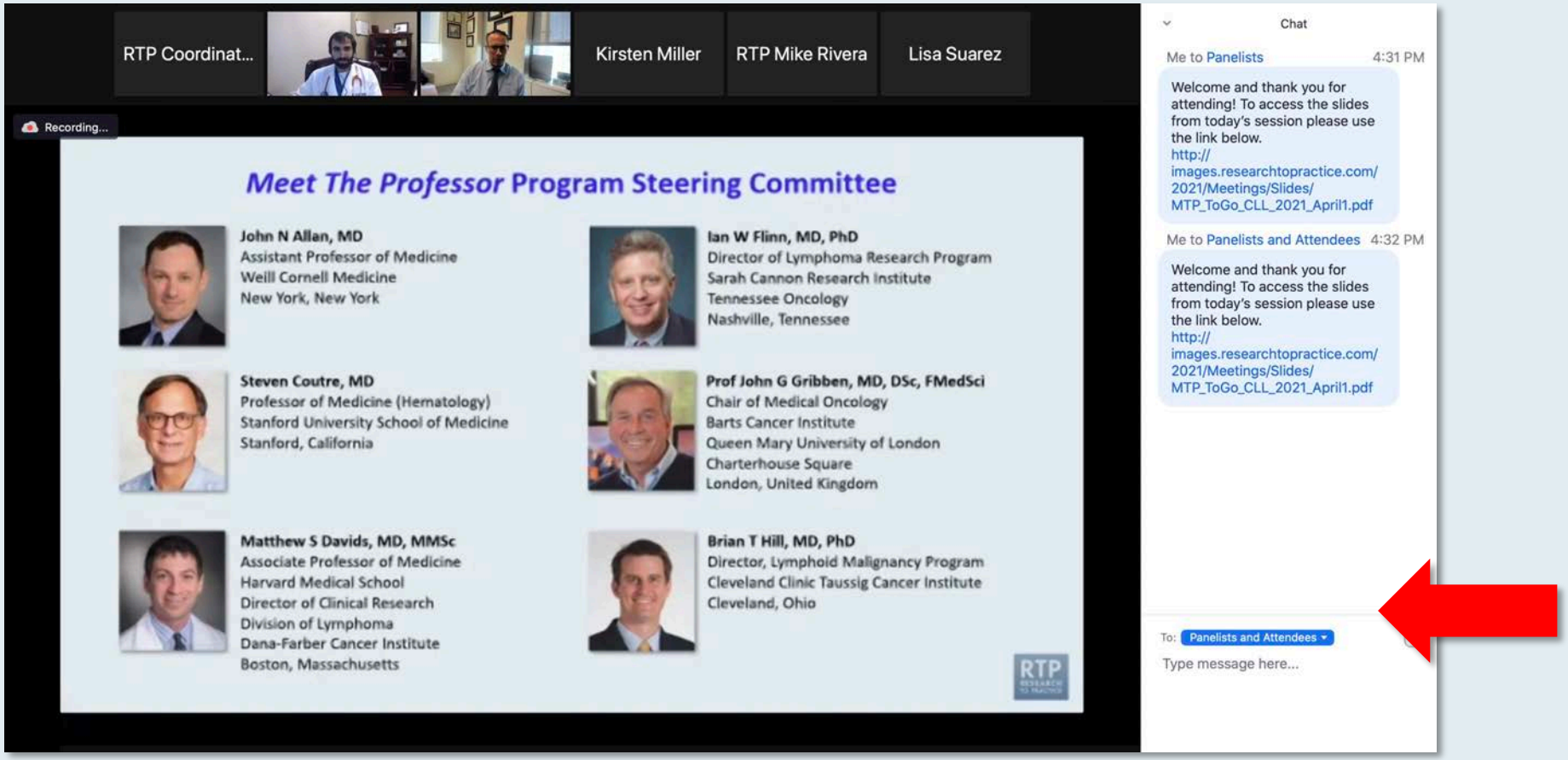

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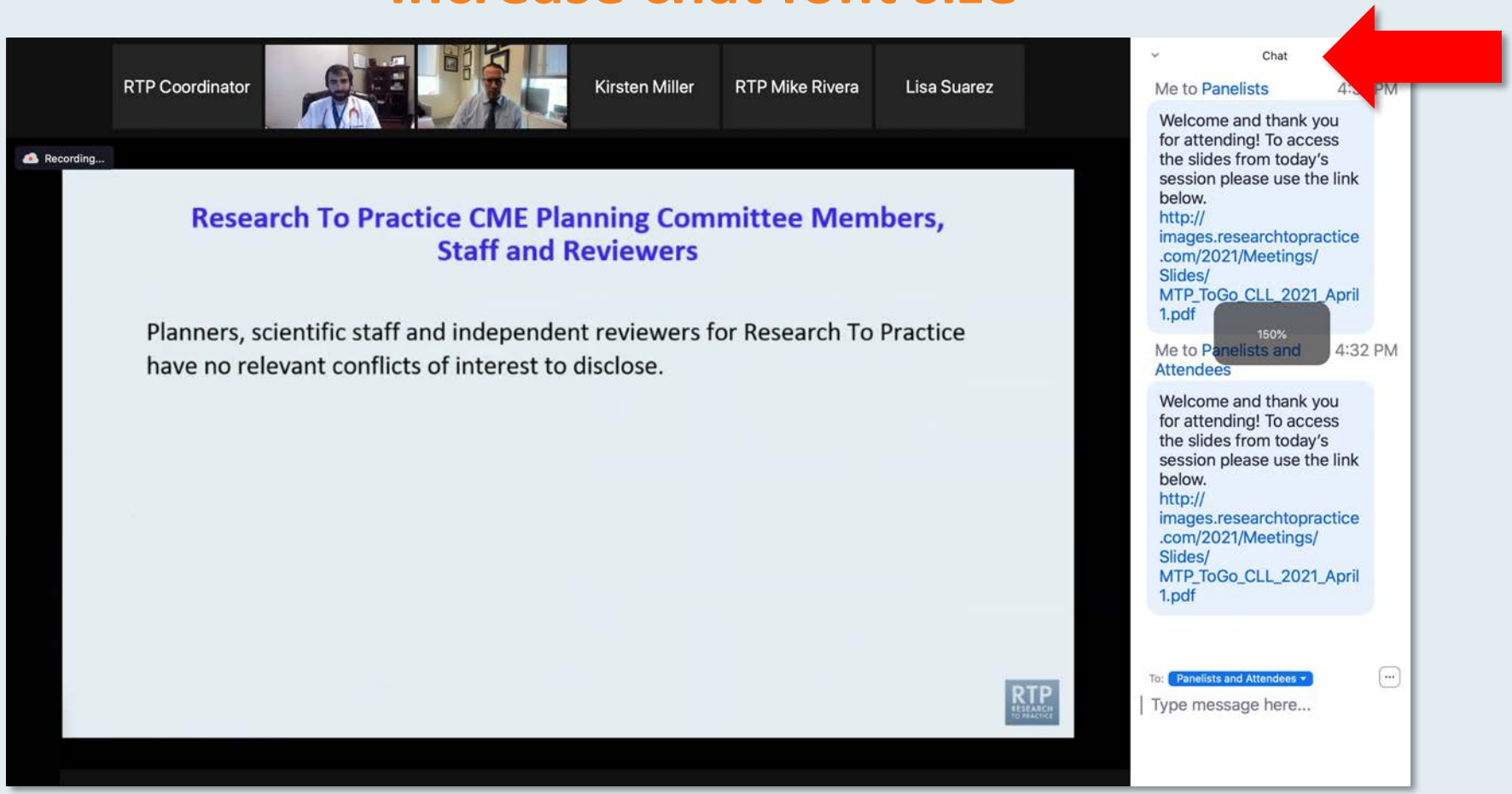

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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Advances in the Management of Cholangiocarcinoma

DR MITESH BORAD

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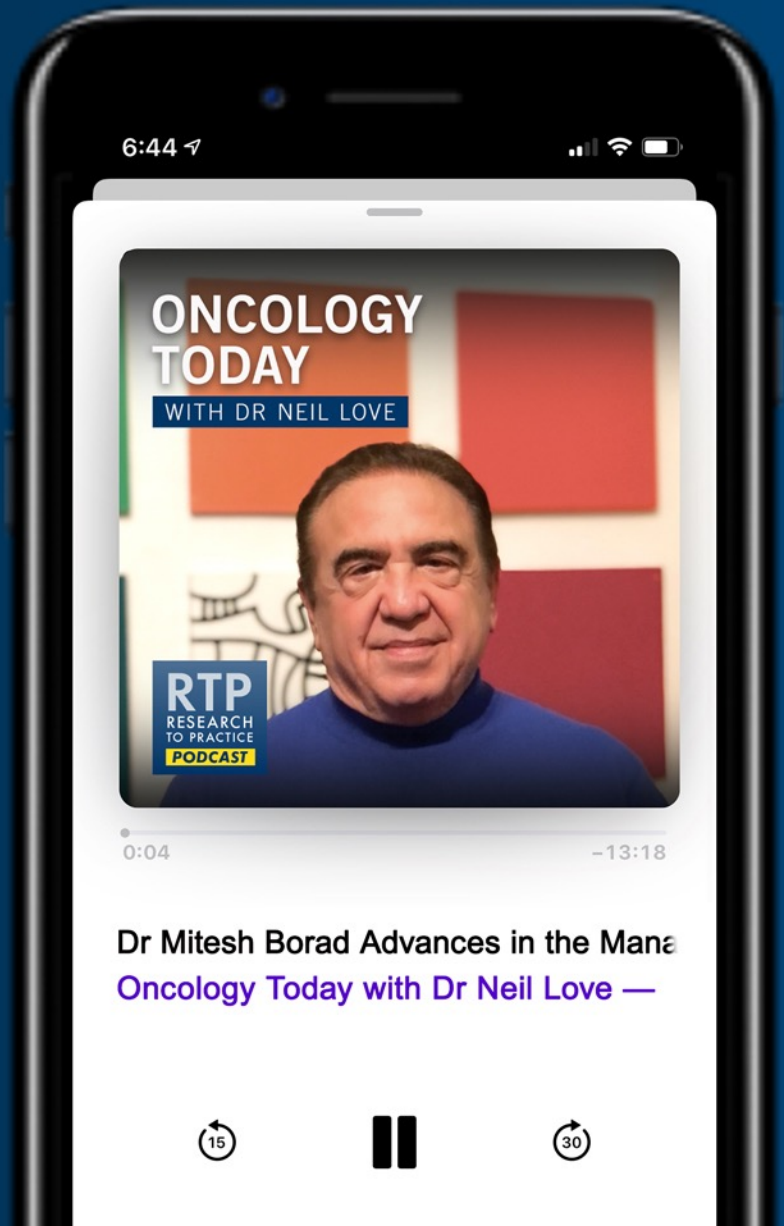

Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Gynecologic Cancers

Thursday, August 26, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas J Herzog, MD
Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Chronic Lymphocytic Leukemia

A Virtual CME Satellite Symposium Series in Conjunction with the Society of Hematologic Oncology 2021 Annual Meeting

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Mitchell R Smith, MD, PhD
Philip A Thompson, MB, BS

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Wednesday, September 1, 2021
5:00 PM – 6:00 PM ET

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Joyce F Liu, MD, MPH

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RESEARCH TO PRACTICE

Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

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Daniel A Pollyea, MD, MS
David Sallman, MD
Eunice S Wang, MD

Moderator

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Thank you for joining us!

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

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Meet The Professor Program Participating Faculty

Dirk Arnold, MD, PhD
Director
Asklepios Tumorzentrum Hamburg
Asklepios Klinik Altona
Hamburg, Germany

Johanna Bendell, MD
Chief Development Officer
Director, Drug Development Unit Nashville
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee

Tanios Bekaii-Saab, MD
Professor, Mayo Clinic College of Medicine and Science
Program Leader, Gastrointestinal Cancer
Mayo Clinic Cancer Center
Consultant, Mayo Clinic in Arizona
Phoenix, Arizona

Daniel Catenacci, MD
Associate Professor, Department of Medicine
Section of Hematology and Oncology
Director, Interdisciplinary Gastrointestinal Oncology Program
Assistant Director, Translational Research
Comprehensive Cancer Center
The University of Chicago Medical Center and Biological Sciences
Chicago, Illinois

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Meet The Professor Program Participating Faculty

Kristen K Ciombor, MD, MSCI
Assistant Professor of Medicine
Division of Hematology/Oncology
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

Eileen M O'Reilly, MD
Winthrop Rockefeller Endowed Chair in Medical Oncology
Section Head, Hepatopancreaticobiliary and Neuroendocrine Cancers
Co-Director, Medical Initiatives
David M Rubenstein Center for Pancreatic Cancer Research
Attending Physician, Member
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College
New York, New York

Wells A Messersmith, MD
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Associate Director for Translational Research
University of Colorado Cancer Center
Aurora, Colorado

Philip A Philip, MD, PhD, FRCP
Kathryn Cramer Endowed Chair in Cancer Research
Professor of Oncology and Pharmacology
Leader, GI and Neuroendocrine Oncology
Vice President of Medical Affairs
Karmanos Cancer Institute
Wayne State University
Detroit, Michigan

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Meet The Professor Program Participating Faculty

Alan P Venook, MD
The Madden Family Distinguished Professor of
Medical Oncology and Translational Research
Shorenstein Associate Director
Program Development
Helen Diller Family Comprehensive Cancer Center
University of California, San Francisco
San Francisco, California

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Zev Wainberg, MD, MSc
Co-Director, GI Oncology Program
Director of Early Phase Clinical Research
Jonsson Comprehensive Cancer Center
UCLA School of Medicine
Los Angeles, California

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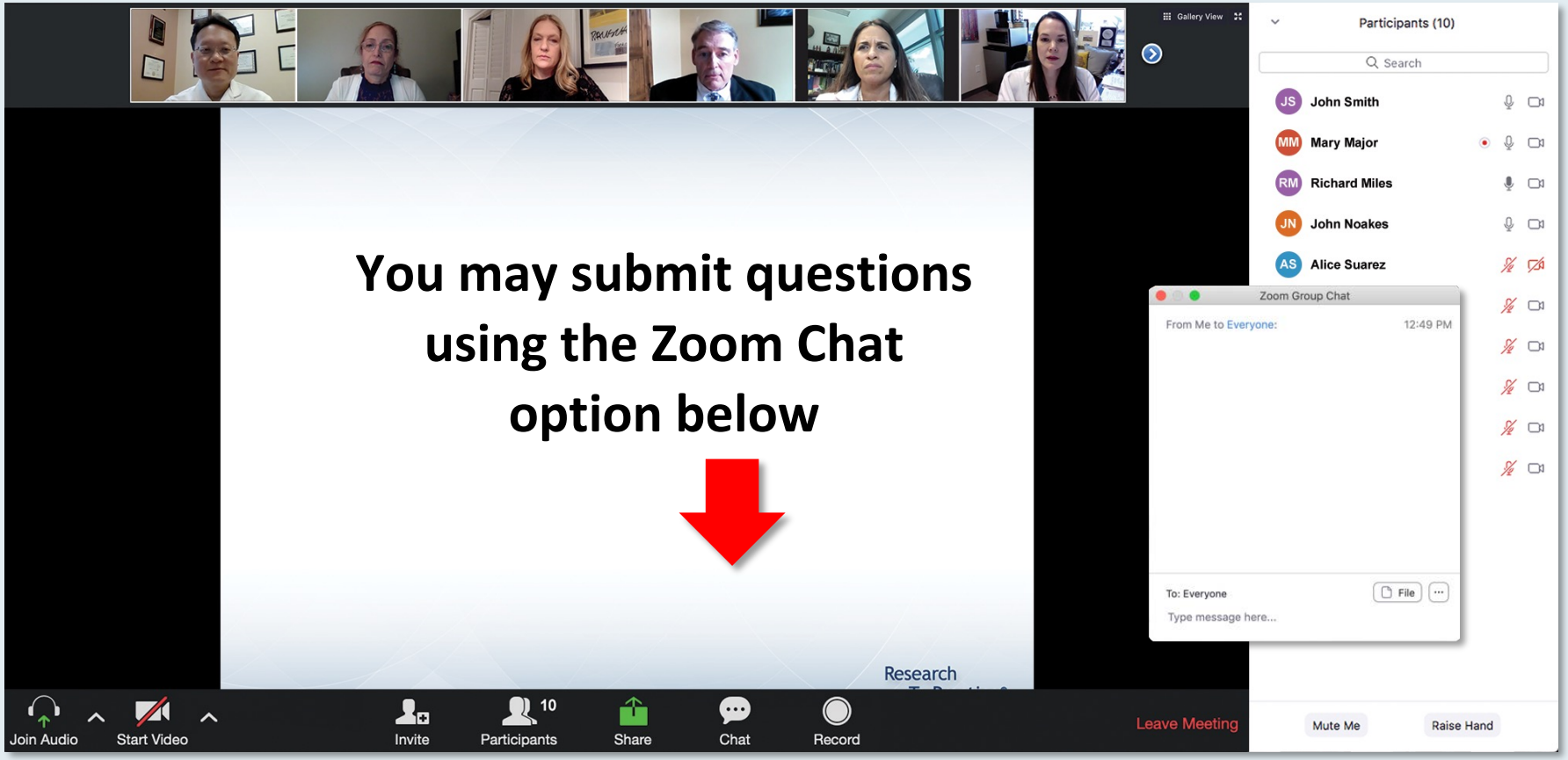

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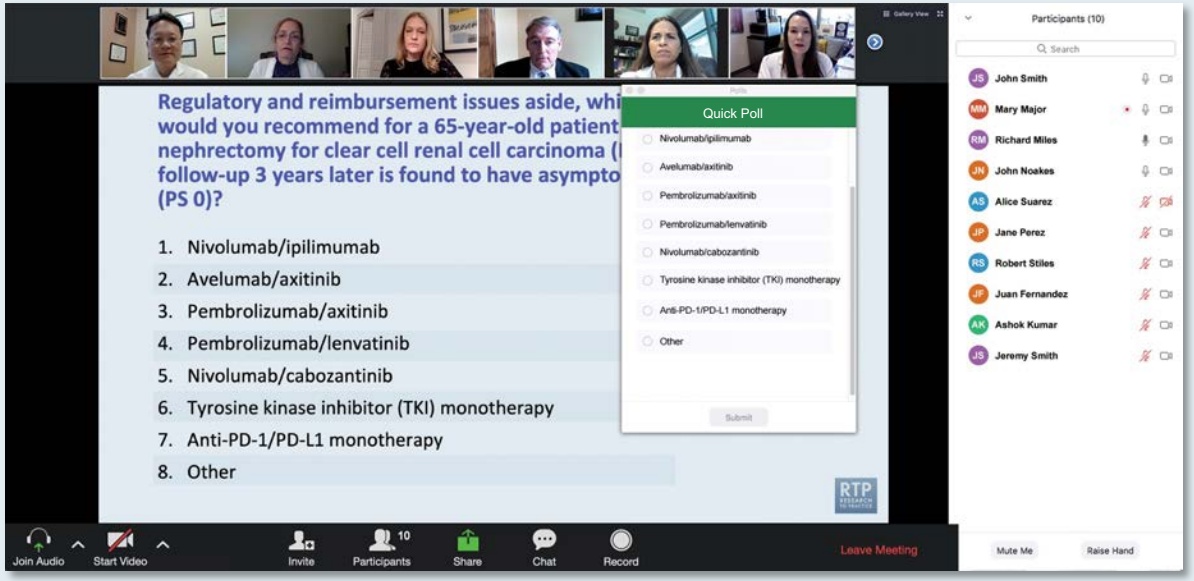

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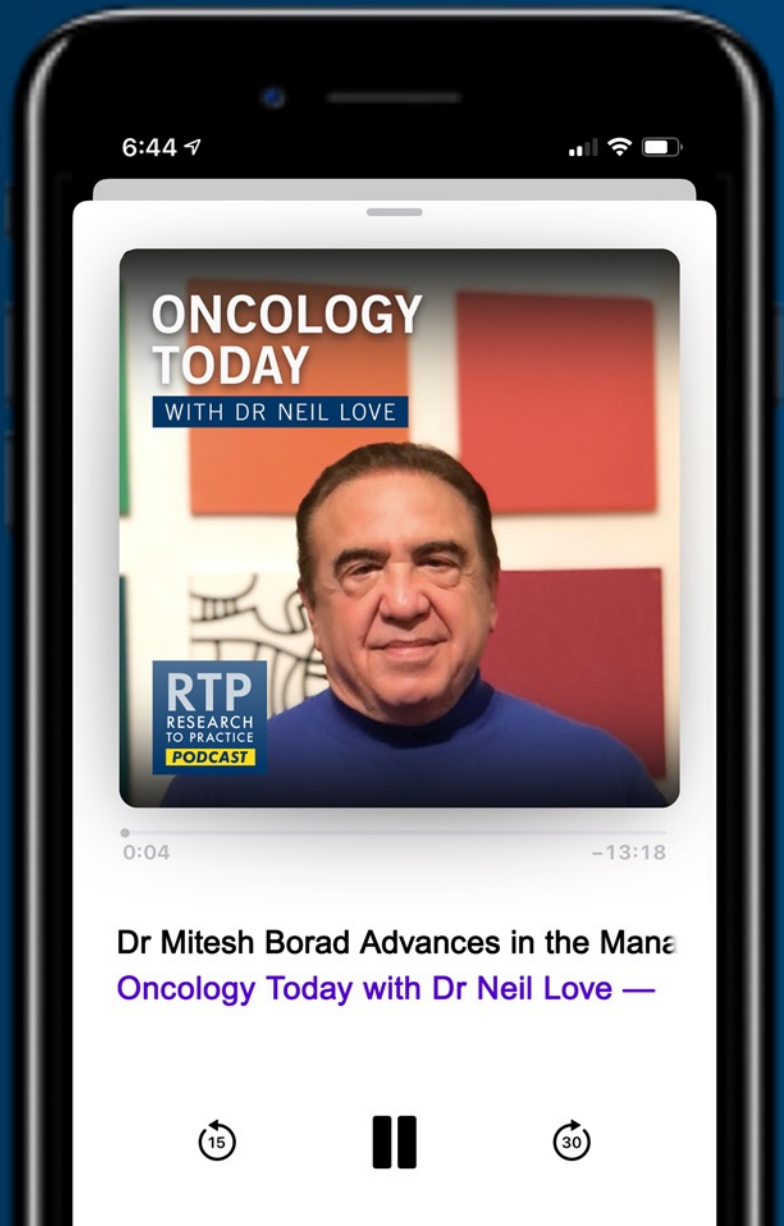

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Philip L Brooks, MD
Hematologist/Medical Oncologist
Cancer Care of Maine
Northern Light Eastern Maine Medical Center
Brewer, Maine

Rahul Gosain, MD
Guthrie Corning Cancer Center
Corning, New York

Gigi Chen, MD
Diablo Valley Oncology and Hematology Medical Group
Pleasant Hill, California

Ranju Gupta, MD
Attending Physician
Co-Director, Cardio-Oncology Program
LVPG Hematology Oncology Associates
Lehigh Valley Health Network
Bethlehem, Pennsylvania

Philip Glynn, MD
Director, Medical Oncology
Mercy Medical Center
Springfield, Massachusetts

Sulfi Ibrahim, MD
Reid Health
Richmond, Indiana

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Meet The Professor with Dr Messersmith

MODULE 1: Cases from Drs Chen and Ibrahim

- Dr Chen: A 68-year-old woman with MMR-proficient T3N0 rectal cancer
- Dr Ibrahim: A 40-year-old man with MSI-high metastatic colon cancer

MODULE 2: Beyond the Guidelines; Key Data – Colorectal Cancer

MODULE 3: Cases from Drs Brooks and Gosain

- Dr Brooks: A 55-year-old man with MSS esophageal cancer – PD-L1 CPS 10
- Dr Gosain: A 56-year-old man with HER2-positive, MSS gastroesophageal junction cancer

MODULE 4: Beyond the Guidelines; Key Data – Gastroesophageal, Esophageal Cancers

MODULE 5: Cases from Drs Glynn and Gupta

- Dr Glynn: A 74-year-old man with hepatocellular carcinoma (HCC) and cirrhosis
- Dr Gupta: An 80-year-old woman with metastatic HCC

MODULE 6: Beyond the Guidelines; Key Data – HCC

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Case Presentation – Dr Chen: A 68-year-old woman with MMR-proficient T3N0 rectal cancer

Dr Gigi Chen

- Presented with hematochezia
- Colonoscopy: Ulcerated mass 5 cm from the anal verge
- Biopsy: T3N0 adenocarcinoma, MMR proficient
- Patient desires to preserve her sphincter

Questions

- What would be the best treatment for her, whether this would be chemoradiation followed by surgery or total neoadjuvant chemotherapy?

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Case Presentation – Dr Ibrahim: A 40-year-old man with MSI-high metastatic colon cancer

Dr Sulfi Ibrahim

- Stage IIIC adenocarcinoma of the right colon, 19/25 lymph nodes positive → Surgery
- Adjuvant FOLFOX which was very poorly tolerated (Oxaliplatin x 4, 5-FU/LV x 6)
- Metastatic disease to the retroperitoneum within 12 months of completing adjuvant chemotherapy
- Irinotecan/bevacizumab with a good response → Bevacizumab maintenance → PD in retroperitoneum
- Restarted on Irinotecan/bevacizumab, with minor response
  - MSS, patient chose not to pursue germline testing despite a strong family history of colon cancer
- NGS testing: MSI high
- Treatment changed to Ipilimumab and nivolumab
  - Admitted to the hospital with a diffuse erythematous rash, mild increase in his creatinine and bilirubin
  - High-dose steroids with improvement in his rash and normalization of labs
  - Imaging after two doses: No evidence of disease
- Currently on maintenance monthly nivolumab
- Germline testing: Positive for Lynch syndrome

Case Presentation – Dr Ibrahim: A 40-year-old man with MSI-high metastatic colon cancer (continued)

Dr Sulfi Ibrahim

Questions

- ***How often do you get discordant results between IHC for microsatellite instability between immunohistochemistry and next-generation sequencing?***
- ***Does combination ipilimumab/nivolumab provide a better chance of durable response compared to single-agent pembrolizumab?***
- ***After hospitalized for ICI toxicity, I discontinued ipilimumab and continued nivolumab. Is that reasonable?***

Case Presentation – Dr Ibrahim: A 40-year-old man with MSI-high metastatic colon cancer (continued)

Dr Sulfi Ibrahim

RESULT: POSITIVE

One Pathogenic variant identified in MLH1. MLH1 is associated with autosomal dominant Lynch syndrome and autosomal recessive constitutional mismatch repair deficiency syndrome.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
MLH1	c.1381A>T (p.Lys461*)	heterozygous	PATHOGENIC

About this test

This diagnostic test evaluates 30 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

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MODULE 6: Beyond the Guidelines; Key Data – HCC

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, MSS, pan-RAS wild-type, BRAF wild-type metastatic colorectal cancer (mCRC)?

1. Chemotherapy
2. Chemotherapy + anti-VEGF antibody
3. Chemotherapy + anti-EGFR antibody
4. Chemotherapy + immunotherapy
5. Other

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, MSS, pan-RAS wild-type, BRAF wild-type metastatic colorectal cancer (mCRC)?

 Prof Arnold	FOLFOX + cetuximab	 Dr Ciombor	FOLFOX/CAPOX + bevacizumab
 Dr Bekaii-Saab	FOLFOXIRI + bevacizumab	 Dr O'Reilly	FOLFOX/CAPOX + bevacizumab
 Dr Bendell	FOLFOXIRI + bevacizumab	 Dr Venook	FOLFOXIRI + bevacizumab
 Dr Catenacci	FOLFIRI + bevacizumab	 Dr Wainberg	FOLFOX/CAPOX + bevacizumab

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What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, pan-RAS wild-type, BRAF wild-type, MSI-high mCRC?

1. Pembrolizumab
2. Nivolumab
3. Nivolumab/ipilimumab
4. Chemotherapy
5. Chemotherapy + anti-VEGF antibody
6. Chemotherapy + anti-EGFR antibody
7. Chemotherapy + immunotherapy
8. Other

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, pan-RAS wild-type, BRAF wild-type, MSI-high mCRC?

 Prof Arnold	Pembrolizumab	 Dr Ciombor	Pembrolizumab
 Dr Bekaii-Saab	Pembrolizumab	 Dr O'Reilly	Pembrolizumab
 Dr Bendell	Pembrolizumab	 Dr Venook	Pembrolizumab
 Dr Catenacci	Pembrolizumab	 Dr Wainberg	Pembrolizumab

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Regulatory and reimbursement issues aside, for a patient with pan-RAS wild-type mCRC with a BRAF V600E mutation, in what line of therapy would you generally administer BRAF-targeted therapy?

 Prof Arnold	Second line	 Dr Ciombor	Second line
 Dr Bekaii-Saab	Second line	 Dr O'Reilly	Second line
 Dr Bendell	Second line	 Dr Venook	Second line
 Dr Catenacci	Second line	 Dr Wainberg	Second line

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For a patient with mCRC with a BRAF V600E mutation to whom you would administer BRAF-targeted therapy, what would be your preferred treatment?

1. Irinotecan + vemurafenib + EGFR antibody
2. Dabrafenib + trametinib + EGFR antibody
3. Encorafenib + binimetinib + EGFR antibody
4. Encorafenib + EGFR antibody
5. Other

For a patient with mCRC with a BRAF V600E mutation to whom you would administer BRAF-targeted therapy, what would be your preferred treatment?

 Prof Arnold	Encorafenib + cetuximab	 Dr Ciombor	Encorafenib + panitumumab
 Dr Bekaii-Saab	Encorafenib + panitumumab	 Dr O'Reilly	Encorafenib + cetuximab
 Dr Bendell	Encorafenib + panitumumab	 Dr Venook	Encorafenib + panitumumab
 Dr Catenacci	Encorafenib + cetuximab	 Dr Wainberg	Encorafenib + cetuximab

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A Single-Institution Experience Using Total Neoadjuvant Therapy to Treat Locally-Advanced Rectal Cancer

ABSTRACT #64

Tyler Friedrich, Ashley Glode, Whitney Herter, Robert Lentz, Sunnie Kim, Alexis Leal, S. Lindsey Davis, William Purcell, Jon Vogel, Michelle Cowan, Steven Ahrendt, Ana Gleisner, Elisa Birnbaum, Martin McCarter, Tracey Schefter, Wells Messersmith, Brandon Chapman, and Christopher Lieu

University of Colorado
Anschutz Medical Campus

Presented By Tyler Friedrich at 2021 Gastrointestinal Cancers Symposium

A Phase II Study Investigating Cabozantinib in Patients with Refractory Metastatic Colorectal Cancer (AGICC 17CRC01)

Scott AJ et al.

Gastrointestinal Cancers Symposium 2020;Abstract 103.

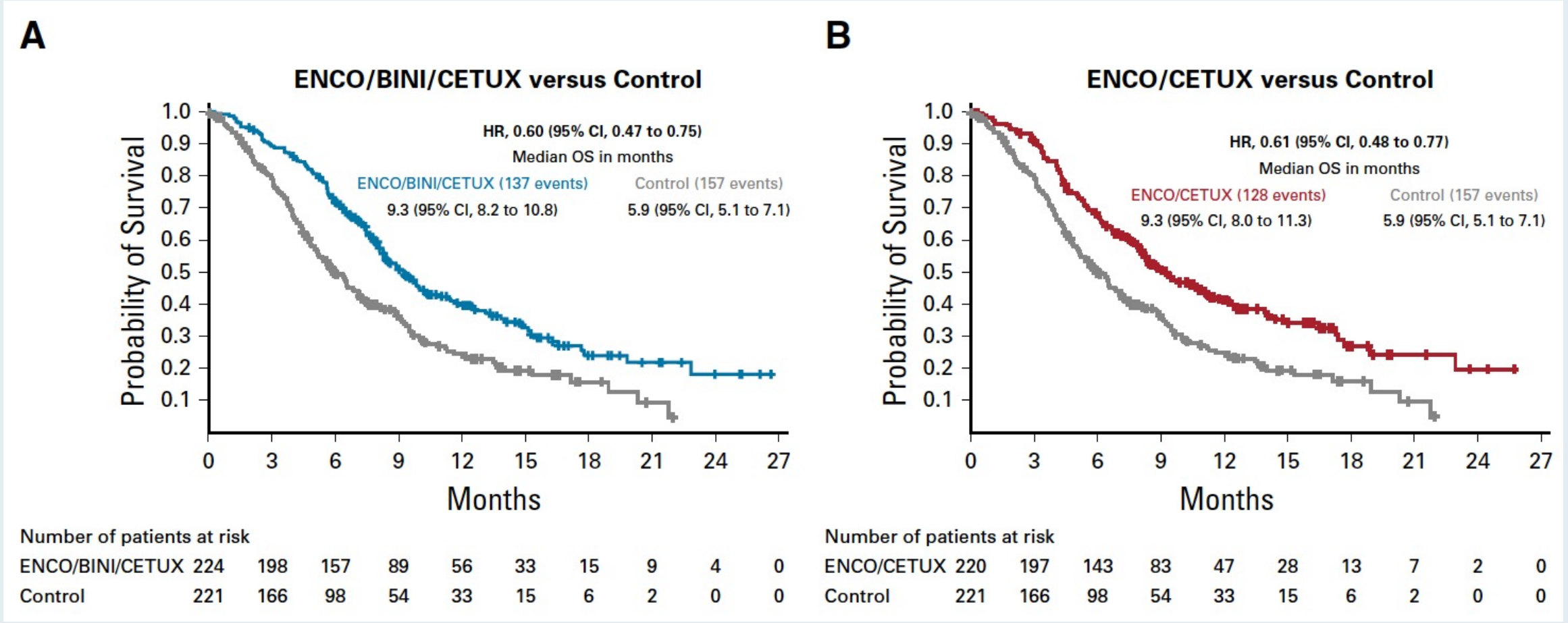
rapid communications

Encorafenib Plus Cetuximab as a New Standard of Care for Previously Treated *BRAF* V600E–Mutant Metastatic Colorectal Cancer: Updated Survival Results and Subgroup Analyses from the BEACON Study

Josep Tabernero, MD, PhD[1]; Axel Grothey, MD[2]; Eric Van Cutsem, MD, PhD[3]; Rona Yaeger, MD[4]; Harpreet Wasan, MD[5]; Takayuki Yoshino, MD, PhD[6]; Jayesh Desai, MBBS[7]; Fortunato Ciardiello, MD, PhD[8]; Fotios Loupakis, MD, PhD[9]; Yong Sang Hong, MD, PhD[10]; Neeltje Steeghs, MD, PhD[11]; Tormod Kyrre Guren, MD, PhD[12]; Hendrik-Tobias Arkenau, MD, PhD[13]; Pilar Garcia-Alfonso, MD[14]; Elena Elez, MD, PhD[1]; Ashwin Gollerkeri, MD[15]; Kati Maharry, PhD[15]; Janna Christy-Bittel, MSN[15]; and Scott Kopetz, MD, PhD[16]

J Clin Oncol 2021;39(4):273-84.

BEACON: Overall Survival Results



Tabanero J et al. *J Clin Oncol* 2021;39(4):273-84.

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ESMO WORLD CONGRESS ON Gastrointestinal Cancer

ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated *BRAF*^{V600E}–mutant metastatic colorectal cancer

Eric Van Cutsem, Julien Taieb, Rona Yaeger, Takayuki Yoshino, Evaristo Maiello, Elena Elez Fernandez, Jeroen Dekervel, Paul Ross, Ana Ruiz Casado, Janet Graham, Takeshi Kato, Jose Carlos Ruffinelli, Thierry André, Edith Carrière Roussel, Isabelle Klauck, Mélanie Groc, Axel Grothey, Jean-Claude Vedovato, Josep Tabernero*

** University Hospitals Leuven, Belgium*

ANCHOR CRC: encorAfenib, biNimetinib and Cetuximab in subjects witH previOusly untreated BRAF-mutant ColoRectal Cancer

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

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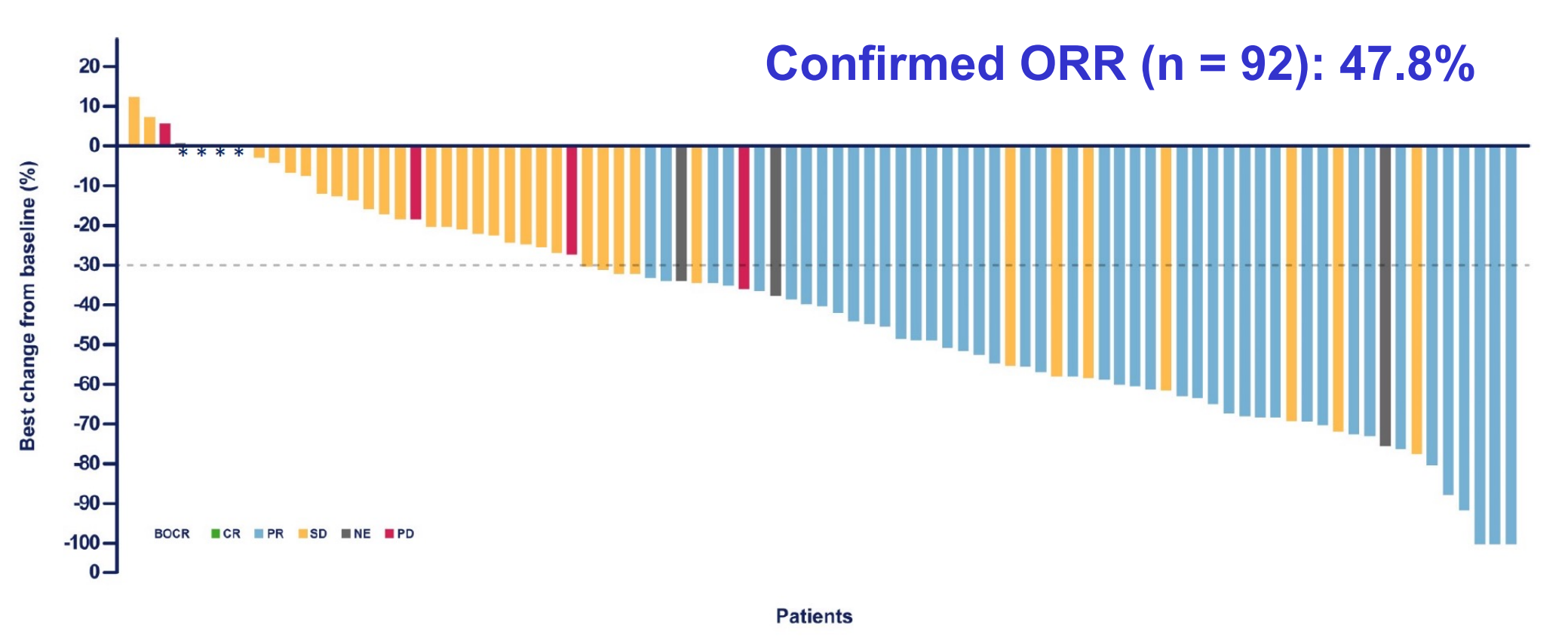
ANCHOR CRC: Results Summary



- OS was 17.2 mos (with a median follow-up of 14.4 mos)
- The triplet combination was well-tolerated and there were no unexpected toxicities

Van Cutsem E et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

BREAKWATER Study Design

An open-label, multicenter, randomized phase 3 study of 1st line encorafenib plus cetuximab with or without chemotherapy versus standard of care therapy in patients with metastatic *BRAF* V600E-mutant mCRC

Safety lead-in

Patients with *BRAF*^{V600E} mutant mCRC with 0 to 1 prior regimens in the metastatic setting

Phase 3

Patients with *BRAF*^{V600E} mutant mCRC and no prior systemic therapy in the metastatic setting

Encorafenib + cetuximab + mFOLFOX6
N=30
Encorafenib + cetuximab + FOLFIRI
N=30

Dosages
- Encorafenib, 300 mg PO QD
- Cetuximab, 500 mg/m² IV Q2W
- **FOLFOX, full dose IV Q2W**
- FOLFIRI, full dose IV Q2W

Randomize 1:1:1*

Arm A**
Encorafenib + cetuximab, N=290

Arm B**
Encorafenib + cetuximab + FOLFOX or FOLFIRI$^{\beta}$, N=290

Control arm§
Physician's choice: FOLFOX, FOLFIRI, FOLFOXIRI, CAPOX, all ± anti-VEGF antibody, N=290

PRIMARY ENDPOINTS
PFS (BICR) Arm A vs Control
AND
PFS (BICR) Arm B vs Control
(BICR, blinded independent central review)

KEY SECONDARY ENDPOINTS
OS Arm A vs Control
AND
OS Arm B vs Control

OTHER ENDPOINTS
- Incidence of DLTs, adverse events, dose modifications/discontinuations due to AEs
- PK including drug-drug interactions

BREAKWATER STUDY

*Stratified by: ECOG PS 0 v. 1, Region US/Canada v. Western Europe v. ROW
**Same dosing as SLI; $^{\beta}$FOLFOX or FOLFIRI based on SLI results; § No crossover.
ClinicalTrials.gov Identifier: NCT04607421

Van Cutsem E et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

FDA Approves New Dosing Regimen for Cetuximab

Press Release – April 6, 2021

"On April 6, 2021, the Food and Drug Administration approved a new dosage regimen of 500 mg/m^2 as a 120-minute intravenous infusion every two weeks (Q2W) for cetuximab for patients with K-Ras wild-type, EGFR-expressing colorectal cancer (mCRC) or squamous cell carcinoma of the head and neck (SCCHN).

The approval was based on population pharmacokinetic (PK) modeling analyses that compared the predicted exposures of cetuximab 500 mg Q2W to observed cetuximab exposures in patients who received cetuximab 250 mg weekly. The application was also supported by pooled analyses of overall response rates, progression-free survival, and overall survival (OS) from published literature in patients with CRC and SCCHN, and OS analyses using real-world data in patients with mCRC who received either the weekly cetuximab or Q2W regimens. In these exploratory analyses, the observed efficacy results were consistent across dosage regimens and supported the results of the population PK modeling analyses.

The most common adverse reactions (incidence ≥25%) to cetuximab are cutaneous adverse reactions (including rash, pruritus, and nail changes), headache, diarrhea, and infection."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-new-dosing-regimen-cetuximab

ESMO WORLD CONGRESS ON Gastrointestinal Cancer

Final Overall Survival for the Phase 3 KN177 Study: Pembrolizumab Versus Chemotherapy in Microsatellite Instability-High/Mismatch Repair Deficient Metastatic Colorectal Cancer

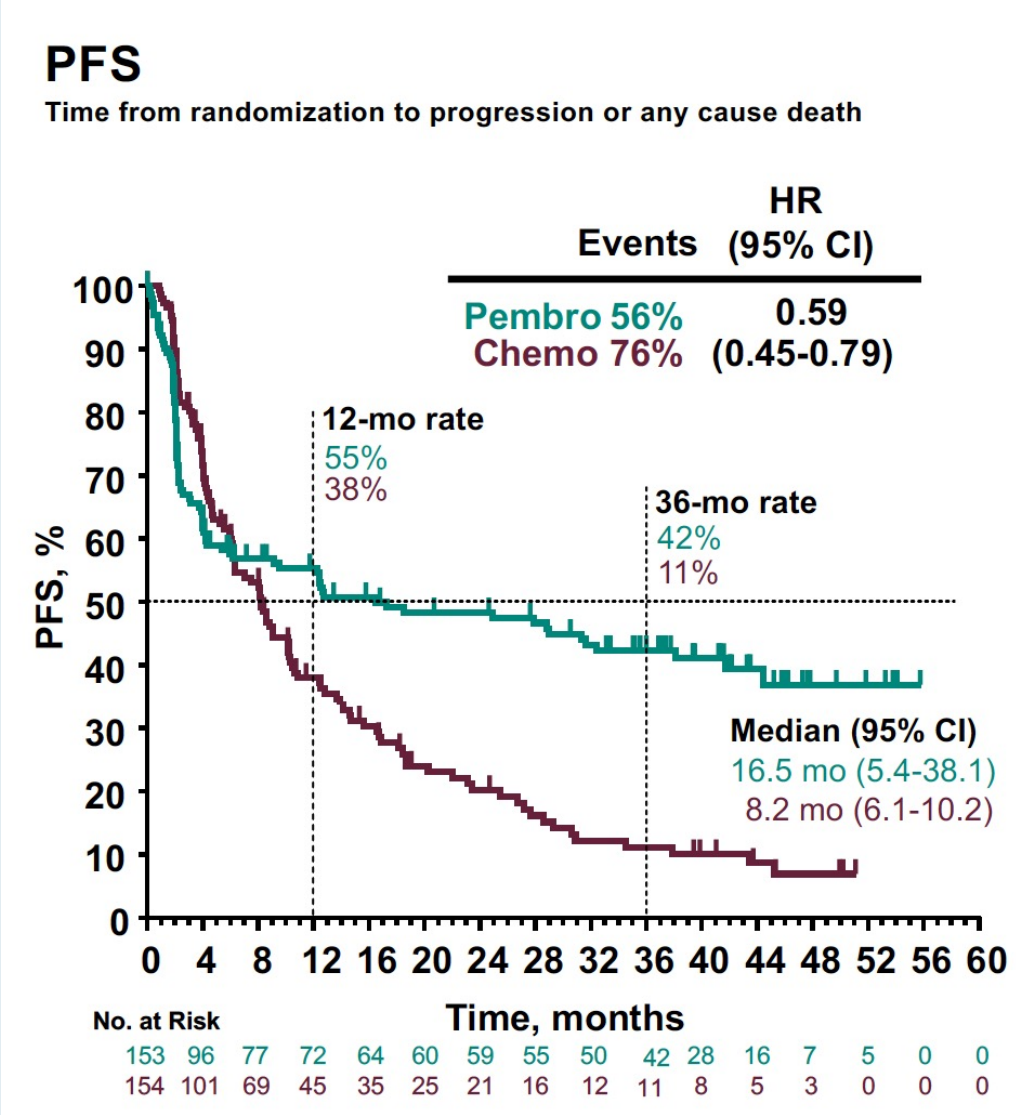
Thierry André,[1] Kai-Keen Shiu,[2] Tae Won Kim,[3] Benny Vittrup Jensen,[4] Lars Henrik Jensen,[5] Cornelis Punt,[6] Denis Smith,[7] Rocio Garcia-Carbonero,[8] Julia Alcaide-Garcia,[9] Peter Gibbs,[10] Christelle de la Fouchardiere,[11] Fernando Rivera,[12] Elena Elez,[13] Johanna Bendell,[14] Dung T. Le,[15] Takayuki Yoshino,[16] Wenyan Zhong,[17] David Fogelman,[18] Patricia Marinello,[18] Luis A. Diaz Jr[19]

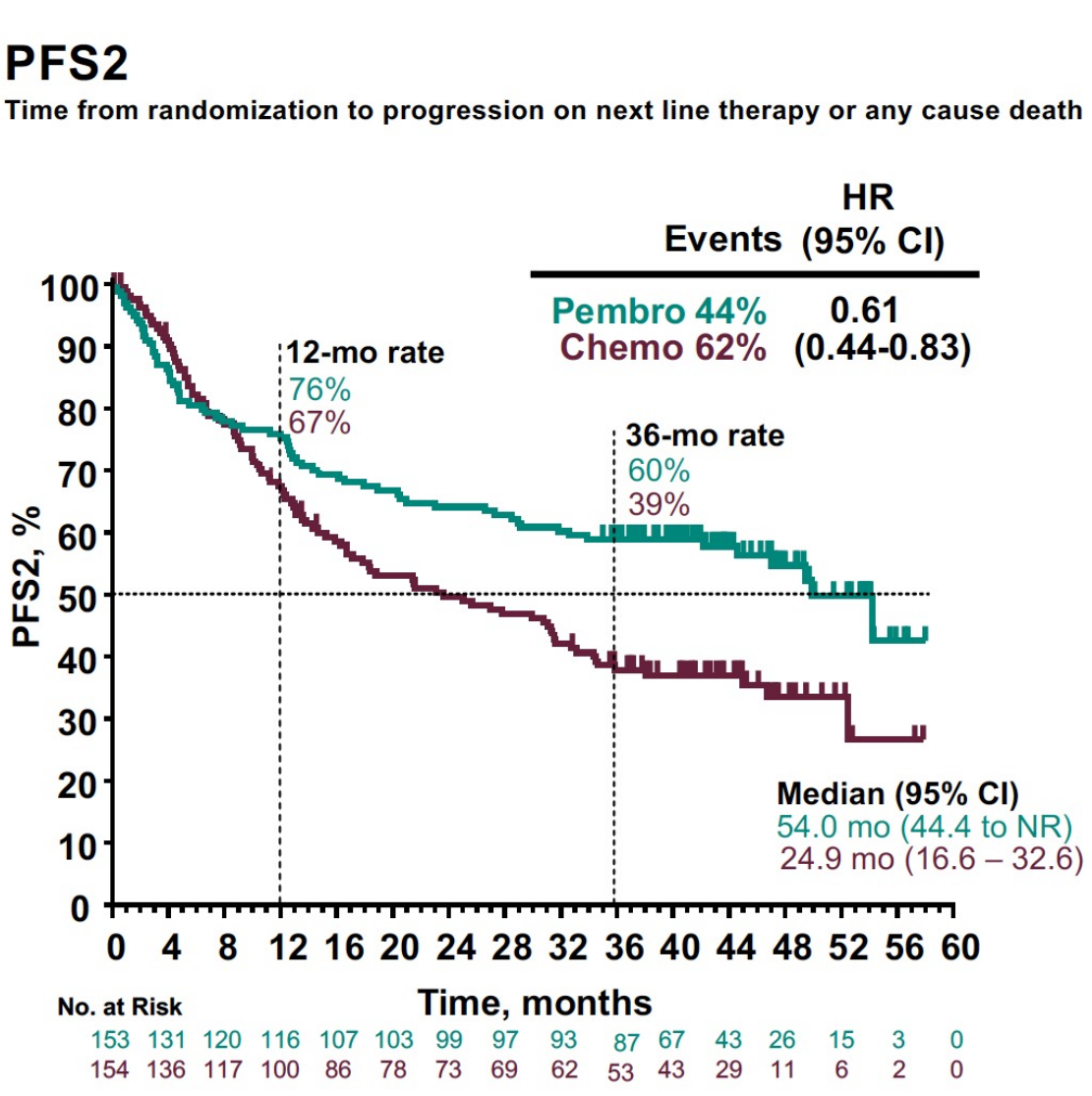
[1]Sorbonne Université and Hôpital Saint Antoine, Paris, France; [2]University College Hospital, NHS Foundation Trust, London, United Kingdom; [3]Asan Medical Center, University of Ulsan, Seoul, Republic of Korea; [4]Herlev and Gentofte Hospital, Herlev, Denmark; [5]University Hospital of Southern Denmark, Vejle, Denmark; [6]Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands; [7]Bordeaux University Hospital, Bordeaux, France; [8]Hospital Universitario 12 de Octubre, Imas12, CNIO, UCM, Madrid, Spain; [9]Hospital Regional Universitario de Malaga, Malaga, Spain; [10]Western Health, St Albans, Australia; [11]Léon Bérard Center, Lyon, France; [12]Hospital Universitario Marques de Valdecilla, IDIVAL, Santander, Spain; [13]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [14]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [15]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [16]National Cancer Center Hospital East, Kashiwa, Japan; [17]MSD China, Beijing, China; [18]Merck & Co., Inc. Kenilworth, NJ, USA; [19]Memorial Sloan Kettering Cancer Center, New York, NY, USA

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

RTP RESEARCH TO PRACTICE

KEYNOTE-177: Progression-Free Survival

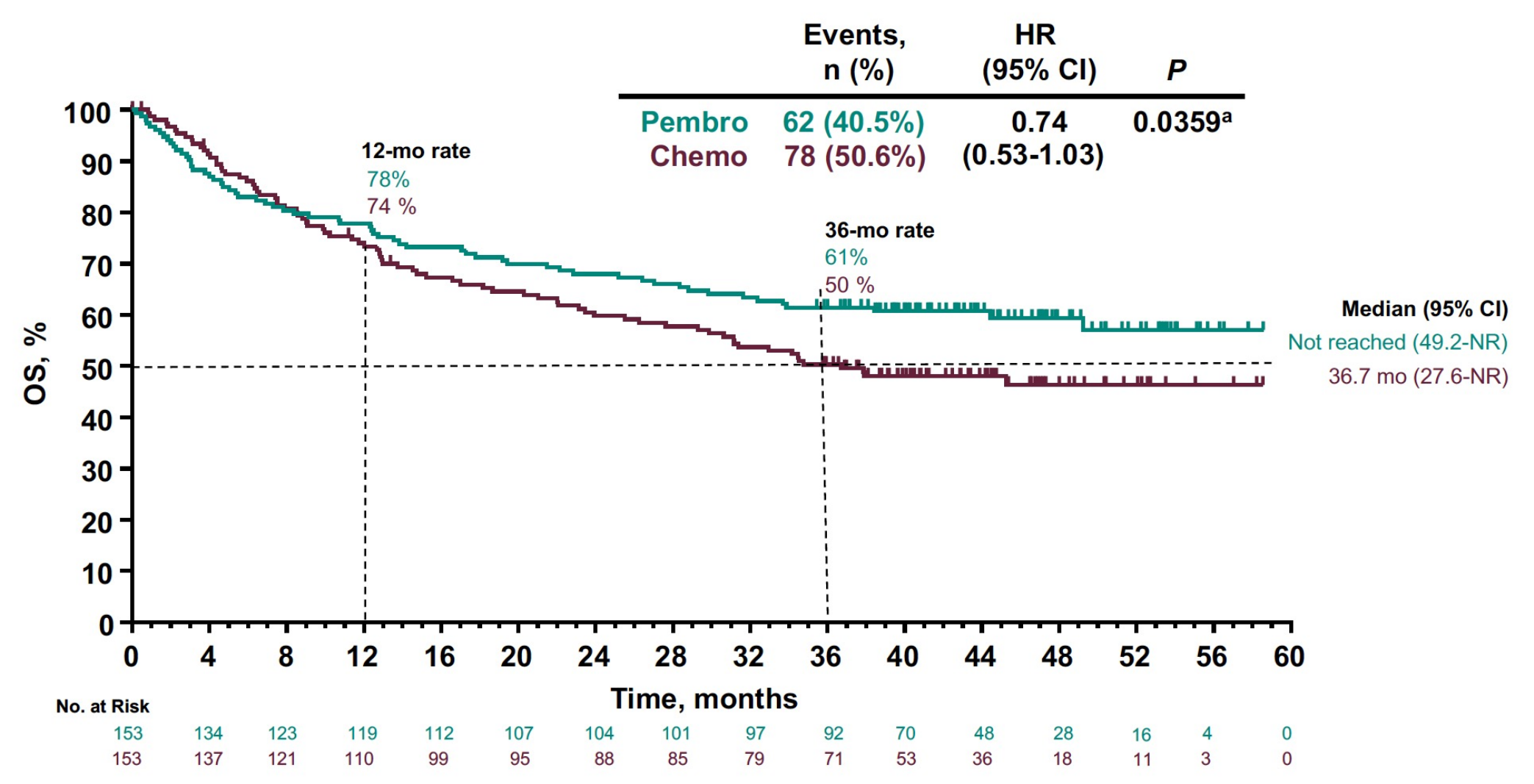




Andre T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

RTP RESEARCH TO PRACTICE

KEYNOTE-177: Overall Survival



Andre T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

ESMO WORLD CONGRESS ON Gastrointestinal Cancer

NIVOLUMAB PLUS LOW-DOSE IPILIMUMAB IN PREVIOUSLY TREATED PATIENTS WITH MICROSATELLITE INSTABILITY-HIGH/ MISMATCH REPAIR-DEFICIENT METASTATIC COLORECTAL CANCER: 4-YEAR FOLLOW-UP FROM CHECKMATE 142

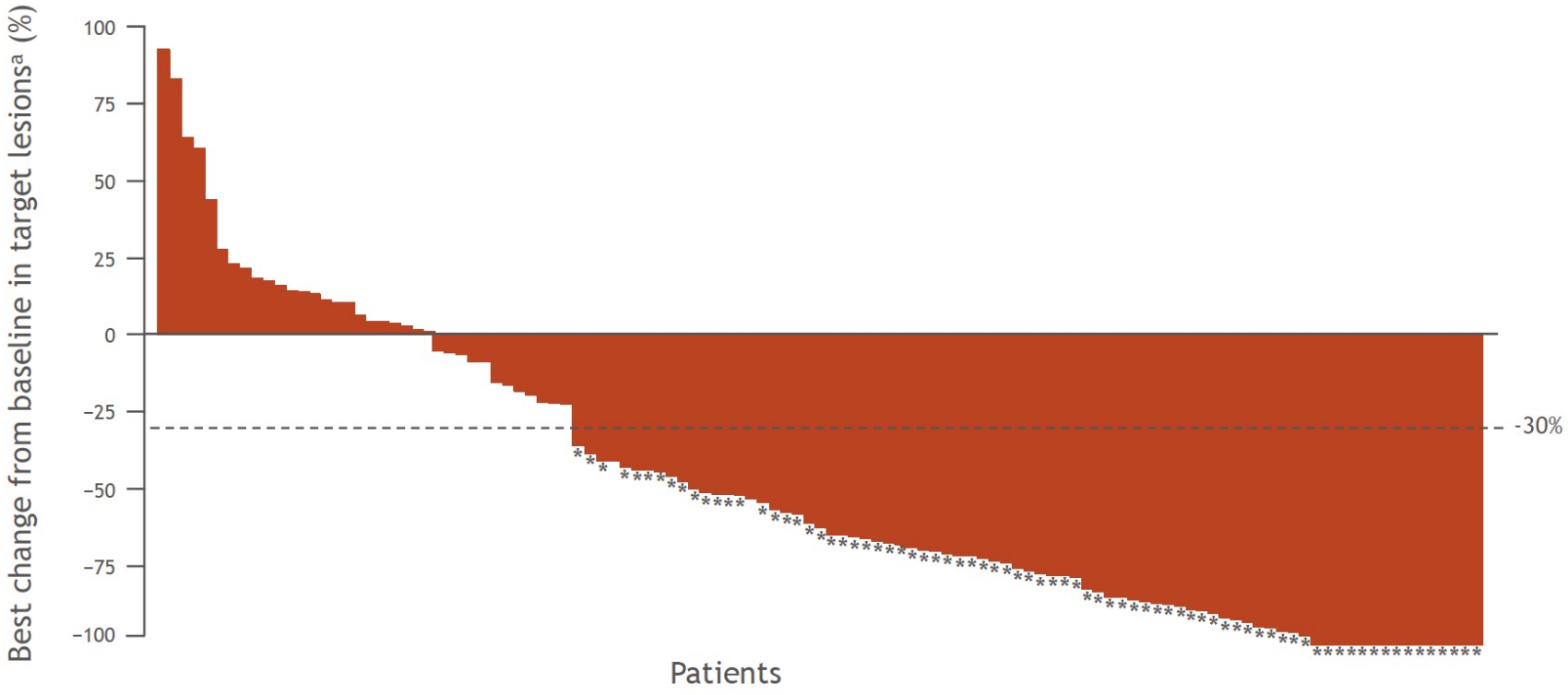
Thierry André,[1] Sara Lonardi,[2] Ka Yeung Mark Wong,[3] Heinz-Josef Lenz,[4] Fabio Gelsomino,[5] Massimo Aglietta,[6] Michael A. Morse,[7] Eric Van Cutsem,[8] Ray McDermott,[9] Andrew Hill,[10] Michael B. Sawyer,[11] Alain Hendlisz,[12] Bart Neyns,[13] Sandzhar Abdullaev,[14] Arteid Memaj,[14] Ming Lei,[14] Scott Kopetz,[15] Michael Overman[15]

[1]Hôpital Saint Antoine, Assistance Publique Hôpitaux de Paris and Sorbonne Université, Paris, France; [2]Istituto Oncologico Veneto IOV-IRCSS, Padova, Italy; [3]Westmead Hospital, Sydney, NSW, Australia; [4]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [5]University Hospital of Modena, Modena, Italy; [6]Candiolo Cancer Institute and University of Torino Medical School, Candiolo, Italy; [7]Duke University Medical Center, Durham, NC, USA; [8]University Hospitals Gasthuisberg/ Leuven and KU Leuven, Leuven, Belgium; [9]St Vincent's University Hospital and Cancer Trials Ireland, Dublin, Ireland; [10]Tasman Oncology Research, Ltd., Southport, QLD, Australia; [11]Cross Cancer Institute and University of Alberta, Edmonton, AB, Canada; [12]Institut Jules Bordet, Brussels, Belgium; [13]Universitair Ziekenhuis Brussel, Brussels, Belgium; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]MD Anderson Cancer Center, Houston, TX, USA

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract SO-27.

RTP RESEARCH TO PRACTICE

CheckMate 142: 4-Year Update of Nivolumab/Ipilimumab as First-Line Therapy in MSI-H/dMMR mCRC



- Most patients (79%) had a reduction in tumor burden from baseline

- Median PFS and OS were not reached
- 48-month PFS rate: 53%
- 48-month OS rate: 70.5%

Andre T et al. World Congress on Gastrointestinal Cancer 2021;Abstract SO-27.

2021 ASCO ANNUAL MEETING

Abstract 3505

DESTINY-CRC01

Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients With HER2-expressing Metastatic Colorectal Cancer: Final Results From a Phase 2, Multicenter, Open-label Study (DESTINY-CRC01)

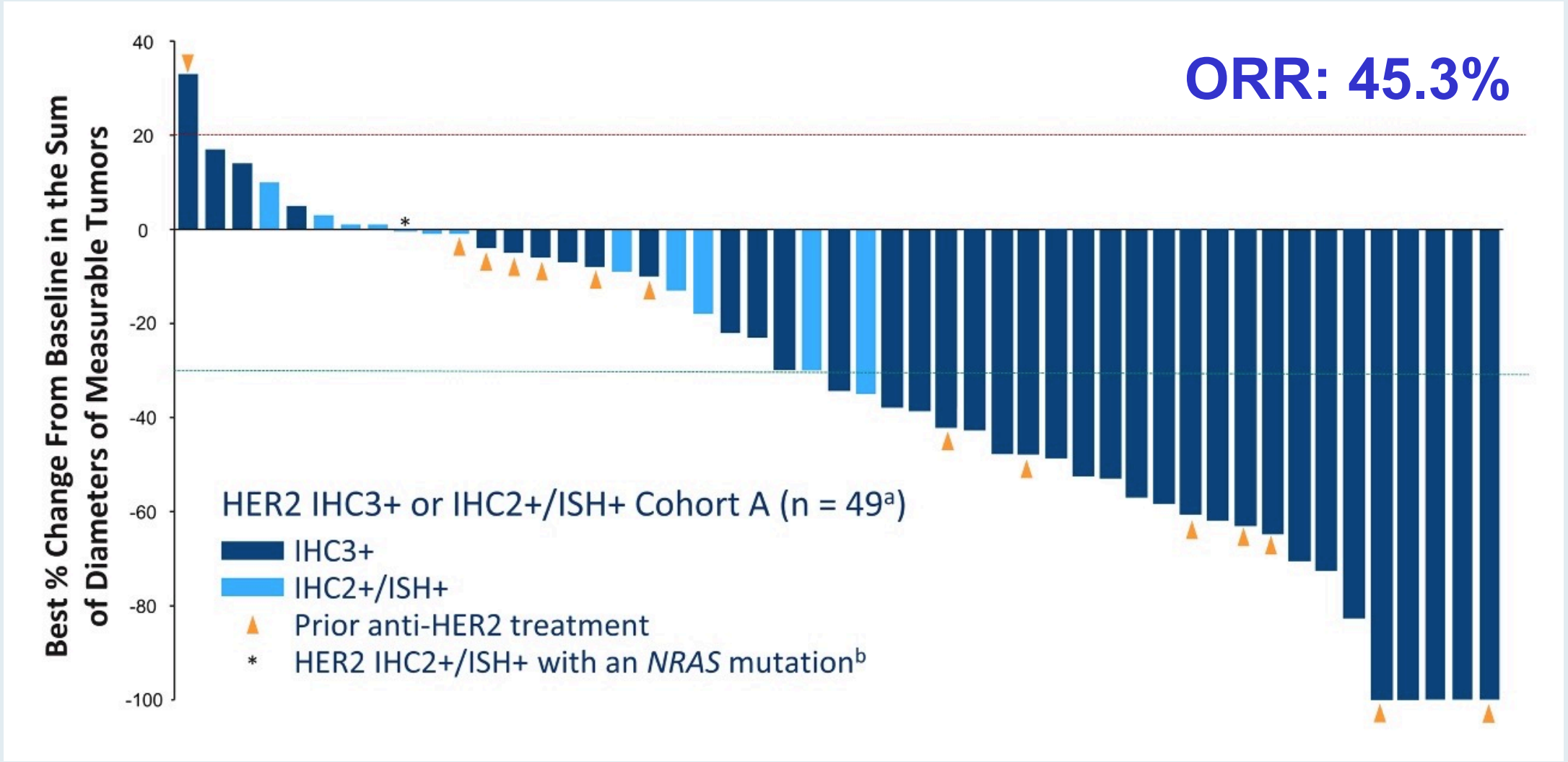
Takayuki Yoshino; National Cancer Center Hospital East, Kashiwa, Japan

June 7, 2021

Additional authors: Maria Di Bartolomeo, Kanwal Raghav, Toshiki Masuishi, Fotios Loupakis, Hisato Kawakami, Kensei Yamaguchi, Tomohiro Nishina, Zev Wainberg, Elena Elez, Javier Rodriguez, Marwan Fakih, Fortunato Ciardiello, Kapil Saxena, Kojiro Kobayashi, Emarjola Bako, Yasuyuki Okuda, Gerold Meinhardt, Axel Grothey, Salvatore Siena

On behalf of the DESTINY-CRC01 investigators

DESTINY-CRC01: Best Change in Tumor Size in Cohort A

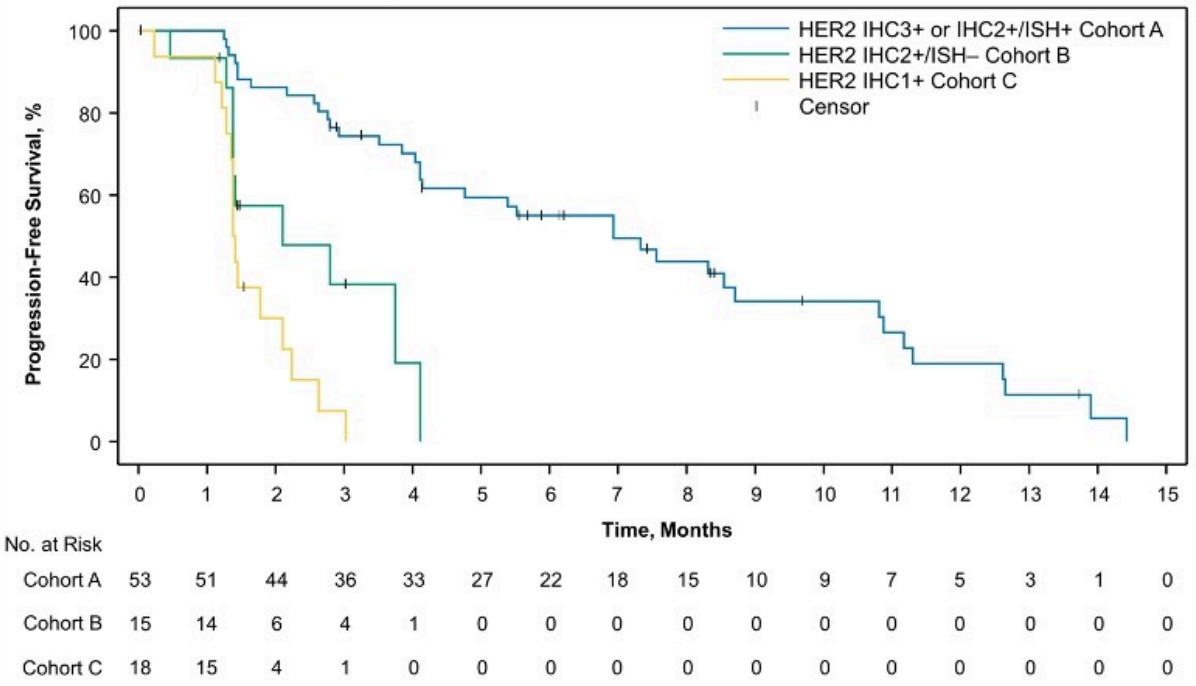


Yoshino T et al. ASCO 2021;Abstract 3500.

RTP RESEARCH TO PRACTICE

DESTINY-CRC01: Progression-Free and Overall Survival

Progression-Free Survival

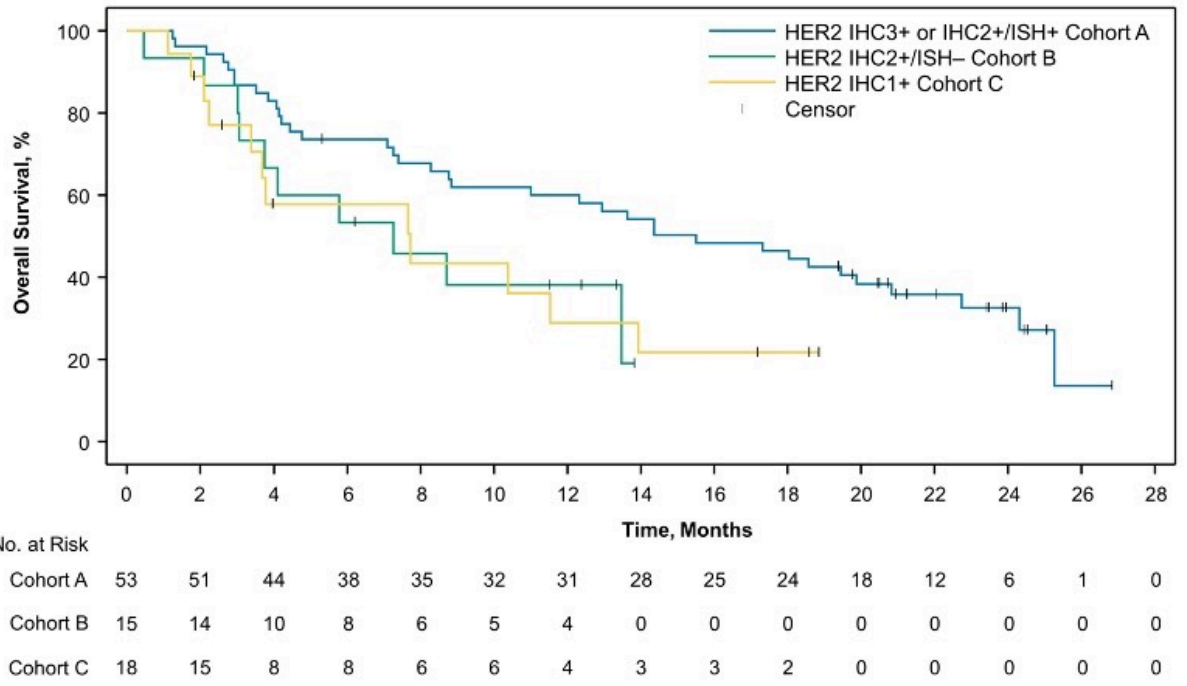


No. at Risk

Cohort A	53	51	44	36	33	27	22	18	15	10	9	7	5	3	1	0
Cohort B	15	14	6	4	1	0	0	0	0	0	0	0	0	0	0	0
Cohort C	18	15	4	1	0	0	0	0	0	0	0	0	0	0	0	0

	HER2 IHC3+ or IHC2+/ISH+ Cohort A (n = 53)	HER2 IHC2+/ISH– Cohort B (n = 15)	HER2 IHC1+ Cohort C (n = 18)
mPFS (95% CI), months	6.9 (4.1-8.7)	2.1 (1.4-4.1)	1.4 (1.3-2.1)

Overall Survival



No. at Risk

Cohort A	53	51	44	38	35	32	31	28	25	24	18	12	6	1	0	
Cohort B	15	14	10	8	6	5	4	0	0	0	0	0	0	0	0	
Cohort C	18	15	8	8	6	6	4	3	3	2	0	0	0	0	0	

	HER2 IHC3+ or IHC2+/ISH+ Cohort A (n = 53)	HER2 IHC2+/ISH– Cohort B (n = 15)	HER2 IHC1+ Cohort C (n = 18)
mOS (95% CI), months	15.5 (8.8-20.8)	7.3 (3.0-NE)	7.7 (2.2-13.9)

Yoshino T et al. ASCO 2021;Abstract 3500.

RTP RESEARCH TO PRACTICE

DESTINY-CRC01 AEs of Special Interest: Interstitial Lung Disease

All Patients (N=86)	n (%)
Grade 1	0
Grade 2	4 (4.7)
Grade 3	1 (1.2)
Grade 4	0
Grade 5	3 (3.5)[a]
Any Grade/Total	8 (9.3)[b,c]

Adjudicated drug-related ILDs:

- Median time to adjudicated onset was 61.0 days (range, 9-165 days)
- 8 of 8 patients received corticosteroids
- 4 patients with grade 2 recovered and 1 patient with grade 3 did not recover (later died due to disease progression)
- Median time from adjudicated onset date to initiation of steroid treatment in the 8 ILD cases was 3.5 days, (range 0-50)

Grade 5 ILDs:

- In the 3 fatal cases adjudicated as drug-related ILD, onset was from 9 days to 120 days (median: 22 days); and death occurred 6-19 days after diagnosis (median: 6 days)

Updated ILD/pneumonitis guidelines recommend to monitor for symptoms, interrupt or discontinue T-DXd, conduct imaging (as clinically indicated), and start steroids as soon as ILD is suspected.

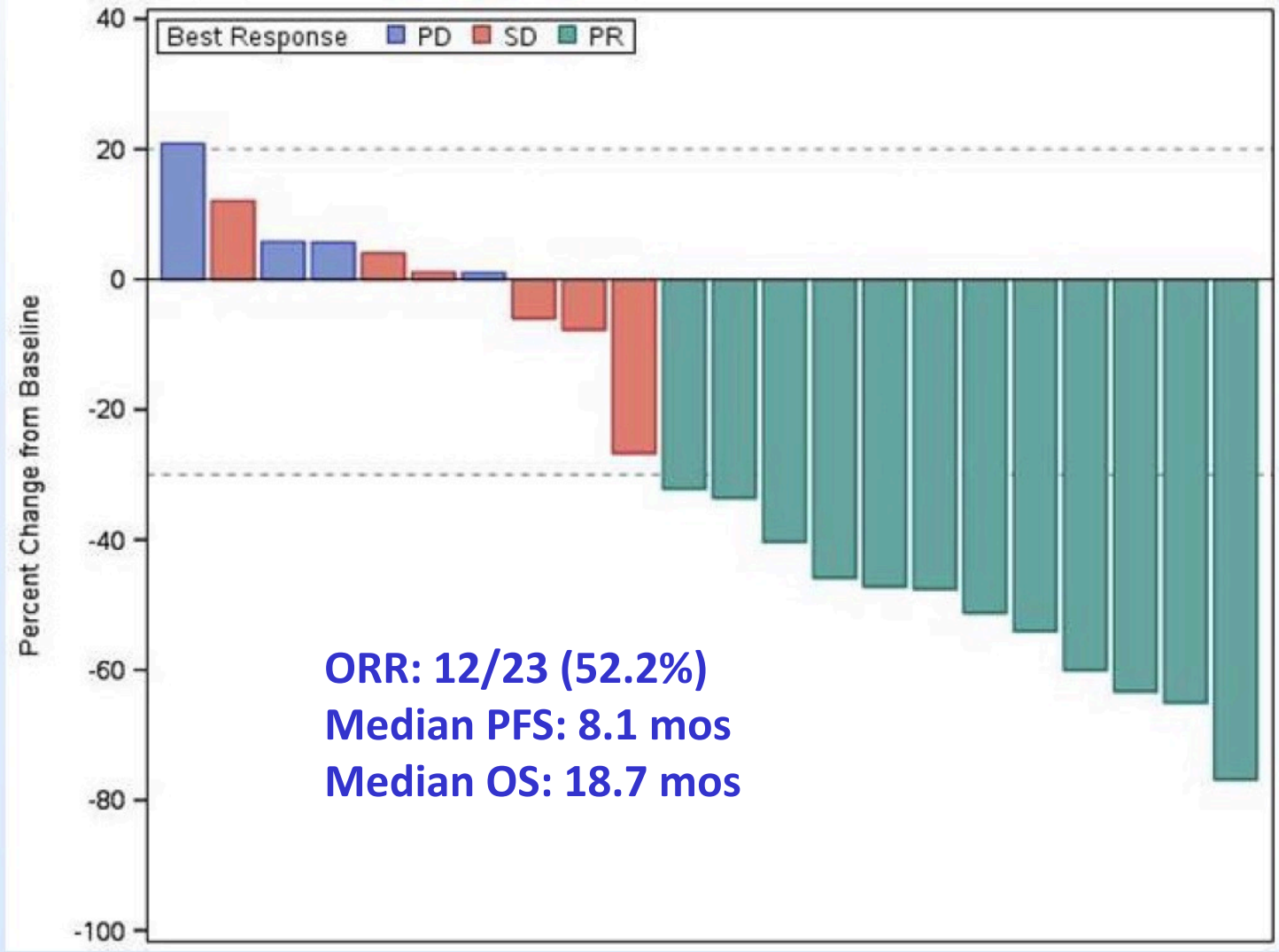
Yoshino T et al. ASCO 2021;Abstract 3500.

Trastuzumab and Tucatinib for the Treatment of HER2 Amplified Metastatic Colorectal Cancer: Initial Results from the MOUNTAINEER Trial

Strickler JH et al.

ESMO 2019;Abstract 527PD.

MOUNTAINEER: Response and Survival



Strickler JH et al. ESMO 2019;Abstract 527PD.

Meet The Professor with Dr Messersmith

MODULE 1: Cases from Drs Chen and Ibrahim

- Dr Chen: A 68-year-old woman with MMR-proficient T3N0 rectal cancer
- Dr Ibrahim: A 40-year-old man with MSI-high metastatic colon cancer

MODULE 2: Beyond the Guidelines; Key Data – Colorectal Cancer

MODULE 3: Cases from Drs Brooks and Gosain

- Dr Brooks: A 55-year-old man with MSS esophageal cancer – PD-L1 CPS 10
- Dr Gosain: A 56-year-old man with HER2-positive, MSS gastroesophageal junction cancer

MODULE 4: Beyond the Guidelines; Key Data – Gastroesophageal, Esophageal Cancers

MODULE 5: Cases from Drs Glynn and Gupta

- Dr Glynn: A 74-year-old man with hepatocellular carcinoma (HCC) and cirrhosis
- Dr Gupta: An 80-year-old woman with metastatic HCC

MODULE 6: Beyond the Guidelines; Key Data – HCC

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TO PRACTICE

Case Presentation – Dr Brooks: A 55-year-old man with MSS esophageal cancer – PD-L1 CPS 10

Dr Philip Brooks

- PMH: Papilloma of nasal cavity and COPD
- 11/2020: Difficulty swallowing solids, with regurgitation
- Diagnosed with poorly differentiated adenocarcinoma, PD-L1 CPS 10, MSS, HER2 equivocal
- CT: Enlarged peri-gastric and pericaval nodes up to 2-cm, 2.5-cm adrenal mass, and multiple liver lesions
- FOLFOX, with discussion about adding ICI
  - Needle biopsy: HER2-positive by FISH
- Trastuzumab added to FOLFOX

Questions

- How is it best to sequence the targeted treatments we have available? How would you approach it when there's progression? If we start with anti-HER2 therapy, would we proceed with another anti-HER2 agent or move to immunotherapy? Is there any role of using them together at some point?
- Would the experts agree with targeting HER2 first rather than with using immunotherapy? Would it be the newer agents that target trastuzumab?

Case Presentation – Dr Gosain: A 56-year-old man with HER2-positive, MSS gastroesophageal junction cancer

Dr Rahul Gosain

- Worsening dysphagia and 10lbs weight loss
- EGD consistent with poorly differentiated adenocarcinoma, MSI stable, HER2-positive, PD-L1 negative
- PET-CT: Gastro-hepatic adenopathy. No other distant disease
- Peri-operative concurrent carbo + paclitaxel + radiation therapy
  - Repeat EGD post treatment consistent with residual disease
- Patient evaluated by surgery but declined surgery

Questions

- Would you consider systemic chemotherapy as palliative treatment?
- Would you consider immunotherapy, despite his PD-L1 or CPS score?
- Is there any data for neoadjuvant trastuzumab?

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Messersmith

MODULE 1: Cases from Drs Chen and Ibrahim

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- Dr Glynn: A 74-year-old man with hepatocellular carcinoma (HCC) and cirrhosis
- Dr Gupta: An 80-year-old woman with metastatic HCC

MODULE 6: Beyond the Guidelines; Key Data – HCC

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 who has experienced disease progression on first-line FOLFOX?

 Prof Arnold	Ramucirumab/ paclitaxel	 Dr Ciombor	FOLFIRI/ramucirumab
 Dr Bekaii-Saab	Test for PD-L1 CPS and administer pembrolizumab if ≥10	 Dr O'Reilly	Ramucirumab/ paclitaxel
 Dr Bendell	Test for PD-L1 CPS and administer pembrolizumab if ≥10	 Dr Venook	Ramucirumab/ paclitaxel
 Dr Catenacci	FOLFIRI/ramucirumab	 Dr Wainberg	Ramucirumab/ paclitaxel

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-positive, MSS adenocarcinoma of the GEJ who has experienced disease progression on first-line FOLFOX/trastuzumab?

 Prof Arnold	Ramucirumab/ paclitaxel	 Dr Ciombor	FOLFIRI/ramucirumab
 Dr Bekaii-Saab	Trastuzumab deruxtecan	 Dr O'Reilly	Trastuzumab deruxtecan
 Dr Bendell	Test for PD-L1 CPS and administer pembrolizumab if ≥10%	 Dr Venook	Ramucirumab/ paclitaxel
 Dr Catenacci	Continue trastuzumab and switch chemotherapy	 Dr Wainberg	Trastuzumab deruxtecan

RTP RESEARCH TO PRACTICE

Impact of Radiation Dose on Postoperative Complications in Esophageal and Gastroesophageal Junction Cancers

Noah Kastelowitz[1], Megan D. Marsh[2], Martin McCarter[2], Robert A. Meguid[2], Narine Wandrey Bhardwaj[2], John D. Mitchell[2], Michael J. Weyant[2], Christopher Scott[2], Tracey Schefter[2], Priscilla Stumpf[2], Stephen Leong[2], Wells Messersmith[2], Christopher Lieu[2], Alexis D. Leal[2], S. Lindsey Davis[2], William T. Purcell[2], Madeleine Kane[2], Sachin Wani[2], Raj Shah[2], Hazem Hammad[2], Steven Edmundowicz[2] and Karyn A. Goodman[3]*

Front Oncol **2021;11:614640.**

Tissue Tumor Mutational Burden (TMB) as a Biomarker of Efficacy with Immune Checkpoint Inhibitors (ICI) in Metastatic Gastrointestinal (mGI) Cancers

Lentz RW et al.

ASCO 2021;Abstract e14559.

Innate Immune Checkpoint Inhibitors: The Next Breakthrough in Medical Oncology?

Robert W. Lentz[1], Meryl D. Colton[2], Siddhartha S. Mitra[3], and Wells A. Messersmith[1]

Mol Cancer Ther 2021;20(6):961-74.

2021 ASCO ANNUAL MEETING

Abstract 2505

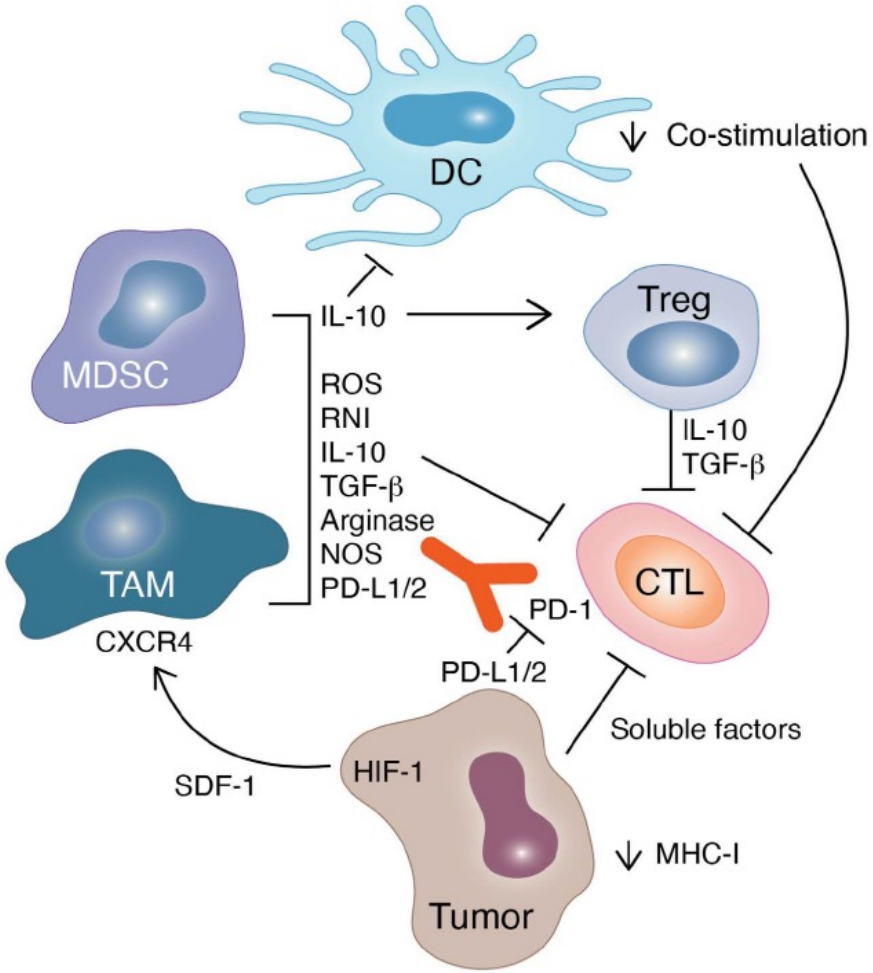
PRELIMINARY CLINICAL AND BIOLOGIC RESULTS OF GB1275, A FIRST-IN-CLASS ORAL CD11B MODULATOR, ALONE AND WITH PEMBROLIZUMAB, IN ADVANCED SOLID TUMORS (KEYNOTE A36)

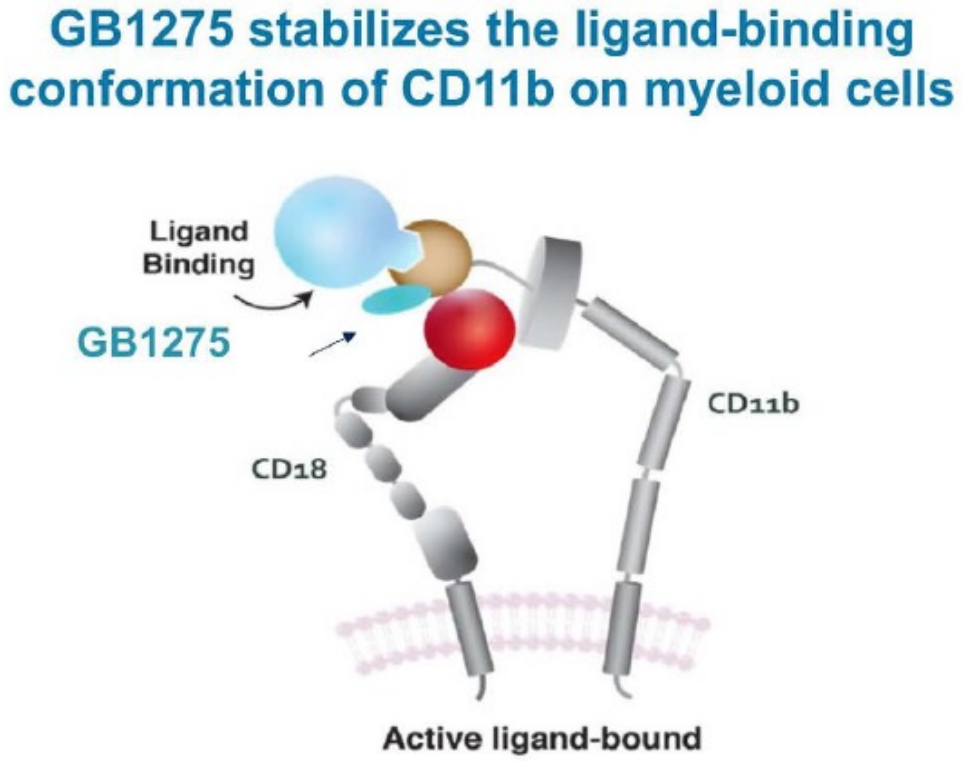
Haeseong Park, MD MPH
Washington University, St. Louis, MO

On behalf of co-authors: Johanna C. Bendell, Wells A. Messersmith, Drew W. Rasco, Johann S. de Bono, John Strickler, Lei Zhou, Laura L. Carter, Jean-Marie Bruey, Jack Li, Kartik Raghupathi, Jakob Dupont, Marya F. Chaney, Wungki Park

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Unique Mechanism of Action of the Oral CD11B Modulator GB1275





Park H et al. ASCO 2021;Abstract 2505.

2021 ASCO ANNUAL MEETING

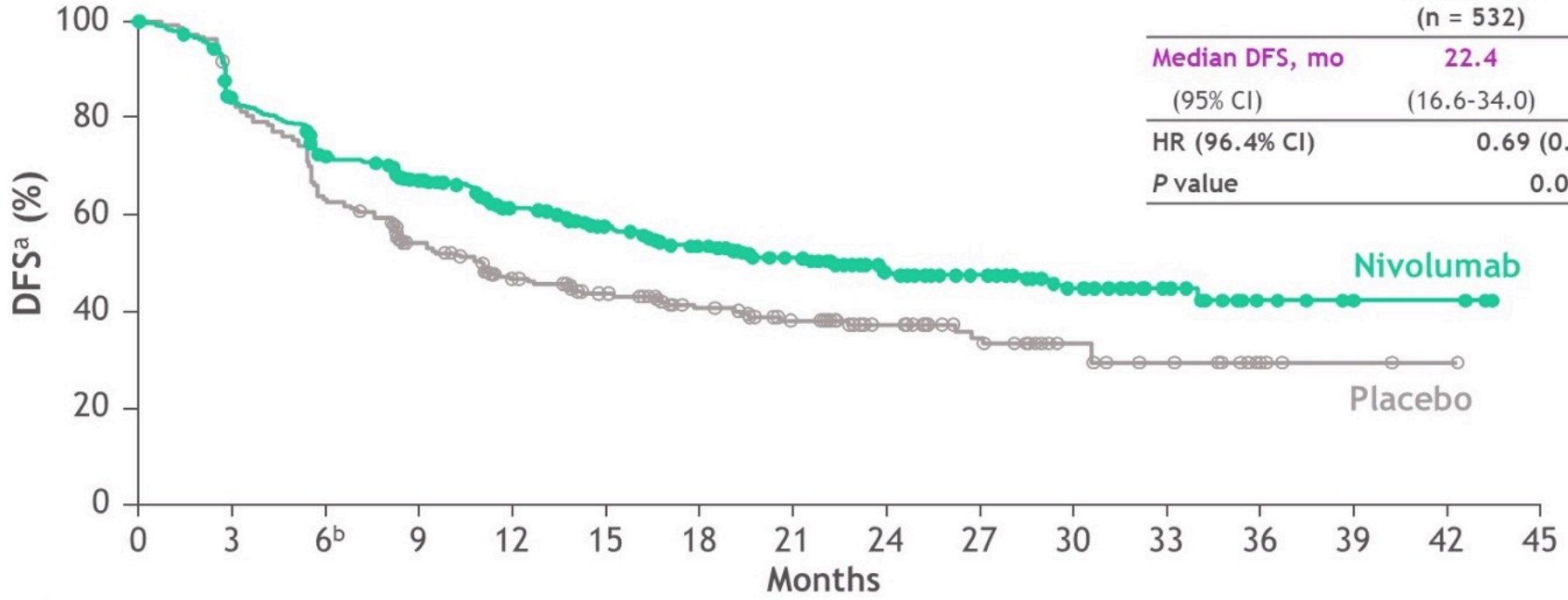
Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

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



	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.

FDA Approves Pembrolizumab in Combination with Chemotherapy for Esophageal or GEJ Carcinoma

Press Release – March 22, 2021

"On March 22, 2021, the Food and Drug Administration approved pembrolizumab in combination with platinum and fluoropyrimidine-based chemotherapy for patients with metastatic or locally advanced esophageal or gastroesophageal (GEJ) (tumors with epicenter 1 to 5 centimeters above the gastroesophageal junction) carcinoma who are not candidates for surgical resection or definitive chemoradiation.

Efficacy was evaluated in KEYNOTE-590 (NCT03189719), a multicenter, randomized, placebo-controlled trial that enrolled 749 patients with metastatic or locally advanced esophageal or gastroesophageal junction carcinoma who were not candidates for surgical resection or definitive chemoradiation.

The recommended pembrolizumab dose for esophageal cancer is 200 mg every 3 weeks or 400 mg every 6 weeks."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-esophageal-or-gej-carcinoma?utm_medium=email&utm_source=govdelivery

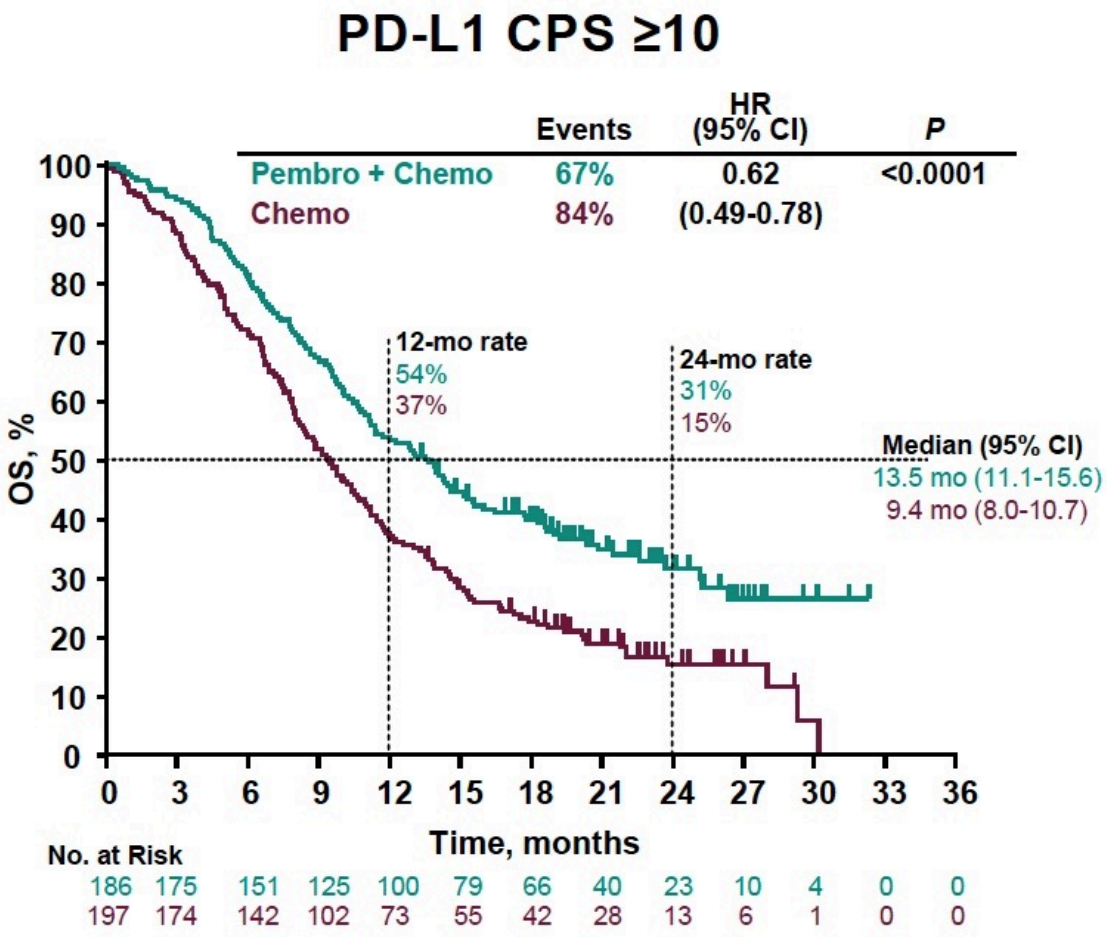
RTP RESEARCH TO PRACTICE

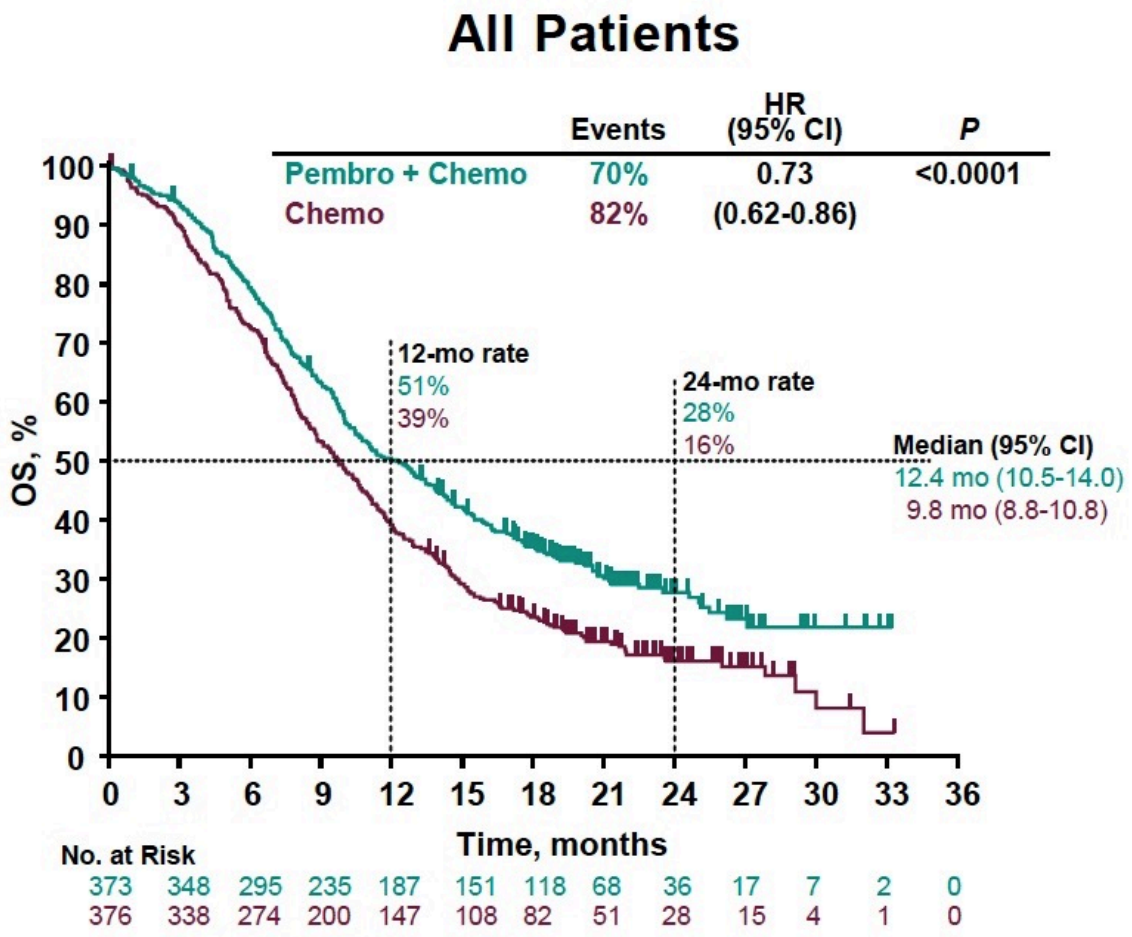
Pembrolizumab plus Chemotherapy versus Chemotherapy as First-Line Therapy in Patients with Advanced Esophageal Cancer: The Phase 3 KEYNOTE-590 Study

Kato K et al.

ESMO 2020;Abstract LBA8_PR.

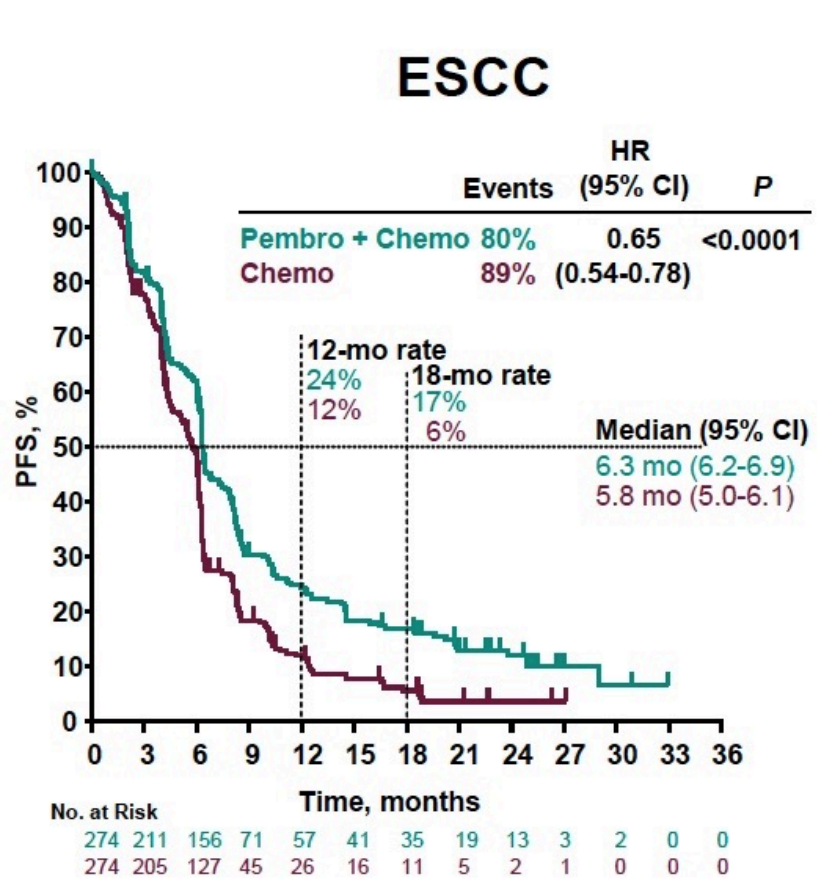
KEYNOTE-590: Overall Survival

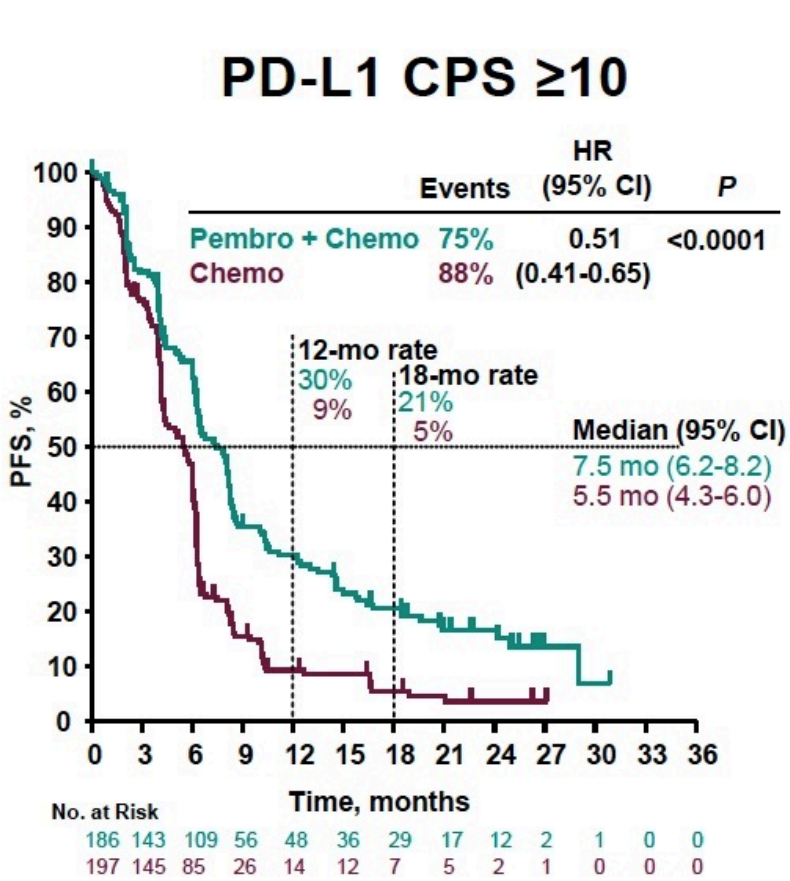


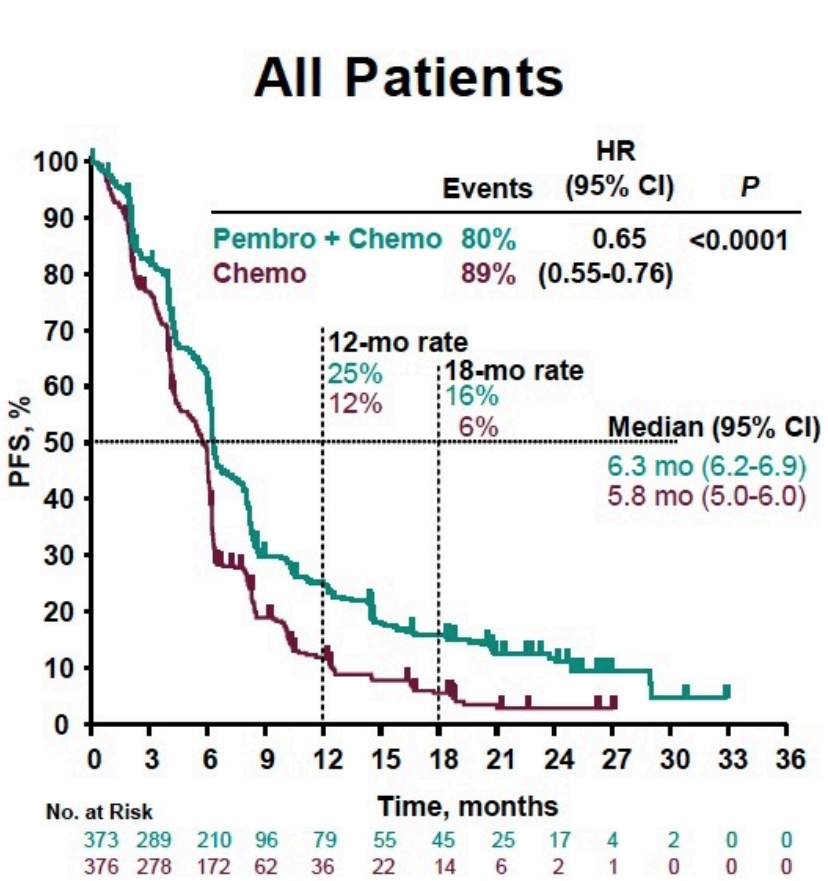


Kato K et al. ESMO 2020;Abstract LBA8_PR.

KEYNOTE-590: Progression-Free Survival







Kato K et al. ESMO 2020;Abstract LBA8_PR.

RTP RESEARCH TO PRACTICE

FDA Approves Nivolumab with Chemotherapy for Front-Line Advanced Gastric Cancer

Press Release – April 16, 2021

"The FDA approved nivolumab in combination with certain types of chemotherapy for the frontline treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma, making it the first approved immunotherapy for this patient population.

The agency based the approval on data from the randomized, multicenter, open-label phase 3 CheckMate-649 trial, designed to evaluate nivolumab – a monoclonal antibody that inhibits tumor growth by enhancing T-cell function – plus chemotherapy in 1,581 patients with previously untreated advanced or metastatic gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma. Of the 789 patients treated in the nivolumab arm, median overall survival was 13.8 months, compared with 11.6 months for patients who received chemotherapy alone."

https://www.cancernetwork.com/view/fda-approves-nivolumab-plus-chemo-for-frontline-advanced-gastric-cancer?utm_source=sfmc&utm_medium=email&utm_campaign=4.16.21_CN_Breaking&eKey=Z2tlbGx5QHJlc2VhcmNodG9wcmFjdGljZS5jb20=

RTP RESEARCH TO PRACTICE

2021 ASCO ANNUAL MEETING

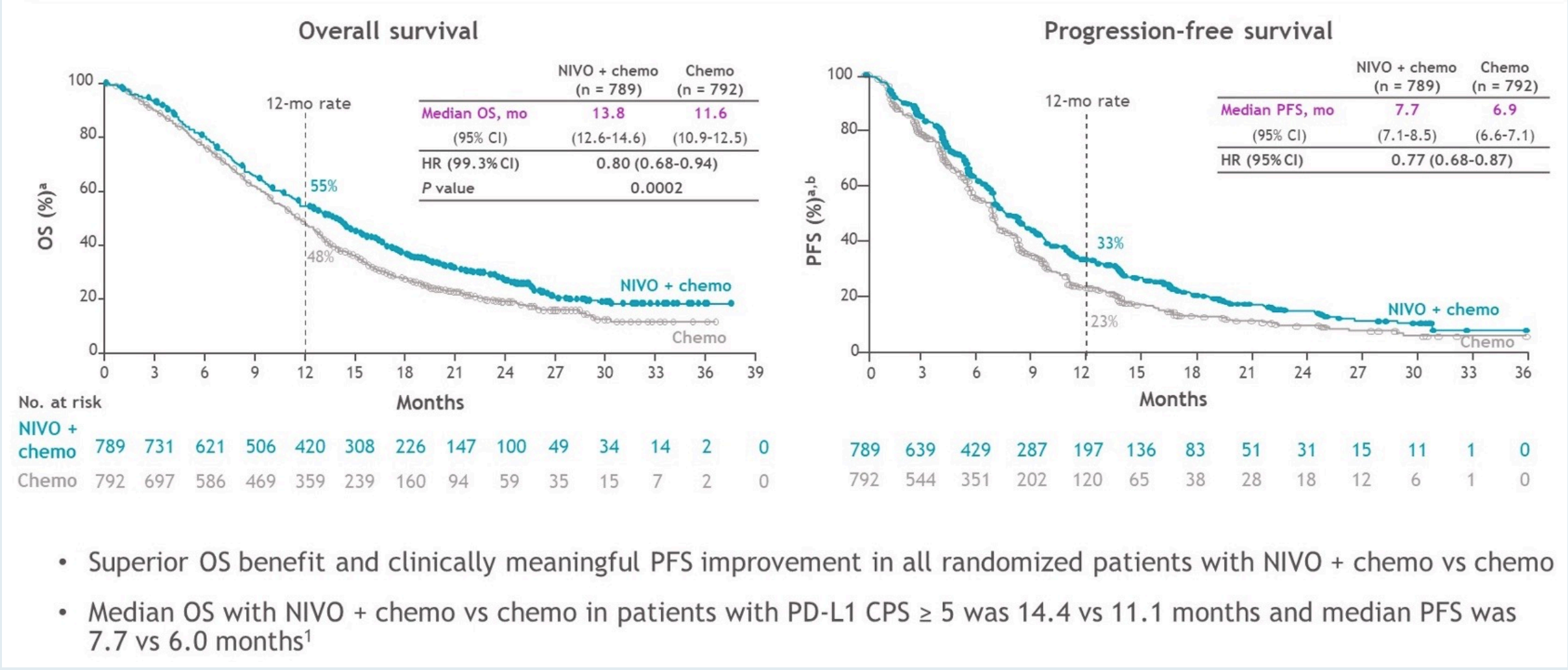
First-line nivolumab plus chemotherapy vs chemotherapy in advanced gastric cancer/ gastroesophageal junction cancer/esophageal adenocarcinoma: expanded efficacy and safety data from CheckMate 649

Markus Moehler,[1] Kohei Shitara,[2] Marcelo Garrido,[3] Pamela Salman,[4] Lin Shen,[5] Lucjan Wyrwicz,[6] Kensei Yamaguchi,[7] Tomasz Skoczylas,[8] Arinilda Campos Bragagnoli,[9] Tianshu Liu,[10] Michael Schenker,[11] Patricio Yanez,[12] Mustapha Tehfe,[13] Mingshun Li,[14] Dana Cullen,[14] Samira Soleymani,[14] Ming Lei,[14] Hong Xiao,[14] Yelena Y. Janjigian,[15] Jaffer A. Ajani[16]

[1]Johannes-Gutenberg University Clinic, Mainz, Germany; [2]National Cancer Center Hospital East, Kashiwa, Japan; [3]Clinica San Carlos de Apoquindo, Pontificia Universidad Católica, Chile; [4]Fundación Arturo López Pérez, Providencia, Chile; [5]Department of Gastrointestinal Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital and Institute, Beijing, China; [6]Klinika Onkologii i Radioterapii, Narodowy Instytut Onkologii, Warszawa, Poland; [7]Cancer Institute Hospital of JFCR, Tokyo, Japan; [8]II Klinika Chirurgii Ogólnej, Gastroenterologicznej i Nowotworów Układu Pokarmowego, Medical University of Lublin, Lublin, Poland; [9]Fundacao Pio Xii Hosp Cancer De Barretos, Barretos, Brazil; [10]Zhongshan Hospital Fudan University, Shanghai, China; [11]SF Nectarie Oncology Center, Craiova, Romania; [12]Universidad de La Frontera, Temuco, Chile; [13]Oncology Center - Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Canada; [14]Bristol Myers Squibb, Princeton, NJ; [15]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY; [16]The University of Texas MD Anderson Cancer Center, Houston, TX

Abstract Number 4002

CheckMate 649 Dual Primary Endpoints: PFS and OS



- Superior OS benefit and clinically meaningful PFS improvement in all randomized patients with NIVO + chemo vs chemo
- Median OS with NIVO + chemo vs chemo in patients with PD-L1 CPS ≥ 5 was 14.4 vs 11.1 months and median PFS was 7.7 vs 6.0 months[1]

Moehler M et al. ASCO 2021;Abstract 4002.

RTP RESEARCH TO PRACTICE

2021 ASCO ANNUAL MEETING

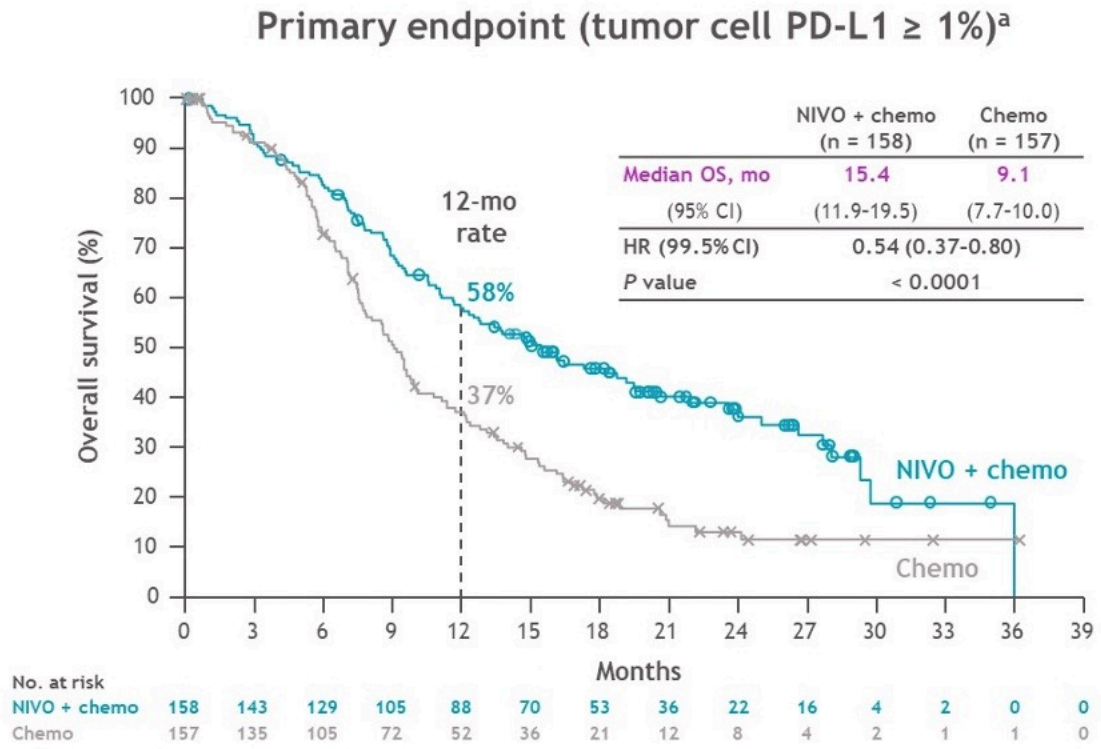
Nivolumab plus ipilimumab or nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced esophageal squamous cell carcinoma: first results of the CheckMate 648 study

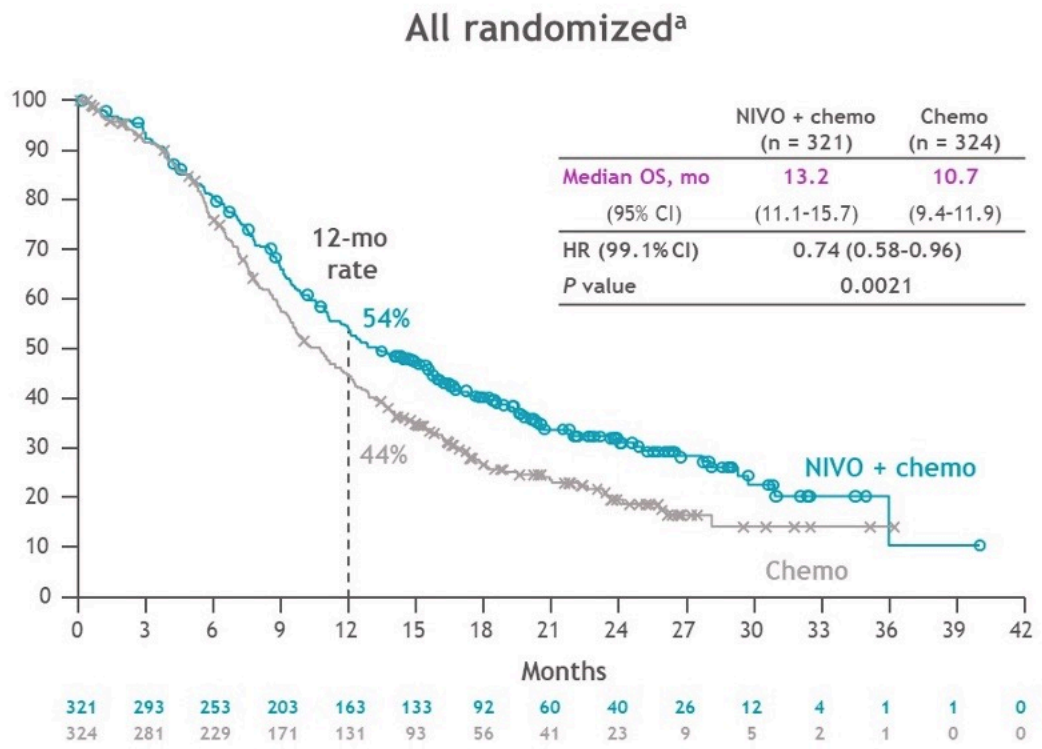
Ian Chau,[1] Yuichiro Doki,[2] Jaffer A. Ajani,[3] Jianming Xu,[4] Lucjan Wyrwicz,[5] Satoru Motoyama,[6] Takashi Ogata,[7] Hisato Kawakami,[8] Chih-Hung Hsu,[9] Antoine Adenis,[10] Farid el Hajbi,[11] Maria Di Bartolomeo,[12] Maria Ignez Braghiroli,[13] Eva Holtved,[14] Ioannis Xynos,[15] Xuan Liu,[15] Ming Lei,[15] Kaoru Kondo,[15] Ken Kato,[16] Yuko Kitagawa[17]

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

Abstract Number LBA4001

CheckMate 648: Overall Survival in Patients with PD-L1 ≥ 1% (Primary Endpoint Along with PFS in PD-L1 ≥ 1%) and in ITT



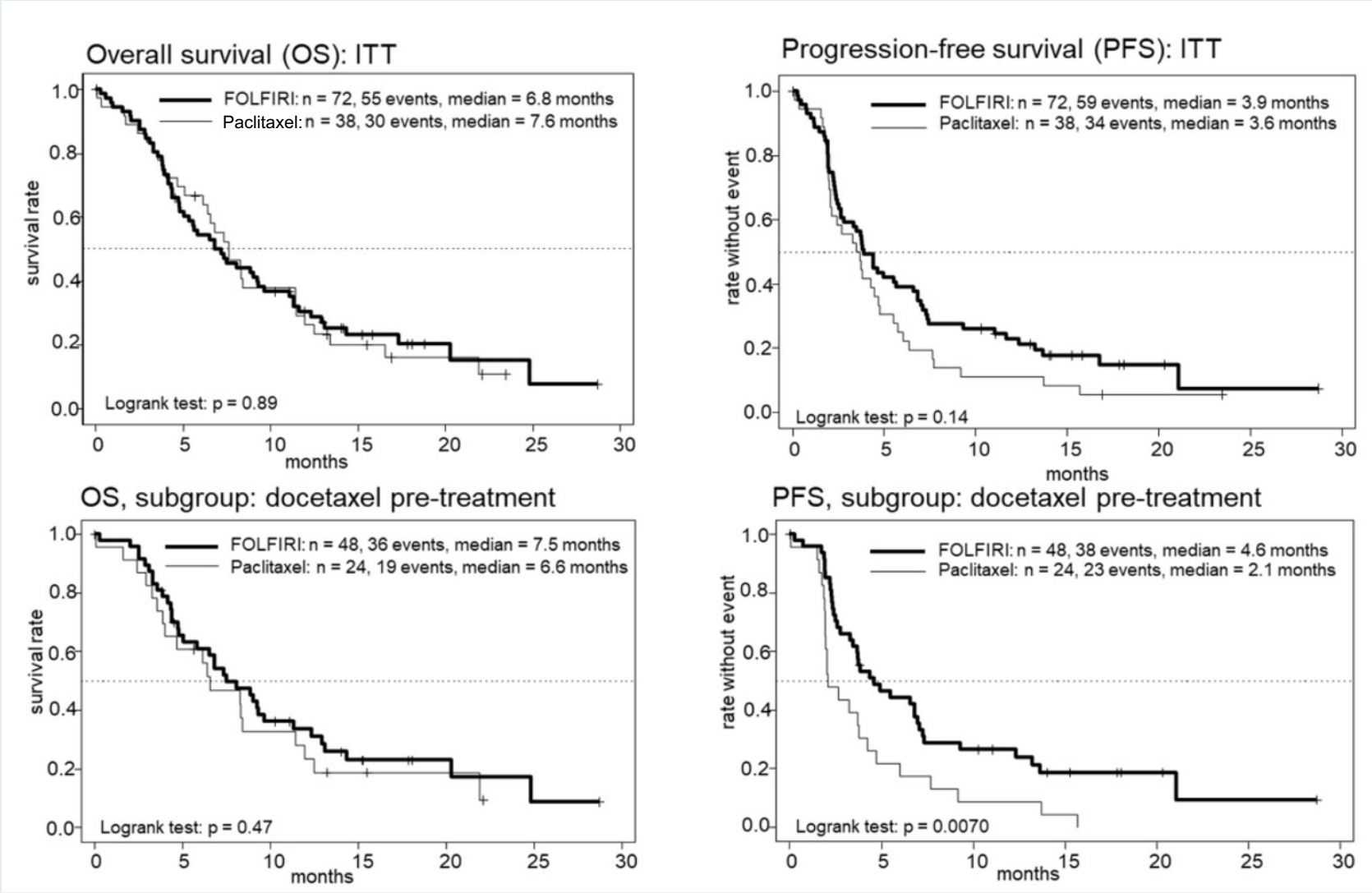


- Superior OS with NIVO + chemo vs chemo in tumor cell PD-L1 ≥ 1% and all randomized populations
  - Tumor cell PD-L1 ≥ 1%: 46% reduction in the risk of death and a 6.3-month improvement in median OS
  - All randomized: 26% reduction in the risk of death and a 2.5-month improvement in median OS

Chau I et al. ASCO 2021;Abstract LBA4001.

RTP RESEARCH TO PRACTICE

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



Lorenzen S et al. ASCO 2020;Abstract 4514.

FDA Approves Trastuzumab Deruxtecan for HER2-Positive Gastric Adenocarcinomas

Press Release – January 15, 2021

"On January 15, 2021, the Food and Drug Administration approved fam-trastuzumab deruxtecan-nxki for adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen.

Efficacy was evaluated in a multicenter, open-label, randomized trial (DESTINY-Gastric01, NCT03329690) in patients with HER2-positive locally advanced or metastatic gastric or GEJ adenocarcinoma who had progressed on at least two prior regimens, including trastuzumab, a fluoropyrimidine- and a platinum-containing chemotherapy. A total of 188 patients were randomized (2:1) to receive fam-trastuzumab deruxtecan-nxki 6.4 mg/kg intravenously every 3 weeks or physician's choice of either irinotecan or paclitaxel monotherapy."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-fam-trastuzumab-deruxtecan-nxki-her2-positive-gastric-adenocarcinomas

2021 ASCO ANNUAL MEETING

Abstract 4048

DESTINY-Gastric01

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with human epidermal growth factor receptor 2–positive advanced gastric cancer or gastroesophageal junction adenocarcinoma: final overall survival results from a randomized, multicenter, open-label, phase 2 study (DESTINY-Gastric01)

Kensei Yamaguchi

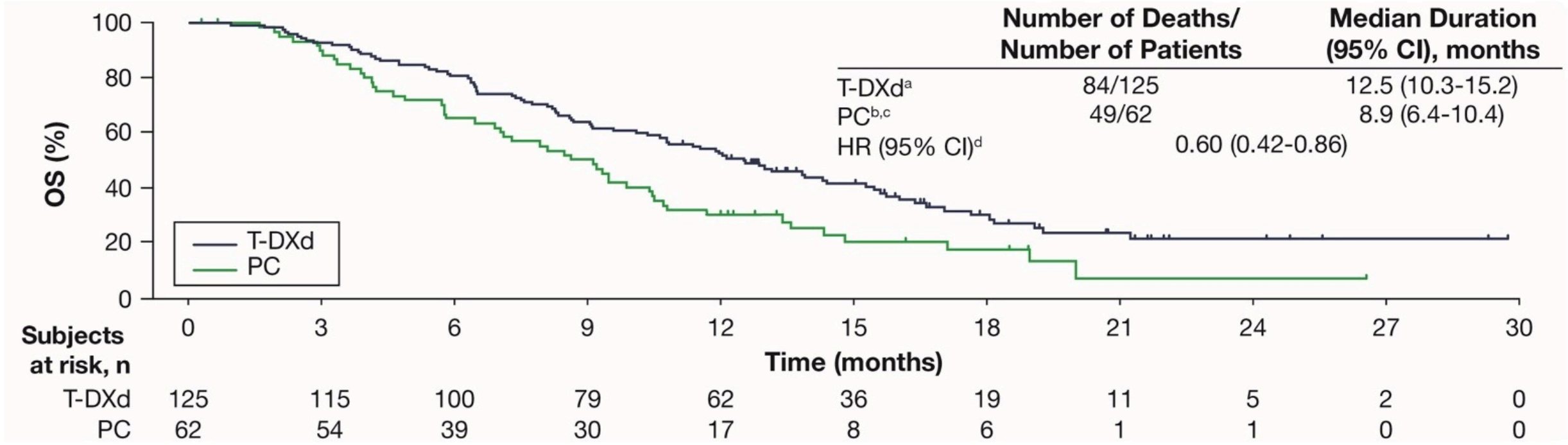
The Cancer Institute Hospital of JFCR, Tokyo, Japan

June 2021

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: Final Overall Survival Analysis



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. ASCO 2021;Abstract 4048.

DESTINY-Gastric01: Selected Adverse Events

Preferred Term, %	T-DXd n = 125			PC Overall n = 62		
	Grade			Grade		
	Any	3	4	Any	3	4
Neutrophil count decreased[b]	64.8	38.4	12.8	35.5	16.1	8.1
Nausea	63.2	5.6	0	46.8	1.6	0
Decreased appetite	60.8	16.8	0	45.2	12.9	0
Anemia[c]	57.6	38.4	0	30.6	21.0	1.6
Platelet count decreased[d]	40.0	9.6	1.6	6.5	1.6	1.6
White blood cell count decreased[e]	38.4	20.8	0	35.5	8.1	3.2

Yamaguchi K et al. ASCO 2021;Abstract 4048.

DESTINY-Gastric01 AEs of Special Interest: Interstitial Lung Disorder

- 16 patients (12.8%) had T-DXd-related ILD, as determined by an independent adjudication committee
  - There were 13 grade 1 or 2, two grade 3, one grade 4, and no grade 5 events
  - There were four ILD events since the primary analysis; one grade 1 and three grade 2
  - Among the 16 total ILD events, the median time to first onset was 102.5 days (range, 36-638 days)
- There was one T-DXd-related death from pneumonia (non-ILD), as reported in the primary analysis

Yamaguchi K et al. ASCO 2021;Abstract 4048.

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

Exploratory Biomarker in Primary HER2-Positive Cohort	Median Overall Survival
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.

FDA Grants Accelerated Approval to Pembrolizumab with Trastuzumab and Chemotherapy as First-Line Therapy for HER2-Positive Gastric Cancer

Press Release – May 5, 2021

"On May 5, 2021, the Food and Drug Administration granted accelerated approval to pembrolizumab in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of patients with locally advanced unresectable or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.

Approval was based on the prespecified interim analysis of the first 264 patients of the ongoing KEYNOTE-811 (NCT03615326) trial, a multicenter, randomized, double-blind, placebo-controlled trial in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma who had not previously received systemic therapy for metastatic disease. Patients were randomized (1:1) to receive pembrolizumab 200 mg or placebo every 3 weeks, in combination with trastuzumab and either fluorouracil plus cisplatin or capecitabine plus oxaliplatin.

The main efficacy measure for this analysis was overall response rate (ORR) assessed by blinded independent review committee. The ORR was 74% in the pembrolizumab arm and 52% in the placebo arm (one-sided p-value < 0.0001, statistically significant). The median duration of response (DoR) was 10.6 months for patients treated with pembrolizumab and 9.5 months for those in the placebo arm."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-pembrolizumab-her2-positive-gastric-cancer

RTP RESEARCH TO PRACTICE

ESMO WORLD CONGRESS ON Gastrointestinal Cancer

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

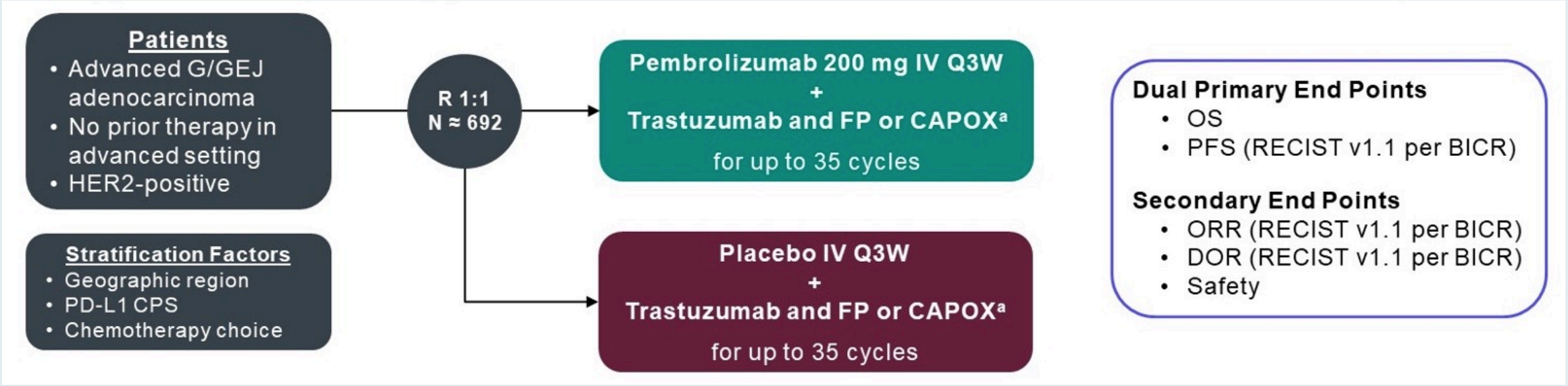
Yelena Y. Janjigian,[1] Akihito Kawazoe,[2] Patricio Yañez,[3] Suxia Luo,[4] Sara Lonardi,[5] Oleksii Kolesnik,[6] Olga Barajas,[7] Yuxian Bai,[8] Lin Shen,[9] Yong Tang,[10] Lucjan S. Wyrwicz,[11] Kohei Shitara,[2] Shukui Qin,[12] Eric Van Cutsem,[13] Josep Tabernero,[14] Lie Li,[15] Chie-Schin Shih,[15]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

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]National Cancer Center Hospital East, Kashiwa, Japan; [3]Universidad de La Frontera, James Lind Cancer Research Center, Temuco, Chile; [4]Henan Cancer Hospital, the Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China; [5]Istituto Oncologico Veneto IOV-IRCCS, Padova, Italy; [6]Medical Center "Oncolife", Zaporizhzhia, Ukraine; [7]Arturo López Pérez Foundation, Santiago, Chile; [8]Harbin Medical University Cancer Hospital, Harbin, China; [9]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, China; [10]Cancer Hospital Affiliated to Xinjiang Medical University, Xinjiang, China; [11]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; [12]Cancer Center of People's Liberation Army, Nanjing, China; [13]University Hospitals Gasthuisberg and KU Leuven, Leuven, Belgium; [14]Vall d'Hebron Hospital Campus and Institute of Oncology (VHIO), IOB-Quiron, UVic-UCC, Barcelona, Spain; [15]Merck & Co., Inc., Kenilworth, NJ, USA; [16]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract LBA4.

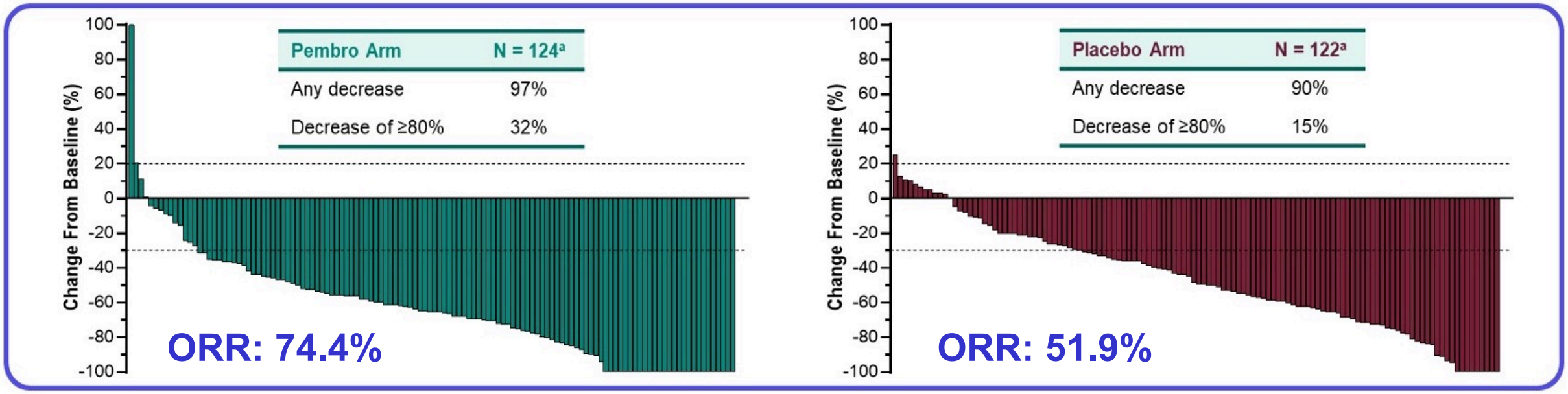
RTP RESEARCH TO PRACTICE

KEYNOTE-811 Phase III Study Design



Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancers 2021;Abstract LBA4.

KEYNOTE-811: Confirmed Response at First Interim Analysis



Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract LBA4.

Meet The Professor with Dr Messersmith

MODULE 1: Cases from Drs Chen and Ibrahim

- Dr Chen: A 68-year-old woman with MMR-proficient T3N0 rectal cancer
- Dr Ibrahim: A 40-year-old man with MSI-high metastatic colon cancer

MODULE 2: Beyond the Guidelines; Key Data – Colorectal Cancer

MODULE 3: Cases from Drs Brooks and Gosain

- Dr Brooks: A 55-year-old man with MSS esophageal cancer – PD-L1 CPS 10
- Dr Gosain: A 56-year-old man with HER2-positive, MSS gastroesophageal junction cancer

MODULE 4: Beyond the Guidelines; Key Data – Gastroesophageal, Esophageal Cancers

MODULE 5: Cases from Drs Glynn and Gupta

- Dr Glynn: A 74-year-old man with hepatocellular carcinoma (HCC) and cirrhosis
- Dr Gupta: An 80-year-old woman with metastatic HCC

MODULE 6: Beyond the Guidelines; Key Data – HCC

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Case Presentation – Dr Glynn: A 74-year-old man with HCC and cirrhosis

Dr Philip Glynn

- 11/2019: Abnormal liver function tests on routine exam
- MRI: Innumerable liver lesions (largest 5.6 cm)
- Biopsy: Moderately differentiated HCC, cirrhosis
- 1/2020: Chemoembolization → Sorafenib
  - Rash, weight loss
- 6/2020: Bevacizumab/atezolizumab, well tolerated, stable disease 12/2020

Question

- What would be the consideration for next line of therapy, whether going to regorafenib or ipi/nivo or cabozantinib?

Case Presentation – Dr Gupta: An 80-year-old woman with metastatic HCC

Dr Ranju Gupta

- PMH: Diabetes, gastroparesis, GERD, hypertension
- 11/2020: Multifocal and metastatic HCC, with right lobe of the liver nearly completely replaced by HCC
  - CT scan: 8.7-cm right hepatic lobe mass, 2.6-cm mass in the posterior segment of the right hepatic lobe. No adenopathy. Liver biopsy consistent with HCC. Alpha-fetoprotein 90.
- Patient not interested in systemic treatment because of her age and comorbid conditions
- 2/2021: Right lobar chemoembolization – 2 months later developed liver abscess status post drainage and antibiotics
- 7/2021 Restaging scans: New right pleural effusion, lung metastases

Questions

- Since the patient does not want to receive chemotherapy and in light of her age and comorbid conditions, what treatment would you recommend?

Meet The Professor with Dr Messersmith

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RTP RESEARCH TO PRACTICE

What would be your current preferred first-line systemic treatment for a 65-year-old patient with HCC, a Child-Pugh B7 score and PS 1?

1. Sorafenib
2. Lenvatinib
3. Atezolizumab/bevacizumab
4. Chemotherapy
5. Other

What would be your current preferred first-line systemic treatment for a 65-year-old patient with HCC, a Child-Pugh B7 score and a PS of 1?

 Prof Arnold	Atezolizumab/ bevacizumab	 Dr Ciombor	Sorafenib
 Dr Bekaii-Saab	Atezolizumab/ bevacizumab	 Dr O'Reilly	Lenvatinib
 Dr Bendell	Atezolizumab/ bevacizumab	 Dr Venook	Atezolizumab/ bevacizumab
 Dr Catenacci	Atezolizumab/ bevacizumab	 Dr Wainberg	Lenvatinib

RTP RESEARCH TO PRACTICE

What would be your most likely second-line systemic therapy for a 65-year-old patient with HCC, a Child-Pugh A score and a PS of 0 who received first-line atezolizumab/bevacizumab with minimal toxicity, had stable disease for 14 months and then experienced disease progression (alpha-fetoprotein, AFP, 2,500 ng/mL)?

 Prof Arnold	Cabozantinib	 Dr Ciombor	Sorafenib
 Dr Bekaii-Saab	Cabozantinib	 Dr O'Reilly	Lenvatinib
 Dr Bendell	Cabozantinib	 Dr Venook	Lenvatinib
 Dr Catenacci	Lenvatinib	 Dr Wainberg	Ramucirumab

RTP RESEARCH TO PRACTICE

What would be your most likely second-line systemic therapy for a 65-year-old patient with HCC, a Child-Pugh A score and a PS of 0 who received first-line standard-dose sorafenib with minimal toxicity, had stable disease for 14 months and then experienced disease progression (AFP 2,500 ng/mL)?

 Prof Arnold	Nivolumab	 Dr Ciombor	Atezolizumab/ bevacizumab
 Dr Bekaii-Saab	Atezolizumab/ bevacizumab	 Dr O'Reilly	Nivolumab/ ipilimumab
 Dr Bendell	Atezolizumab/ bevacizumab	 Dr Venook	Atezolizumab/ bevacizumab
 Dr Catenacci	Atezolizumab/ bevacizumab	 Dr Wainberg	Ramucirumab

RTP RESEARCH TO PRACTICE

What would be your most likely third-line systemic therapy recommendation for an otherwise healthy 65-year-old patient with HCC who experienced disease progression on first-line atezolizumab/bevacizumab and second-line lenvatinib (AFP 2,500 ng/mL)?

 Prof Arnold	Ramucirumab	 Dr Ciombor	Ramucirumab
 Dr Bekaii-Saab	Cabozantinib	 Dr O'Reilly	Nivolumab/ ipilimumab
 Dr Bendell	Cabozantinib	 Dr Venook	Cabozantinib
 Dr Catenacci	Ramucirumab	 Dr Wainberg	Ramucirumab

RTP RESEARCH TO PRACTICE

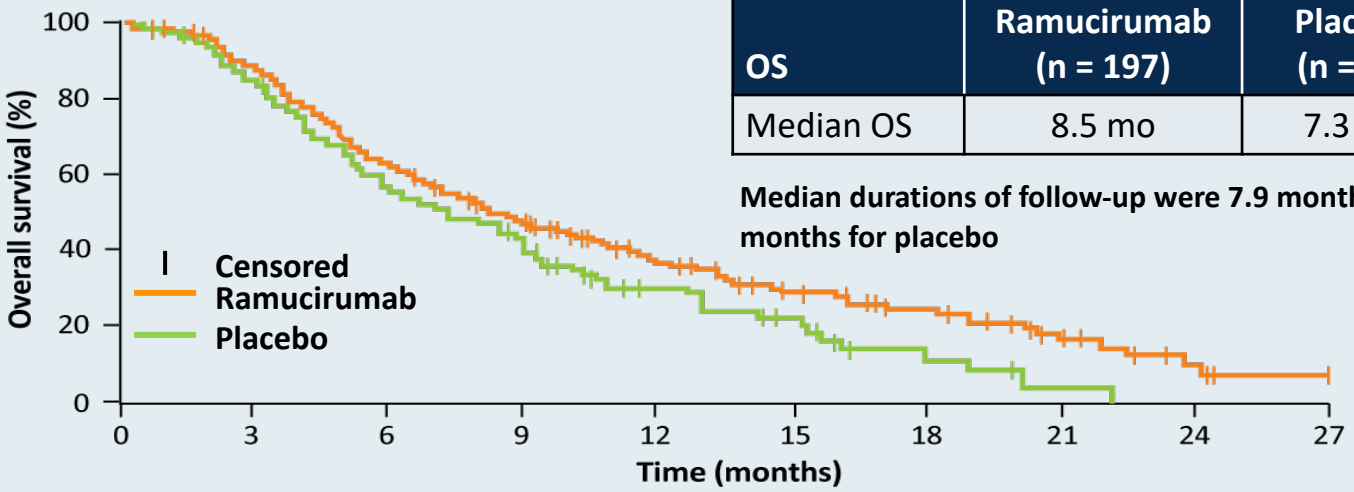
Articles

Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased α-fetoprotein concentrations (REACH-2): a randomised, double-blind, placebo-controlled, phase 3 trial

*Andrew X Zhu, Yoon-Koo Kang, Chia-Jui Yen, Richard S Finn, Peter R Galle, Josep M Llovet, Eric Assenat, Giovanni Brandi, Marc Pracht, Ho Yeong Lim, Kun-Ming Rau, Kenta Motomura, Izumi Ohno, Philippe Merle, Bruno Daniele, Dong Bok Shin, Guido Gerken, Christophe Borg, Jean-Baptiste Hiriart, Takuji Okusaka, Manabu Morimoto, Yanzhi Hsu, Paolo B Abada, Masatoshi Kudo, for the REACH-2 study investigators**

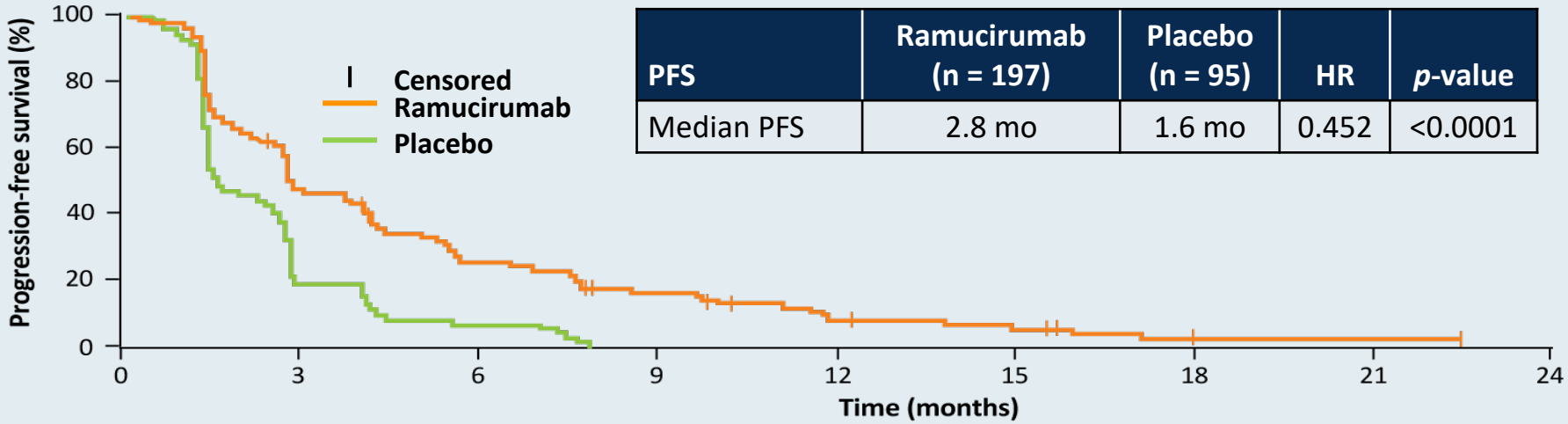
Lancet Oncol 2019;20(2):282-96.

REACH-2: A Phase III Trial of Ramucirumab After Sorafenib for Patients with Advanced HCC and Increased AFP



OS	Ramucirumab (n = 197)	Placebo (n = 95)	HR	*p*-value
Median OS	8.5 mo	7.3 mo	0.710	0.0199

Median durations of follow-up were 7.9 months for ramucirumab, 6.6 months for placebo



PFS	Ramucirumab (n = 197)	Placebo (n = 95)	HR	*p*-value
Median PFS	2.8 mo	1.6 mo	0.452	<0.0001

Grade ≥3 AEs associated with ramucirumab included hypertension and hyponatremia.

Zhu AX et al. ASCO 2018;Abstract 4003; *Lancet Oncol* 2019;20(2):282-96.

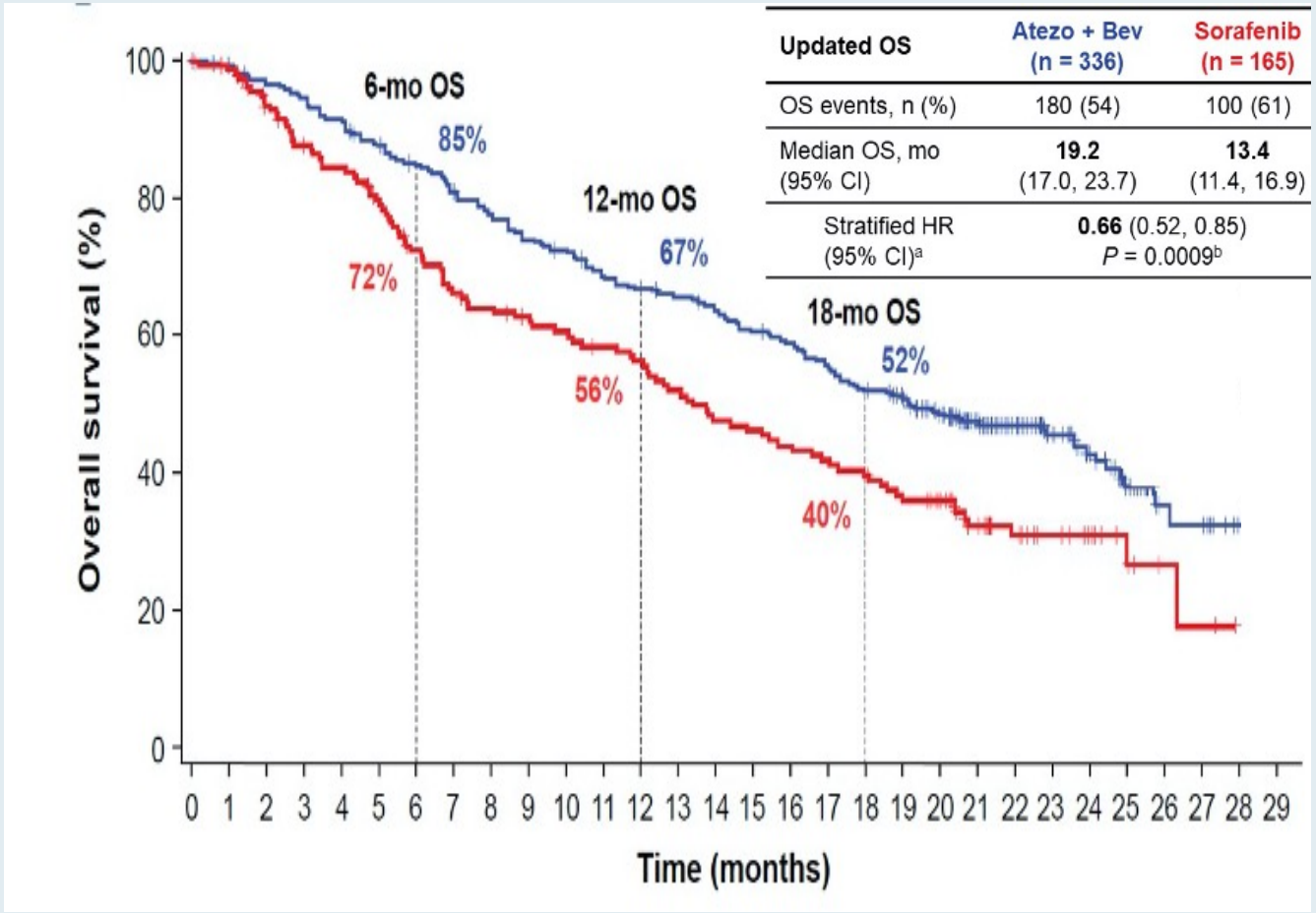
RTP RESEARCH TO PRACTICE

IMbrave150: Updated Overall Survival (OS) Data from a Global, Randomized, Open-Label Phase III Study of Atezolizumab (atezo) + Bevacizumab (bev) versus Sorafenib (sor) in Patients (pts) with Unresectable Hepatocellular Carcinoma (HCC)

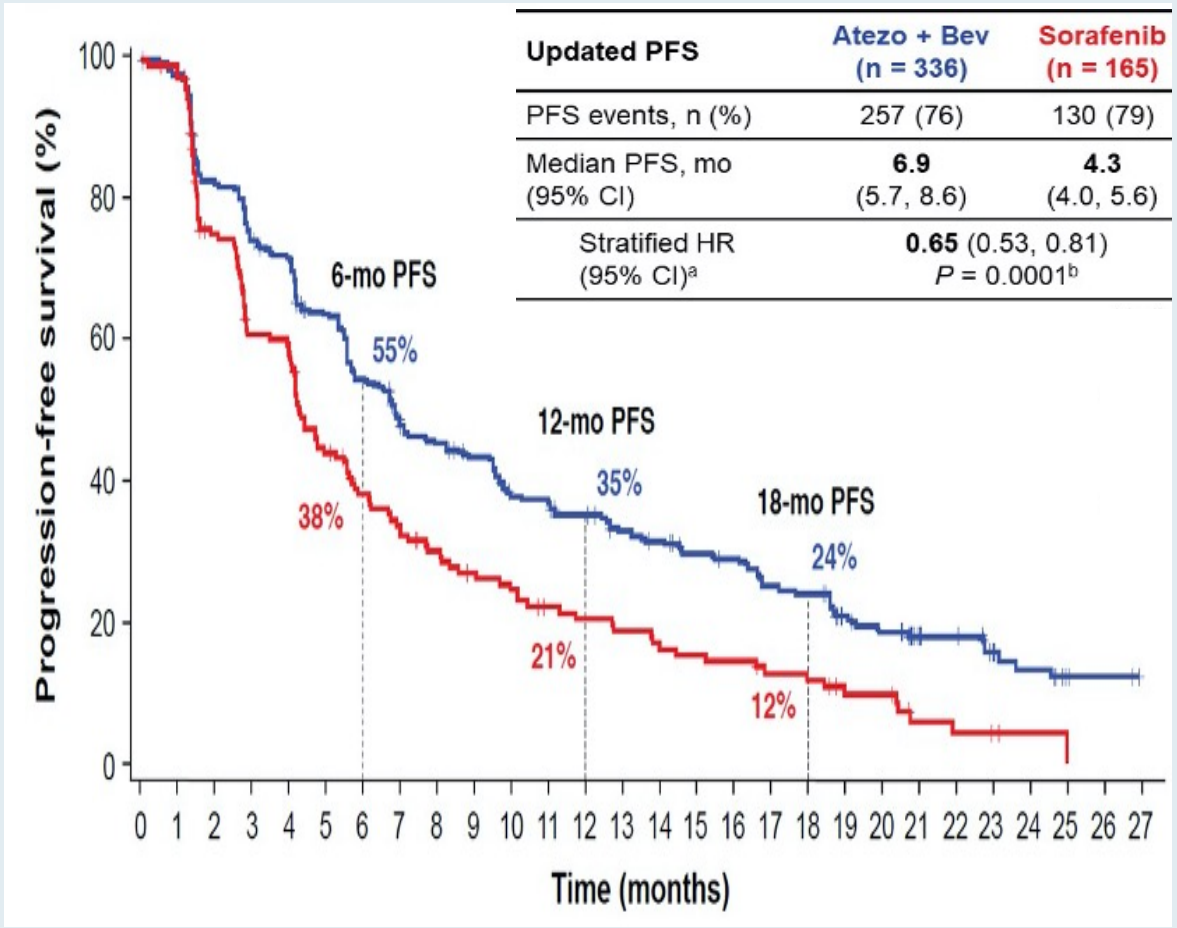
Finn RS et al.

Gastrointestinal Cancers Symposium 2021;Abstract 267.

IMbrave150: Updated OS and PFS (Median Follow-Up = 15.6 Months)



Updated OS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
OS events, n (%)	180 (54)	100 (61)
Median OS, mo (95% CI)	**19.2** (17.0, 23.7)	**13.4** (11.4, 16.9)
Stratified HR (95% CI)[a]	**0.66** (0.52, 0.85) *P* = 0.0009[b]	



Updated PFS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
PFS events, n (%)	257 (76)	130 (79)
Median PFS, mo (95% CI)	**6.9** (5.7, 8.6)	**4.3** (4.0, 5.6)
Stratified HR (95% CI)[a]	**0.65** (0.53, 0.81) *P* = 0.0001[b]	

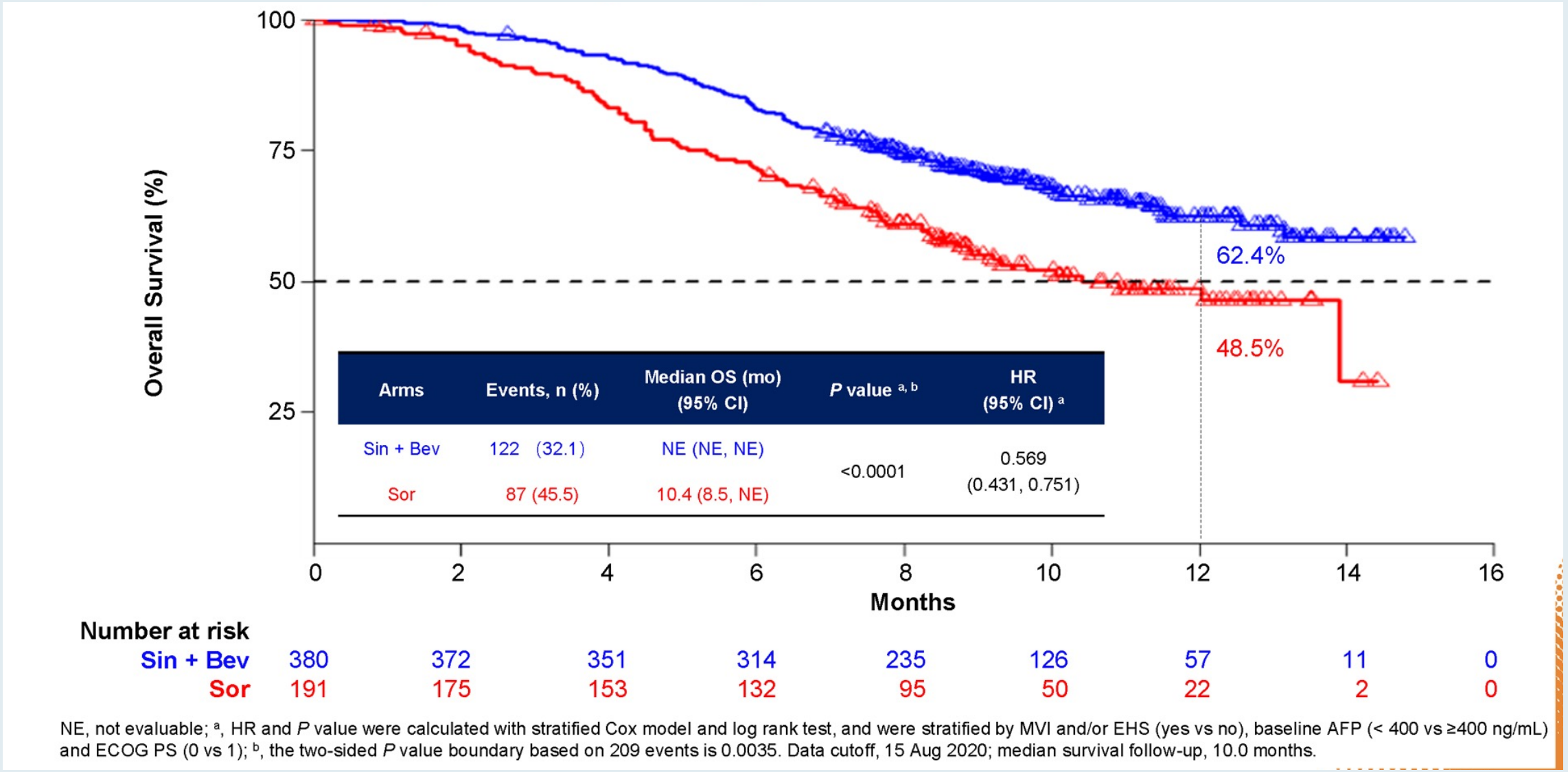
Finn RS et al. Gastrointestinal Cancers Symposium 2021;Abstract 267.

RTP RESEARCH TO PRACTICE

Sintilimab plus Bevacizumab Biosimilar vs Sorafenib as First-Line Treatment for Advanced Hepatocellular Carcinoma (ORIENT-32)

Ren Z et al.
ESMO Asia 2020;Abstract LBA2.

ORIENT-32 Coprimary Endpoint: Overall Survival



Arms	Events, n (%)	Median OS (mo) (95% CI)	*P* value [a, b]	HR (95% CI) [a]
Sin + Bev	122 (32.1)	NE (NE, NE)	<0.0001	0.569 (0.431, 0.751)
Sor	87 (45.5)	10.4 (8.5, NE)		

Number at risk

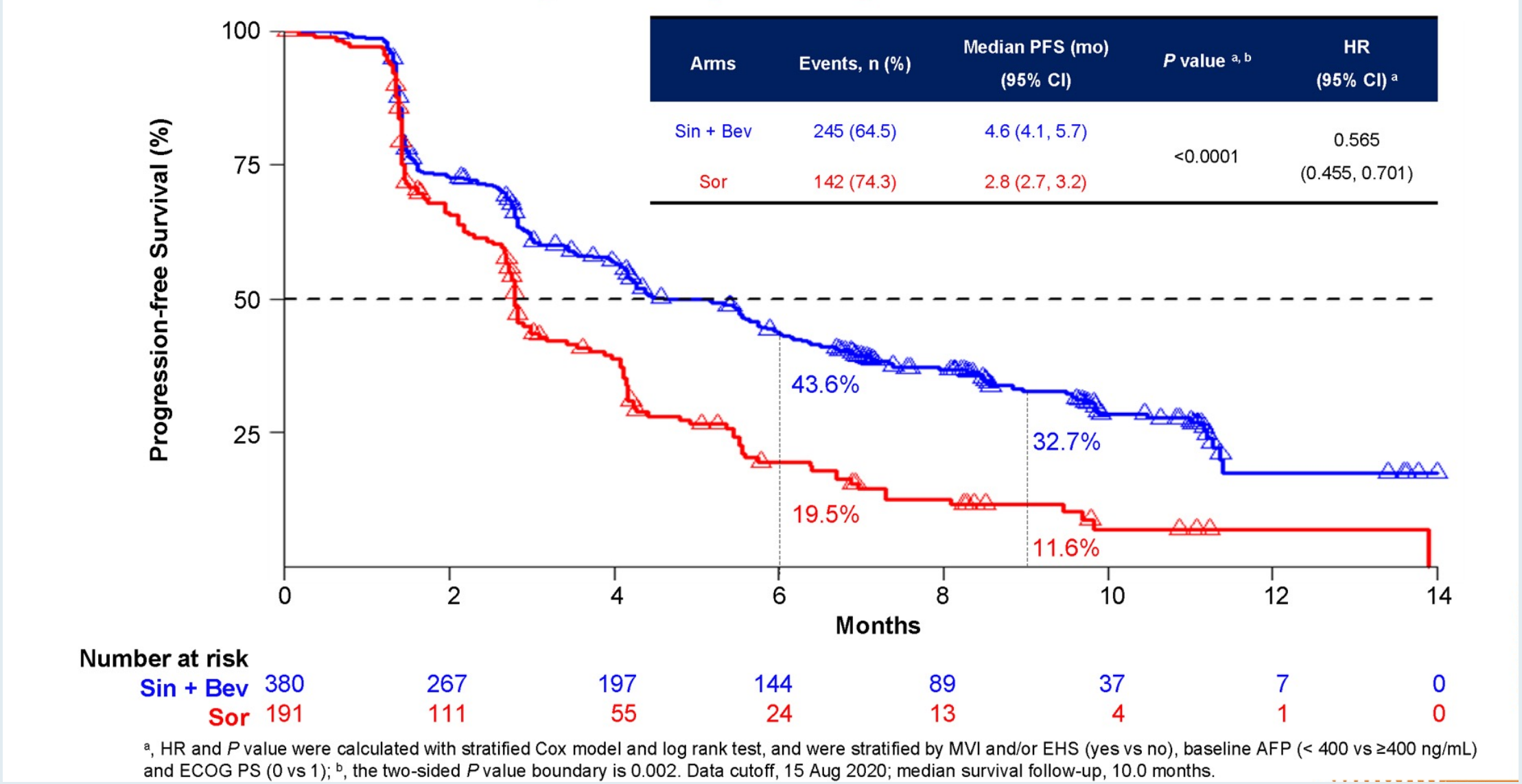
Sin + Bev	380	372	351	314	235	126	57	11	0
Sor	191	175	153	132	95	50	22	2	0

NE, not evaluable; [a], HR and *P* value were calculated with stratified Cox model and log rank test, and were stratified by MVI and/or EHS (yes vs no), baseline AFP (< 400 vs ≥400 ng/mL) and ECOG PS (0 vs 1); [b], the two-sided *P* value boundary based on 209 events is 0.0035. Data cutoff, 15 Aug 2020; median survival follow-up, 10.0 months.

The superior OS benefit with sintilimab plus bev biosimilar was generally consistent across all subgroups

Ren Z et al. ESMO Asia 2020;Abstract LBA2.

ORIENT-32 Coprimary Endpoint: Progression-Free Survival



Arms	Events, n (%)	Median PFS (mo) (95% CI)	*P* value [a, b]	HR (95% CI) [a]
Sin + Bev	245 (64.5)	4.6 (4.1, 5.7)	<0.0001	0.565 (0.455, 0.701)
Sor	142 (74.3)	2.8 (2.7, 3.2)		

Number at risk								
Sin + Bev	380	267	197	144	89	37	7	0
Sor	191	111	55	24	13	4	1	0

[a], HR and *P* value were calculated with stratified Cox model and log rank test, and were stratified by MVI and/or EHS (yes vs no), baseline AFP (< 400 vs ≥400 ng/mL) and ECOG PS (0 vs 1); [b], the two-sided *P* value boundary is 0.002. Data cutoff, 15 Aug 2020; median survival follow-up, 10.0 months.

The superior PFS benefit with sintilimab plus bev biosimilar was generally consistent across all subgroups

Ren Z et al. ESMO Asia 2020;Abstract LBA2.

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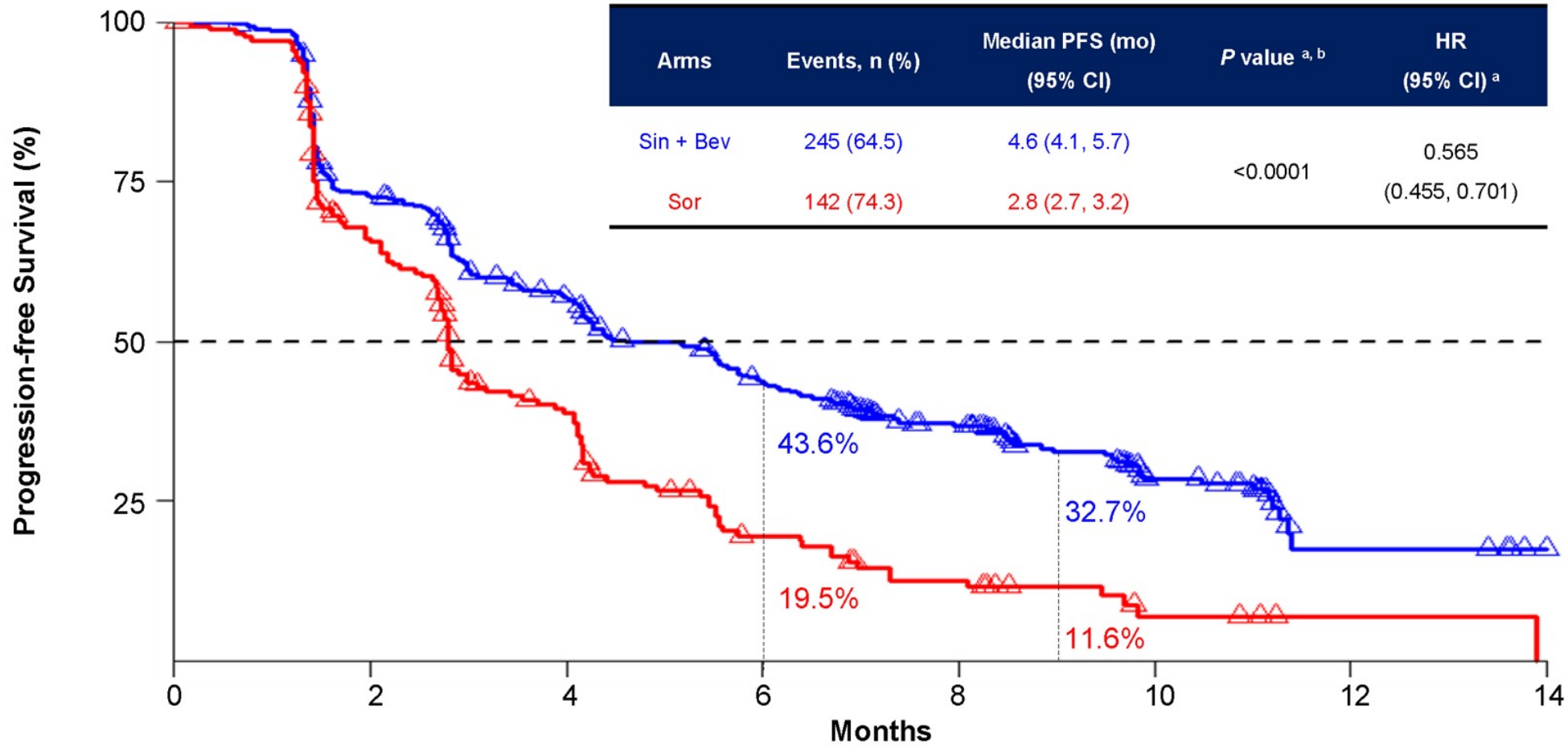
ORIENT-32 Coprimary Endpoint: Progression-Free Survival



Arms	Events, n (%)	Median PFS (mo) (95% CI)	*P* value [a, b]	HR (95% CI) [a]
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The superior PFS benefit with sintilimab plus bev biosimilar was generally consistent across all subgroups

Ren Z et al. ESMO Asia 2020;Abstract LBA2.

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Moderator

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