Meet The Professor

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

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

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, 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, 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 Bekaii-Saab — Disclosures

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Data and Safety Monitoring Board/Committee	AstraZeneca Pharmaceuticals LP, Exelixis Inc, Merck, Pancreatic Cancer Action Network
Inventions/Patents	WO/2018/183488, WO/2019/055687

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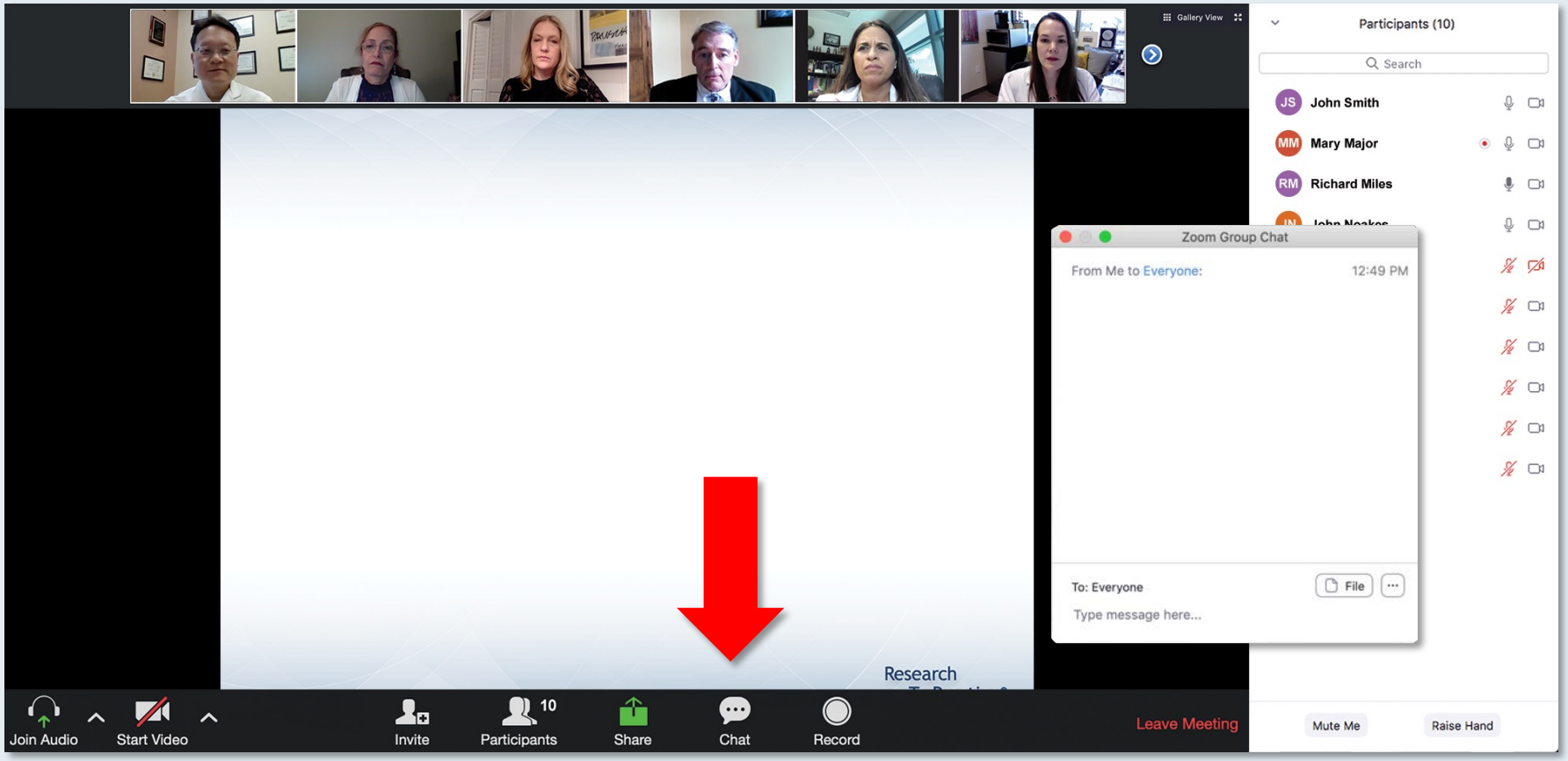
We Encourage Clinicians in Practice to Submit Questions



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

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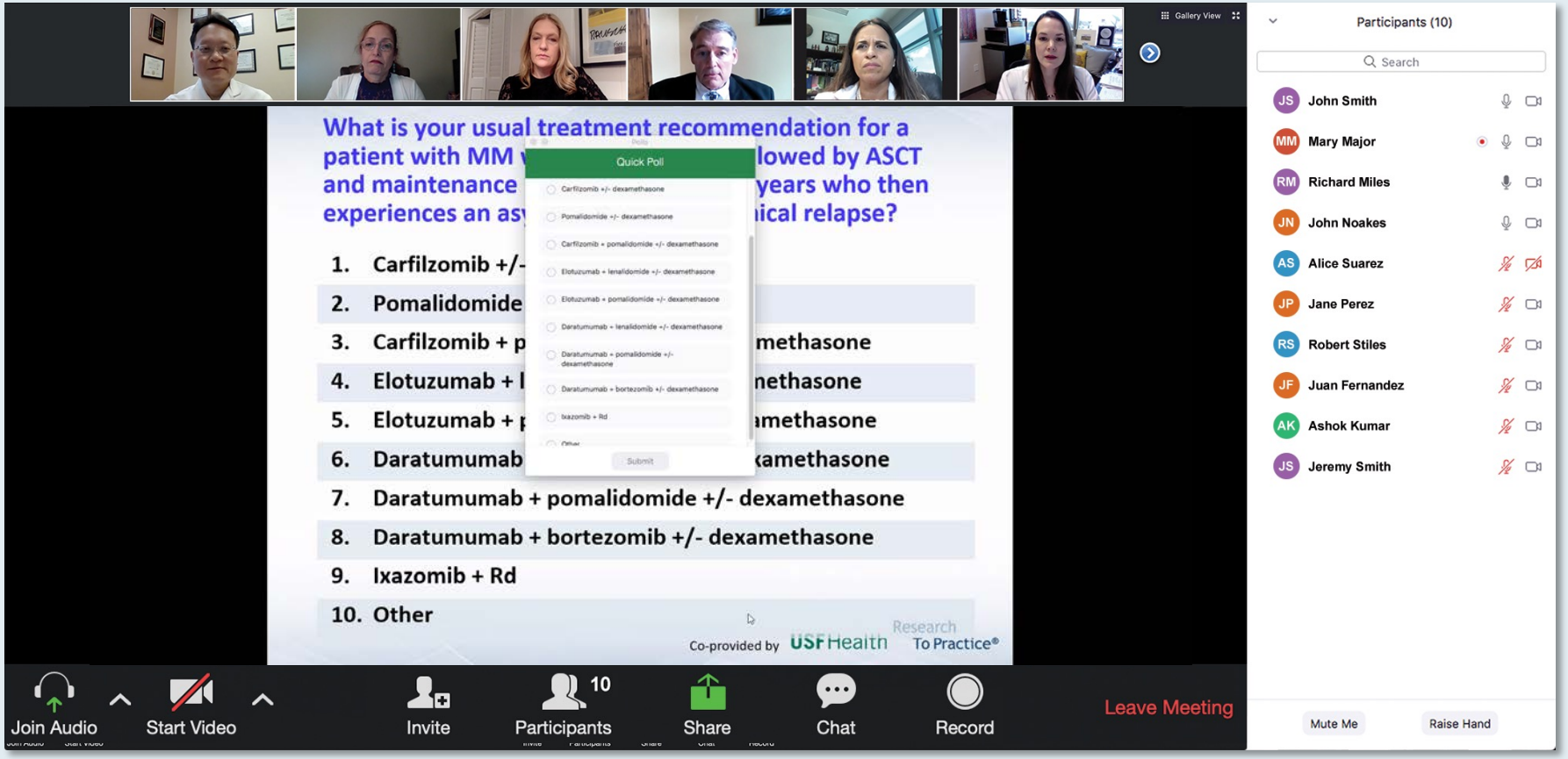
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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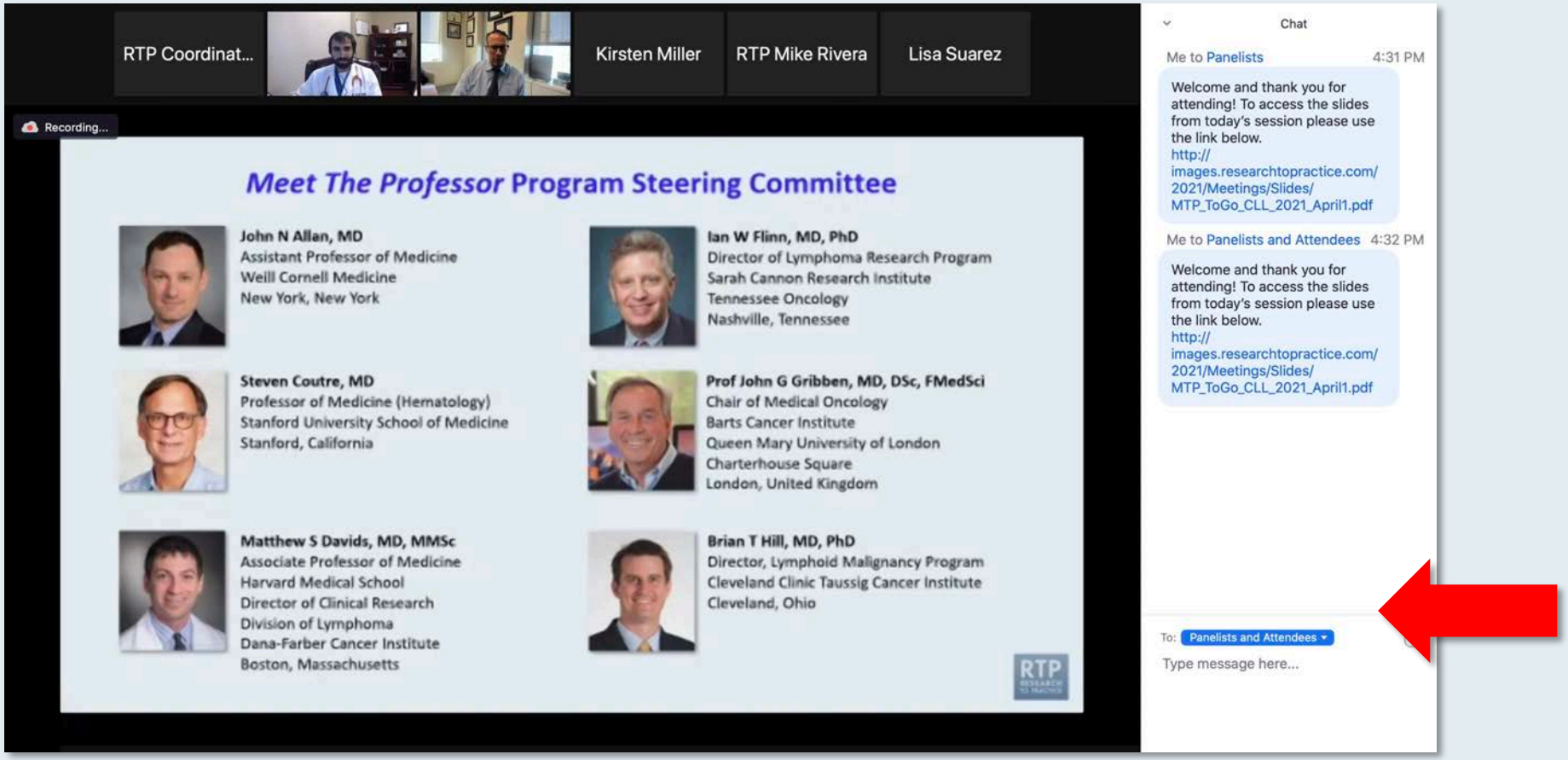
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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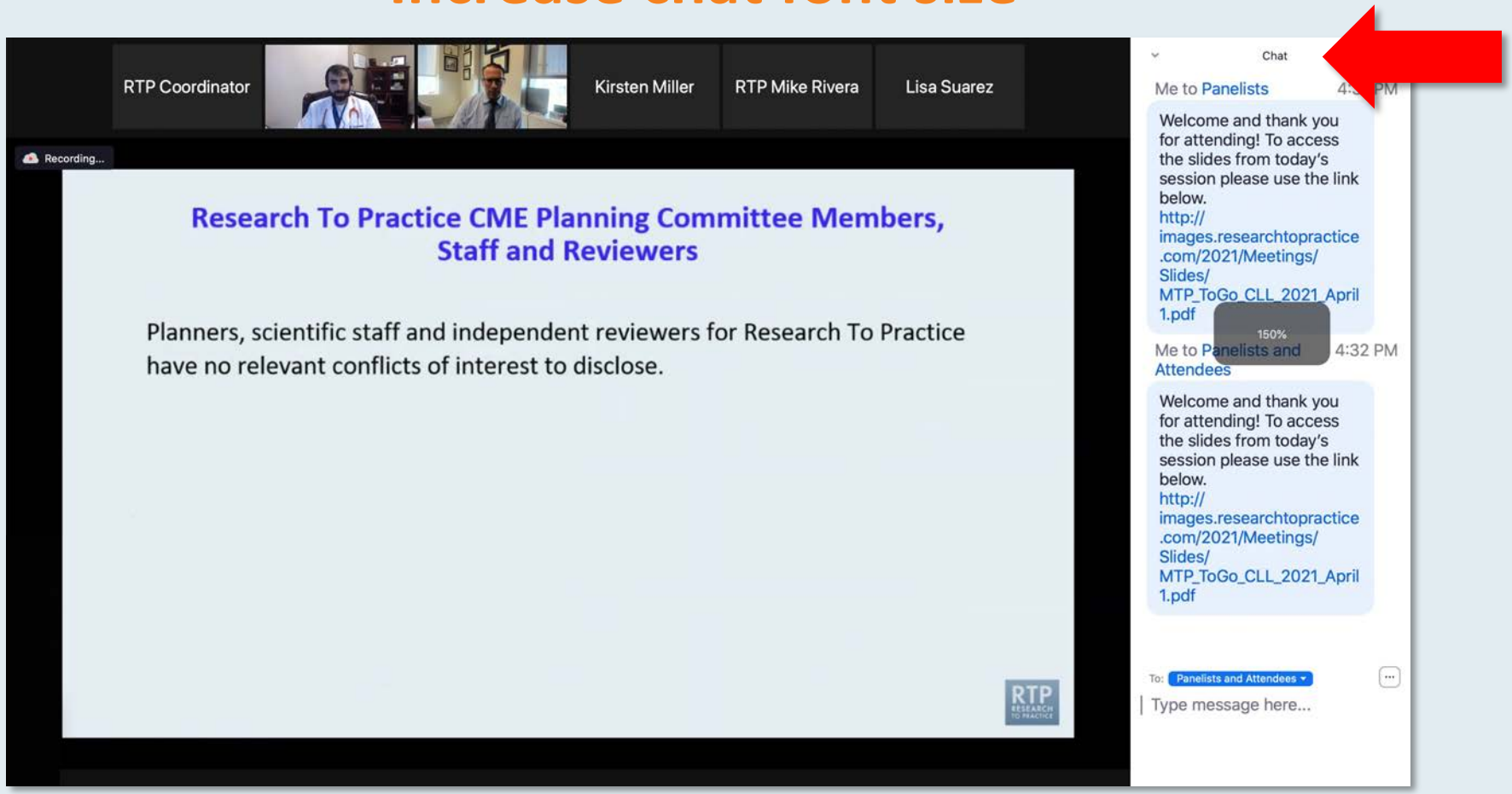
Familiarizing Yourself with the Zoom Interface

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.

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MAYO CLINIC COMPREHENSIVE CANCER CENTER

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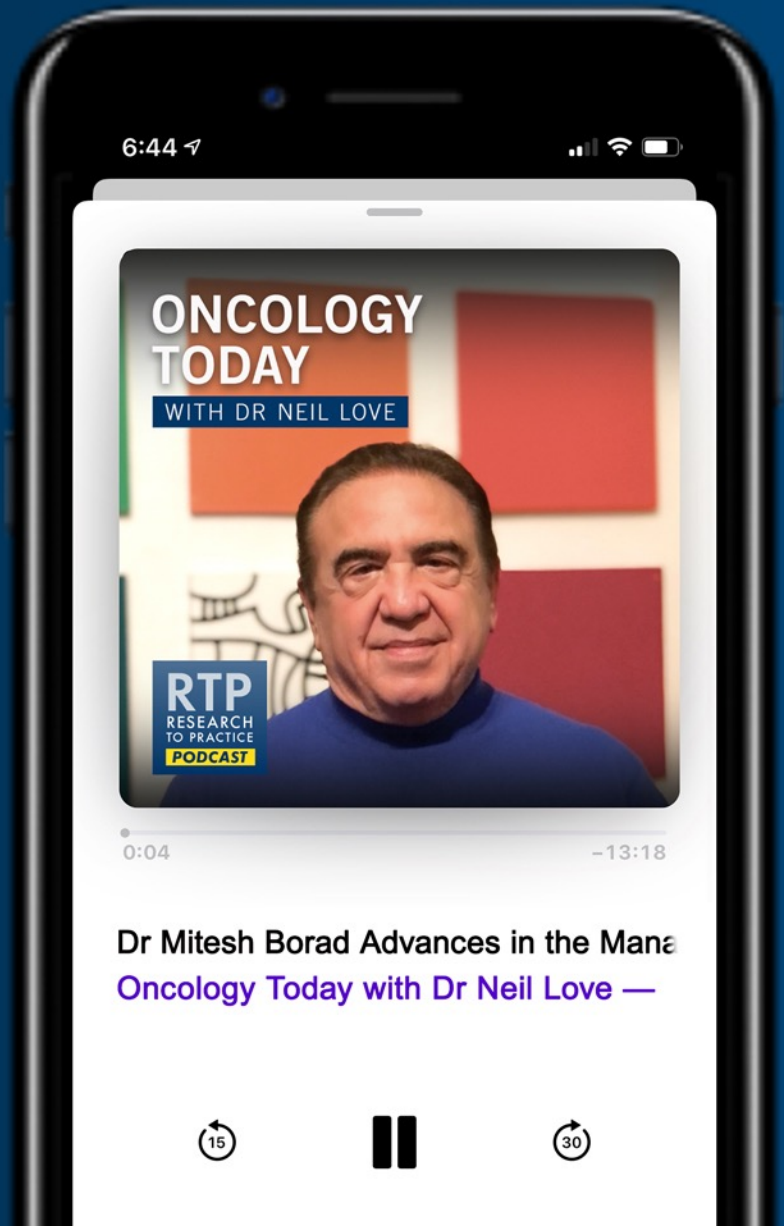

9 Exciting CME/MOC Events You Do Not Want to Miss

A Live Webinar Series Held in Conjunction with the 2021 ASCO Annual Meeting

Metastatic Castration-Resistant Prostate Cancer
Tuesday, July 20
5:00 PM – 6:00 PM ET

Bladder Cancer
Wednesday, July 21
5:00 PM – 6:00 PM ET

Endometrial and Cervical Cancers
Monday, July 26
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Head and Neck Cancer
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A Conversation with the Investigators: Metastatic Castration-Resistant Prostate Cancer

Tuesday, July 20, 2021
5:00 PM – 6:00 PM ET

Faculty

Emmanuel S Antonarakis, MD
Johann de Bono, MBChB, MSc, PhD
Julie N Graff, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Bladder Cancer

Wednesday, July 21, 2021
5:00 PM – 6:00 PM ET

Faculty

Petros Grivas, MD, PhD
Daniel P Petrylak, MD
Arlene Siefker-Radtke, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Thursday, July 22, 2021
5:00 PM – 6:00 PM ET

Faculty

David F McDermott, MD

Moderator

Neil Love, MD

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A Conversation with the Investigators: Endometrial and Cervical Cancers

Monday, July 26, 2021
5:00 PM – 6:00 PM ET

Faculty

Mansoor Raza Mirza, MD
David M O'Malley, MD
Angeles Alvarez Secord, MD, MHSc

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What General Medical Oncologists Want to Know About Targeted Therapy for Non-Small Cell Lung Cancer

Tuesday, July 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Professor Solange Peters, MD, PhD
Zofia Piotrowska, MD, MHS
Gregory J Riely, MD, PhD

Moderator

Neil Love, MD

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What General Medical Oncologists Want to Know About Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Wednesday, July 28, 2021
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Faculty

Mark Awad, MD, PhD
David R Spigel, MD
Heather Wakelee, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Consultant, Mayo Clinic in Arizona
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Meet The Professor Program Participating Faculty

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Director, Drug Development Unit Nashville
Sarah Cannon Research Institute
Tennessee Oncology
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Mayo Clinic Cancer Center
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Director, Interdisciplinary Gastrointestinal Oncology Program
Assistant Director, Translational Research
Comprehensive Cancer Center
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Meet The Professor Program Participating Faculty

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Associate Director for Translational Research
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Co-Director, Medical Initiatives
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Attending Physician, Member
Memorial Sloan Kettering Cancer Center
Professor of Medicine
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New York, New York

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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

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Shorenstein Associate Director
Program Development
Helen Diller Family Comprehensive Cancer Center
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San Francisco, California

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

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Director of Early Phase Clinical Research
Jonsson Comprehensive Cancer Center
UCLA School of Medicine
Los Angeles, California

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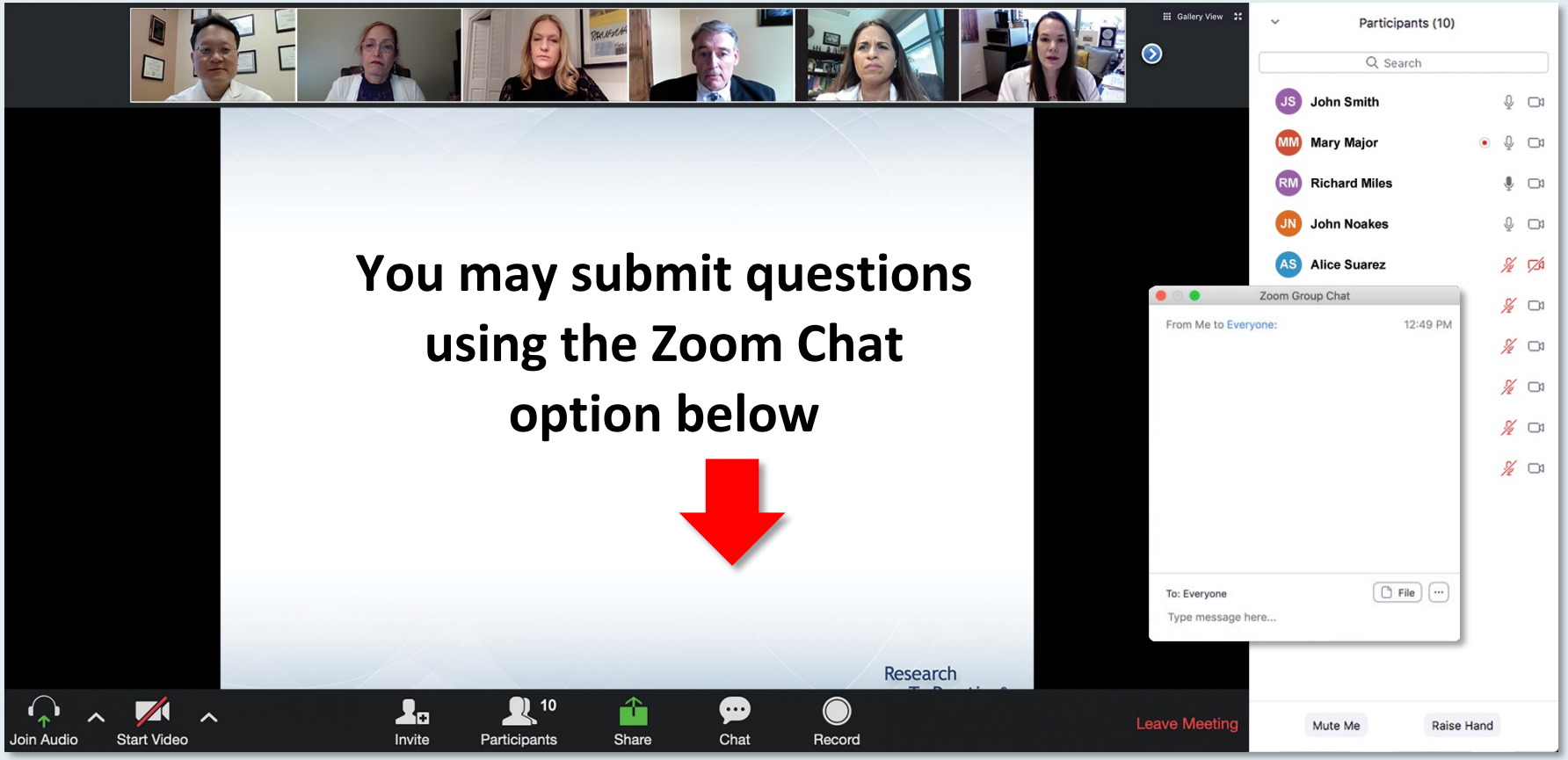

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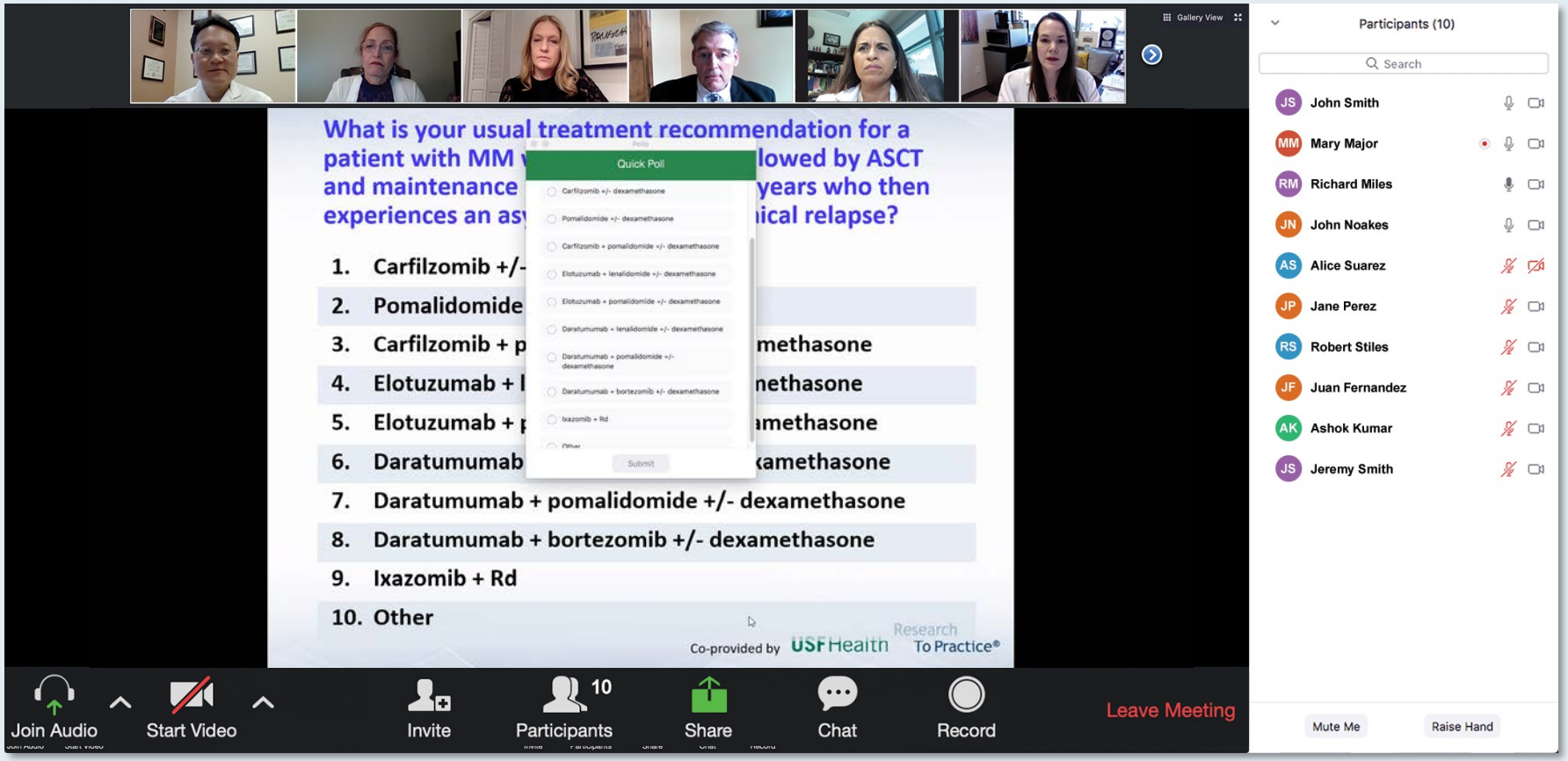

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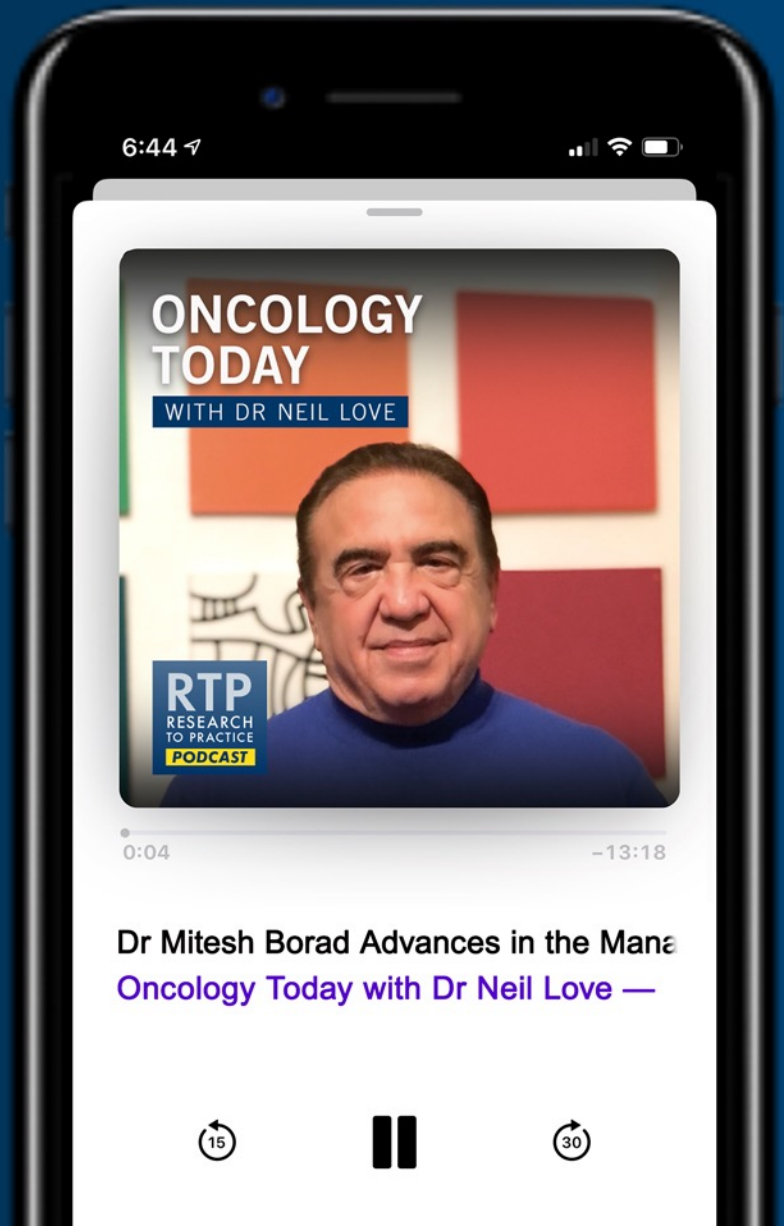

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Angeles Alvarez Secord, MD, MHSc

Moderator

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Neil Love, MD

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David R Spigel, MD
Heather Wakelee, MD

Moderator

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Mayo Clinic Cancer Center
Consultant, Mayo Clinic in Arizona
Phoenix, Arizona

Kristen K Ciombor, MD, MSCI
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

Sulfi Ibrahim, MD
Reid Health
Richmond, Indiana

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

Yanjun Ma, MD
Tennessee Oncology
Murfreesboro, Tennessee

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Meet The Professor with Dr Bekaii-Saab

MODULE 1: Cases from Drs Ibrahim and Ma

- Dr Ibrahim: A 58-year-old man with HIV and esophageal cancer
- Dr Ma: A frail 78-year-old woman with metastatic gastric cancer and brain metastases – PD-L1 CPS 15%, TMB 38.4 mut/Mb
- Dr Ibrahim: An 81-year-old man with metastatic gastroesophageal junction adenocarcinoma and a PD-L1 of 50%

MODULE 2: Beyond the Guidelines; Key Data – Gastroesophageal Cancers

MODULE 3: Cases from Dr Ciombor

- A 51-year-old woman with metastatic colorectal cancer (CRC) and discordant mismatch repair results
- A 53-year-old woman with microsatellite-stable metastatic CRC and a BRAF V600E mutation

MODULE 4: Beyond the Guidelines; Key Data – CRC

MODULE 5: Cases from Dr Gosain

- A 64-year-old man with metastatic sarcomatoid hepatocellular carcinoma (HCC) whose disease progressed from Child-Pugh A6 to B8 while on atezolizumab/bevacizumab
- A 66-year-old man with HCC and untreated hepatitis C

MODULE 6: Beyond the Guidelines; Key Data – HCC

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Case Presentation – Dr Ibrahim: A 58-year-old man with HIV and esophageal cancer

Dr Sulfi Ibrahim

- PMH: HIV-1-positive (well controlled), significant CAD with placement of multiple stents in the past year
- Locally advanced esophageal adenocarcinoma
- Neoadjuvant chemoradiation therapy, with good response and resolution of dysphagia
  - Patient declines esophagectomy
- Recurrent disease in the esophagus only but no other evidence of disease
  - Patient continues to decline surgery
- Patient declines chemotherapy but willing to accept treatment with pembrolizumab (PD-L1: 15%)

Questions

- Is single-agent pembrolizumab an appropriate treatment choice in a patient who has disease confined to the esophagus? Is there any data for responses in such patients? Any other alternate treatment suggestions?
- His HIV-1 disease is controlled on antiretroviral medications – are there any safety concerns for giving PD-L1 or PD-1 directed therapy in a patient with HIV?

Case Presentation – Dr Ma: A frail 78-year-old woman with metastatic gastric cancer and brain metastases – PD-L1 CPS 15%, TMB 38.4 mut/Mb

Dr Yanjun Ma

- 12/2019: EGD, EBUS, Stage IIIB adenocarcinoma of the gastric cardia
- 1/2020: Preoperative FLOT chemotherapy → Perforated diverticulitis requiring prolonged recovery
- 6/2020: Surgery, with 6-cm residual tumor, 10/23 positive nodes, negative surgical margins
  - Difficult post-operative recovery, decline in performance status, attempt at adjuvant chemo aborted
- Three months post-surgery restaging CT: Mild diffuse nodal progression, persistent personality changes
- Isolated right front lobe metastasis → 9/2020: SBRT
- Clinical trial of SN38 toxin binding to HSP90 → 1/2021 restaging scan: Mixed response with persistent increase in brain metastasis and associated edema
- NGS and RNA fusion analysis: High TMB 38.4 mut/Mb, PD-L1 CPS ~15, and PI3K mutation

Case Presentation – Dr Ma: A frail 78-year-old woman with metastatic gastric cancer and brain metastases – PD-L1 CPS 15%, TMB 38.4 mut/Mb (continued)

Dr Yanjun Ma

Questions

- What is your strategy in patients who are too weak after preoperative chemotherapy and surgery to undergo postoperative chemotherapy? Would you suggest surveillance only, or something other than FLOT?
- Since she has a very high tumor mutation burden would you recommend FOLFOX/nivolumab, or single-agent pembrolizumab? Would you forgo FOLFOX and consider a taxane/ramucirumab?
- Would adjuvant nivolumab be an option?

Case Presentation – Dr Ibrahim: An 81-year-old man with metastatic GEJ adenocarcinoma and PD-L1 of 50%

Dr Sulfi Ibrahim

- Work up for progressive dysphagia: GEJ adenocarcinoma with metastases to the liver, PD-L1 50%
  - NGS: No other actionable mutations
- Nivolumab/capecitabine/oxaliplatin, with very good response and resolution of dysphagia
  - Oxaliplatin and capecitabine dose reduced due to his age
- Currently, receiving monthly maintenance nivolumab

Questions

- Is nivolumab/capecitabine/oxaliplatin the optimal regimen to have picked for this patient? Would a non-chemotherapy-containing regimen of ipilimumab and nivolumab have also been a reasonable choice?

Meet The Professor with Dr Bekaii-Saab

MODULE 1: Cases from Drs Ibrahim and Ma

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MODULE 6: Beyond the Guidelines; Key Data – HCC

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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

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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

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2021 ASCO ANNUAL MEETING

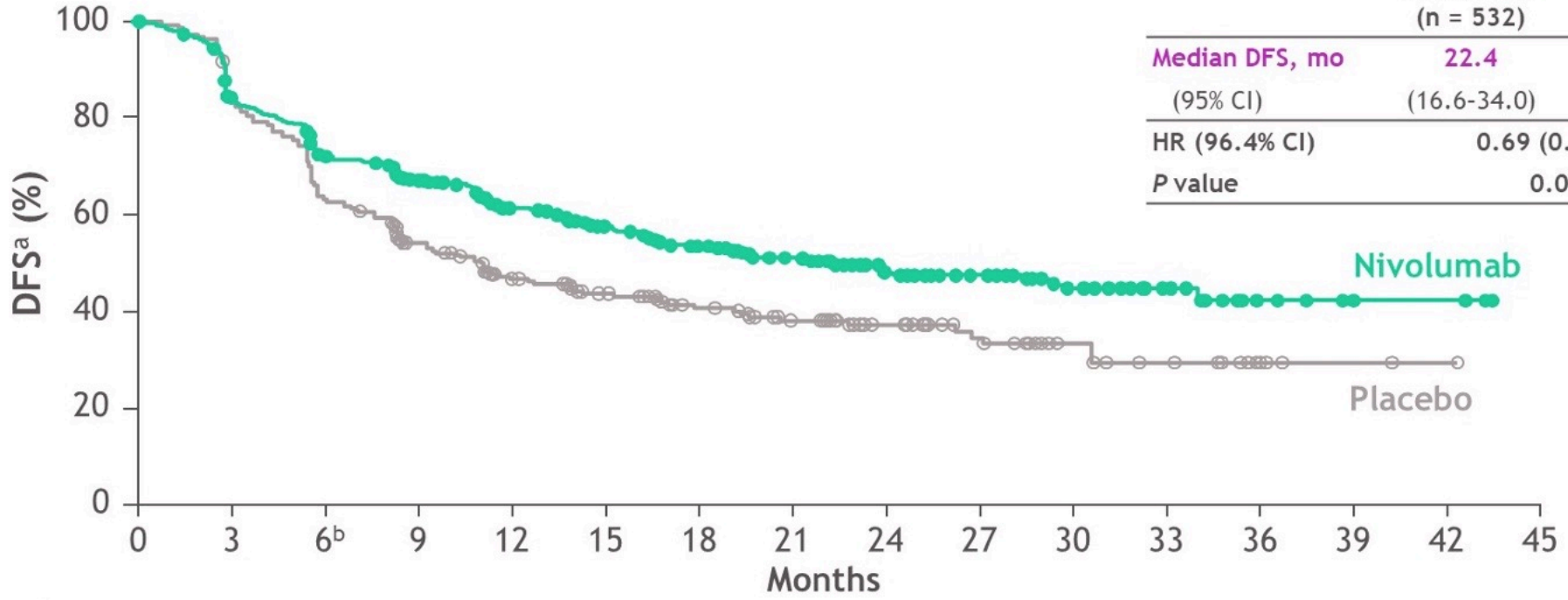
Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

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

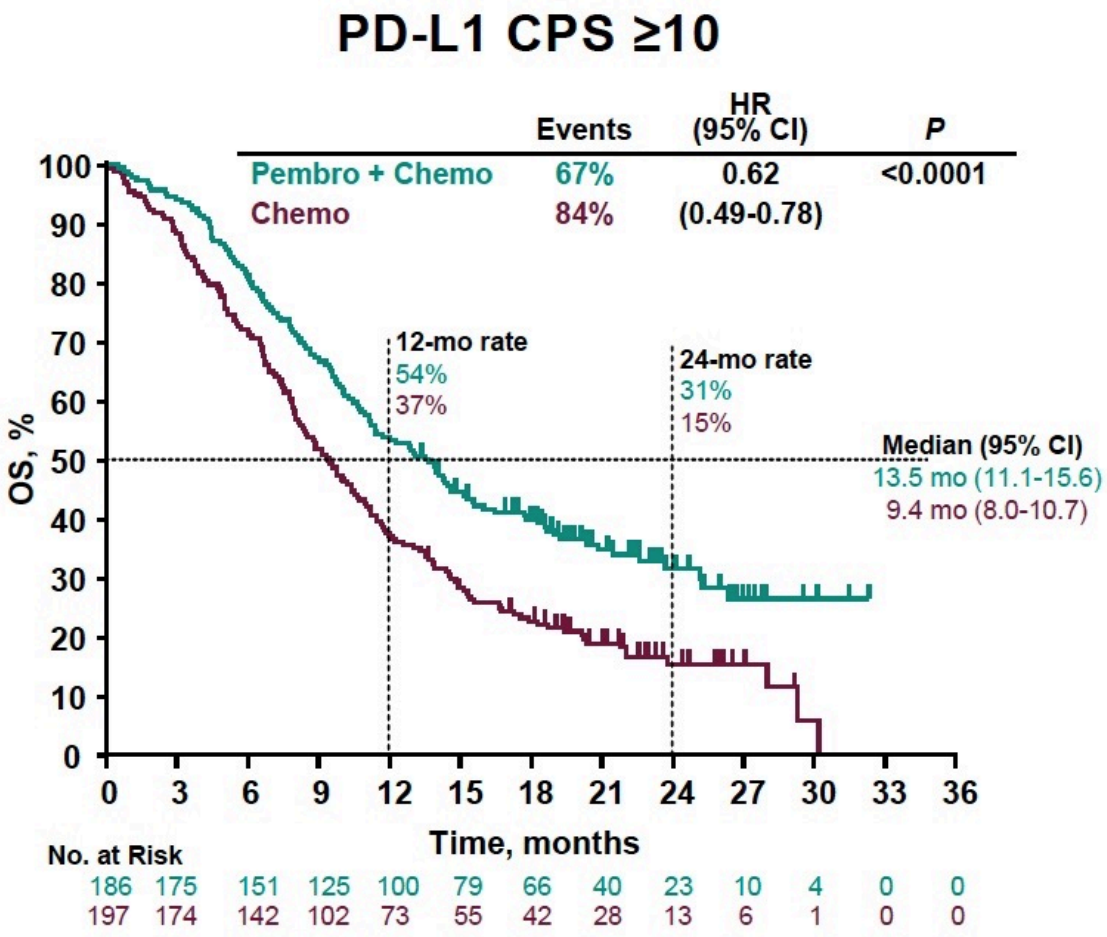
RTP RESEARCH TO PRACTICE

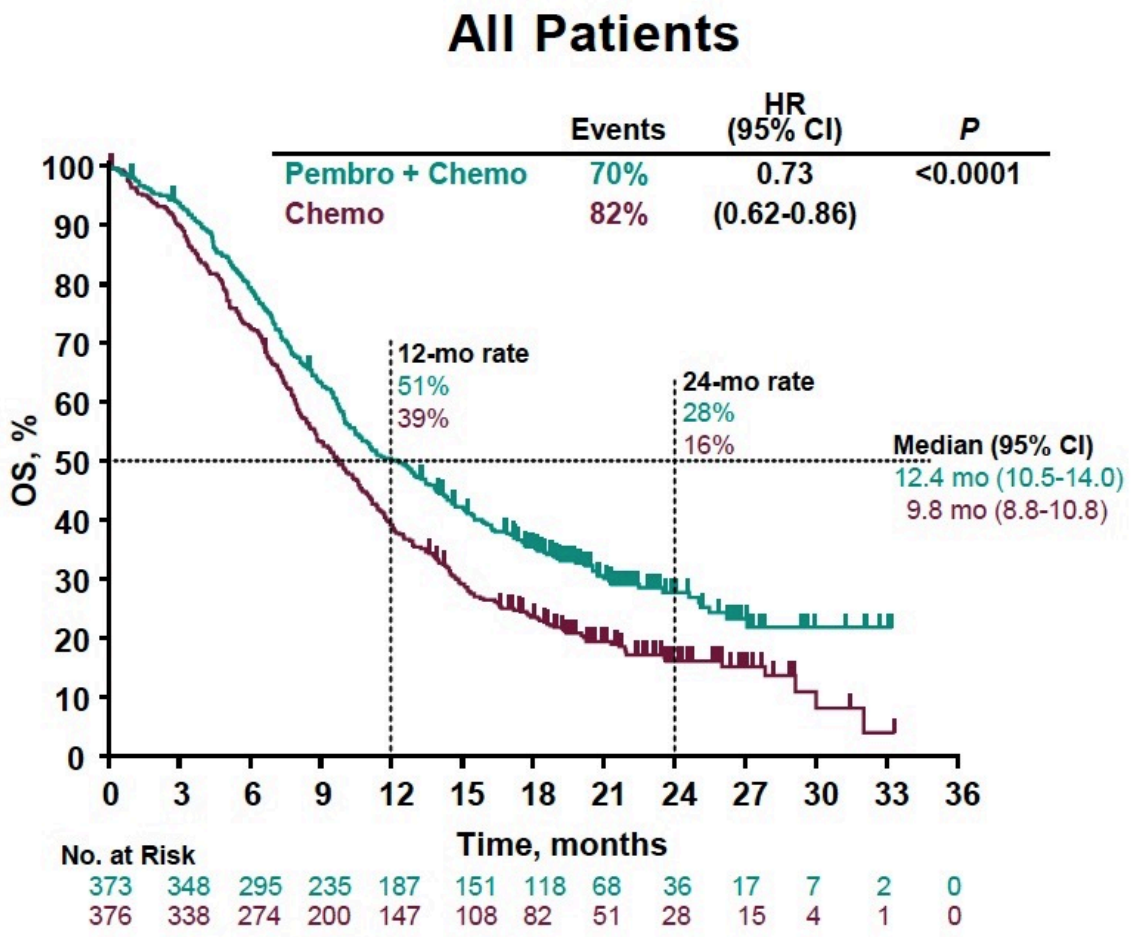
Pembrolizumab plus Chemotherapy versus Chemotherapy as First-Line Therapy in Patients with Advanced Esophageal Cancer: The Phase 3 KEYNOTE-590 Study

Kato K et al.

ESMO 2020;Abstract LBA8_PR.

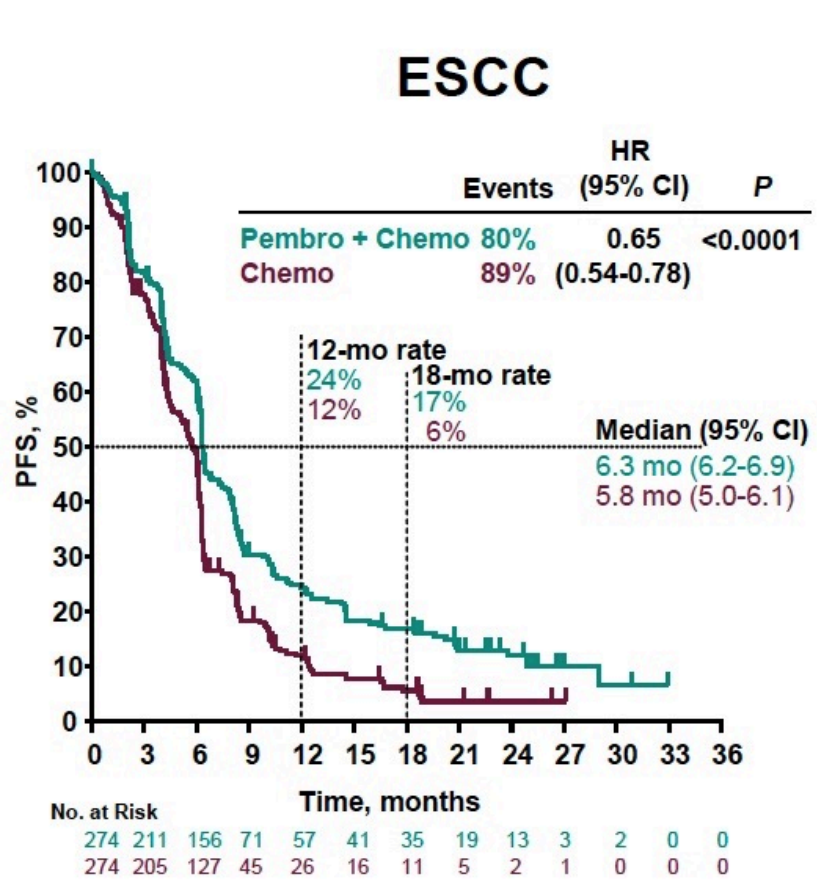
KEYNOTE-590: Overall Survival

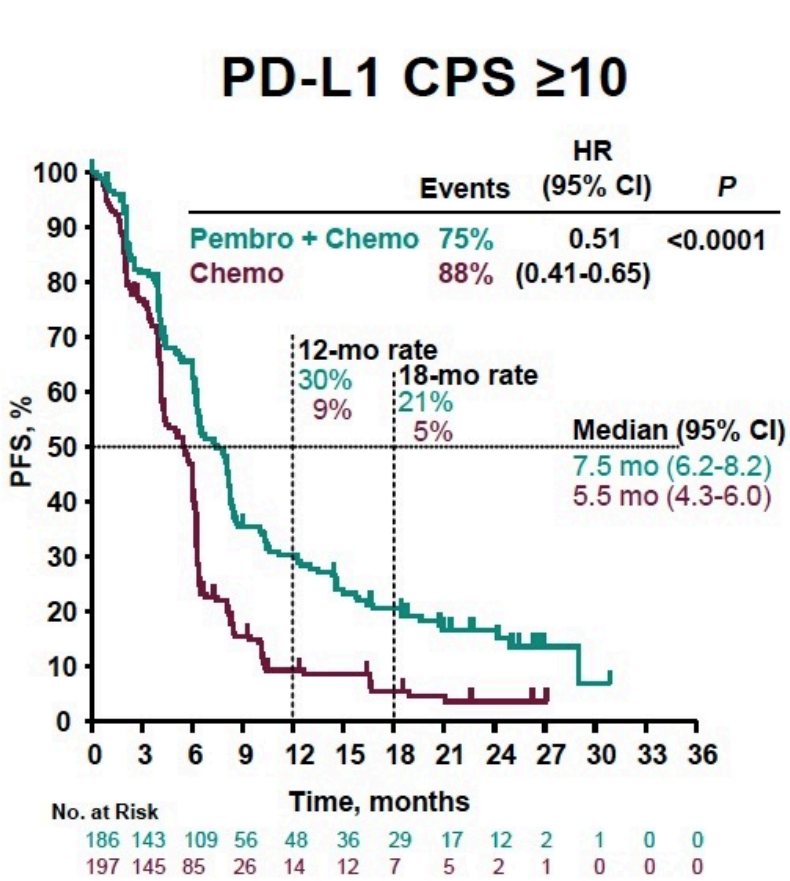


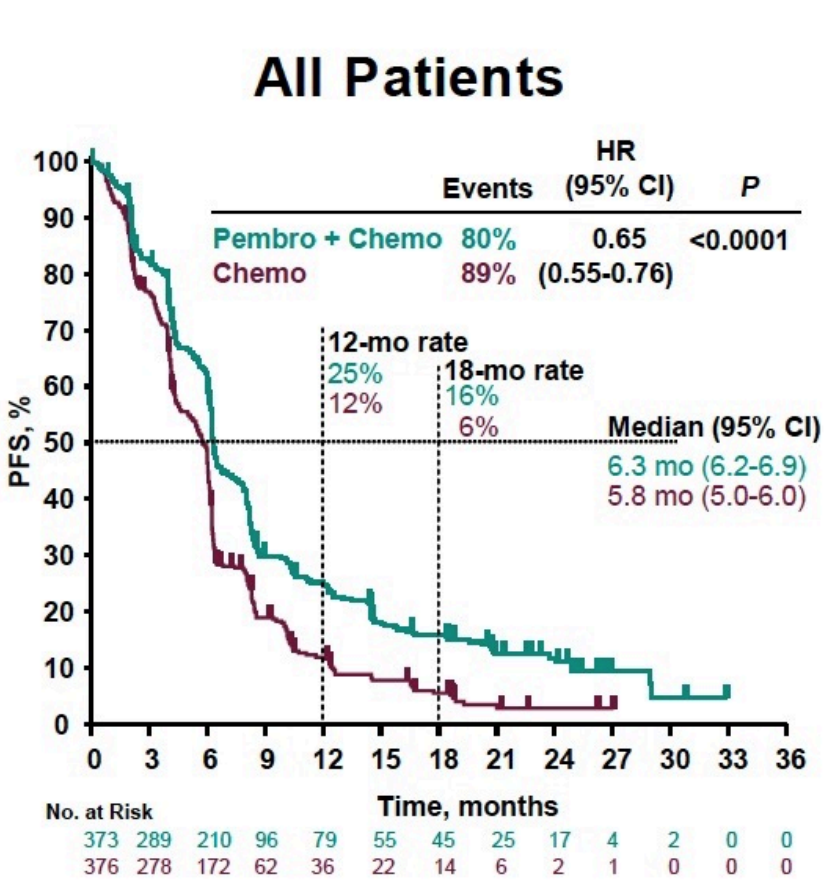


Kato K et al. ESMO 2020;Abstract LBA8_PR.

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

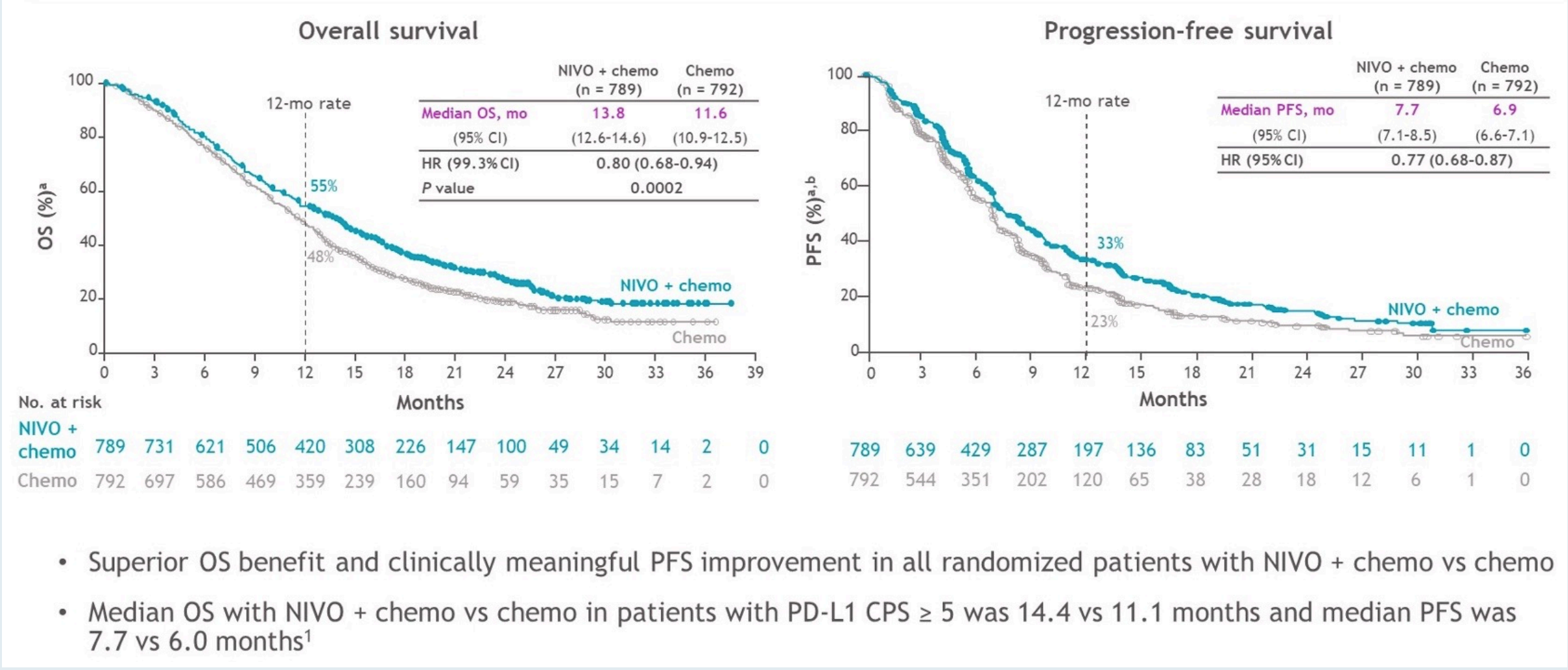
First-line nivolumab plus chemotherapy vs chemotherapy in advanced gastric cancer/ gastroesophageal junction cancer/esophageal adenocarcinoma: expanded efficacy and safety data from CheckMate 649

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

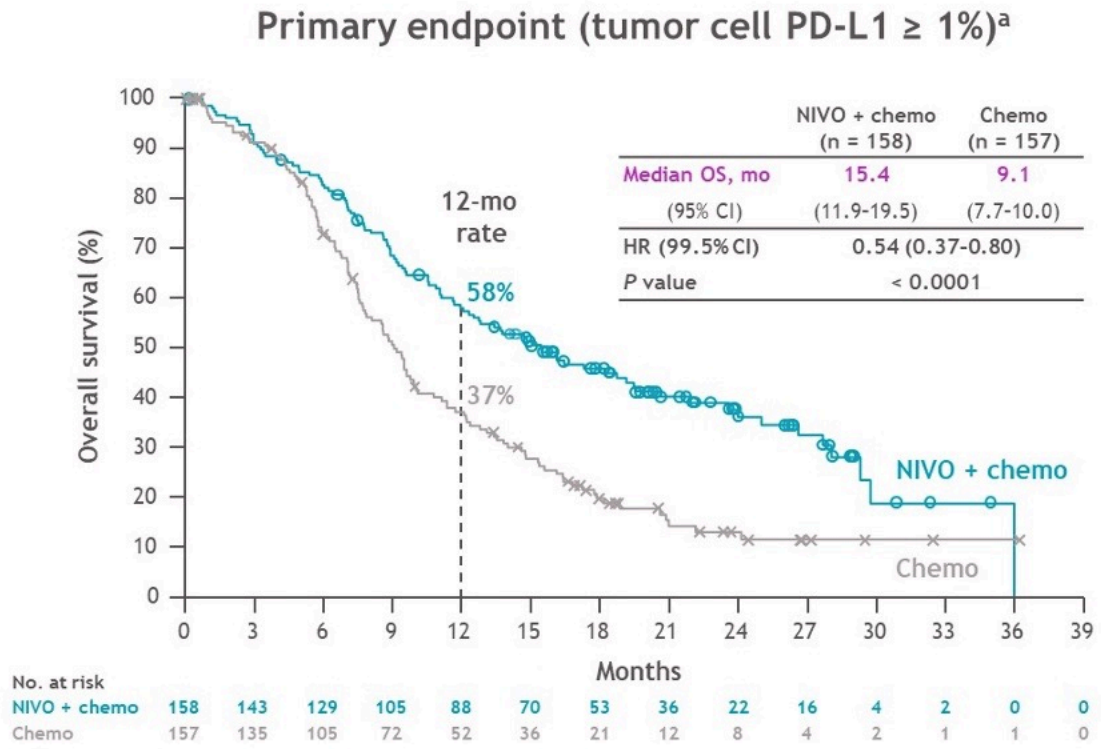
Nivolumab plus ipilimumab or nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced esophageal squamous cell carcinoma: first results of the CheckMate 648 study

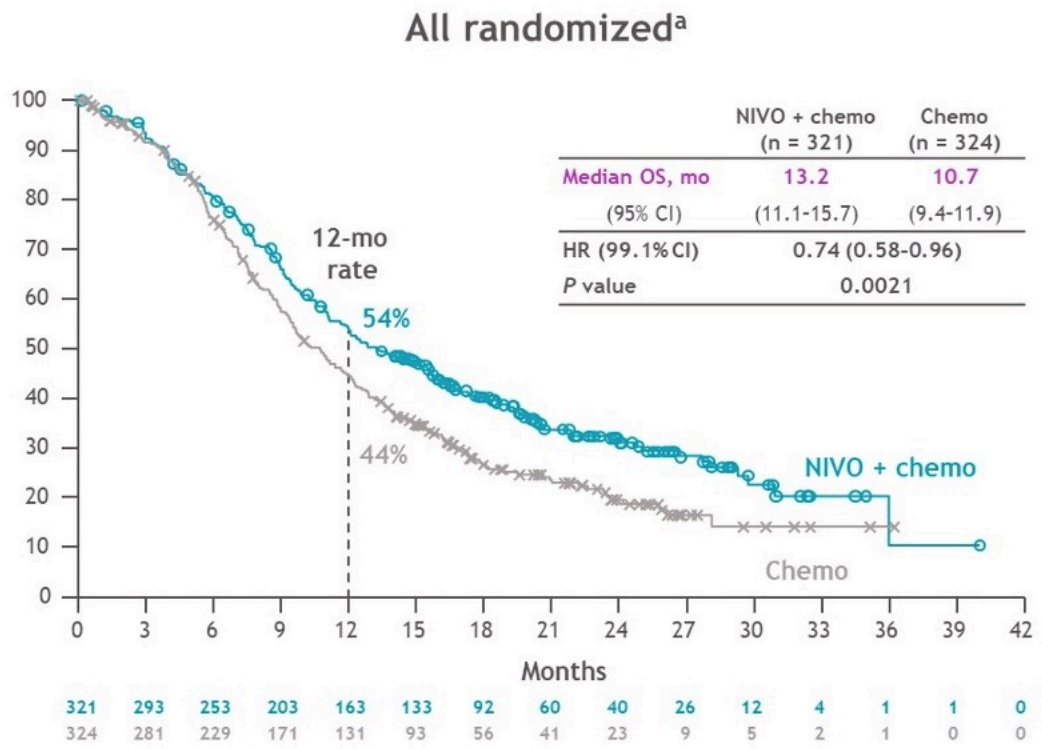
Ian Chau,[1] Yuichiro Doki,[2] Jaffer A. Ajani,[3] Jianming Xu,[4] Lucjan Wyrwicz,[5] Satoru Motoyama,[6] Takashi Ogata,[7] Hisato Kawakami,[8] Chih-Hung Hsu,[9] Antoine Adenis,[10] Farid el Hajbi,[11] Maria Di Bartolomeo,[12] Maria Ignez Braghiroli,[13] Eva Holtved,[14] Ioannis Xynos,[15] Xuan Liu,[15]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



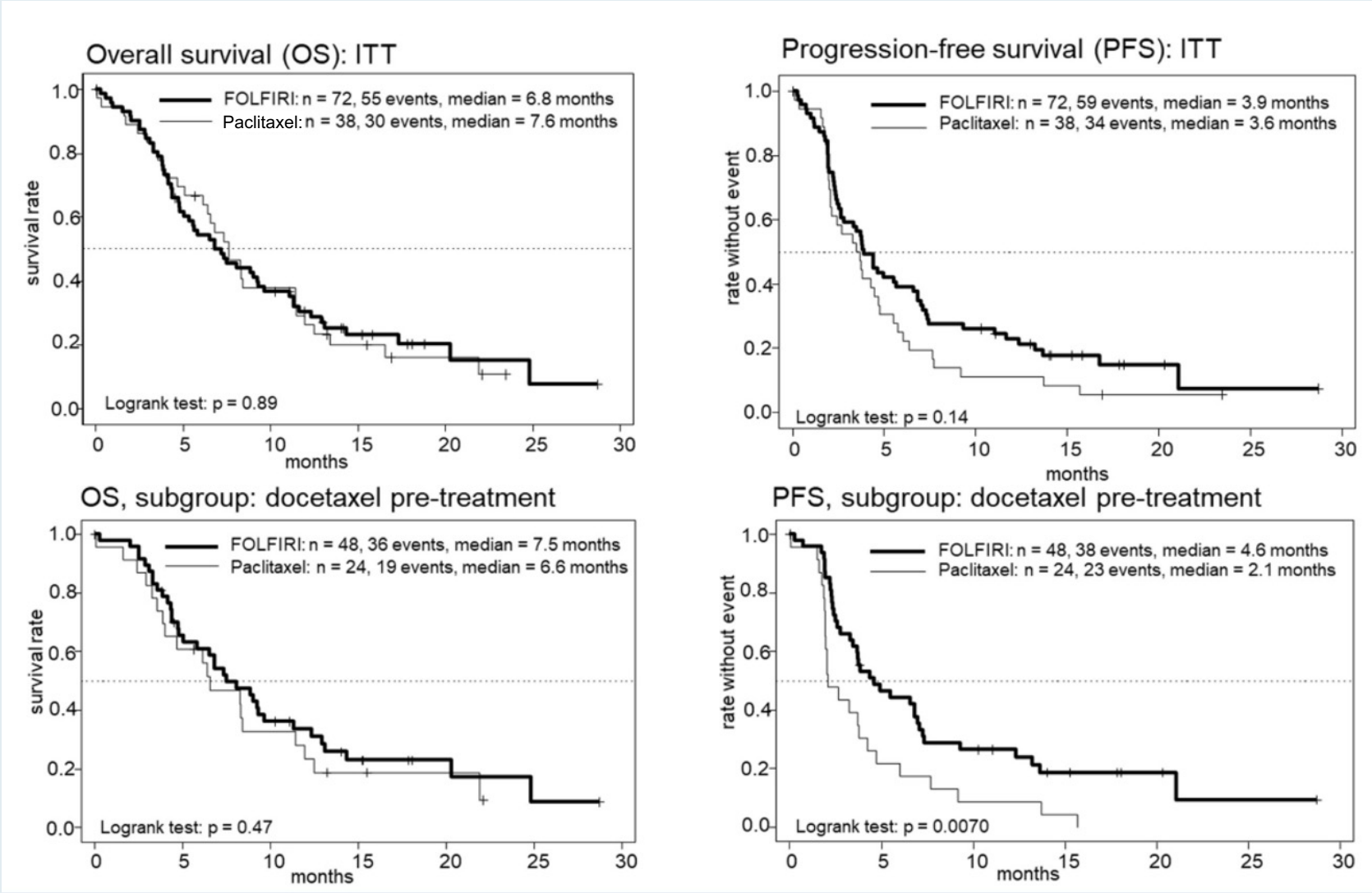


- Superior OS with NIVO + chemo vs chemo in tumor cell PD-L1 ≥ 1% and all randomized populations
  - Tumor cell PD-L1 ≥ 1%: 46% reduction in the risk of death and a 6.3-month improvement in median OS
  - All randomized: 26% reduction in the risk of death and a 2.5-month improvement in median OS

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

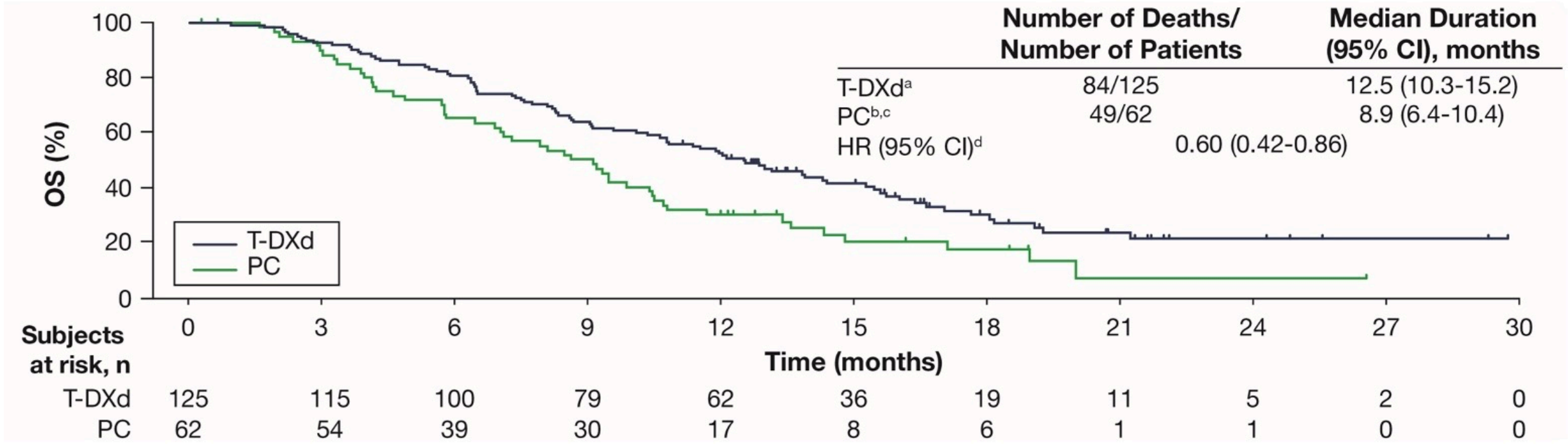
The Cancer Institute Hospital of JFCR, Tokyo, Japan

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.

RTP RESEARCH TO PRACTICE

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

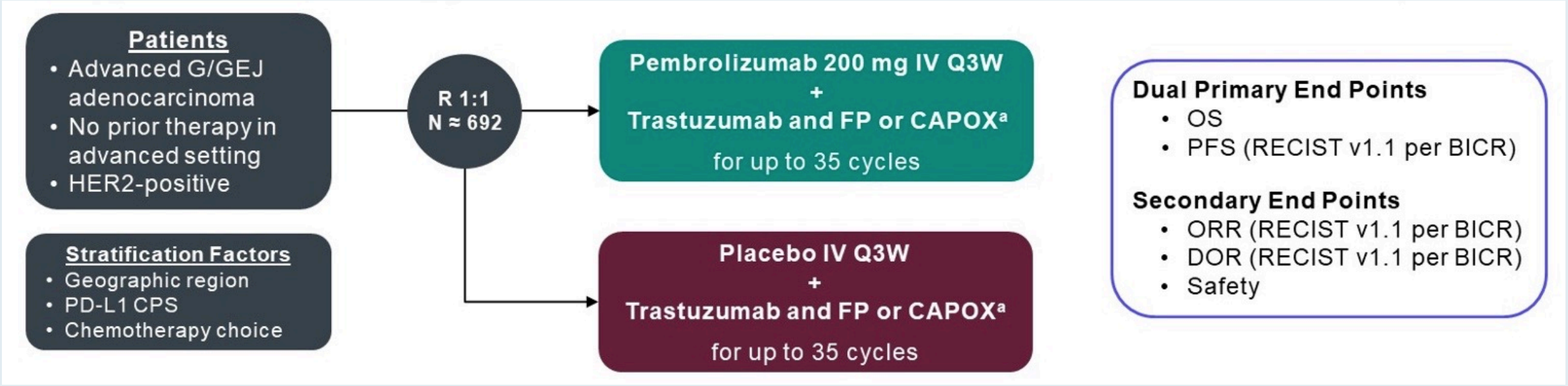
Yelena Y. Janjigian,[1] Akihito Kawazoe,[2] Patricio Yañez,[3] Suxia Luo,[4] Sara Lonardi,[5] Oleksii Kolesnik,[6] Olga Barajas,[7] Yuxian Bai,[8] Lin Shen,[9] Yong Tang,[10] Lucjan S. Wyrwicz,[11] Kohei Shitara,[2] Shukui Qin,[12] Eric Van Cutsem,[13] Josep Tabernero,[14] Lie Li,[15] Chie-Schin Shih,[15]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

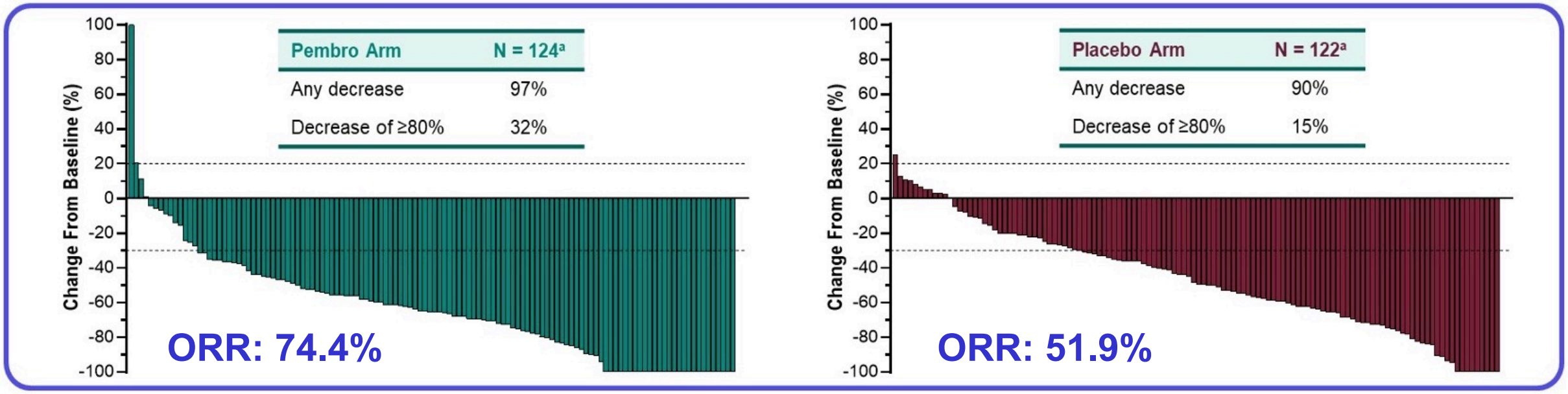
RTP RESEARCH TO PRACTICE

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 Bekaii-Saab

MODULE 1: Cases from Drs Ibrahim and Ma

- Dr Ibrahim: A 58-year-old man with HIV and esophageal cancer
- Dr Ma: A frail 78-year-old woman with metastatic gastric cancer and brain metastases – PD-L1 CPS 15%, TMB 38.4 mut/Mb
- Dr Ibrahim: An 81-year-old man with metastatic gastroesophageal junction adenocarcinoma and a PD-L1 of 50%

MODULE 2: Beyond the Guidelines; Key Data – Gastroesophageal Cancers

MODULE 3: Cases from Dr Ciombor

- A 51-year-old woman with metastatic colorectal cancer (CRC) and discordant mismatch repair results
- A 53-year-old woman with microsatellite-stable metastatic CRC and a BRAF V600E mutation

MODULE 4: Beyond the Guidelines; Key Data – CRC

MODULE 5: Cases from Dr Gosain

- A 64-year-old man with metastatic sarcomatoid hepatocellular carcinoma (HCC) whose disease progressed from Child-Pugh A6 to B8 while on atezolizumab/bevacizumab
- A 66-year-old man with HCC and untreated hepatitis C

MODULE 6: Beyond the Guidelines; Key Data – HCC

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Ciombor: A 51-year-old woman with metastatic CRC and discordant MMR results

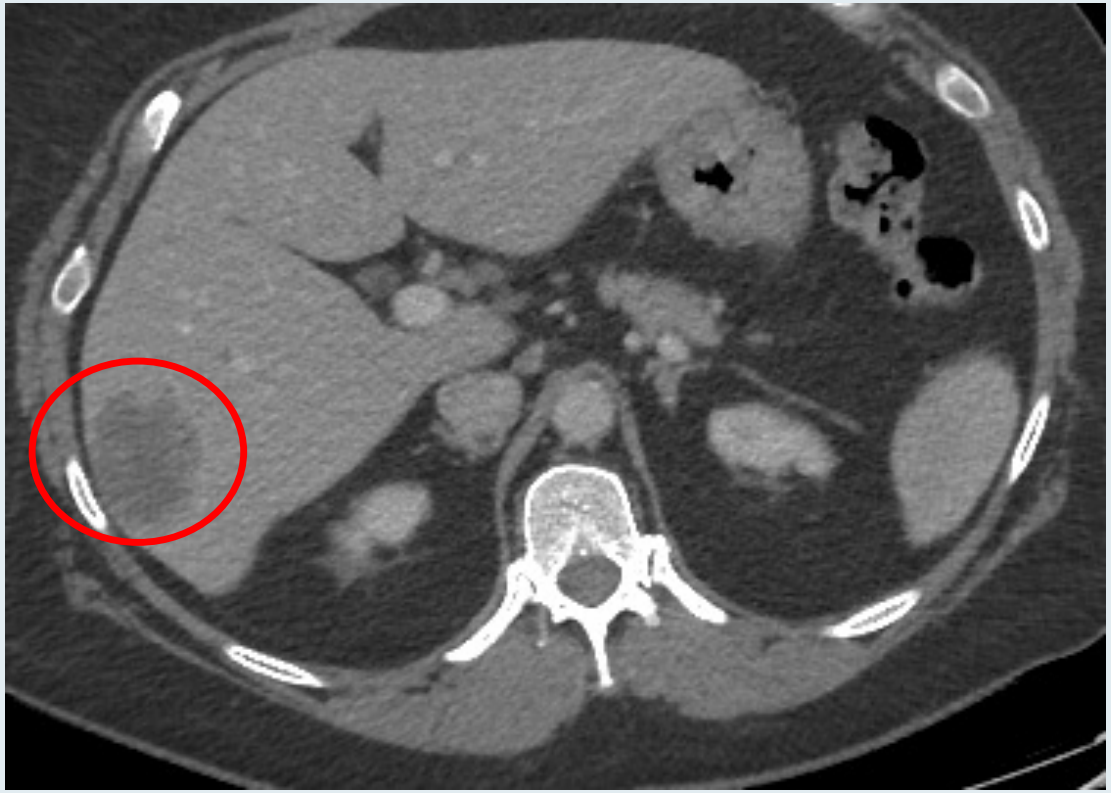
Dr Kristen Ciombor

- PMH: HTN, DM, rectal bleeding
- Colonoscopy: 5-cm rectal cancer; MRI Pelvis: Multiple unresectable liver metastases
  - Primary: MMR proficient; Liver metastases: MMR deficient
- Nivolumab/ipilimumab x 2 cycles, with CEA 44.5 → 2.1, marked improvement in liver and rectum
  - Appendicitis → diagnosed with adrenal insufficiency, thyroiditis (levothyroxine, high-dose steroids)
- Liver metastasectomy, with only one focus of cancer remaining in right liver parenchyma
- Molecular profiling (Blood, rectal tumor): MSS, TMB 5-6
- Short course of RT → TME
- Continued improvement in rectal tumor despite no systemic therapy since 11/2020

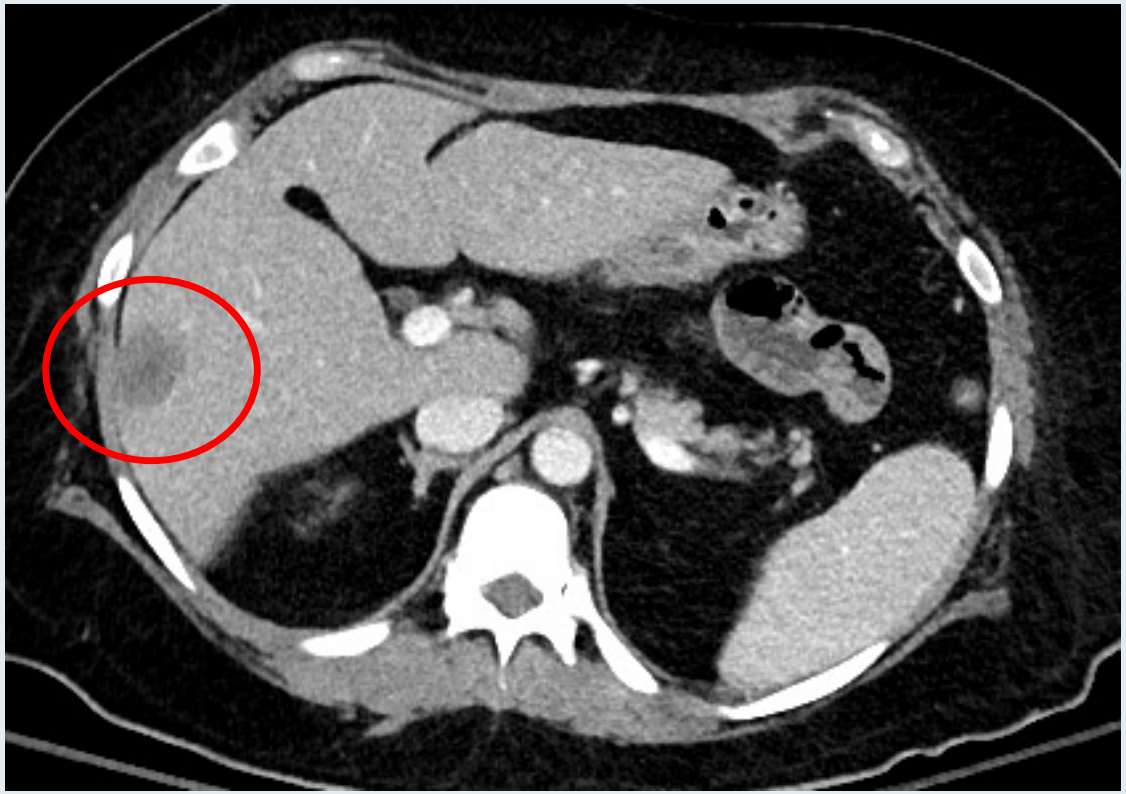
Case Presentation – Dr Ciombor: A 51-year-old woman with metastatic CRC and discordant MMR results

Dr Kristen Ciombor

Hepatic Metastasis



Continued Shrinkage of Hepatic Metastasis after Nivolumab/Ipilimumab x 2



RTP RESEARCH TO PRACTICE

Case Presentation – Dr Ciombor: A 53-year-old woman with MSS metastatic CRC and a BRAF V600E mutation

Dr Kristen Ciombor

- Presents with de novo metastatic CRC, with a right-sided colon primary, CEA: 52.7
- NGS: MSS, KRAS/NRAS wild type, BRAF V600E mutation, FGFR1 amplification
- FOLFOX/bevacizumab, with great response x 10 cycles
  - Oxaliplatin discontinued due to PN, bevacizumab discontinued due to mucosal bleeding
- At PD: Encorafenib/panitumumab x 8 months
- FOLFIRI → FOLFOXIRI → yttrium-90

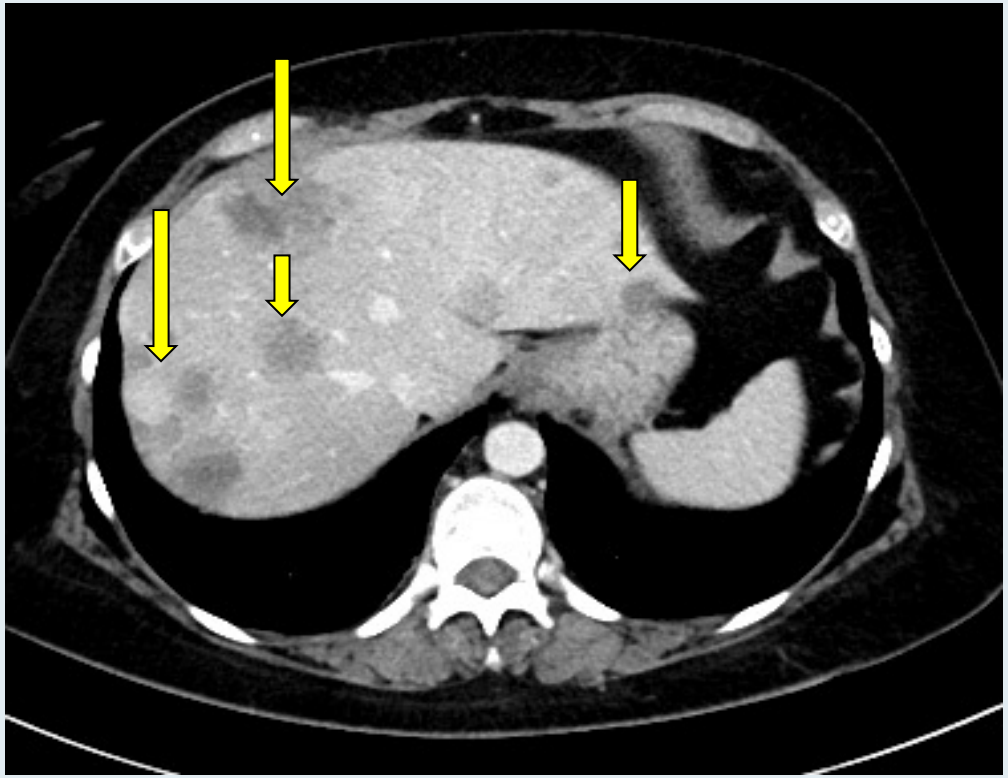
Questions

- This patient was started on FOLFOX/bevacizumab, but subsequent molecular data showed that she was KRAS/NRAS wild type but BRAF V600E mutant. Would that change what you were doing as first-line therapy, even though she is feeling better and her CEA is starting to drop? Would you escalate therapy to FOLFOXIRI/bev?
- In patients with BRAF V600E-mutant colorectal cancer do you use BRAF inhibition in the first line setting or second line and beyond? Based on the BEACON CRC data, are you using doublet therapy with anti-EGFR and BRAF inhibitors? Are you adding the MEK inhibitor in? Are there certain subtypes in which you might consider the triplet?

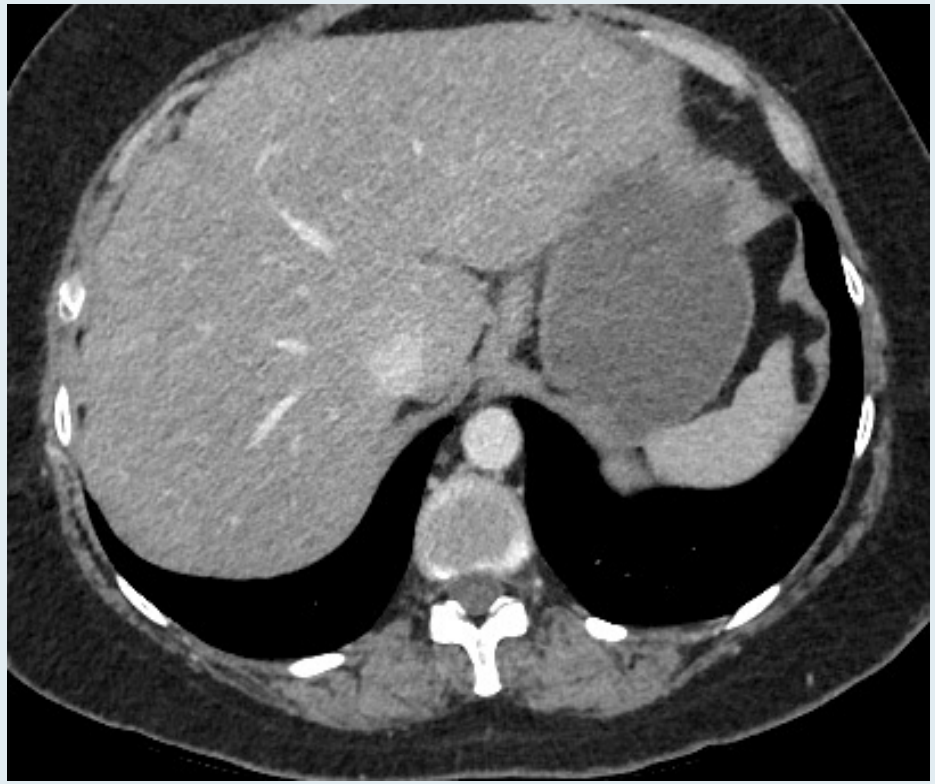
Case Presentation – Dr Ciombor: A 53-year-old woman with MSS metastatic CRC and a BRAF V600E mutation

Dr Kristen Ciombor

Multiple Liver Lesions Before FOLFOX/Bevacizumab



Best Response to FOLFOX/Bev → 5-FU Maintenance



RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Bekaii-Saab

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MODULE 6: Beyond the Guidelines; Key Data – HCC

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

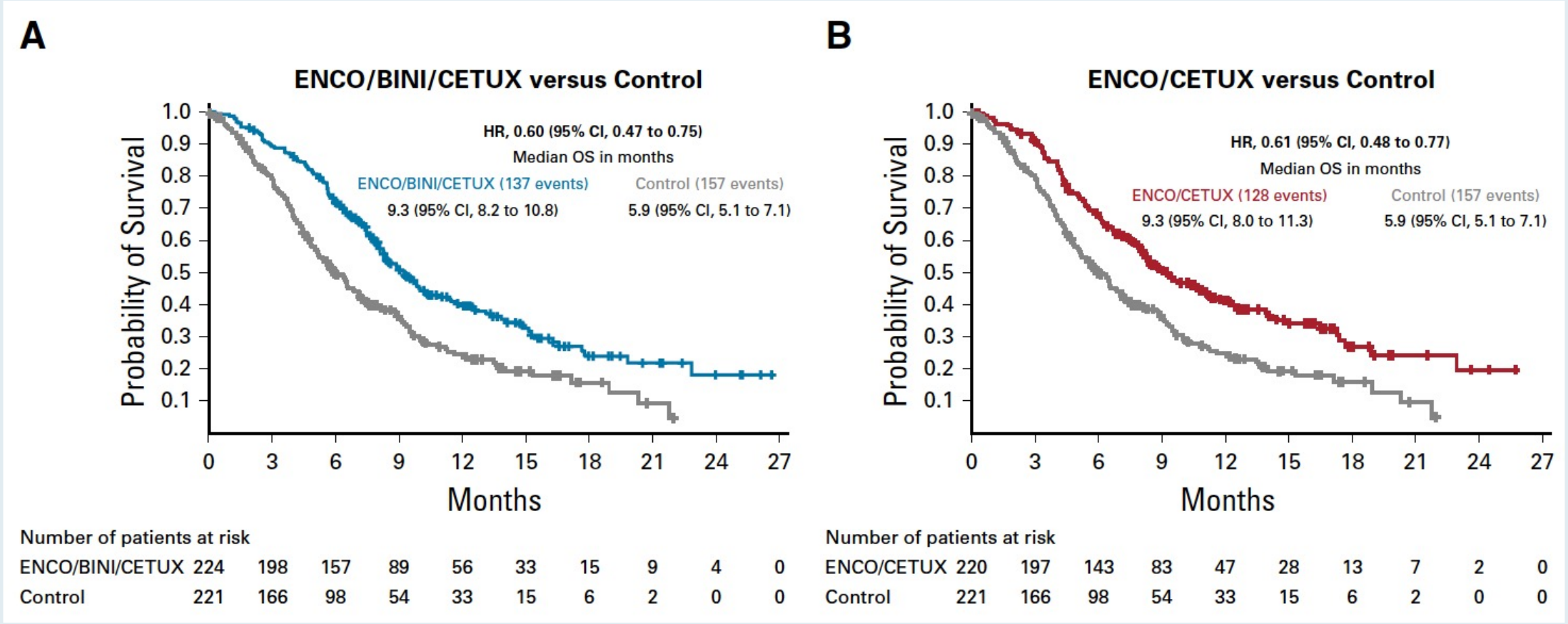
rapid communications

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.

RTP RESEARCH TO PRACTICE

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*

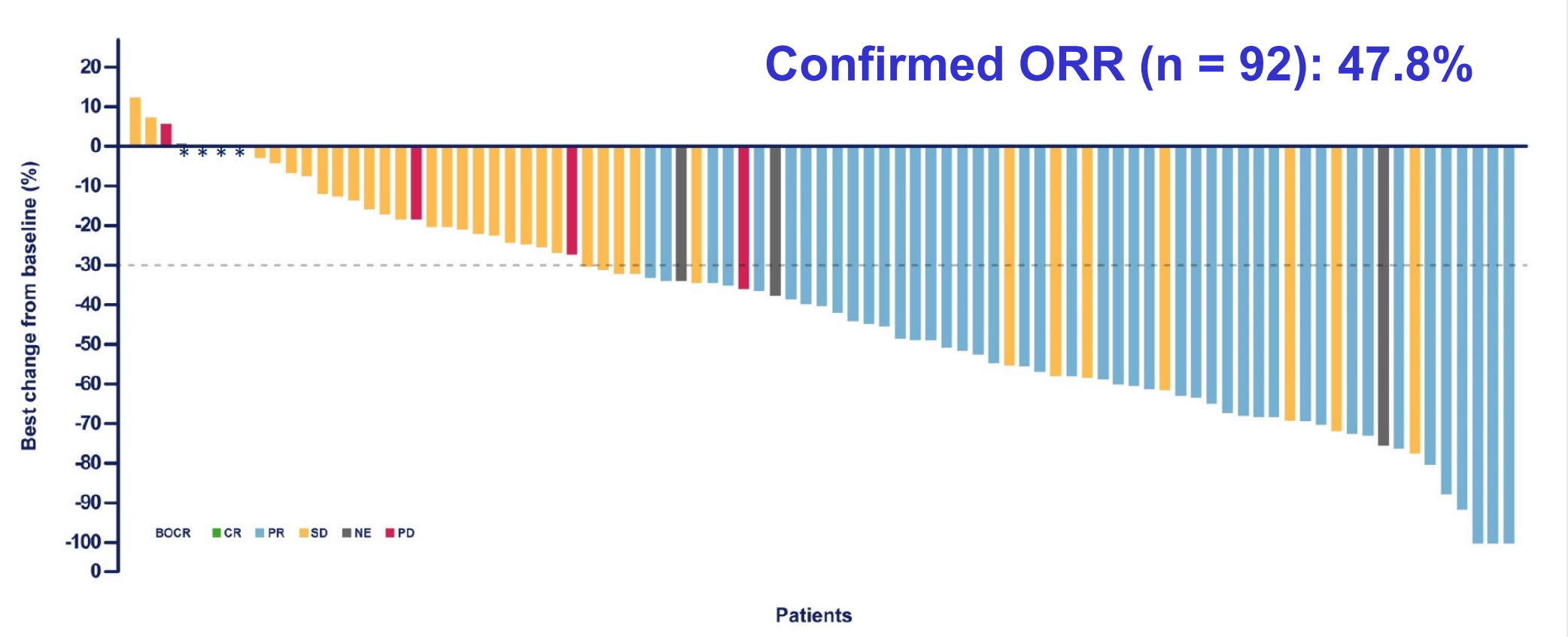
** University Hospitals Leuven, Belgium*

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.

RTP RESEARCH TO PRACTICE

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

BioDrugs (2020) 34:349–362

REVIEW ARTICLE

The Role of Immune Checkpoint Inhibitors in Colorectal Adenocarcinoma

Daniel R. Almquist[1] · Daniel H. Ahn[1] · Tanios S. Bekaii-Saab[1]

Potential Mechanisms of Resistance to ICI Therapies in CRC

Almquist DR et al. BioDrugs 2020;34(3):349-62.

Oncologist 2021;[Online ahead of print].

The Oncologist®

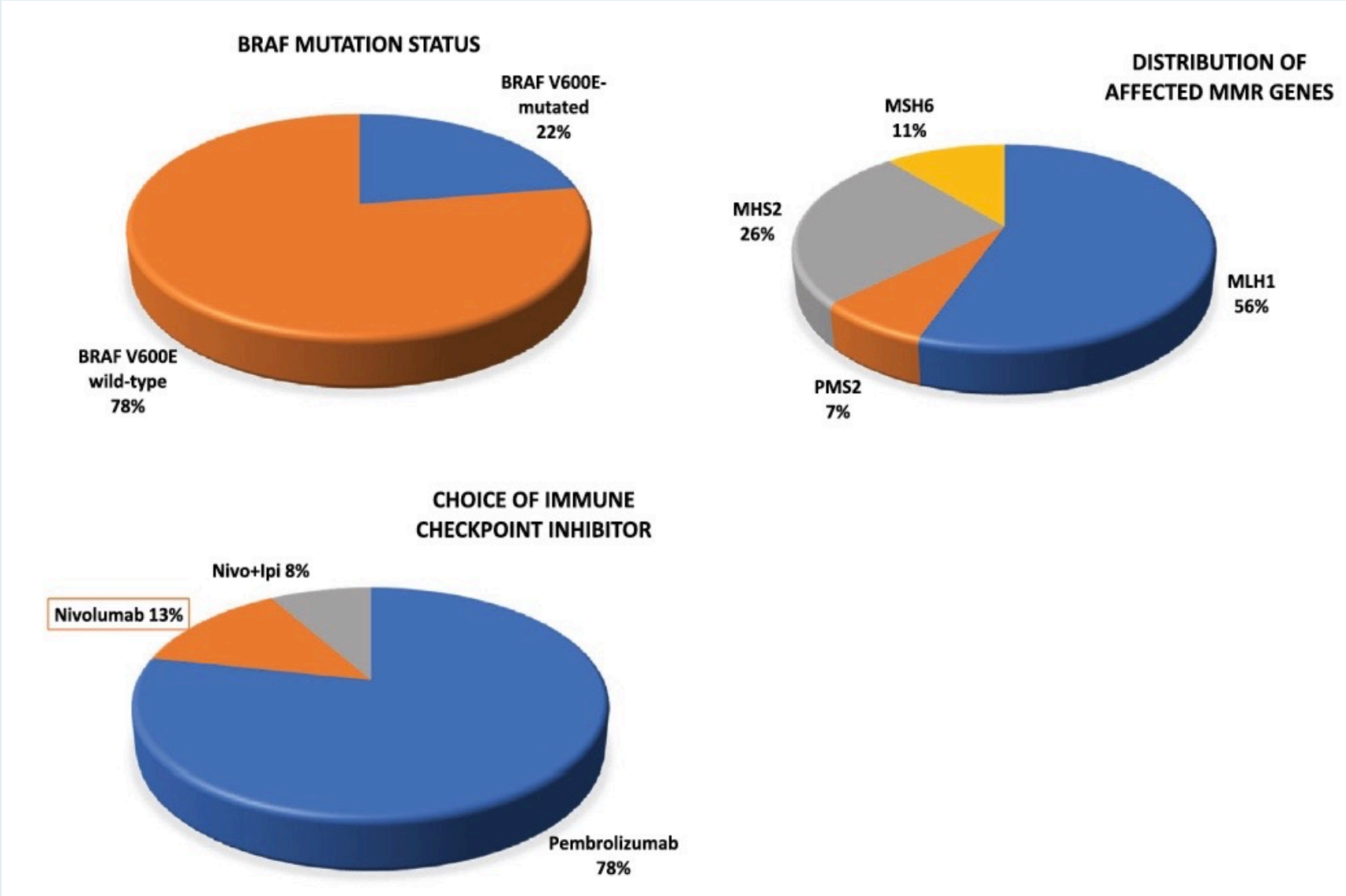
Gastrointestinal Cancer

Mismatch Repair (MMR) Gene Alteration and BRAF V600E Mutation Are Potential Predictive Biomarkers of Immune Checkpoint Inhibitors in MMR-Deficient Colorectal Cancer

Ibrahim Halil Sahin,[a] Subir Goyal,[b] Yoanna Pumpalova,[c] Mohamad B. Sonbol,[d] Satya Das,[e] Sigurdis Haraldsdottir,[f] Daniel Ahn,[d] Kristen K. Ciombor,[e] Zhengjia Chen,[b] Amber Draper,[b] Jordan Berlin,[e] Tanios Bekaii-Saab,[d] Gregory B. Lesinski,[b] Bassel F. El-Rayes,[b] Christina Wu[b]

[a]H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA; [b]Emory University School of Medicine, Winship Cancer Institute, Atlanta, Georgia, USA; [c]Stanford University Cancer Institute, Stanford, California, USA; [d]Mayo Clinic, Rochester, Minnesota, USA; [e]Vanderbilt University Ingram Cancer Center, Nashville, Tennessee, USA; [f]Dana-Farber Cancer Institute, Boston, Massachusetts, USA

Distribution of Clinical and Molecular Variables in the Cohort of Interest



Sahin IH et al. *Oncologist* 2021;[Online ahead of print].

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

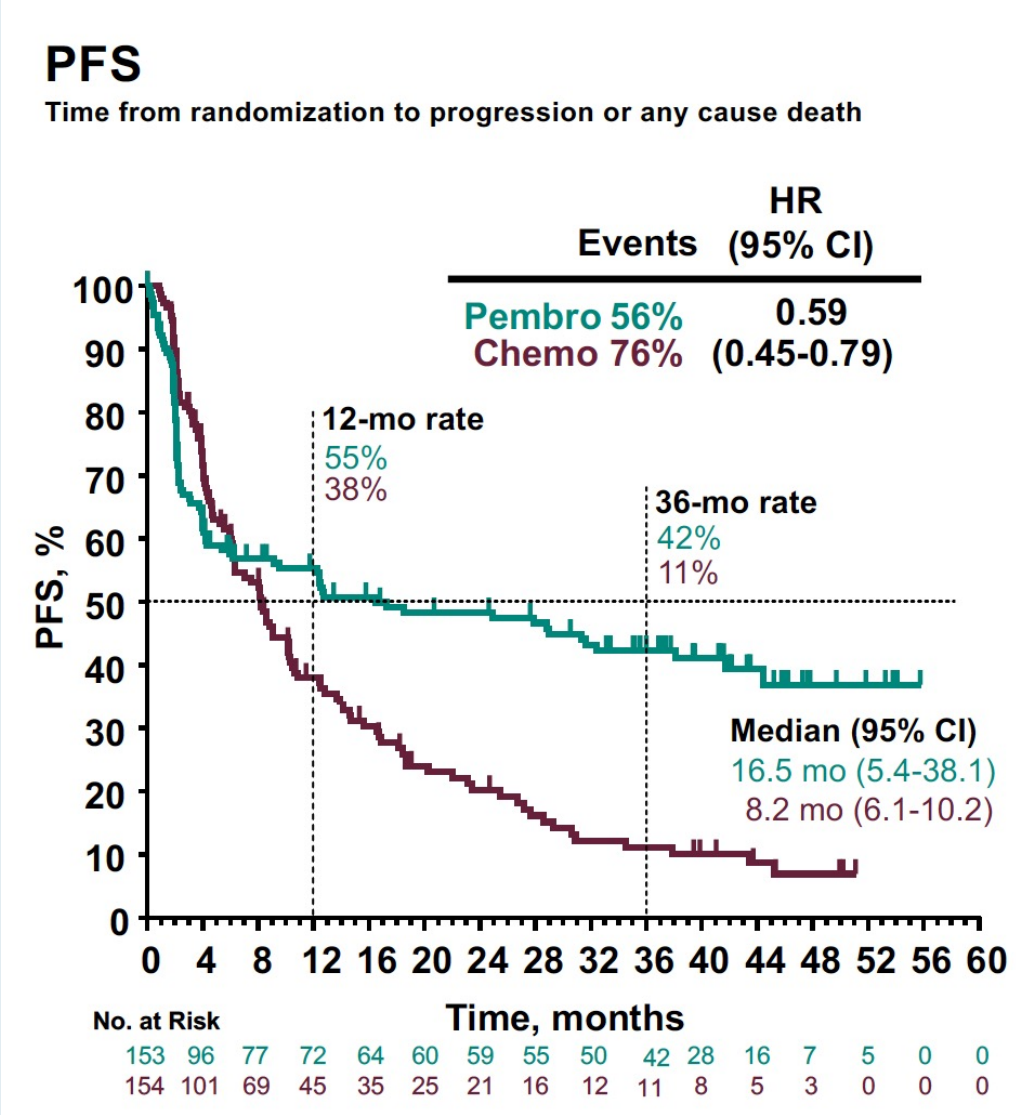
Thierry André,[1] Kai-Keen Shiu,[2] Tae Won Kim,[3] Benny Vittrup Jensen,[4] Lars Henrik Jensen,[5] Cornelis Punt,[6] Denis Smith,[7] Rocio Garcia-Carbonero,[8] Julia Alcaide-Garcia,[9] Peter Gibbs,[10] Christelle de la Fouchardiere,[11] Fernando Rivera,[12] Elena Elez,[13] Johanna Bendell,[14] Dung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

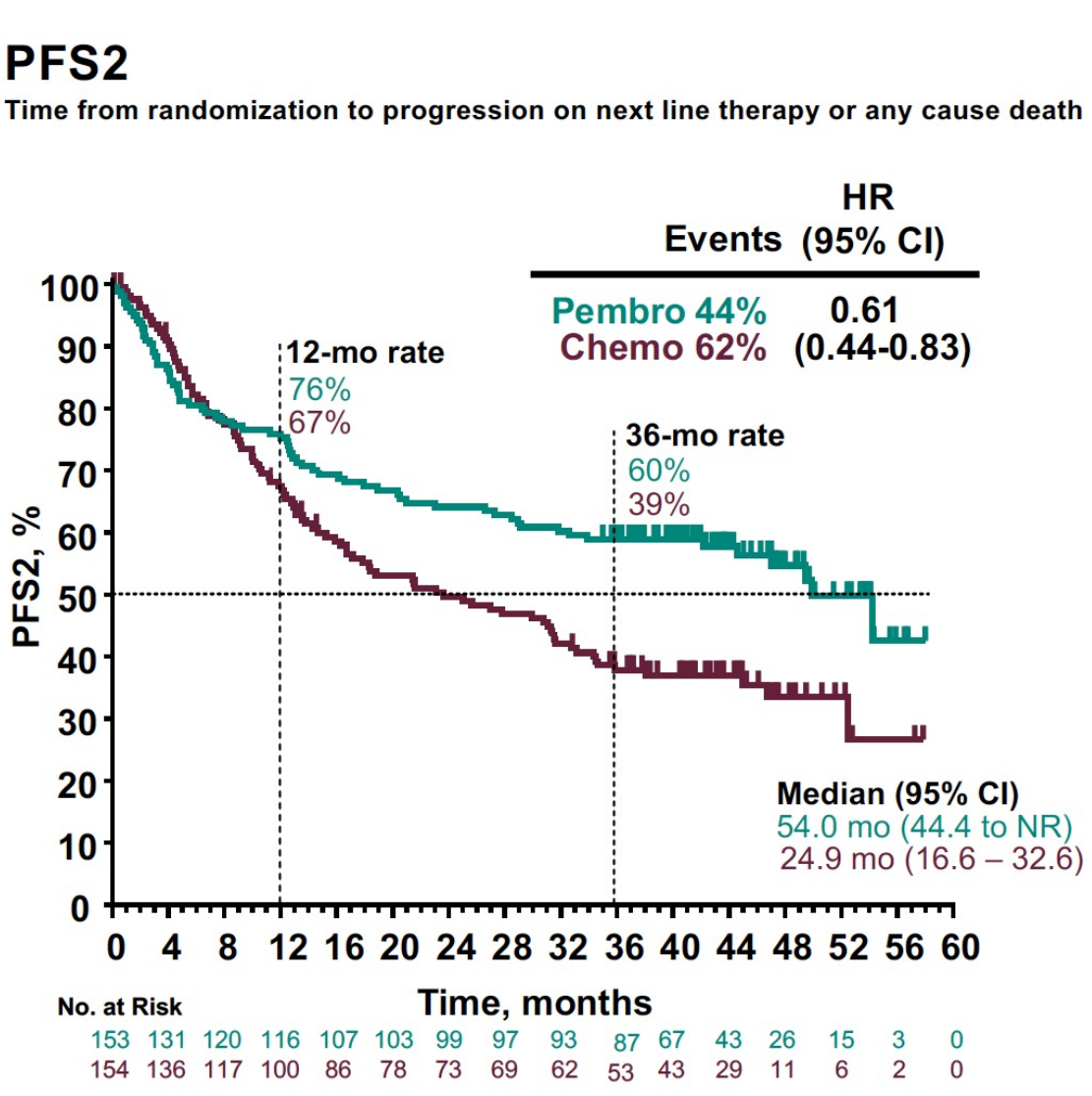
[1]Sorbonne Université and Hôpital Saint Antoine, Paris, France; [2]University College Hospital, NHS Foundation Trust, London, United Kingdom; [3]Asan Medical Center, University of Ulsan, Seoul, Republic of Korea; [4]Herlev and Gentofte Hospital, Herlev, Denmark; [5]University Hospital of Southern Denmark, 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

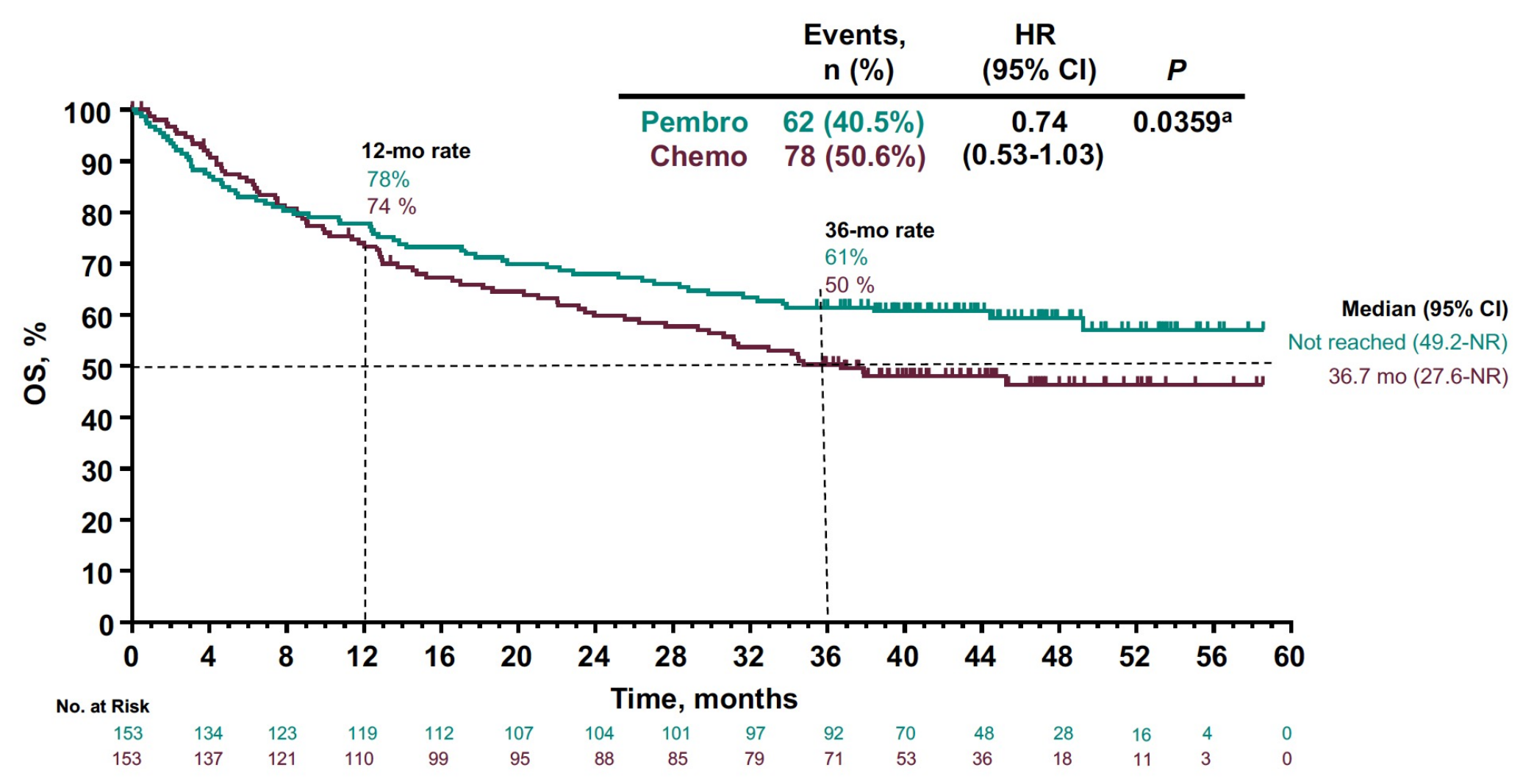




Andre T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

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

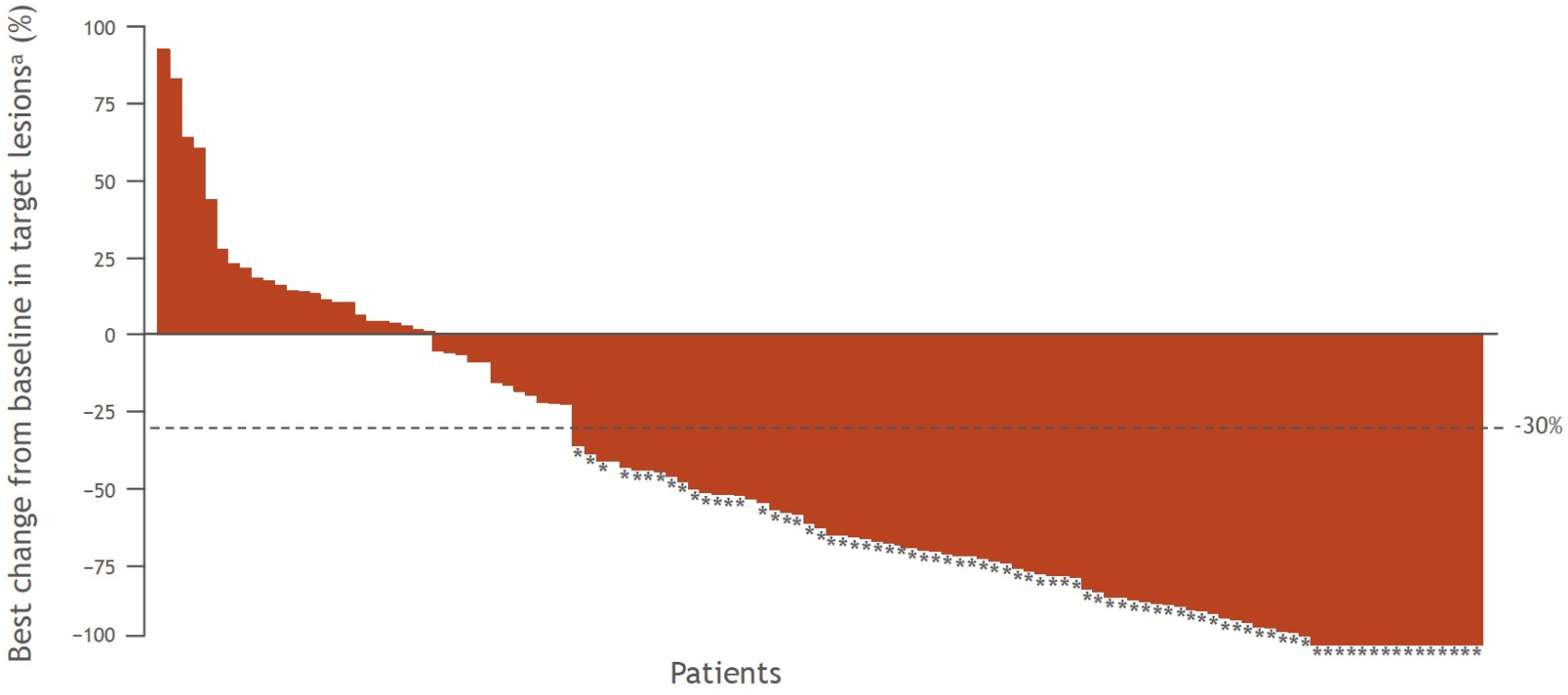
Thierry André,[1] Sara Lonardi,[2] Ka Yeung Mark Wong,[3] Heinz-Josef Lenz,[4] Fabio Gelsomino,[5] Massimo Aglietta,[6] Michael A. Morse,[7] Eric Van Cutsem,[8] Ray McDermott,[9] Andrew Hill,[10] Michael B. Sawyer,[11] Alain Hendlisz,[12] Bart Neyns,[13] Sandzhar Abdullaev,[14] Arteid Memaj,[14] Ming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

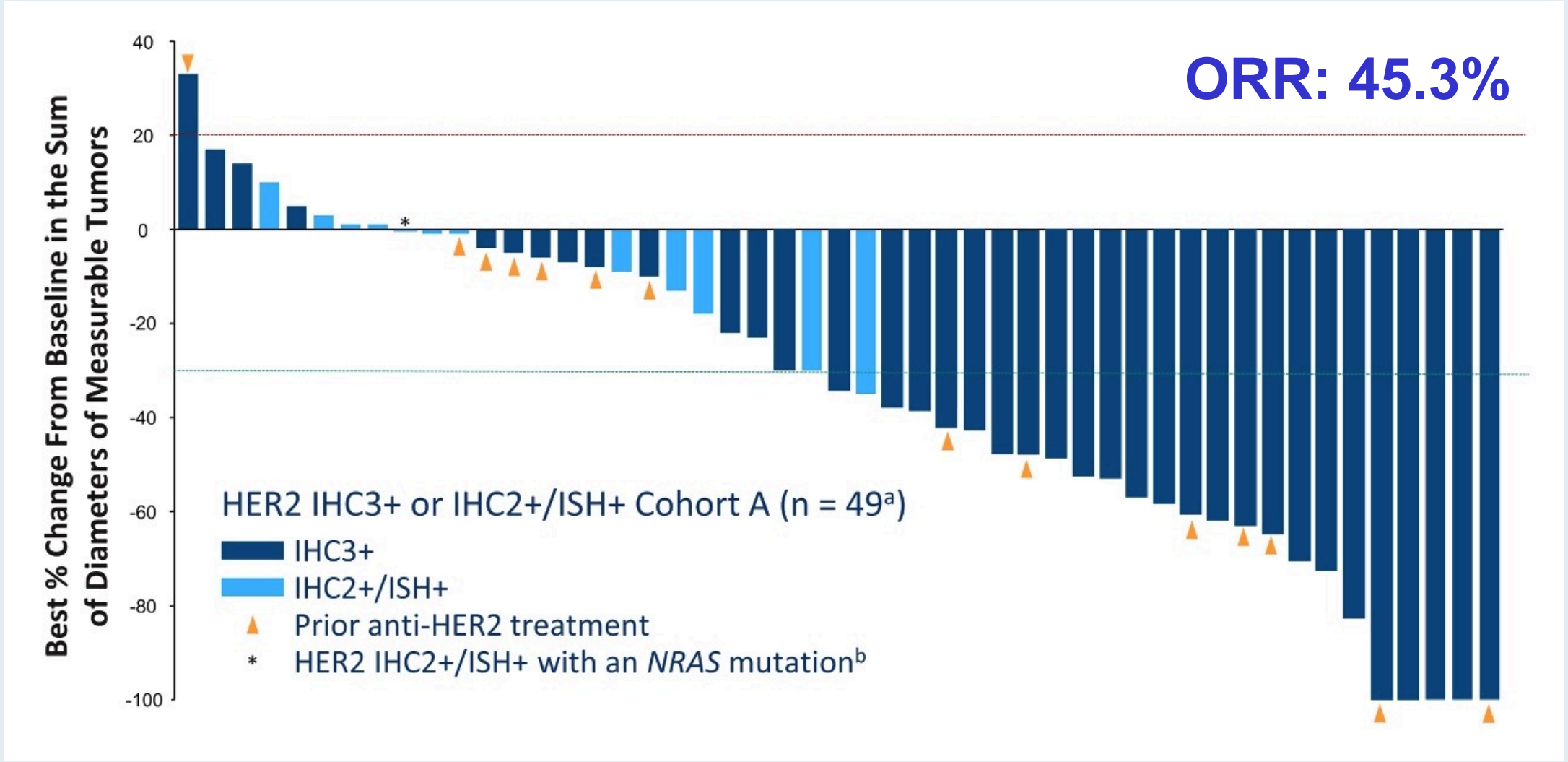
Takayuki Yoshino; National Cancer Center Hospital East, Kashiwa, Japan

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

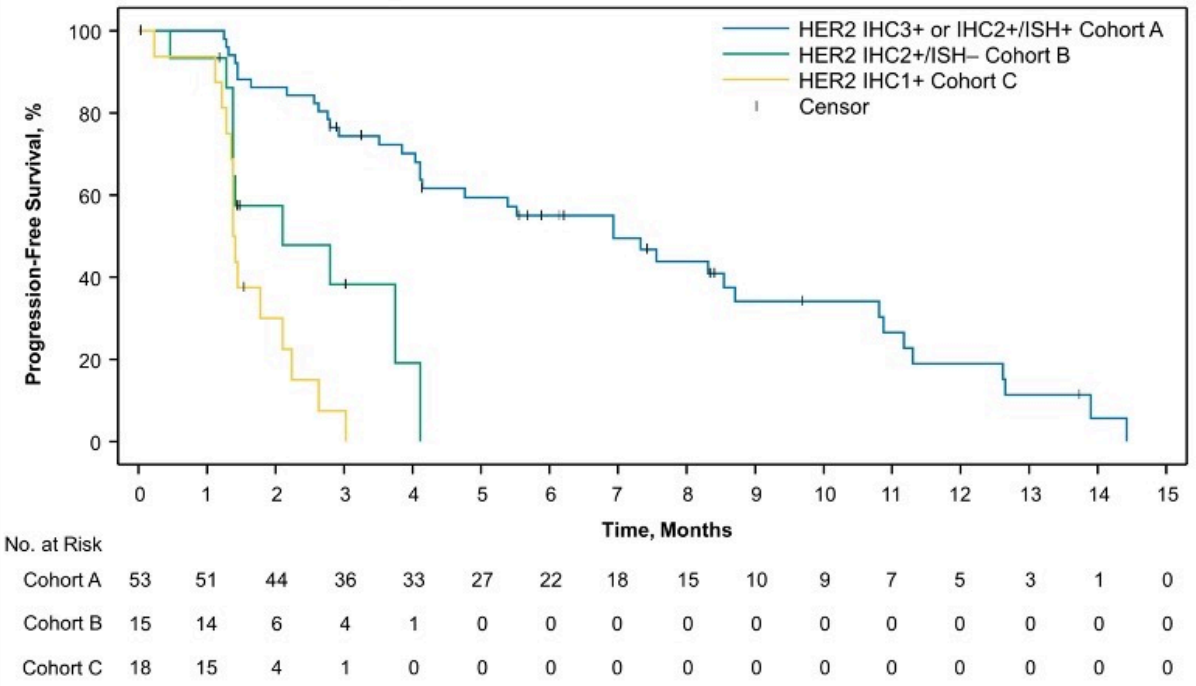


Yoshino T et al. ASCO 2021;Abstract 3500.

RTP RESEARCH TO PRACTICE

DESTINY-CRC01: Progression-Free and Overall Survival

Progression-Free Survival

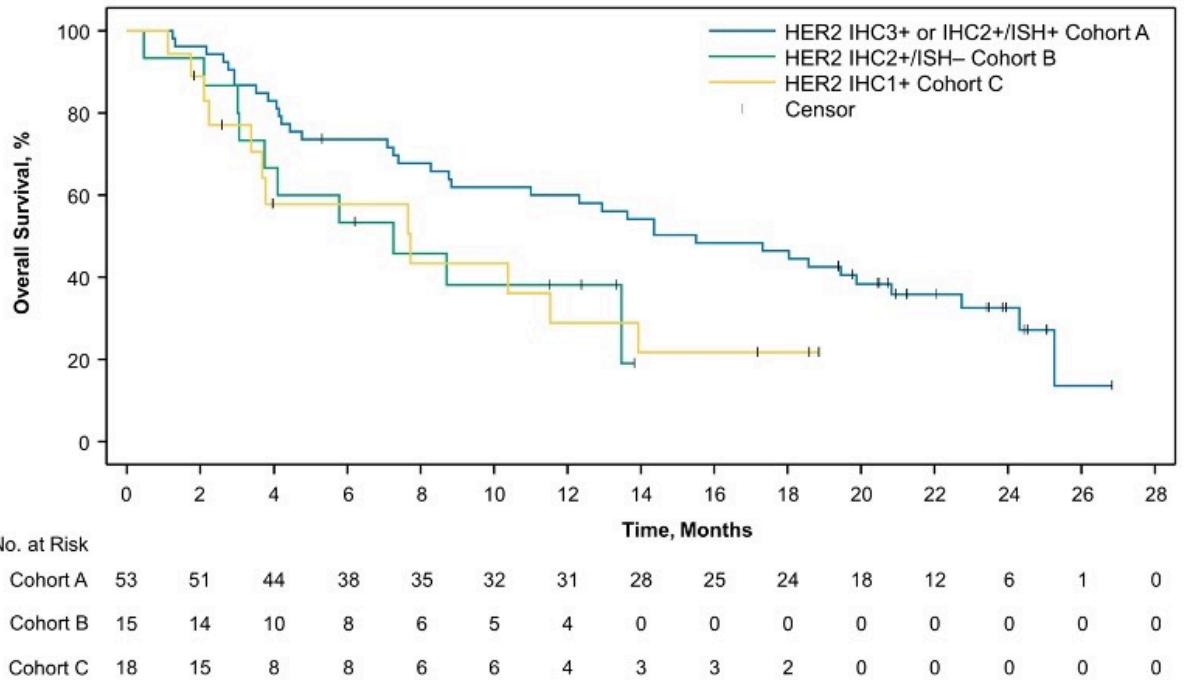


No. at Risk

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.

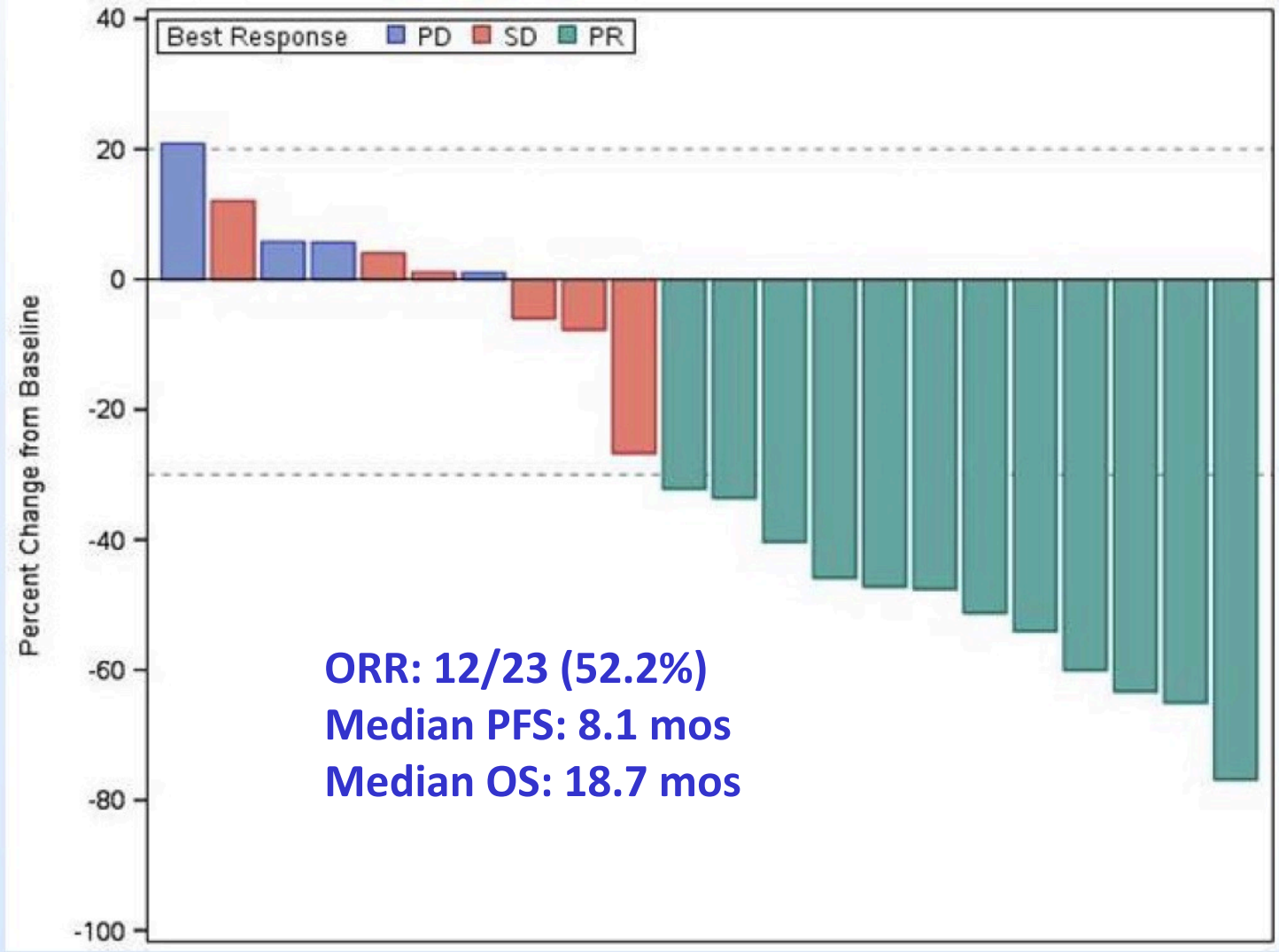
Yoshino T et al. ASCO 2021;Abstract 3500.

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.

Oncologist 2021;[Online ahead of print].

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Symptom Management and Supportive Care

Preemptive Versus Reactive Topical Clobetasol for Regorafenib-Induced Hand-Foot Reactions: A Preplanned Analysis of the ReDOS Trial

Aminah Jatoi,[a] Fang-Shu Ou,[a] Daniel H. Ahn,[b] Tyler J. Zemla,[a] Jennifer G. Le-Rademacher,[a] Patrick Boland,[c] Kristen K. Ciombor,[d] Nisha L. Jacobs,[e] Boris Pasche,[f] James M. Cleary,[g] Jeannine S. McCune,[h] Katrina S. Pedersen,[i] Afsaneh Barzi,[h] E. Gabriela Chiorean,[j] Erica N. Heying,[a] Heinz-Josef Lenz,[k] Jeff A. Sloan,[a] Axel Grothey,[l] Mario E. Lacouture,[m] Tanios Bekaii-Saab[b]

[a]Mayo Clinic, Rochester, Minnesota, USA; [b]Mayo Clinic, Scottsdale, Arizona, USA; [c]Roswell Park Cancer Institute, Buffalo, New York, USA; [d]Vanderbilt University, Nashville, Tennessee, USA; [e]Minnesota Hematology Oncology, Coon Rapids, Minnesota, USA; [f]Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, USA; [g]Dana-Farber Cancer Institute, Boston, Massachusetts, USA; [h]City of Hope, Duarte, California, USA; [i]Washington University in St. Louis, St. Louis, Missouri, USA; [j]University of Washington, Seattle, Washington, USA; [k]USC Norris Comprehensive Cancer Center, California, Los Angeles, USA; [l]West Cancer Center, Germantown, Tennessee, USA; [m]Memorial Sloan Kettering Cancer Center, New York, New York, USA

Meet The Professor with Dr Bekaii-Saab

MODULE 1: Cases from Drs Ibrahim and Ma

- Dr Ibrahim: A 58-year-old man with HIV and esophageal cancer
- Dr Ma: A frail 78-year-old woman with metastatic gastric cancer and brain metastases – PD-L1 CPS 15%, TMB 38.4 mut/Mb
- Dr Ibrahim: An 81-year-old man with metastatic gastroesophageal junction adenocarcinoma and a PD-L1 of 50%

MODULE 2: Beyond the Guidelines; Key Data – Gastroesophageal Cancers

MODULE 3: Cases from Dr Ciombor

- A 51-year-old woman with metastatic colorectal cancer (CRC) and discordant mismatch repair results
- A 53-year-old woman with microsatellite-stable metastatic CRC and a BRAF V600E mutation

MODULE 4: Beyond the Guidelines; Key Data – CRC

MODULE 5: Cases from Dr Gosain

- A 64-year-old man with metastatic sarcomatoid hepatocellular carcinoma (HCC) whose disease progressed from Child-Pugh A6 to B8 while on atezolizumab/bevacizumab
- A 66-year-old man with HCC and untreated hepatitis C

MODULE 6: Beyond the Guidelines; Key Data – HCC

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Gosain: A 64-year-old man with metastatic sarcomatoid HCC whose disease progressed from Child-Pugh A6 to B8 while on atezolizumab/bevacizumab

Dr Rahul Gosain

- PMH: Cirrhosis from alcohol (quit 5 years ago), active smoker, being followed for thrombocytopenia
- 12/2020: AFP increased from baseline of 6.4 to 15.2; Ultrasound without new findings
  - MRI c/w multifocal liver lesions, largest 4.5 cm
  - CT chest/pelvis c/w pulmonary nodules, enlarged periportal nodes
  - Liver biopsy: HCC, sarcomatoid histology, PD-L1 CPS 10, ***Child-Pugh A6*** (albumin 3.3)

Questions

- What's the utility of ultrasound versus MRI as a screening tool for HCC?

Case Presentation – Dr Gosain: A 64-year-old man with metastatic sarcomatoid HCC whose disease progressed from Child-Pugh A6 to B8 while on atezolizumab/bevacizumab (continued)

Dr Rahul Gosain

- 12/2020: AFP increased from baseline of 6.4 to 15.2; Ultrasound without new findings
  - MRI c/w multifocal liver lesions, largest 4.5 cm
  - CT chest/pelvis c/w pulmonary nodules, enlarged periportal nodes
  - Liver biopsy: HCC, sarcomatoid histology, PD-L1 CPS 10, ***Child-Pugh A6*** (albumin 3.3)
  - ***EGD: Negative for varices***
- ***Bevacizumab/atezolizumab, but required paracentesis for worsening ascites before cycle 3***
  - ***Now Child-Pugh B8***

Questions

- The patient progressed from Child-Pugh A6 to B8 while on bevacizumab/atezolizumab, which isn't approved in this setting. Should I switch treatment now?
- If he progresses, are there any good alternative treatment options?
- How often and in what circumstances would you consider doing a biopsy despite this being classic HCC on your MRI?
- How important is knowing the histology? Will it change treatment?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Gosain: A 66-year-old man with HCC and untreated hepatitis C

Dr Rahul Gosain

- Known history of untreated hepatitis C
- 12/2019: 8.5-cm liver mass and porta vein thrombus, diagnosed with Child-Pugh B7 HCC
- Lenvatinib 12mg decreased to 8mg with up-trending LFTs
  - Further rapid rise in LFTs but now with drastic rise in Hep C viral load (while AFP was down trending: 2842)
- Treated his active hepatitis C for 8 weeks
  - AFP at 4718 and scans consistent with further progression of his liver lesion
- Lenvatinib re-started
  - AFP is now down-trending (1718) and scans are stable

Questions

- Do you treat patients with untreated hepatitis C any differently? Is it more likely that you'll treat their hepatitis C first and then their metastatic disease?

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Bekaii-Saab

MODULE 1: Cases from Drs Ibrahim and Ma

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- Dr Ma: A frail 78-year-old woman with metastatic gastric cancer and brain metastases – PD-L1 CPS 15%, TMB 38.4 mut/Mb
- Dr Ibrahim: An 81-year-old man with metastatic gastroesophageal junction adenocarcinoma and a PD-L1 of 50%

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MODULE 3: Cases from Dr Ciombor

- A 51-year-old woman with metastatic colorectal cancer (CRC) and discordant mismatch repair results
- A 53-year-old woman with microsatellite-stable metastatic CRC and a BRAF V600E mutation

MODULE 4: Beyond the Guidelines; Key Data – CRC

MODULE 5: Cases from Dr Gosain

- A 64-year-old man with metastatic sarcomatoid hepatocellular carcinoma (HCC) whose disease progressed from Child-Pugh A6 to B8 while on atezolizumab/bevacizumab
- A 66-year-old man with HCC and untreated hepatitis C

MODULE 6: Beyond the Guidelines; Key Data – HCC

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

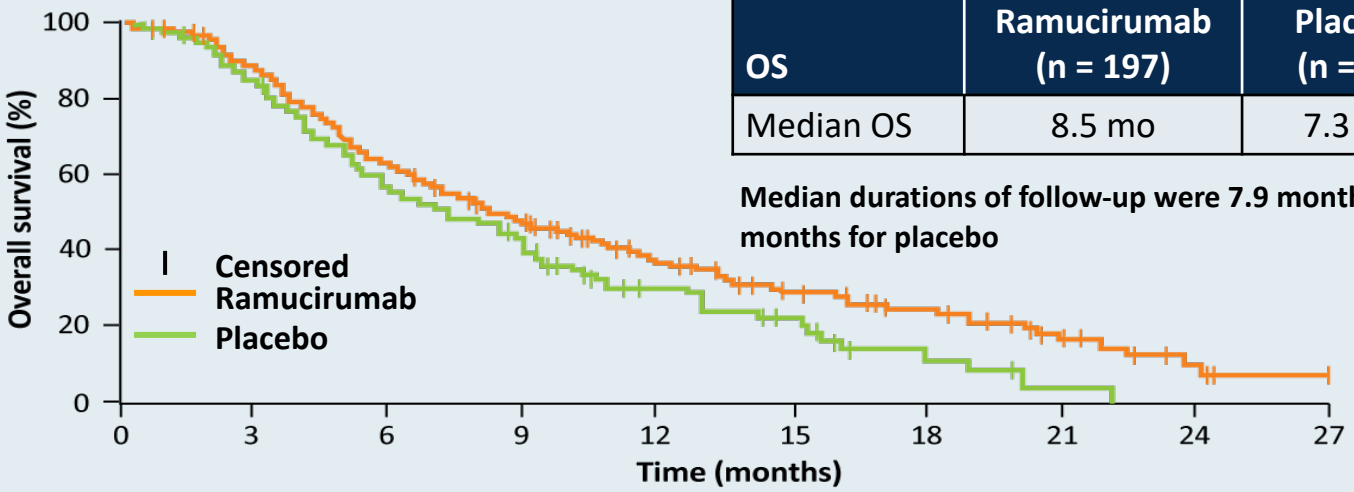
Articles

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**

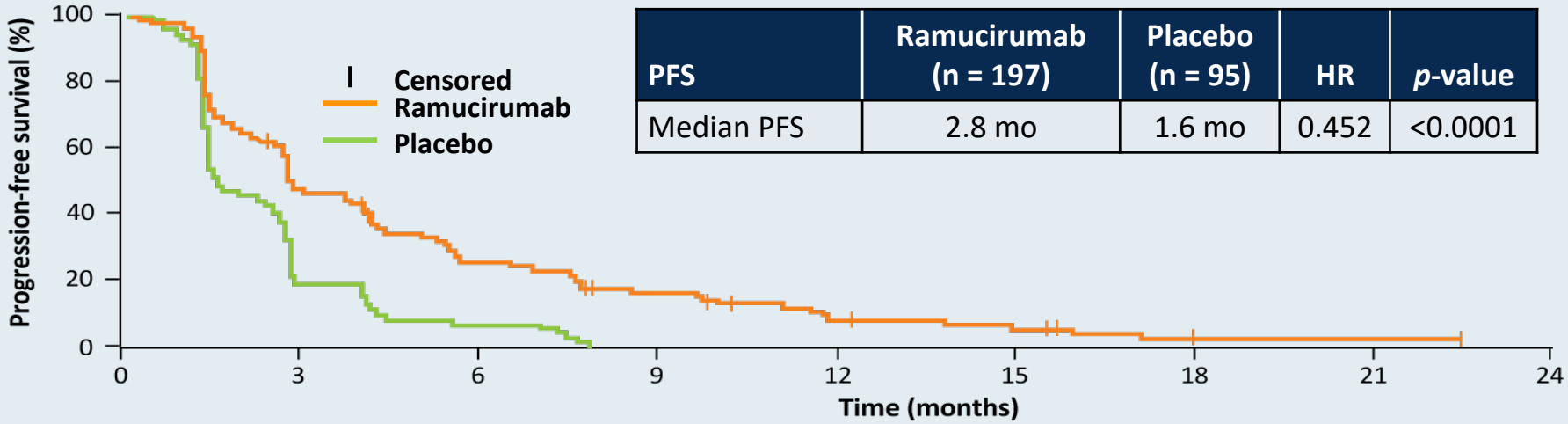
Lancet Oncol 2019;20(2):282-96.

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.

Combination Immunotherapy for Hepatocellular Carcinoma: Where Are We Currently?

Pedro Luiz Serrano Uson Junior, MD[1,2,3] Bolni Marius Nagalo, PhD[1,2,3,4] Daniel H. Ahn, MD[1] Tanios Bekaii-Saab, MD[1] Mitesh J. Borad, MD[1,2,3,4]

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[2] Center for Individualized Medicine, Mayo Clinic, Rochester, Minnesota
[3] Mayo Clinic Cancer Center, Mayo Clinic, Phoenix, Arizona
[4] Department of Molecular Medicine, Mayo Clinic, Rochester, Minnesota

Address for correspondence Mitesh J. Borad, MD, Division of Hematology and Medical Oncology, Department of Molecular Medicine, Mayo Clinic, 5777 E Mayo Blvd, Phoenix, AZ 85054, (e-mail: borad.mitesh@mayo.edu).

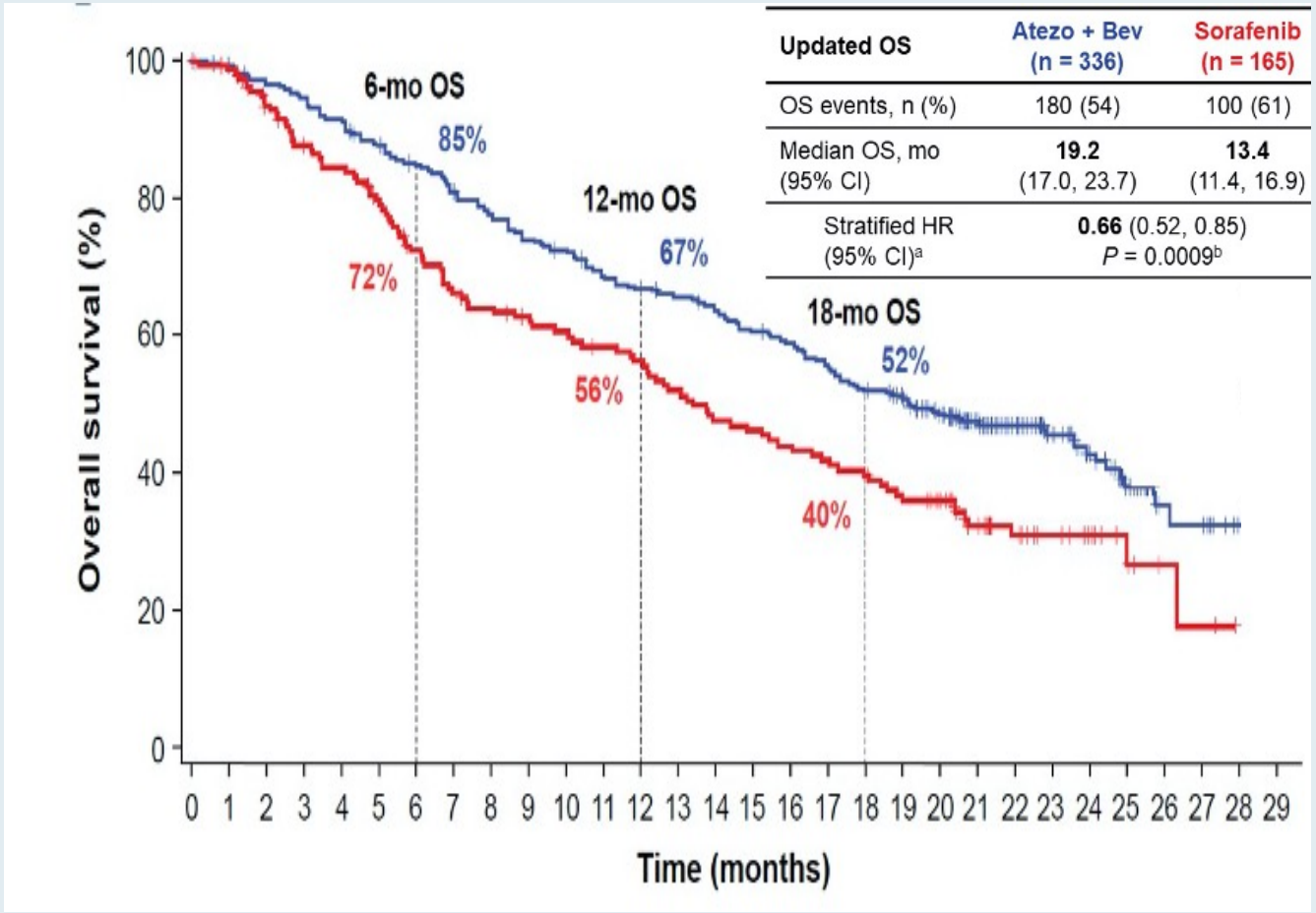
Semin Liver Dis 2021;41:136–141.

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)

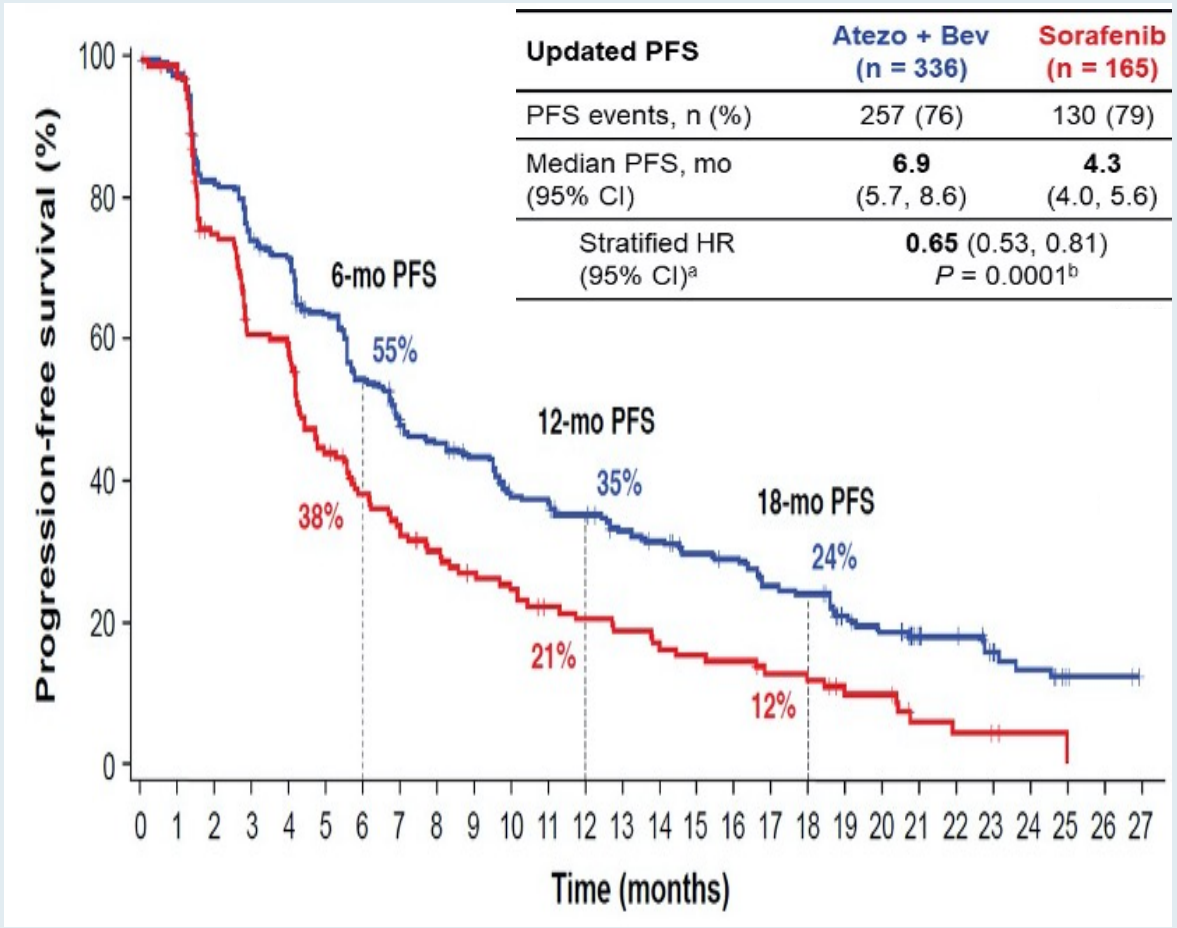
Finn RS et al.

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.

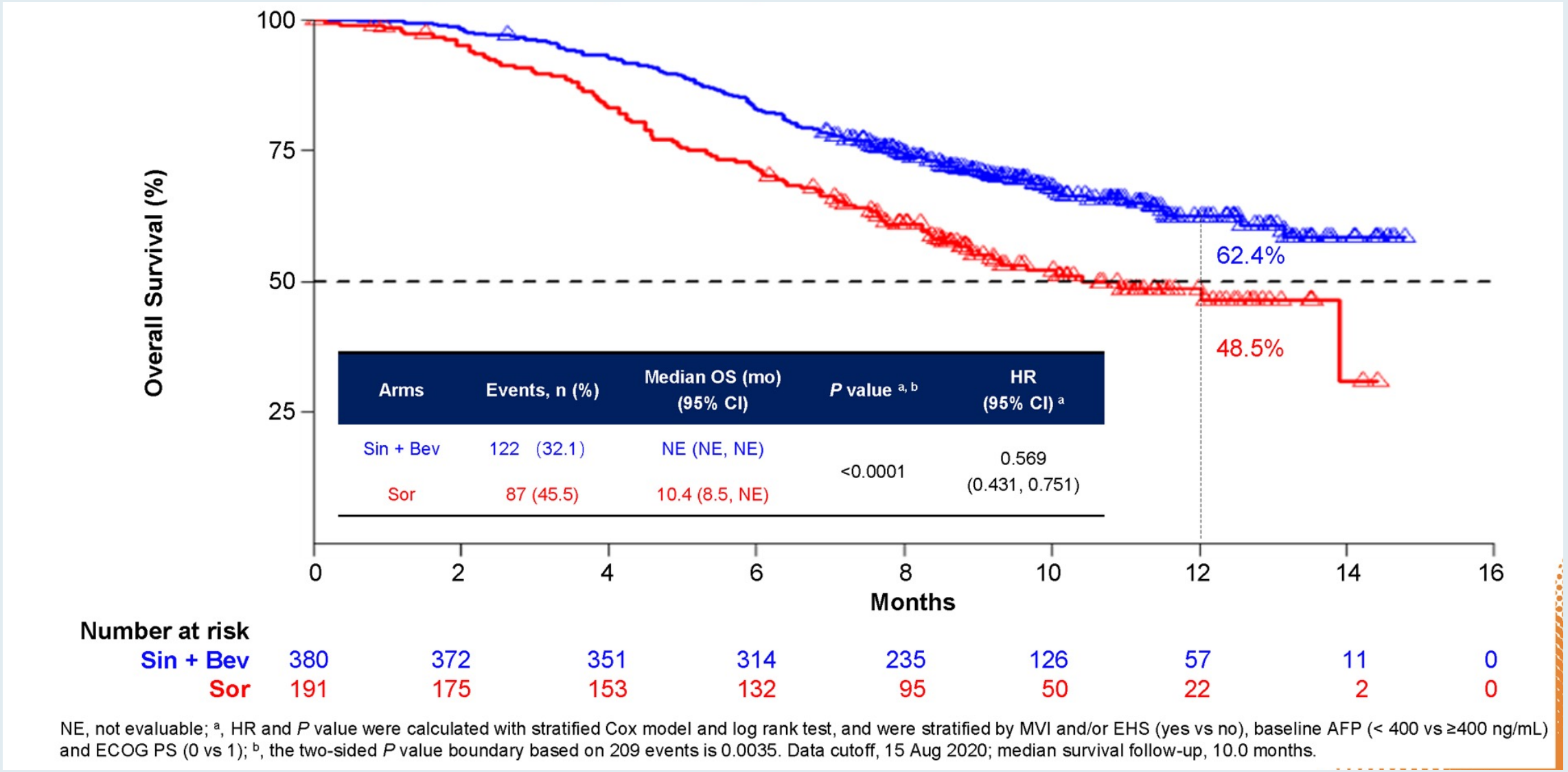
RTP RESEARCH TO PRACTICE

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

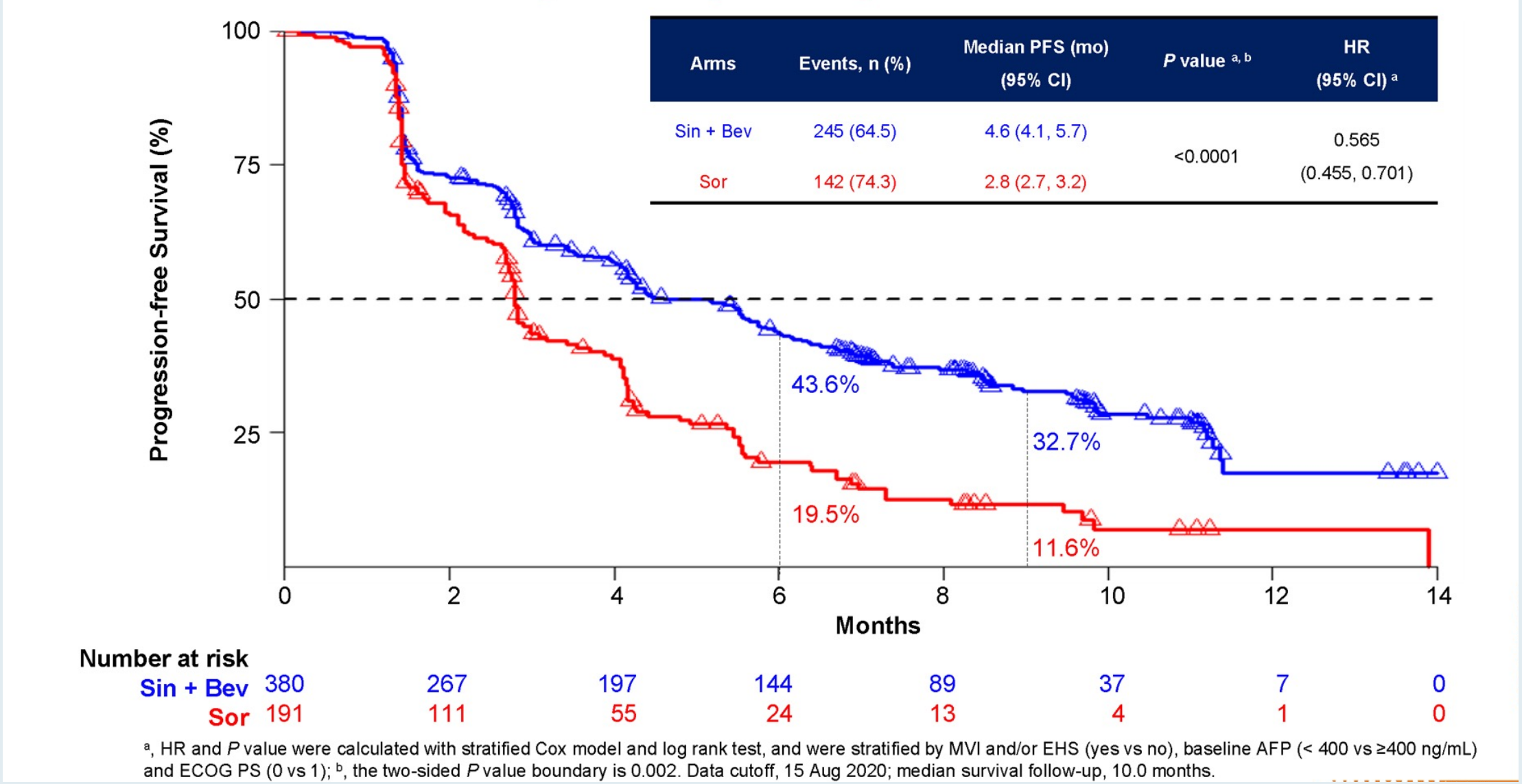
Sin + Bev	380	372	351	314	235	126	57	11	0
Sor	191	175	153	132	95	50	22	2	0

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

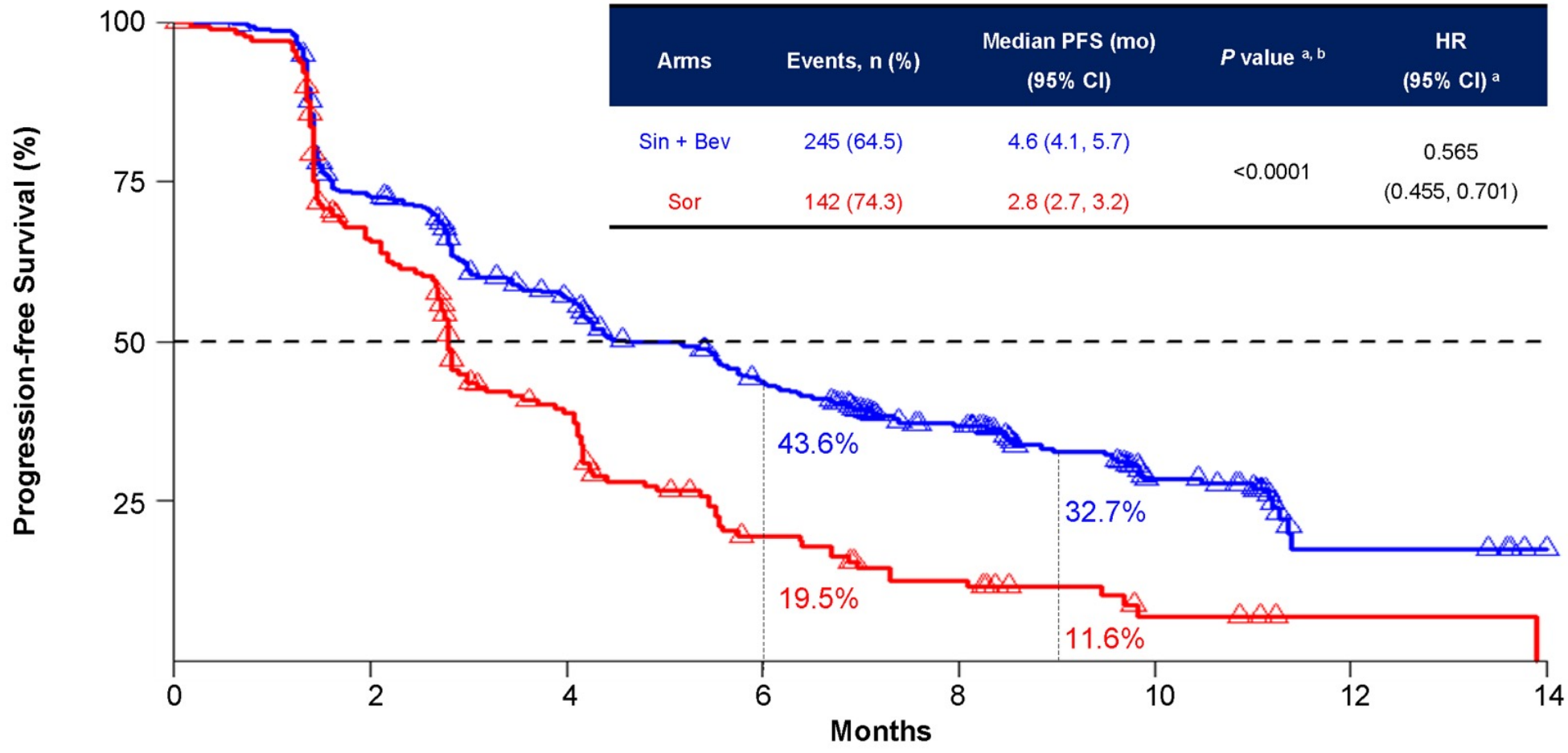
[a], HR and *P* value were calculated with stratified Cox model and log rank test, and were stratified by MVI and/or EHS (yes vs no), baseline AFP (< 400 vs ≥400 ng/mL) and ECOG PS (0 vs 1); [b], the two-sided *P* value boundary is 0.002. Data cutoff, 15 Aug 2020; median survival follow-up, 10.0 months.

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

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

RTP RESEARCH TO PRACTICE

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.

Am J Med 2020:S0002-9343(20)31098-6

REVIEW

THE AMERICAN JOURNAL of MEDICINE®

Contemporary Management of Pancreatic Cancer from an Internist Perspective

Qurat ul Ain Riaz Sipra, MD,[a,1] Mahnoor Islam, MBBS,[b,1] Irbaz Bin Riaz, MD, MS,[c] Jin Zhaohui, MD,[d] Hani M. Babiker, MD,[e] Tanios S. Bekaii-Saab, MD,[c] Mohamad Bassam Sonbol, MD[c]

[a]Banner University Medical Center, University of Arizona, Tucson; [b]Dow Medical University, Karachi City, Sindh, Pakistan; [c]Mayo Clinic, Phoenix, Ariz; [d]Mayo Clinic, Rochester, Minn; [e]University of Arizona Cancer Center, Tucson.

A Conversation with the Investigators: Metastatic Castration-Resistant Prostate Cancer

Tuesday, July 20, 2021
5:00 PM – 6:00 PM ET

Faculty

Emmanuel S Antonarakis, MD
Johann de Bono, MBChB, MSc, PhD
Julie N Graff, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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