Meet The Professor

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

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
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Professor of Medicine
Weill Cornell Medical College
New York, New York

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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, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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

Dr O'Reilly — Disclosures

Consulting Agreements	Agios Pharmaceuticals Inc, Alnylam Pharmaceuticals Inc, AstraZeneca Pharmaceuticals LP, Autem Medical, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Berry Genomics, Celgene Corporation, Cend Therapeutics Inc, CytomX Therapeutics, Eisai Inc, Exelixis Inc, Flatiron Health, Genentech, a member of the Roche Group, Genoscience Pharma, Helio Health, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, MiNA Therapeutics, QED Therapeutics, Rafael Pharmaceuticals Inc, RedHill Biopharma Ltd, Silenseed Ltd, SillaJen, Sobi, Surface Oncology, TheraBionic, twoXAR Inc, Vector Pharma, Yiviva
Contracted Research	Agios Pharmaceuticals Inc, Arcus Biosciences, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BioNTech, Bristol-Myers Squibb Company, Celgene Corporation, Flatiron Health, Genentech, a member of the Roche Group, Genoscience Pharma, Incyte Corporation, Polaris Pharmaceuticals, Puma Biotechnology Inc, QED Therapeutics, SillaJen, Yiviva

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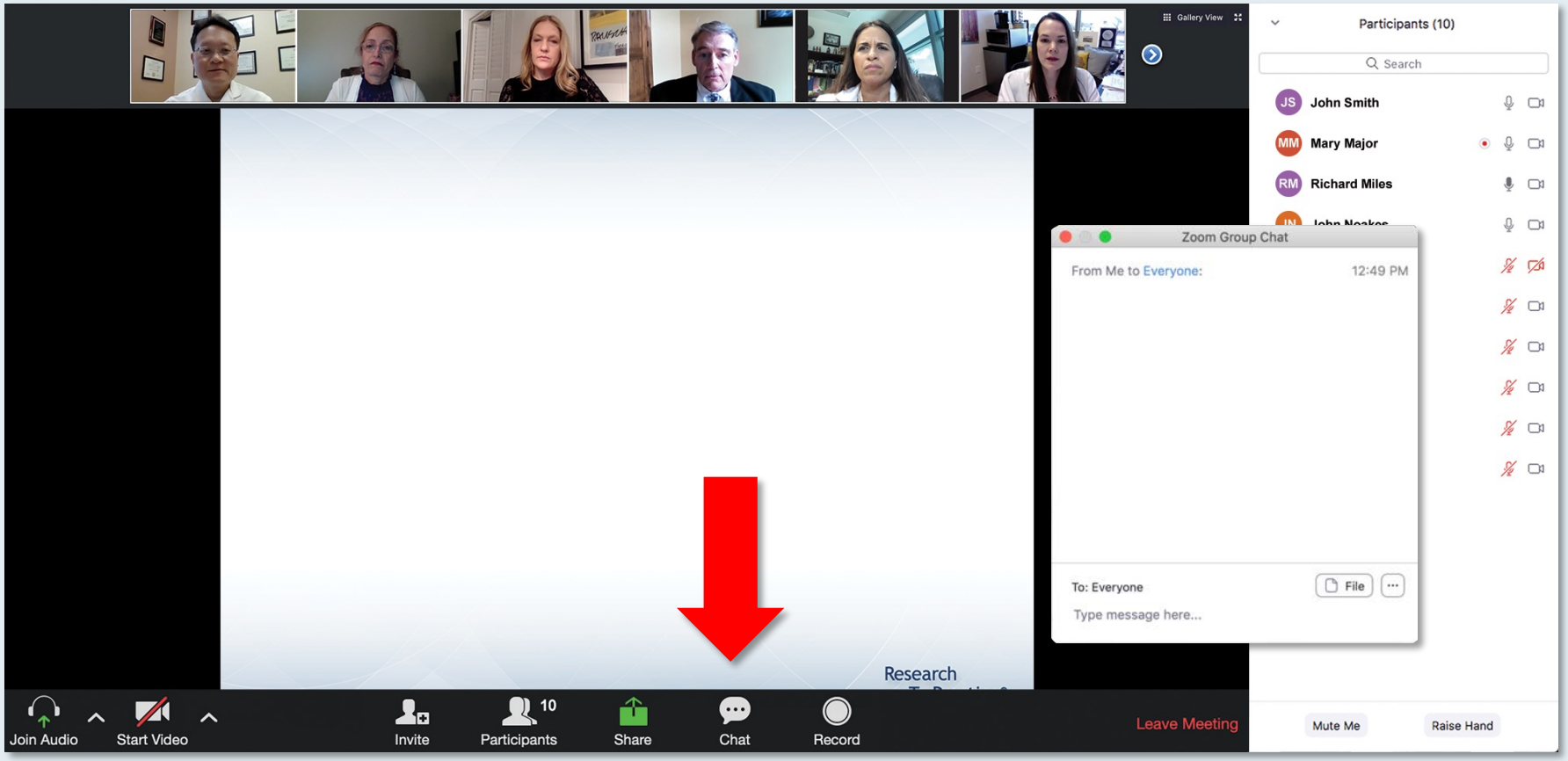

Feel free to submit questions now before the program begins and throughout the program.

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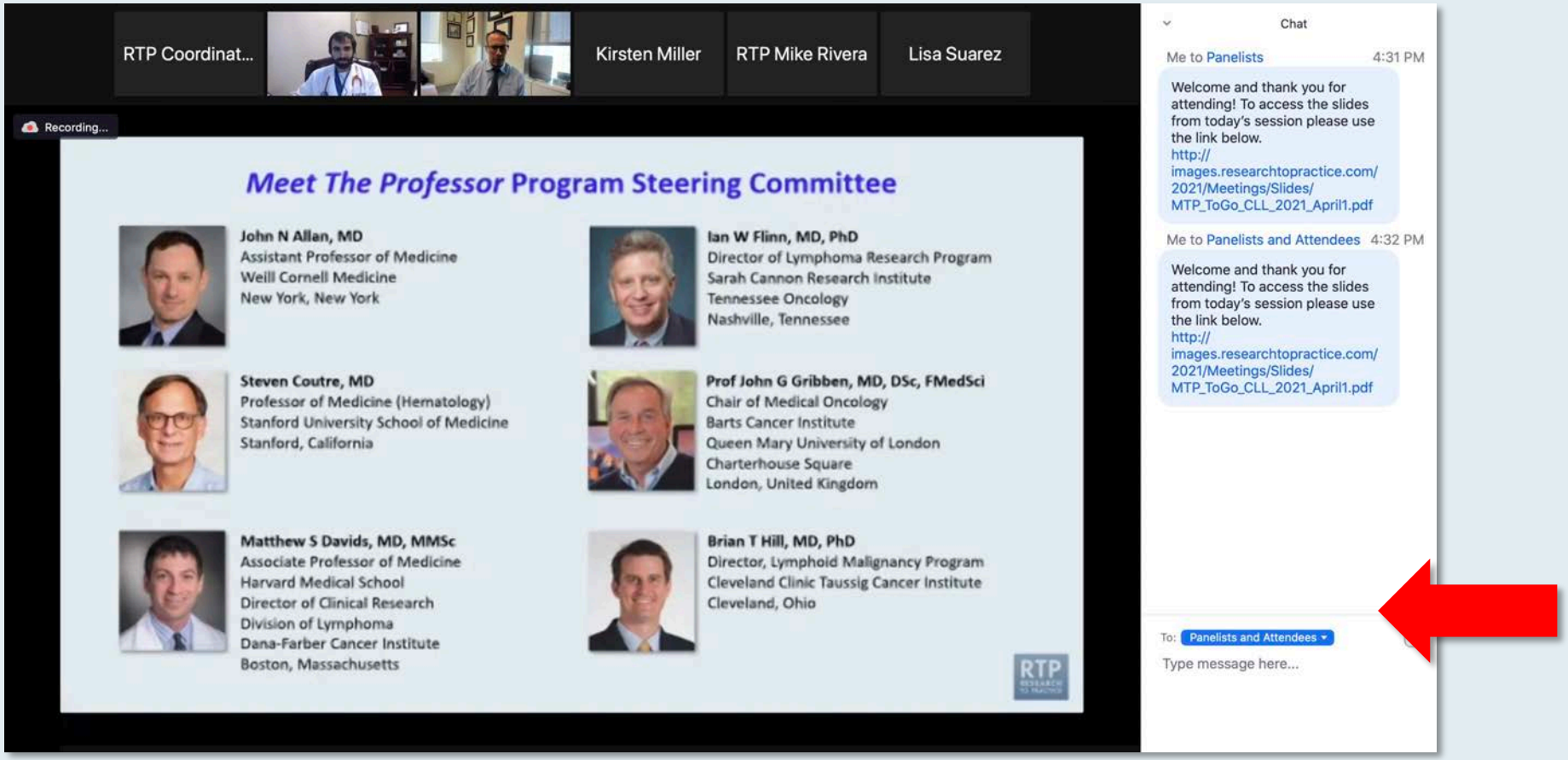
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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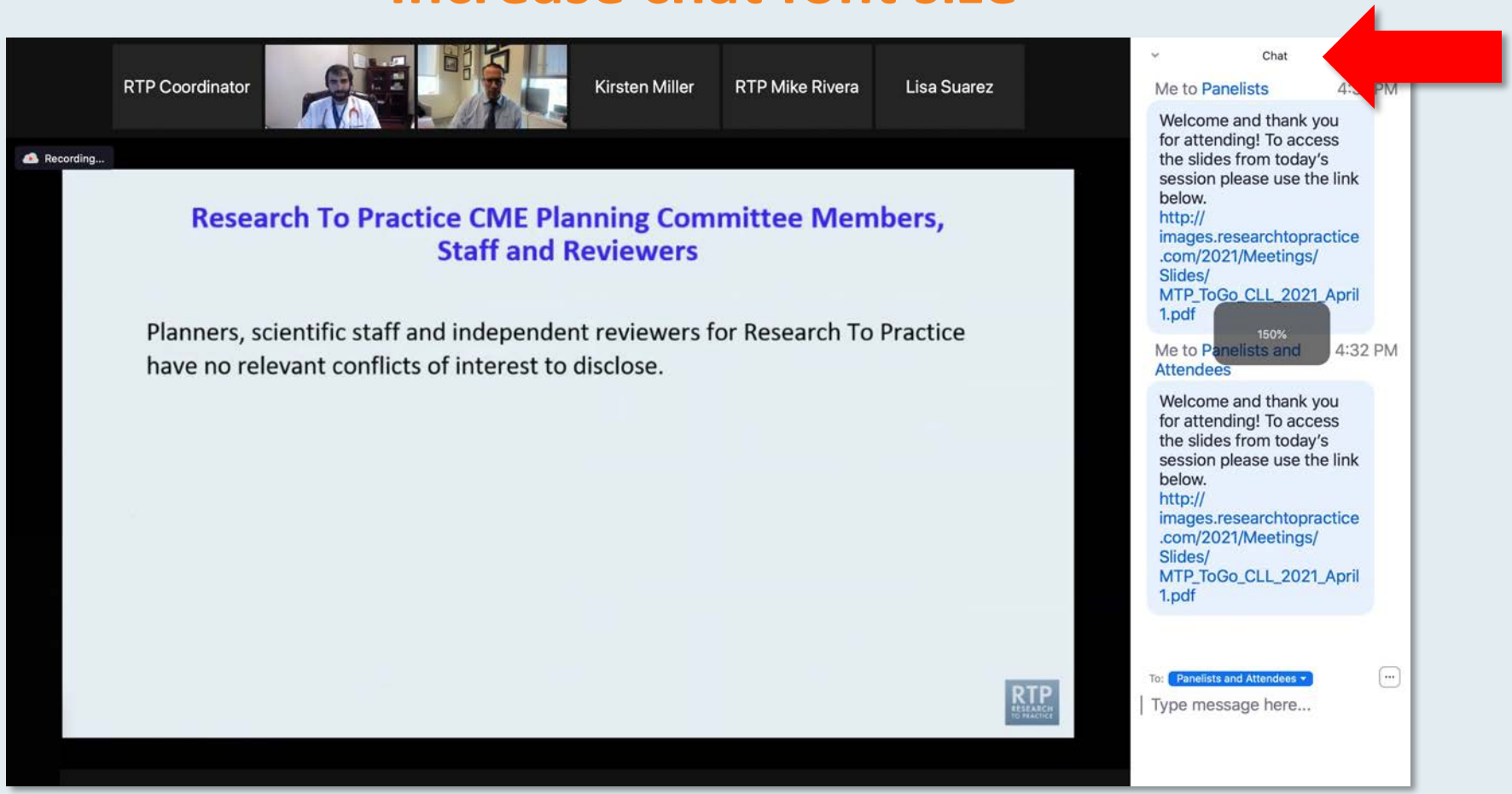
Familiarizing Yourself with the Zoom Interface

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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WITH DR NEIL LOVE

Key Presentations on Gastrointestinal Cancers from the 2021 ASCO Annual Meeting

DR KRISTEN CIOMBOR

VANDERBILT-INGRAM CANCER CENTER

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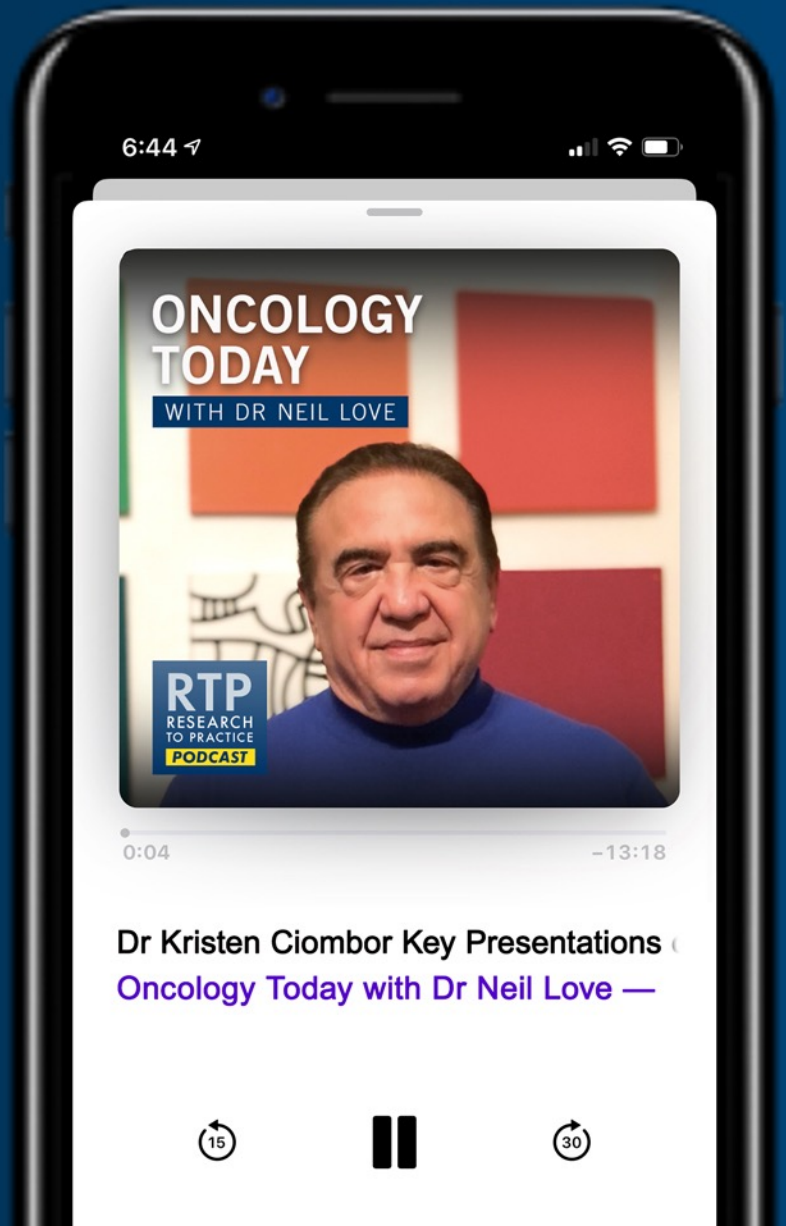

Meet The Professor

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

Monday, October 11, 2021
5:00 PM – 6:00 PM ET

Faculty

Elizabeth R Plimack, MD, MS

Moderator

Neil Love, MD

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Tuesday, October 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Wednesday, October 13, 2021
5:00 PM – 6:00 PM ET

Faculty

Erika Hamilton, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Triple-Negative Breast Cancer

Wednesday, October 20, 2021
5:00 PM – 6:00 PM ET

Faculty

Aditya Bardia, MD, MPH

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Recent Advances and Future Directions in Oncology: A Daylong Multitumor Educational Webinar in Partnership with Florida Cancer Specialists

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Saturday, October 23, 2021
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Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD
Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH
David R Spigel, MD
Saad Zafar Usmani, MD, MBA
Andrew D Zelenetz, MD, PhD
Additional faculty to be announced.

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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New York, New York

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Meet The Professor Program Participating Faculty

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Director
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Asklepios Klinik Altona
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Johanna Bendell, MD
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Program Leader, Gastrointestinal Cancer
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Director, Interdisciplinary Gastrointestinal Oncology Program
Assistant Director, Translational Research
Comprehensive Cancer Center
The University of Chicago Medical Center and Biological Sciences
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Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

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Memorial Sloan Kettering Cancer Center
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Kathryn Cramer Endowed Chair in Cancer Research
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Karmanos Cancer Institute
Wayne State University
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Jonsson Comprehensive Cancer Center
UCLA School of Medicine
Los Angeles, California

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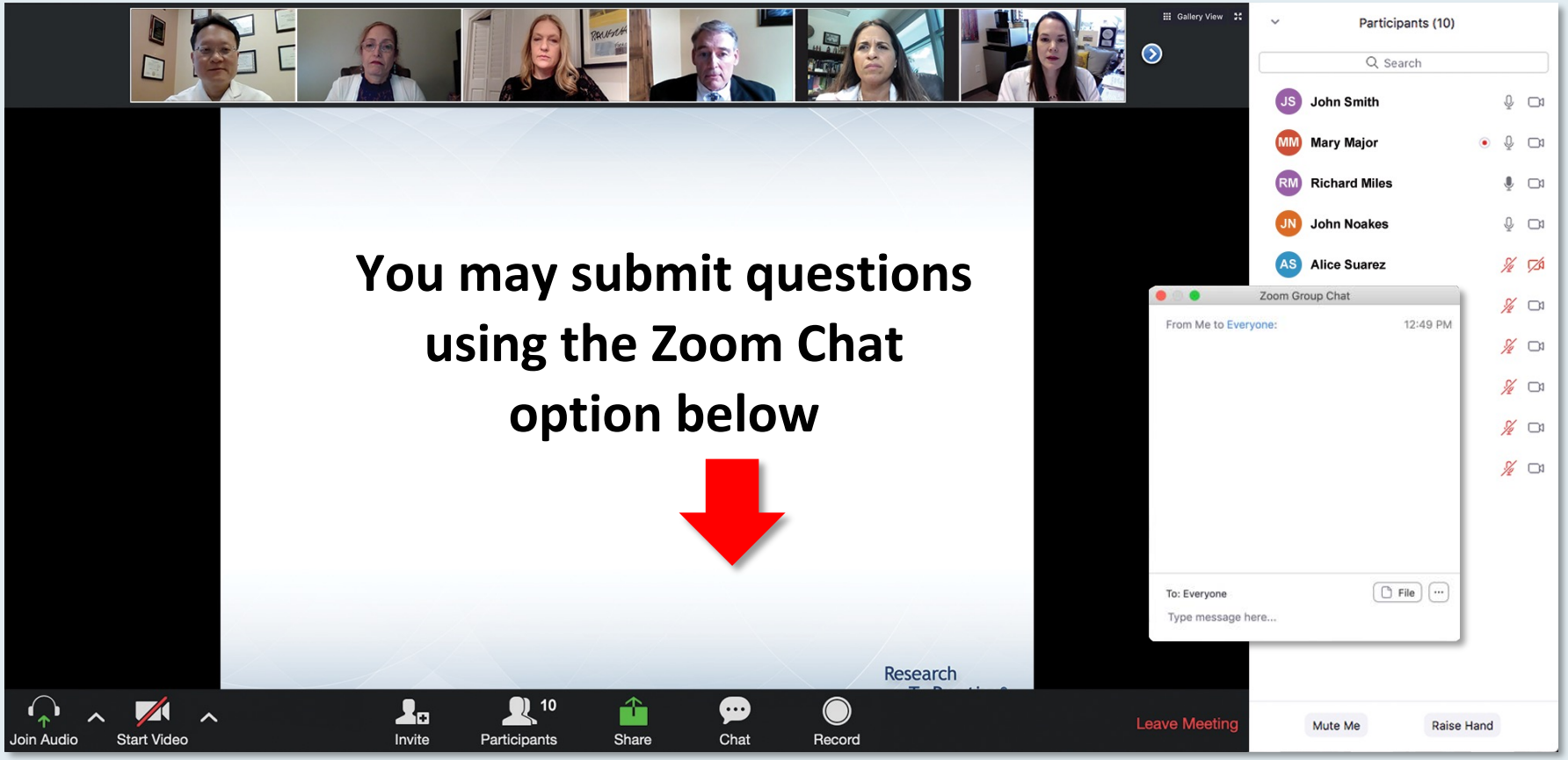

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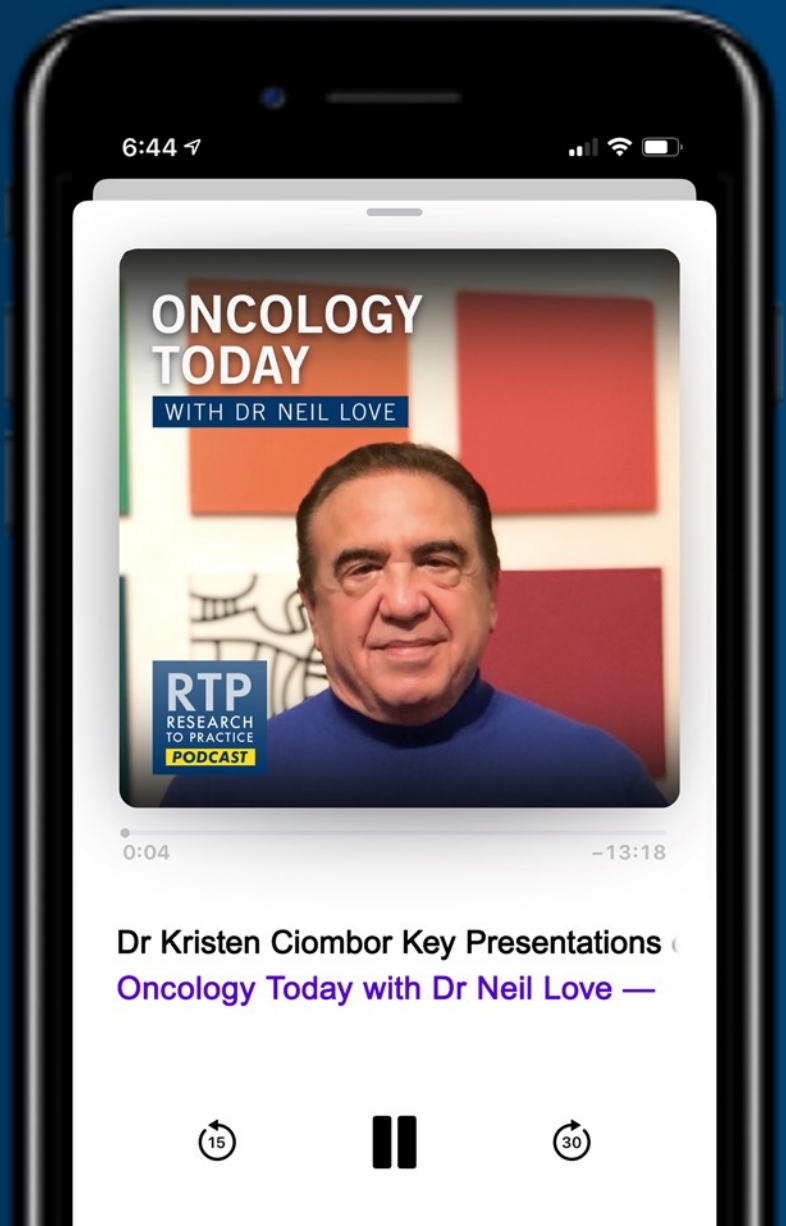

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Module 1: Breast Cancer – 9:30 AM – 10:20 AM

Module 2: Lung Cancer – 10:30 AM – 11:20 AM

Module 3: Gastrointestinal Cancers – 11:30 AM – 12:20 PM

Module 4: Genitourinary Cancers – 12:30 PM – 1:20 PM

Module 5: CLL and Lymphomas – 1:30 PM – 2:20 PM

Module 6: Multiple Myeloma – 2:30 PM – 3:20 PM

Module 7: AML and MDS – 3:30 PM – 4:20 PM

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Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

Nikesh Jasani, MD
Texas Oncology-Cypress
Houston, Texas

Farshid Dayyani, MD, PhD
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Department of Medicine
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Orange, California

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Director of Gastrointestinal
Oncology Program
Saint Luke's Cancer Institute
University of Missouri-Kansas
City School of Medicine
Kansas City, Missouri

Sulfi Ibrahim, MD
Hematology/Oncology
Reid Health
Richmond, Indiana

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Meet The Professor with Dr O'Reilly

MODULE 1: Journal Club with Dr O'Reilly — Pancreatic Cancer

MODULE 2: Case Presentations

- Dr Dayyani: A 54-year-old man with MSI-high metastatic colorectal cancer
- Dr Schafer: A 60-year-old woman with MSS metastatic sigmoid adenocarcinoma and a somatic BRCA2 mutation
- Dr Ciombor: A 60-year-old man with metastatic esophageal adenocarcinoma – PD-L1 CPS 70
- Dr Ibrahim: A 60-year-old man with infiltrative hepatocellular carcinoma
- Dr Dayyani: A 62-year-old woman with metastatic cholangiocarcinoma – FGFR2 rearrangement, MSS, TMB low

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

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Clinical Review & Education

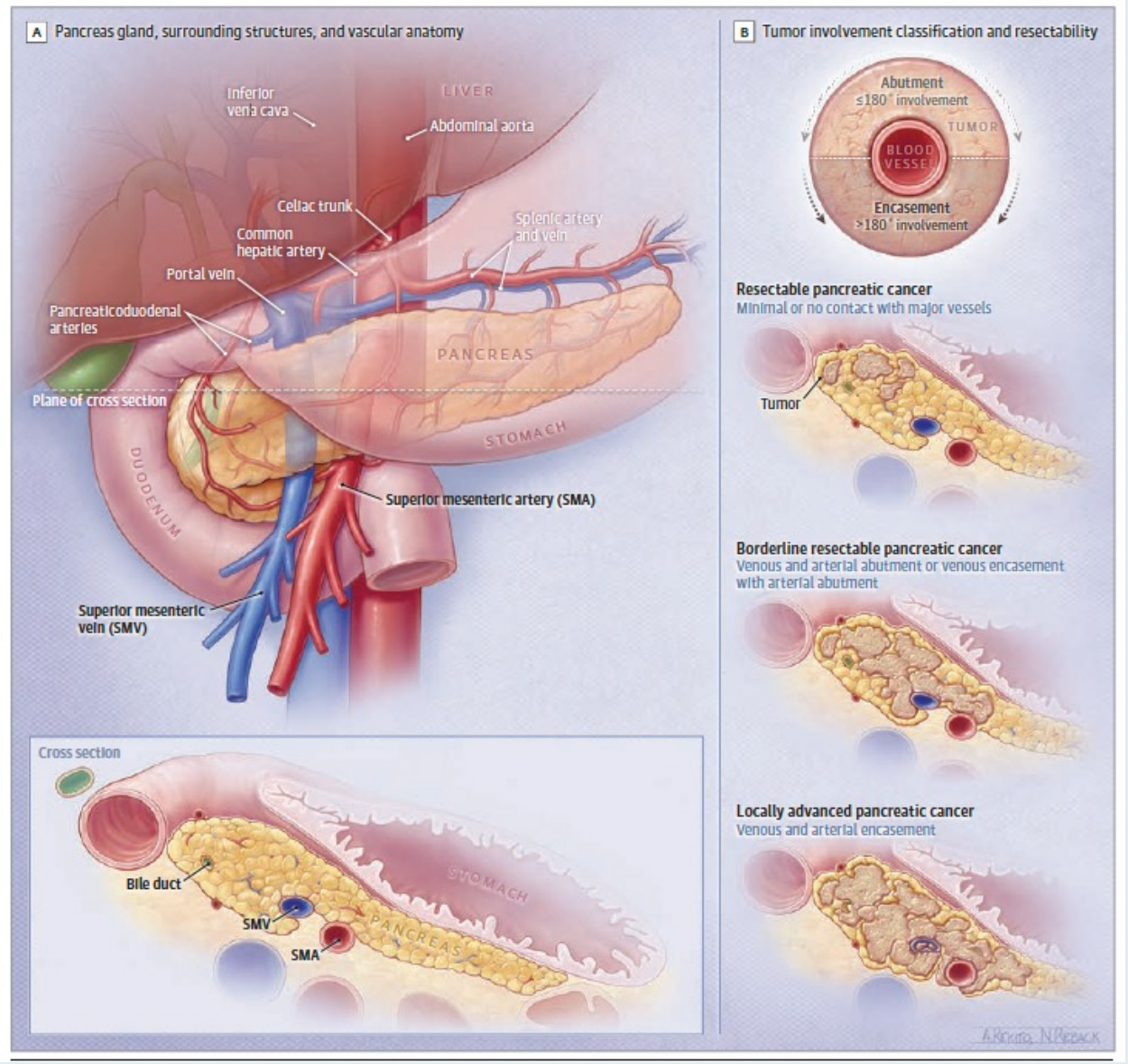
JAMA | Review

Pancreatic Cancer
A Review

Wungki Park, MD; Akhil Chawla, MD; Eileen M. O'Reilly, MD

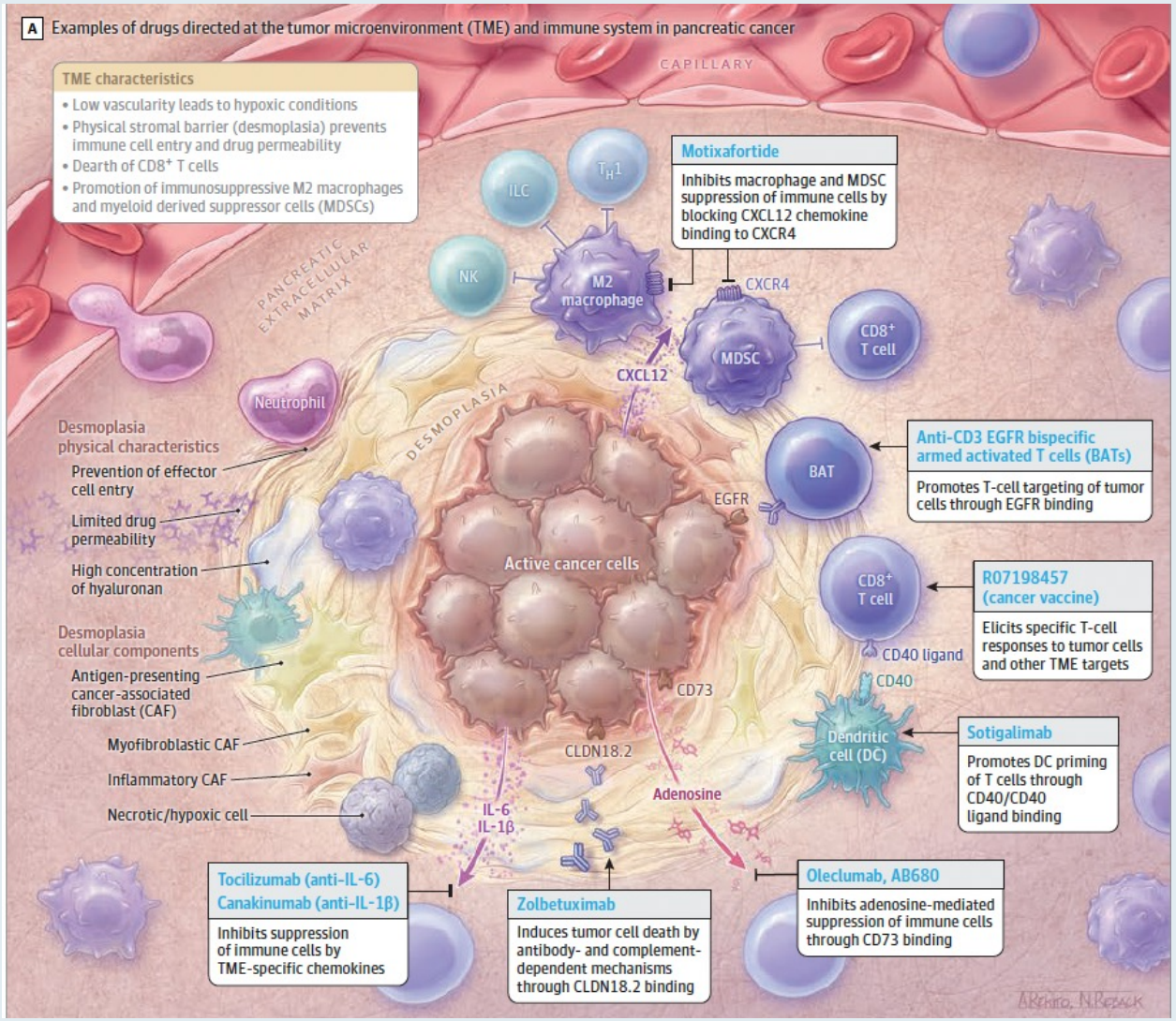
JAMA 2021;326(9):851-62.

Spectrum of Localized Pancreatic Cancer



Park W et al. *JAMA* 2021;326(9):851-62.

Novel Targets and Agents in Development for Pancreatic Cancer



B Select drugs in development for pancreatic cancer

TME directed

	Class, mechanism, or target	Agent
STROMA DIRECTED	CSF-1 receptor on MDSCs	Pexidartinib
	Connective tissue growth factor	Pamrevlumab
	Vitamin D receptor	Paricalcitol
	FAK inhibition	Defactinib
IMMUNE DIRECTED	Checkpoint inhibition (PD-1, CTLA4)	Pembrolizumab, ipilimumab
	Mismatch repair deficiency–related variants and neoantigens	Pembrolizumab,[a] nivolumab
	Mesothelin, CEA	Chimeric antigen receptor T cells
	Various (eg, prostate stem cell antigen)	Allogenic natural killer (NK) cells, NK T cells

Tumor cell directed

	Class, mechanism, or target	Agent
DDR	Poly (ADB-ribose) polymerase inhibition	Olaparib,[a] rucaparib
	Checkpoint inhibition (PD-1, CTLA4)	Pembrolizumab, ipilimumab
	WEE1 inhibition	Adavosertib
KRAS DIRECTED	Autophagy	Hydroxychloroquine
	Small interfering RNA	siG12D LoDER (G12D, G12V)
	Allele-specific inhibition	Sotorasib, adagrasib (G12C)
	Vaccines	ELI-002 peptide
OTHER	CA 19-9	BNT321 monoclonal antibody
	Tumor cell mitochondria	Devimistat
	Asparagine, glutamine metabolism	Eryaspase
	NRG1 fusion (*KRAS* wild type)	Zenocutuzumab
	NTRK fusion (*KRAS* wild type)	Entrectinib,[a] larotrectinib[a]

ADB indicates adenosine diphosphate; CA, carbohydrate antigen; CEA, carcinoembryonic antigen; CSF, colony-stimulating factor; DDR, DNA damage repair, EGFR, epidermal growth factor receptor; ILC, innate lymphoid cell; and T_H1, type 1 helper T cell.

[a] Approved by the US Food and Drug Administration or guideline-endorsed for pancreatic cancer.

Park W et al. *JAMA* 2021;326(9):851-62.

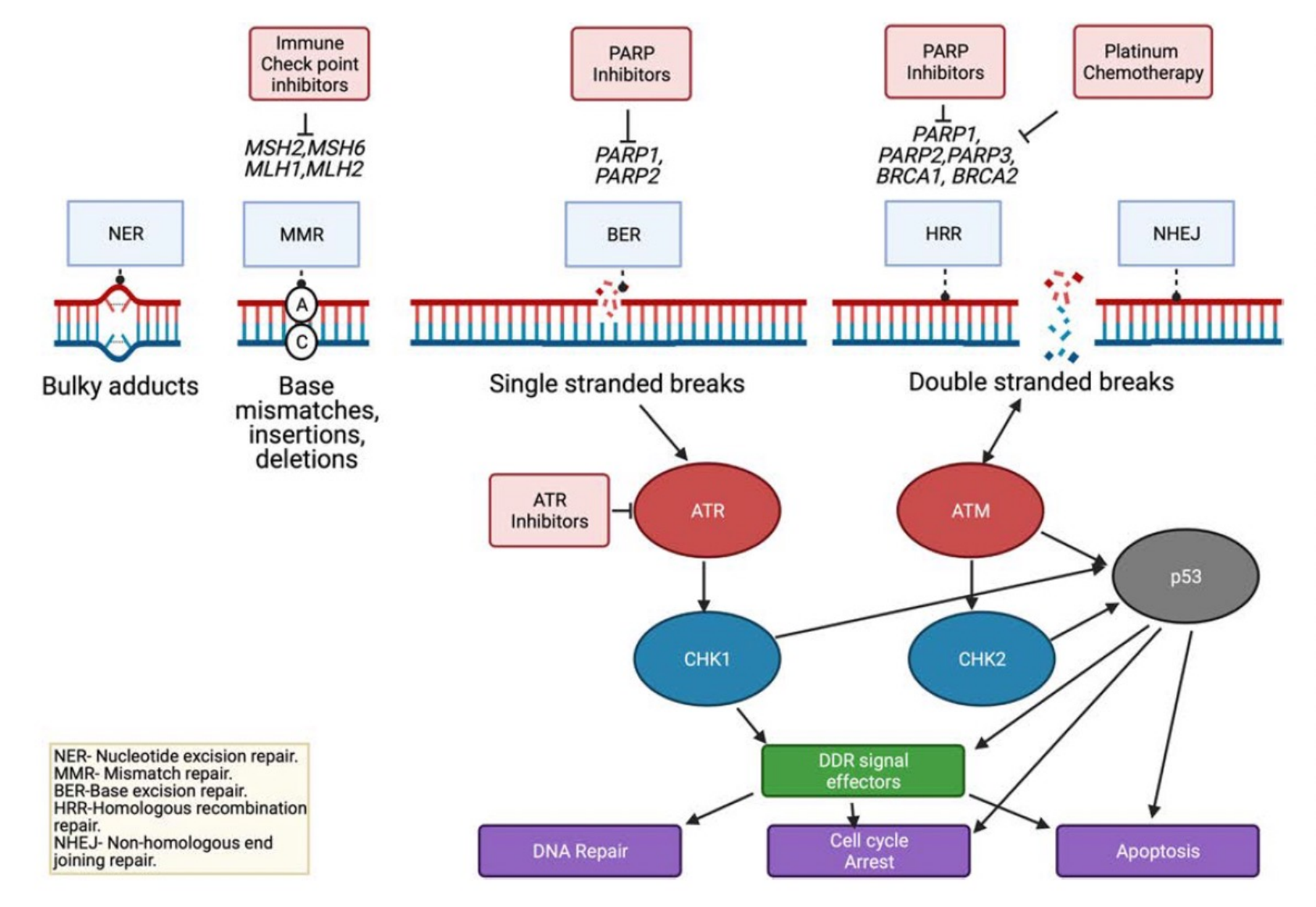
Cancer and Metastasis Reviews 2021;[Online ahead of print].
https://doi.org/10.1007/s10555-021-09983-1

Targeting DNA damage repair pathways in pancreas cancer

Fionnuala Crowley[1,2,3] · Wungki Park[1,4,5,6] · Eileen M. O'Reilly[1,4,6]

Received: 8 May 2021 / Accepted: 30 July 2021

Targeting DDR Pathways in Pancreas Cancer



Crowley F et al. *Cancer Metasis Rev* 2021;[Online ahead of print].

Gastrointestinal Cancers Symposium 2021

Abstract 639

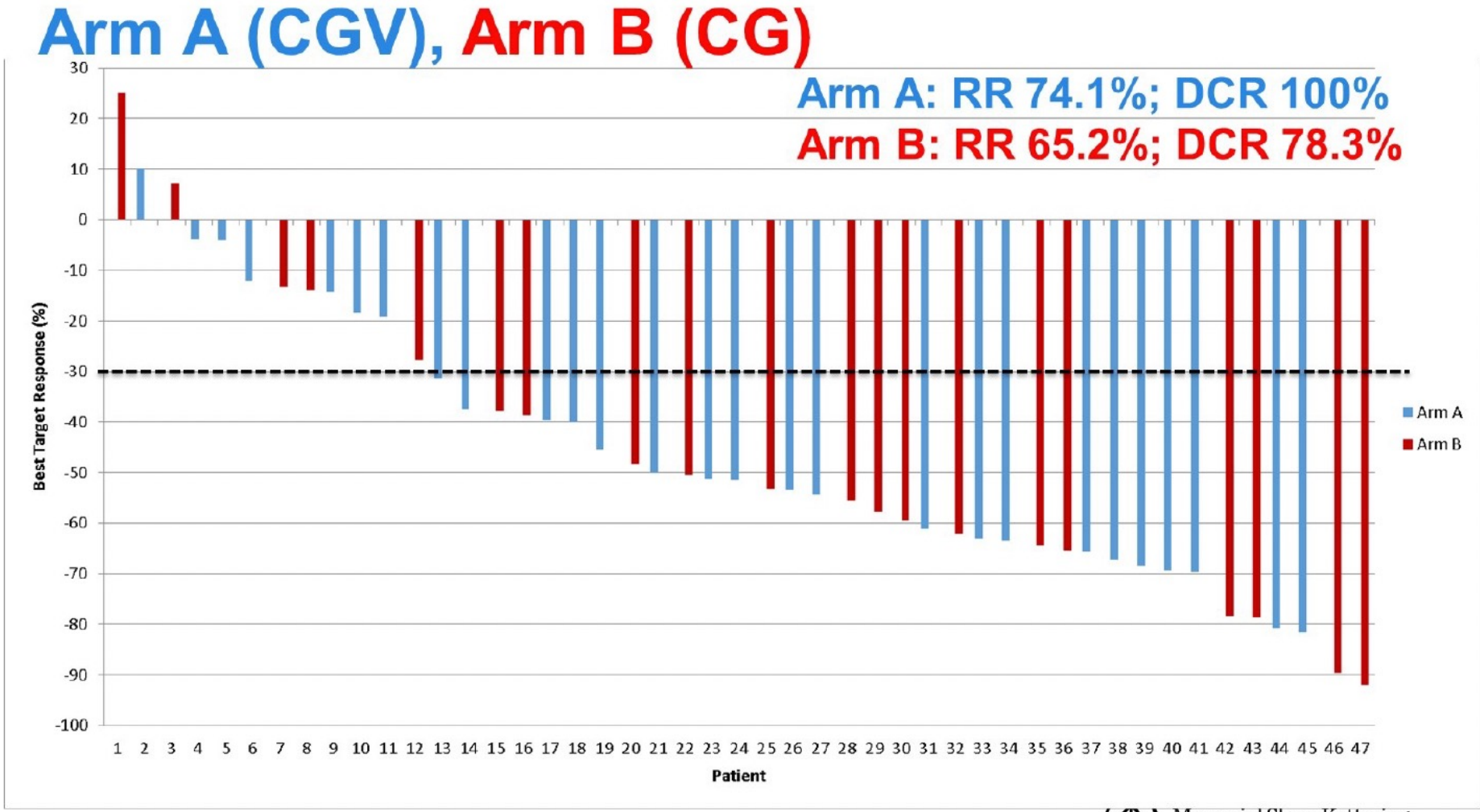
Memorial Sloan Kettering Cancer Center

Randomized, Multicenter, Phase II Trial of Gemcitabine, Cisplatin +/- Veliparib in Patients with Pancreas Adenocarcinoma and a known Germline *BRCA/PALB2* Mutation

Eileen M. O'Reilly, MD[1]; Jonathan W. Lee, MSc[1]; Mark Zalupski, MD[2]; Marinela Capanu[1]; Jennifer Park, BS[1]; Talia Golan, MD[3]; Esther Tahover, MD[4]; Maeve A. Lowery, MD[5]; Joanne F. Chou, MPH[1]; Vaibhav Sahai, MBBS, MS[2]; Robin Brenner, RN, BSN[1]; Hedy L. Kindler, MD[6]; Kenneth H. Yu, MD[1]; Alice Zervoudakis, MD[1]; Shreya Vemuri, BS[1]; Zsofia K. Stadler, MD[1]; Richard K. G. Do, MD, PhD[1]; Neesha Dhani, MD, PhD[7]; Alice P. Chen, MD[8]; and David P. Kelsen, MD[1]

[1]Memorial Sloan Kettering Cancer Center, New York, NY. [2]University of Michigan, Ann Arbor, MI. [3]Chaim Sheba Medical Center at Tel HaShomer, Tel HaShomer, Israel. [4]The Oncology Institute, Sha'are Zedek Medical Center, Jerusalem, Israel. [5]Trinity College, Dublin, Ireland. [6]University of Chicago, Chicago, IL. [7]Princess Margaret Cancer Centre-University Health Network, Toronto, Ontario, Canada. [8]National Cancer Institute, Bethesda, MD

Primary Endpoint: RECIST Response



RR: Response Rate; DCR: Disease Control Rate

O'Reilly EM et al. Gastrointestinal Cancers Symposium 2021;Abstract 639.

Phase II, Open-Label, Randomized Study of First-Line Zolbetuximab plus Gemcitabine and *Nab*-Paclitaxel (GN) in Claudin 18.2-Positive Metastatic Pancreatic Cancer (mPC)

Park W et al.

ASCO 2020;Abstract TPS4667.

2021 ASCO ANNUAL MEETING

Abstract 3003

Efficacy and safety of zenocutuzumab in advanced pancreatic cancer and other solid tumors harboring NRG1 fusions

Alison M Schram

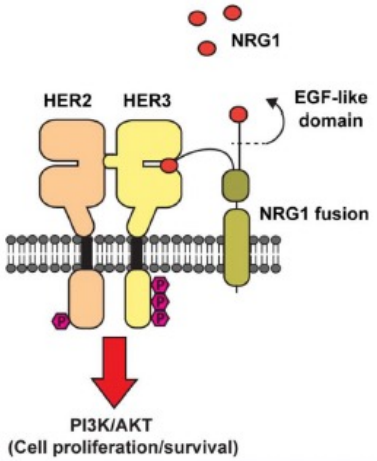
Memorial Sloan Kettering Cancer Center, NY, USA

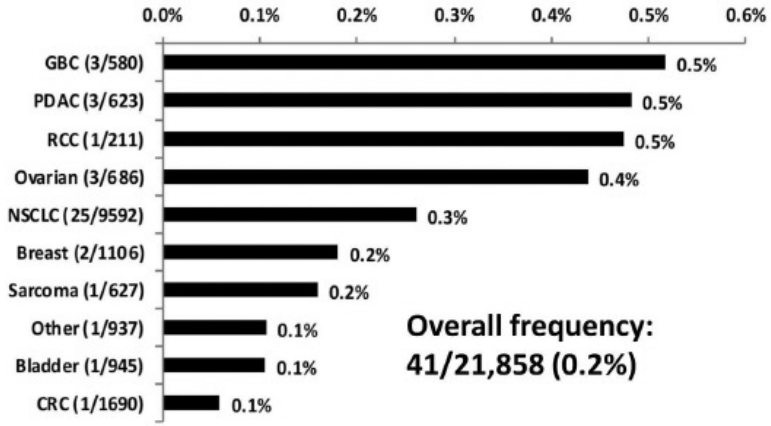
04 June 2021

AM Schram, EM O'Reilly, GM O'Kane, K Goto, DW Kim, C Neuzillet, P Martin-Romano, M Duruisseaux, M Nagasaka, J Rodon, BA Weinberg, K Umemoto, SH I Ou, T Macarulla, C de la Fouchardiere, AK Joe, E Wasserman, V Stalbovskaya, J Ford, AE Drilon

NRG1 Fusions are Clinically Actionable Targets

- Neuregulin 1 (NRG1) is a ligand that binds to HER3, promoting HER2/HER3 heterodimerization and activation of PI3K/AKT/mTOR signaling
- Chromosomal rearrangements involving NRG1 are rare oncogenic drivers in solid tumors, enriched in *KRASwt* PDAC and lung IMA
- Numerous NRG1 fusion partners identified (e.g., CD74, ATP1B1, SDC4)
- NRG1 fusion positive (NRG1+) *in vitro* and *in vivo* models are sensitive to HER2/HER3 directed therapy





Fernandez-Cuesta et al. Cancer Discov. 2014;4:415-22
Schram et al. J Clin Oncol. 2019;37:3129
Jonna et al. J Clin Oncol. 2020;38:3113
Jonna et al. Clin Cancer Res. 2019;25:4966–7

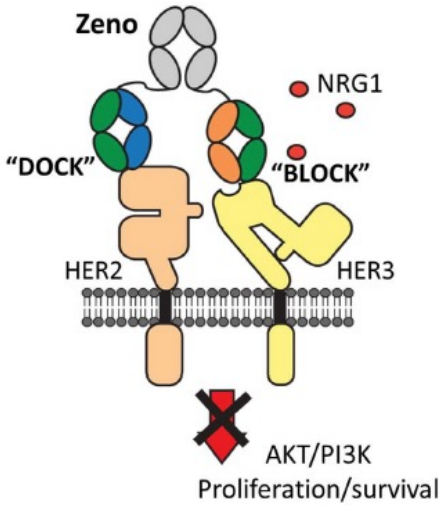
Presented By: **Alison Schram**

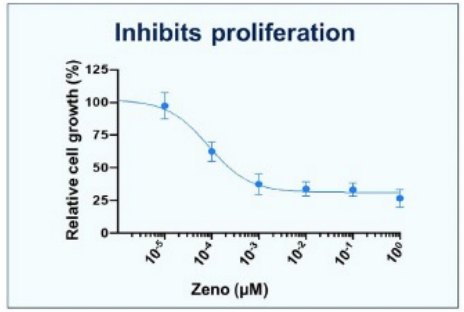
2021 ASCO ANNUAL MEETING

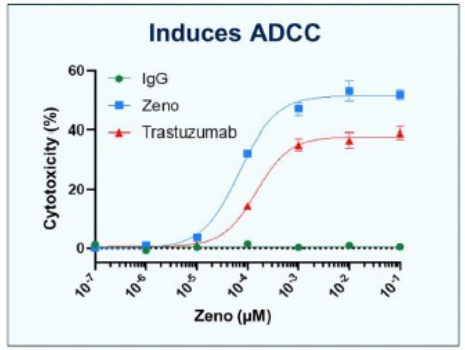
Schram AM. ASCO 2021;Abstract 3003.

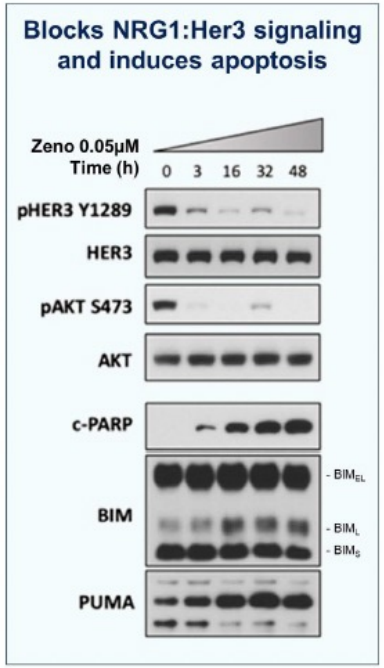
Zenocutuzumab: A Novel Therapeutic Paradigm for NRG1+ Cancers

- Common light chain bispecific Biclonics® antibody with enhanced ADCC activity
- Docks on HER2 and blocks NRG1 interaction with HER3
- Potent inhibition of cell growth and molecular signaling (pHER3, PI3K) at 0.01 µM
- Orphan drug and fast-track designations were granted









MDA-MB-175-VII (*DOC4-NRG1* fusion)

Geuijen et al. Cancer Cell. 2018;33:922-36
Odintsov et al. AACR. 2021; abstract 956

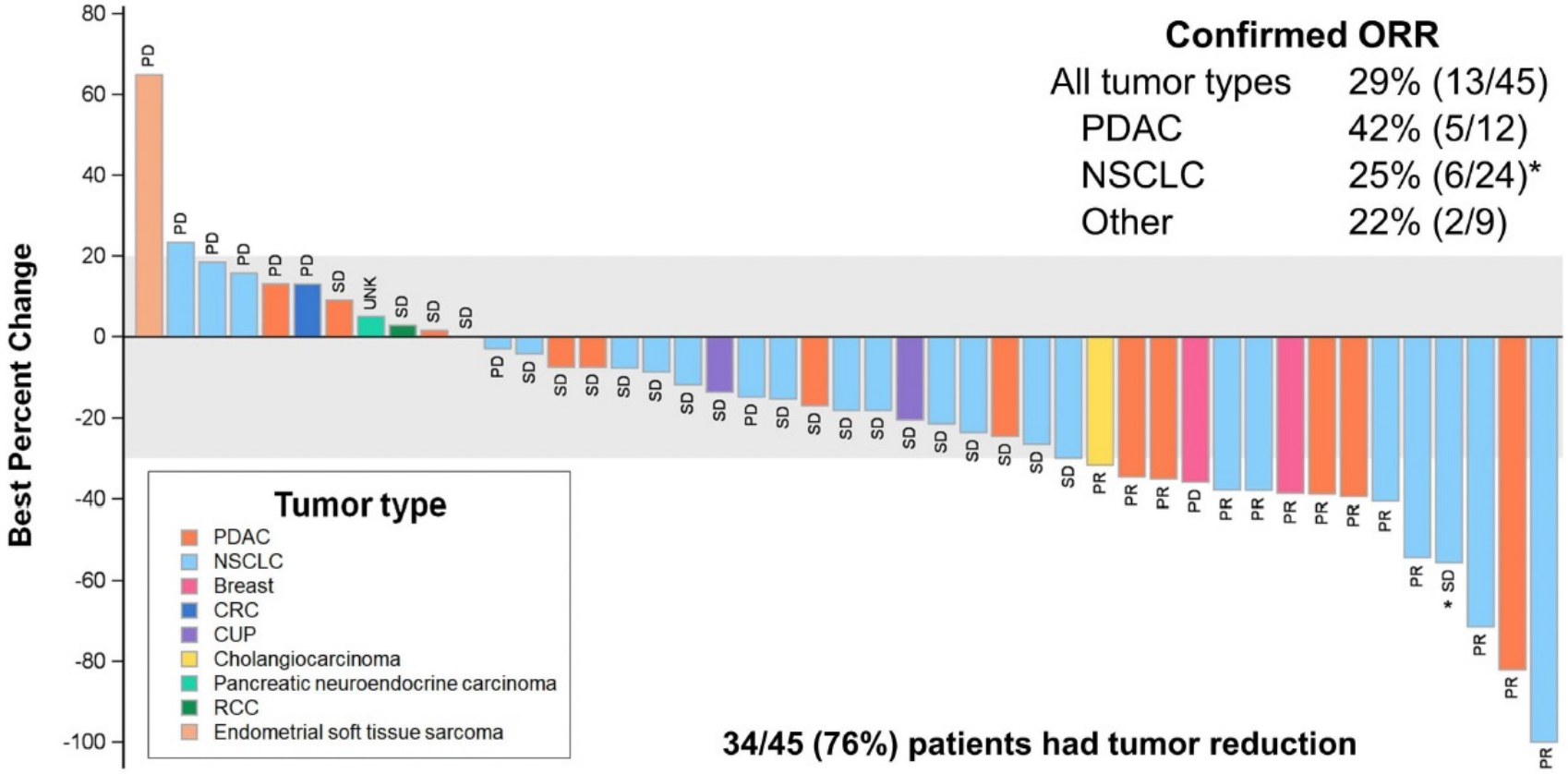
Presented By: **Alison Schram**

2021 ASCO ANNUAL MEETING

Schram AM. ASCO 2021;Abstract 3003.

Efficacy Regardless of NRG1+ Tumor Type

Best Percent change in Target Lesions from Baseline



* One additional PR confirmed after the cutoff date; NSCLC ORR 29% (7/24)

Presented By: **Alison Schram**

2021 ASCO ANNUAL MEETING

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Schram AM. ASCO 2021;Abstract 3003.

Meet The Professor with Dr O'Reilly

MODULE 1: Journal Club with Dr O'Reilly — Pancreatic Cancer

MODULE 2: Case Presentations

- Dr Dayyani: A 54-year-old man with MSI-high metastatic colorectal cancer
- Dr Schafer: A 60-year-old woman with MSS metastatic sigmoid adenocarcinoma and a somatic BRCA2 mutation
- Dr Ciombor: A 60-year-old man with metastatic esophageal adenocarcinoma – PD-L1 CPS 70
- Dr Ibrahim: A 60-year-old man with infiltrative hepatocellular carcinoma
- Dr Dayyani: A 62-year-old woman with metastatic cholangiocarcinoma – FGFR2 rearrangement, MSS, TMB low

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Dayyani: A 54-year-old man with microsatellite instability (MSI)-high metastatic colorectal cancer

Dr Farshid Dayyani

- Colonoscopy: Obstructing right colon cancer
- 11/2019 CT CAP: Large colonic hepatic flexure mass, mesenteric LAD and left hepatic lesions
- ctDNA testing: MSI high

Question

- If you're thinking about sequencing systemic therapy, hopefully followed by resection of the primary tumor and liver metastases, would you choose induction with a checkpoint inhibitor alone based on KEYNOTE-177?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Dayyani: A 54-year-old man with MSI-high metastatic colorectal cancer (continued)

Dr Farshid Dayyani

- Colonoscopy: Obstructing right colon cancer
- 11/2019 CT CAP: Large colonic hepatic flexure mass, mesenteric LAD and left hepatic lesions
- ctDNA testing: MSI high
- 2/2020: FOLFOX/pembrolizumab x 6 → 8/2020 laparoscopic partial colectomy, left hepatectomy, microwave of liver lesion → Pathology: ypT3N0 with liver-only necrosis

Question

- Would you administer adjuvant treatment? For how long? And with what agent?

Case Presentation – Dr Schafer: A 60-year-old woman with microsatellite stable (MSS) metastatic sigmoid adenocarcinoma and a somatic BRCA2 mutation

Dr Liudmila Schafer

- 9/2019: S/p left hemicolectomy for Stage IIIB sigmoid colon cancer
- Adjuvant FOLFOX x 3, with oxaliplatin discontinued due to toxicity; 5-FU discontinued after 10 cycles
- 9/2020: New left hydronephrosis, progression of liver lesions → Capecitabine/bevacizumab
- 11/2020: PD, with new liver lesions → Irinotecan/bevacizumab
  - Stable disease on last CT scan
- NGS: Somatic BRCA2 mutations, MSS, KRAS-mutated, BRAF wildtype, NRAS wildtype, HER2-negative, TRK-negative, TMB 6 mut/Mb

Questions

- What would you recommend on the next progression of her disease – regorafenib, TAS-102?
- Would you use bevacizumab, even though she has previous exposure to that treatment?
- Is there any role for PARP inhibitors?

RTP RESEARCH TO PRACTICE

Incorporation of immune checkpoint inhibitor therapy into the management of gastric, GEJ and esophageal cancers

Dr Nikesh Jasani

Case Presentation – Dr Ciombor: A 60-year-old man with metastatic esophageal adenocarcinoma – PD-L1 CPS 70

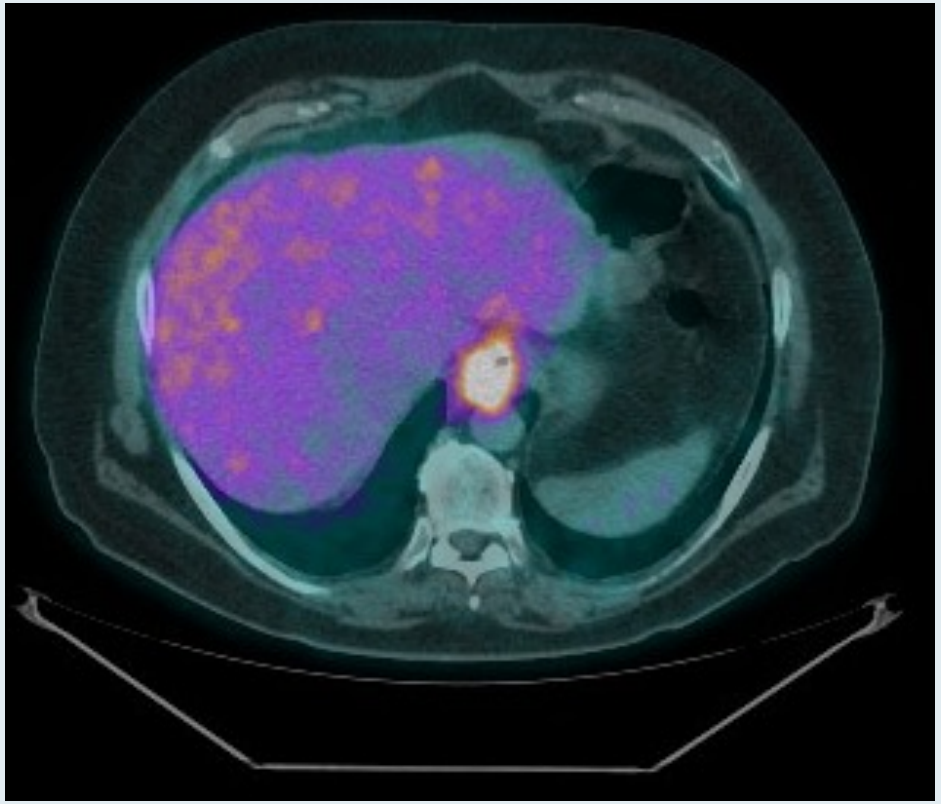
Dr Kristen Ciombor

- PMH: HTN, HLD, DM
- Presented with dysphagia which he attributed to recent stress; esophagram showed distal esophageal stricture
- EGD: large friable mass with stenosis from 36 to 41 cm from incisors; biopsy: intramucosal carcinoma
- CT C/A/P: esophageal mass and mildly enlarged paraesophageal nodes, 8-mm omental nodule, 1.2-cm lesion in right liver
- Diagnostic laparoscopy: omental nodule positive for adenocarcinoma
- FOLFOX x 4 cycles → SD
- Palliative radiation for significant dysphagia
- Molecular testing: MSS, CDH1 E243K mut, KRAS G12D mut, TP53 mut, HER2-; PD-L1 CPS 70
- Switched to pembrolizumab x 1 year
- Reimaging showed CR; EGD w/ biopsy without residual tumor (reactive changes, eosinophils)
- Now in IO treatment holiday and still in CR

Case Presentation – Dr Ciombor: A 60-year-old man with metastatic esophageal adenocarcinoma – PD-L1 CPS 70 (continued)

Dr Kristen Ciombor

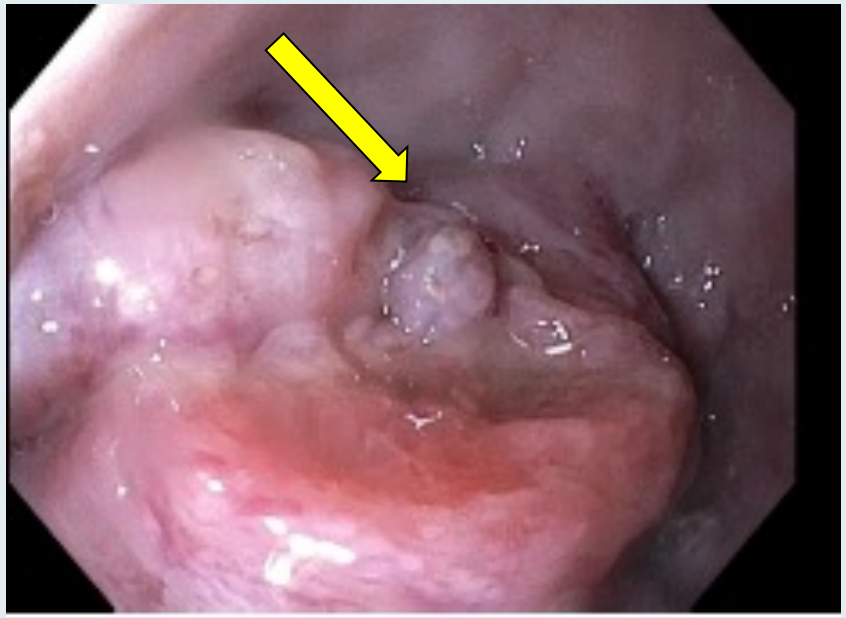
CR after pembrolizumab therapy

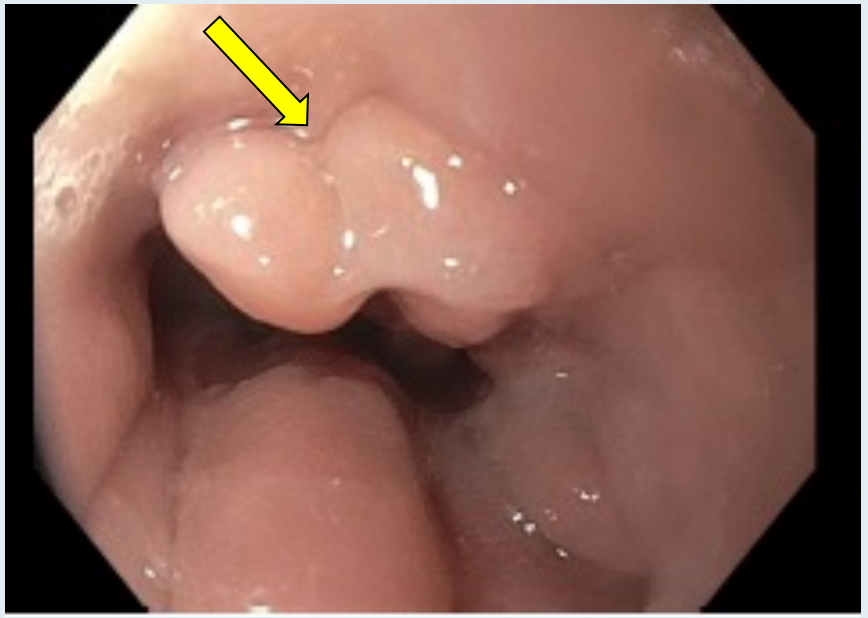


Case Presentation – Dr Ciombor: A 60-year-old man with metastatic esophageal adenocarcinoma – PD-L1 CPS 70 (continued)

Dr Kristen Ciombor

EGD after pembrolizumab therapy





Case Presentation – Dr Ibrahim: A 60-year-old man with infiltrative hepatocellular carcinoma

Dr Sulfi Ibrahim

- Right upper quadrant pain → Workup: Multiple liver and lung metastases
- Liver biopsy c/w poorly differentiated carcinoma on radiographic imaging
- Diagnosed at tertiary care center with infiltrative type HCC
- Patient rapidly declining; bilirubin 1 to 10 in one week
- Atezolizumab/bevacizumab

Questions

- What is the optimal management of infiltrative type HCC?
- Would you use atezolizumab and bevacizumab in patients with Child-Pugh B or Child-Pugh C HCC?

Case Presentation – Dr Dayyani: A 62-year-old woman with metastatic cholangiocarcinoma — FGFR2 rearrangement, MSS, TMB low

Dr Farshid Dayyani

- 7/2017: Diagnosed with intrahepatic cholangiocarcinoma
- 12/2017: Completed adjuvant gemcitabine/cisplatin x 5 cycles
- 1/2018: Underwent right hepatic lobectomy → capecitabine (d/c due to colitis/mucositis)
  - Patient switched to gemcitabine/cisplatin; completed 7/2018
- 3/2019: CT identifies suspected liver and lung metastases
- NGS: FGFR2-AHCYL1 fusion | MSS | TMB low
- 6/2019: Patient enrolled on MATCH trial and began treatment with erdafitinib
  - Multiple dose interruptions and reductions due to hyperphosphatemia, serous retinopathy (reversible), mucositis and increasing PPE
- 7/2020: Continued partial response in single liver lesion, and only lung micronodules
- 9/2020: Patient opted to come off trial due to recurrent PPE, mucositis on lowest dose

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MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

RTP RESEARCH TO PRACTICE

Colorectal Cancer

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

Gastric/GEJ

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

Hepatocellular

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

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RTP RESEARCH TO PRACTICE

Colorectal Cancer

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TO PRACTICE

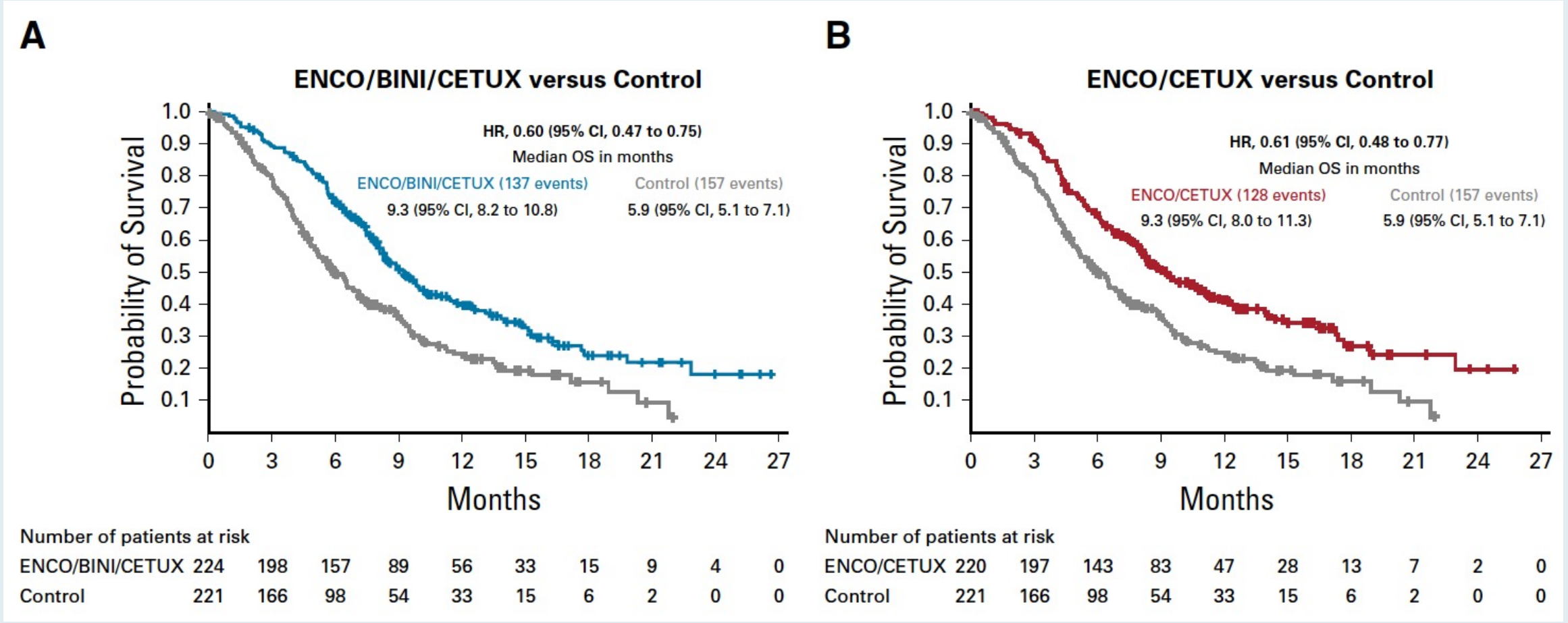
rapid communications

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*

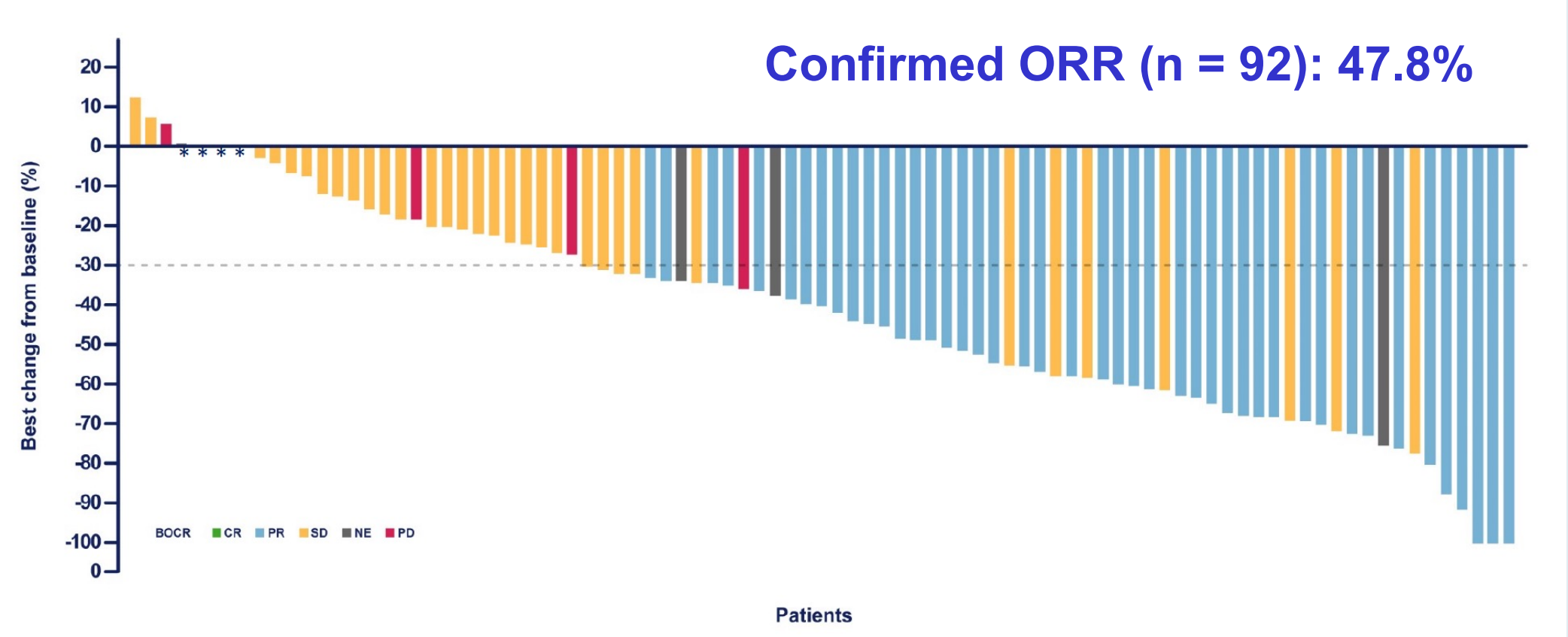
** University Hospitals Leuven, Belgium*

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

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

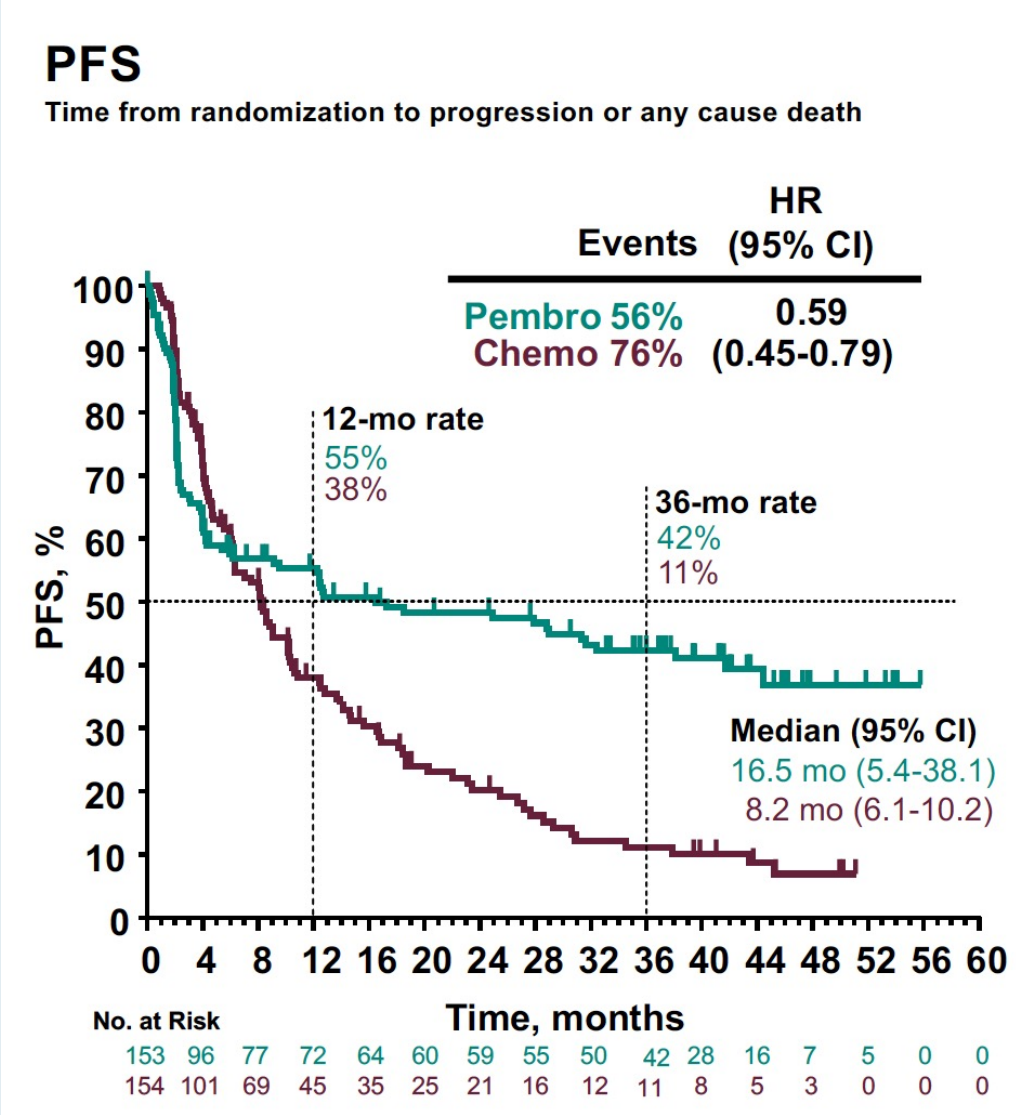
Thierry André,[1] Kai-Keen Shiu,[2] Tae Won Kim,[3] Benny Vittrup Jensen,[4] Lars Henrik Jensen,[5] Cornelis Punt,[6] Denis Smith,[7] Rocio Garcia-Carbonero,[8] Julia Alcaide-Garcia,[9] Peter Gibbs,[10] Christelle de la Fouchardiere,[11] Fernando Rivera,[12] Elena Elez,[13] Johanna Bendell,[14] Dung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

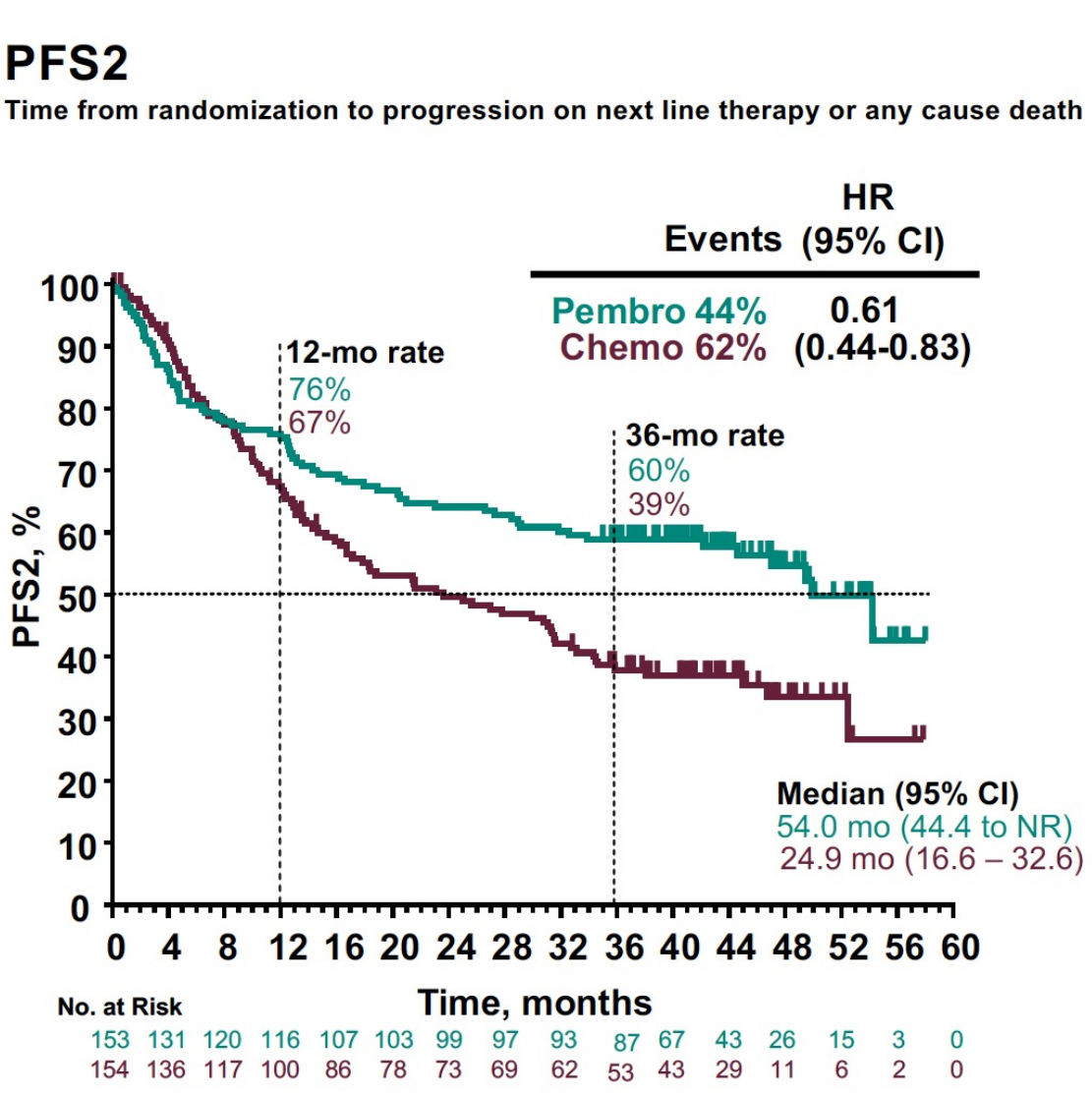
[1]Sorbonne Université and Hôpital Saint Antoine, Paris, France; [2]University College Hospital, NHS Foundation Trust, London, United Kingdom; [3]Asan Medical Center, University of Ulsan, Seoul, Republic of Korea; [4]Herlev and Gentofte Hospital, Herlev, Denmark; [5]University Hospital of Southern Denmark,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

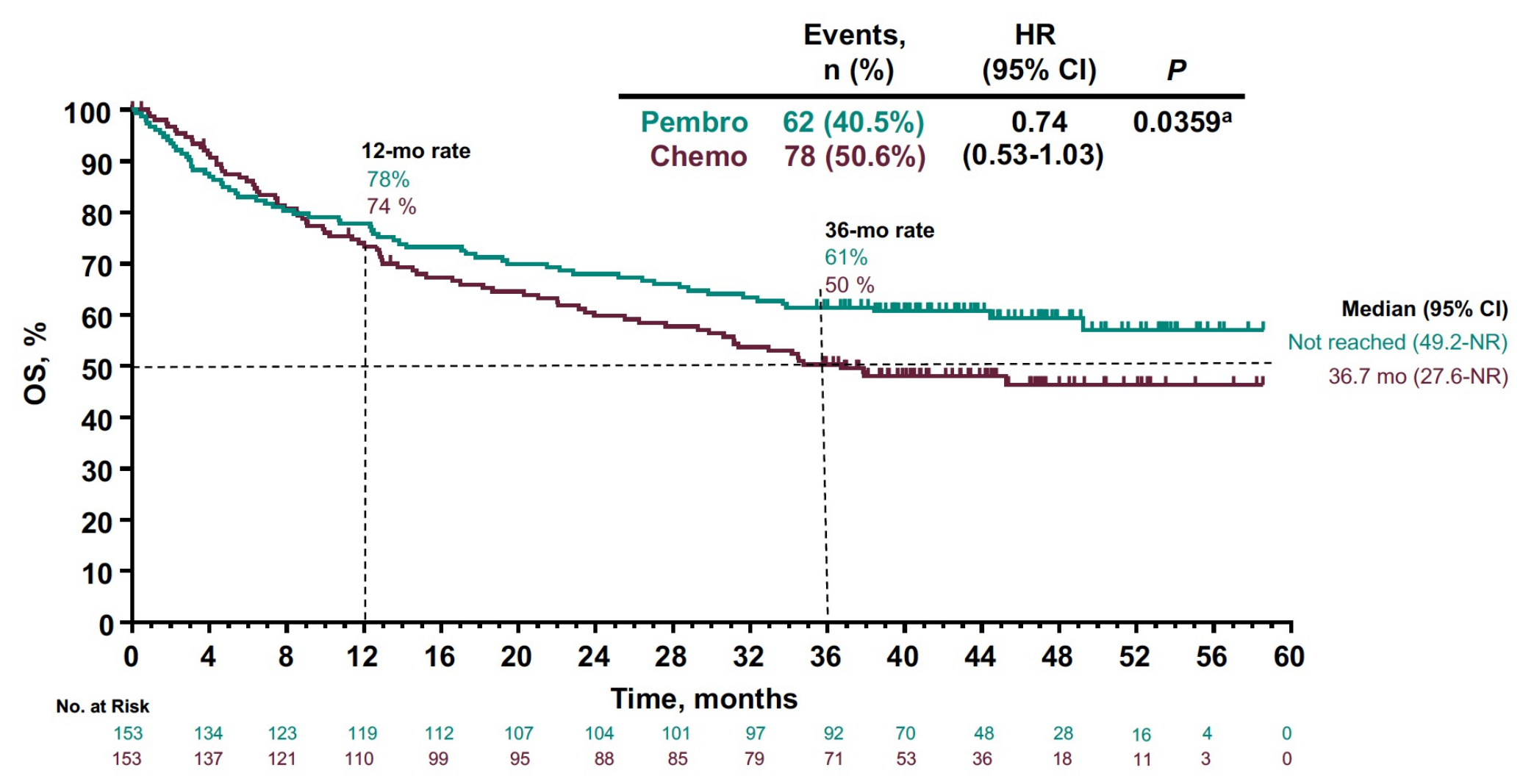




Andre T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

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

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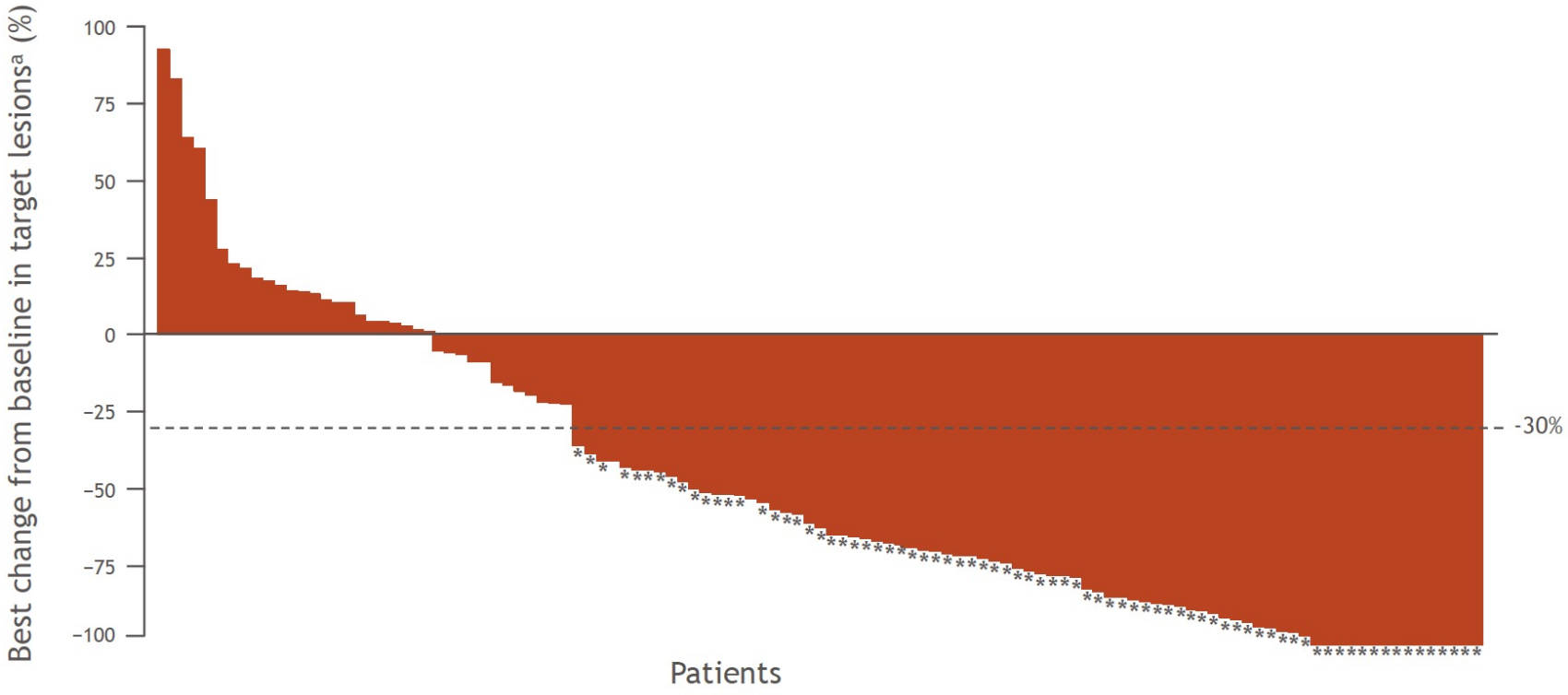
ESMO World Congress on Gastrointestinal Cancer 2021;Abstract SO-27.

RTP RESEARCH TO PRACTICE

CheckMate 142: Four-Year Update of Nivolumab/Ipilimumab as First-Line Therapy for 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.

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Dostarlimab-gxly for dMMR Advanced Solid Tumors

Press Release – August 17, 2021

"The Food and Drug Administration granted accelerated approval to dostarlimab-gxly for adult patients with mismatch repair deficient (dMMR) recurrent or advanced solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.

Today, the FDA also approved the VENTANA MMR RxDx Panel as a companion diagnostic device to select patients with dMMR solid tumors for treatment with dostarlimab-gxly.

The efficacy of dostarlimab was evaluated in the GARNET Trial (NCT02715284), a non-randomized, multicenter, open-label, multi-cohort trial. The efficacy population consisted of 209 patients with dMMR recurrent or advanced solid tumors who progressed following systemic therapy and had no satisfactory alternative treatment."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dostarlimab-gxly-dmmr-advanced-solid-tumors

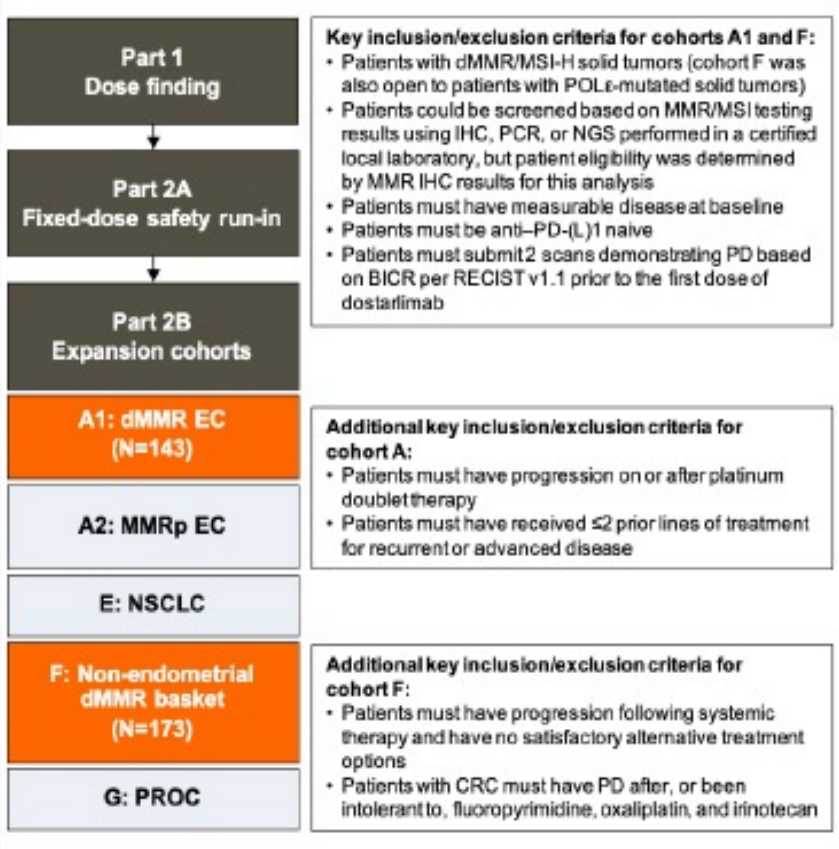
Antitumor Activity of Dostarlimab in Patients with Mismatch Repair–Deficient (dMMR) Tumors: A Combined Analysis of 2 Cohorts in the GARNET Study

Berton D et al.

ASCO 2021;Abstract 2564.

GARNET: Trial Design and Antitumor Activity

Trial Design



Primary Endpoint Analysis

Variable	Cohort A1 (n=103)	Cohort F (n=106)	Cohorts A1 + F (n=209)
Median follow-up time, mo[a]	20.4	16.7	17.5
Confirmed responses, n	46	41	87
ORR, % (95% CI)[b]	44.7 (34.9–54.8)	38.7 (29.4–48.6)	41.6 (34.9–48.6)
CR, n (%)	11 (10.7)	8 (7.5)	19 (9.1)
PR, n (%)	35 (34.0)	33 (31.1)	68 (32.5)
SD, n (%)	13 (12.6)	26 (24.5)	39 (18.7)
PD, n (%)	39 (37.9)	32 (30.2)	71 (34.0)
NE, n (%)	5 (4.9)	7 (6.6)	3 (1.4)
Disease control rate, % (95% CI)[c]	57.3 (47.2–67.0)	63.2 (53.3–72.4)	60.3 (53.3–67.0)
Duration of response, median (range), mo	34.7 (2.63 to 35.78+)	NR (5.59 to 30.13+)	34.7 (2.63 to 35.78+)

Antitumor Activity by Tumor Type

		Confirmed ORR (RECIST v1.1)	
Tumor type	**Patients, N**	**n (%)**	**95% CI, %**
Overall	**209**	**87 (41.6)**	**(34.9–48.6)**
EC	**103**	**46 (44.7)**	**(34.9–54.8)**
CRC	**69**	**25 (36.2)**	**(25.0–48.7)**
Non-CRC	**37**	**16 (43.2)**	**(27.1–60.5)**
Small-intestinal cancer	12	4 (33.3)	(9.9–65.1)
Gastric and gastroesophageal junction cancer	8	3 (37.5)	(8.5–75.5)
Pancreatic carcinoma	4	SD, 3 PD	
Ovarian cancer	2	PR, SD	
Hepatocellular carcinoma	2	PR, PD	
Biliary neoplasm	2	2 CR	
Breast cancer	1	CR	
Adrenal cortical carcinoma	1	PR	
Malignant neoplasm of the female genitals	1	PR	
Pleural cancer	1	PR	
Unknown origin	1	PR	
Renal cell carcinoma	1	SD	
Esophageal cancer	1	PD	

Berton D et al. ASCO 2021;Abstract 2564.

GARNET Combined Cohort Analysis: Adverse Events

	Cohort A1 (N=143)	Cohort F (N=173)	Cohorts A1 + F (N=316)
Safety summary, n (%)			
Any TEAE	140 (97.9)	167 (96.5)	307 (97.2)
Any-grade TRAE	100 (69.9)	119 (68.8)	219 (69.3)
Grade ≥3 TEAE	72 (50.3)	85 (49.1)	157 (49.7)
Grade ≥3 TRAE	23 (16.1)	20 (11.6)	43 (13.6)
Treatment-related SAE	15 (10.5)	13 (7.5)	28 (8.9)
Any TRAE leading to discontinuation	8 (5.6)	8 (4.6)	16 (5.1)
TRAE leading to death[a]	0	2 (1.2)	2 (0.6)
TEAEs in ≥1% of patients leading to discontinuation, n (%)			
ALT increased	2 (1.4)	2 (1.2)	4 (1.3)
Any-grade TEAEs in ≥20% of patients, n (%)			
Anemia	45 (31.5)	55 (31.8)	100 (31.6)
Diarrhea	40 (28.0)	43 (24.9)	83 (26.3)
Asthenia	35 (24.5)	42 (24.3)	77 (24.4)
Nausea	45 (31.5)	26 (15.0)	71 (22.5)
Fatigue	36 (25.2)	28 (16.2)	64 (20.3)
Grade ≥3 TEAEs in ≥2% of patients, n (%)			
Anemia	21 (14.7)	13 (7.5)	34 (10.8)
Abdominal pain	7 (4.9)	6 (3.5)	13 (4.1)
Hyponatremia	6 (4.2)	5 (2.9)	11 (3.5)
Sepsis	4 (2.8)	6 (3.5)	10 (3.2)
ALT increased	3 (2.1)	5 (2.9)	8 (2.5)
Acute kidney injury	4 (2.8)	3 (1.7)	7 (2.2)
Lipase increased	3 (2.1)	4 (2.3)	7 (2.2)

	Cohort A1 (N=143)	Cohort F (N=173)	Cohorts A1 + F (N=316)
Grade ≥2 irTEAEs in ≥5% of patients, n (%)			
Diarrhea	12 (8.4)	11 (6.4)	23 (7.3)
Hypothyroidism	11 (7.7)	9 (5.2)	20 (6.3)
ALT increased	4 (2.8)	12 (6.9)	16 (5.1)
Grade ≥3 irTEAEs in ≥1% of patients, n (%)			
ALT increased	3 (2.1)	5 (2.9)	8 (2.5)
Lipase increased	3 (2.1)	4 (2.3)	7 (2.2)
AST increased	1 (0.7)	4 (2.3)	5 (1.6)
Diarrhea	3 (2.1)	2 (1.2)	5 (1.6)
Hyperglycemia	1 (0.7)	3 (1.7)	4 (1.3)

[a]1 hepatic ischemia and 1 suicide.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ir, immune-related; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Berton D et al. ASCO 2021;Abstract 2564.

Safety and efficacy of anti–PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study

Thierry André[1], Dominique Berton[2], Giuseppe Curigliano[3], Susan L. Ellard[4], Jose Manuel Trigo Perez[5], Hendrik-Tobias Arkenau[6], Cyril Abdeddaim[7], Victor Moreno[8], Wei Guo[9], Ellie Im[9], Naureen Starling[10]

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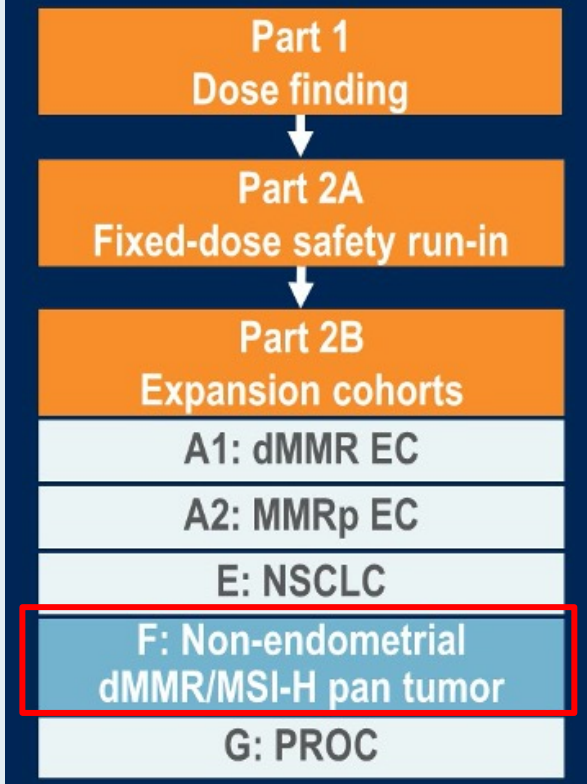
Abstract 9

PRESENTED AT: Gastrointestinal Cancers Symposium

#GI21

GARNET: Methods, Patient Characteristics and Antitumor Activity

Cohorts



Patient Characteristics

Characteristic	Cohort F N=106
Median age, years (range)	61.5 (24–85)
Sex, n (%)	
Male	58 (55)
Female	48 (45)
ECOG performance status, n (%)	
0	42 (40)
1	64 (60)
Histology, n (%)	
Colorectal	69 (65)
Small intestine	12 (11)
Gastric and gastroesophageal junction	8 (8)
Pancreatic carcinoma	4 (4)
Ovarian	2 (2)
Hepatocellular carcinoma	2 (2)
Other[a]	9 (8)

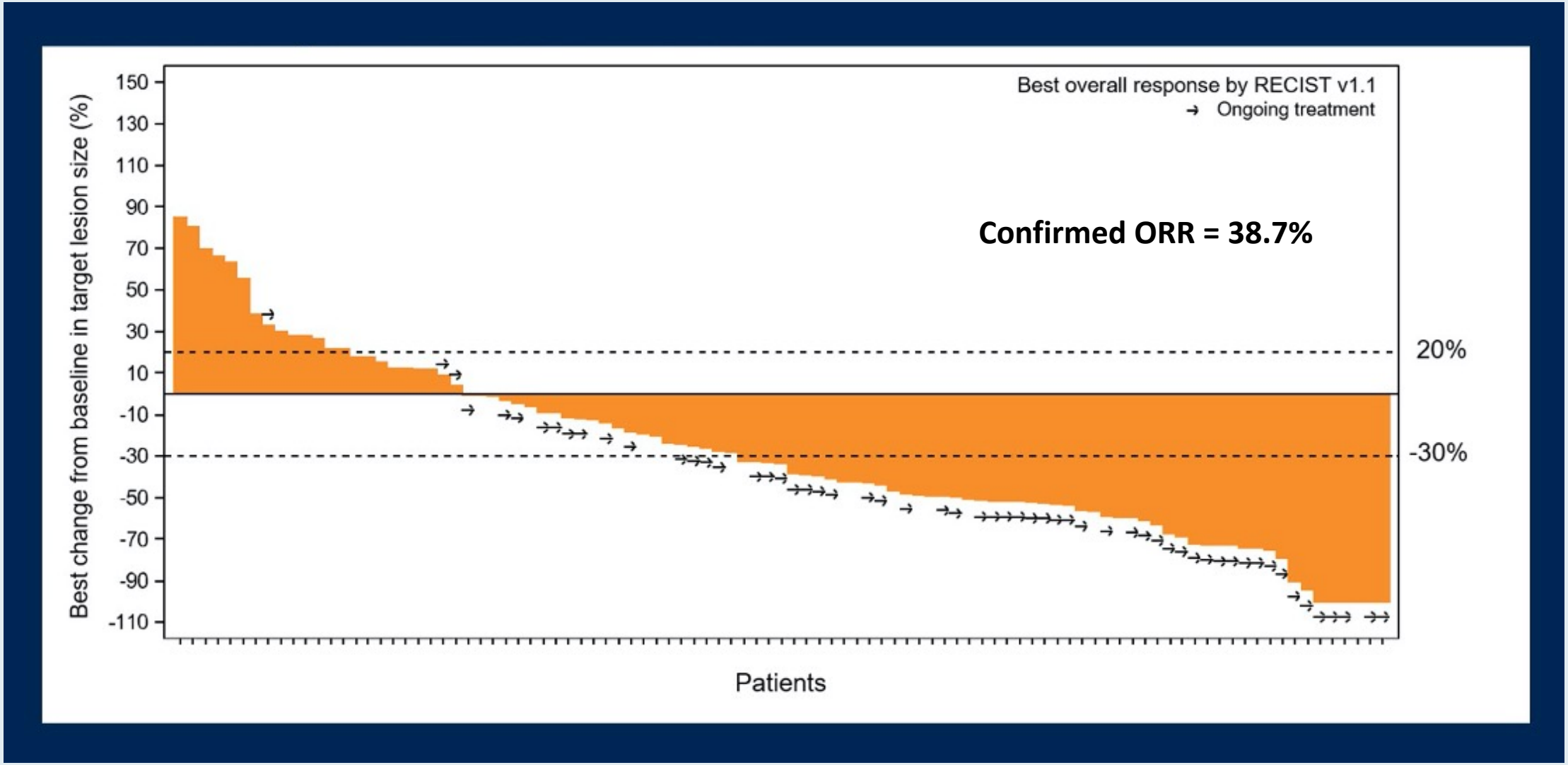
Response

Tumor type	Patients, N	Confirmed ORR (RECIST v1.1) n	95% CI[a]
Overall	**106**	**41 (38.7%)**	**(29.4%–48.6%)**
CRC	**69**	**25 (36.2%)**	**(25.0%–48.7%)**
Non-CRC	**37**	**16 (43.2%)**	**(27.1%–60.5%)**
Small intestinal cancer	12	4 (33.3%)	(9.9%–65.1%)
Gastric and gastroesophageal junction	8	3 (37.5%)	(8.5%–75.5%)
Pancreatic carcinoma	4	SD, 3 PD	
Ovarian cancer	2	PR, SD	
Hepatocellular carcinoma	2	PR, PD	
Biliary neoplasm	1	CR	
Breast cancer	1	CR	
Gallbladder	1	CR	
Adrenal cortical	1	PR	
Genital neoplasm malignant female	1	PR	
Pleural	1	PR	
Unknown origin	1	PR	
Renal cell carcinoma	1	SD	
Esophageal cancer	1	PD	

dMMR = mismatch repair-deficient; EC = endometrial cancer; MMRp = mismatch mutation repair-proficient; NSCLC = non-small cell lung cancer; PROC = platinum-resistant ovarian cancer

Andre T et al. Gastrointestinal Cancers Symposium 2021;Abstract 9.

GARNET Cohort F: Best Volume Change in Target Lesions



Andre T et al. Gastrointestinal Cancers Symposium 2021;Abstract 9.

GARNET Cohort F: Adverse Events

Preferred term, n (%)	Cohort F (N=144[a])
Any grade TRAEs occurring in ≥5% of pts	
Asthenia	19 (13)
Diarrhea	18 (13)
Pruritis	18 (13)
Arthralgia	13 (9)
Fatigue	13 (9)
Hypothyroidism	12 (8)
Rash	12 (8)
AST increased	11 (8)
ALT increased	9 (6)
Nausea	8 (6)

Preferred term, n (%)	Cohort F (N=144[a])
Grade ≥3 TRAEs occurring in ≥1% of pts	
Lipase increased[b]	2 (1)
Hyperlipasemia[c]	2 (1)
Grade ≥3 irTRAEs	
Lipase increased	2 (1)
Adrenal insufficiency	1 (<1)
ALT increased	1 (<1)
AST increased	1 (<1)
Diarrhea	1 (<1)
Hyperthyroidism	1 (<1)
Rash	1 (<1)

Andre T et al. Gastrointestinal Cancers Symposium 2021;Abstract 9.

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)

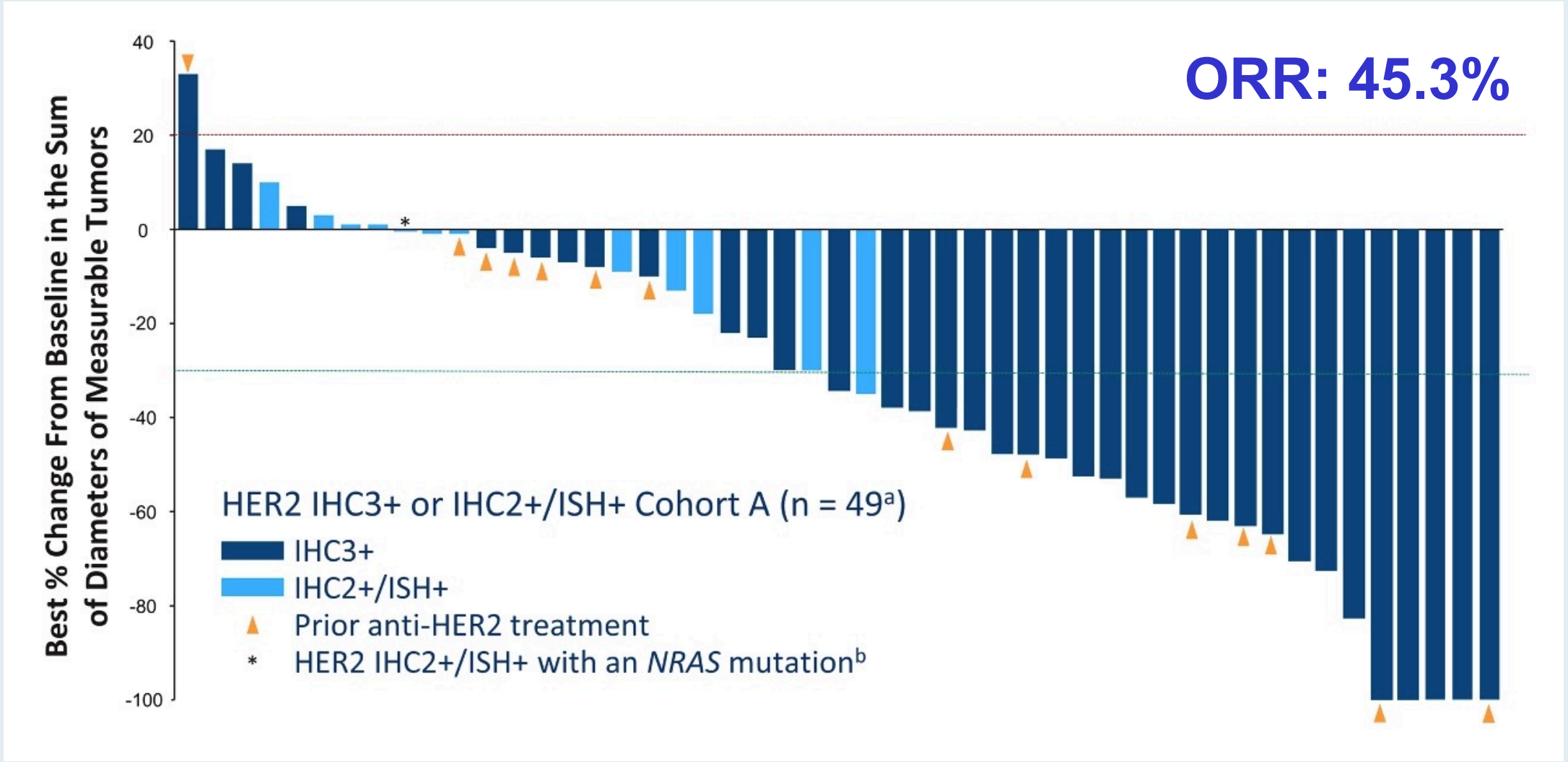
Takayuki Yoshino; National Cancer Center Hospital East, Kashiwa, Japan

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

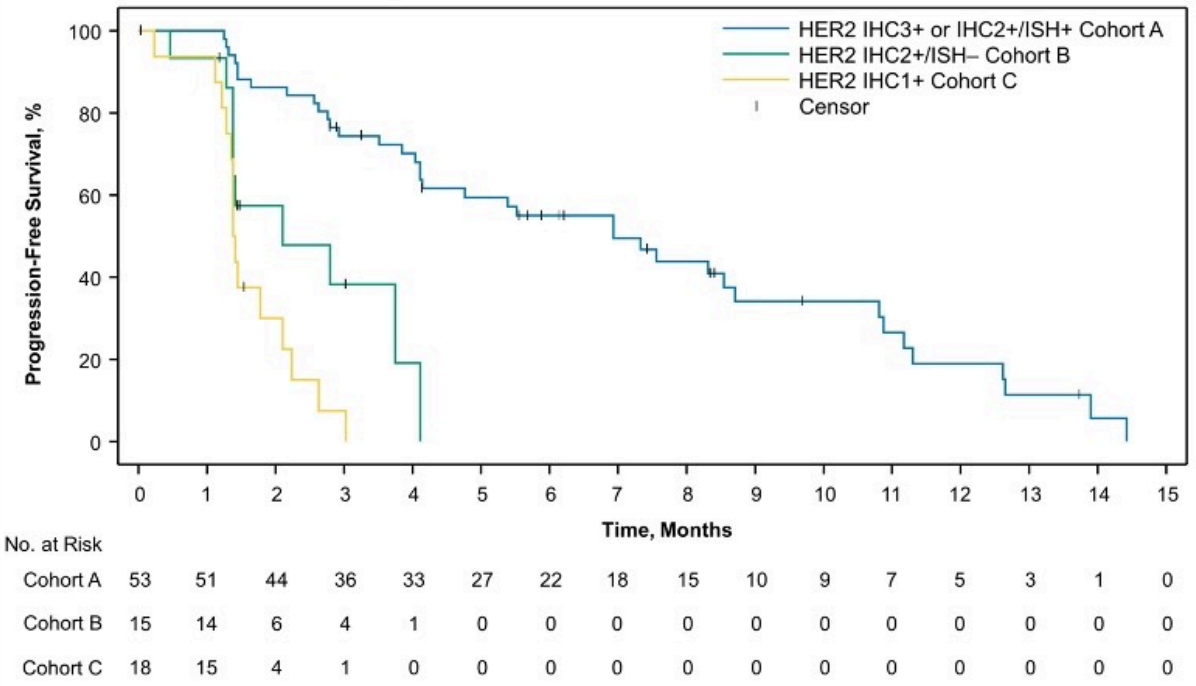


Yoshino T et al. ASCO 2021;Abstract 3500.

RTP RESEARCH TO PRACTICE

DESTINY-CRC01: Progression-Free and Overall Survival

Progression-Free Survival

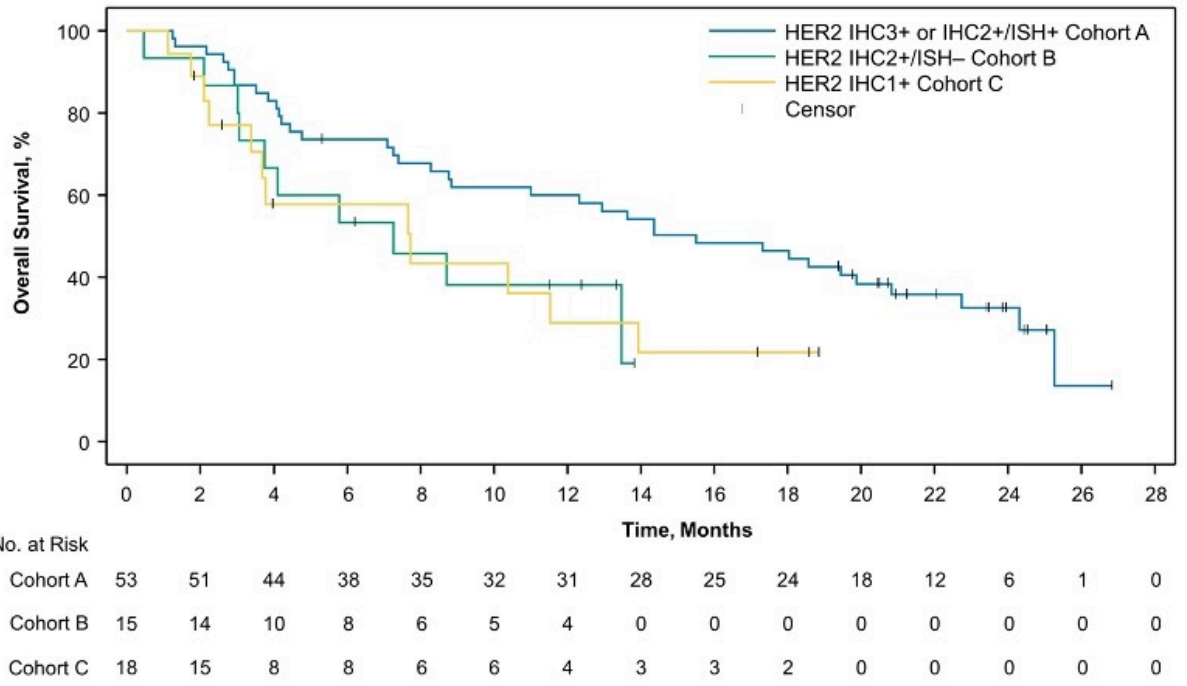


No. at Risk

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.

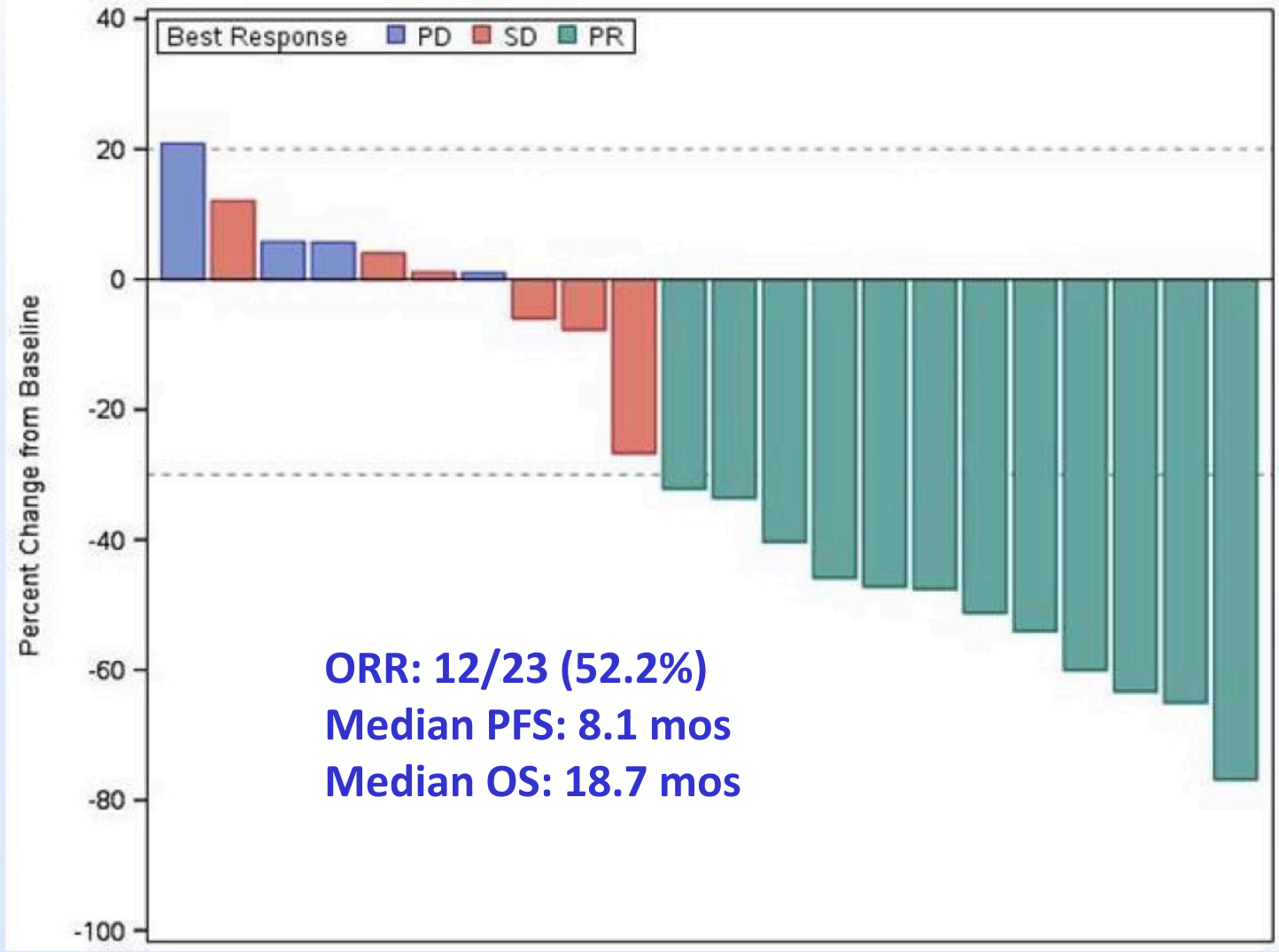
Yoshino T et al. ASCO 2021;Abstract 3500.

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.

Gastric/GEJ/Esophageal Cancer

2021 ASCO ANNUAL MEETING

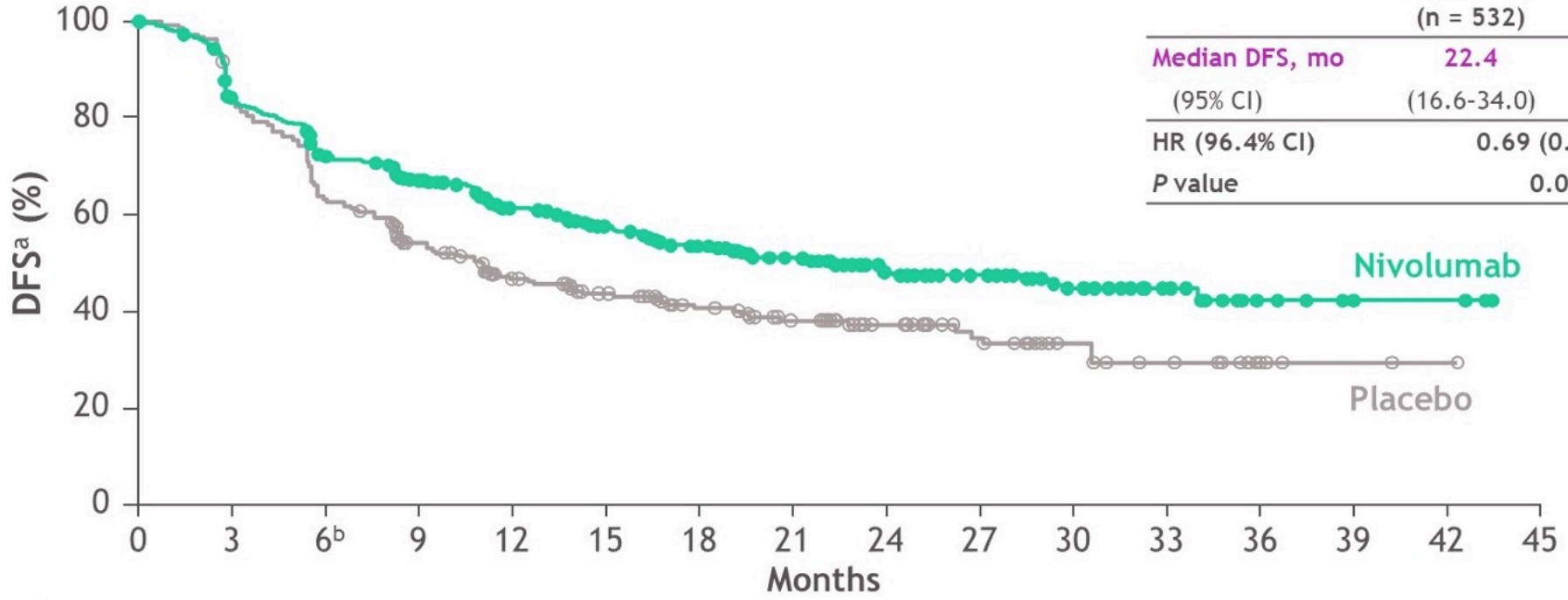
Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

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

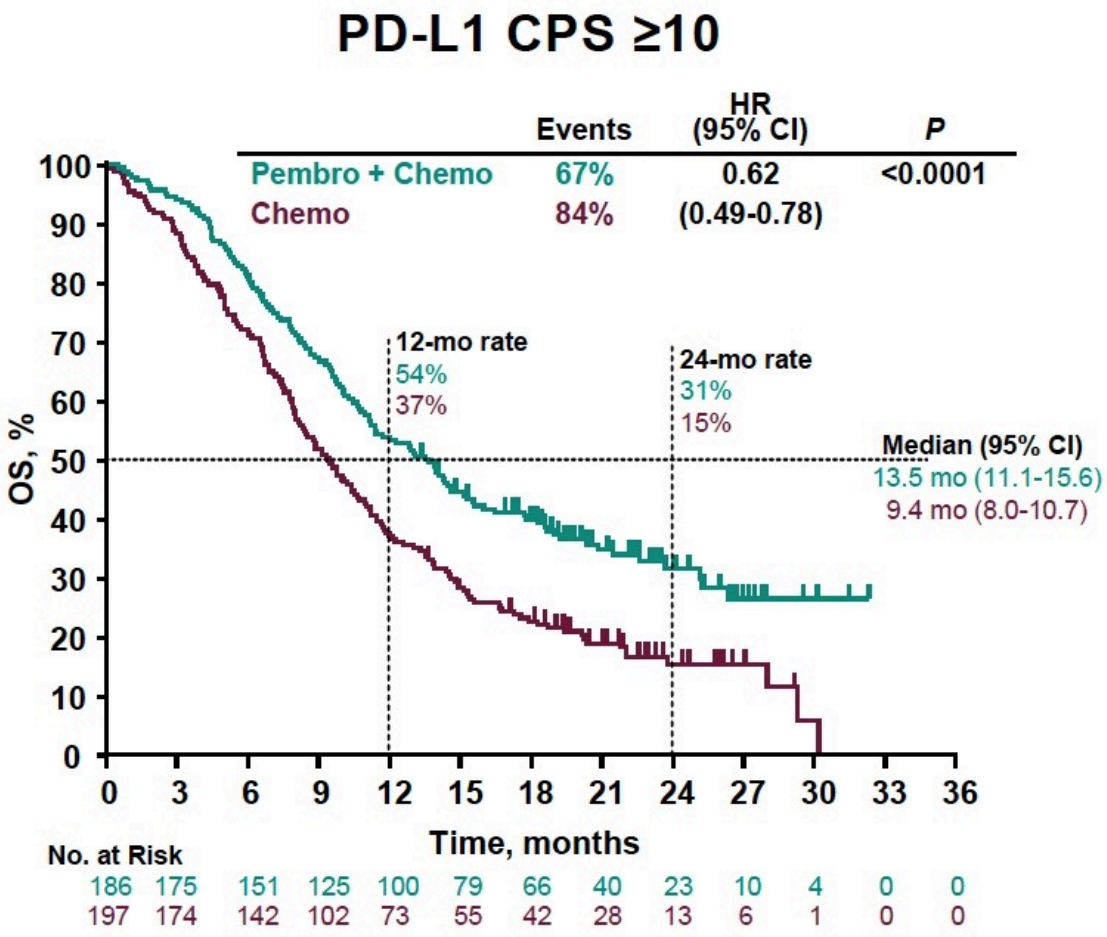
RTP RESEARCH TO PRACTICE

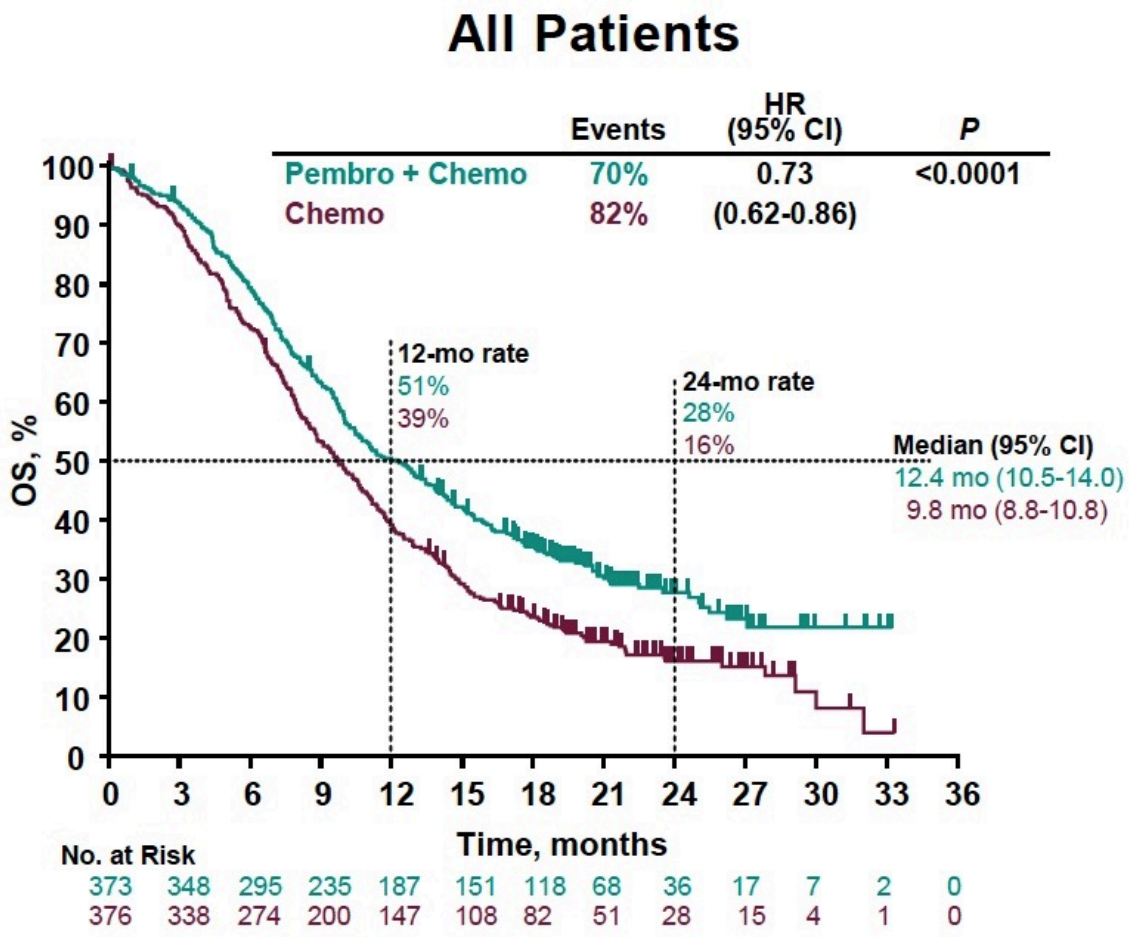
Pembrolizumab plus Chemotherapy versus Chemotherapy as First-Line Therapy in Patients with Advanced Esophageal Cancer: The Phase 3 KEYNOTE-590 Study

Kato K et al.

ESMO 2020;Abstract LBA8_PR.

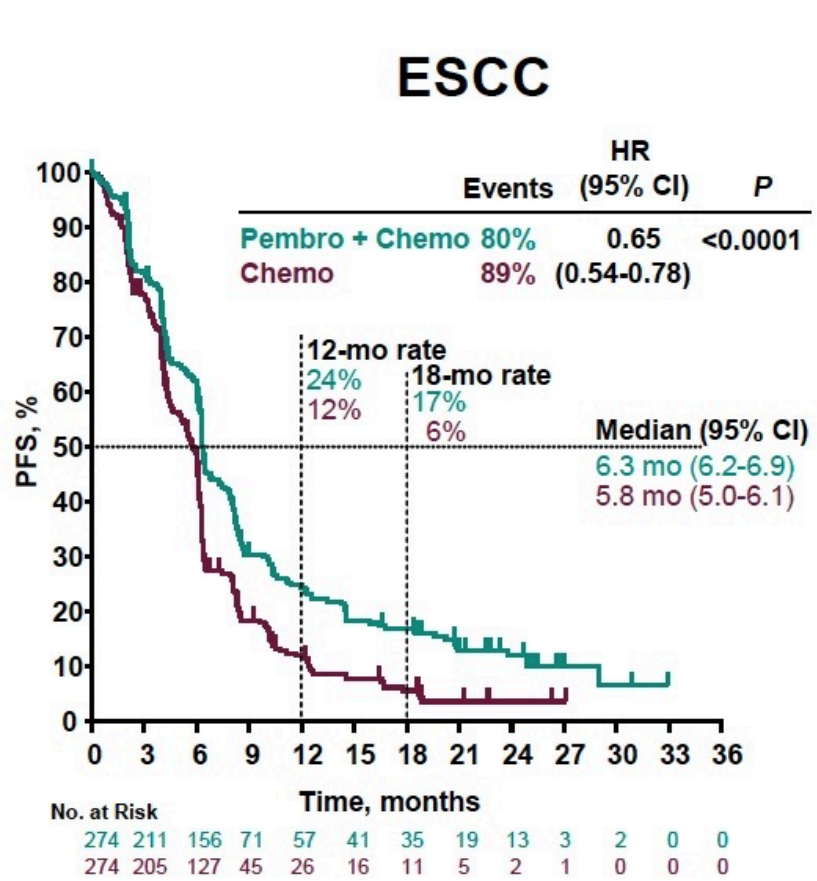
KEYNOTE-590: Overall Survival

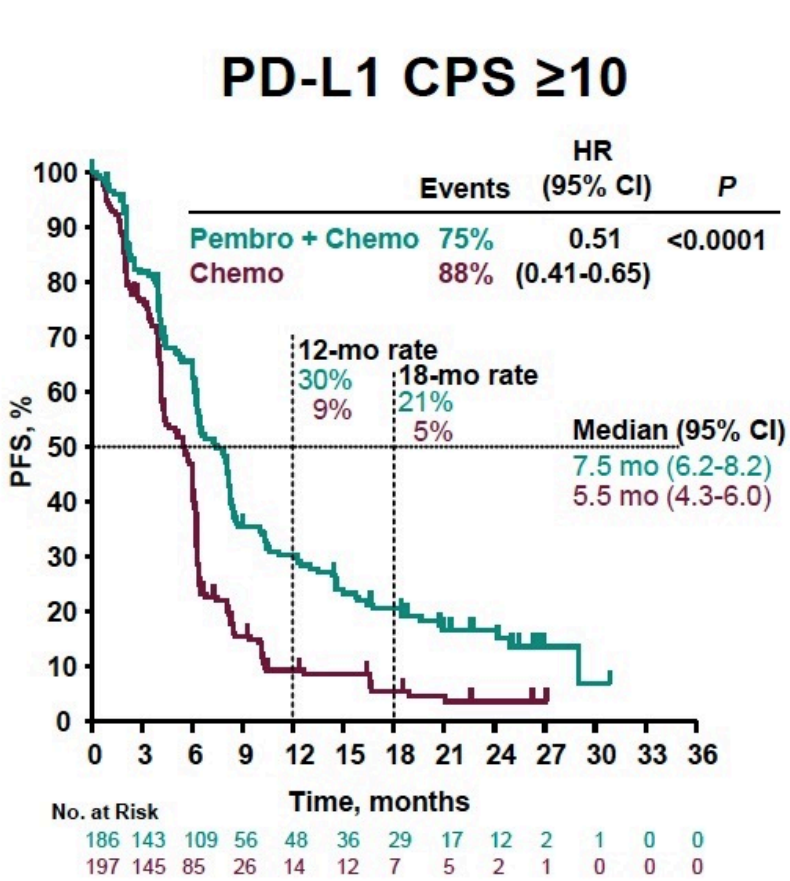


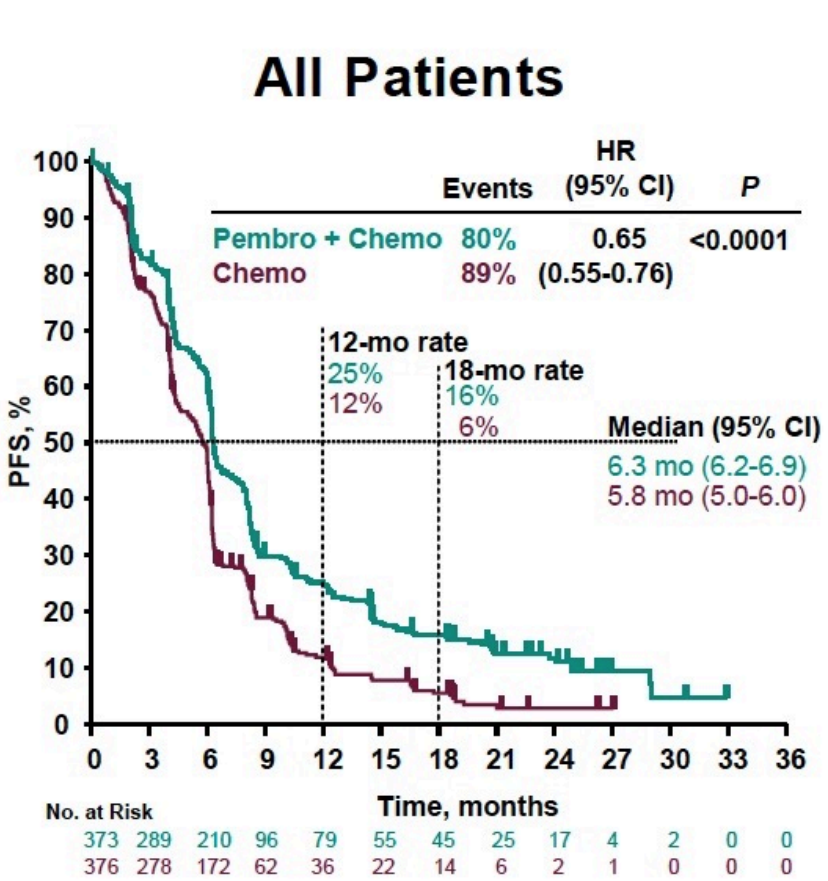


Kato K et al. ESMO 2020;Abstract LBA8_PR.

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

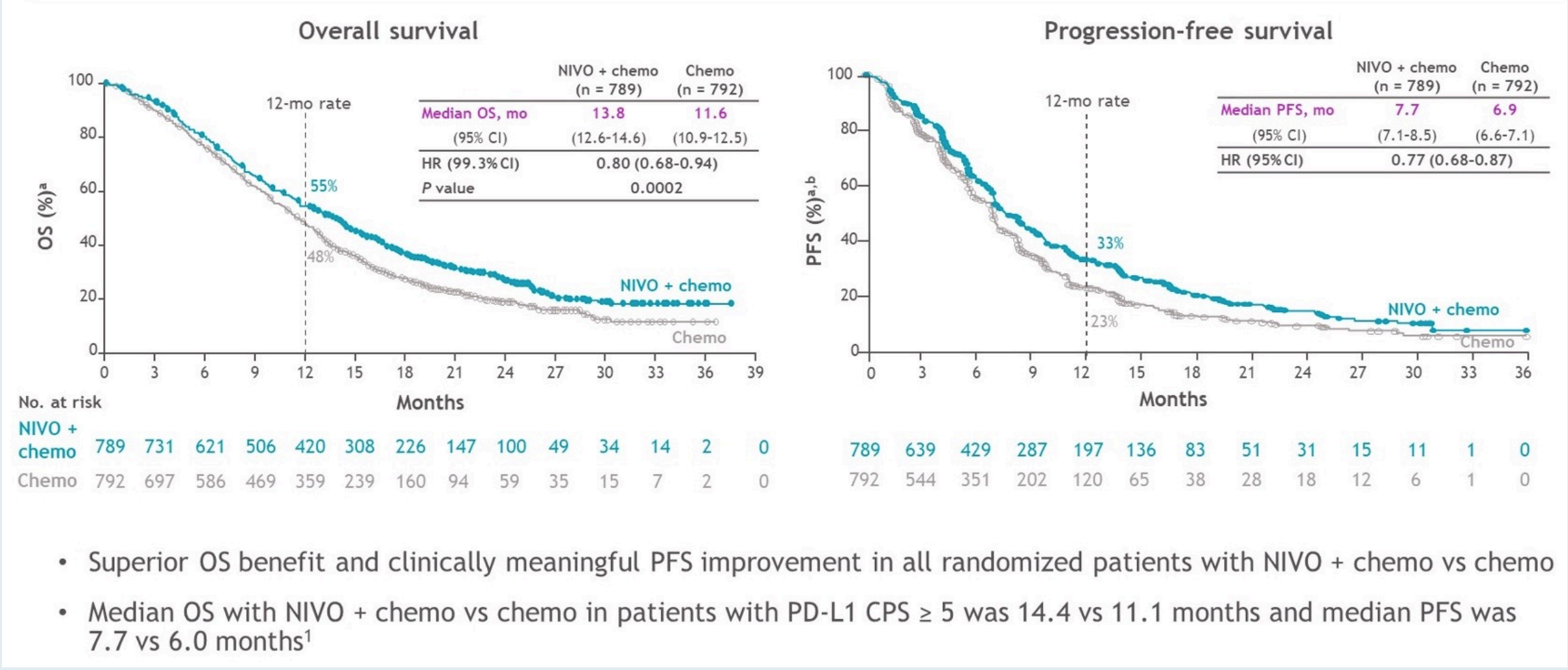
First-line nivolumab plus chemotherapy vs chemotherapy in advanced gastric cancer/ gastroesophageal junction cancer/esophageal adenocarcinoma: expanded efficacy and safety data from CheckMate 649

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

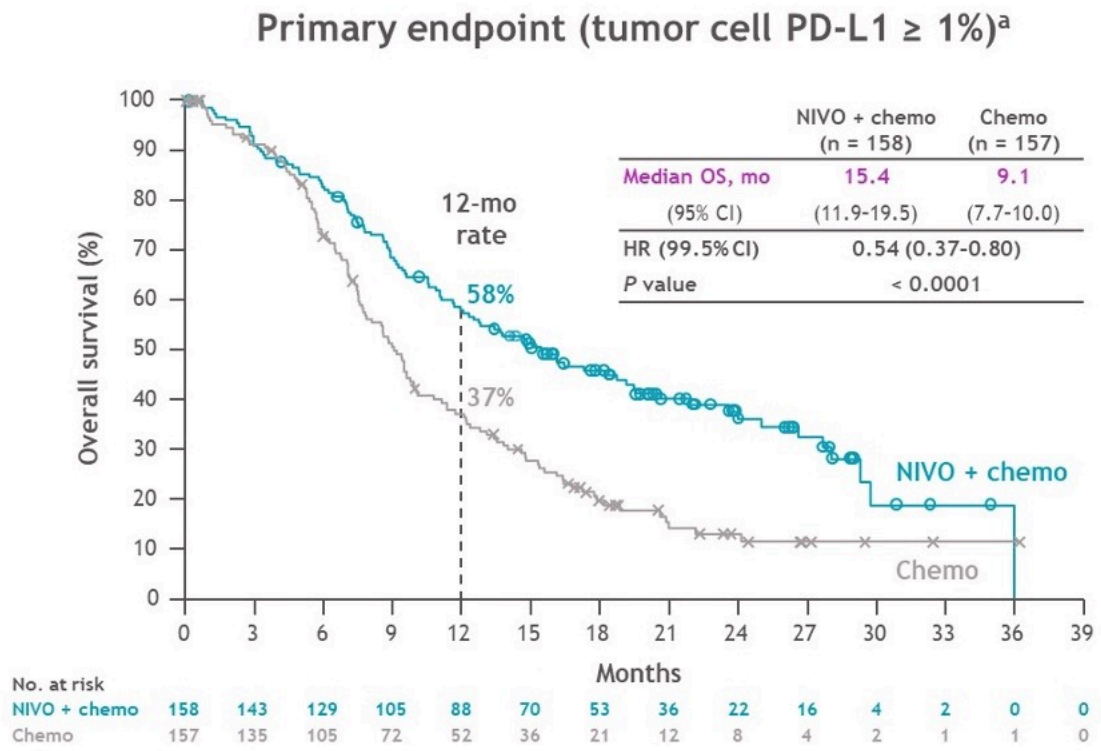
Nivolumab plus ipilimumab or nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced esophageal squamous cell carcinoma: first results of the CheckMate 648 study

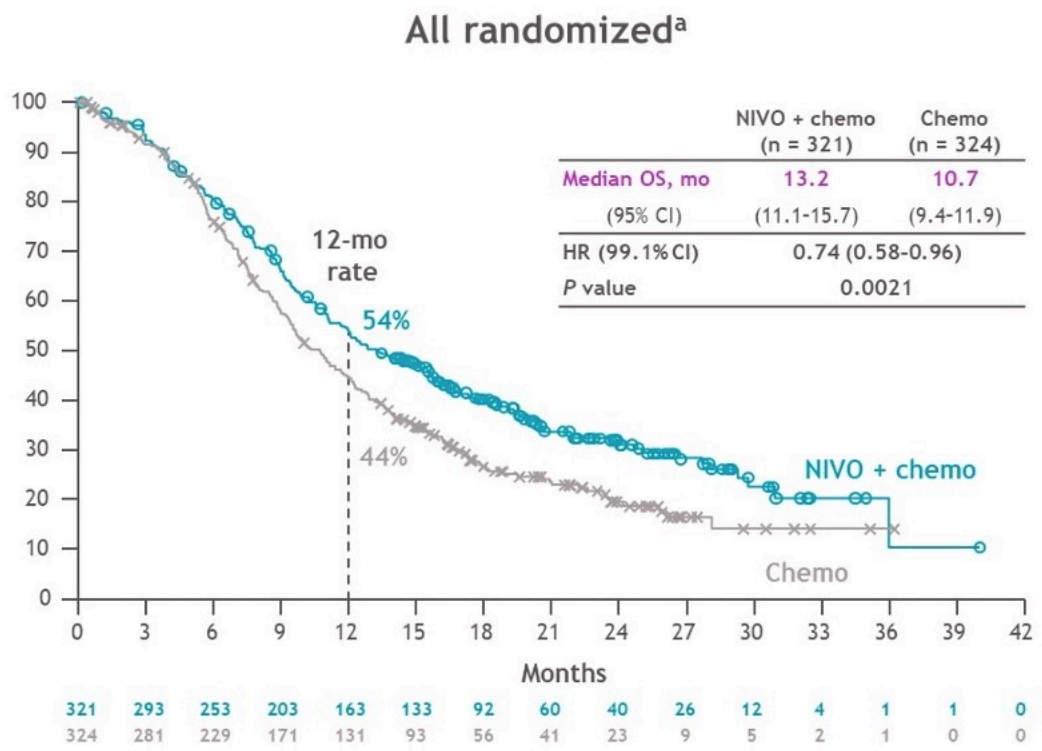
Ian Chau,[1] Yuichiro Doki,[2] Jaffer A. Ajani,[3] Jianming Xu,[4] Lucjan Wyrwicz,[5] Satoru Motoyama,[6] Takashi Ogata,[7] Hisato Kawakami,[8] Chih-Hung Hsu,[9] Antoine Adenis,[10] Farid el Hajbi,[11] Maria Di Bartolomeo,[12] Maria Ignez Braghiroli,[13] Eva Holtved,[14] Ioannis Xynos,[15] Xuan Liu,[15] 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 for Patients with PD-L1 ≥1% (Primary Endpoint Along with PFS in PD-L1 ≥1%) and in ITT Population



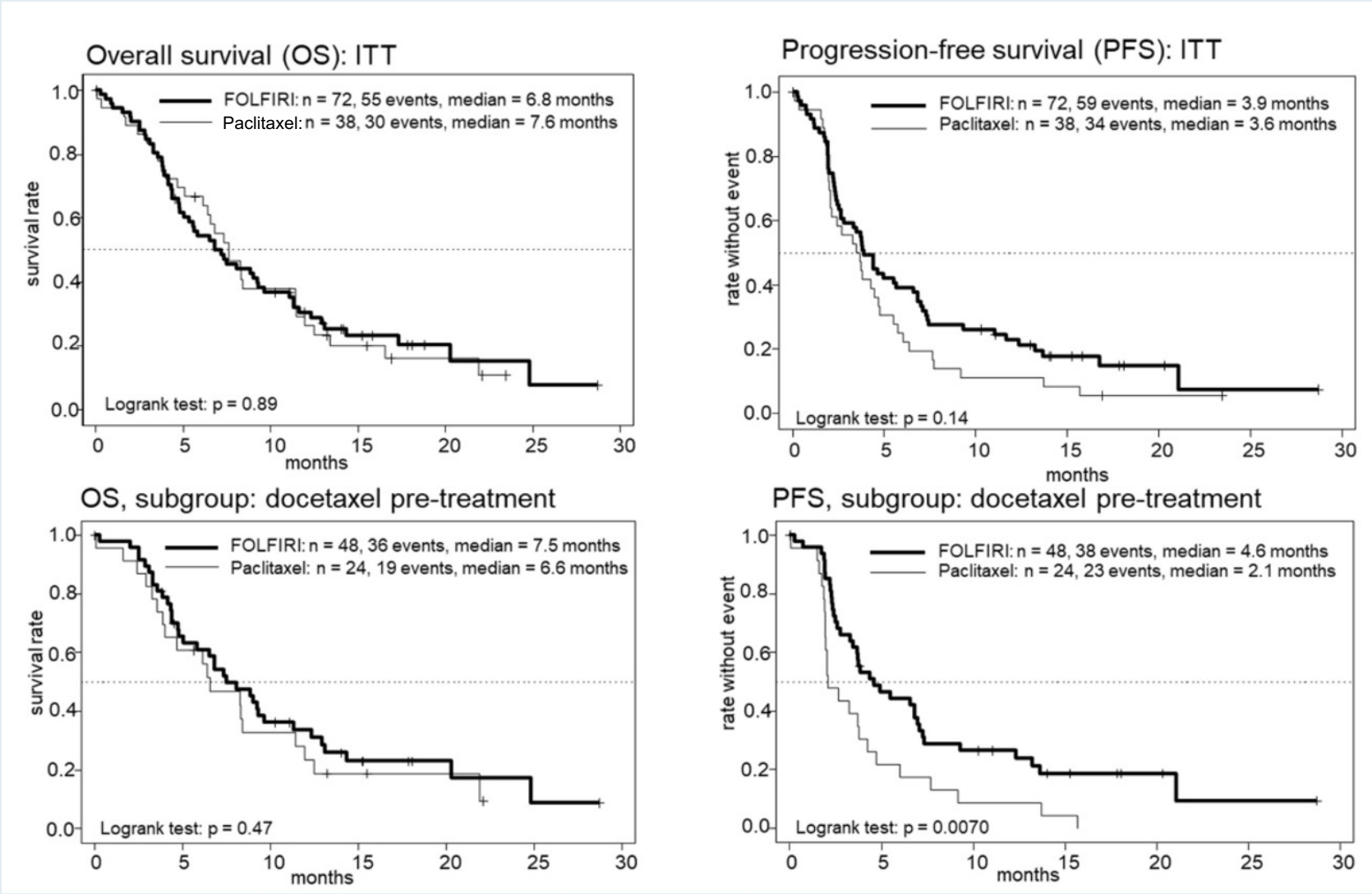


- Superior OS with NIVO + chemo vs chemo in tumor cell PD-L1 ≥ 1% and all randomized populations
  - Tumor cell PD-L1 ≥ 1%: 46% reduction in the risk of death and a 6.3-month improvement in median OS
  - All randomized: 26% reduction in the risk of death and a 2.5-month improvement in median OS

Chau I et al. ASCO 2021;Abstract LBA4001.

RTP RESEARCH TO PRACTICE

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



Lorenzen S et al. ASCO 2020;Abstract 4514.

RTP RESEARCH TO PRACTICE

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

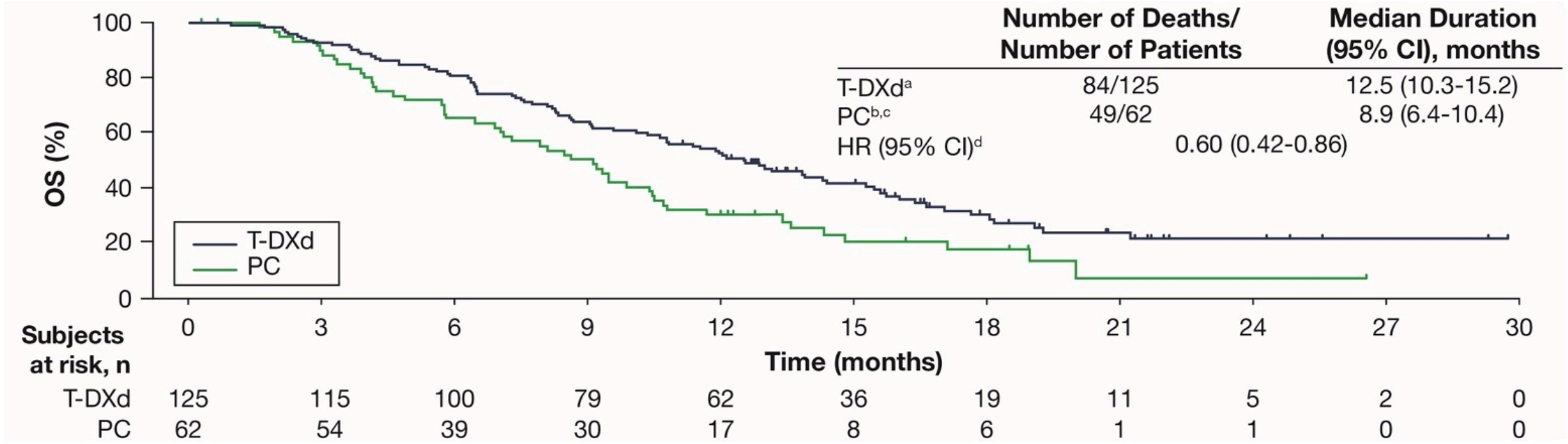
The Cancer Institute Hospital of JFCR, Tokyo, Japan

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

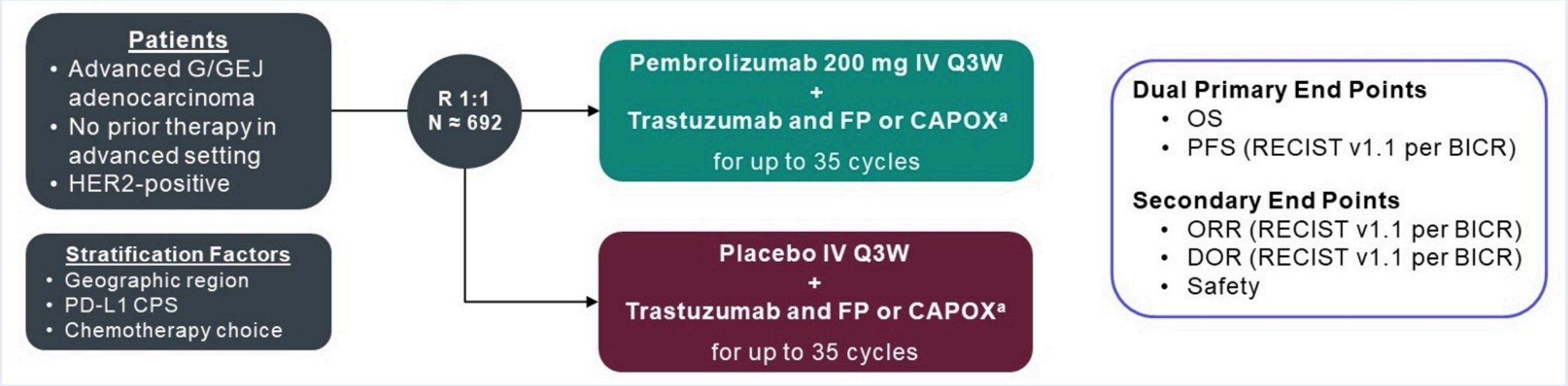
Yelena Y. Janjigian,[1] Akihito Kawazoe,[2] Patricio Yañez,[3] Suxia Luo,[4] Sara Lonardi,[5] Oleksii Kolesnik,[6] Olga Barajas,[7] Yuxian Bai,[8] Lin Shen,[9] Yong Tang,[10] Lucjan S. Wyrwicz,[11] Kohei Shitara,[2] Shukui Qin,[12] Eric Van Cutsem,[13] Josep Tabernero,[14] Lie Li,[15] Chie-Schin Shih,[15]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

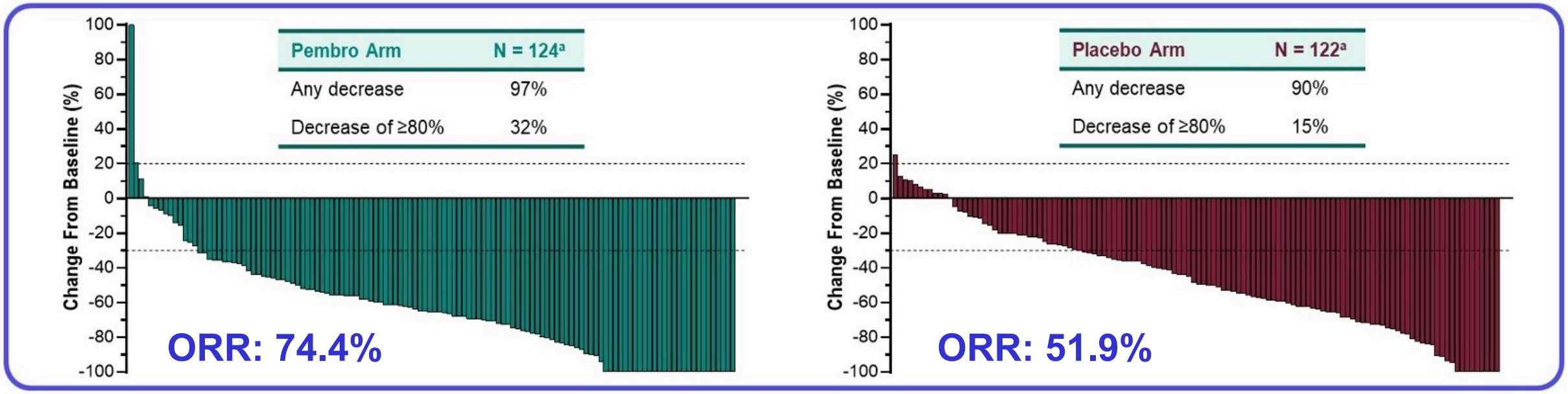
RTP RESEARCH TO PRACTICE

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.

Hepatocellular Carcinoma

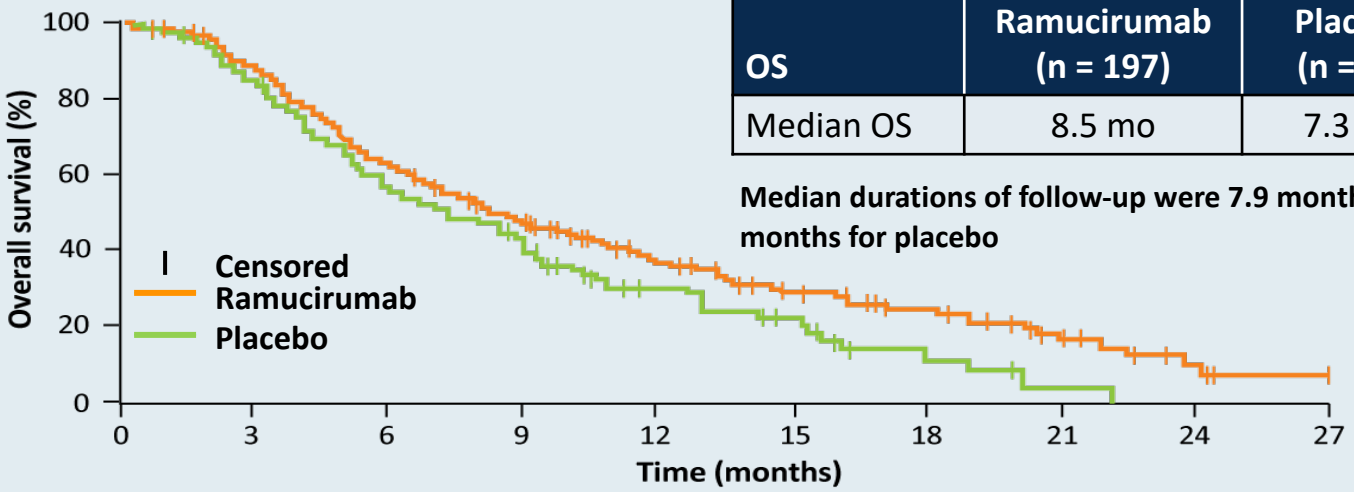
Articles

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**

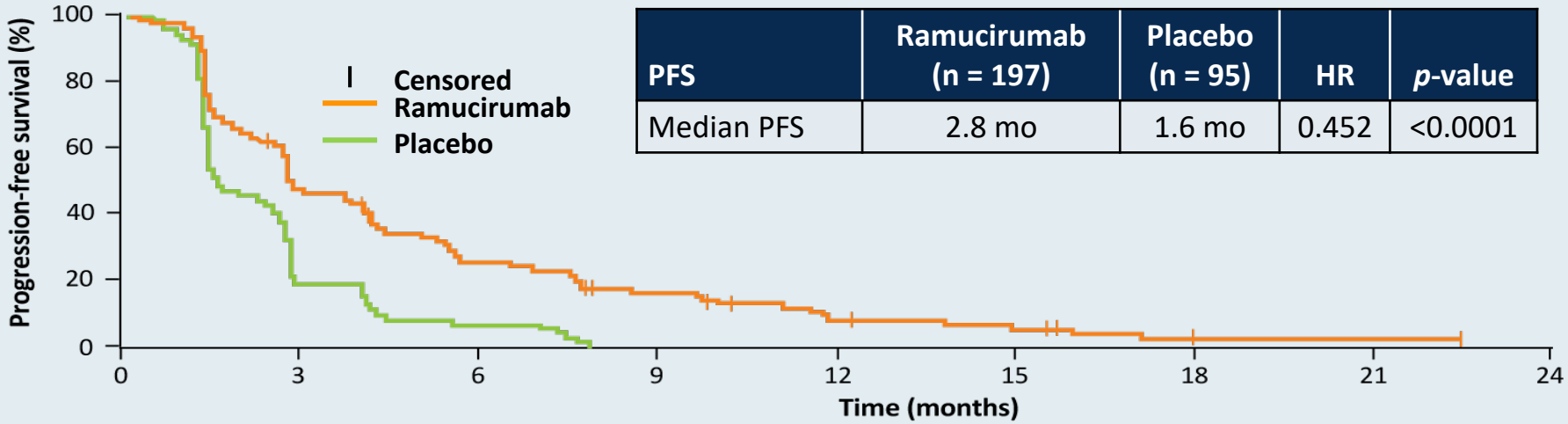
Lancet Oncol 2019;20(2):282-96.

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

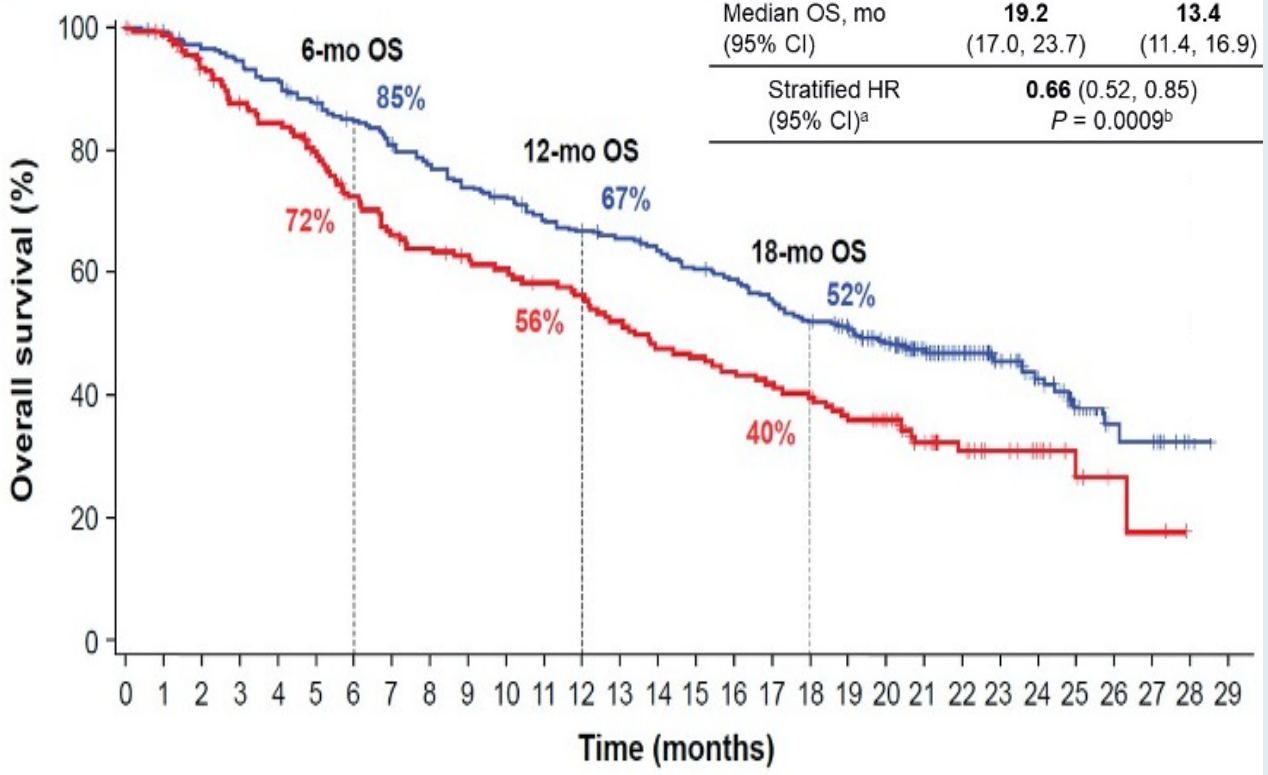
IMbrave150: Updated Overall Survival (OS) Data from a Global, Randomized, Open-Label Phase III Study of Atezolizumab (atezo) + Bevacizumab (bev) versus Sorafenib (sor) in Patients (pts) with Unresectable Hepatocellular Carcinoma (HCC)

Finn RS et al.

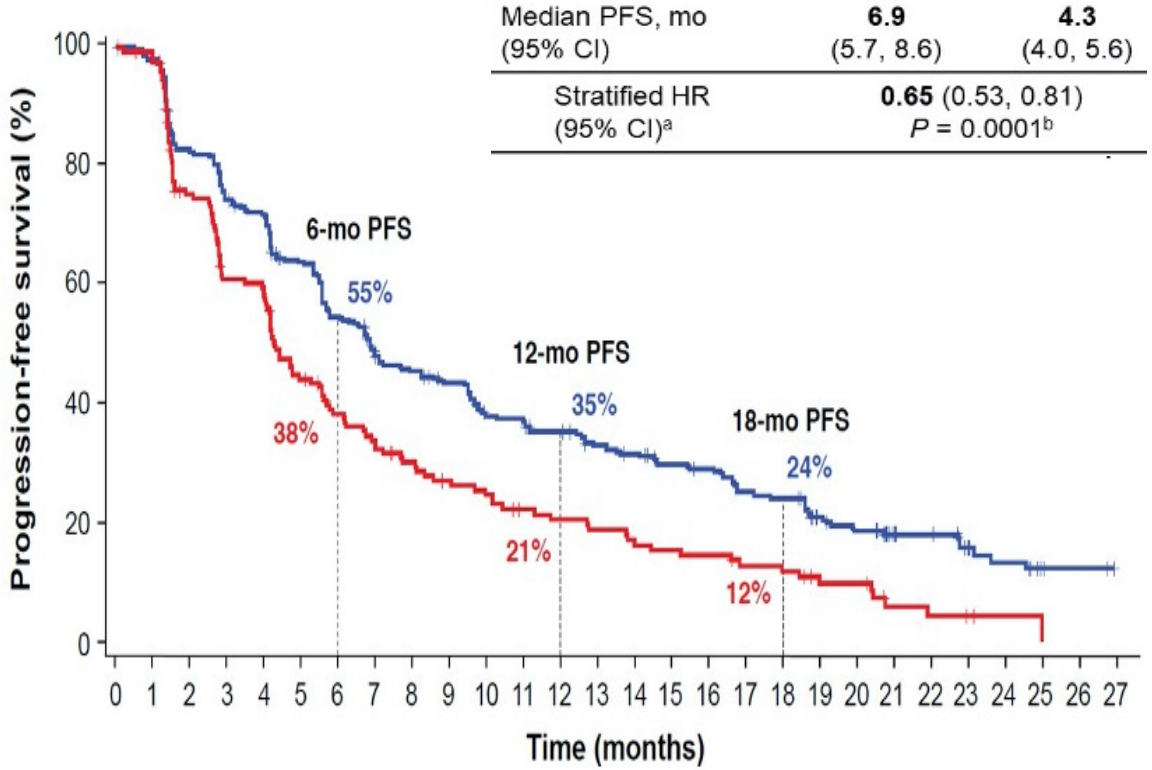
Gastrointestinal Cancers Symposium 2021;Abstract 267.

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]	



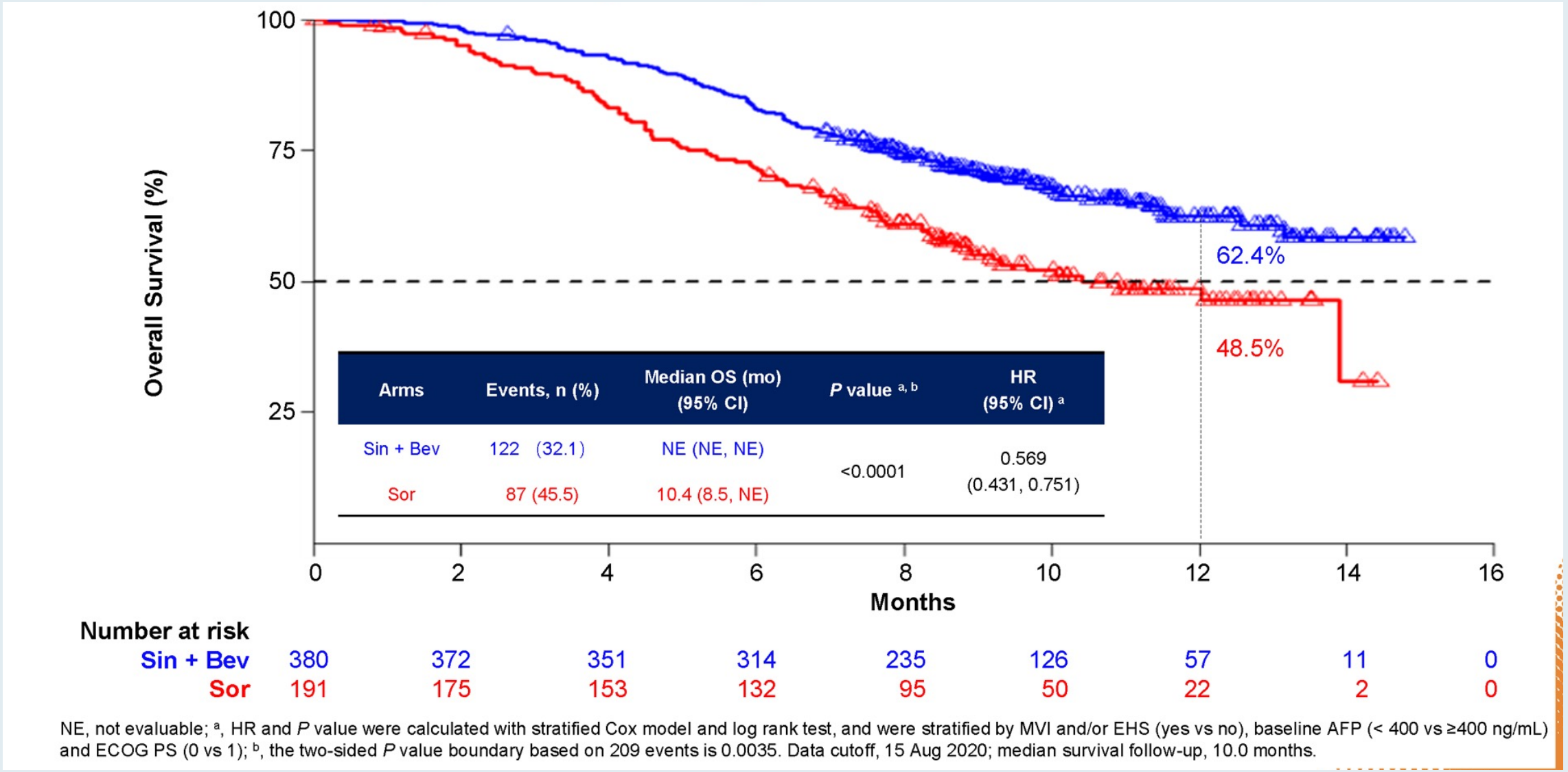
Finn RS et al. Gastrointestinal Cancers Symposium 2021;Abstract 267.

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

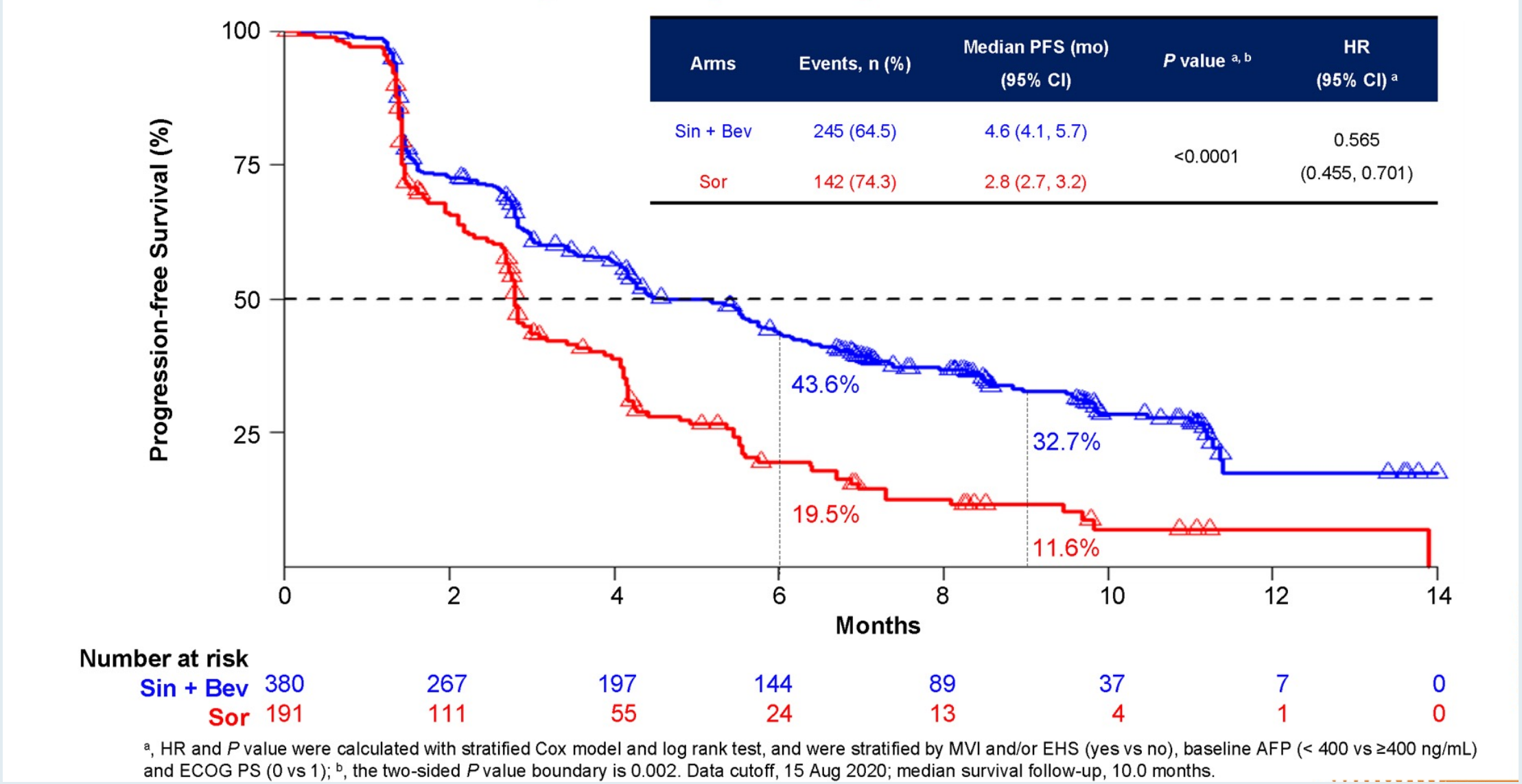
Sin + Bev	380	372	351	314	235	126	57	11	0
Sor	191	175	153	132	95	50	22	2	0

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.

RTP RESEARCH TO PRACTICE

Meet The Professor

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

Monday, October 11, 2021
5:00 PM – 6:00 PM ET

Faculty

Elizabeth R Plimack, MD, MS

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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