Meet The Professor

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

Dirk Arnold, MD, PhD
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Commercial Support

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Dr Love — Disclosures

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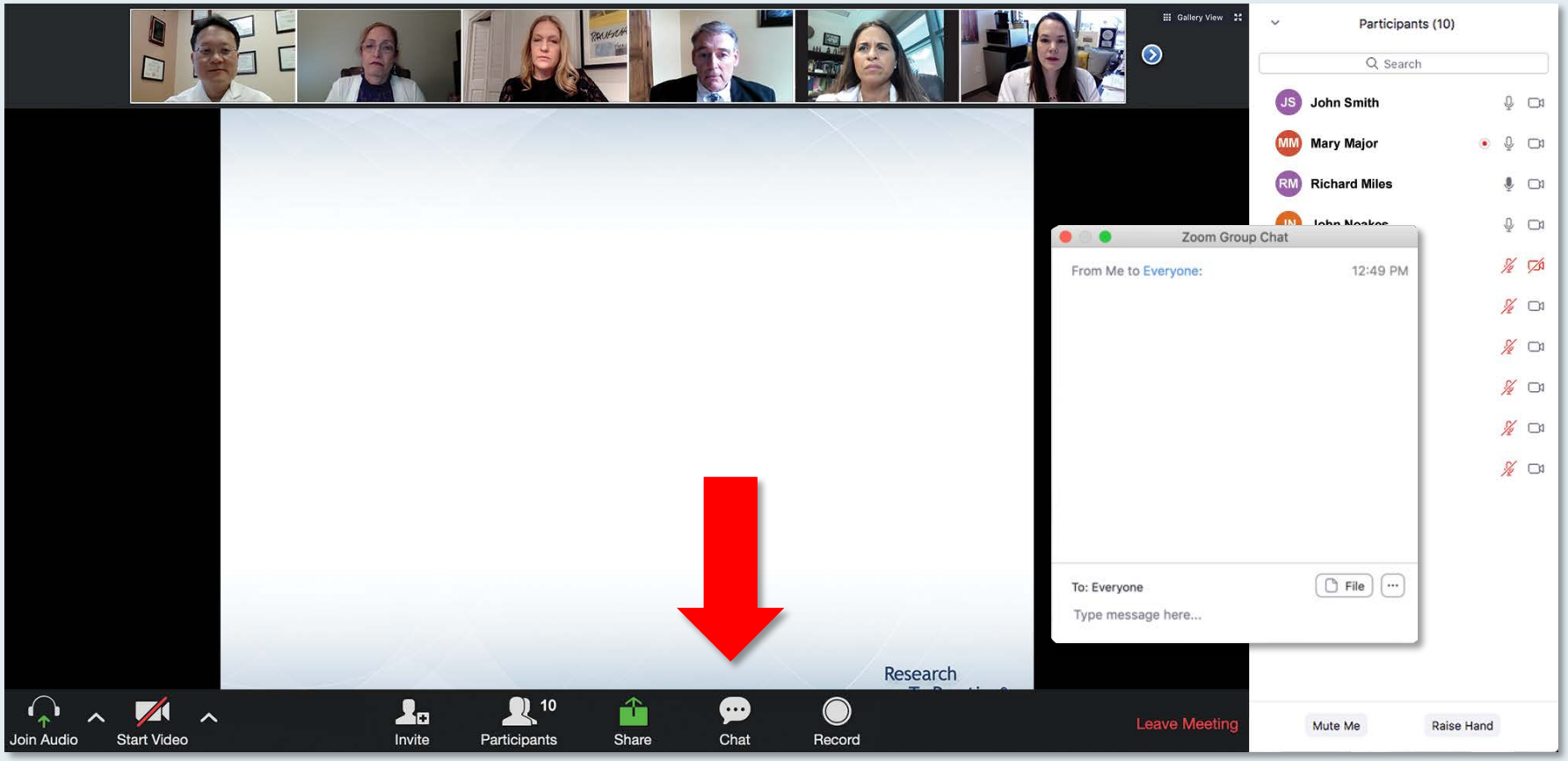
We Encourage Clinicians in Practice to Submit Questions



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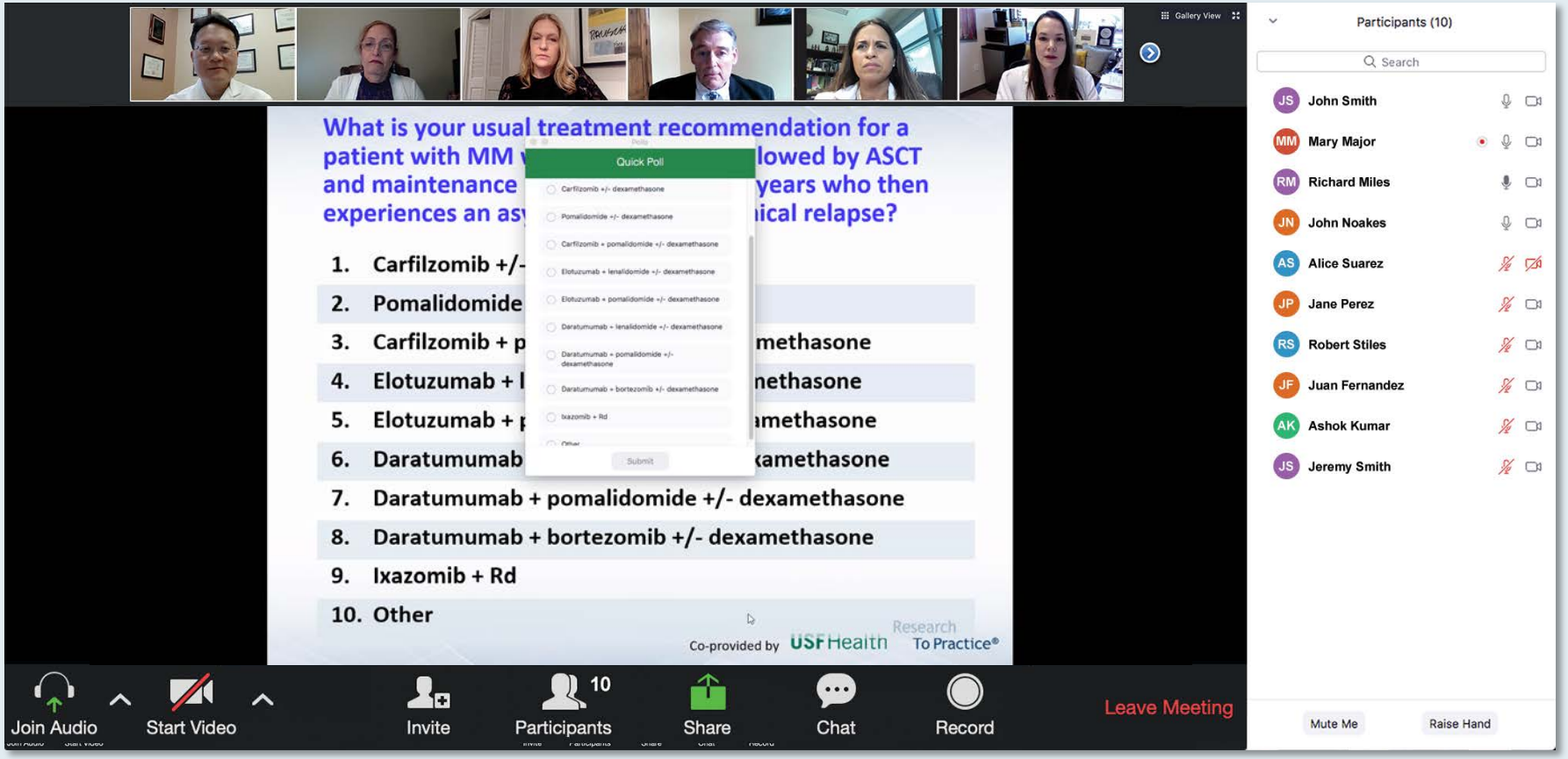

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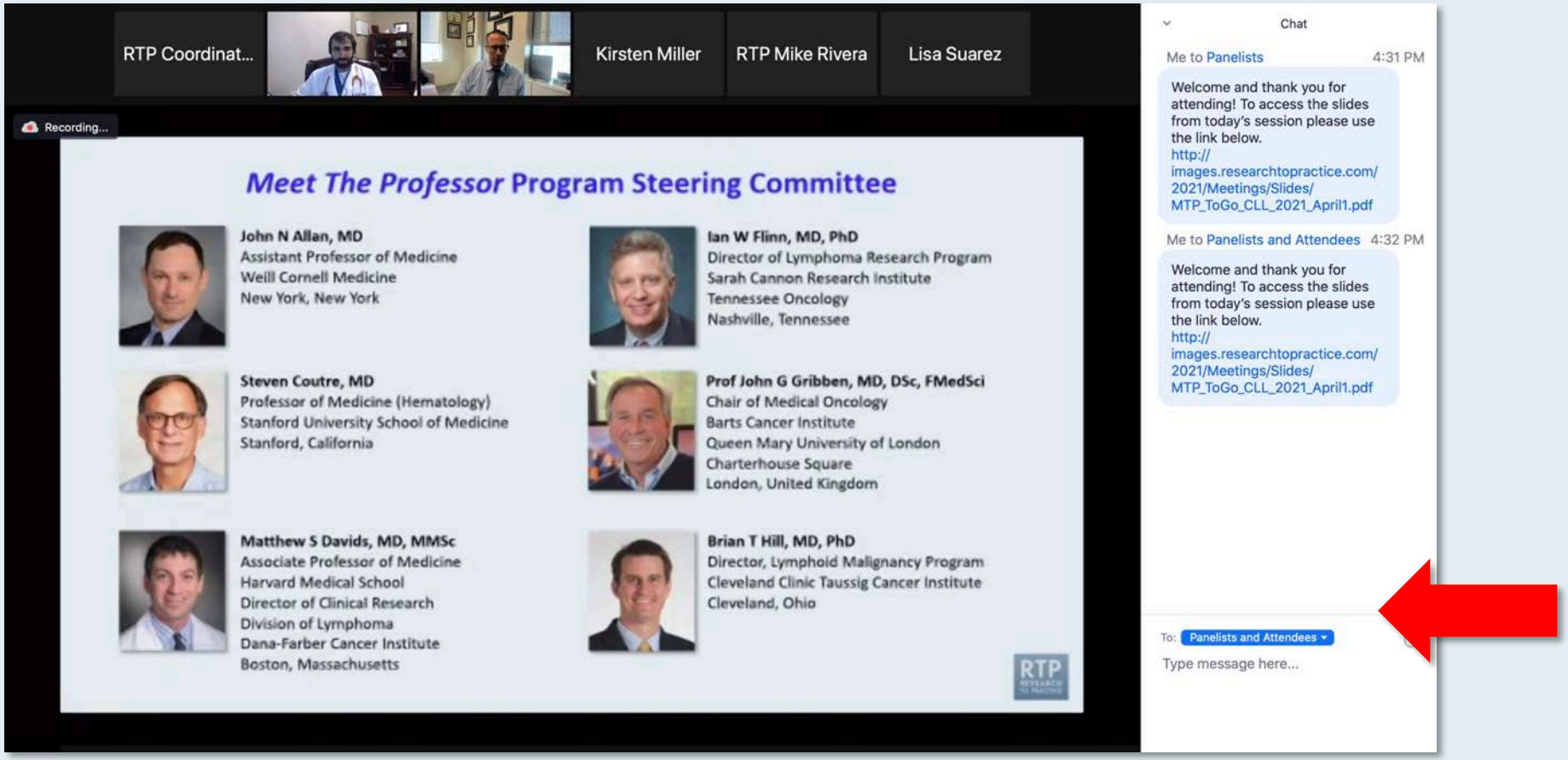

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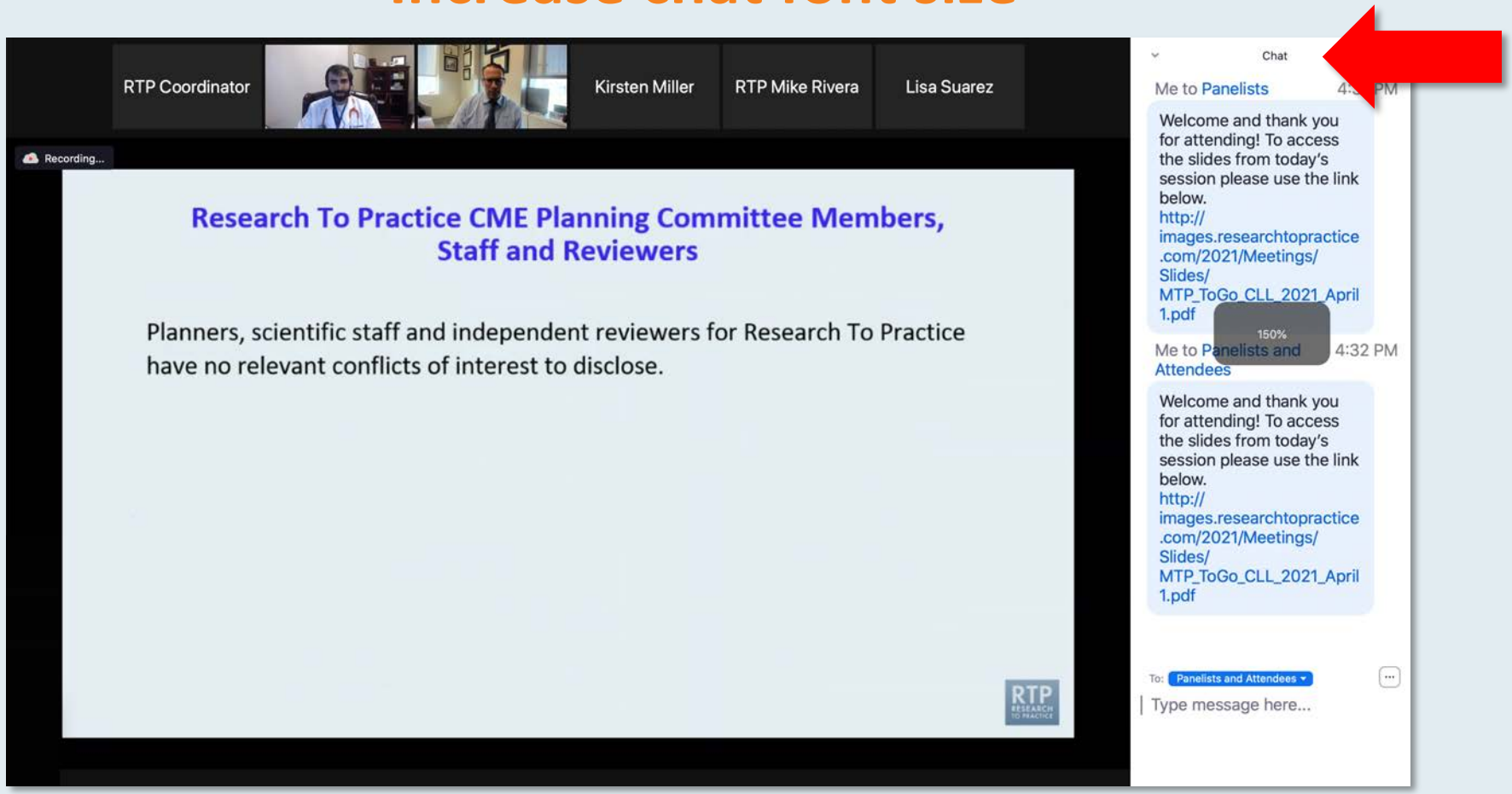

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You may do this as many times as you need for readability.

Ask the Investigators: Applying Emerging Clinical Research to the Care of Patients with Gastroesophageal Cancers

A Satellite Educational Symposium Held in Conjunction with the 2021 AACR Virtual Annual Meeting

Monday, April 12, 2021
6:30 PM – 7:30 PM ET

Faculty

Joseph Chao, MD
Yelena Y Janjigian, MD

Moderator

Neil Love, MD

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Meet The Professor

Management of Chronic Lymphocytic Leukemia

Thursday, April 15, 2021
5:00 PM – 6:00 PM ET

Faculty

John N Allan, MD

Moderator

Neil Love, MD

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Dissecting the Decision: Investigator Perspectives on Key Issues in the Management of Common Cancers

A Complimentary NCPD Live Webinar Series Hosted in Conjunction with the 46th Annual ONS Congress

Breast Cancer
Tuesday, April 20, 2021
8:30 AM – 10:00 AM ET

Non-Small Cell Lung Cancer
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Acute Myeloid Leukemia
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12:00 PM – 1:00 PM ET

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In Partnership with Project Echo® and Florida Cancer Specialists

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WITH DR NEIL LOVE

Key Recent Data Sets in Gastrointestinal Cancers

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Meet The Professor Program Participating Faculty

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Asklepios Tumorzentrum Hamburg
Asklepios Klinik Altona
Hamburg, Germany

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Meet The Professor Program Participating Faculty

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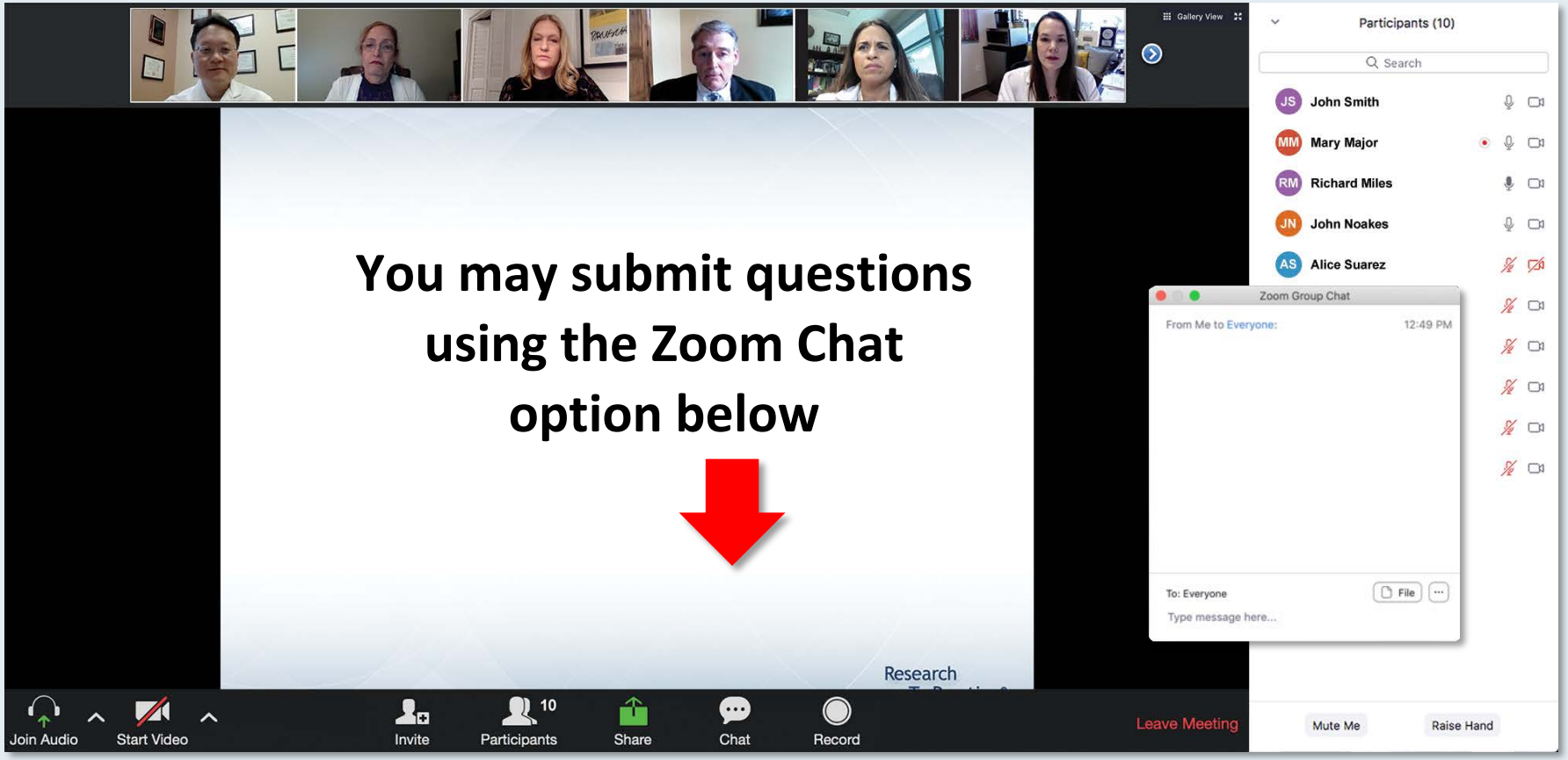

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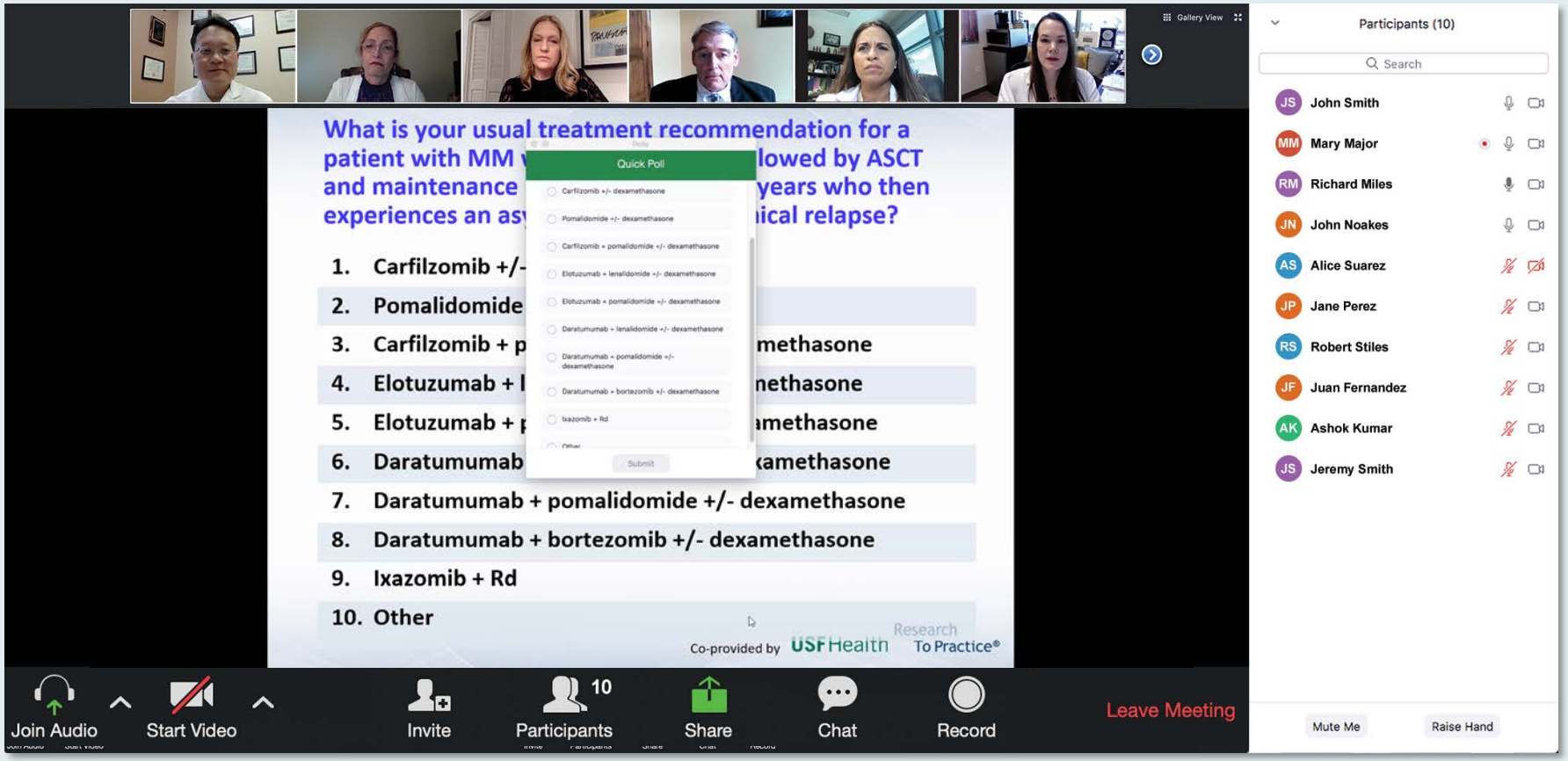

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Erik J Rupard, MD
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Reading Hospital and Medical Center
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Liudmila N Schafer, MD
Associate Professor of Medicine
Director of Gastrointestinal Oncology Program
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University of Missouri-Kansas City School of Medicine
Kansas City, Missouri

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Meet The Professor with Prof Arnold

MODULE 1: Case from Dr Schafer

- An 82-year-old woman with mismatch repair-deficient metastatic colorectal cancer – BRAF V600E mutation (Parts 1 and 2)

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

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MODULE 7: Gastrointestinal Cancers Journal Club with Prof Arnold

MODULE 8: Recent Data Sets

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Schafer: An 82-year-old woman with MMR-deficient metastatic colorectal cancer – BRAF V600E mutation (Part 1)

Dr Liudmila Schafer

- 2017 Hemicolectomy for sigmoid diverticulosis
- 3/2019 Stage IIIA right colon cancer s/p right hemicolectomy → FOLFOX x 6
  - 1/2020 Imaging: NED
  - MMR deficient (HML1 absent, PMS2 absent), BRAF V600E mutation, TMB: 40 mut/Mb
- 4/2020 Rising CEA (48), with PD in mesenteric lymph nodes
- Pembrolizumab intiated
  - 6/2020 Radiologic CR, CEA: 48 → 21
- Development of spongiotic dermatitis with perivascular mixed inflammation

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Case Presentation – Dr Schafer: An 82-year-old woman with MMR-deficient metastatic colorectal cancer (Part 1 continued)

Dr Liudmila Schafer

MSI status	High
Germline variants	None
TMB	40 mut/mb
MMR	Deficient (PMS2 and MLH1 absent)
PD-L1	Tumor: <1%, tumor-associated immune: 10%
HRD	Not detected
Genomic variants	BRAF V600E, BRCA2 P.E2981fs, BRCA1 p.K339fs
RNA	MGMT underexpressed
Neo-antigen prediction	45 antigenic
Immune infiltration	CD8 6%
Signatera	2.1 MTM/mL

Case Presentation – Dr Schafer: An 82-year-old woman with MMR-deficient metastatic colorectal cancer – BRAF V600E mutation (Part 2)

Dr Liudmila Schafer

- 2017 Hemicolectomy for sigmoid diverticulosis
- 3/2019 Stage IIIA right colon cancer s/p right hemicolectomy → FOLFOX x 6
  - 1/2020 Imaging: NED
  - MMR deficient (HML1 absent, PMS2 absent), BRAF V600E mutation, TMB: 40 mut/Mb
- 4/2020 Rising CEA (48), with PD in mesenteric lymph nodes
- ***Pembrolizumab, with spongiotic dermatitis not responding well to steroids and other treatment modalities***
- ***12/2020 New FDG activity in the lymph nodes***
- ***CEA: 21 → 170***

Questions

- ***What would you use in the second-line setting, considering her skin toxicities?***
- ***Would she be a candidate for encorafenib and cetuximab in light of her dermatologic toxicities?***

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Meet The Professor with Prof Arnold

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

1. FOLFOX/CAPOX
2. FOLFOX/CAPOX + bevacizumab
3. FOLFOX/CAPOX + EGFR antibody
4. FOLFOXIRI
5. FOLFOXIRI + bevacizumab
6. FOLFOXIRI + EGFR antibody
7. Other

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)?

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

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

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

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

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

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

 Prof Arnold	Encorafenib + EGFR antibody	 Dr Grothey	Encorafenib + EGFR antibody
 Dr Bekaii-Saab	Encorafenib + EGFR antibody	 Dr O'Reilly	Encorafenib + EGFR antibody
 Dr Bendell	Encorafenib + EGFR antibody	 Dr Venook	Encorafenib + EGFR antibody
 Dr Ciombor	Encorafenib + EGFR antibody	 Dr Wainberg	Encorafenib + binimetinib + EGFR antibody

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

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

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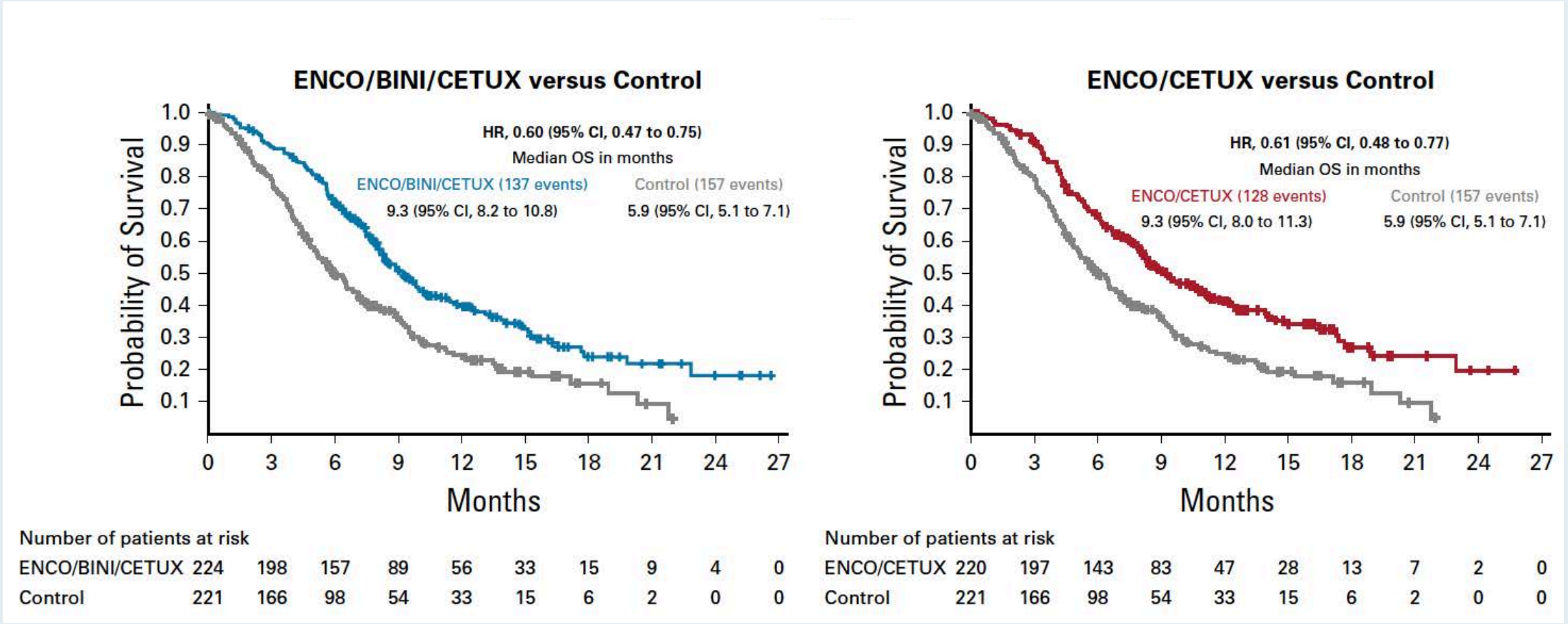
rapid communications

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

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

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

BEACON: Overall Survival Results



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

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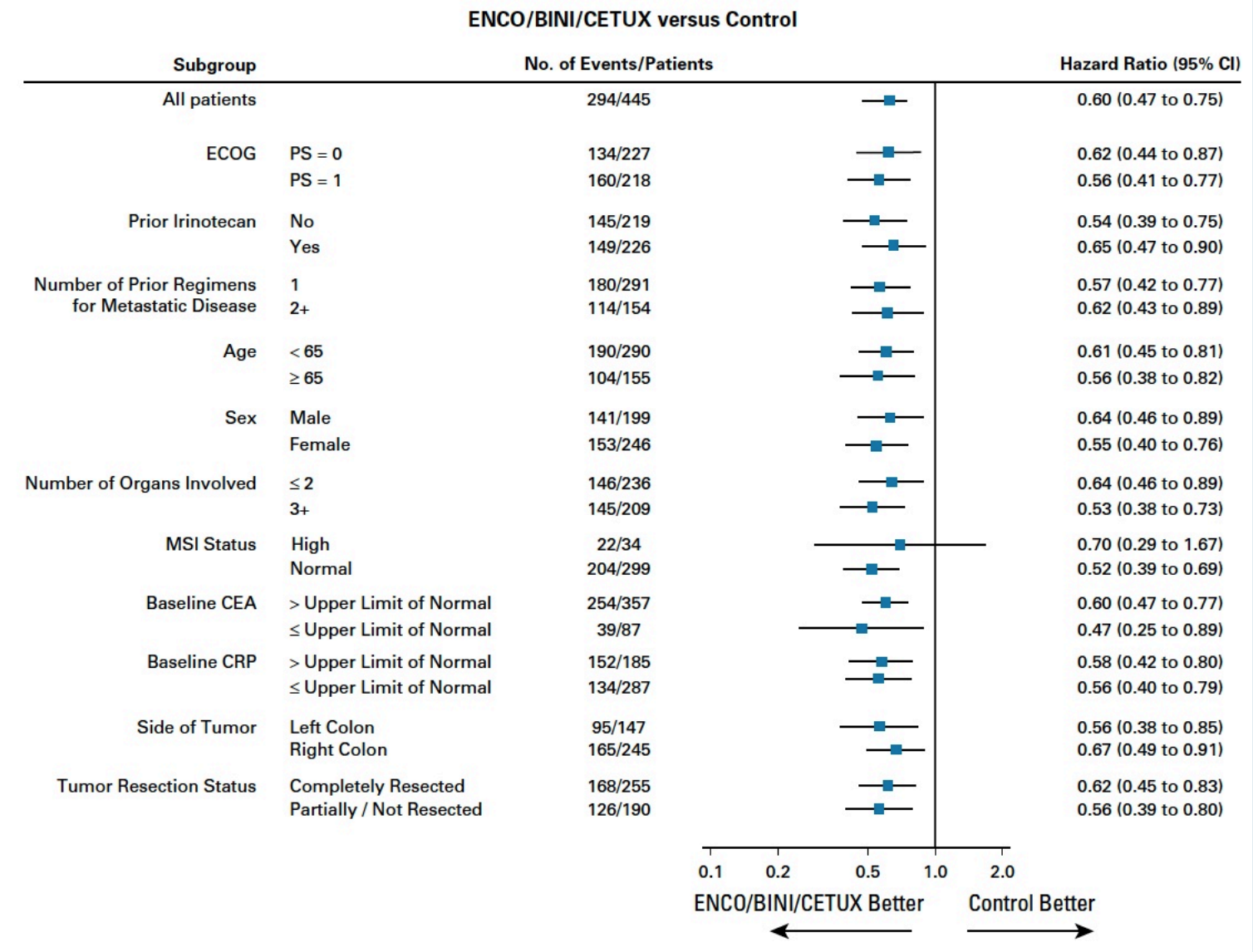
BEACON: Subgroup Analysis of Overall Survival



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Case Presentation – Dr Rupard: A 79-year-old woman with metastatic GEJ cancer and a prolonged response to ramucirumab but with proteinuria (Part 1)

Dr Erik Rupard

- 2014: GEJ adenocarcinoma s/p neoadjuvant FOLFOX → R0 resection
- Rapid relapse in her liver → Ramucirumab with intent to add taxane, but rapid PR
- 2/2020: After 5 years, ramucirumab held due to proteinuria (leg/orthostasis)
- Proteinuria did not respond to ACE inhibitor therapy
- 5FU x 2 months but developed NSTEMI

Case Presentation – Dr Rupard: A 79-year-old woman with metastatic GEJ cancer and a prolonged response to ramucirumab but with proteinuria (Part 2)

Dr Erik Rupard

- 2014: GEJ adenocarcinoma s/p neoadjuvant FOLFOX → R0 resection
- Rapid relapse in her liver → Ramucirumab with intent to add taxane, but rapid PR
- 2/2020: After 5 years, ramucirumab held due to proteinuria (leg/orthostasis)
- Proteinuria did not respond to ACE inhibitor therapy
- 5FU x 2 months but developed NSTEMI
- ***NGS: TMB 12 mut/Mb, PD-L1 CPS 6***
- ***Currently, 6 months off treatment without relapse but has developed ovarian cancer***

Questions

- ***How often, if at all, have you encountered anti-VEGF therapy-related proteinuria to be a life-limiting problem?***
- ***Have you seen such durable objective response to ramucirumab, in her case lasting 5 years?***

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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 Grothey	Trastuzumab deruxtecan
 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 Ciombor	FOLFIRI/ramucirumab	 Dr Wainberg	Trastuzumab deruxtecan

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Regulatory and reimbursement issues aside, in which line of therapy if any would you generally recommend an anti-PD-1/PD-L1 antibody (with or without chemotherapy) for a 65-year-old patient with metastatic HER2-negative, MSS adenocarcinoma of the gastroesophageal junction (GEJ) with a PD-L1 combined positive score (CPS) of 0?

1. First line
2. Second line
3. Third line
4. Beyond third line
5. I would not recommend an anti-PD-1/PD-L1 antibody

Regulatory and reimbursement issues aside, in which line of therapy would you generally recommend an anti-PD-1/PD-L1 antibody (with or without chemotherapy) for a 65-year-old patient with metastatic HER2-negative, microsatellite-stable (MSS) adenocarcinoma of the gastroesophageal junction (GEJ) with a PD-L1 combined positive score (CPS) of 0?

 Prof Arnold	Beyond third line — nivolumab or pembrolizumab	 Dr Grothey	Would not recommend an anti-PD-1/PD-L1 antibody
 Dr Bekaii-Saab	Would not recommend an anti-PD-1/PD-L1 antibody	 Dr O'Reilly	Beyond third line — nivolumab or pembrolizumab
 Dr Bendell	Beyond third line — nivolumab	 Dr Venook	Would not recommend an anti-PD-1/PD-L1 antibody
 Dr Ciombor	Would not recommend an anti-PD-1/PD-L1 antibody	 Dr Wainberg	Would not recommend an anti-PD-1/PD-L1 antibody

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy if any would you generally recommend an anti-PD-1/PD-L1 antibody (with or without chemotherapy) for a 65-year-old patient with metastatic HER2-negative, MSS adenocarcinoma of the GEJ with a PD-L1 CPS of 5?

1. First line
2. Second line
3. Third line
4. Beyond third line
5. I would not recommend an anti-PD-1/PD-L1 antibody

Regulatory and reimbursement issues aside, in which line of therapy would you generally recommend an anti-PD-1/PD-L1 antibody (with or without chemotherapy) for a 65-year-old patient with metastatic HER2-negative, MSS adenocarcinoma of the GEJ with a PD-L1 CPS of 5?

 Prof Arnold	First line — pembrolizumab or nivolumab with CAPOX/FOLFOX	 Dr Grothey	First line — nivolumab/FOLFOX
 Dr Bekaii-Saab	First line — nivolumab/FOLFOX	 Dr O'Reilly	First line — nivolumab/FOLFOX
 Dr Bendell	First line — nivolumab/FOLFOX	 Dr Venook	First line — nivolumab or pembrolizumab + FOLFOX
 Dr Ciombor	First line — nivolumab/FOLFOX	 Dr Wainberg	First line — nivolumab + FOLFOX or CAPOX

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally recommend an anti-PD-1/PD-L1 antibody (with or without chemotherapy) for a 65-year-old patient with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 0%?

 Prof Arnold	Second line — nivolumab	 Dr Grothey	Would not recommend an anti-PD-1/PD-L1 antibody
 Dr Bekaii-Saab	First line — pembrolizumab/ FOLFOX	 Dr O'Reilly	First line — pembrolizumab/ FOLFOX
 Dr Bendell	First line — pembrolizumab/ FOLFOX	 Dr Venook	Second line — nivolumab or pembrolizumab
 Dr Ciombor	Would not recommend an anti-PD-1/PD-L1 antibody	 Dr Wainberg	First line — pembrolizumab + 5-FU/platinum

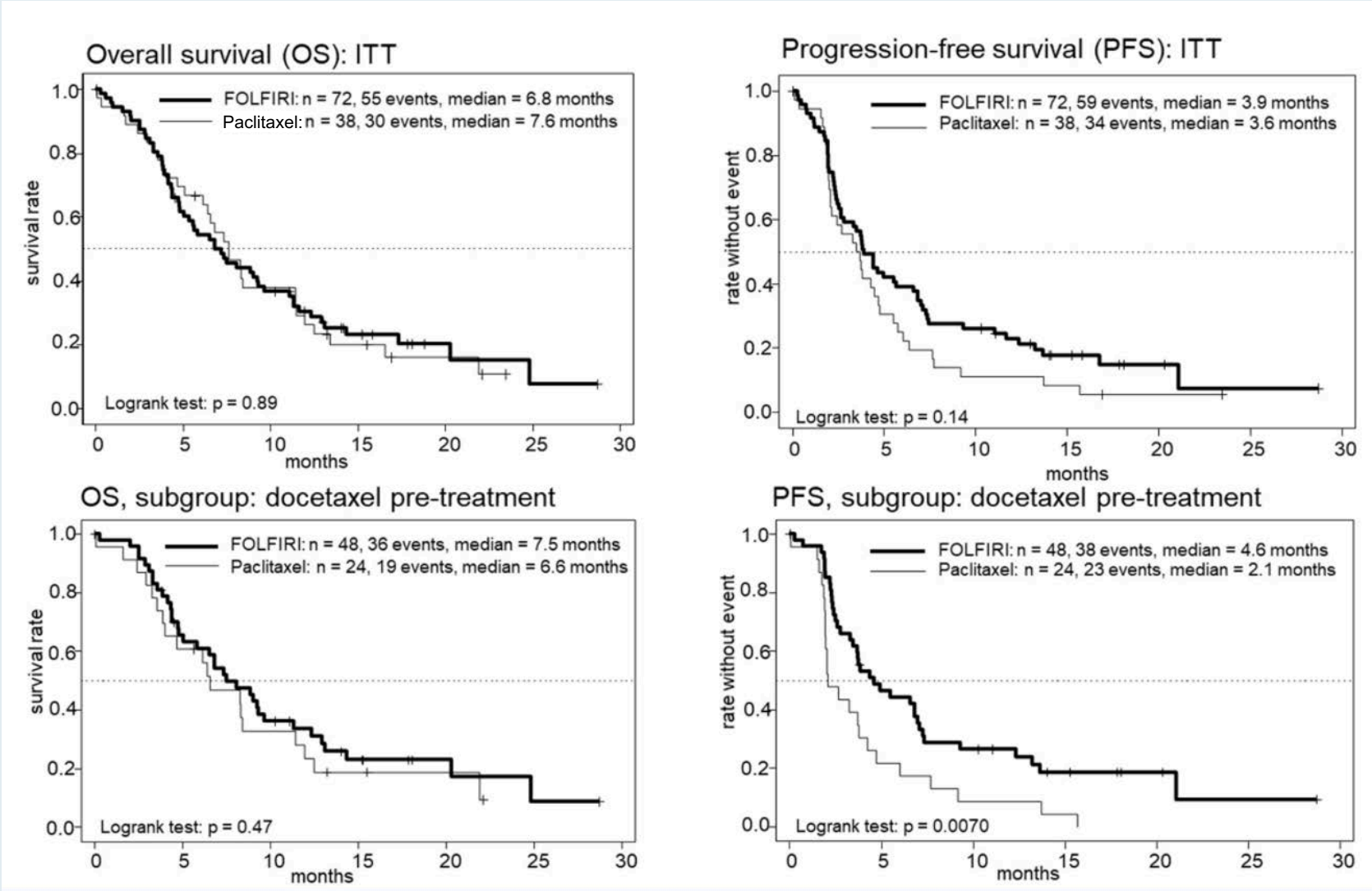
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally recommend an anti-PD-1/PD-L1 antibody (with or without chemotherapy) for a 65-year-old patient with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 5?

 Prof Arnold	First line — pembrolizumab + platinum-based chemo with taxane or 5-FU	 Dr Grothey	Second line — pembrolizumab
 Dr Bekaii-Saab	First line — pembrolizumab/ FOLFOX	 Dr O'Reilly	First line – Pembrolizumab/ FOLFOX
 Dr Bendell	First line — pembrolizumab/ FOLFOX	 Dr Venook	Second line — nivolumab or pembrolizumab
 Dr Ciombor	Second line — nivolumab	 Dr Wainberg	First line — pembrolizumab + 5-FU/platinum

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.

RTP RESEARCH TO PRACTICE

FDA Approves Pembrolizumab 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.

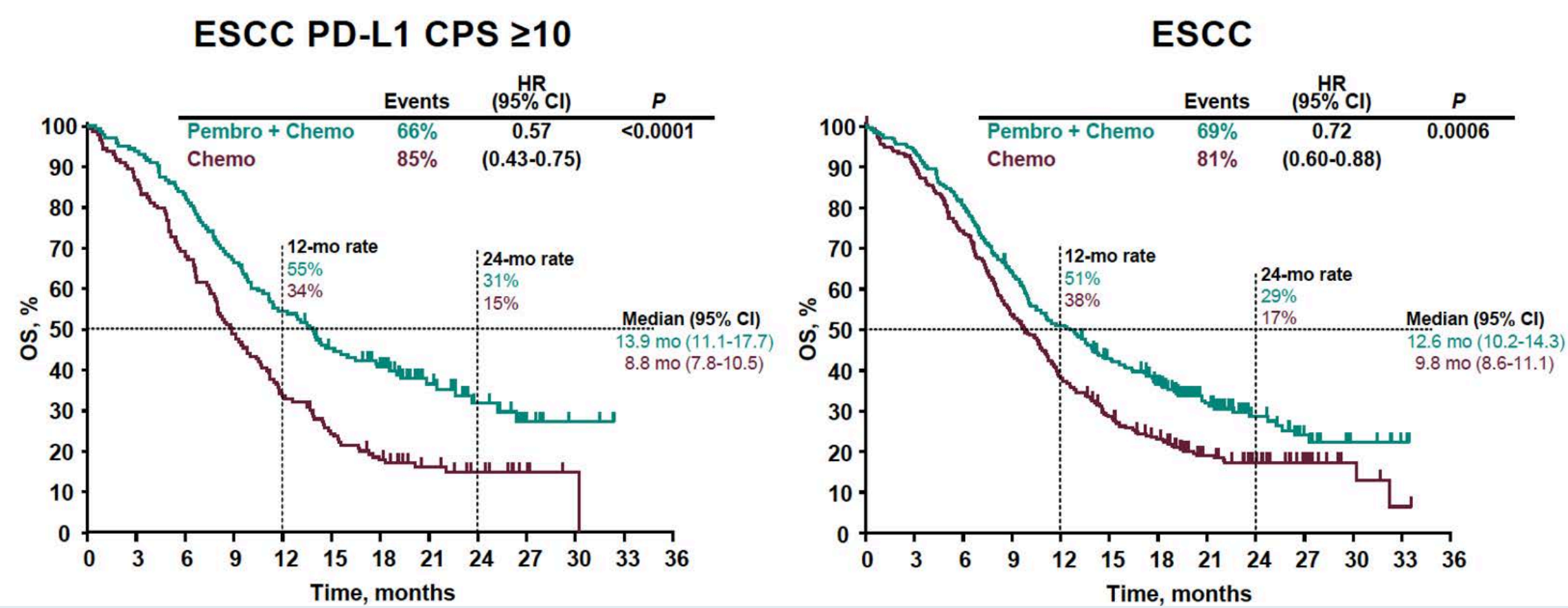
The recommended pembrolizumab dose for esophageal cancer is 200 mg every 3 weeks or 400 mg every 6 weeks."

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

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.

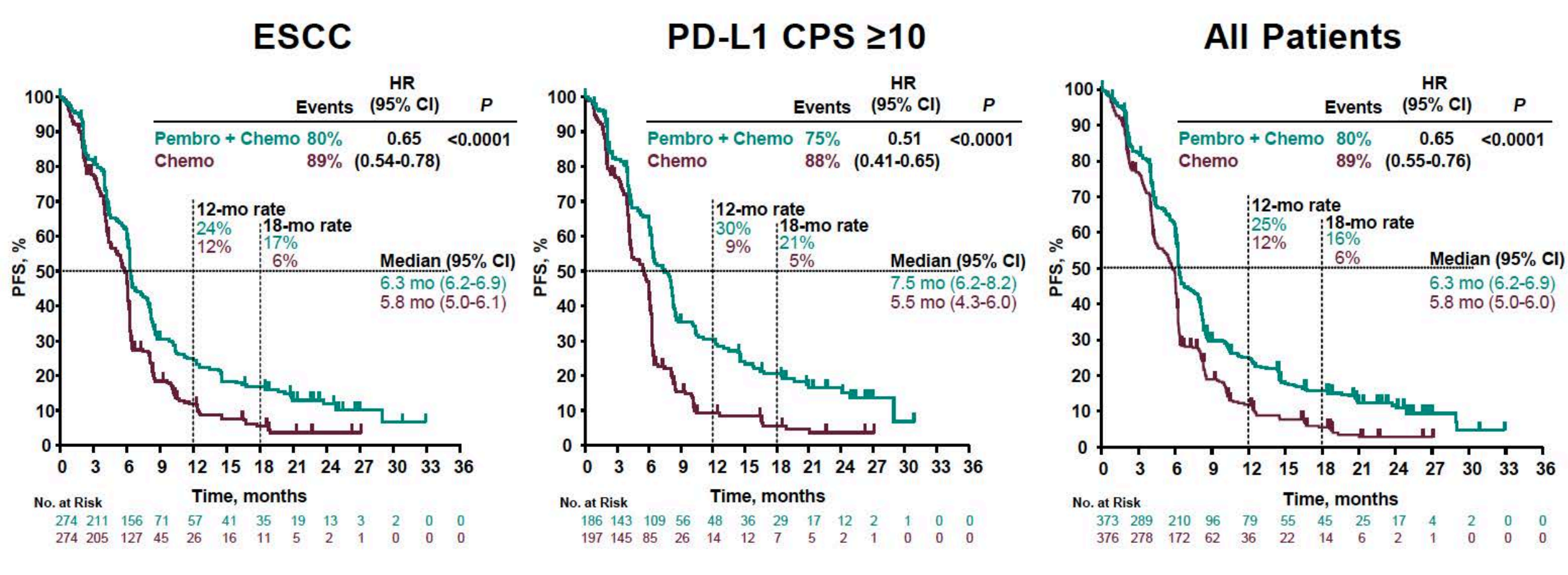
KEYNOTE-590: Overall Survival



Median OS	Pembro + Chemo	Chemo	HR (*p*-value)
All patients	12.4 mo	9.8 mo	0.73 (<0.0001)
PD-L1 CPS ≥ 10	13.5 mo	9.4 mo	0.62 (<0.0001)

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

Positive Topline Results Announced from CheckMate 648 Study: Nivolumab with Chemotherapy and Nivolumab with Ipilimumab Demonstrate Superior Survival Benefit

Press Release – April 8, 2021

Positive topline results were announced from the Phase III CheckMate 648 trial evaluating treatment with nivolumab and chemotherapy or nivolumab and ipilimumab compared to chemotherapy alone for patients with unresectable advanced or metastatic esophageal squamous cell carcinoma.

"In the study, nivolumab plus chemotherapy demonstrated a statistically significant and clinically meaningful benefit for the primary and secondary endpoints of overall survival in patients whose tumors express PD-L1 and in the all-randomized patient population at the pre-specified interim analysis. Additionally, nivolumab plus chemotherapy demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of progression-free survival by blinded independent central review (BICR) in patients whose tumors express PD-L1.

Nivolumab plus ipilimumab also met its primary and secondary endpoints by demonstrating statistically significant and clinically meaningful improvement in overall survival in patients whose tumors express PD-L1 and in the all-randomized population. Nivolumab plus ipilimumab did not meet its other primary endpoint of progression-free survival by BICR in patients whose tumors express PD-L1."

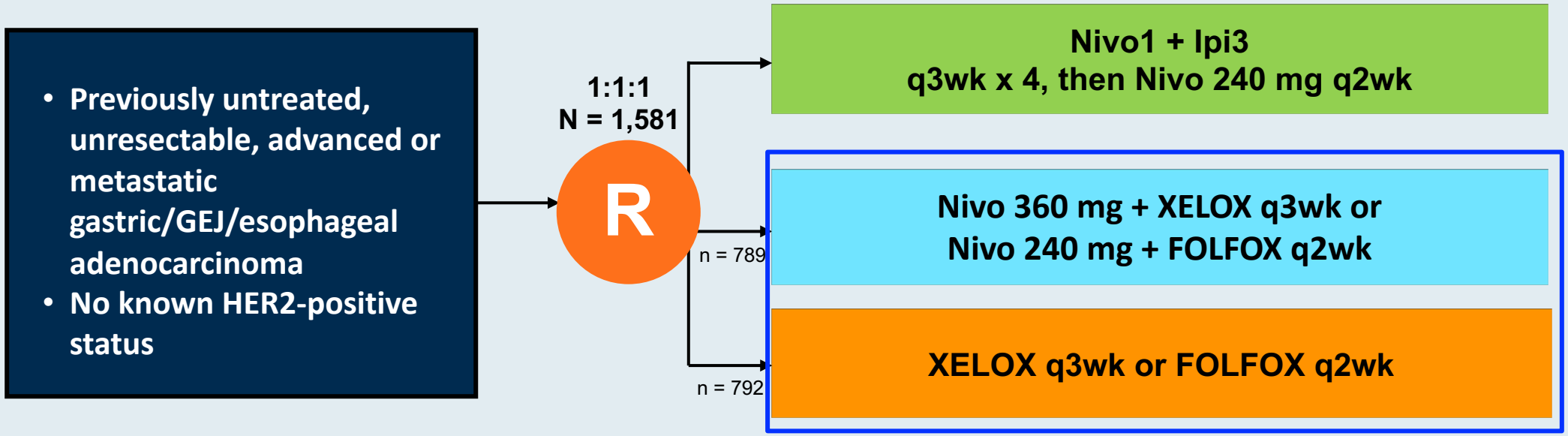
https://news.bms.com/news/corporate-financial/2021/Bristol-Myers-Squibb-Announces-Opdivo-nivolumab-plus-Chemotherapy-and-Opdivo-plus-Yervoy-ipilimumab-Demonstrate-Superior-Survival-Benefit-Compared-to-Chemotherapy-in-Unresectable-Advanced-or-Metastatic-Esophageal-Squamous-Cell-Carcinoma/default.aspx

Nivolumab (Nivo) plus Chemotherapy (Chemo) versus Chemo as First-Line (1L) Treatment for Advanced Gastric Cancer/Gastroesophageal Junction Cancer (GC/GEJC)/Esophageal Adenocarcinoma (EAC): First Results of the CheckMate 649 Study

Moehler M et al.

ESMO 2020;Abstract LBA6.

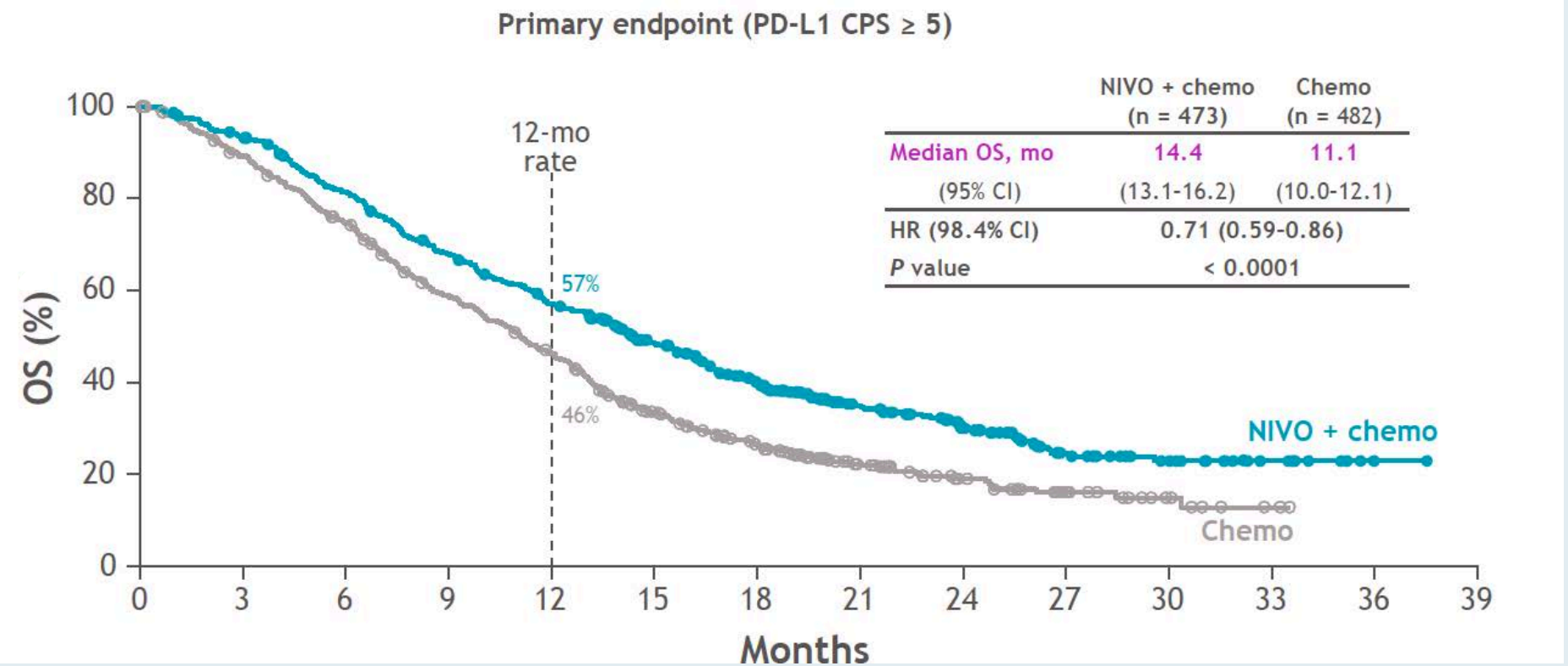
CheckMate 649 Phase III Schema



Co-Primary Endpoints
Progression-free survival (PFS),
Overall survival (OS)

Moehler M et al. ESMO 2020;Abstract LBA6.

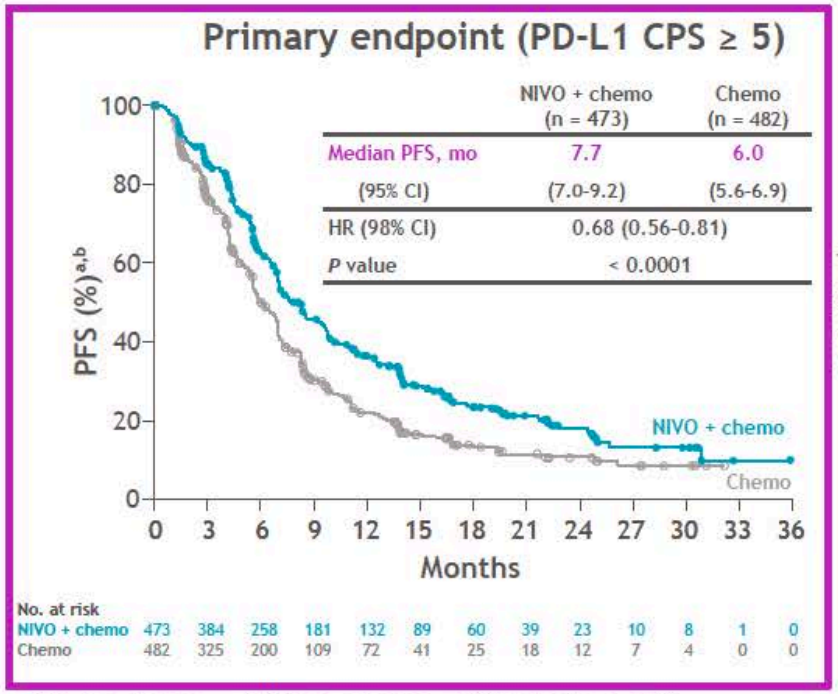
CheckMate 649: Overall Survival



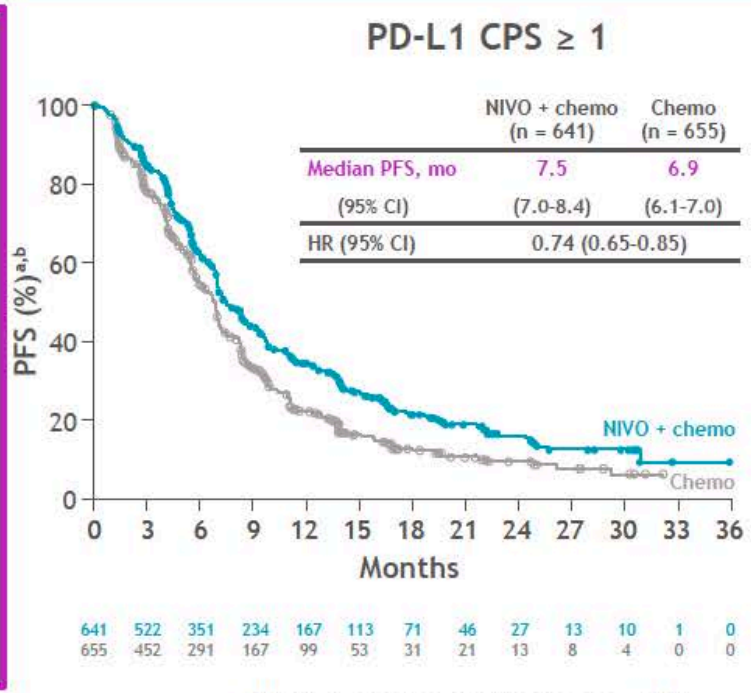
Median OS	Nivo + Chemo (n = 641)	Chemo (n = 655)	HR (*p*-value)
PD-L1 CPS ≥ 1	14.0 mo	11.3 mo	0.77 (0.0001)
All treated patients	13.8 mo	11.6 mo	0.80 (0.0002)

Moehler M et al. ESMO 2020;Abstract LBA6.

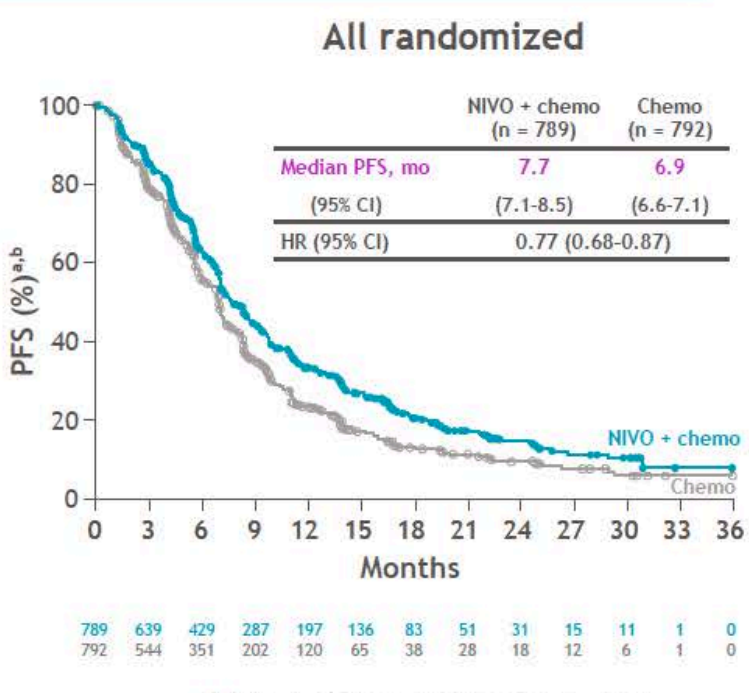
CheckMate 649: Progression-Free Survival



12-mo rate: NIVO + chemo, 36%; chemo, 22%



NIVO + chemo, 34%; chemo, 22%



NIVO + chemo, 33%; chemo, 23%

Moehler M et al. ESMO 2020;Abstract LBA6.

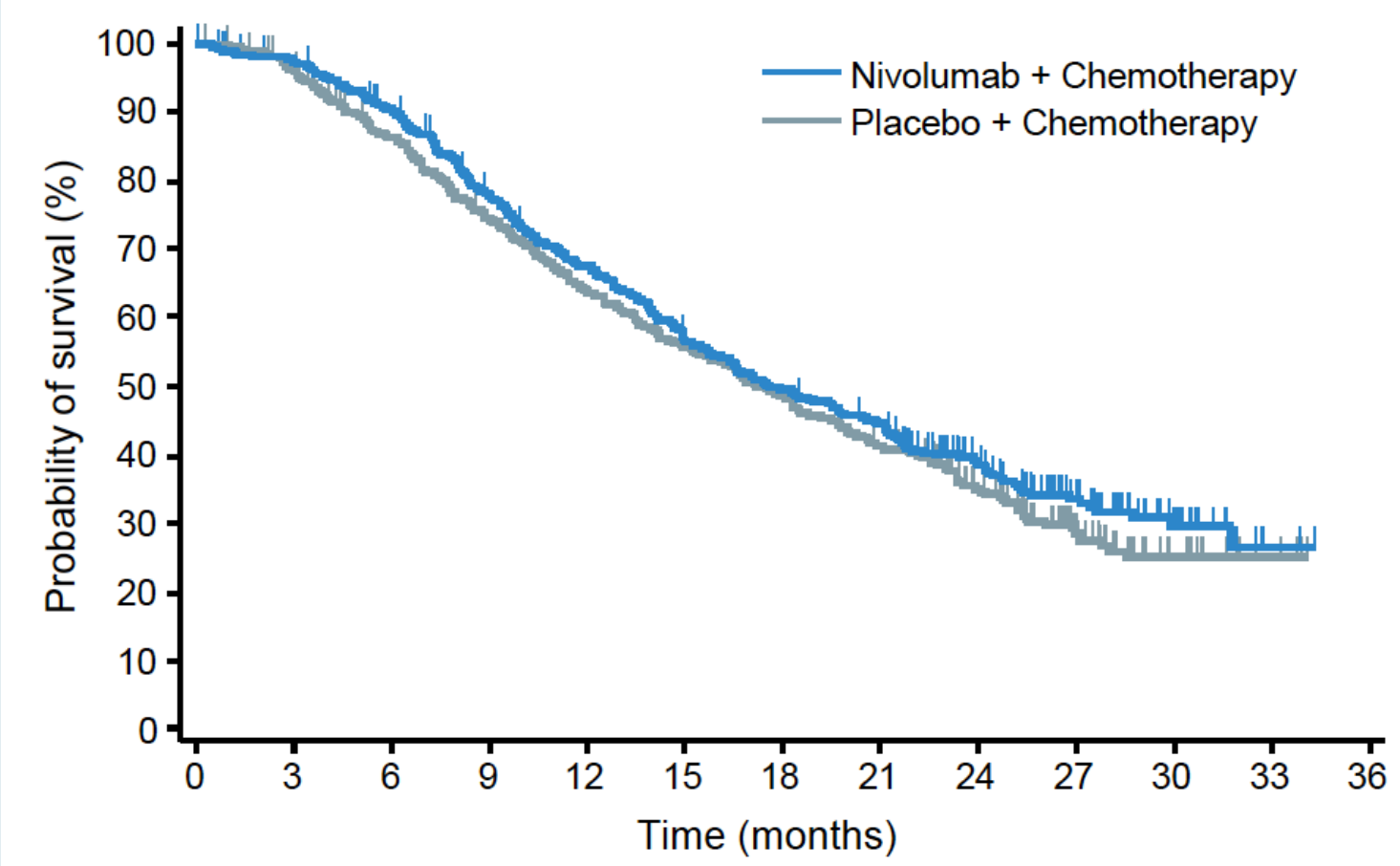
RTP RESEARCH TO PRACTICE

Nivolumab plus Chemotherapy versus Chemotherapy Alone in Patients with Previously Untreated Advanced or Recurrent Gastric/Gastroesophageal Junction (G/GEJ) Cancer: ATTRACTION-4 (ONO-4538-37) Study

Boku N et al.

ESMO 2020;Abstract LBA7_PR.

ATTRACTION-4: Final Analysis of OS



	Nivo + chemo (n = 362)	Placebo + chemo (n = 362)	HR (*p*-value)
Median OS	17.45 mo	17.15 mo	0.90 (0.257)

Boku N et al. ESMO 2020;Abstract LBA7_PR.

RTP RESEARCH TO PRACTICE

Meet The Professor with Prof Arnold

MODULE 1: Case from Dr Schafer

- An 82-year-old woman with mismatch repair-deficient metastatic colorectal cancer – BRAF V600E mutation (Parts 1 and 2)

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

MODULE 3: Case from Dr Rupard

- A 79-year-old woman with metastatic gastroesophageal junction cancer and a prolonged response to ramucirumab but with proteinuria (Parts 1 and 2)

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

MODULE 5: Case from Dr Ciombor

- A 58-year-old man with Child-Pugh A hepatocellular carcinoma and bleeding hemangioma of the hard palate (Parts 1 and 2)

MODULE 6: Beyond the Guidelines; Key Data – Hepatocellular Carcinoma

MODULE 7: Gastrointestinal Cancers Journal Club with Prof Arnold

MODULE 8: Recent Data Sets

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Case Presentation – Dr Ciombor: A 58-year-old man with Child-Pugh A HCC and bleeding hemangioma of the hard palate (Part 1)

Dr Kristen Ciombor

- PMH: Treated hepatitis C, cirrhosis
- HCC screening: AFP 995, asymptomatic
  - MRI abdomen: Several new liver lesions, portal vein tumor thrombus
  - Incidental diagnosis (biopsy-proven): Hemangioma of hard palate
- Concerns regarding anti-VEGF therapy due to bleeding hemangioma

Case Presentation – Dr Ciombor: A 58-year-old man with Child-Pugh A HCC and bleeding hemangioma of the hard palate (Part 2)

Dr Kristen Ciombor

- PMH: Treated hepatitis C, cirrhosis → HCC screening: AFP 995, asymptomatic
  - MRI abdomen: Several new liver lesions, portal vein tumor thrombus
  - Incidental diagnosis (biopsy-proven): Hemangioma of hard palate
- ***Nivolumab, with SD***
  - ***3 months later: Major CVA requiring tissue plasminogen activator (tPA); recovered with rehab***
- ***Resumed nivolumab x 1 year***
  - ***Grade 3 autoimmune hepatitis (resolved with steroids), discontinued nivolumab***
- ***Subsequent MRI: Ongoing decrease in liver lesions, AFP nadir 6***
- ***Nivolumab "holiday" x 20 months***

Questions

- ***Currently he's doing very well on his IO holiday, but if his disease progresses what would you do next? Would you feel comfortable in the setting of a prior Grade 3 autoimmune hepatitis rechallenging him? Now that he's a couple of years out from his stroke would you feel comfortable going to the anti-VEGF therapy?***

RTP RESEARCH TO PRACTICE

Meet The Professor with Prof Arnold

MODULE 1: Case from Dr Schafer

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MODULE 8: Recent Data Sets

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would be your current preferred first-line systemic treatment for a 65-year-old patient with HCC, a Child-Pugh A score and a PS of 0?

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

What would be your current preferred first-line systemic treatment for a 65-year-old patient with hepatocellular carcinoma (HCC), a Child-Pugh A score and a performance status (PS) of 0?

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

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, 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?

1. Sorafenib
2. Lenvatinib
3. Cabozantinib
4. Atezolizumab/bevacizumab
5. Chemotherapy
6. 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 Grothey	Atezolizumab/ bevacizumab
 Dr Bekaii-Saab	Atezolizumab/ bevacizumab	 Dr O'Reilly	Lenvatinib
 Dr Bendell	Atezolizumab/ bevacizumab	 Dr Venook	Atezolizumab/ bevacizumab
 Dr Ciombor	Sorafenib	 Dr Wainberg	Lenvatinib

RTP RESEARCH TO PRACTICE

What would be your second-line therapy for a 65-year-old patient with HCC, a Child-Pugh B7 score and PS 1 who received first-line atezolizumab/bevacizumab and experienced disease progression after 14 months (AFP 2,500 ng/mL)?

1. Cabozantinib
2. Lenvatinib
3. Anti-PD-1 antibody
4. Nivolumab/ipilimumab
5. Ramucirumab
6. Regorafenib
7. Sorafenib
8. Other

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 4 months and then experienced disease progression (AFP 2,500 ng/mL)?

 Prof Arnold	Nivolumab	 Dr Grothey	Atezolizumab/ bevacizumab
 Dr Bekaii-Saab	Atezolizumab/ bevacizumab	 Dr O'Reilly	Nivolumab/ ipilimumab
 Dr Bendell	Atezolizumab/ bevacizumab	 Dr Venook	Atezolizumab/ bevacizumab
 Dr Ciombor	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 lenvatinib with minimal toxicity, had stable disease for 14 months and then experienced disease progression (AFP 2,500 ng/mL)?

 Prof Arnold	Cabozantinib	 Dr Grothey	Atezolizumab/ bevacizumab
 Dr Bekaii-Saab	Atezolizumab/ bevacizumab	 Dr O'Reilly	Atezolizumab/ bevacizumab
 Dr Bendell	Atezolizumab/ bevacizumab	 Dr Venook	Atezolizumab/ bevacizumab
 Dr Ciombor	Atezolizumab/ bevacizumab	 Dr Wainberg	Nivolumab

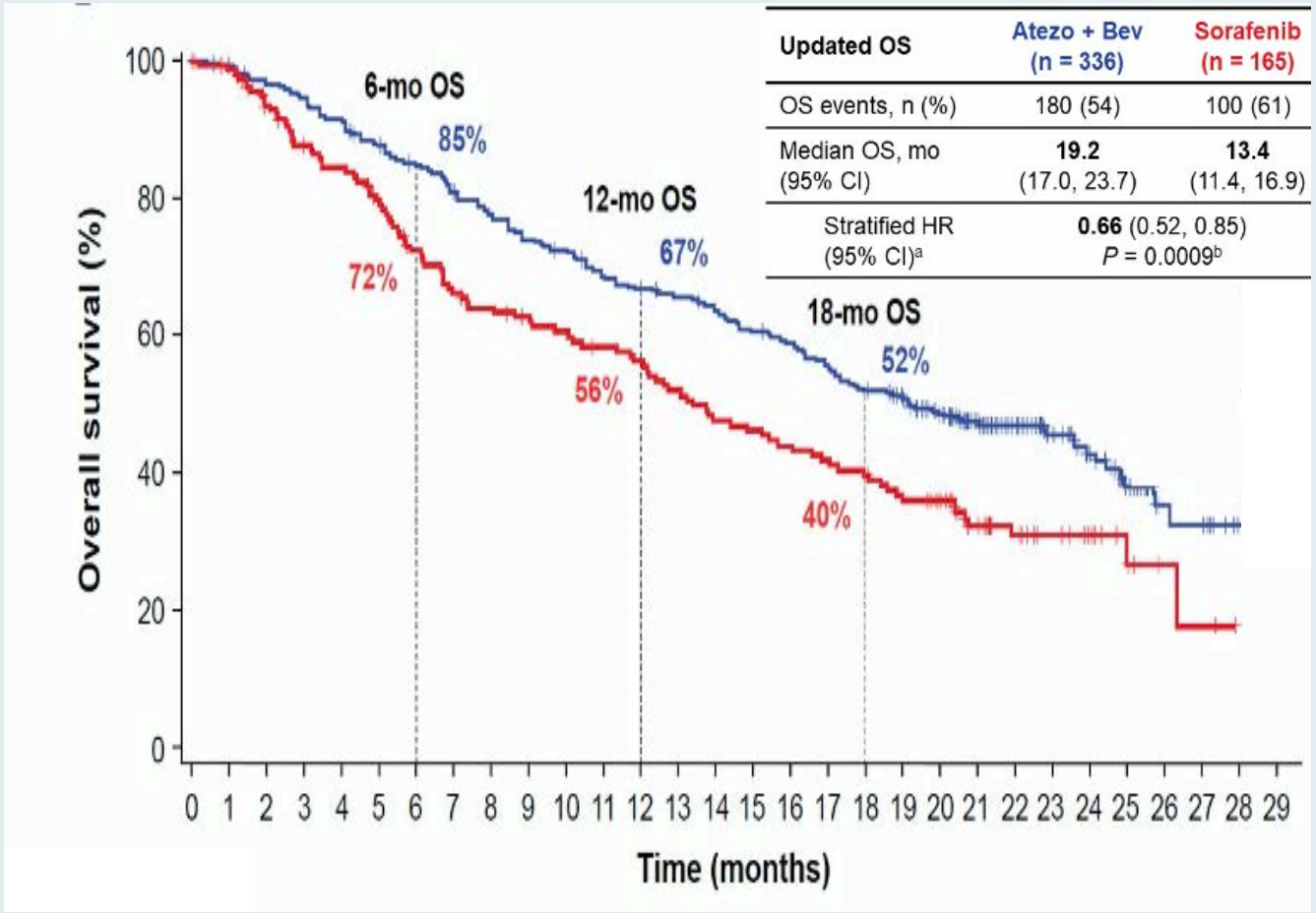
RTP RESEARCH TO PRACTICE

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)

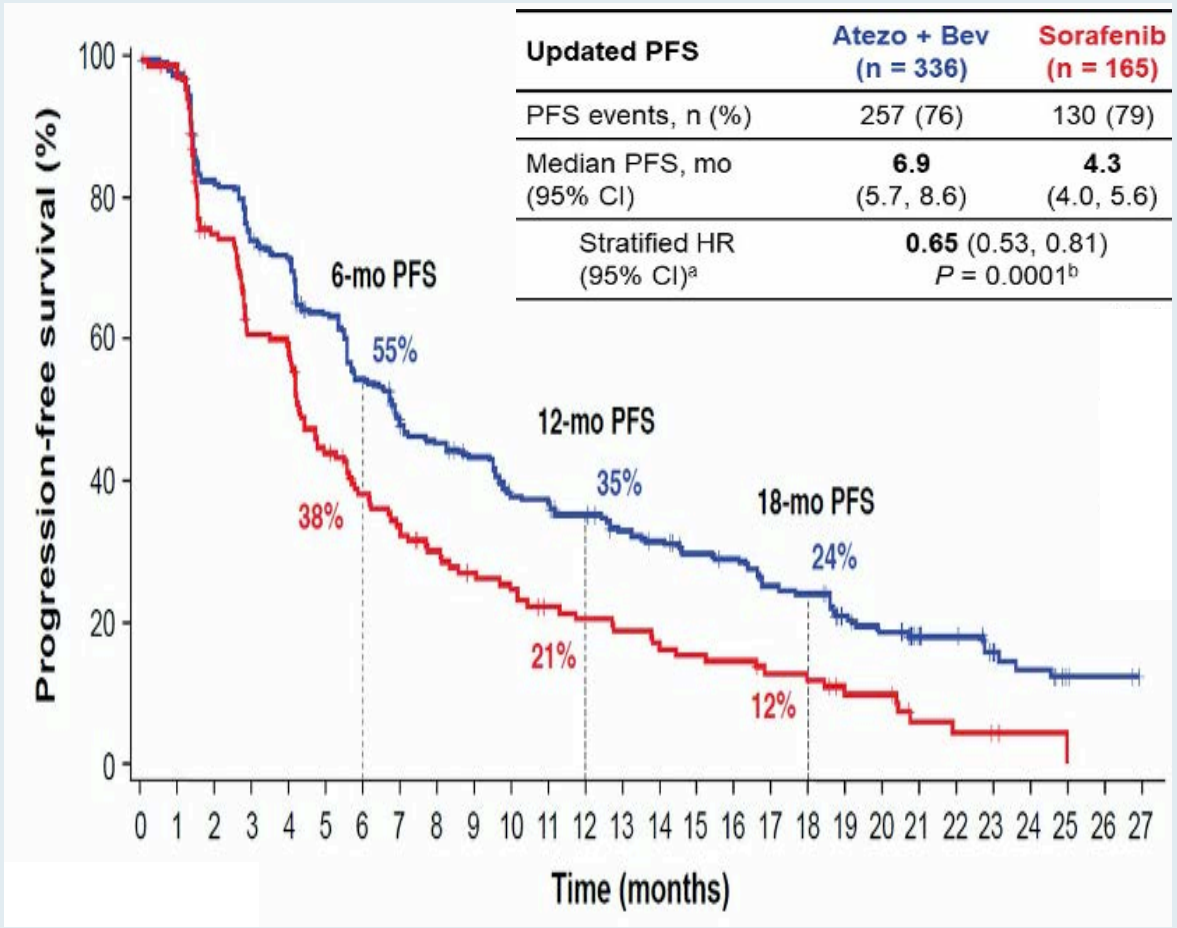
Finn RS et al.

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.

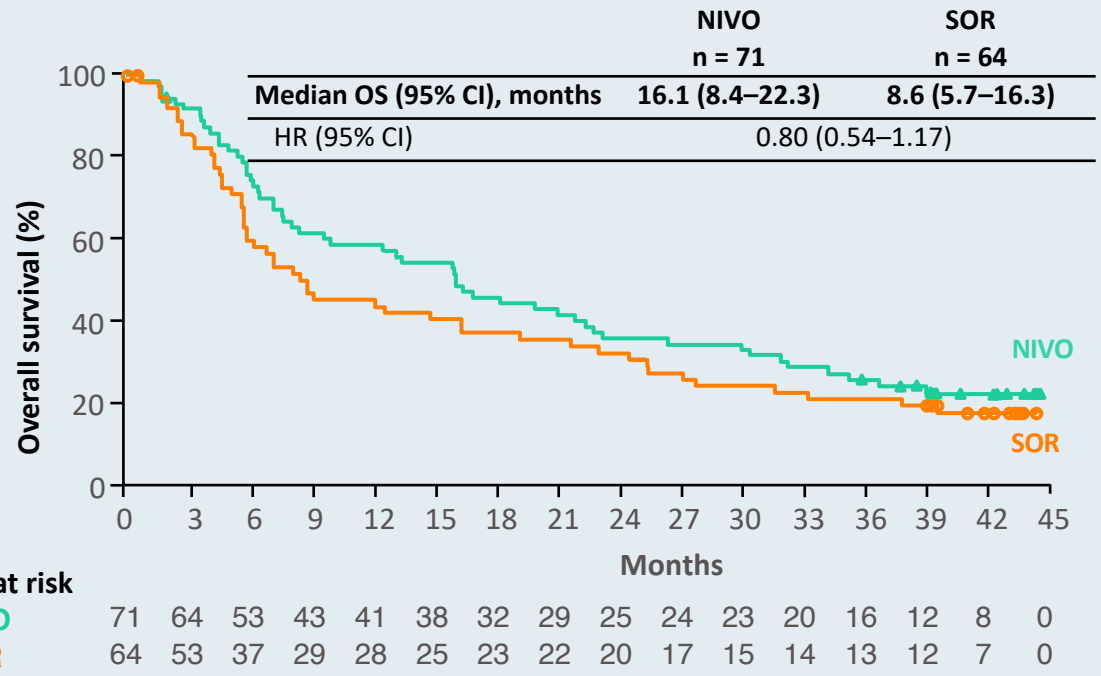
RTP RESEARCH TO PRACTICE

CheckMate 459: Long-Term Efficacy Outcomes with Nivolumab versus Sorafenib as First-line Treatment in Patients with Advanced Hepatocellular Carcinoma

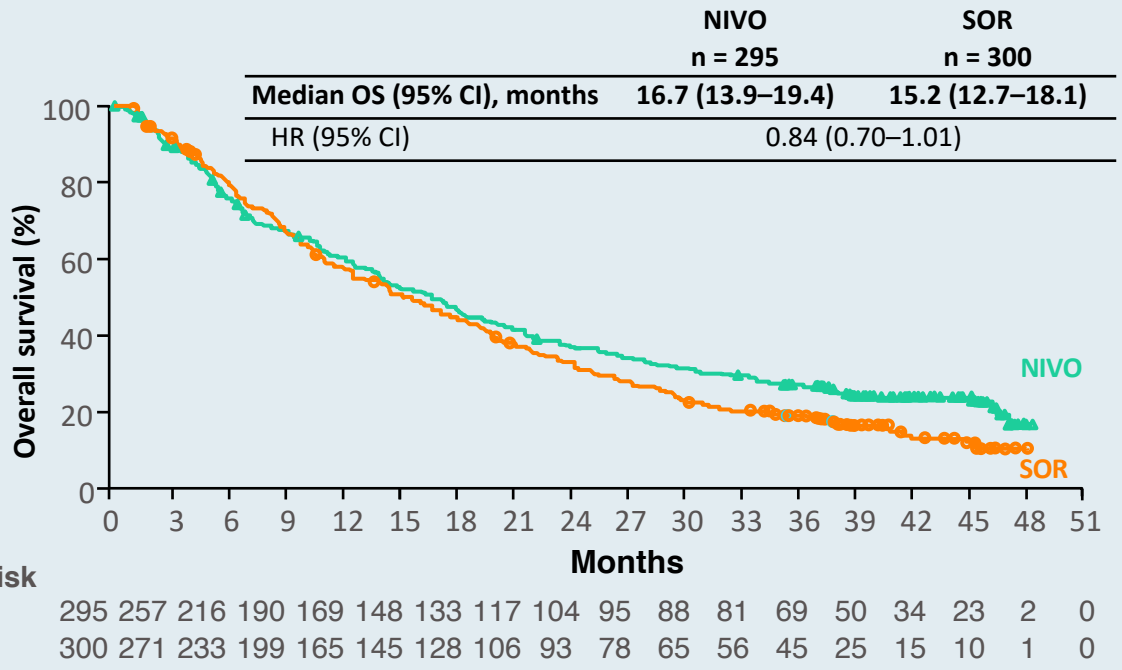
Sangro B et al.
ESMO World GI Congress 2020;Abstract LBA-3.

CheckMate 459: Overall Survival by PD-L1 Expression with First-Line Sorafenib in Advanced HCC

Tumor cell PD-L1 expression ≥ 1%



Tumor cell PD-L1 expression < 1%



- OS in the PD-L1 ≥ 1% group was longer in the NIVO arm compared to the SOR arm

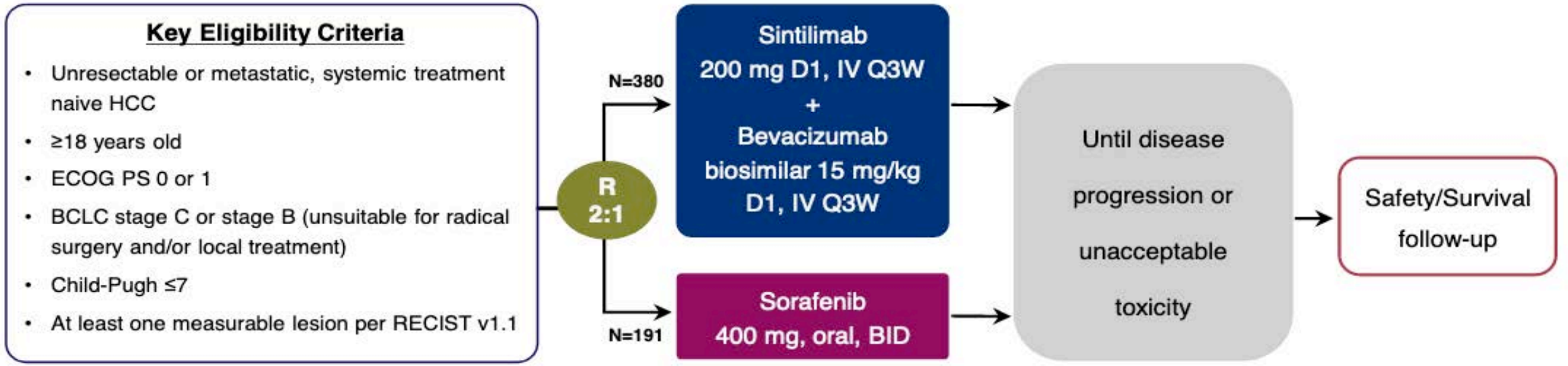
Sangro B et al. ESMO World GI Congress 2020;Abstract LBA-3.

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.

Phase III ORIENT-32 Trial of Sintilimab plus Bevacizumab Biosimilar vs Sorafenib as First-Line Therapy for Advanced HCC



Stratification factors

- **Macrovascular invasion** (MVI) **and/or extrahepatic metastasis** (EHS) (yes/no)
- **Baseline alpha fetoprotein** (AFP; < 400 / ≥400 ng/mL)
- **ECOG PS** (0/1)

Co-primary endpoints

- OS
- PFS by independent radiologic review committee (IRRC) per RECIST v1.1

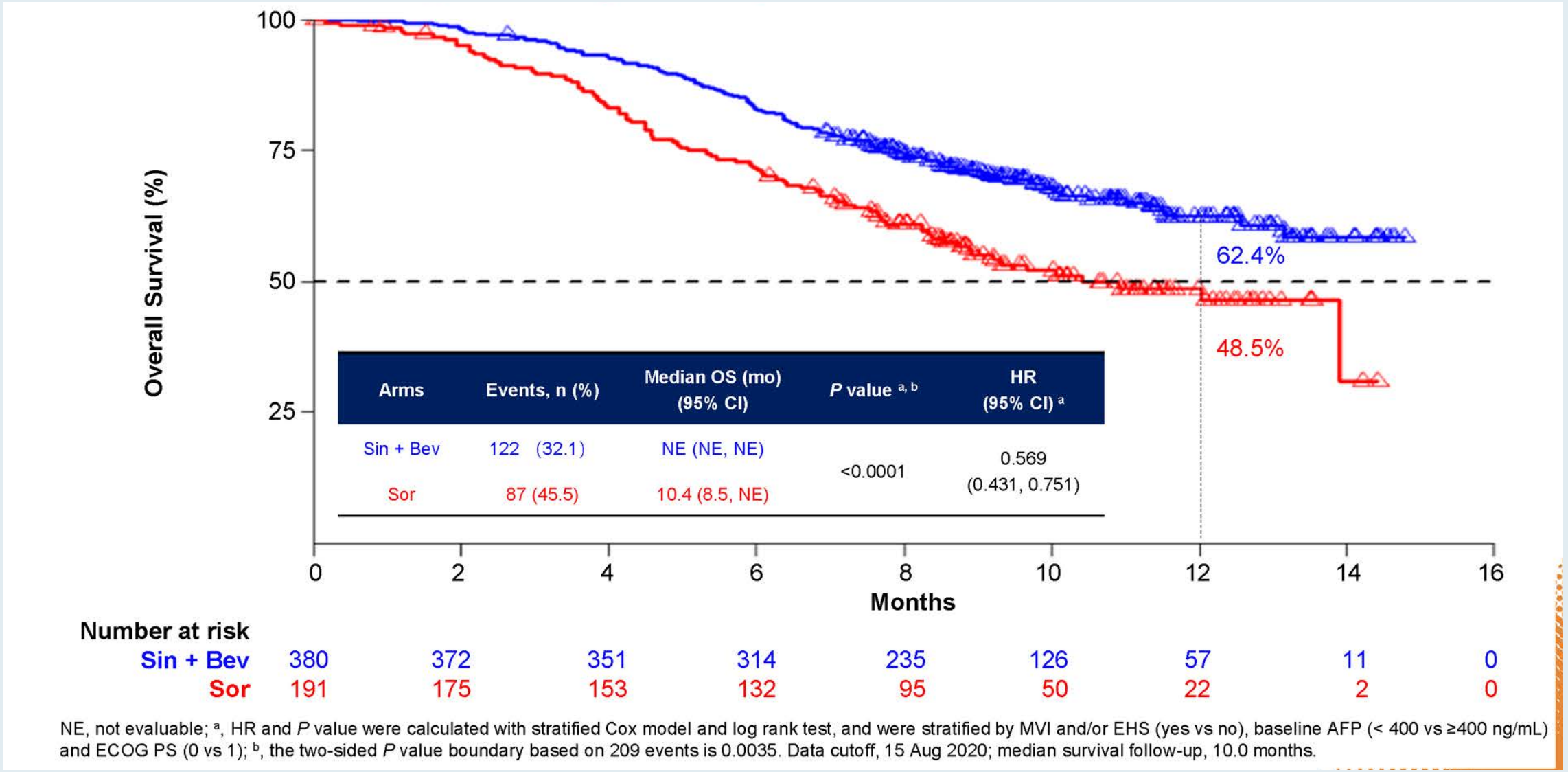
Key secondary endpoints

- PFS by investigator per RECIST v1.1
- ORR by IRRC and investigator per RECIST v1.1
- ORR by IRRC per HCC mRECIST

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

RTP RESEARCH TO PRACTICE

ORIENT-32 Coprimary Endpoint: Overall Survival



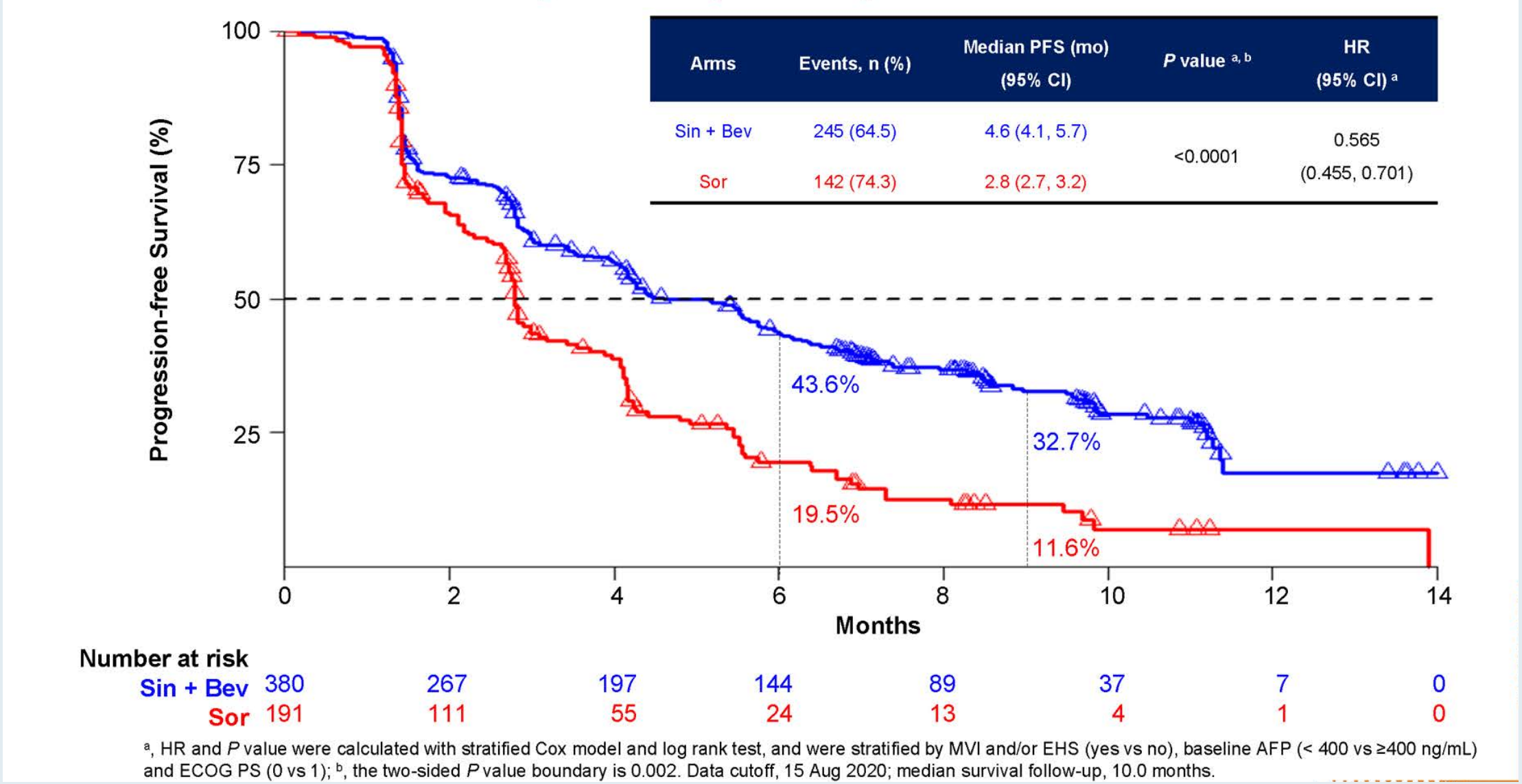
NE, not evaluable; [a], HR and *P* value were calculated with stratified Cox model and log rank test, and were stratified by MVI and/or EHS (yes vs no), baseline AFP (< 400 vs ≥400 ng/mL) and ECOG PS (0 vs 1); [b], the two-sided *P* value boundary based on 209 events is 0.0035. Data cutoff, 15 Aug 2020;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

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]
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)		

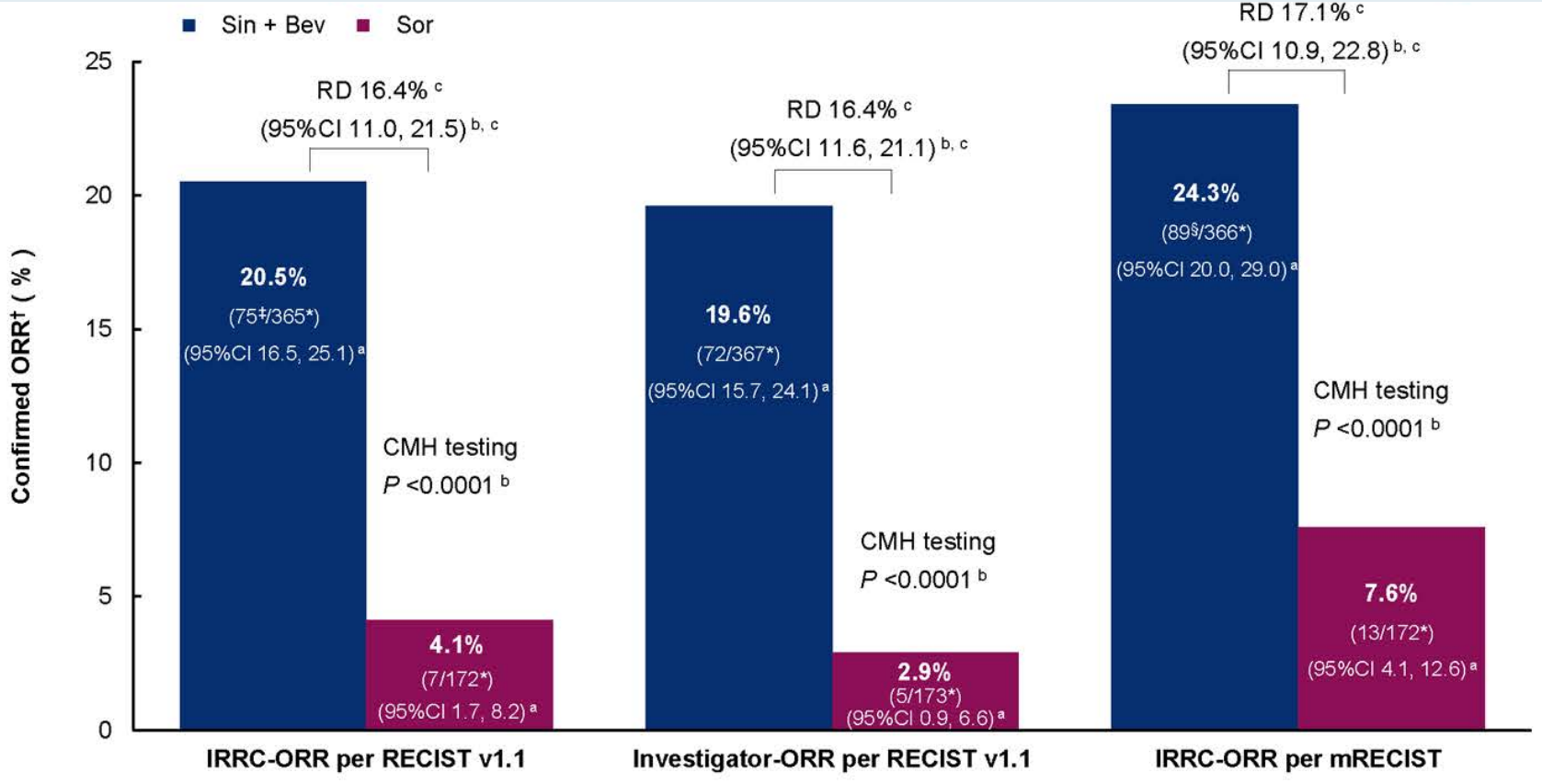
Number at risk								
Sin + Bev	380	267	197	144	89	37	7	0
Sor	191	111	55	24	13	4	1	0

[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.

ORIENT-32: Response Rate and Duration of Response



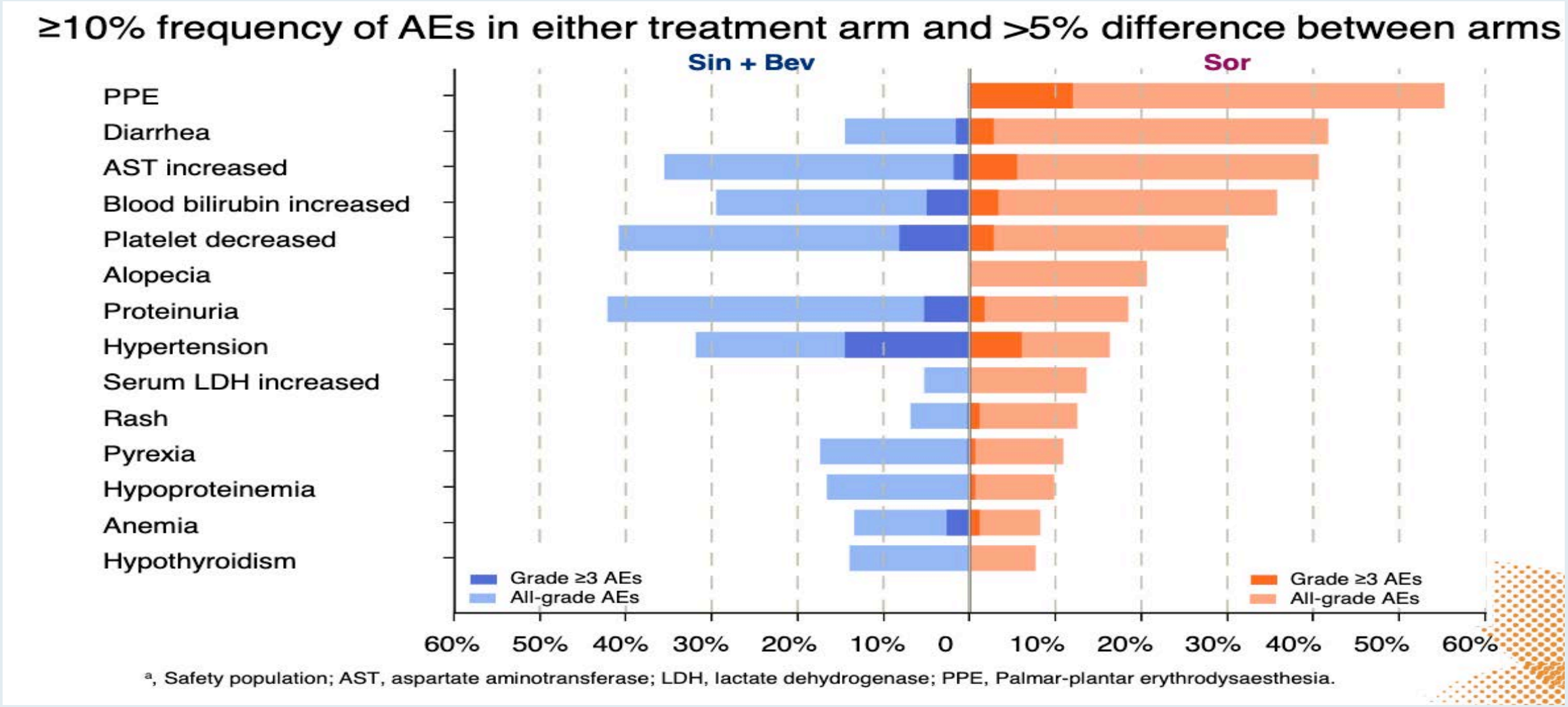
Median DOR, months	**NE**	**9.8**	**NE**	**NE**	**NE**	**6.6**
(95% CI)	(NE, NE)	(2.8, NE)	(NE, NE)	(2.5, NE)	(8.2, NE)	(2.6, NE)

*, response-evaluable population
†, defined as a response (complete or partial) confirmed by two consecutive tumor assessments with at least 28-day interval
‡, 3 subjects who had 2 consecutive partial responses (PRs) cross cutoff date were included
§, 2 patients who had 2 consecutive PRs cross cutoff date were included

a, 95% CI was calculated using Clopper-Pearson method
b, the stratification factors included MVI and/or EHS (yes vs. no), AFP (< 400 vs ≥400 ng/mL) and ECOG PS (0 vs 1)
c, RD, rate difference = $ORR_{Sin+Bev} - ORR_{Sor}$, and was calculated using stratified M-N method
NE, not evaluable.

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

ORIENT-32: Safety



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

Meet The Professor with Prof Arnold

MODULE 1: Case from Dr Schafer

- An 82-year-old woman with mismatch repair-deficient metastatic colorectal cancer – BRAF V600E mutation (Parts 1 and 2)

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

MODULE 3: Case from Dr Rupard

- A 79-year-old woman with metastatic gastroesophageal junction cancer and a prolonged response to ramucirumab but with proteinuria (Parts 1 and 2)

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

MODULE 5: Case from Dr Ciombor

- A 58-year-old man with Child-Pugh A hepatocellular carcinoma and bleeding hemangioma of the hard palate (Parts 1 and 2)

MODULE 6: Beyond the Guidelines; Key Data – Hepatocellular Carcinoma

MODULE 7: Gastrointestinal Cancers Journal Club with Prof Arnold

MODULE 8: Recent Data Sets

RTP RESEARCH TO PRACTICE

Neoadjuvant Chemoradiation (CRT) for Locally Advanced Rectal Cancer (LARC) with or without Oxaliplatin (OX): Individual Patient Data (IPD) Meta-analysis of Three Randomized Controlled Trials (RCTs) with Subgroup Analyses of Age Cohorts

Fontana E et al.

ASCO 2020;Abstract 4074.

European Journal of Cancer 144 (2021) 281–290

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Quality of life in rectal cancer patients with or without oxaliplatin in the randomised CAO/ARO/AIO-04 phase 3 trial

Rebekka Kosmala [a,*], Emmanouil Fokas [b,c,d,e], Michael Flentje [a], Rolf Sauer [g], Torsten Liersch [k], Ullrich Graeven [f], Rainer Fietkau [g], Werner Hohenberger [h], Dirk Arnold [i], Ralf-Dieter Hofheinz [j], Michael Ghadimi [k], Philipp Ströbel [l], Ludger Staib [m], Gerhard G. Grabenbauer [n], Gunnar Folprecht [q], Simon Kirste [o], Wolfgang Uter [p], Christine Gall [p], Claus Rödel [b,c,d,e], Bülent Polat [a,**] on behalf of the German Rectal Cancer Study Group

Survival Outcomes Among Older Adults (OA) Receiving Second-Line Therapy for Metastatic CRC (mCRC): 5,289 Patients (pts) from the ARCAD Clinical Trials Program

McCleary NJ et al.
ASCO 2020;Abstract 7009.

ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Microsatellite instability (MSI-H) is associated with a high immunoscore but not with PD-L1 expression or increased survival in patients (pts.) with metastatic colorectal cancer (mCRC) treated with oxaliplatin (ox) and fluoropyrimidine (FP) with and without bevacizumab (bev): a pooled analysis of the AIO KRK 0207 and RO91 trials

Stefanie Noepel-Duennebacke[1] · Hendrik Juette[2] · Karsten Schulmann[3] · Ulrich Graeven[4] · Rainer Porschen[5] · Jan Stoehlmacher[6] · Susanna Hegewisch-Becker[7] · Arne Raulf[8] · Dirk Arnold[9] · Anke Reinacher-Schick[1] · Aandrea Tannapfel[2]

J Cancer Res Clin Oncol 2021;[Online ahead of print].

Predicting Resistance to First-Line FOLFOX plus Bevacizumab in Metastatic Colorectal Cancer: Final Results of the Multicenter, International PERMAD Trial

Seufferlein T et al.

Gastrointestinal Cancers Symposium;Abstract 115.

Review

Clin Colorectal Cancer 2021;20(1):42-51.e3

Clinical and Regulatory Considerations for the Use of Bevacizumab Biosimilars in Metastatic Colorectal Cancer

Julien Taïeb,[1] Enrique Aranda,[2] Sherif Raouf,[3] Helen Dunn,[4] Dirk Arnold[5]

Oncologist 2020;25(10):e1428-32.

The Oncologist®

Commentary

The Oncology Data Network (ODN): Methodology, Challenges, and Achievements

Ashley Woolmore,[a] Dirk Arnold,[b] Jean-Yves Blay,[c] Christian Buske,[d] Alfredo Carrato,[e] Winald Gerritsen,[f] Marc Peeters,[g] Jesus Garcia-Foncillas,[h] David Kerr[i]

Meet The Professor with Prof Arnold

MODULE 1: Case from Dr Schafer

- An 82-year-old woman with mismatch repair-deficient metastatic colorectal cancer – BRAF V600E mutation (Parts 1 and 2)

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

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MODULE 8: Recent Data Sets

RTP RESEARCH TO PRACTICE

Colorectal Cancer

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FDA Approves Encorafenib in Combination with Cetuximab for Metastatic Colorectal Cancer with a BRAF V600E Mutation

Press Release – April 8, 2020

"On April 8, 2020, the Food and Drug Administration approved encorafenib in combination with cetuximab for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, detected by an FDA-approved test, after prior therapy.

Efficacy was evaluated in a randomized, active-controlled, open-label, multicenter trial (BEACON CRC; NCT02928224). Eligible patients were required to have BRAF V600E mutation-positive metastatic CRC with disease progression after one or two prior regimens.

The recommended encorafenib dose is 300 mg orally once daily in combination with cetuximab."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-encorafenib-combination-cetuximab-metastatic-colorectal-cancer-braf-v600e-mutation

RTP RESEARCH TO PRACTICE

FDA Approves Pembrolizumab for First-Line Treatment of MSI-H/dMMR Colorectal Cancer

Press Release – June 29, 2020

"On June 29, 2020, the Food and Drug Administration approved pembrolizumab for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer.

Approval was based on KEYNOTE-177 (NCT02563002), a multicenter, international, open-label, active-controlled, randomized trial that enrolled 307 patients with previously untreated unresectable or metastatic MSI-H or dMMR colorectal cancer. Determination of MSI or MMR tumor status was made locally using polymerase chain reaction (PCR) or immunohistochemistry (IHC), respectively.

The recommended pembrolizumab dose for MSI-H/dMMR colorectal cancer is 200 mg every 3 weeks or 400 mg every 6 weeks."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-pembrolizumab-first-line-treatment-msi-hdmmr-colorectal-cancer

RTP RESEARCH TO PRACTICE

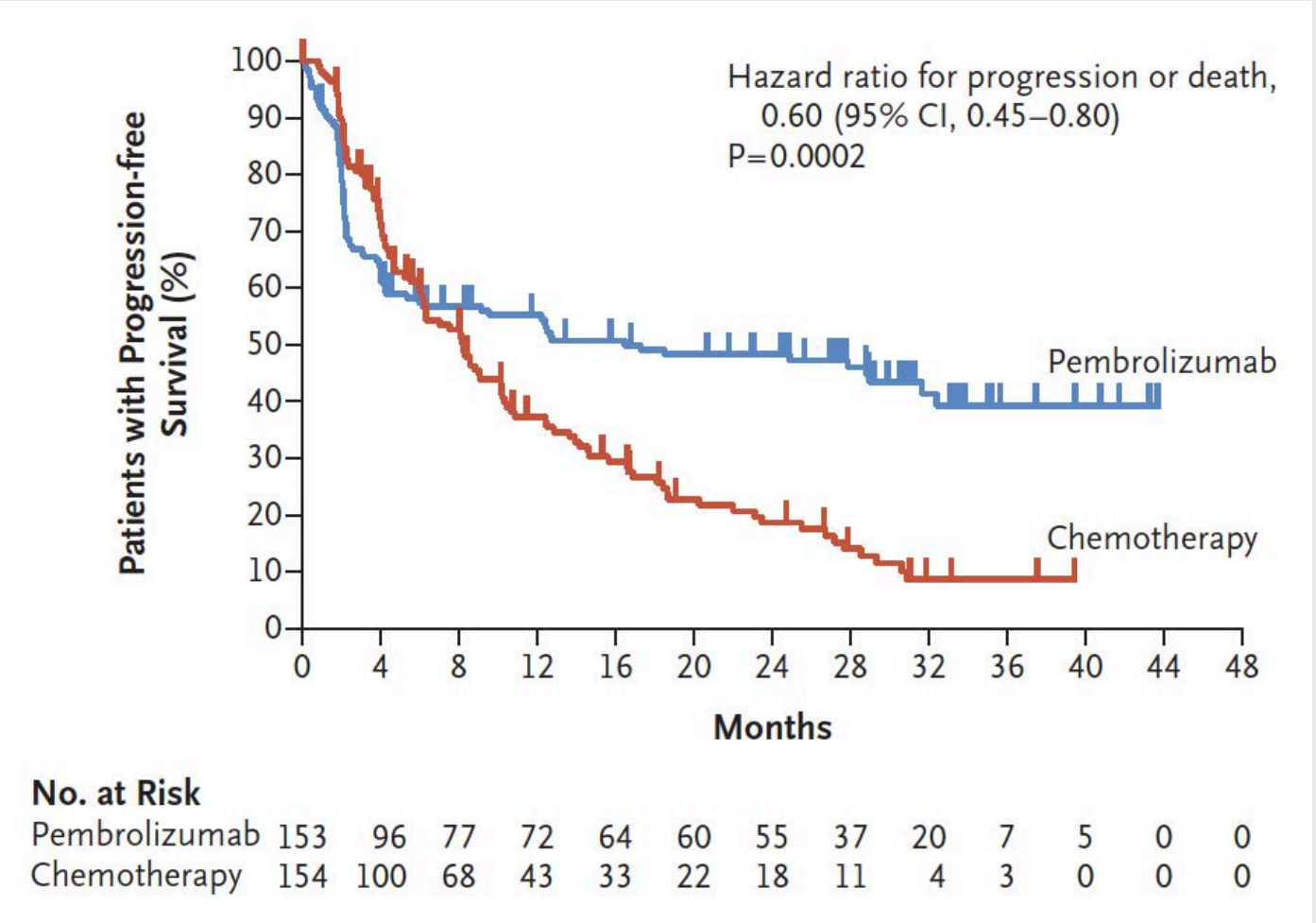
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 3, 2020 VOL. 383 NO. 23

Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

T. André, K.-K. Shiu, T.W. Kim, B.V. Jensen, L.H. Jensen, C. Punt, D. Smith, R. Garcia-Carbonero, M. Benavides, P. Gibbs, C. de la Fouchardiere, F. Rivera, E. Elez, J. Bendell, D.T. Le, T. Yoshino, E. Van Cutsem, P. Yang, M.Z.H. Farooqui, P. Marinello, and L.A. Diaz, Jr., for the KEYNOTE-177 Investigators*

KEYNOTE-177: Primary Survival Endpoints



At the time of data cutoff, data on overall survival were still evolving.

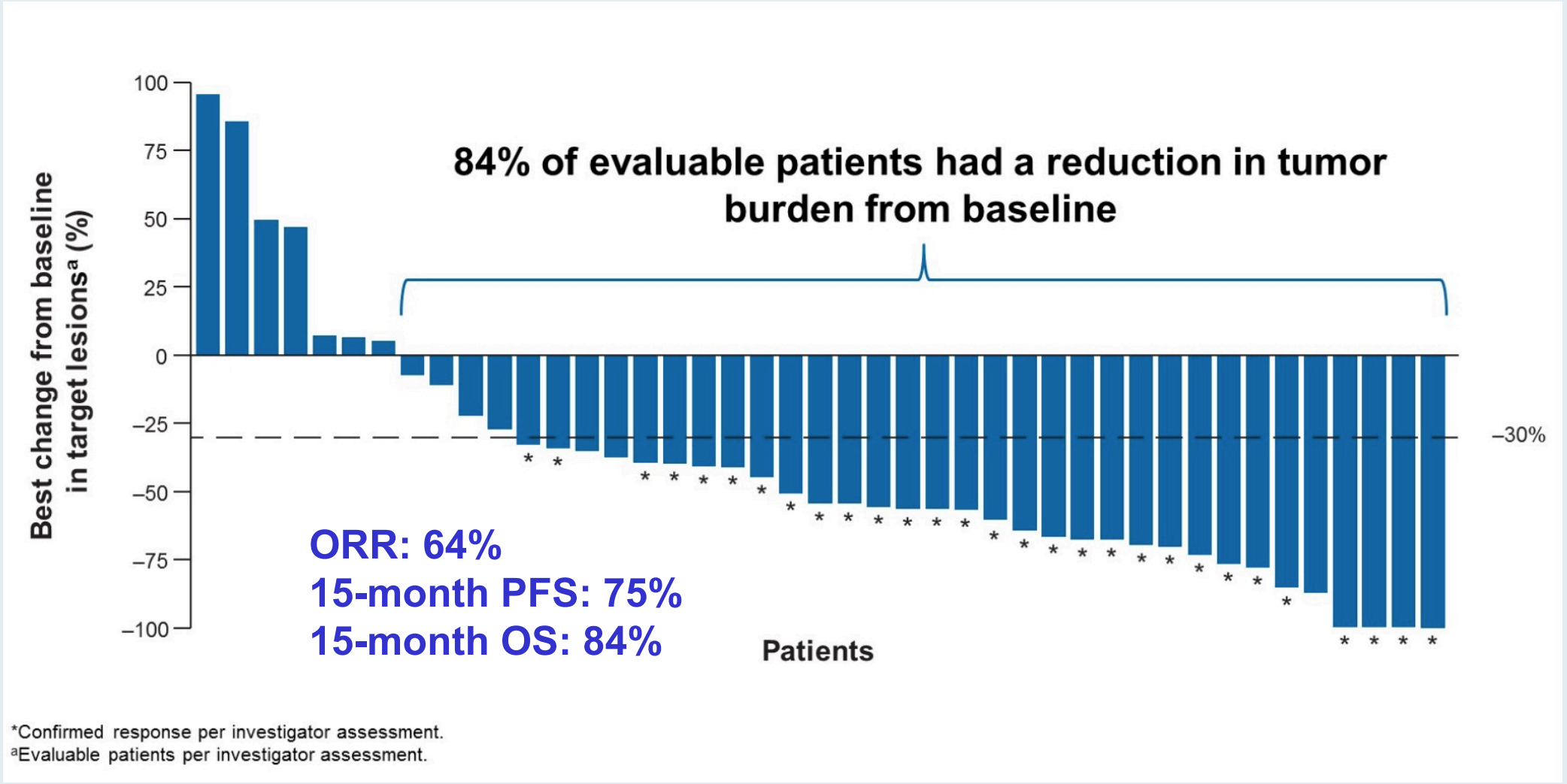
André T et al. *N Engl J Med* 2020;383(23):2207-18.

Nivolumab plus Low-Dose Ipilimumab as First-Line Therapy in Microsatellite Instability-High/DNA Mismatch Repair Deficient mCRC: Clinical Update

Lenz H-J et al.

Gastrointestinal Cancers Symposium 2020;Abstract 11.

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



*Confirmed response per investigator assessment.
[a]Evaluable patients per investigator assessment.

Lenz H-J et al. Gastrointestinal Cancers Symposium 2020;Abstract 11.

RTP RESEARCH TO PRACTICE

A Phase II, Multicenter, Open-Label Study of Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients (pts) with HER2-Expressing Metastatic Colorectal Cancer (mCRC): DESTINY-CRC01

Siena S et al.

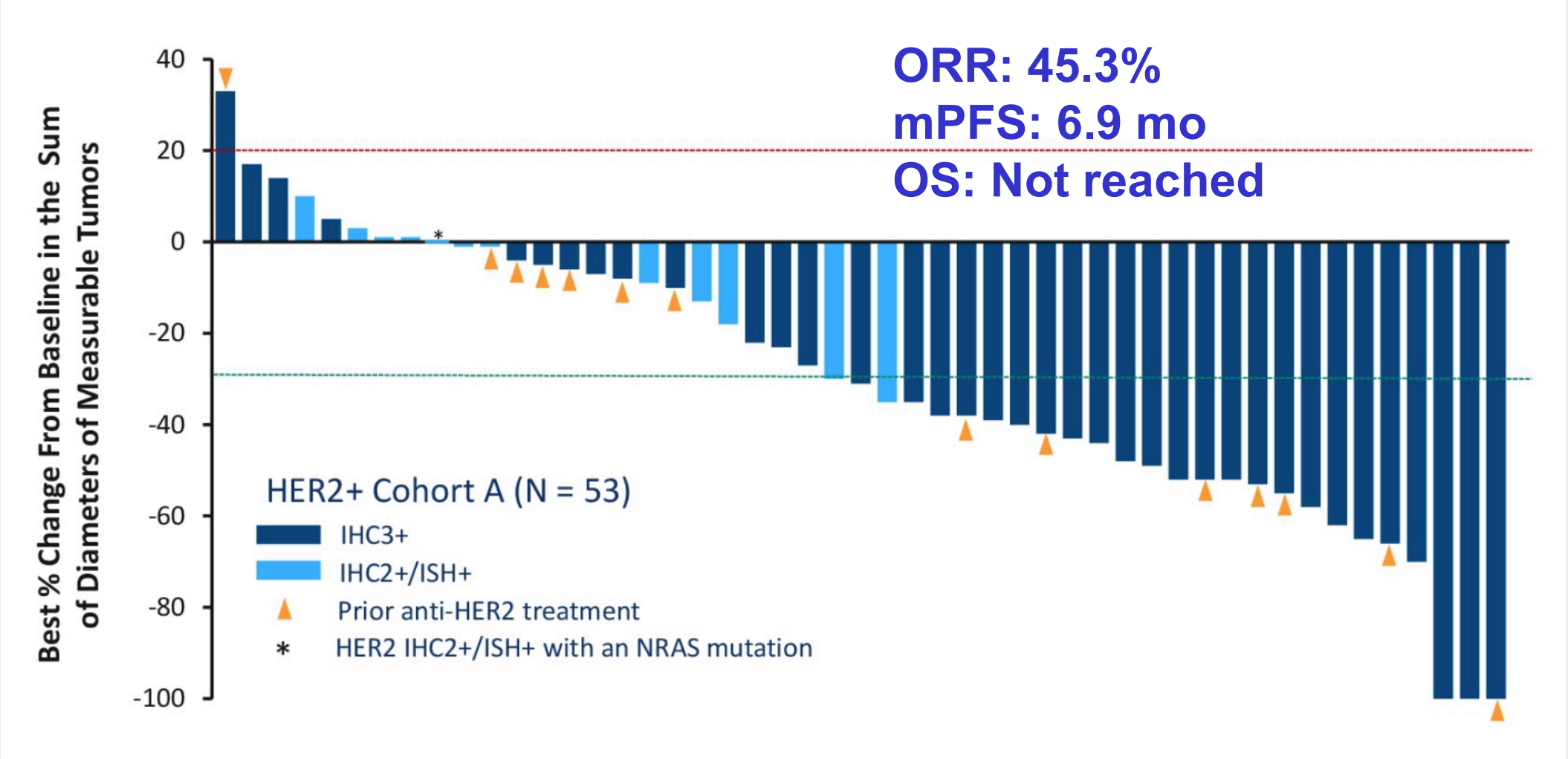
ASCO 2020;Abstract 4000.

DESTINY-CRC01: Response Rates

	HER2+ Cohort A (N = 53)
Confirmed ORR by ICR	**45.3% (n = 24)** (95% CI, 31.6%-59.6%)
CR	1.9% (n = 1)
PR	43.4% (n = 23)
SD	37.7% (n = 20)
PD	9.4% (n = 5)
Not evaluable	7.5% (n = 4)[a]
Disease control rate	83.0% (95% CI, 70.2%-91.9%)
Duration of response, median	Not reached (95% CI, 4.2 months-NE)

Siena S et al. ASCO 2020;Abstract 4000.

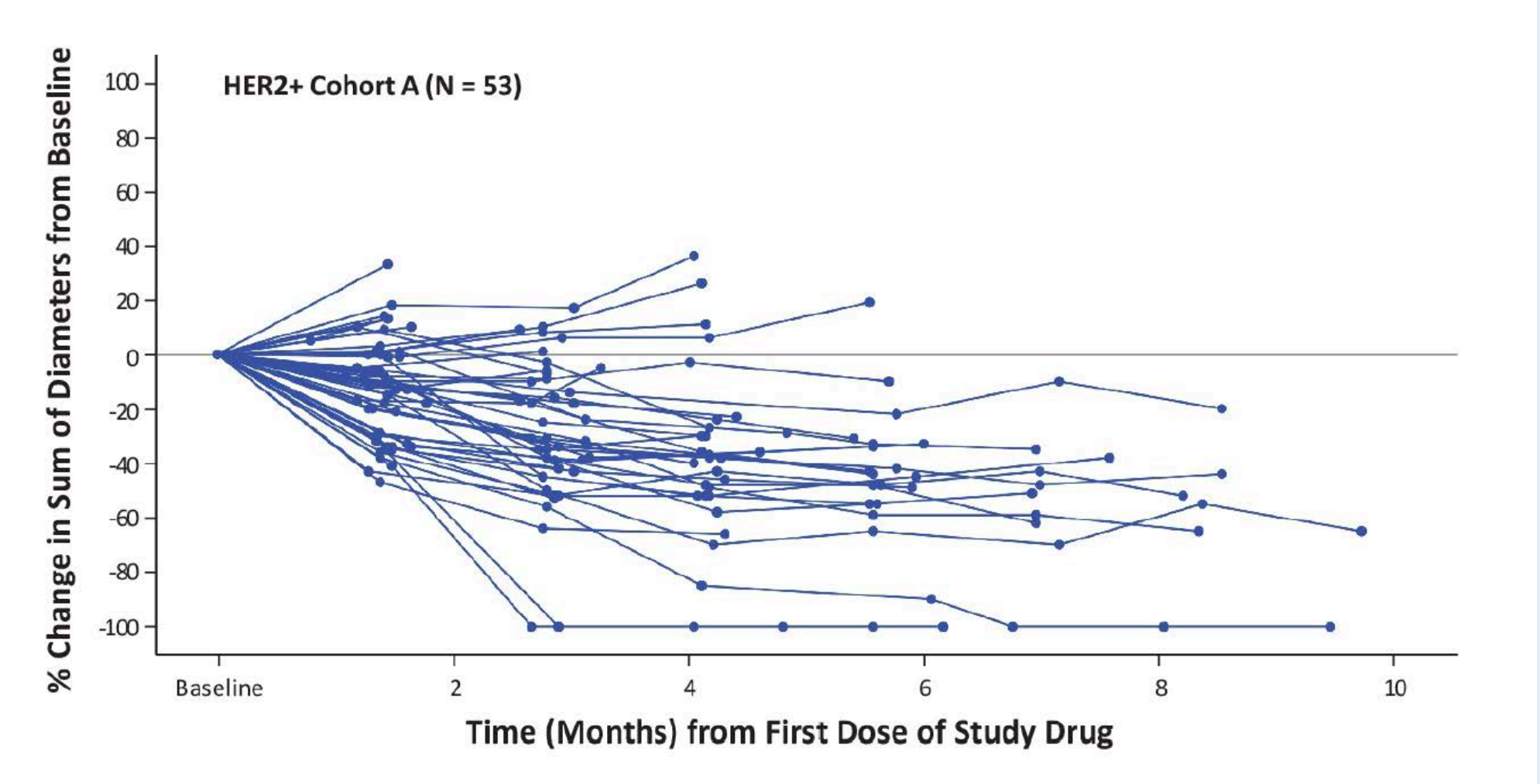
DESTINY-CRC01: Best Change in Tumor Size Over Time



Siena S et al. ASCO 2020;Abstract 4000.

RTP RESEARCH TO PRACTICE

DESTINY-CRC01: Tumor Shrinkage Over Time



Siena S et al. ASCO 2020;Abstract 4000.

DESTINY-CRC01: AEs of Special Interest

	All Patients (N = 78)					
Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial Lung Disease	0	2 (2.6)	1 (1.3)	0	2 (2.6)	5 (6.4)

Among the 5 total events:

- Median time to investigator-reported onset was 80 days (range, 22-132)
- 5 of 5 patients with grade ≥ 2 ILD received corticosteroids
- 2 patients recovered, 1 did not recover (later died due to disease progression), and 2 died
- In the 2 fatal cases, onset was from 40-126 days, both received steroids as part of treatment, and death occurred 6-18 days after diagnosis

Protocol recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected

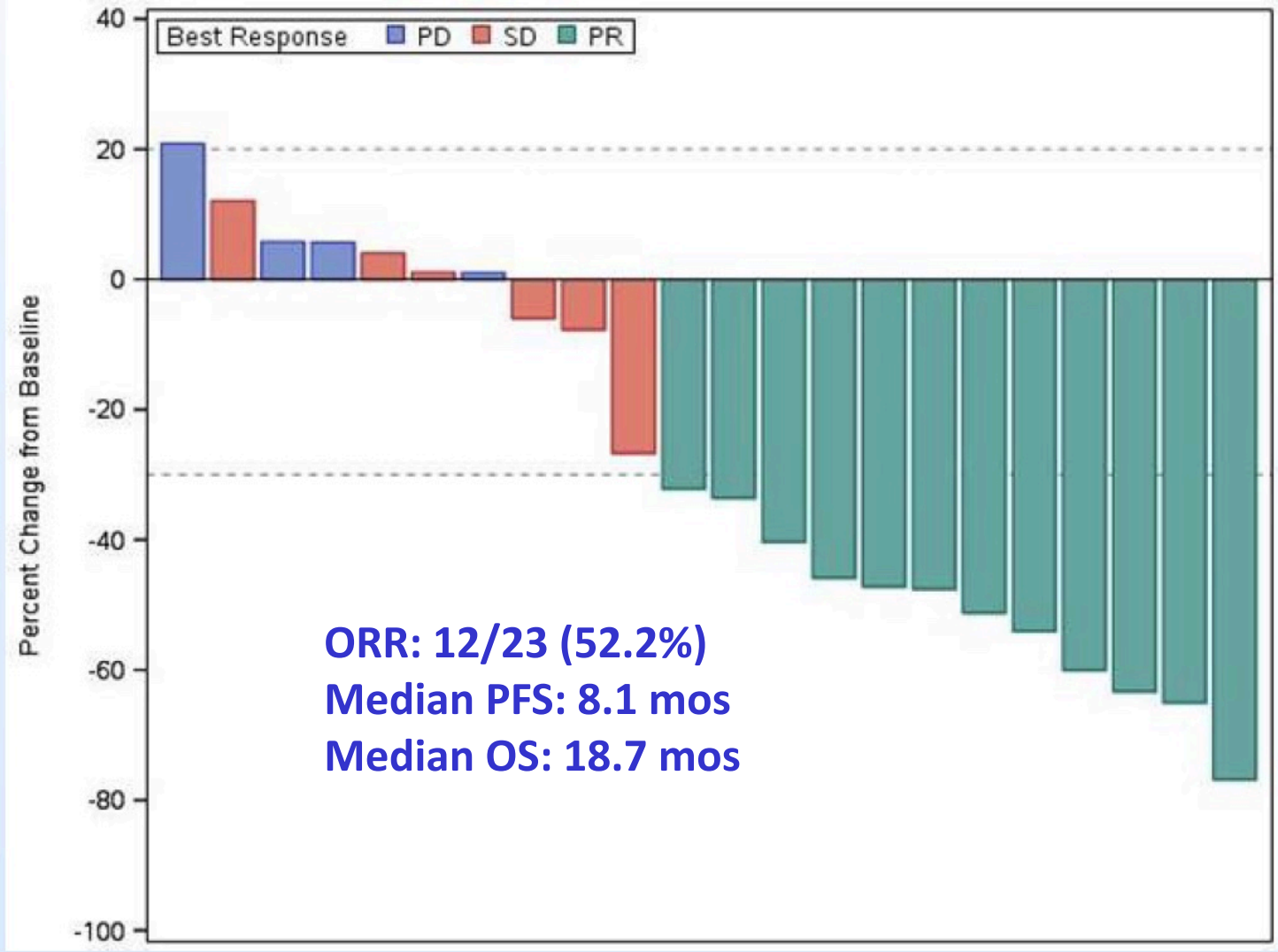
Siena S et al. ASCO 2020;Abstract 4000.

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/Gastroesophageal Cancer

RTP
RESEARCH
TO PRACTICE

Original Investigation

September 3, 2020

Efficacy and Safety of Pembrolizumab or Pembrolizumab Plus Chemotherapy vs Chemotherapy Alone for Patients With First-line, Advanced Gastric Cancer

The KEYNOTE-062 Phase 3 Randomized Clinical Trial

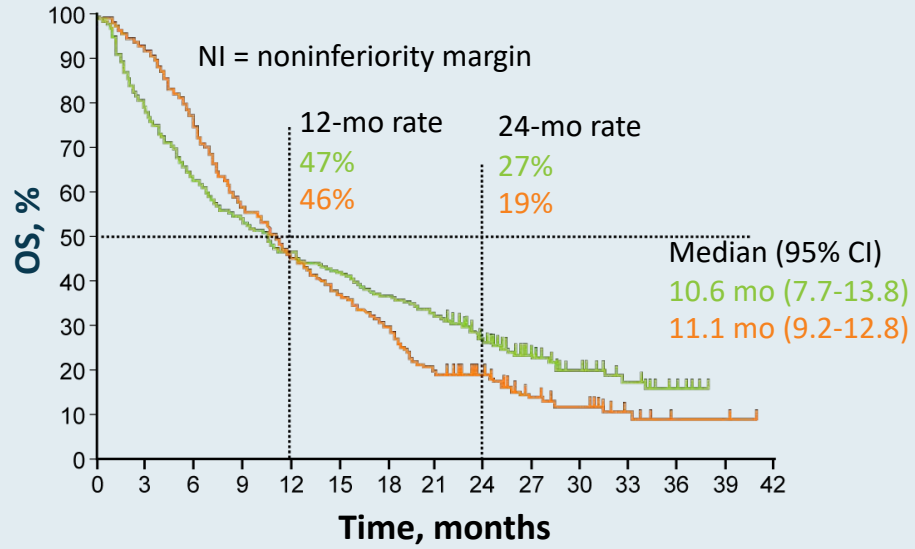
Kohei Shitara, MD[1]; Eric Van Cutsem, MD[2]; Yung-Jue Bang, MD[3]; et al

» Author Affiliations

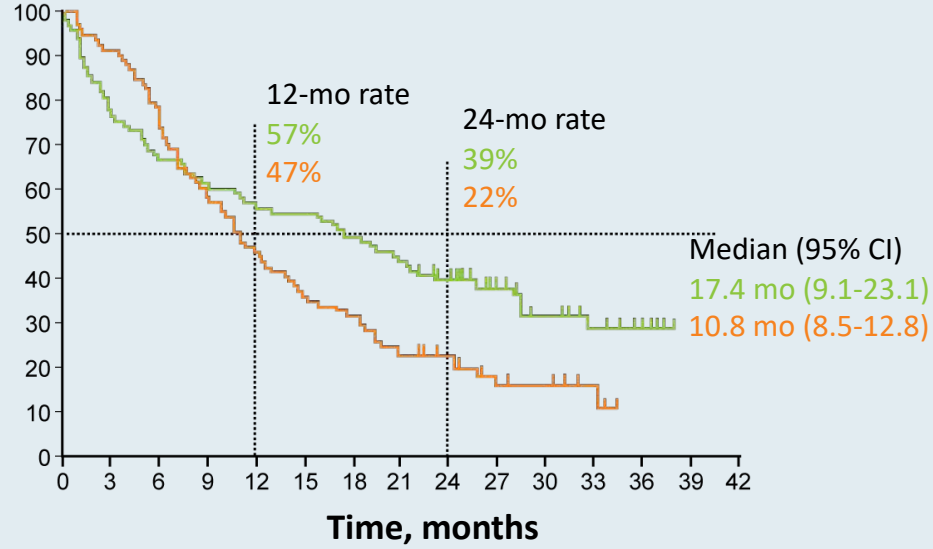
JAMA Oncol. 2020;6(10):1571-1580. doi:10.1001/jamaoncol.2020.3370

KEYNOTE-062: Overall Survival by PD-L1 CPS Score

OS: CPS ≥1	Events	HR	NI
Pembro alone	79%	0.91	1.2
Chemo	86%		



OS: CPS ≥10	Events	HR
Pembro alone	66%	0.69
Chemo	83%	



- Pembrolizumab was noninferior to chemotherapy for OS in patients with CPS ≥1, and a clinically meaningful improvement in OS was reported with pembro vs chemo for patients with CPS ≥10.
- Pembrolizumab + chemotherapy did not show superior OS for patients with CPS ≥1 or CPS ≥10, and the combination did not show superior PFS for patients with CPS ≥1.

Shitara K et al. *JAMA Oncol* 2020;6(10):1571-80.

RTP RESEARCH TO PRACTICE

FDA Approves fam-Trastuzumab Deruxtecan-nxki for HER2-Positive Gastric Adenocarcinomas

Press Release – January 15, 2020

"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."

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

The NEW ENGLAND JOURNAL of MEDICINE

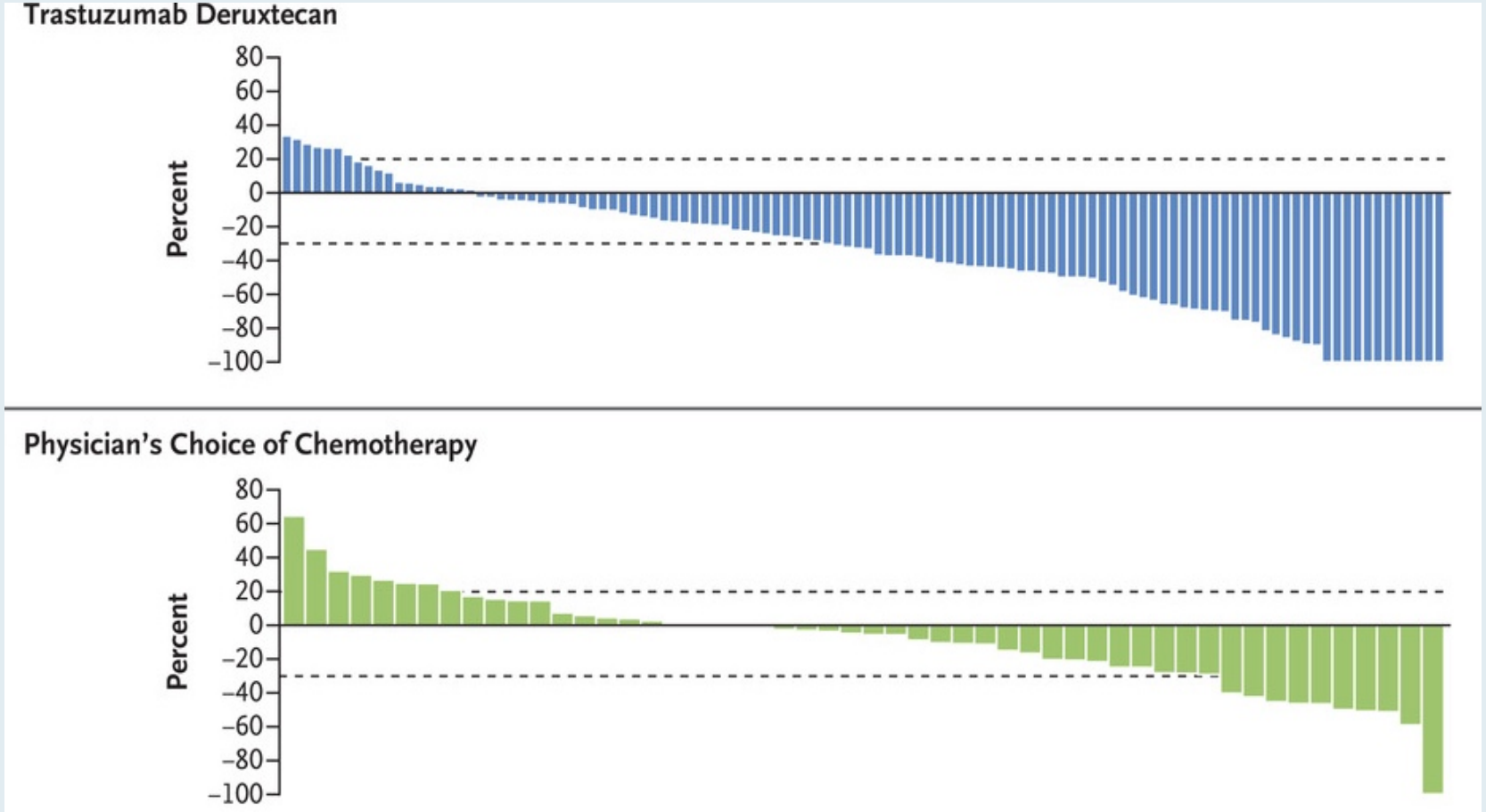
ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Gastric Cancer

K. Shitara, Y.-J. Bang, S. Iwasa, N. Sugimoto, M.-H. Ryu, D. Sakai, H.-C. Chung, H. Kawakami, H. Yabusaki, J. Lee, K. Saito, Y. Kawaguchi, T. Kamio, A. Kojima, M. Sugihara, and K. Yamaguchi, for the DESTINY-Gastric01 Investigators*

***N Engl J Med* 2020;382(25):2419-30.**

DESTINY-Gastric01:Trastuzumab Deruxtecan in Previously Treated HER2-Positive Gastric Cancer

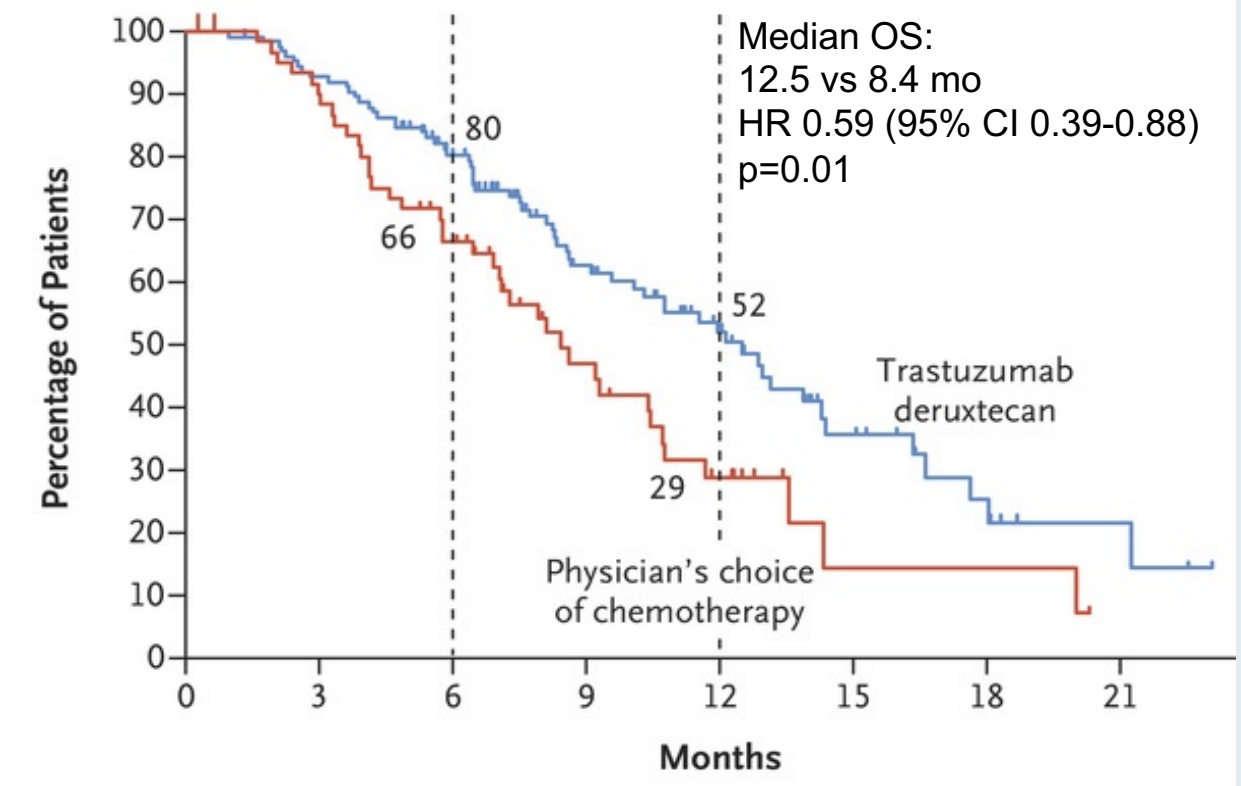


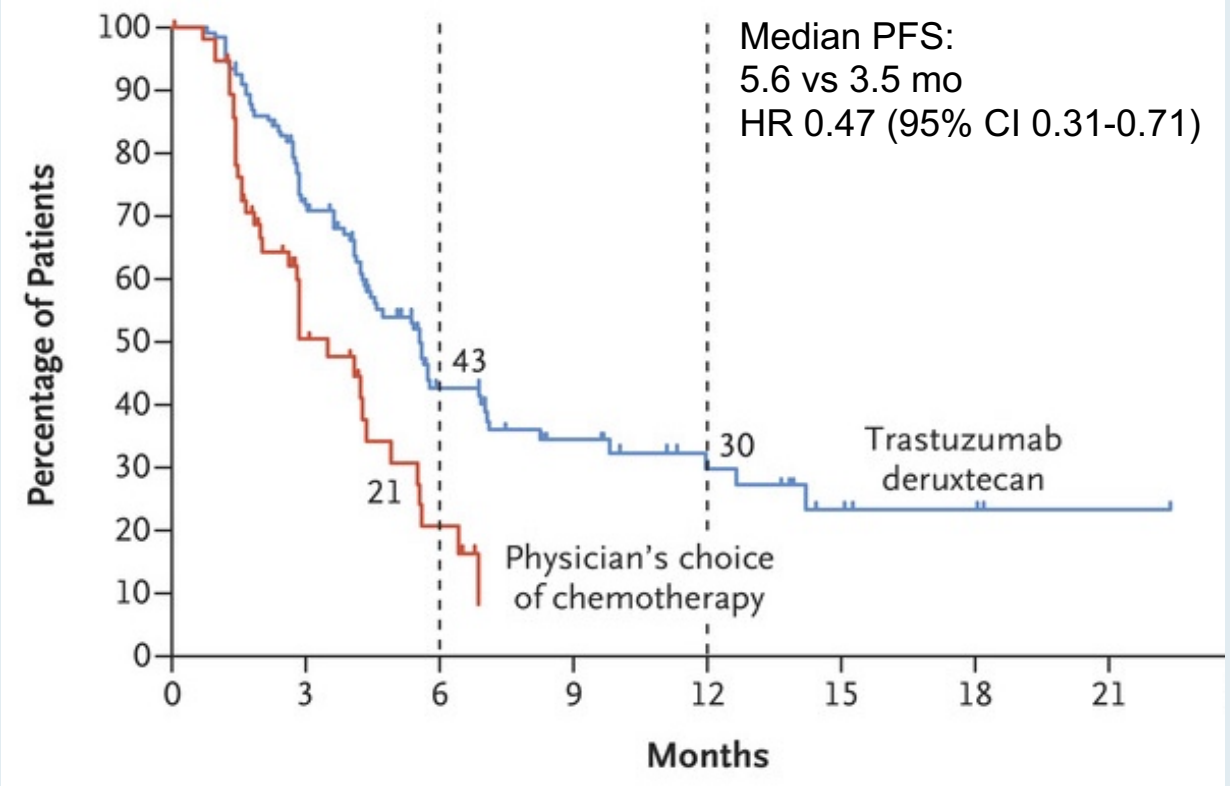
	T-DXd (n = 119)	PC (n = 56)
ORR	**51%**	**14%**
Confirmed ORR	**43%**	**12%**
CR	8%	0%
PR	34%	12%

Shitara K et al. *N Engl J Med* 2020;382(25):2419-30.

RTP RESEARCH TO PRACTICE

DESTINY-Gastric01: Survival Results





Shitara K et al. *N Engl J Med* 2020;382(25):2419-30.

DESTINY-Gastric01: Select Adverse Events

Adverse event	Trastuzumab deruxtecan (n = 125)			Physician's choice of chemo (n = 62)		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Neutrophil count decreased	63%	38%	13%	35%	16%	8%
Anemia	58%	38%	0	31%	21%	2%
Platelet count decreased	39%	10%	2%	6%	2%	2%
White cell count decreased	38%	21%	0	35%	8%	3%
Fatigue	22%	7%	0	24%	3%	0
Lymphocyte count decreased	22%	6%	5%	3%	0	2%

- A total of 12 patients (10%) in the trastuzumab deruxtecan group had drug-related interstitial lung disease or pneumonitis compared to 0 patients in the physician's choice group
- 1 drug-related death (pneumonia) occurred in the trastuzumab deruxtecan group

Shitara K et al. *N Engl J Med* 2020;382(25):2419-30.

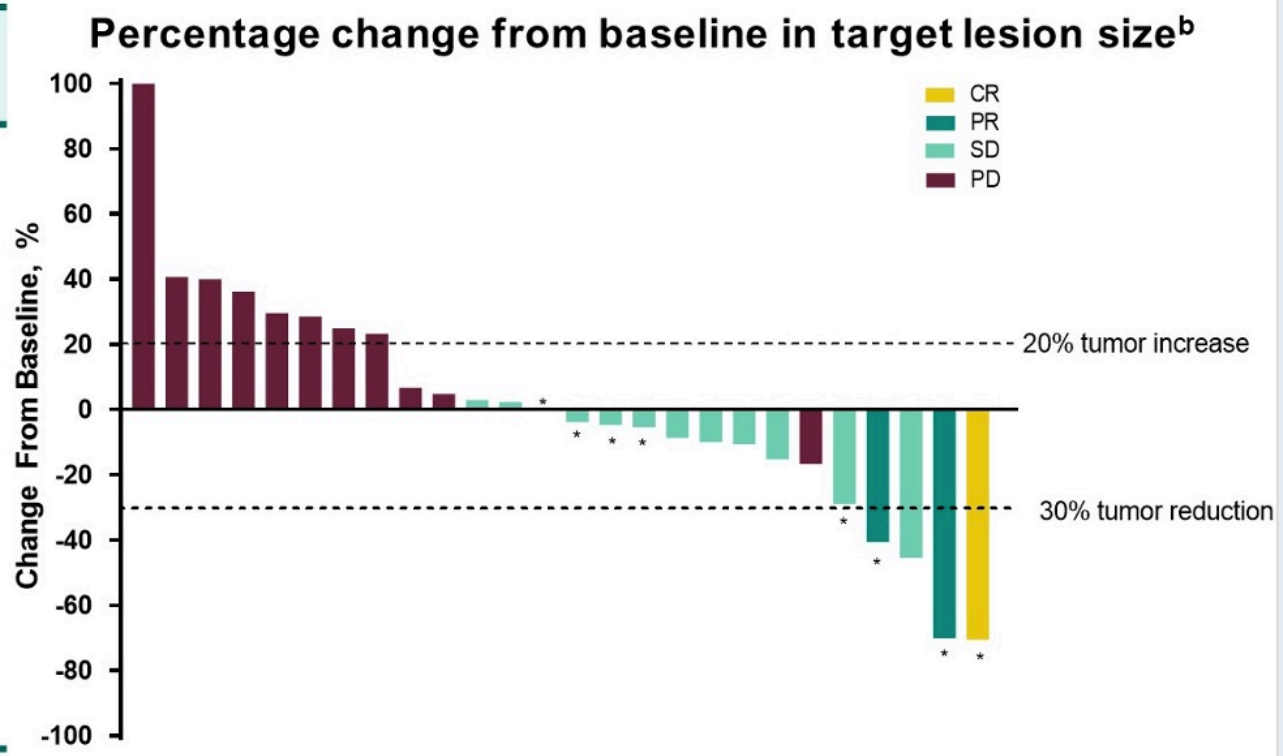
LEAP-005: A Phase II Multicohort Study of Lenvatinib plus Pembrolizumab in Patients with Previously Treated Selected Solid Tumors: Results from the Gastric Cancer Cohort

Chung HC et al.

Gastrointestinal Cancers Symposium 2021;Abstract 230.

LEAP-005: Antitumor Activity

	N = 31
ORR, % (95% CI)	10 (2–26)
DCR,[a] % (95% CI)	48 (30–67)
Best overall response, n (%)[b]	
CR	1 (3)
PR	2 (6)
SD	12 (39)
PD	11 (35)
No assessment[c]	5 (16)
DOR, median (range), mo	NR (2.1+ to 2.3+)

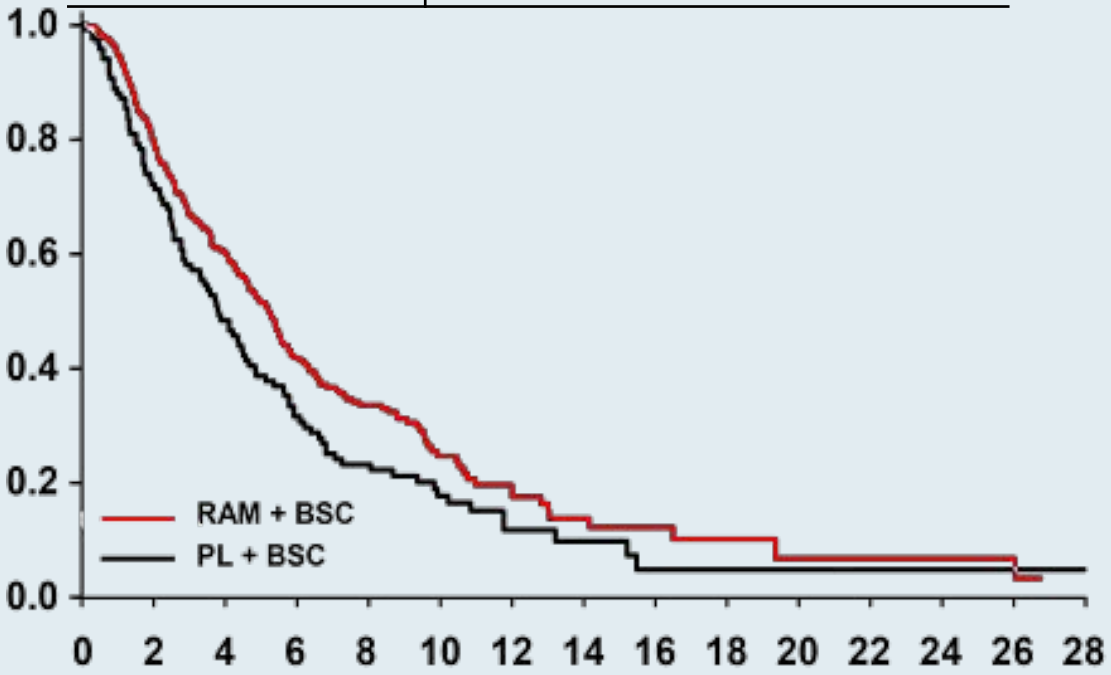


CI, confidence interval; CR, complete response; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Defined as best overall response of CR, PR or SD. [b]Both patients with PR had PD-L1 CPS ≥1; patient with CR had PD-L1 CPS <1. [c]Patient had no post-baseline imaging.
*Patient with treatment ongoing.
Data cutoff date: April 10, 2020.

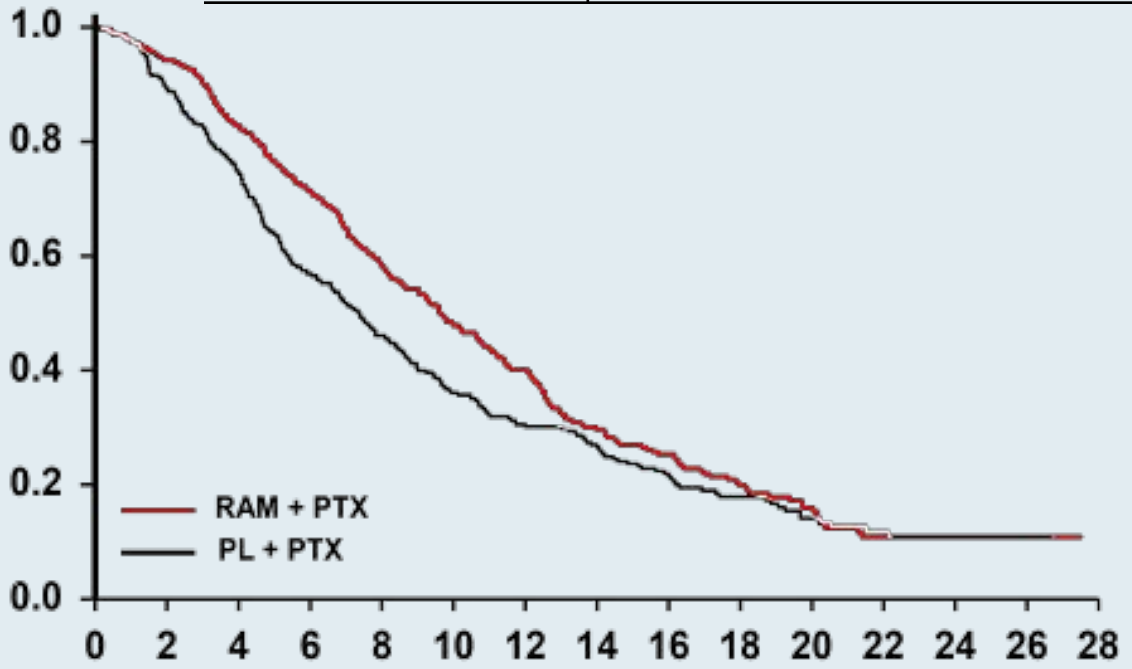
Chung HC et al. Gastrointestinal Cancers Symposium 2021;Abstract 230.

Overall Survival Results from 2 Phase III Trials of Ramucirumab as Second-Line Treatment for Advanced Gastric or GEJ Adenocarcinoma REGARD and RAINBOW

REGARD[1] OS	RAM	Placebo	*p*-value
Median (mo)	**5.2**	**3.8**	**0.047**
HR (95% CI)	**0.776 (0.603-0.998)**		



RAINBOW[2] OS	RAM	Placebo	*p*-value
Median (mo)	**9.6**	**7.4**	**0.017**
HR (95% CI)	**0.807 (0.678-0.962)**		



Abbreviations: BSC = best supportive care; PL = placebo; PTX = paclitaxel; RAM = ramucirumab

Muro K et al. Gastrointestinal Cancers Symposium 2017;Abstract 03 (Plots); [1] Fuchs CS et al. *Lancet* 2014;383(9911):31-9; [2] Wilke H et al. *Lancet Oncol* 2014;15(11):1224-35.

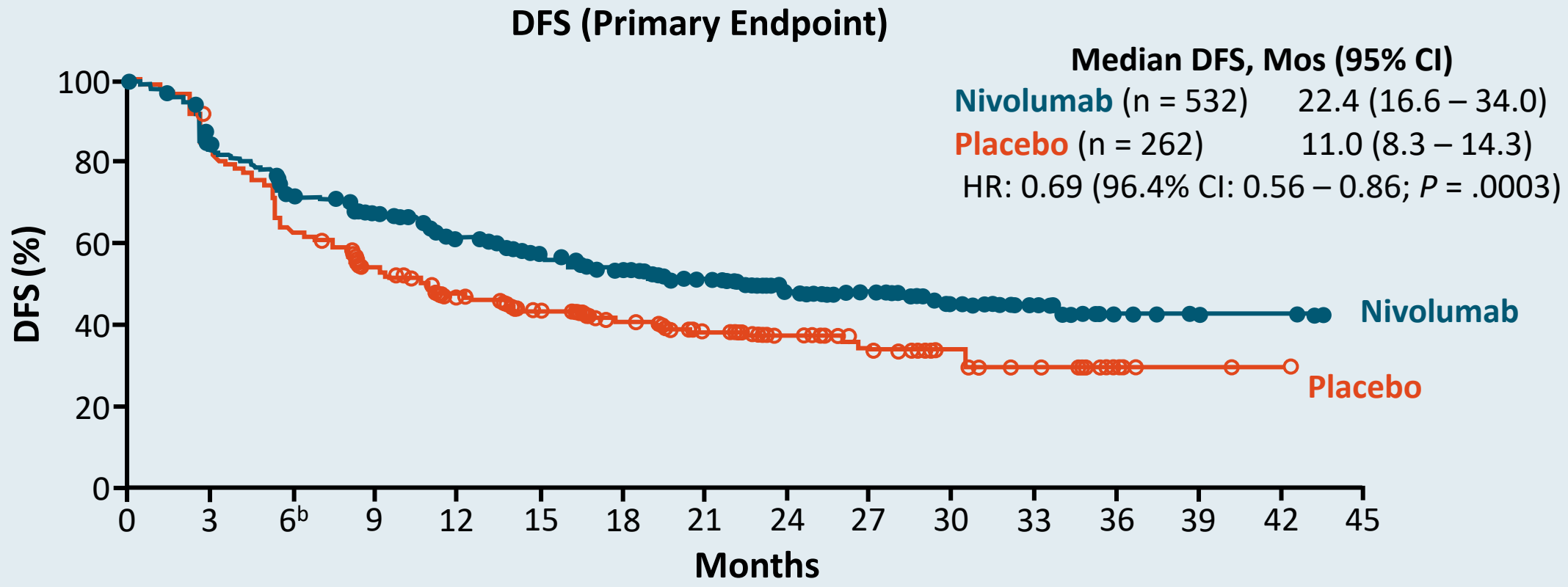
Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer (EC/GEJC) Following Neoadjuvant Chemoradiation Therapy (CRT): First Results of the CheckMate 577 Study

Kelly RJ et al

ESMO 2020;Abstract LBA9_PR

CheckMate 577: Adjuvant Nivolumab Following Neoadjuvant CRT/Resection in Esophageal/GEJ Cancer

- Randomized phase III trial of **adjuvant** **nivolumab** vs **placebo** following neoadjuvant CRT + surgical resection* for pts with stage II/III **esophageal/GEJ adenocarcinoma/SCC** (N = 794)



*Residual pathologic disease ≥ ypT1 or ≥ ypN1.

Kelly RJ et al. ESMO 2020;Abstract LBA9_PR.

FDA Approves Nivolumab for Esophageal Squamous Cell Carcinoma

Press Release – June 10, 2020

"On June 10, 2020, the Food and Drug Administration approved nivolumab for patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

Efficacy was investigated in ATTRACTION-3 (NCT02569242), a multicenter, randomized (1:1), active-controlled, open-label trial in 419 patients with unresectable advanced, recurrent, or metastatic ESCC.

The recommended nivolumab dose for ESCC is 240 mg every 2 weeks or 480 mg every 4 weeks."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-nivolumab-esophageal-squamous-cell-carcinoma

RTP RESEARCH TO PRACTICE

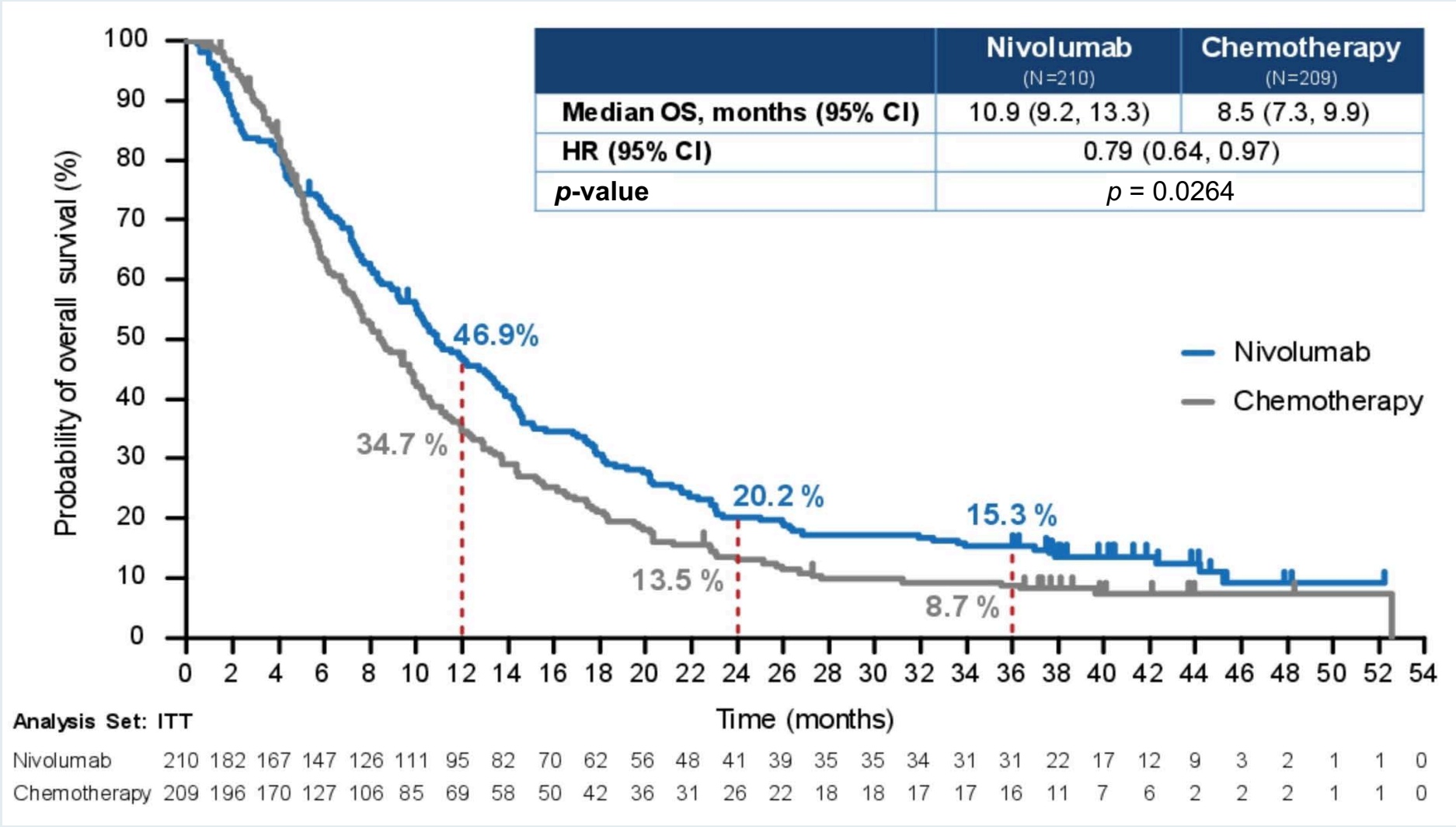
Three-year Follow-up of ATTRACTION-3: A Phase III Study of Nivolumab (Nivo) in Patients with Advanced Esophageal Squamous Cell Carcinoma (ESCC) That Is Refractory or Intolerant to Previous Chemotherapy

Chin K et al.

Gastrointestinal Cancers Symposium 2021;Abstract 204.

ATTRACTION-3: Three-Year Overall Survival Update

	Nivolumab (N=210)	Chemotherapy (N=209)
Median OS, months (95% CI)	10.9 (9.2, 13.3)	8.5 (7.3, 9.9)
HR (95% CI)	0.79 (0.64, 0.97)	
***p*-value**	*p* = 0.0264	



Chin K et al. Gastrointestinal Cancers Symposium 2021;Abstract 204.

RTP RESEARCH TO PRACTICE

Hepatocellular Cancer

FDA Approves First-Line Atezolizumab with Bevacizumab for Unresectable or Metastatic HCC

Press Release – May 29, 2020

"On May 29, 2020, the Food and Drug Administration approved atezolizumab in combination with bevacizumab for patients with unresectable or metastatic hepatocellular carcinoma who have not received prior systemic therapy.

Efficacy was investigated in IMbrave150 (NCT03434379), a multicenter, international, open-label, randomized trial in patients with locally advanced unresectable or metastatic hepatocellular carcinoma who had not received prior systemic therapy. A total of 501 patients were randomized (2:1) to receive either atezolizumab 1200 mg as an intravenous infusion (IV) followed by bevacizumab 15 mg/kg IV on the same day, every 3 weeks, or sorafenib orally twice daily."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-atezolizumab-plus-bevacizumab-unresectable-hepatocellular-carcinoma

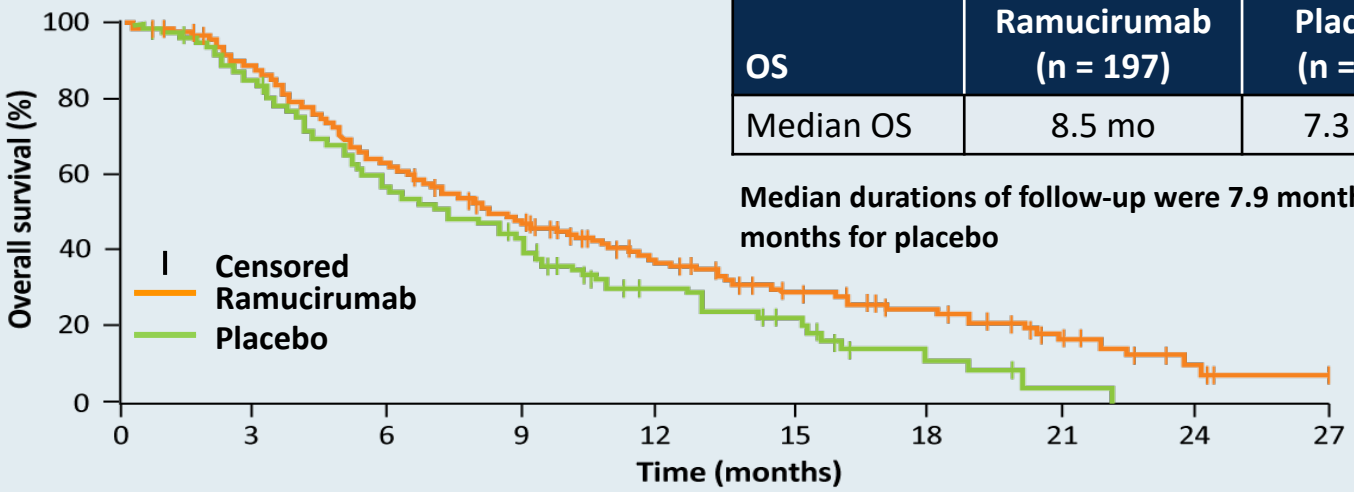
Articles

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**

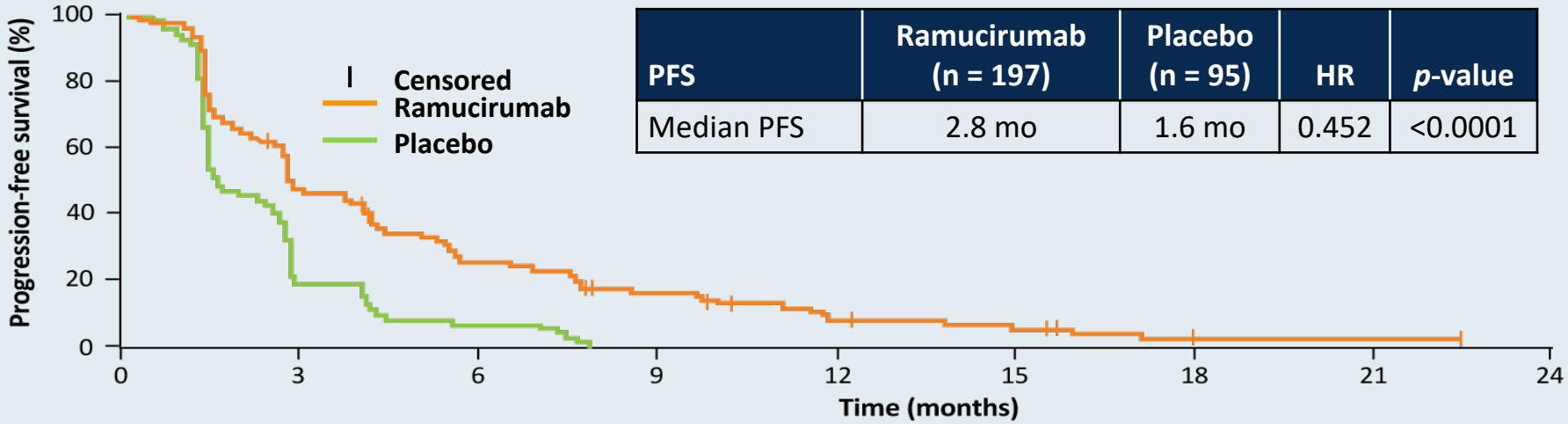
Lancet Oncol 2019;20(2):282-96.

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

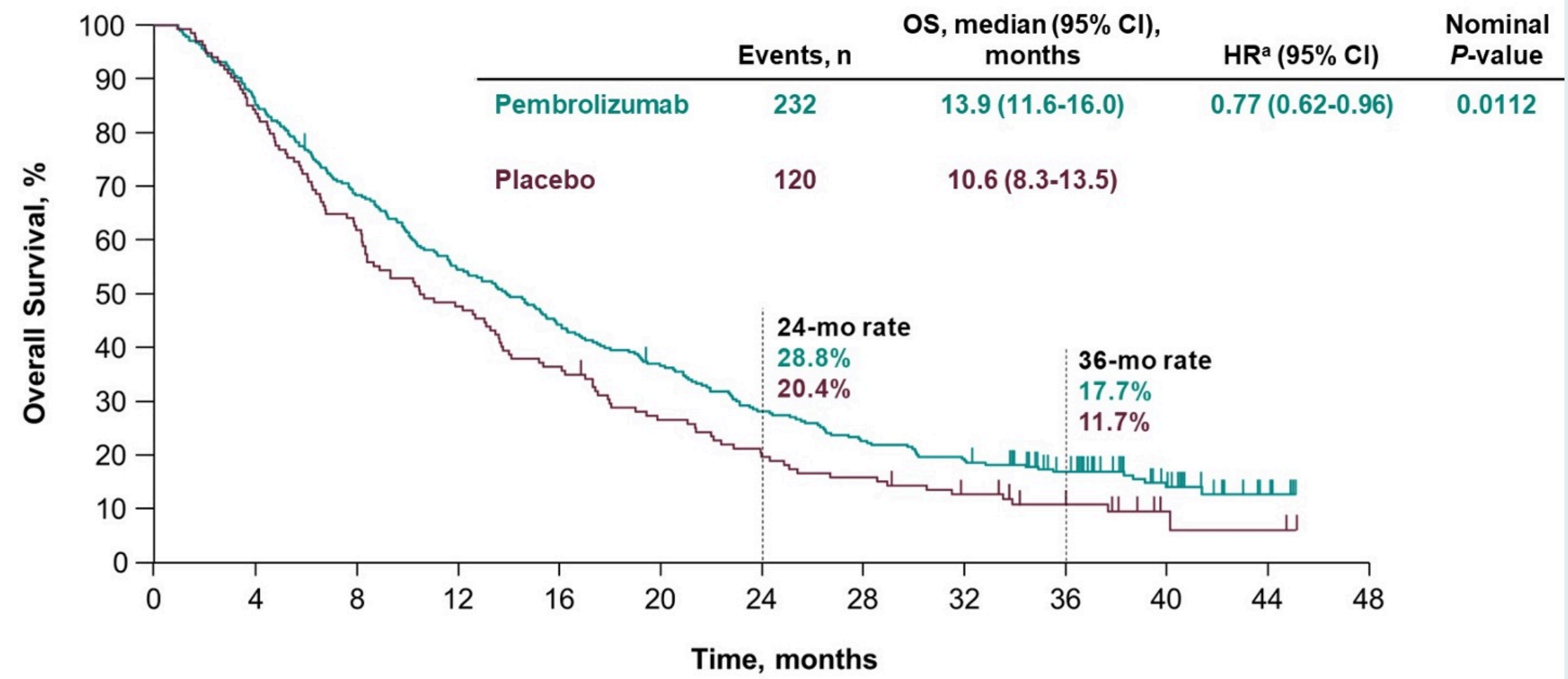
Pembrolizumab versus Placebo in Patients with Advanced Hepatocellular Carcinoma Previously Treated with Sorafenib: Updated Data from the Randomized, Phase 3 KEYNOTE-240 Study

Merle P et al.

Gastrointestinal Cancers Symposium 2021;Abstract 268.

KEYNOTE-240: Updated OS
Hazard Ratios Maintained with Longer Follow-Up

Overall Survival



Merle P et al. Gastrointestinal Cancers Symposium 2021;Abstract 268.

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Nivolumab and Ipilimumab Combination for HCC

Press Release – March 10, 2020

"On March 10, 2020, the Food and Drug Administration granted accelerated approval to the combination of nivolumab and ipilimumab for patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Efficacy of the combination was investigated in Cohort 4 of CHECKMATE-040, (NCT01658878) a multicenter, multiple cohort, open-label trial conducted in patients with HCC who progressed on or were intolerant to sorafenib. A total of 49 patients received nivolumab 1 mg/kg in combination with ipilimumab 3 mg/kg every 3 weeks for four doses, followed by single-agent nivolumab 240 mg every 2 weeks until disease progression or unacceptable toxicity.

The main efficacy outcome measures were overall response rate and duration of response as determined by blinded independent central review (BICR) using RECIST v1.1. ORR was 33% (n=16; 95% CI: 20, 48), with 4 complete responses and 12 partial responses. Response duration ranged from 4.6 to 30.5+ months, with 31% of responses lasting at least 24 months."

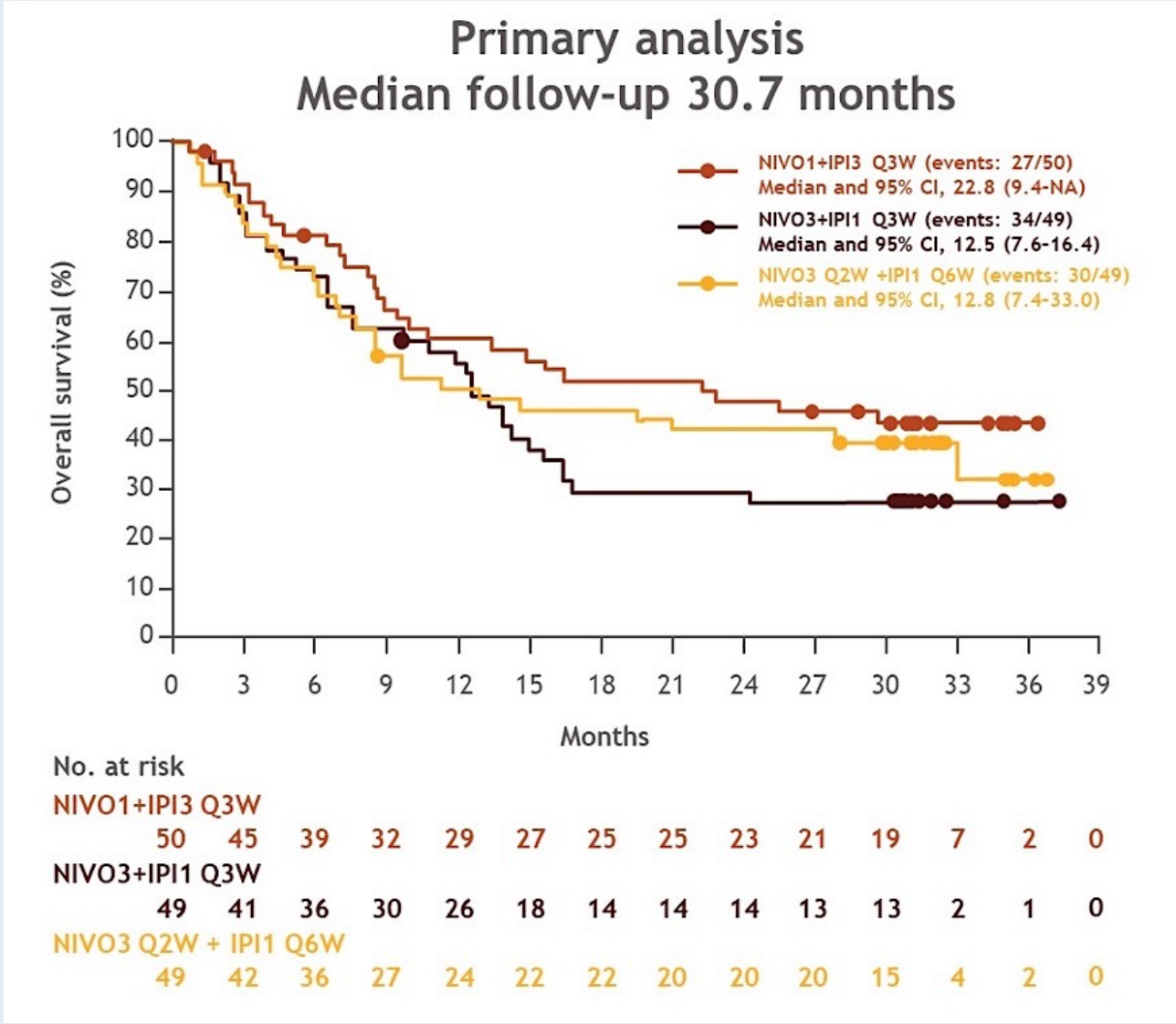
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-nivolumab-and-ipilimumab-combination-hepatocellular-carcinoma

Nivolumab (NIVO) plus Ipilimumab (IPI) Combination Therapy in Patients (Pts) with Advanced Hepatocellular Carcinoma (aHCC): Long-Term Results from CheckMate 040

El-Khoueiry AB et al.

Gastrointestinal Cancers Symposium 2021;Abstract 269.

CheckMate 040: Updated Overall Survival with Ipilimumab/Nivolumab



El-Khoueiry AB et al. Gastrointestinal Cancers Symposium 2021;Abstract 269.

RTP RESEARCH TO PRACTICE

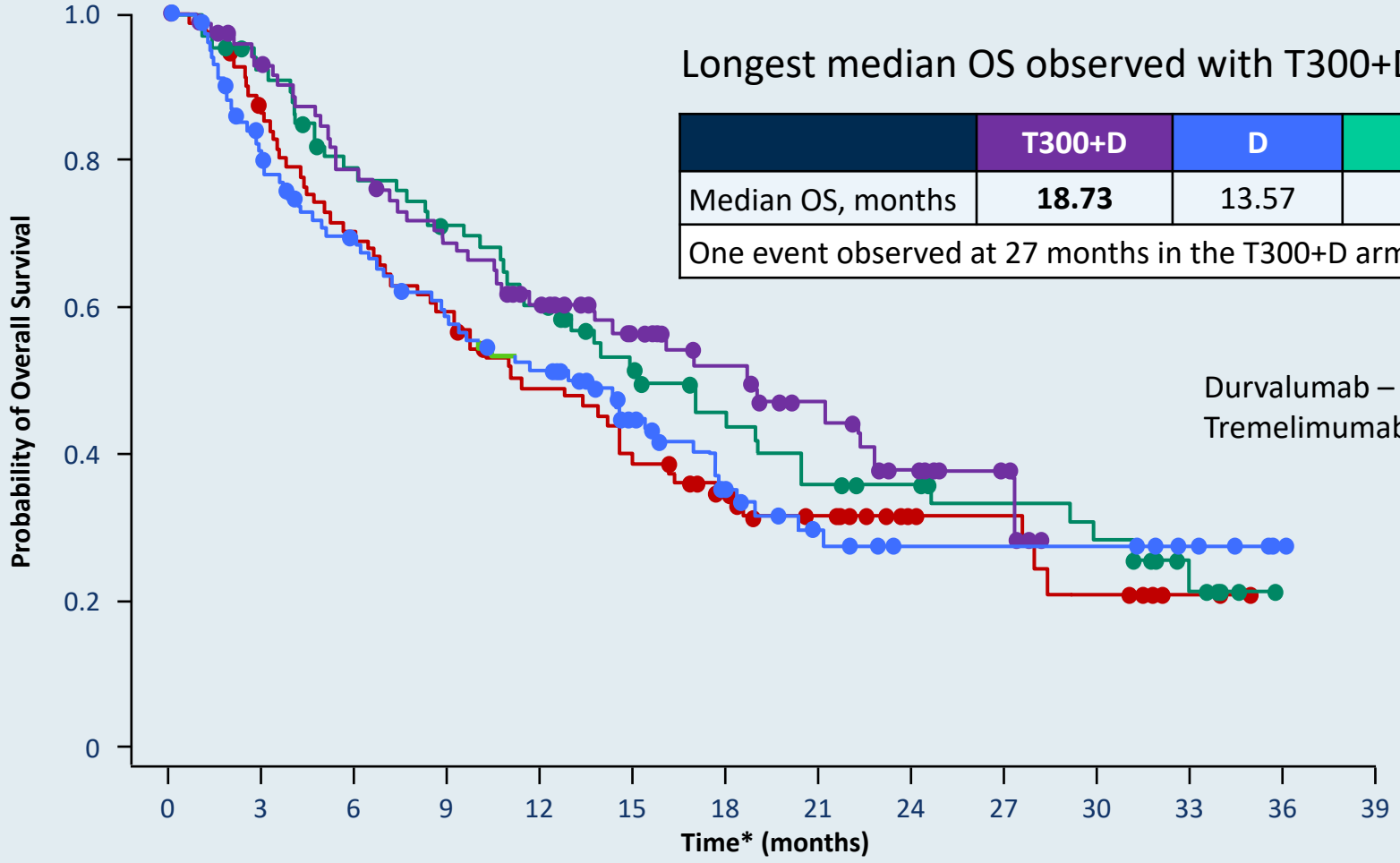
Efficacy, Tolerability, and Biologic Activity of a Novel Regimen of Tremelimumab (T) in Combination with Durvalumab (D) for Patients (pts) with Advanced Hepatocellular Carcinoma (aHCC)

Kelley RK et al.
ASCO 2020;Abstract 4508.

The Novel Regimen of Tremelimumab in Combination with Durvalumab Provides a Favorable Safety Profile and Clinical Activity for Patients with Advanced Hepatocellular Carcinoma

Sangro B et al.
ESMO World GI Congress 2020;Abstract O-6.

Study 22: Overall Survival



Longest median OS observed with T300+D

	T300+D	D	T	T75+D
Median OS, months	**18.73**	13.57	15.11	11.30
One event observed at 27 months in the T300+D arm				

Durvalumab – anti-PD1
Tremelimumab - anti-CTLA4

Number of patients at risk														
T300+D	75	67	56	48	39	30	22	16	10	5	0	0	0	0
D	104	78	65	54	46	31	20	14	8	8	8	5	1	0
T	69	62	51	45	38	29	23	18	16	13	11	5	0	0
T75+D	84	69	56	48	38	30	23	17	10	9	6	2	0	0

Sangro B et al. ESMO World GI Congress 2020;Abstract O-6; Kelley RK et al. ASCO 2020;Abstract 4508.

Ask the Investigators: Applying Emerging Clinical Research to the Care of Patients with Gastroesophageal Cancers

A Satellite Educational Symposium Held in Conjunction with the 2021 AACR Virtual Annual Meeting

Monday, April 12, 2021
6:30 PM – 7:30 PM ET

Faculty

Joseph Chao, MD
Yelena Y Janjigian, 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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