Meet The Professor

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

Alan P Venook, MD

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

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Commercial Support

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Dr Love — Disclosures

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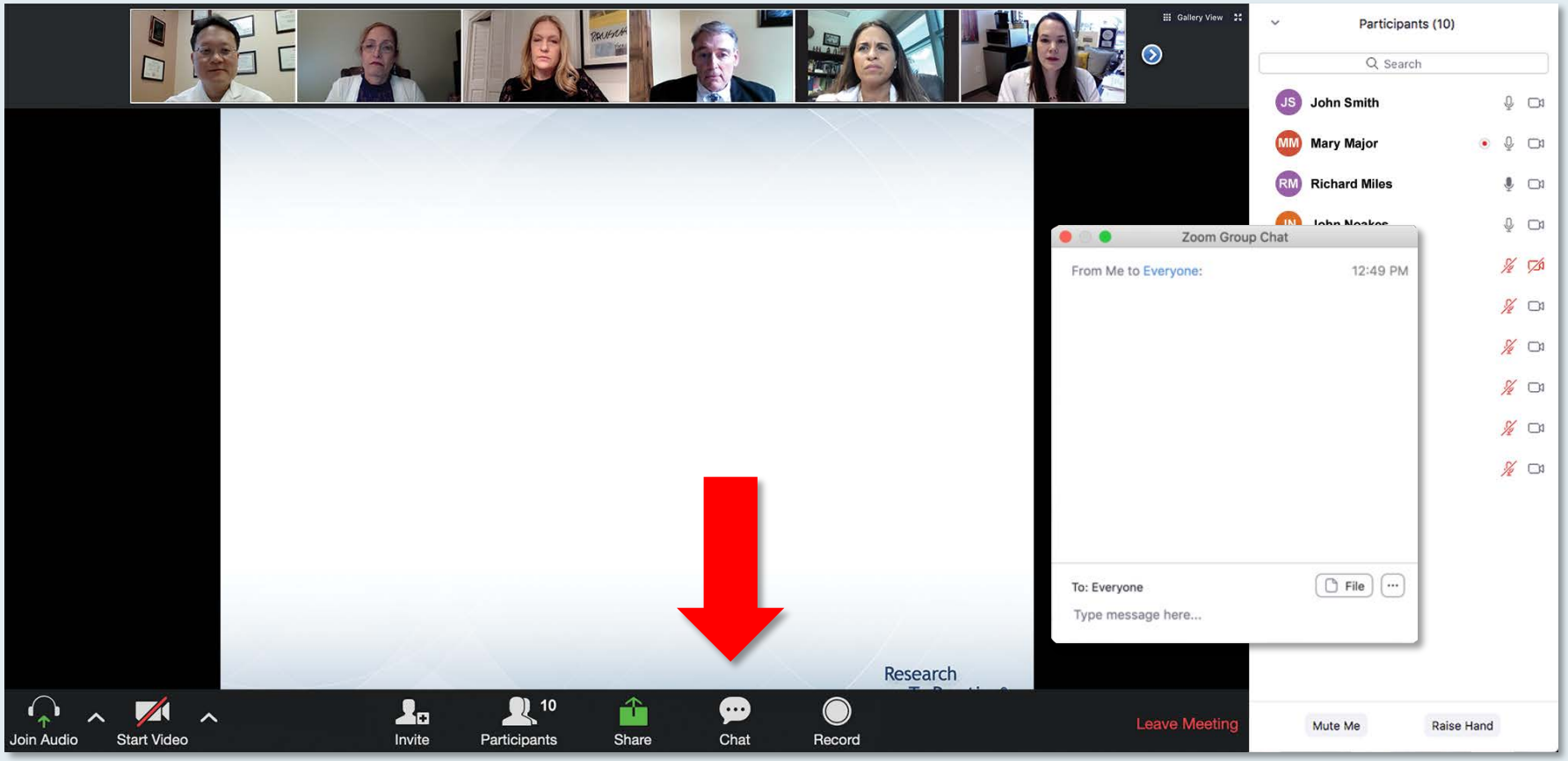
We Encourage Clinicians in Practice to Submit Questions



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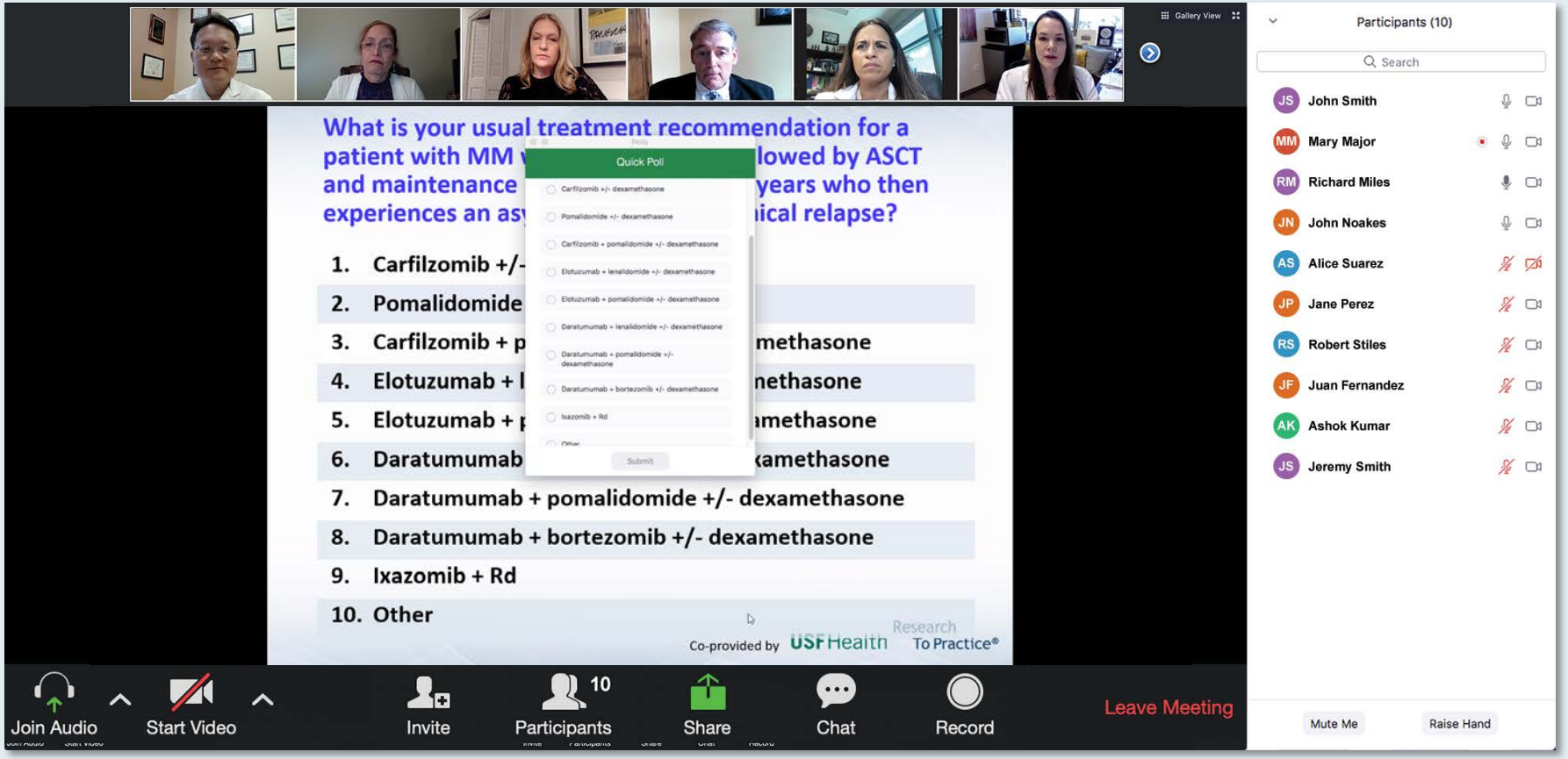

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Dissecting the Decision: Clinical and Nursing Investigators Provide Practical Perspectives on Key Issues in Cancer Care

Part 2 — HER2-Positive Breast Cancer

Thursday, March 18, 2021
5:00 PM – 6:00 PM ET

Faculty

Jamie Carroll, APRN, MSN, CNP
Sara Hurvitz, MD

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss the Role of PARP Inhibition in the Care of Actual Patients with Ovarian Cancer

Saturday, March 20, 2021
4:00 PM – 5:00 PM ET

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Susana Banerjee, MBBS, MA, PhD
Richard T Penson, MD, MRCP
Shannon N Westin, MD, MPH

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Meet The Professor

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

Thursday, March 25, 2021
5:00 PM – 6:00 PM ET

Faculty

Robert J Motzer, MD

Moderator

Neil Love, MD

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Meet The Professor

Management of Chronic Lymphocytic Leukemia

Monday, March 29, 2021
5:00 PM – 6:00 PM ET

Faculty

Philip A Thompson, MB, BS

Moderator

Neil Love, MD

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Monday, April 5, 2021
5:00 PM – 6:00 PM ET

Faculty

Bradley J Monk, MD

Moderator

Neil Love, MD

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Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

Tuesday, April 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Sumanta K Pal, 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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WITH DR NEIL LOVE

Key Recent Data Sets in Gastrointestinal Cancers

DR PHILIP A PHILIP

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Meet The Professor Program Participating Faculty

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Associate Director for Translational Research
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West Cancer Center and Research Institute
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Attending Physician, Member
Memorial Sloan Kettering Cancer Center
Professor of Medicine
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New York, New York

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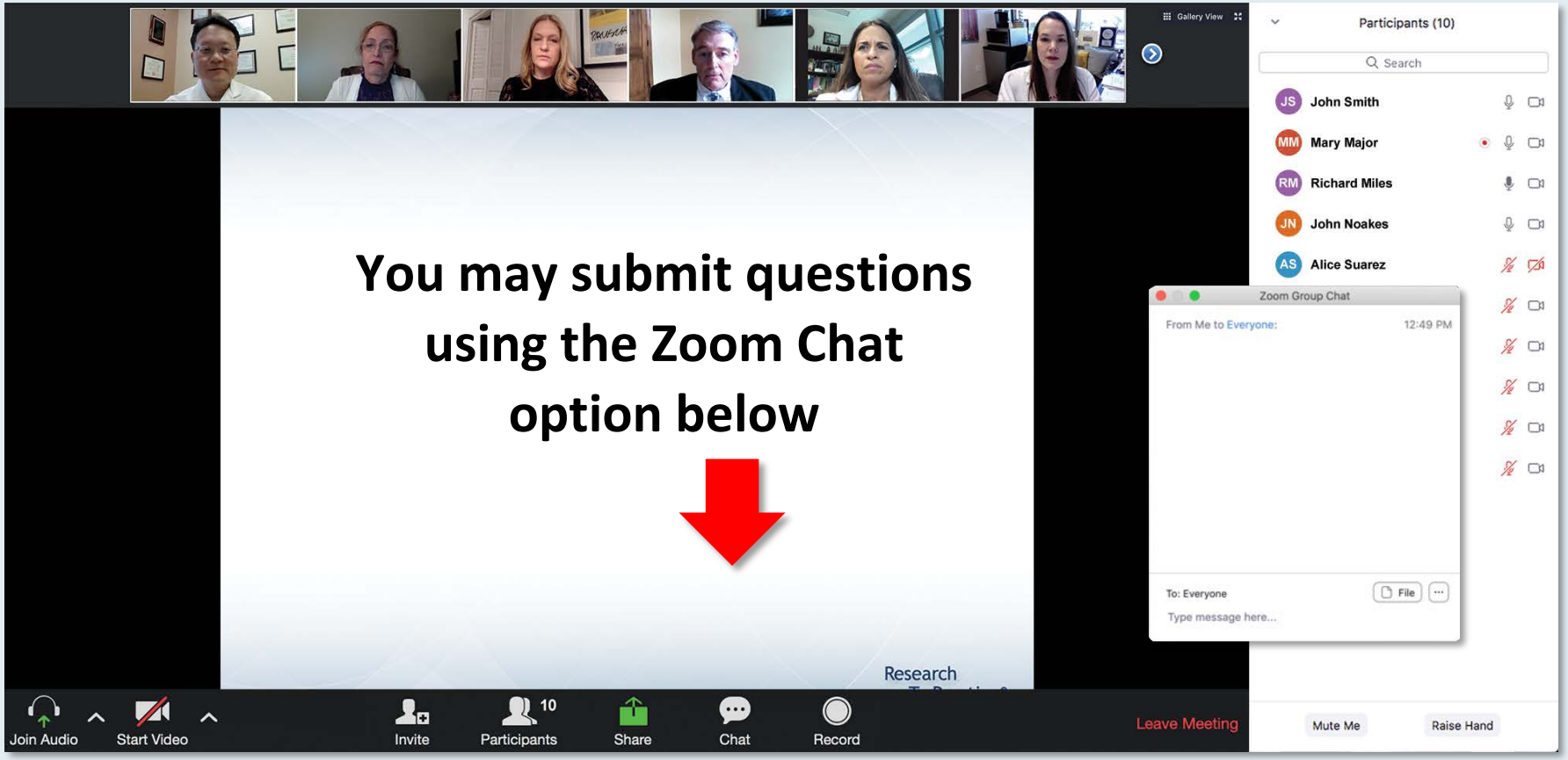

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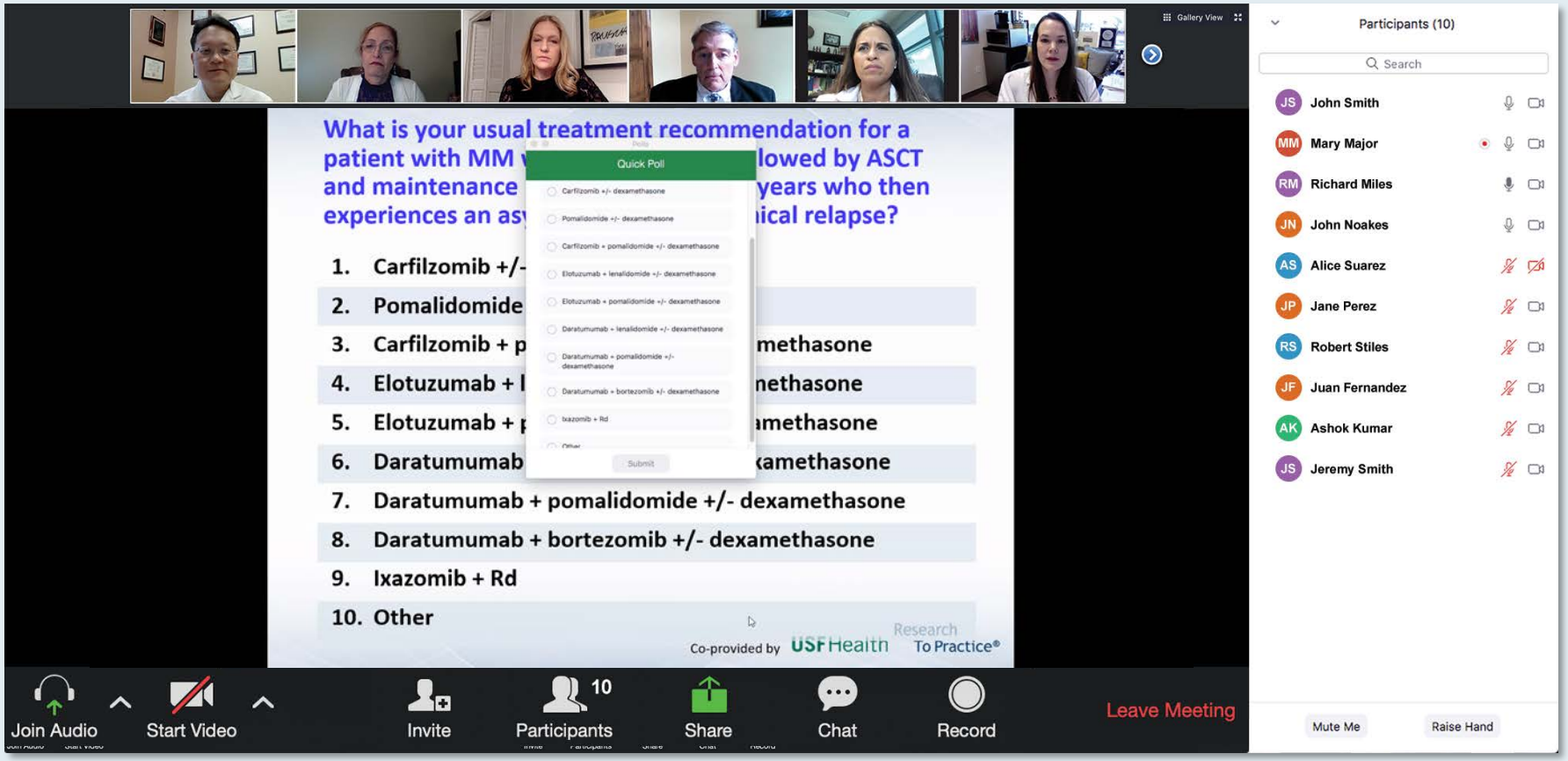

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Akron, Ohio

Mamta Choksi, MD
Florida Cancer Specialists and Research Institute
New Port Richey, Florida

Kelly Yap, MD
Assistant Clinical Professor
City of Hope
Arcadia, California

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Meet The Professor with Dr Venook

MODULE 1: Cases from Drs Bachow and Matt-Amaral

- Dr Bachow: A 73-year-old woman with dMMR metastatic colorectal cancer – BRAF mutation
- Dr Matt-Amaral: A 74-year-old woman with MMR-proficient metastatic colorectal cancer

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

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- Dr Gosain: A 72-year-old man with MSS metastatic GEJ adenocarcinoma – PD-L1 CPS 20, HER2-negative
- Dr Yap: A 54-year-old man with MSS metastatic esophageal adenocarcinoma – PD-L1 CPS 15, HER2-positive

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

MODULE 5: Cases from Drs Brenner and Choksi

- Dr Brenner: An 84-year-old man with Child-Pugh A cirrhosis and advanced hepatocellular carcinoma (HCC)
- Dr Choksi: A 63-year-old woman with Child-Pugh B cirrhosis and advanced HCC

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Case Presentation – Dr Bachow: A 73-year-old woman with dMMR metastatic colorectal cancer – BRAF mutation

Dr Spencer Bachow

- PMH: Limited stage small cell lung cancer with paraneoplastic CIDP (still receiving IV Ig); MPN with JAK2 mutation on ASA/hydroxyurea
- 2020: diagnosis of pT3N2 colon adenocarcinoma, hypermethylated MMR phenotype w/ BRAF mutation
  - Peripheral blood shows JAK2V617F mutation; platelet count 900,000
- 5-FU/leucovorin alone initiated due to CIDP and 5 cycles completed
- Interval CT scan of the chest, abdomen, and pelvis shows 2 new lesions in the liver
- Germline testing is pending; platelet count has improved on hydroxyurea
- After much discussion, patient elects for pembrolizumab therapy despite CIDP-like picture that is present

Questions

- In patients with Stage III colon cancer that are MSI-high or dMMR who have a contraindication to oxaliplatin, is adjuvant PD-1 or PD-L1 therapy a reasonable option? Is there a potential role for adjuvant irinotecan-based therapy?

Case Presentation – Dr Matt-Amaral: A 74-year-old woman with MMR-proficient metastatic colorectal cancer

Dr Laurie Matt-Amaral

- PMH: Stage IIIC colon cancer, right hemicolectomy, FOLFOX
- 6/2017: Stage IV recurrence of colon cancer, KRAS wildtype → FOLFIRI with cetuximab
  - Cetuximab later held due to neuropathy
- 10/2018: PD in peritoneal nodules → regorafenib
- 6/2019: PD → TAS-102
- 11/2019: PD → FOLFIRI with cetuximab
  - Cetuximab discontinued in cycle 13, bevacizumab added in
- 3/2020 – scans show continued stable disease

Question

- Given that this patient progressed through all prescribed treatments, would you have done the same as I did and returned to the original treatment regimen from which she derived some disease control?

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

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

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

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

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Have you administered or would you administer a BRAF inhibitor in combination with an EGFR antibody as first-line therapy to a patient with mCRC with a BRAF V600E mutation who could not tolerate or did not wish to receive chemotherapy?

 Prof Arnold	I have	 Dr Grothey	I have
 Dr Bekaii-Saab	I have	 Dr O'Reilly	I have not but would for the right patient
 Dr Bendell	I have not but would for the right patient	 Dr Venook	I have
 Dr Ciombor	I have not but would for the right patient	 Dr Wainberg	I have

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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

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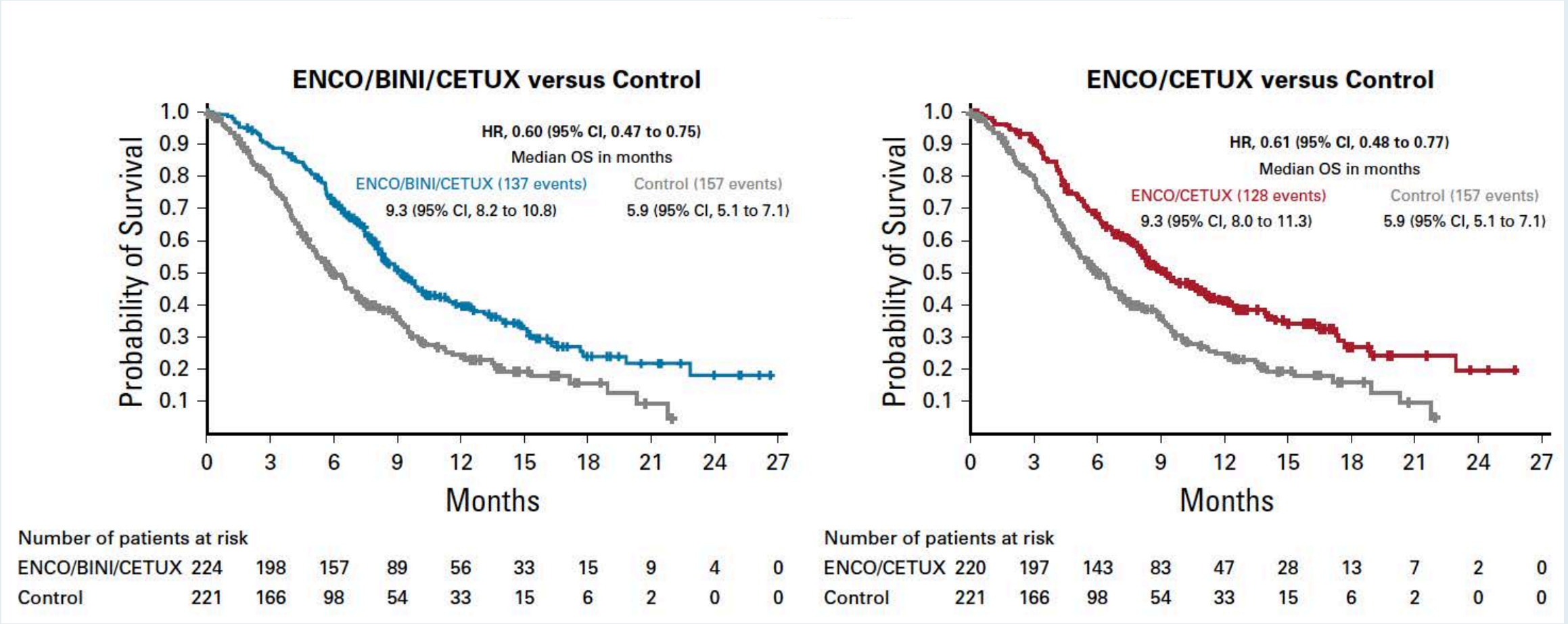
rapid communications

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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Case Presentation – Dr Gosain: A 72-year-old man with MSS metastatic GEJ adenocarcinoma – PD-L1 CPS 20, HER2-negative

Dr Rahul Gosain

- 8/2019: Presents with worsening dysphagia and fatigue, 20-pound weight loss
  - Imaging shows multiple liver lesions and EGD consistent with large ulcerated mass at the GEJ extending to the stomach cardia
  - GEJ and liver biopsy results consistent with poorly differentiated carcinoma
- FOLFOX initiated with palliative intent; oxaliplatin was dropped after cycle 10 due to neuropathy
- Remarkable response in liver lesions and primary lesion
- Repeat EGD to retract stent with scarring (biopsy with no malignant cells)
- Patient has been maintained on 5-FU alone; 1 isolated liver lesion persists

Questions

- In a patient such as this, would you consider giving them directed therapy to the liver and continuing with 5-FU, as we tend to do with colon cancer?
- Is there any role for a chemotherapy holiday versus maintenance 5-FU?

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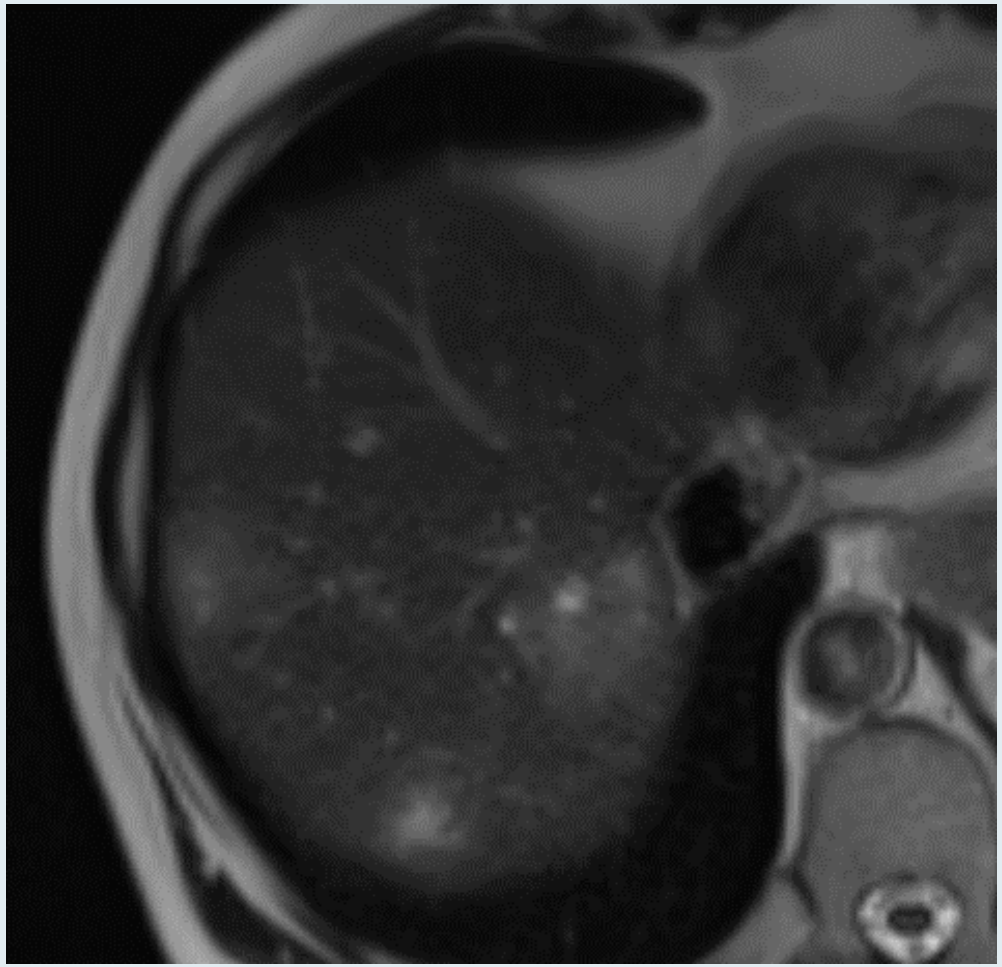
Case Presentation – Dr Gosain: A 72-year-old man with MSS metastatic GEJ adenocarcinoma – PD-L1 CPS 20, HER2-negative (continued)

Dr Rahul Gosain



Case Presentation – Dr Yap: A 54-year-old man with MSS metastatic esophageal adenocarcinoma – PD-L1 CPS 15, HER2-positive

Dr Kelly Yap

- Diagnosed with Stage IV esophageal carcinoma
- Biomarker testing: MSS, HER2-positive, PD-L1 CPS 15
- FOLFOX/trastuzumab initiated; oxaliplatin was eventually discontinued due to neuropathy
- PD noted → FOLFIRI/ramucirumab

Questions

- For this patient at first progression what would be the best treatment option?
- If the patient progresses on the current regimen of FOLFIRI and ramucirumab, is there a role for trastuzumab deruxtecan in this HER2-positive esophageal cancer?
- In a patient with a high PD-L1 CPS how would an immune checkpoint inhibitor fit into their treatment algorithm? Which immune checkpoint inhibitor would be favored? What about the combination of chemotherapy with an immune checkpoint inhibitor?

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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

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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 GEJ with a PD-L1 CPS of 1?

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 1?

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

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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 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 1?

 Prof Arnold	Second line — nivolumab	 Dr Grothey	Third 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

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

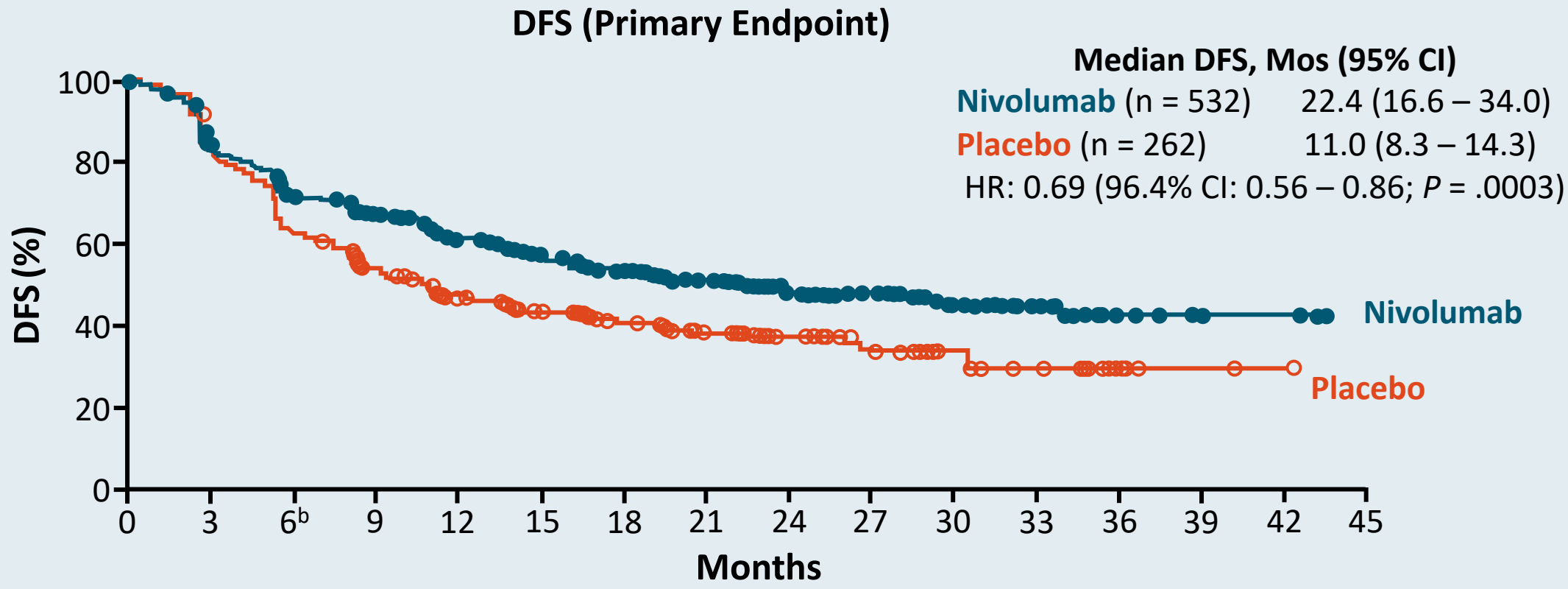
Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer (EC/GEJC) Following Neoadjuvant Chemoradiation Therapy (CRT): First Results of the CheckMate 577 Study

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.

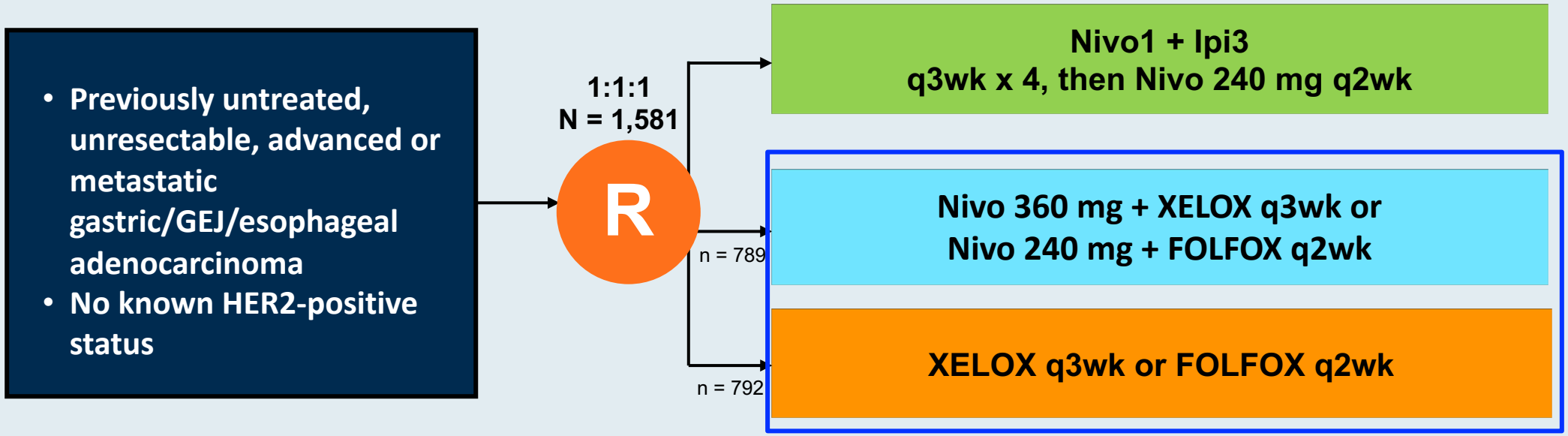
RTP RESEARCH TO PRACTICE

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.

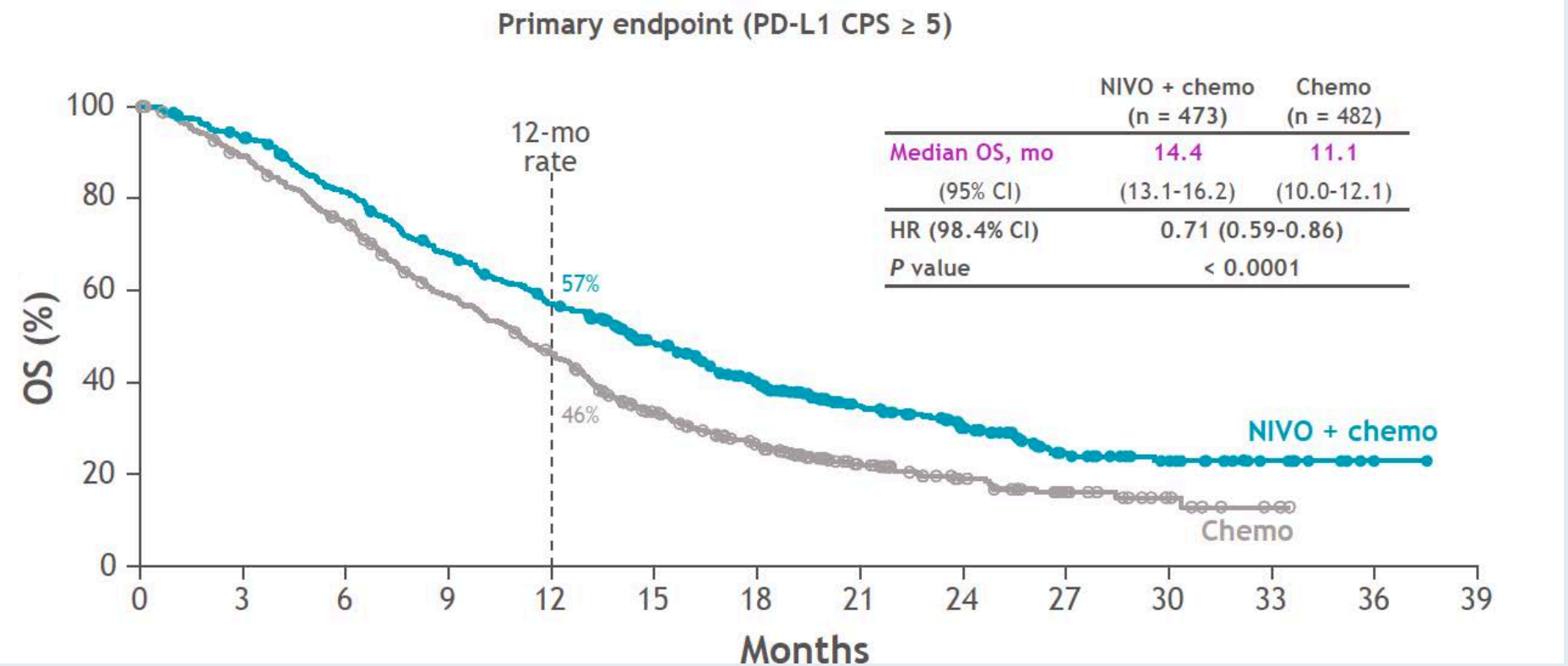
CheckMate 649 Phase III Schema



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

Moehler M et al. ESMO 2020;Abstract LBA6.

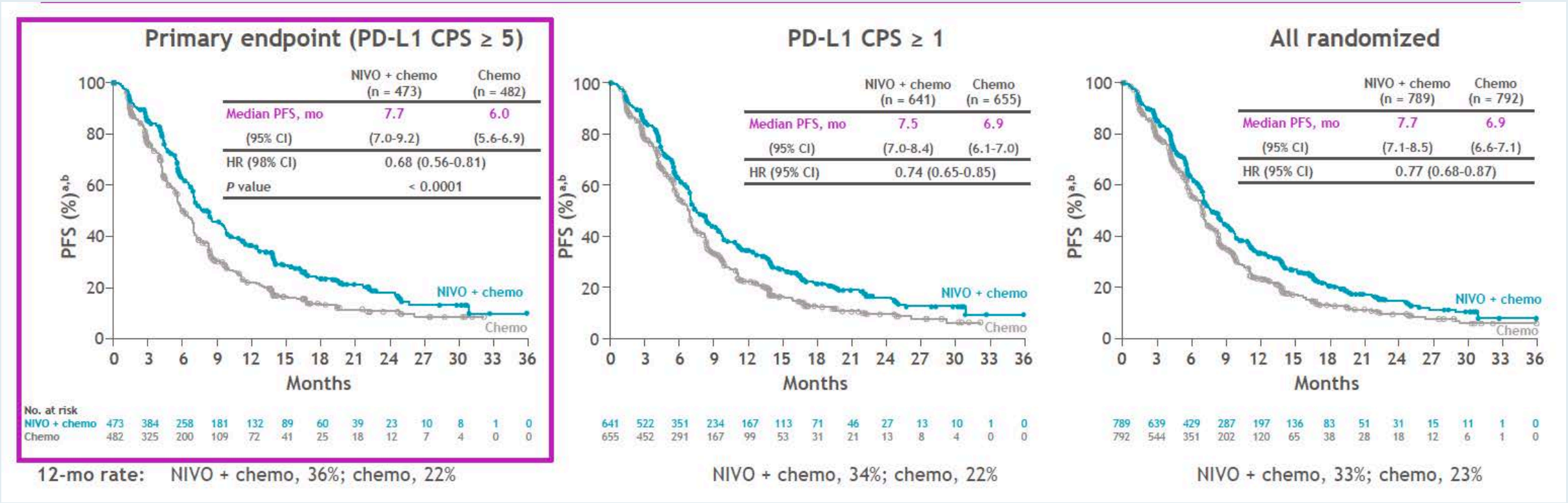
CheckMate 649: Overall Survival



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

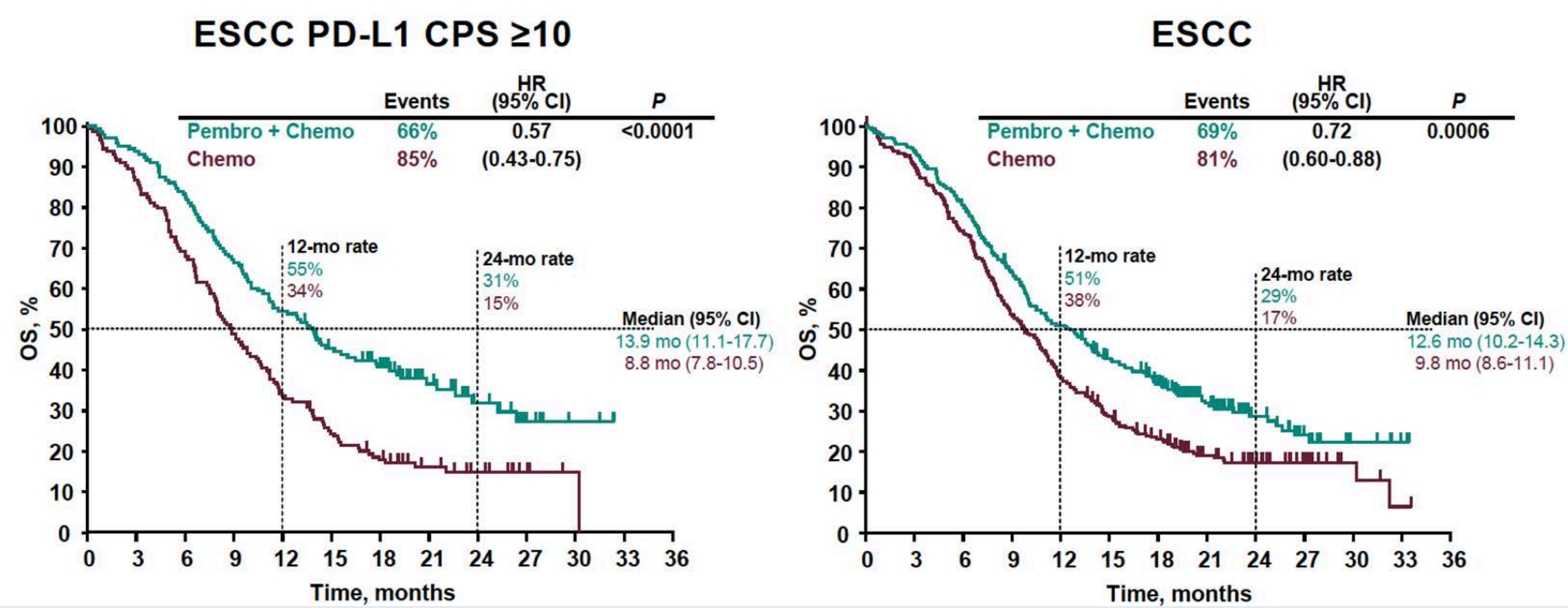


Moehler M et al. ESMO 2020;Abstract LBA6.

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.

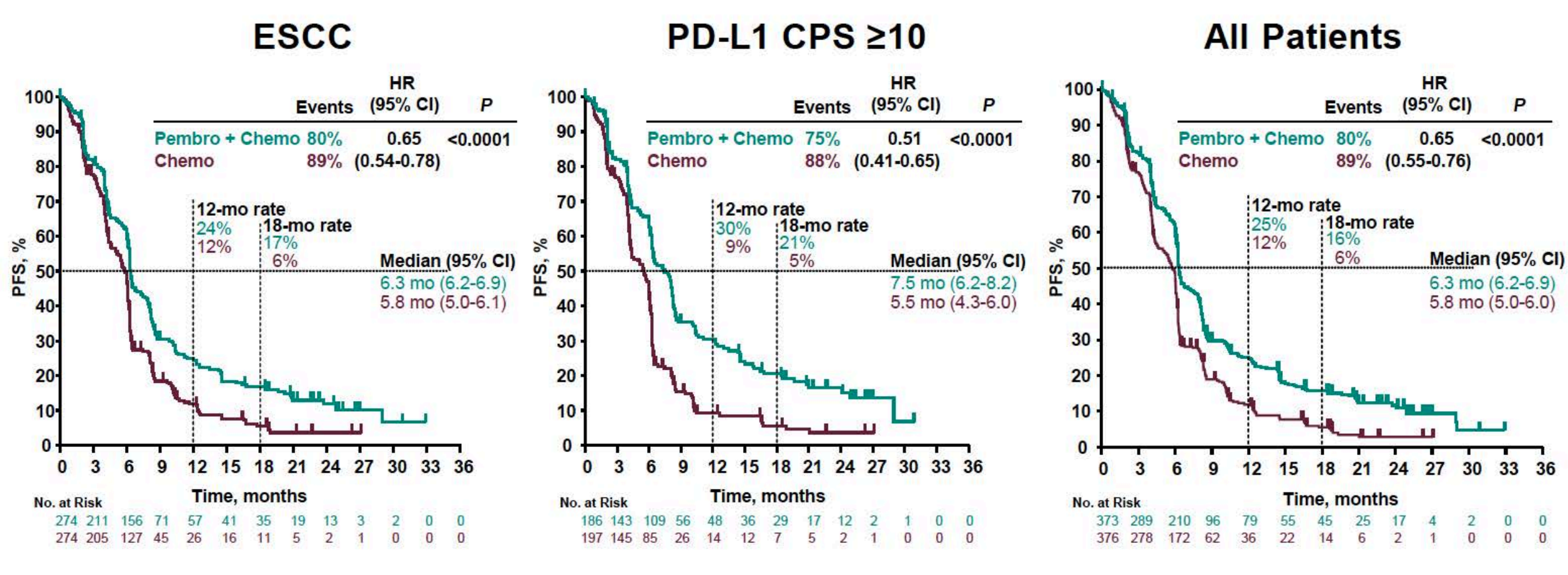
KEYNOTE-590: Overall Survival



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

Meet The Professor with Dr Venook

MODULE 1: Cases from Drs Bachow and Matt-Amaral

- Dr Bachow: A 73-year-old woman with dMMR metastatic colorectal cancer – BRAF mutation
- Dr Matt-Amaral: A 74-year-old woman with MMR-proficient metastatic colorectal cancer

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

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- Dr Gosain: A 72-year-old man with MSS metastatic GEJ adenocarcinoma – PD-L1 CPS 20, HER2-negative
- Dr Yap: A 54-year-old man with MSS metastatic esophageal adenocarcinoma – PD-L1 CPS 15, HER2-positive

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MODULE 5: Cases from Drs Brenner and Choksi

- Dr Brenner: An 84-year-old man with Child-Pugh A cirrhosis and advanced HCC
- Dr Choksi: A 63-year-old woman with Child-Pugh B cirrhosis and advanced HCC

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

MODULE 7: Gastrointestinal Cancers Journal Club with Dr Venook

MODULE 8: Recent Data Sets

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TO PRACTICE

Case Presentation – Dr Brenner: An 84-year-old man with Child-Pugh A cirrhosis and advanced HCC

Dr Warren Brenner

- 10/2019: Diagnosis of Child-Pugh A HCC with underlying liver cirrhosis believed to be secondary to steatohepatitis; radiofrequency ablation
- 9/2020: Recurrent disease in liver with small cardiophrenic right-sided lymph node involvement
  - Cryoablation of the tumor and of the lymph node mass; procedure complicated by right lung pneumothorax due to a chest tube and brief hospitalization
- 12/2020: PD with increasing enhancement along capsular surface of upper margin of the liver
- Atezolizumab with bevacizumab initiated

Questions

- Is atezolizumab and bevacizumab now considered the standard up-front therapy for patients with advanced HCC with maintained liver function? Is there any concern in patients who have baseline low platelets in giving bevacizumab?
- Is there still a role for doing any genetic testing of HCC? Is there any data regarding PD-L1 staining and response to immunotherapy?

Case Presentation – Dr Choksi: A 63-year-old woman with Child-Pugh B cirrhosis and advanced HCC

Dr Mamta Choksi

- PMH: hemochromatosis and liver cirrhosis
- 6/2017: Diagnosis of well differentiated HCC with steatohepatitis features;
  PET/CT showed a liver lesion with mild splenomegaly
  - Deemed high-risk for liver surgery due to her liver cirrhosis with underlying hemochromatosis
  - Radiofrequency ablation
- 10/2020: PET shows right and left liver lesions; elevated AFP 15.89
- Interventional radiologist concerned about her underlying cardiac, pulmonary and liver conditions
- 1/2021: After discussion, nivolumab 240 mg q2weeks is initiated

Question

- What treatment approach would you recommend for this patient?

Meet The Professor with Dr Venook

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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 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 (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 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 Grothey	Lenvatinib
 Dr Bekaii-Saab	Cabozantinib	 Dr O'Reilly	Lenvatinib
 Dr Bendell	Cabozantinib	 Dr Venook	Lenvatinib
 Dr Ciombor	Sorafenib	 Dr Wainberg	Ramucirumab

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 B7 score and a PS of 1 who received first-line atezolizumab/bevacizumab with minimal toxicity, had stable disease for 14 months and then experienced disease progression (AFP 2,500 ng/mL)?

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

RTP RESEARCH TO PRACTICE

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."

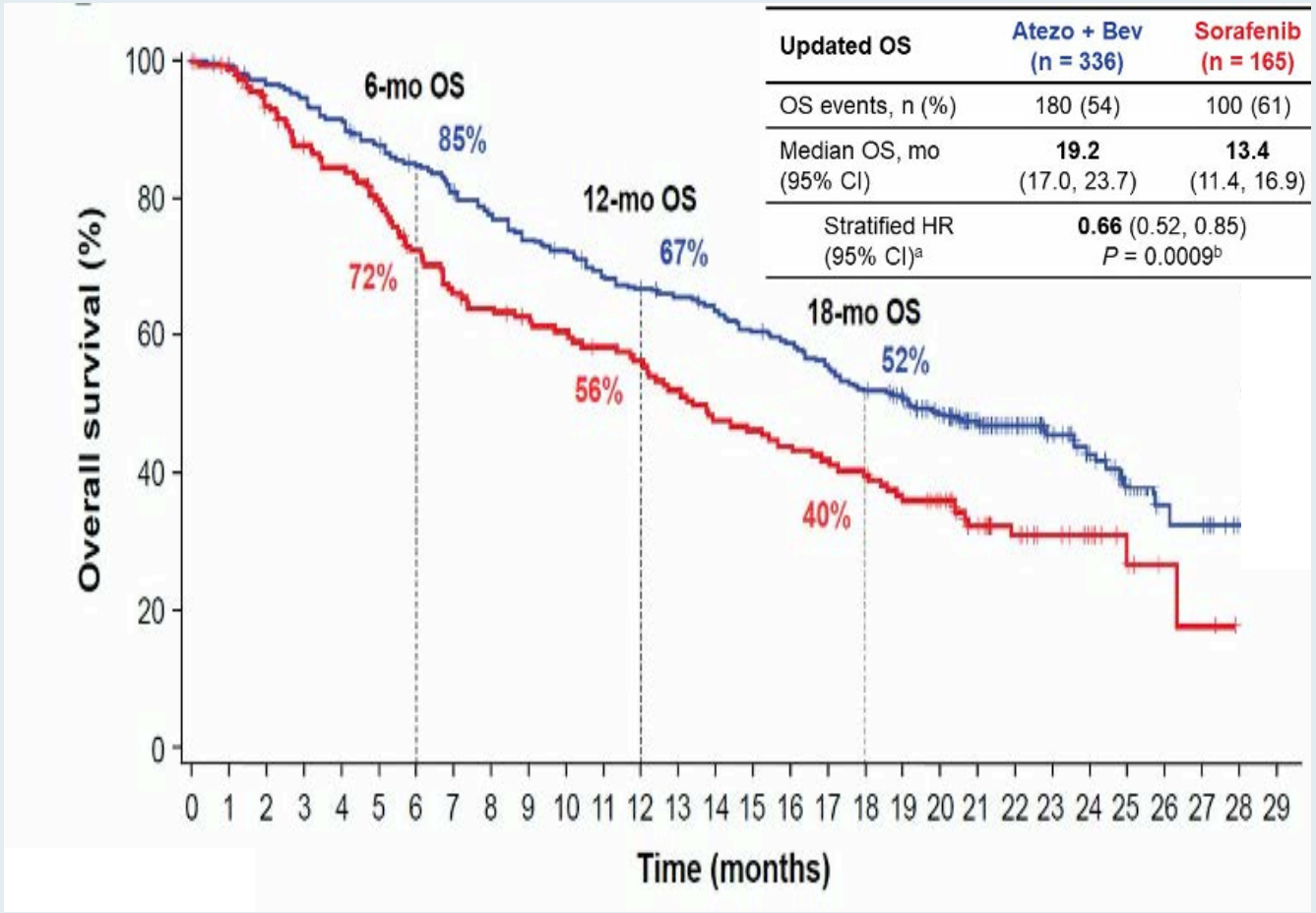
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-atezolizumab-plus-bevacizumab-unresectable-hepatocellular-carcinoma

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)

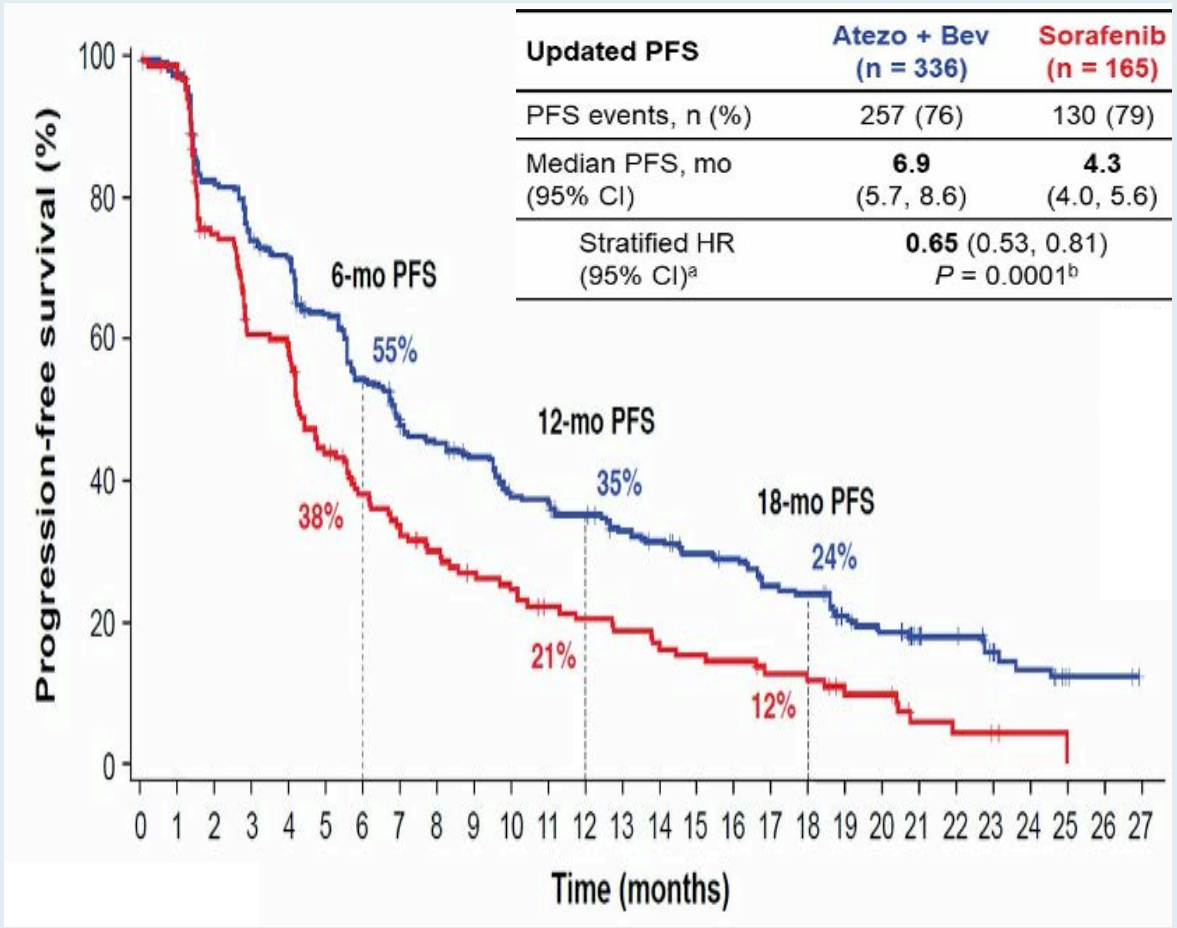
Finn RS et al.

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

IMbrave150: Safety Data

Overall Safety Summary

AEs, n (%)	Atezo + bev (n=329)	Sorafenib (n=156)
Any grade AEs	323 (98)	154 (99)
Treatment-related	276 (84)	147 (94)
Grade 3/4 AEs	186 (57)	86 (55)
Treatment-related Grade 3/4	117 (**36**)	71 (**46**)
Grade 5 AEs	15 (5)	9 (6)
Treatment-related Grade 5	6 (**2**)	1 (**0.6**)
Serious AEs	125 (38)	48 (31)
Treatment-related	56 (17)	24 (15)
AE leading to withdrawal from any drug	51 (16)	16 (10)
AE leading to dose interruption of any treatment	163 (50)	64 (41)
AE leading to dose modification of sorafenib	0	58 (37)

Common AEs (Any Grade ≥15%)

	Atezo + bev (n=329)		Sorafenib (n=156)	
n (%)	All	G3/4	All	G3/4
Hypertension	98 (30)	50 (15)	38 (24)	19 (12)
Fatigue	67 (20)	8 (2)	29 (19)	5 (3)
Proteinuria	66 (20)	10 (3)	11 (7)	1 (0.6)
AST increased	64 (20)	23 (7)	26 (17)	8 (5)
Pruritus	64 (20)	0	15 (10)	0
Diarrhoea	62 (19)	6 (2)	77 (49)	8 (5)
Pyrexia	59 (18)	4 (1)	15 (10)	2 (1)
Decreased appetite	58 (18)	4 (1)	38 (24)	6 (4)
PPES	3 (1)	0	75 (48)	13 (8)
Rash	41 (13)	0	27 (17)	4 (3)
Abdominal pain	40 (12)	4 (1)	27 (17)	4 (3)
Nausea	40 (12)	1 (0.3)	25 (16)	1 (0.6)

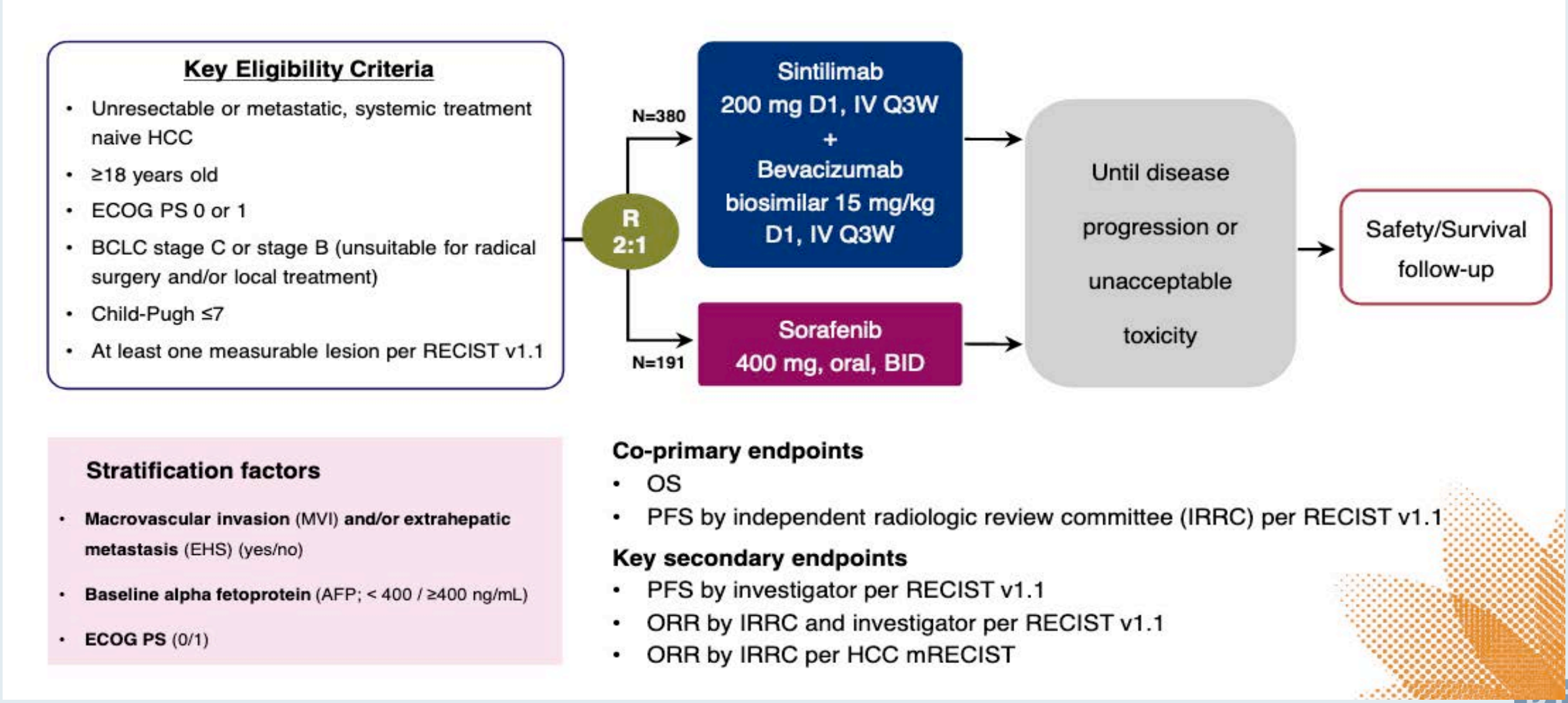
Cheng AL et al. ESMO Asia 2019;Abstract LBA3.

Courtesy of Ahmed Kaseb, MD

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

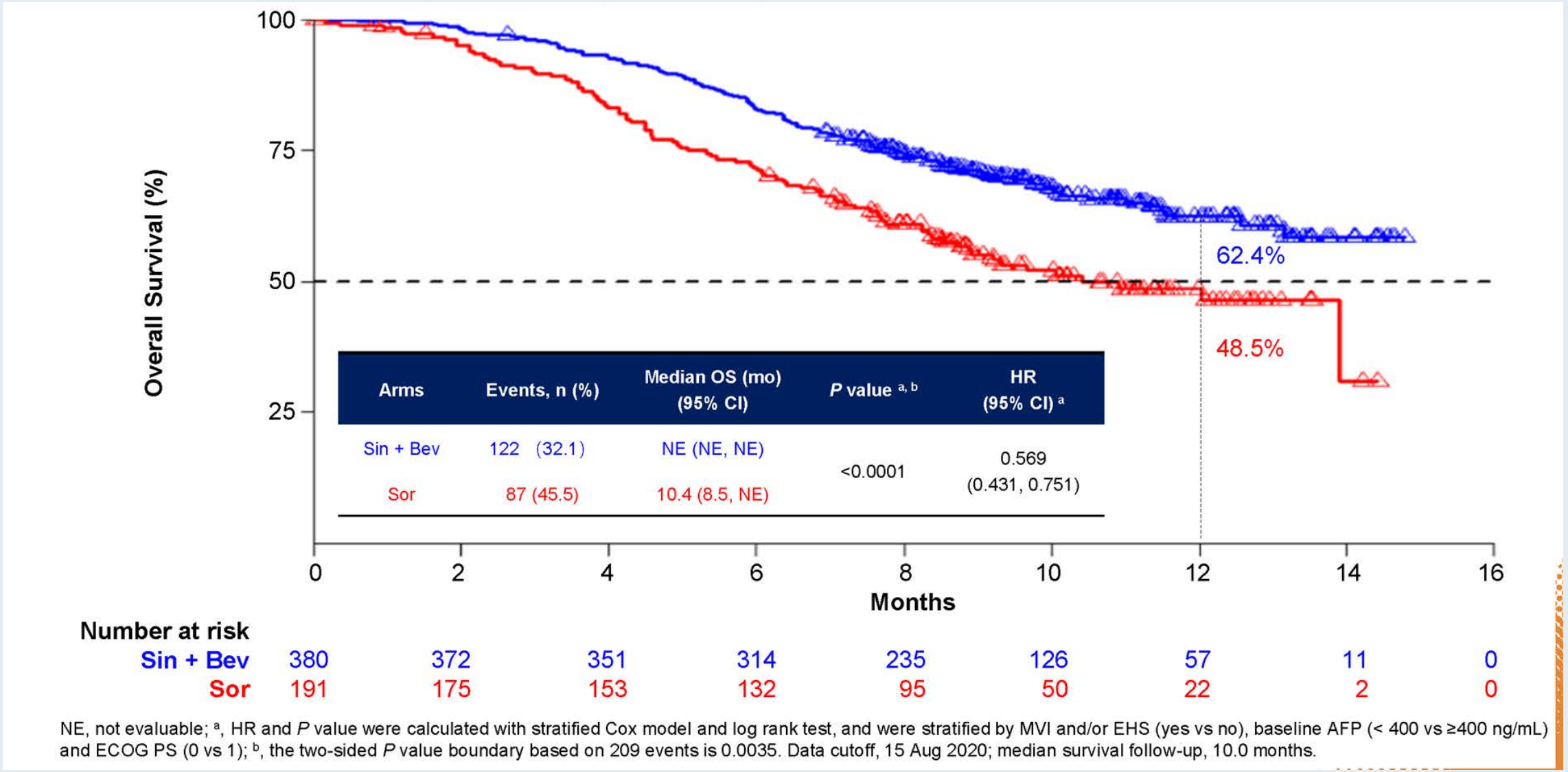
Ren Z et al. ESMO Asia 2020;Abstract LBA2.

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



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

ORIENT-32 Coprimary Endpoint: Overall Survival



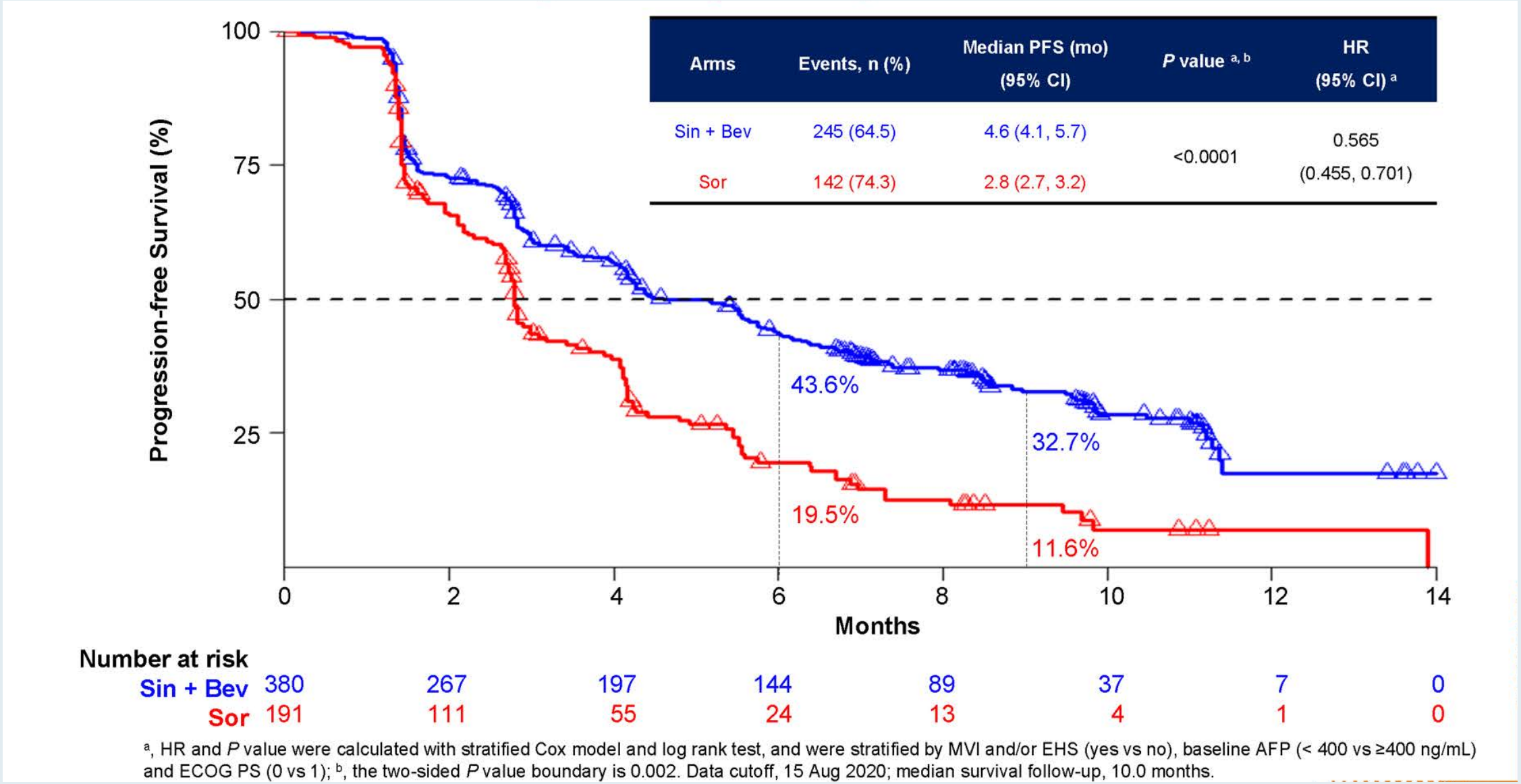
NE, not evaluable; [a], HR and *P* value were calculated with stratified Cox model and log rank test, and were stratified by MVI and/or EHS (yes vs no), baseline AFP (< 400 vs ≥400 ng/mL) and ECOG PS (0 vs 1); [b], the two-sided *P* value boundary based on 209 events is 0.0035. Data cutoff, 15 Aug 2020;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



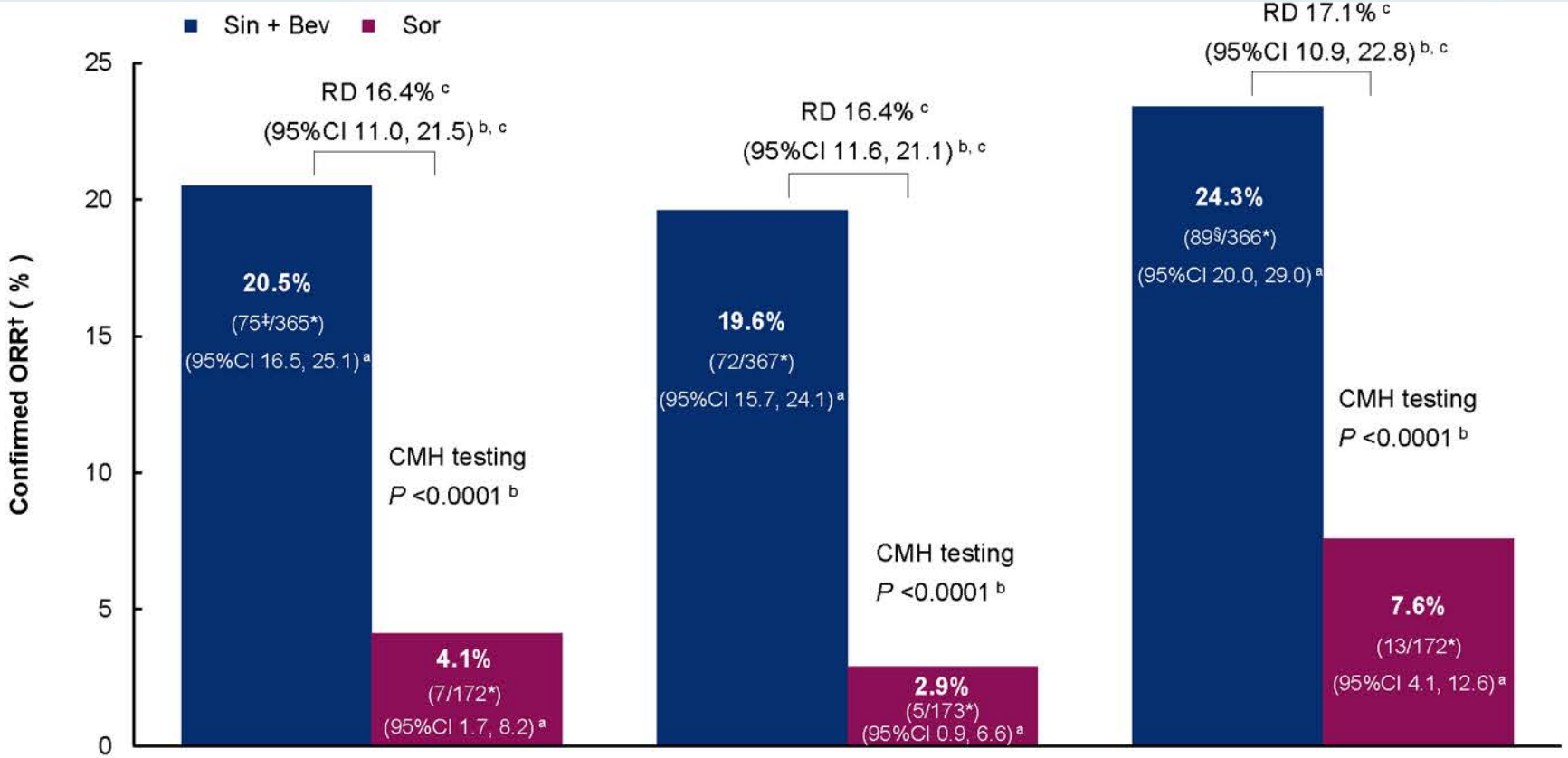
a, HR and *P* value were calculated with stratified Cox model and log rank test, and were stratified by MVI and/or EHS (yes vs no), baseline AFP (< 400 vs ≥400 ng/mL) and ECOG PS (0 vs 1); b, the two-sided *P* value boundary is 0.002. Data cutoff, 15 Aug 2020; median survival follow-up, 10.0 months.

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

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

RTP RESEARCH TO PRACTICE

ORIENT-32: Response Rate and Duration of Response



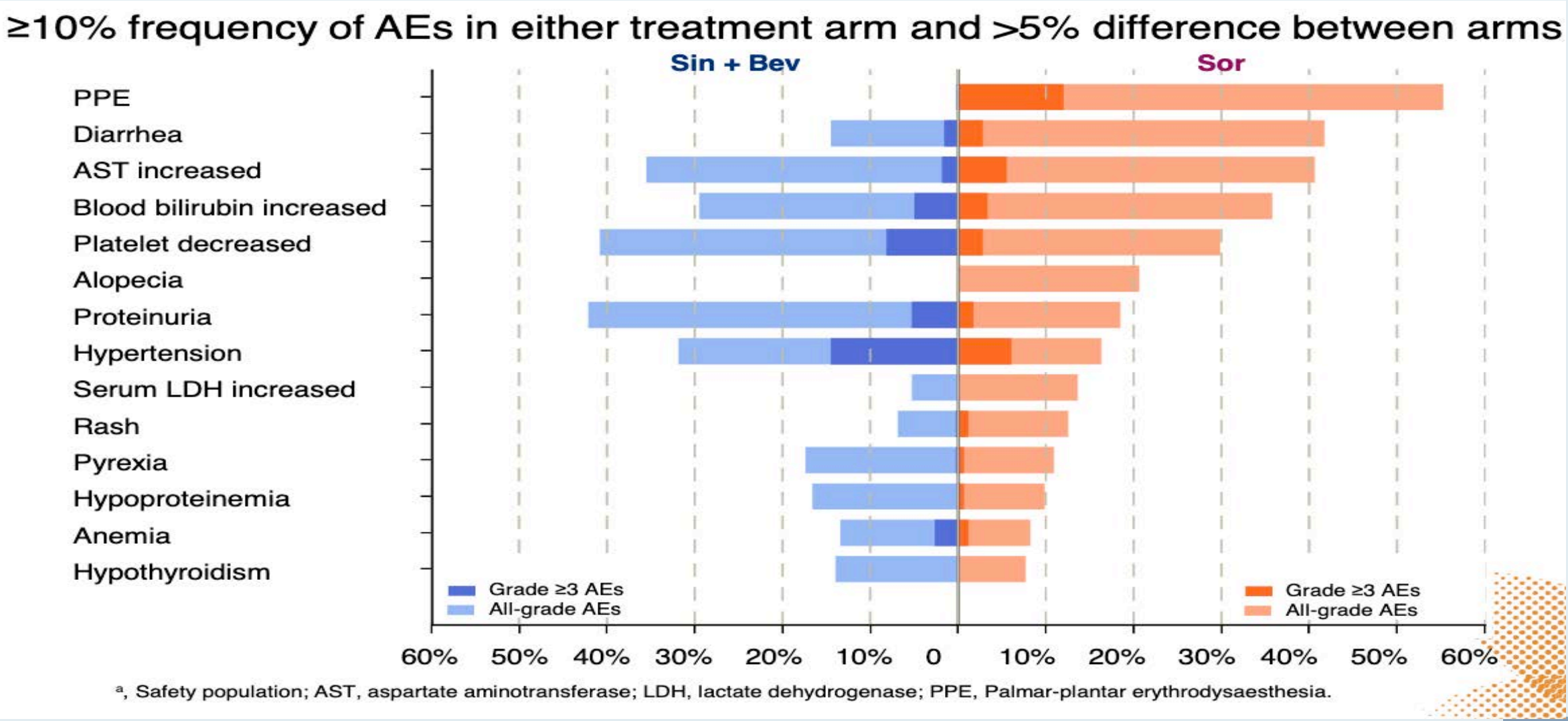
	IRRC-ORR per RECIST v1.1		Investigator-ORR per RECIST v1.1		IRRC-ORR per mRECIST	
Median DOR, months	**NE**	**9.8**	**NE**	**NE**	**NE**	**6.6**
(95% CI)	(NE, NE)	(2.8, NE)	(NE, NE)	(2.5, NE)	(8.2, NE)	(2.6, NE)

*, 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 Dr Venook

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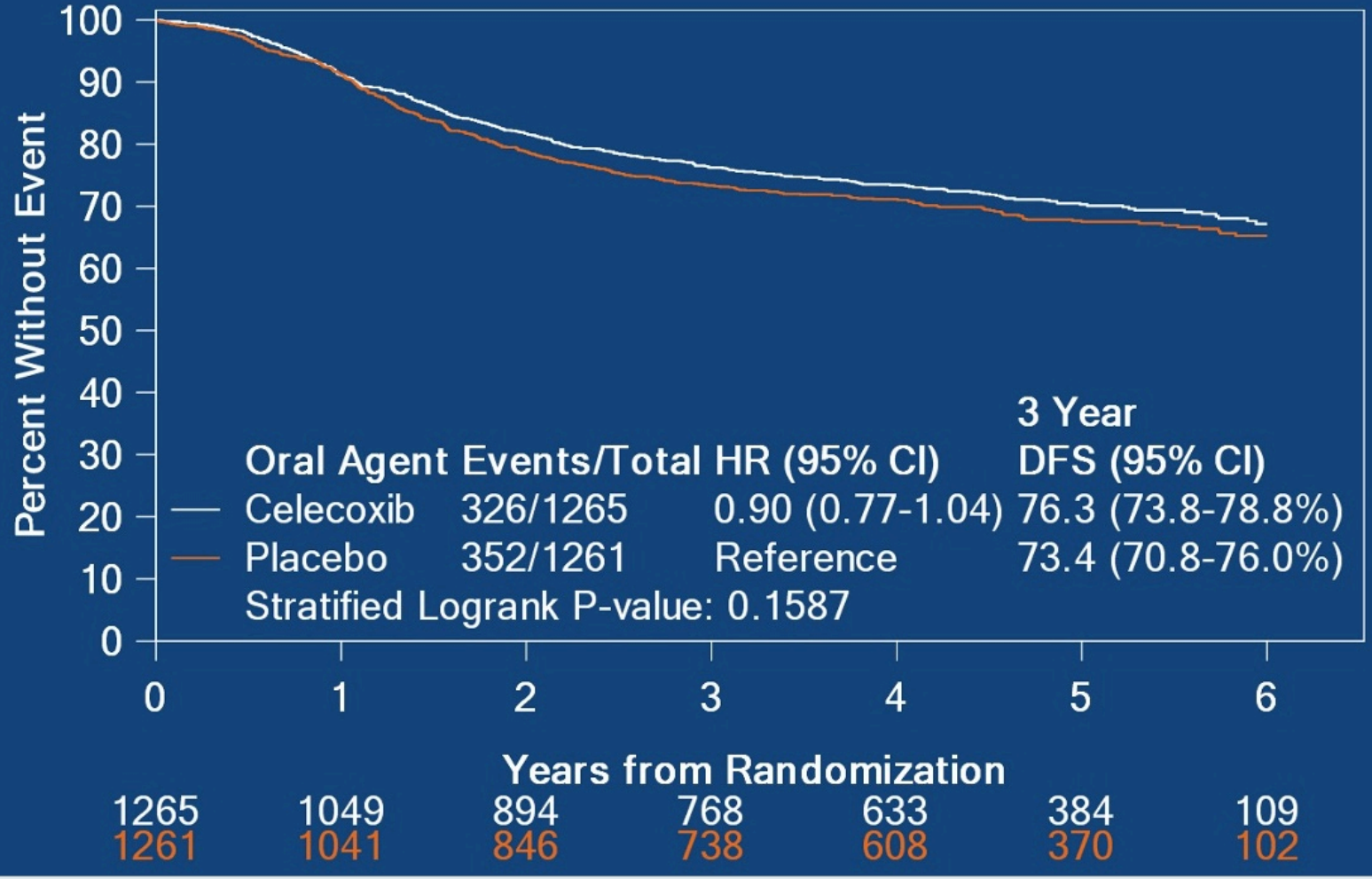
RTP RESEARCH TO PRACTICE

Celecoxib in addition to standard adjuvant therapy with 5-fluorouracil, leucovorin, oxaliplatin (FOLFOX) in stage III colon cancer: Results from CALGB/SWOG 80702

Jeffrey A. Meyerhardt, Qian Shi, Charles S. Fuchs, Donna Niedzwiecki, Tyler Zemla, Priya Kumthekar, Katherine A. Guthrie, Felix Couture, Philip Kuebler, Johanna C. Bendell, Pankaj Kumar, Dequincy Lewis, Benjamin Tan, Monica Bertagnolli, Axel Grothey, Howard S. Hochster, Richard M. Goldberg, Alan Venook, Charles Blanke, Anthony F. Shields

ASCO 2020;Abstract 4003

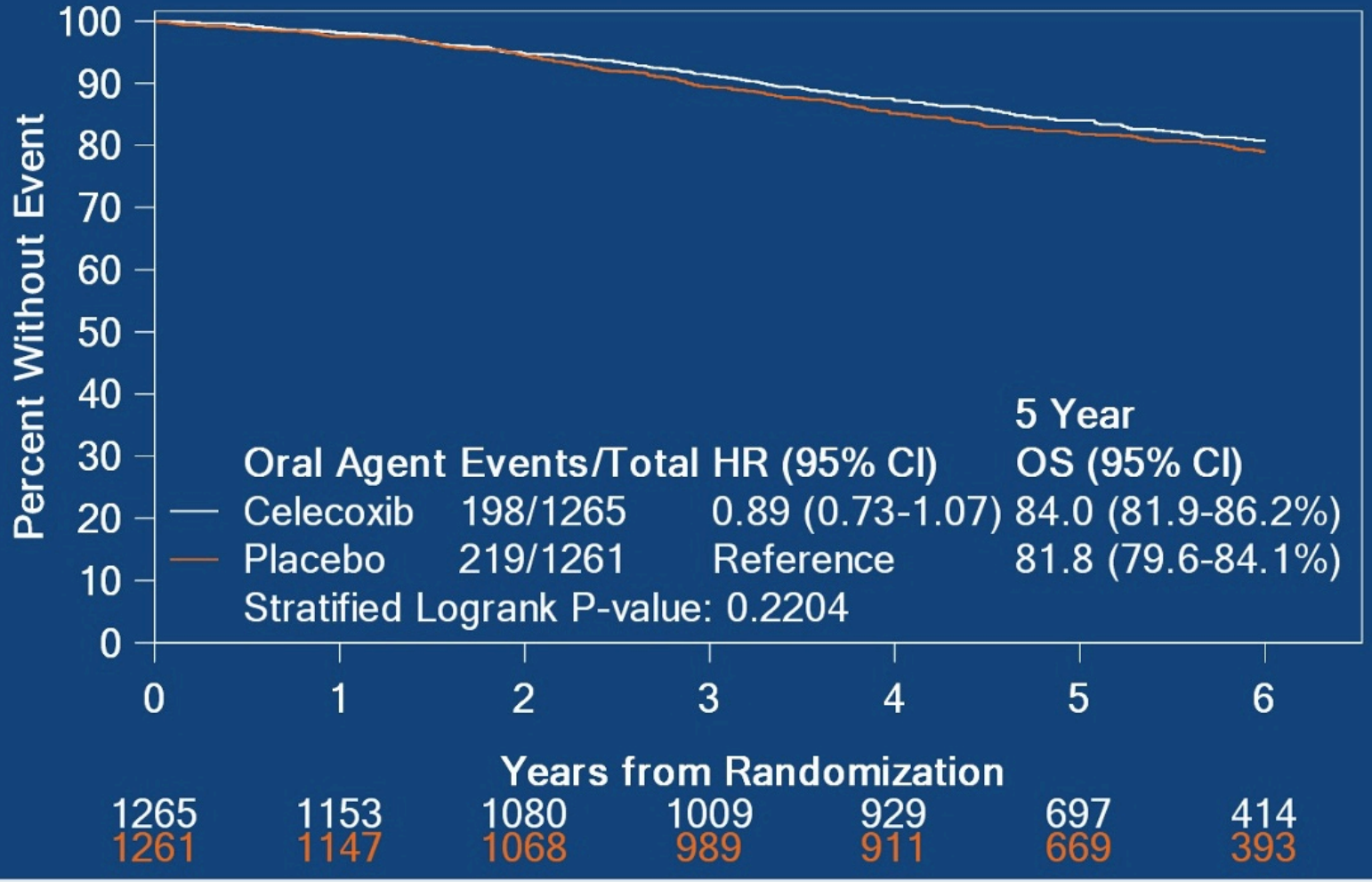
Disease-Free Survival (Celecoxib v Placebo)*



* Censored at 6 years from study entry

Meyerhardt JA et al. ASCO 2020;Abstract 4003.

Overall Survival (Celecoxib v Placebo) *



* Censored at 6 years from study entry

Meyerhardt JA et al. ASCO 2020;Abstract 4003.

CONSENSUS STATEMENT

Nat Rev Clin Oncol 2020;17(12):757-70

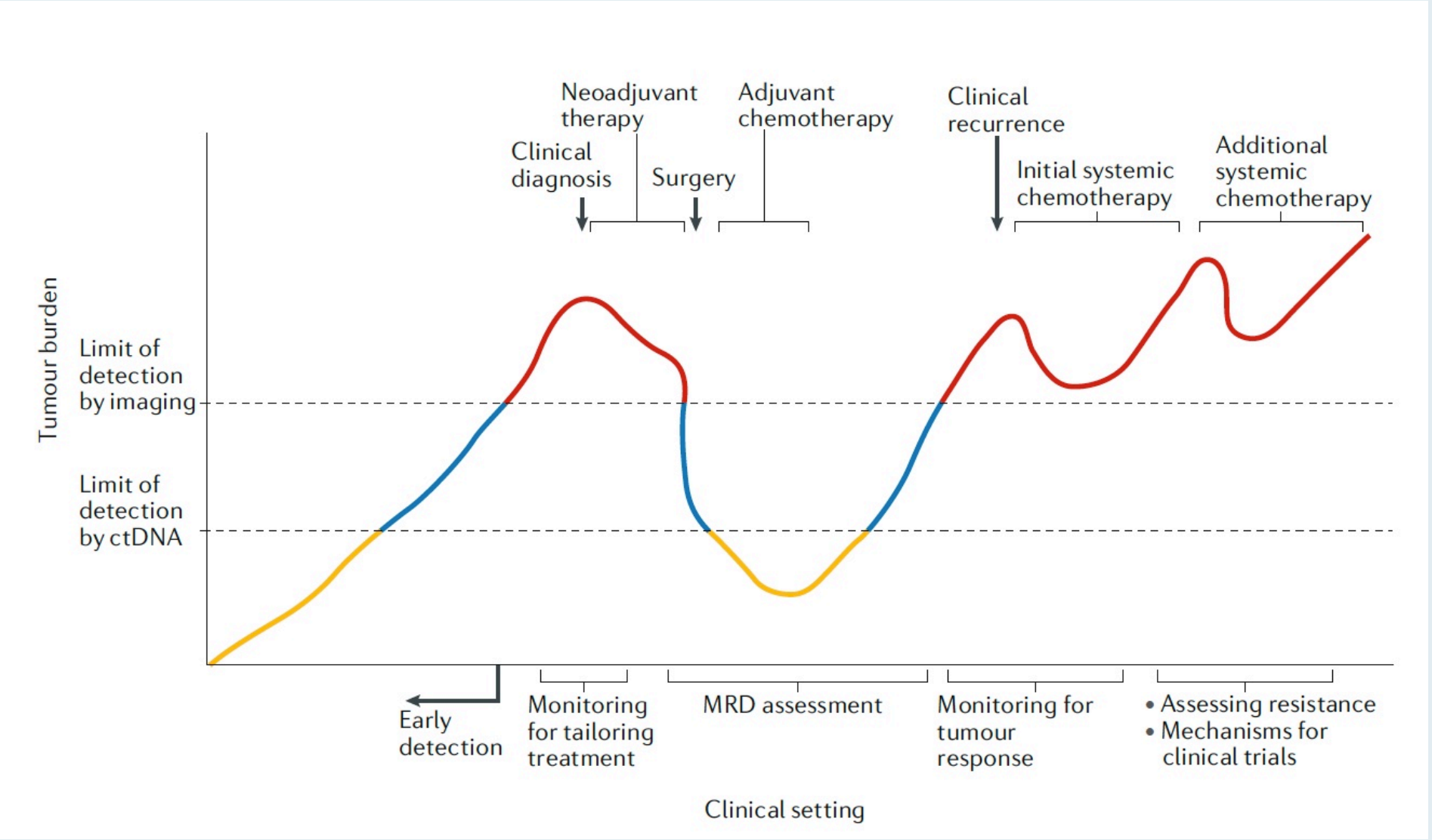
OPEN

Check for updates

ctDNA applications and integration in colorectal cancer: an NCI Colon and Rectal–Anal Task Forces whitepaper

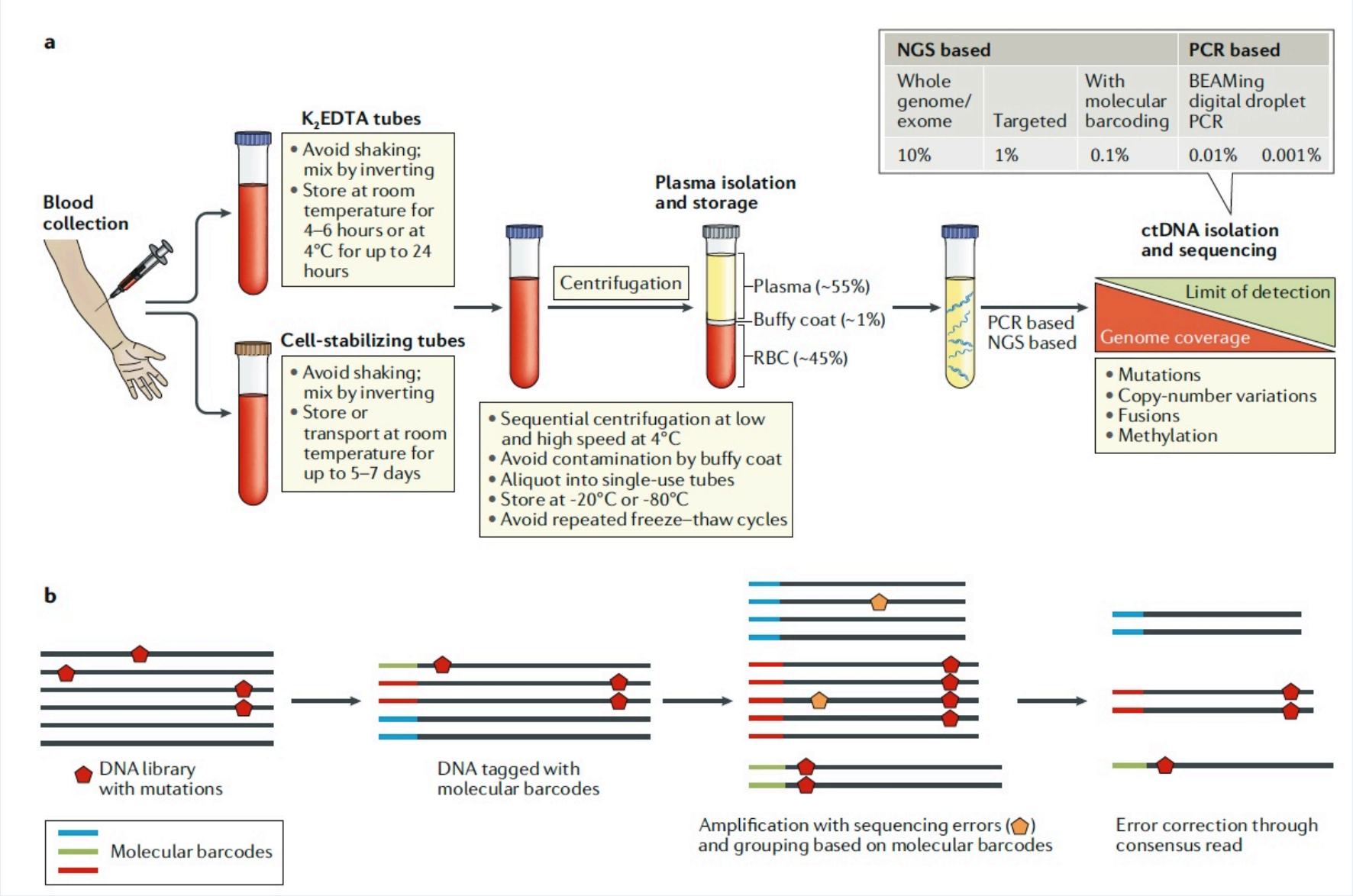
Arvind Dasari[1,40]✉, Van K. Morris[1,40], Carmen J. Allegra[2], Chloe Atreya[3], Al B. Benson III[4], Patrick Boland[5], Ki Chung[6], Mehmet S. Copur[7], Ryan B. Corcoran[8], Dustin A. Deming[9], Andrea Dwyer[10], Maximilian Diehn[11], Cathy Eng[1], Thomas J. George[12], Marc J. Gollub[13], Rachel A. Goodwin[14], Stanley R. Hamilton[15], Jaclyn F. Hechtman[16], Howard Hochster[17], Theodore S. Hong[18], Federico Innocenti[19], Atif Iqbal[20], Samuel A. Jacobs[21], Hagen F. Kennecke[22], James J. Lee[23], Christopher H. Lieu[24], Heinz-Josef Lenz[25], O. Wolf Lindwasser[26], Clara Montagut[27], Bruno Odisio[28], Fang-Shu Ou[29], Laura Porter[30], Kanwal Raghav[1], Deborah Schrag[31], Aaron J. Scott[32], Qian Shi[29], John H. Strickler[33], Alan Venook[34], Rona Yaeger[35], Greg Yothers[36], Y. Nancy You[37], Jason A. Zell[38,39] and Scott Kopetz[1]

Clinical Applications of ctDNA



Dasari A et al. *Nat Rev Clin Oncol* 2020;17(12):757-70.

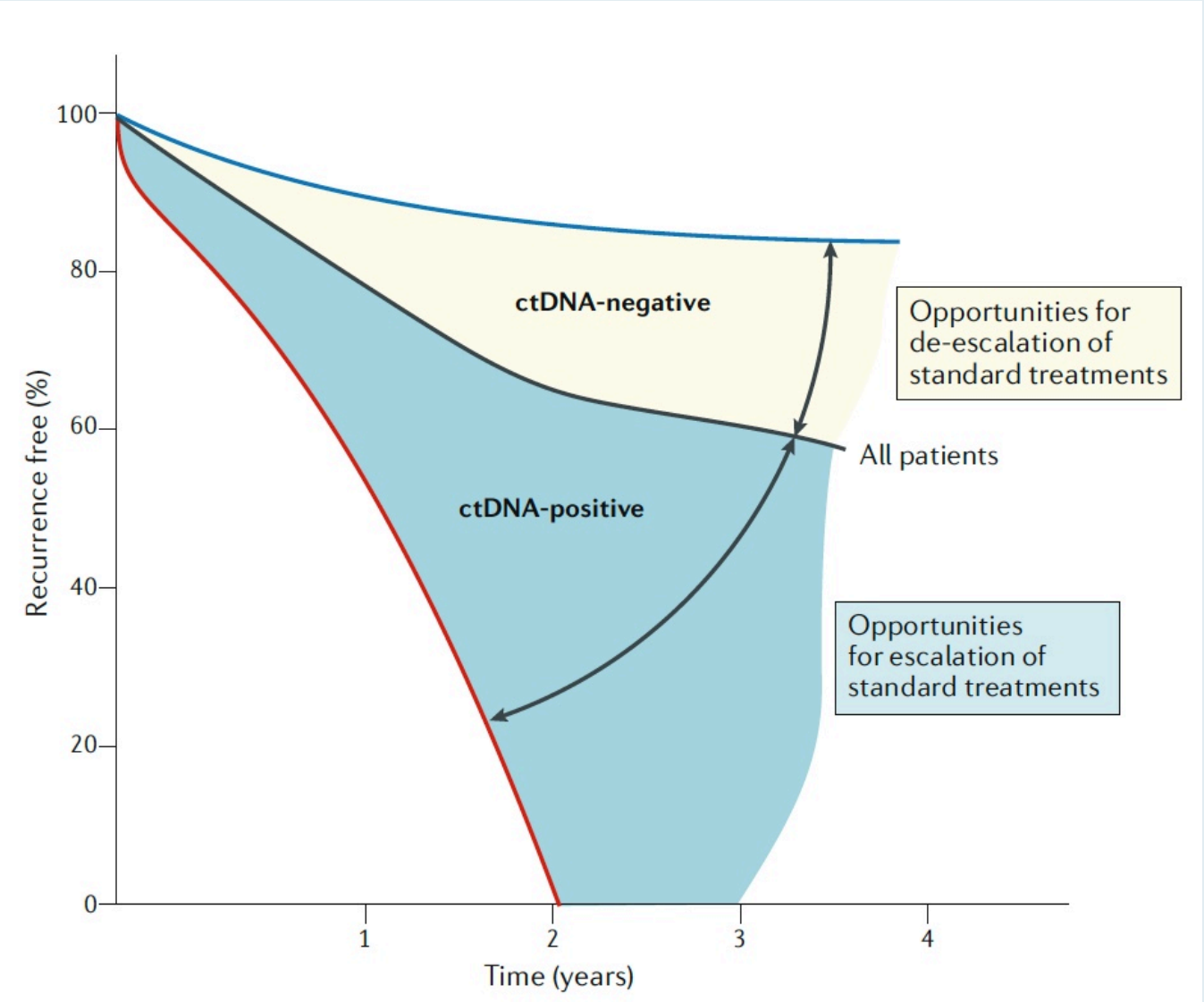
ctDNA Isolation and Analysis



Dasari A et al. *Nat Rev Clin Oncol* 2020;17(12):757-70.

RTP RESEARCH TO PRACTICE

Applications of ctDNA in Tailoring the Aggressiveness of Adjuvant Therapy



Dasari A et al. *Nat Rev Clin Oncol* 2020;17(12):757-70.

Rebecca A. Snyder[1]
Keith Fournier[2]
Richard Royal[3]
Alan P. Venook[4]
George J. Chang[2,5]

[1]*Departments of Surgery and Public Health, Brody School of Medicine at East Carolina University, Greenville, NC*
[2]*Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*
[3]*Department of Surgical Oncology, Maine Medical Center, Portland, ME*
[4]*Department of Medicine, Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA*
[5]*Department of Health Services Research, The University of Texas MD Anderson Cancer Center, Houston, TX*

Clinical Colorectal Cancer, Vol. 19, No. 1, 1-4

Heated Intraperitoneal Chemotherapy for Colorectal Carcinomatosis: Emerging Evidence

Clinical Colorectal Cancer, Vol. 19, No. 1, 1-4

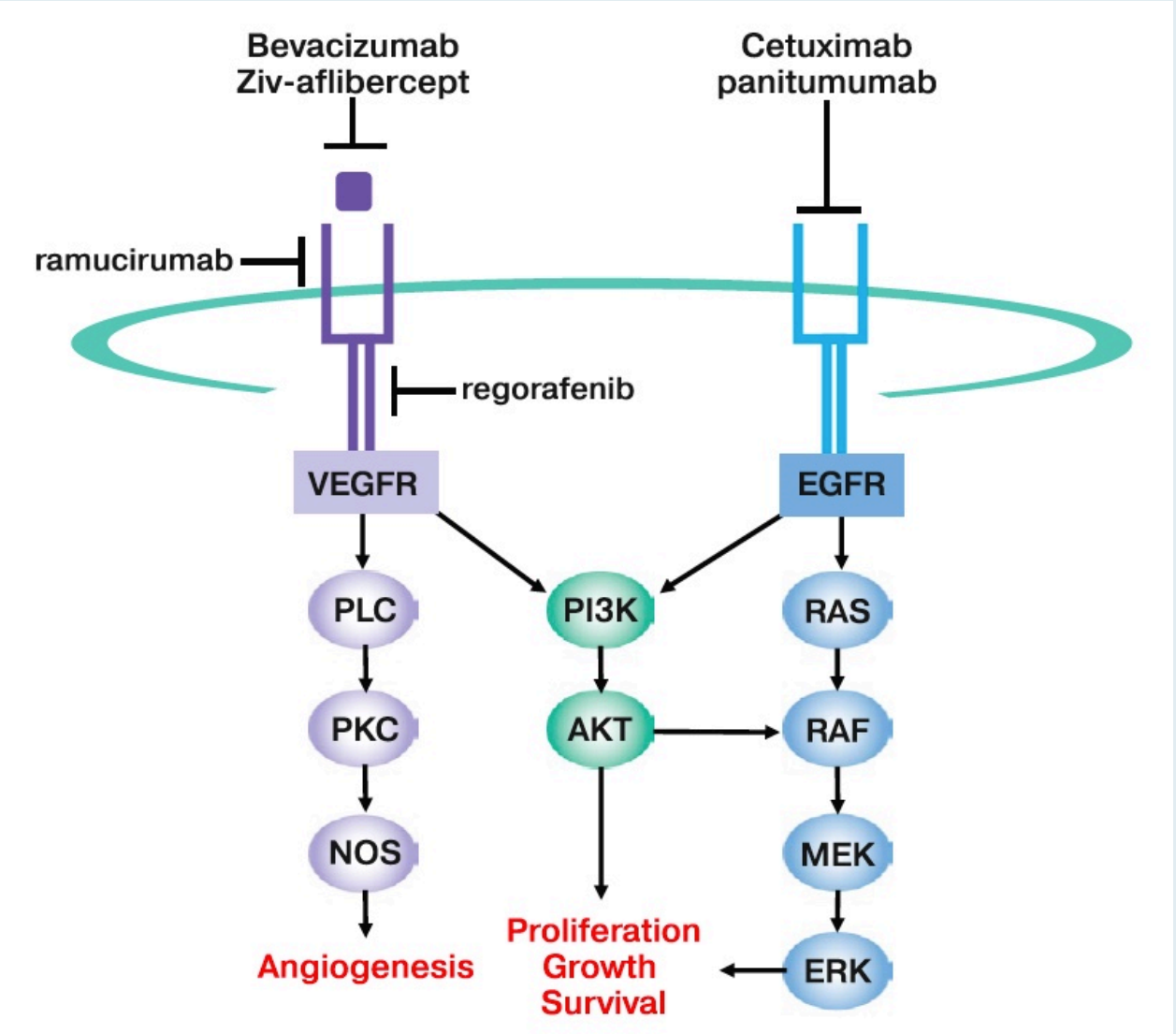
Cancer 2019;125(23):4139-47

Review Article

Targeted Therapy for Colorectal Cancer Metastases: A Review of Current Methods of Molecularly Targeted Therapy and the Use of Tumor Biomarkers in the Treatment of Metastatic Colorectal Cancer

Sorbarikor Piawah, MD, MPH ; and Alan P. Venook, MD

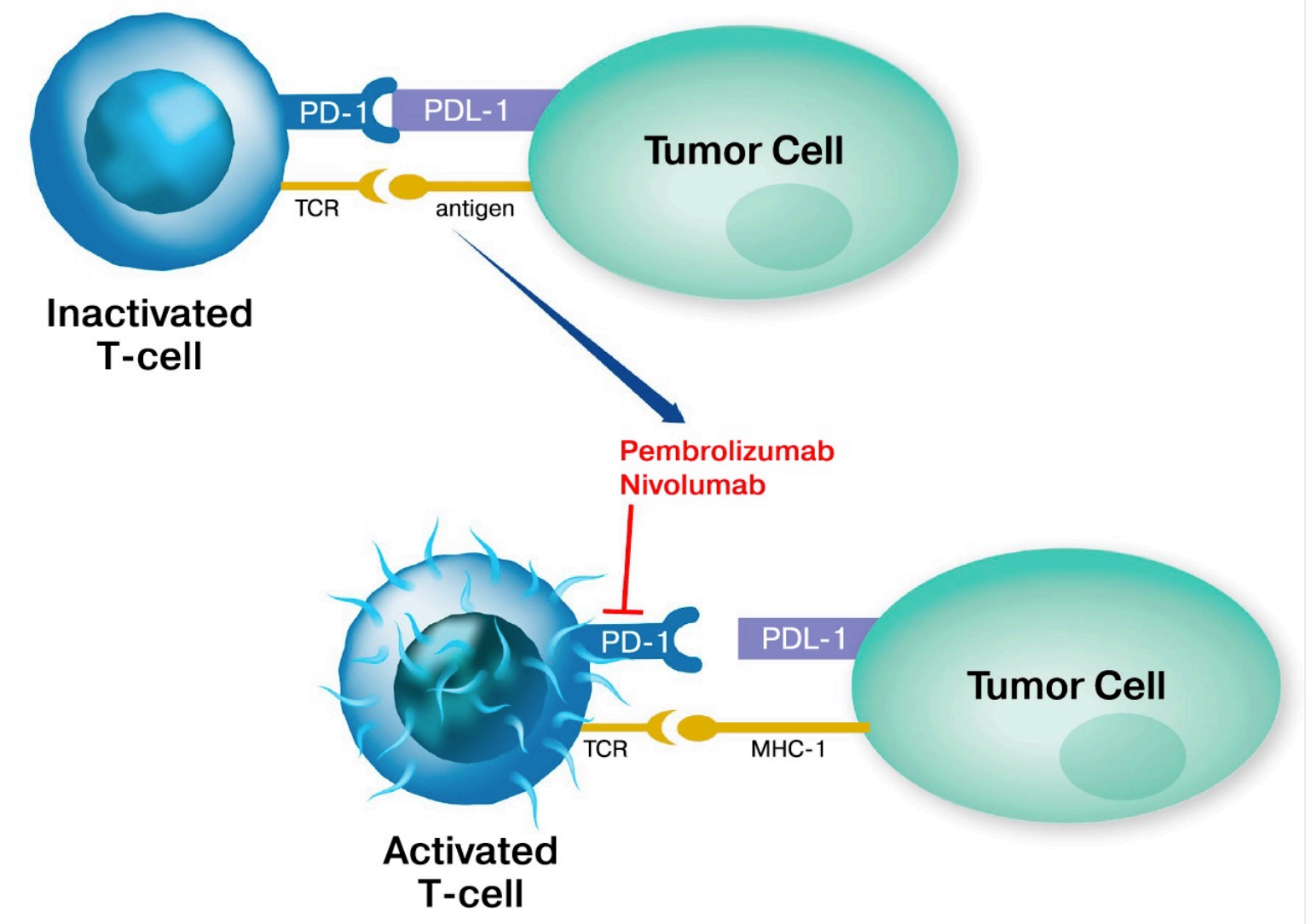
Schematic Depiction of VEGFR and EGFR Cascades and Mechanism of Targeted Therapies



Piawah S, Venook AP. *Cancer* 2019;125(23):4139-47.

RTP RESEARCH TO PRACTICE

Depiction of PD-1 Inhibition by Pembrolizumab and Nivolumab



Piawah S, Venook AP. *Cancer* 2019;125(23):4139-47.

Toxicity and Efficacy of 1st Line Cetuximab (cetux)-Based Therapy in RAS Wildtype (WT) Older Patients (pts) with Metastatic Colorectal Cancer (mCRC): A Pooled Analysis from 1,274 pts in the ARCAD Database

Papamichael D et al.

ESMO 2020;Abstract 432P.

Sex Differences in Efficacy and Toxicity of First-Line Treatment of Metastatic Colorectal Cancer (CRC): An Analysis of 18,399 Patients in the ARCAD Database

Wagner AD et al.
ASCO 2020;Abstract 4029.

Prognostic and Predictive Impact of Primary Tumor Sidedness in First-Line Trials for Advanced Colorectal Cancer: An Analysis of 7,828 Patients in the ARCAD Database

Yin J et al.

Gastrointestinal Cancers Symposium 2020;Abstract 188.

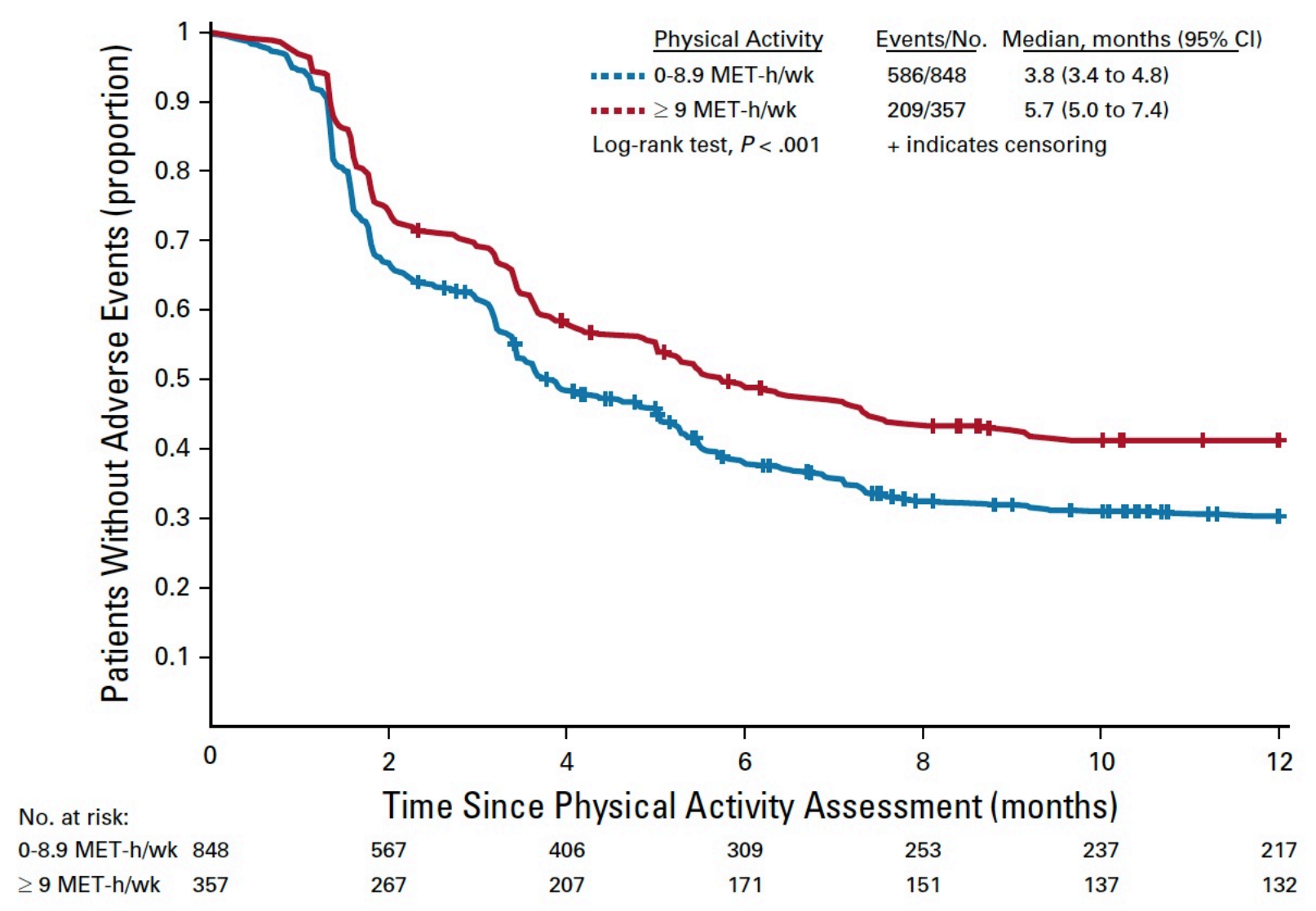
original report

Associations of Physical Activity With Survival and Progression in Metastatic Colorectal Cancer: Results From Cancer and Leukemia Group B (Alliance)/SWOG 80405

Brendan J. Guercio, MD[1]; Sui Zhang, MS[2]; Fang-Shu Ou, PhD[3]; Alan P. Venook, MD[4]; Donna Niedzwiecki, PhD[5]; Heinz-Josef Lenz, MD[6]; Federico Innocenti, MD, PhD[7]; Bert H. O'Neil, MD[8]; James E. Shaw, MD[9]; Blase N. Polite, MD[10]; Howard S. Hochster, MD[11]; James N. Atkins, MD[12]; Richard M. Goldberg, MD[13]; Kaori Sato, MS[2]; Kimmie Ng, MD, MPH[2]; Erin Van Blarigan, ScD[4]; Robert J. Mayer, MD[2]; Charles D. Blanke, MD[14,15]; Eileen M. O'Reilly, MD[16]; Charles S. Fuchs, MD, MPH[17]; and Jeffrey A. Meyerhardt, MD, MPH[2]

J Clin Oncol 2019;37(29):2620-31

Kaplan-Meier Curve for Any First-Time Adverse Event Stratified by Physical Activity Level



Guercio BJ et al. *J Clin Oncol* 2019;37(29):2620-31.

original report

Mutational Analysis of Patients With Colorectal Cancer in CALGB/SWOG 80405 Identifies New Roles of Microsatellite Instability and Tumor Mutational Burden for Patient Outcome

Federico Innocenti, MD, PhD[1]; Fang-Shu Ou, PhD[2]; Xueping Qu, PhD[3]; Tyler J. Zemla, MS[2]; Donna Niedzwiecki, PhD[4]; Rachel Tam[3]; Shilpi Mahajan, PhD[3]; Richard M. Goldberg, MD[5]; Monica M. Bertagnolli, MD[6]; Charles D. Blanke, MD[7]; Hanna Sanoff, MD[1]; James Atkins, MD[8]; Blasé Polite, MD[9]; Alan P. Venook, MD[10]; Heinz-Josef Lenz, MD[11]; and Omar Kabbarah, PhD[3]

J Clin Oncol 2019;37(14):1217-27

Radiomic Signatures to Predict Survival in Patients with Advanced Hepatocellular Carcinoma (HCC) Treated with Sorafenib +/- Doxorubicin: Correlative Science from CALGB 80802 (Alliance)

Dercle L et al.

Gastrointestinal Cancers Symposium 2021;Abstract 343.

Meet The Professor with Dr Venook

MODULE 1: Cases from Drs Bachow and Matt-Amaral

- Dr Bachow: A 73-year-old woman with dMMR metastatic colorectal cancer – BRAF mutation
- Dr Matt-Amaral: A 74-year-old woman with MMR-proficient metastatic colorectal cancer

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

MODULE 3: Cases from Drs Gosain and Yap

- Dr Gosain: A 72-year-old man with MSS metastatic GEJ adenocarcinoma – PD-L1 CPS 20, HER2-negative
- Dr Yap: A 54-year-old man with MSS metastatic esophageal adenocarcinoma – PD-L1 CPS 15, HER2-positive

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

MODULE 5: Cases from Drs Brenner and Choksi

- Dr Brenner: An 84-year-old man with Child-Pugh A cirrhosis and advanced HCC
- Dr Choksi: A 63-year-old woman with Child-Pugh B cirrhosis and advanced HCC

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

MODULE 7: Gastrointestinal Cancers Journal Club with Dr Venook

MODULE 8: Recent Data Sets

RTP RESEARCH TO PRACTICE

Colorectal Cancer

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

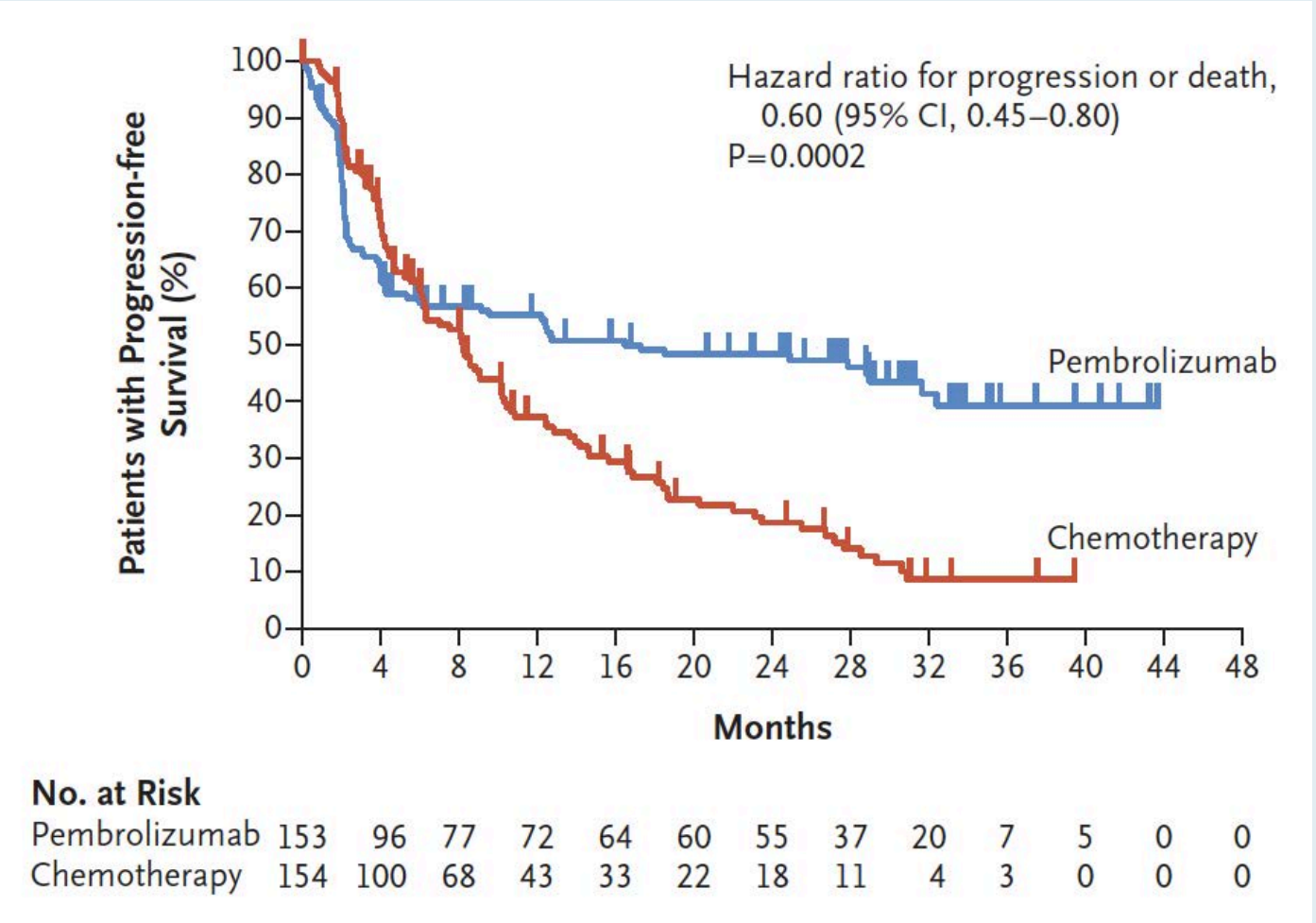
The NEW ENGLAND JOURNAL of MEDICINE

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.

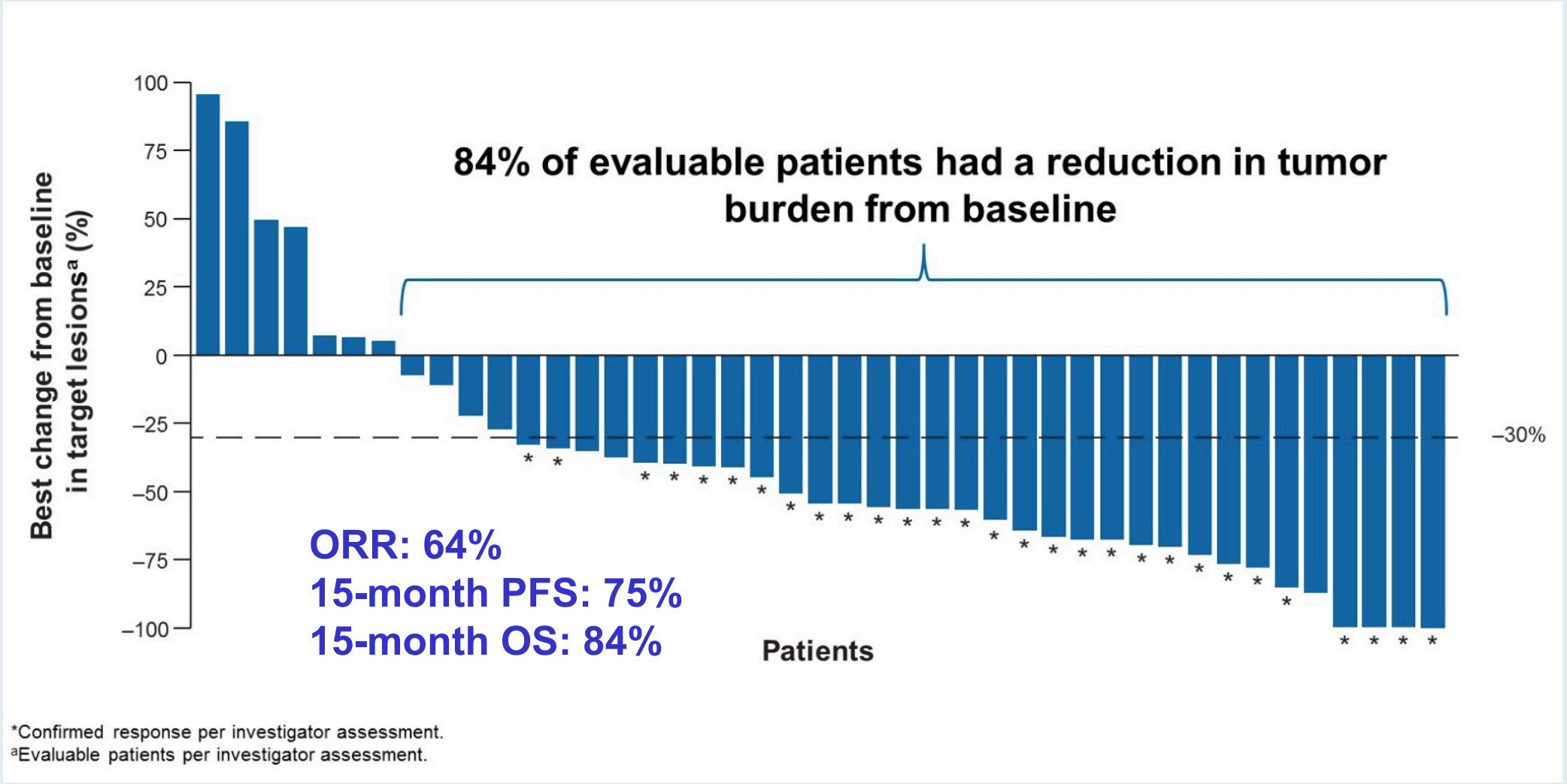
André T et al. *N Engl J Med* 2020;383(23):2207-18.

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.

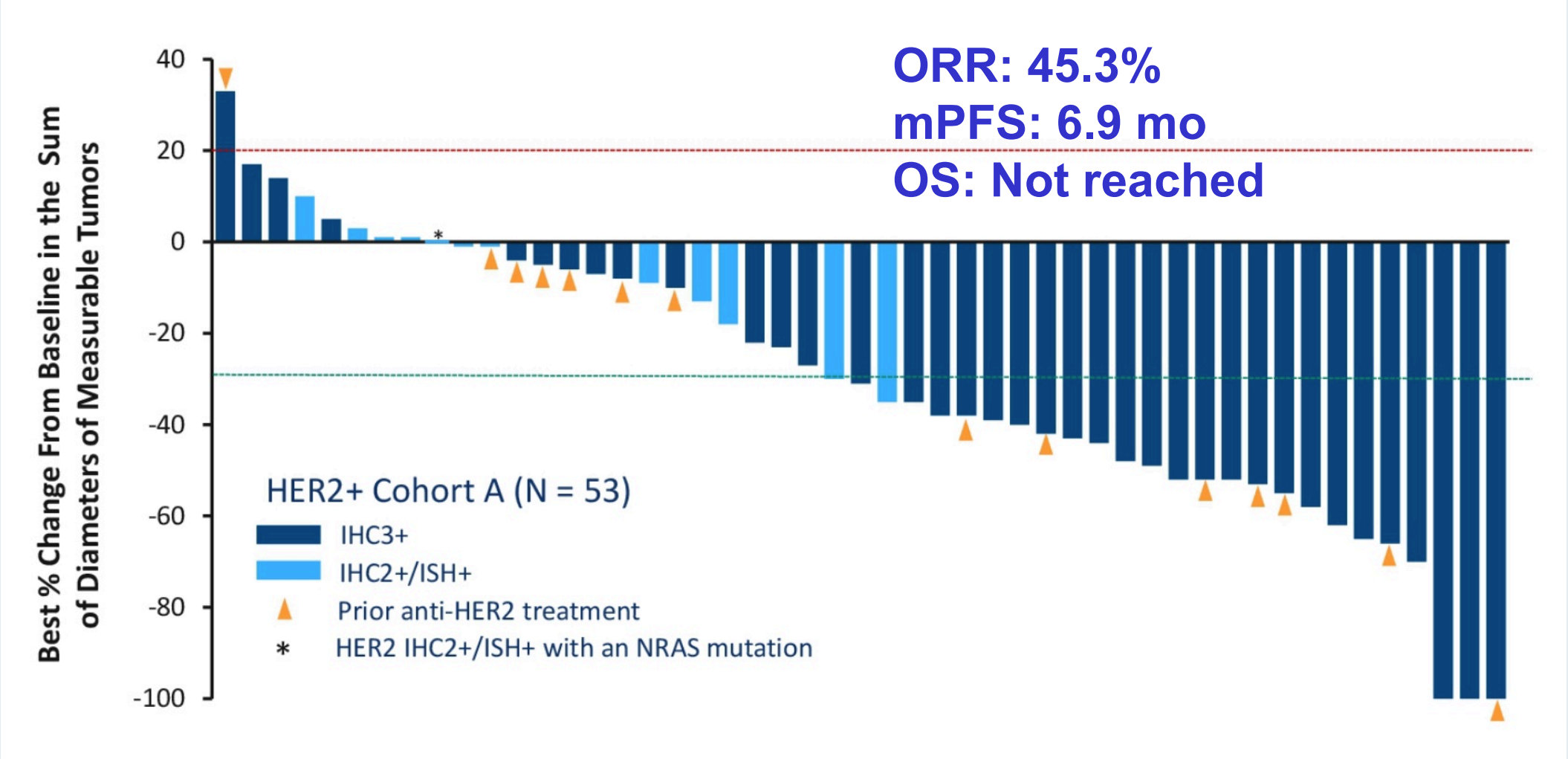
ASCO 2020;Abstract 4000.

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.

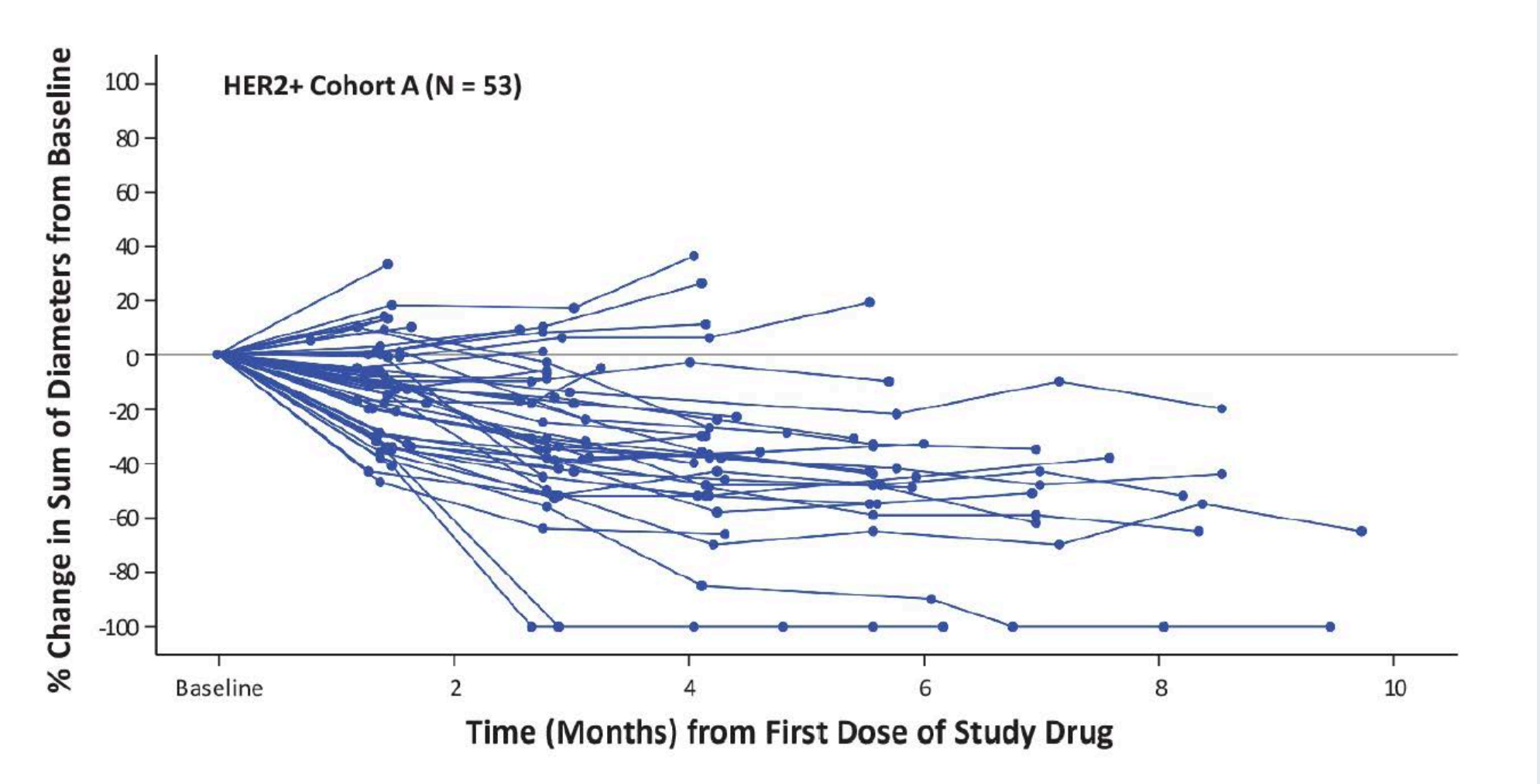
DESTINY-CRC01: Best Change in Tumor Size Over Time



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

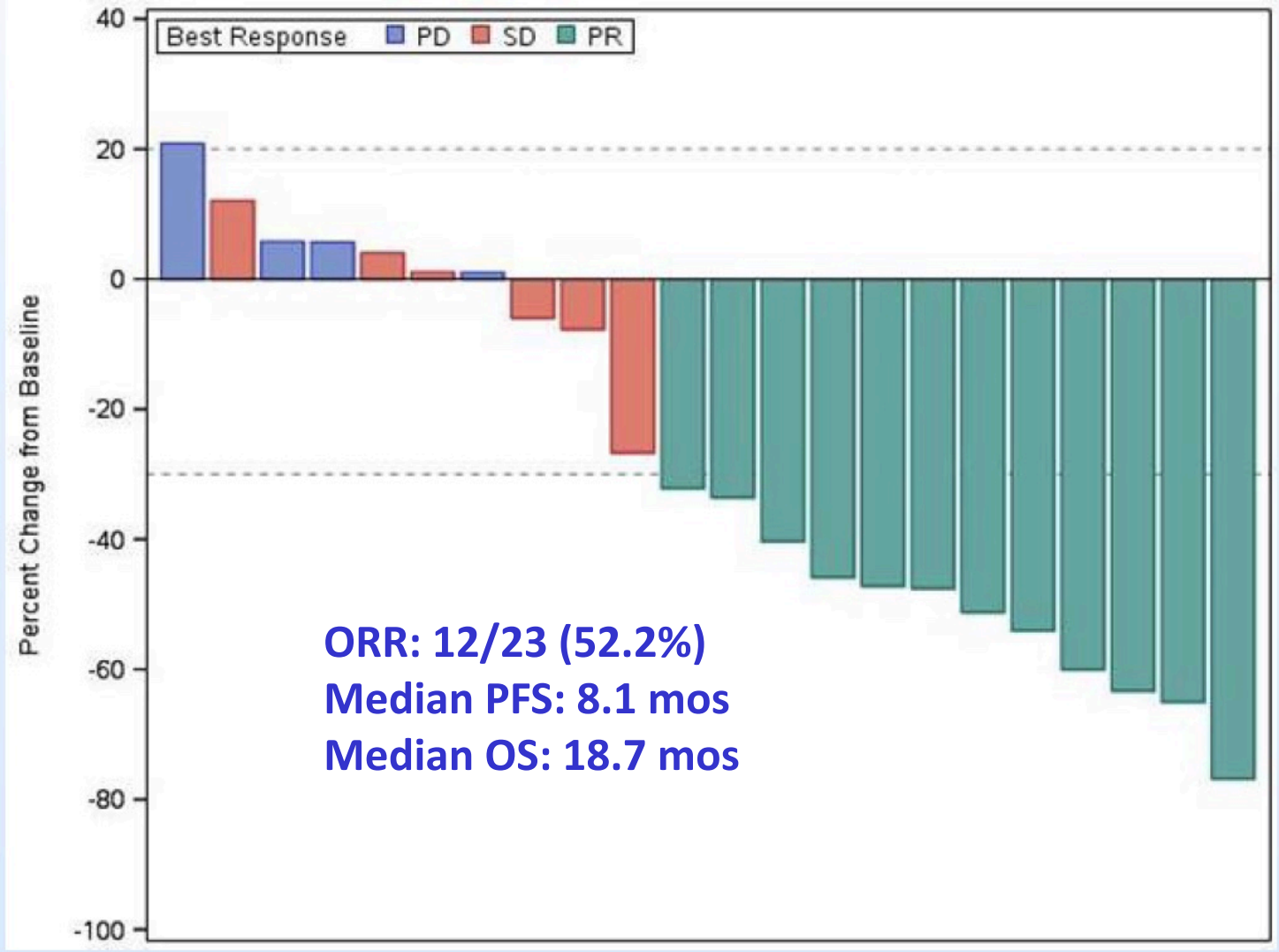
Siena S et al. ASCO 2020;Abstract 4000.

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

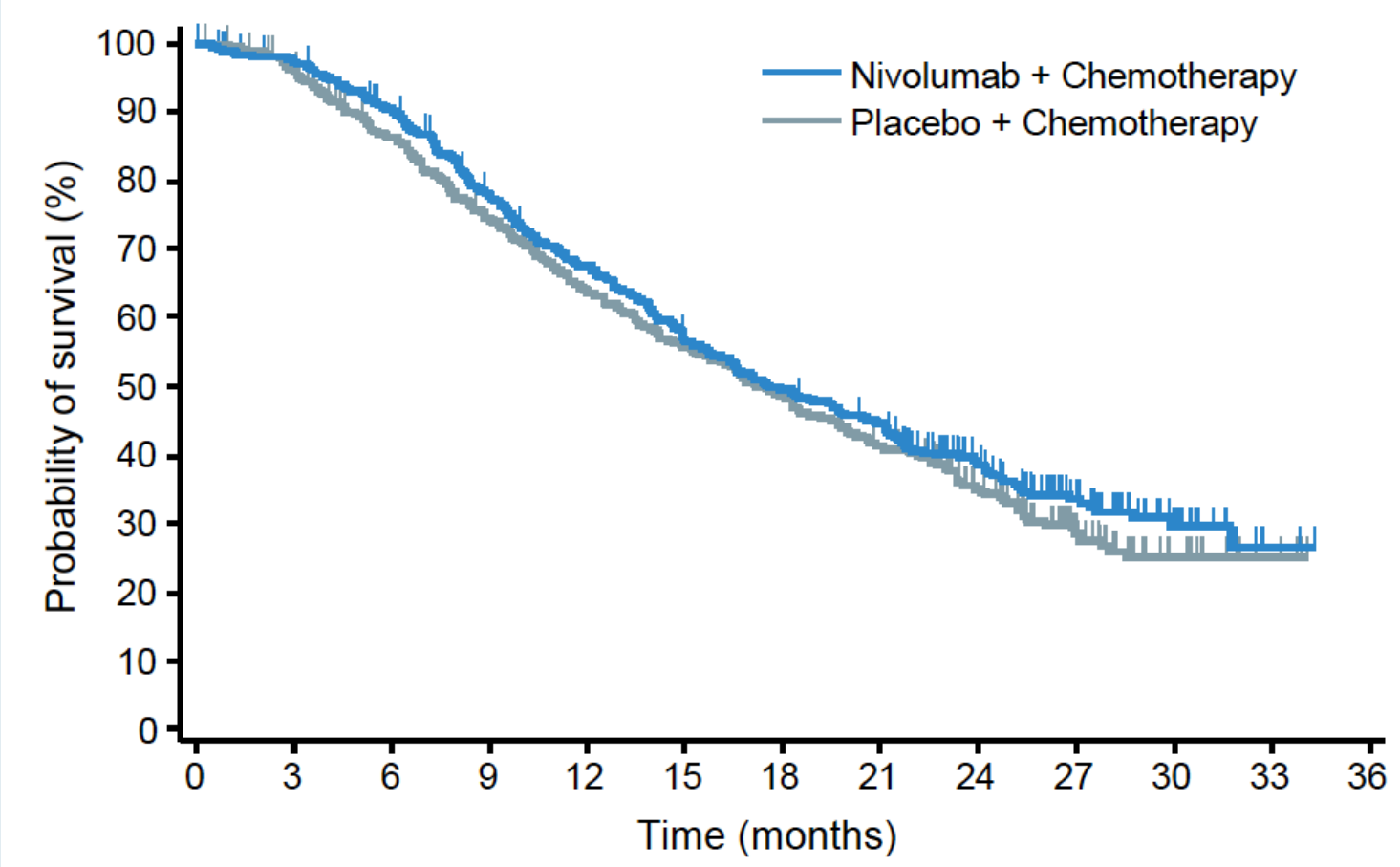
RTP
RESEARCH
TO PRACTICE

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

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

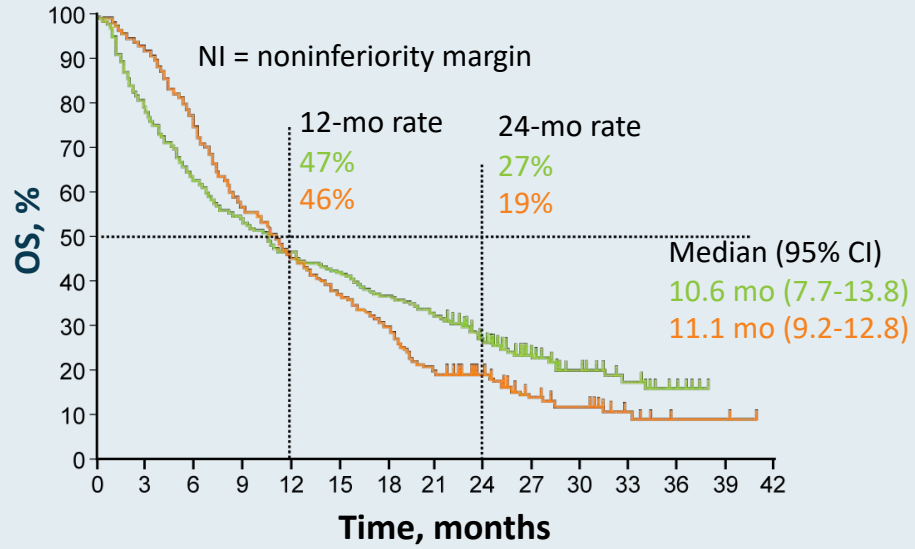
Kohei Shitara, MD[1]; Eric Van Cutsem, MD[2]; Yung-Jue Bang, MD[3]; et al

» Author Affiliations

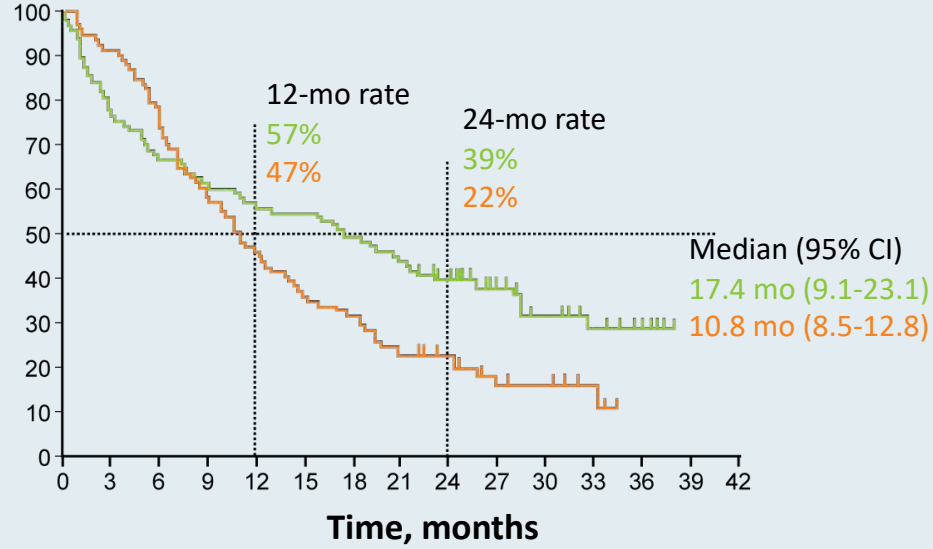
JAMA Oncol. 2020;6(10):1571-1580. doi:10.1001/jamaoncol.2020.3370

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

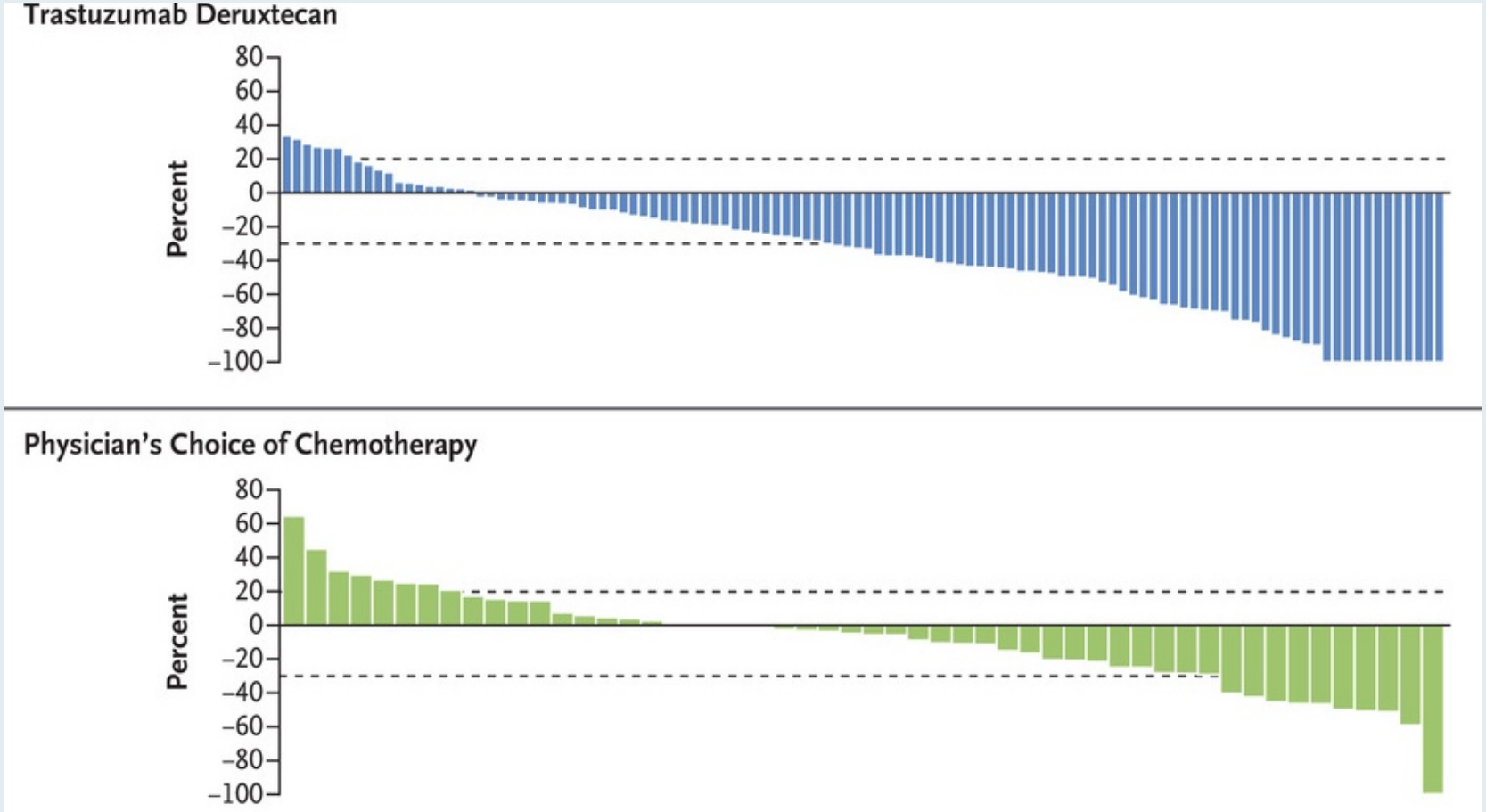
ORIGINAL ARTICLE

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

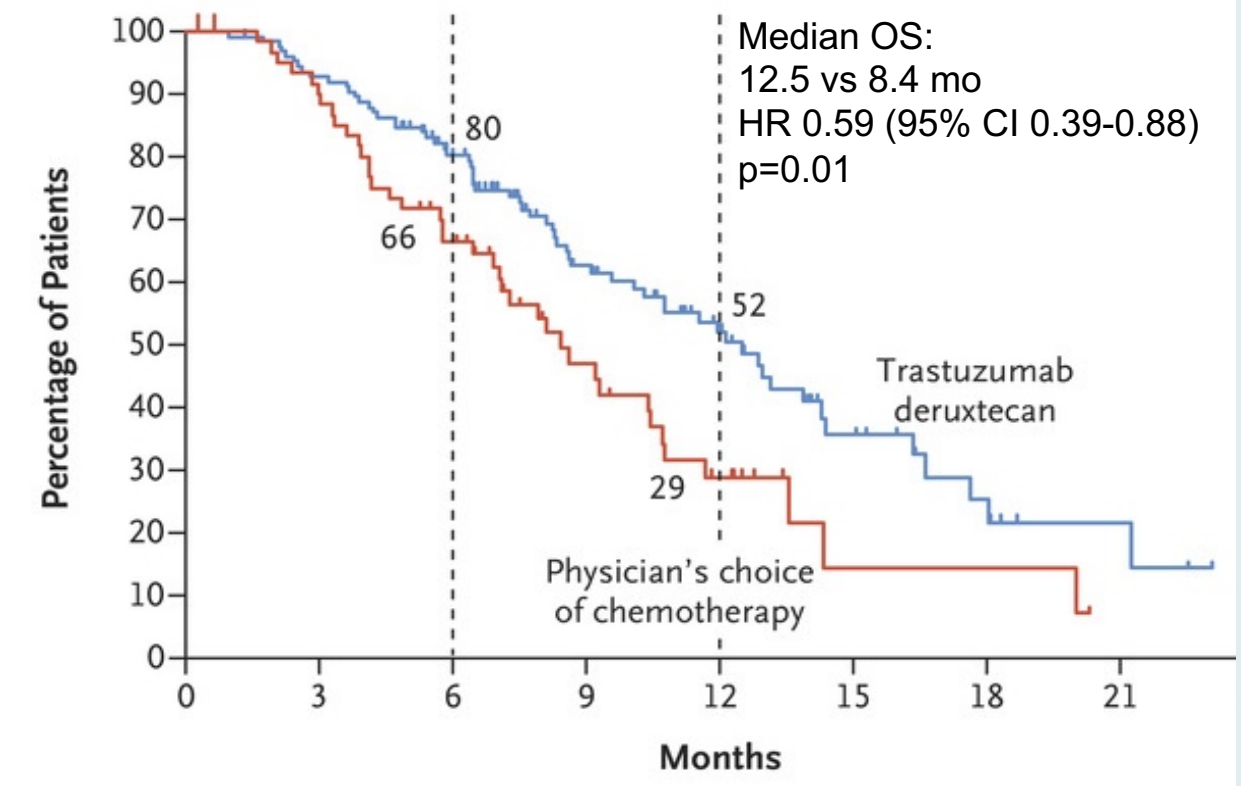


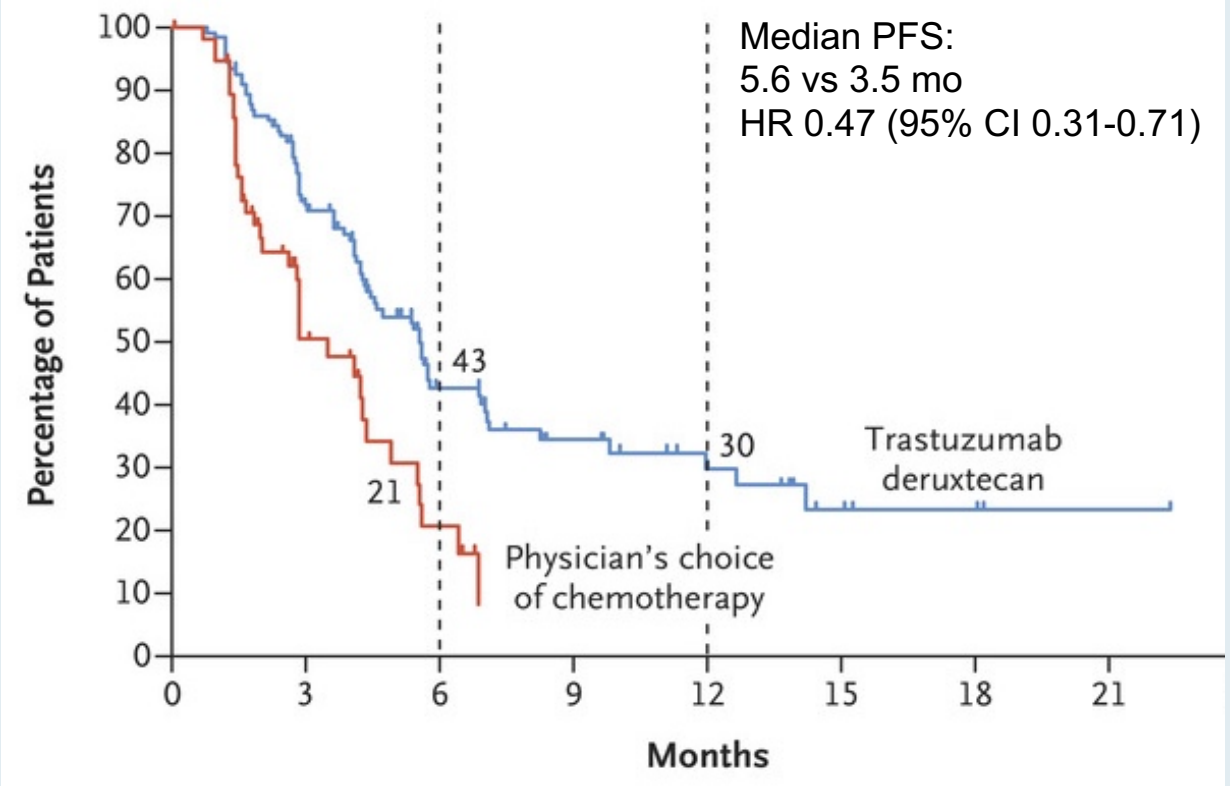
	T-DXd (n = 119)	PC (n = 56)
ORR	**51%**	**14%**
Confirmed ORR	**43%**	**12%**
CR	8%	0%
PR	34%	12%

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.

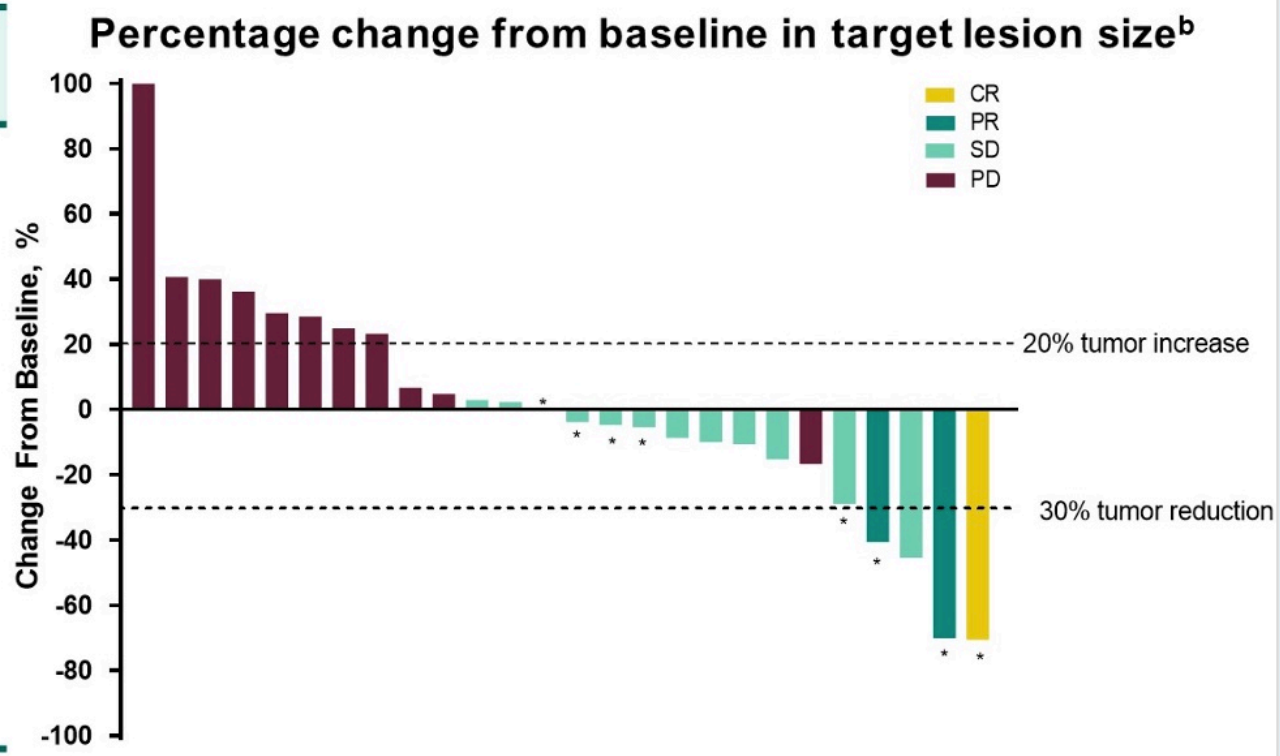
LEAP-005: A Phase II Multicohort Study of Lenvatinib plus Pembrolizumab in Patients with Previously Treated Selected Solid Tumors: Results from the Gastric Cancer Cohort

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+)

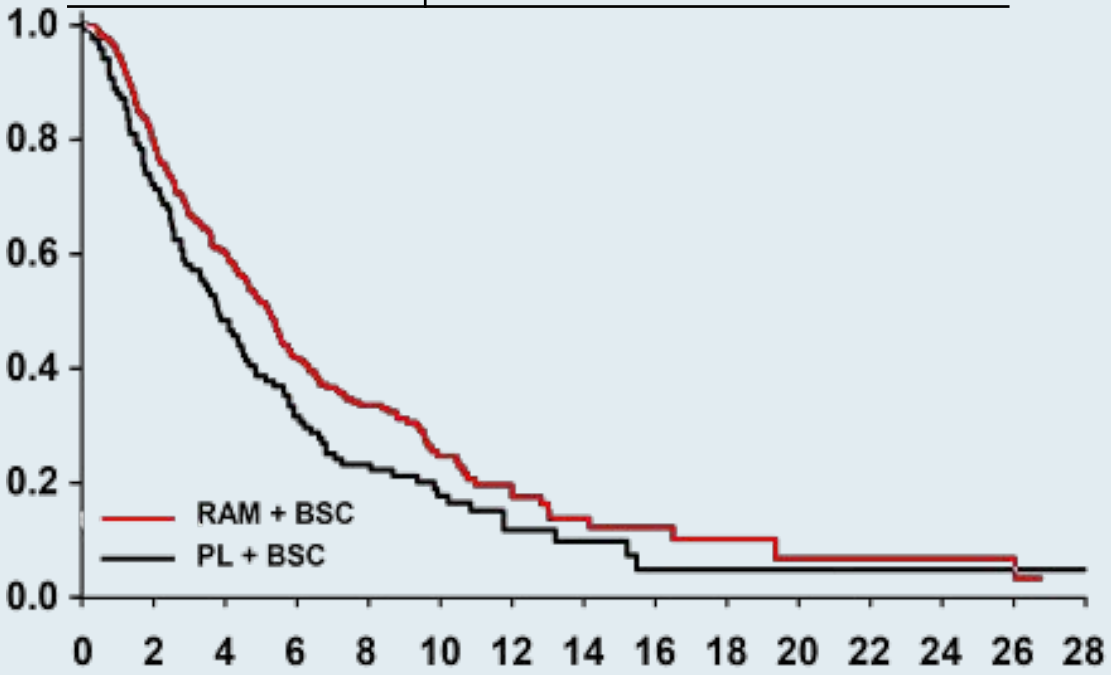


CI, confidence interval; CR, complete response; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Defined as best overall response of CR, PR or SD. [b]Both patients with PR had PD-L1 CPS ≥1; patient with CR had PD-L1 CPS <1. [c]Patient had no post-baseline imaging.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

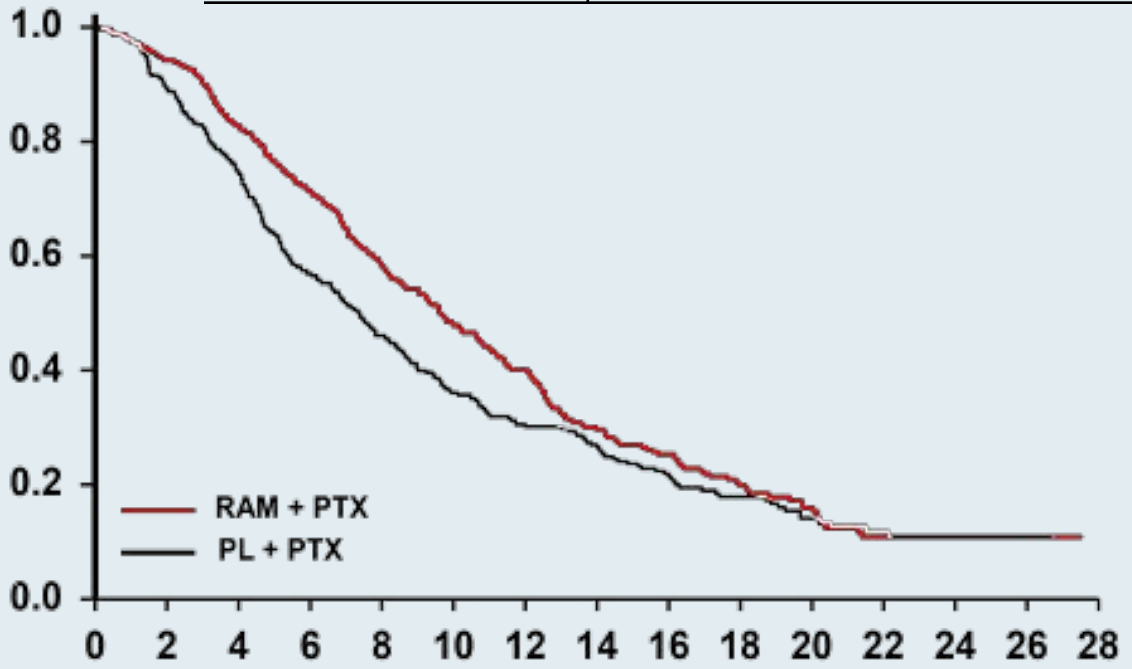
Chung HC et al. Gastrointestinal Cancers Symposium 2021; Abstract 230.

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)**		



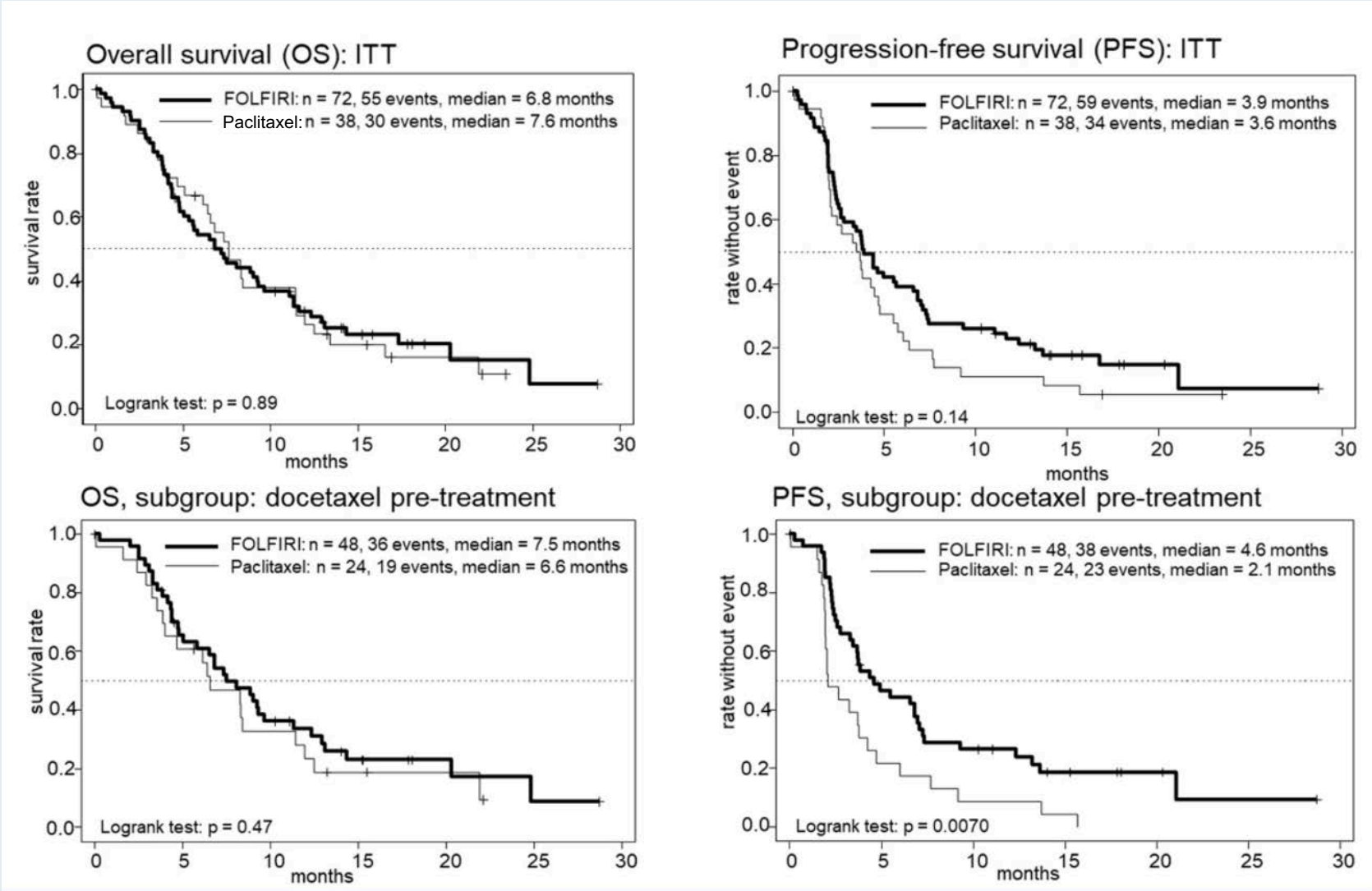
RAINBOW[2] OS	RAM	Placebo	*p*-value
Median (mo)	**9.6**	**7.4**	**0.017**
HR (95% CI)	**0.807 (0.678-0.962)**		



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.

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



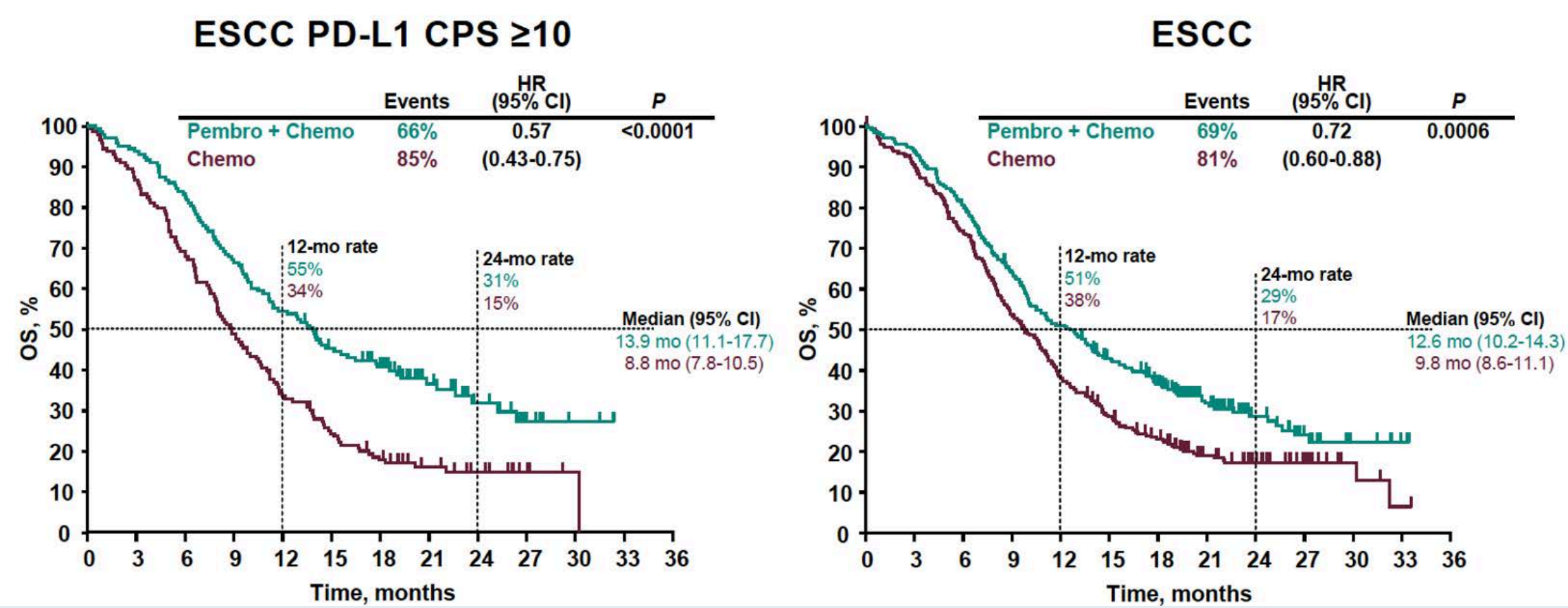
Lorenzen S et al. ASCO 2020;Abstract 4514.

RTP RESEARCH TO PRACTICE

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.

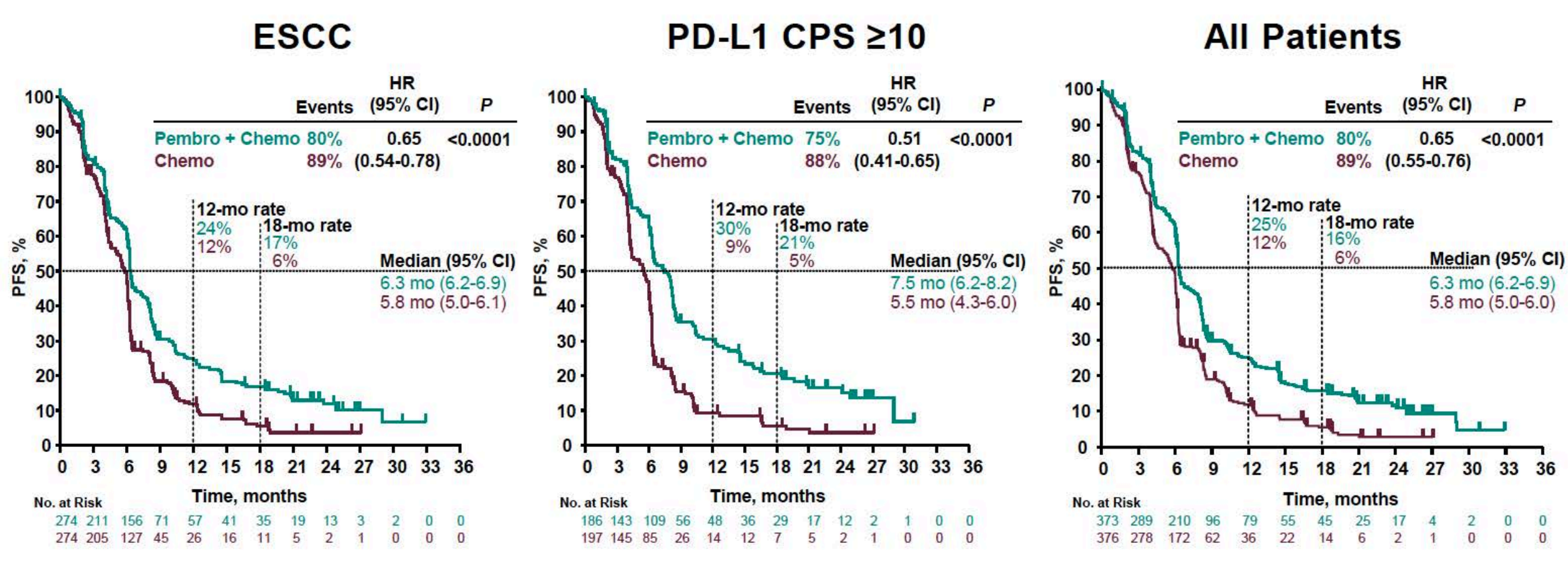
KEYNOTE-590: Overall Survival



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

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

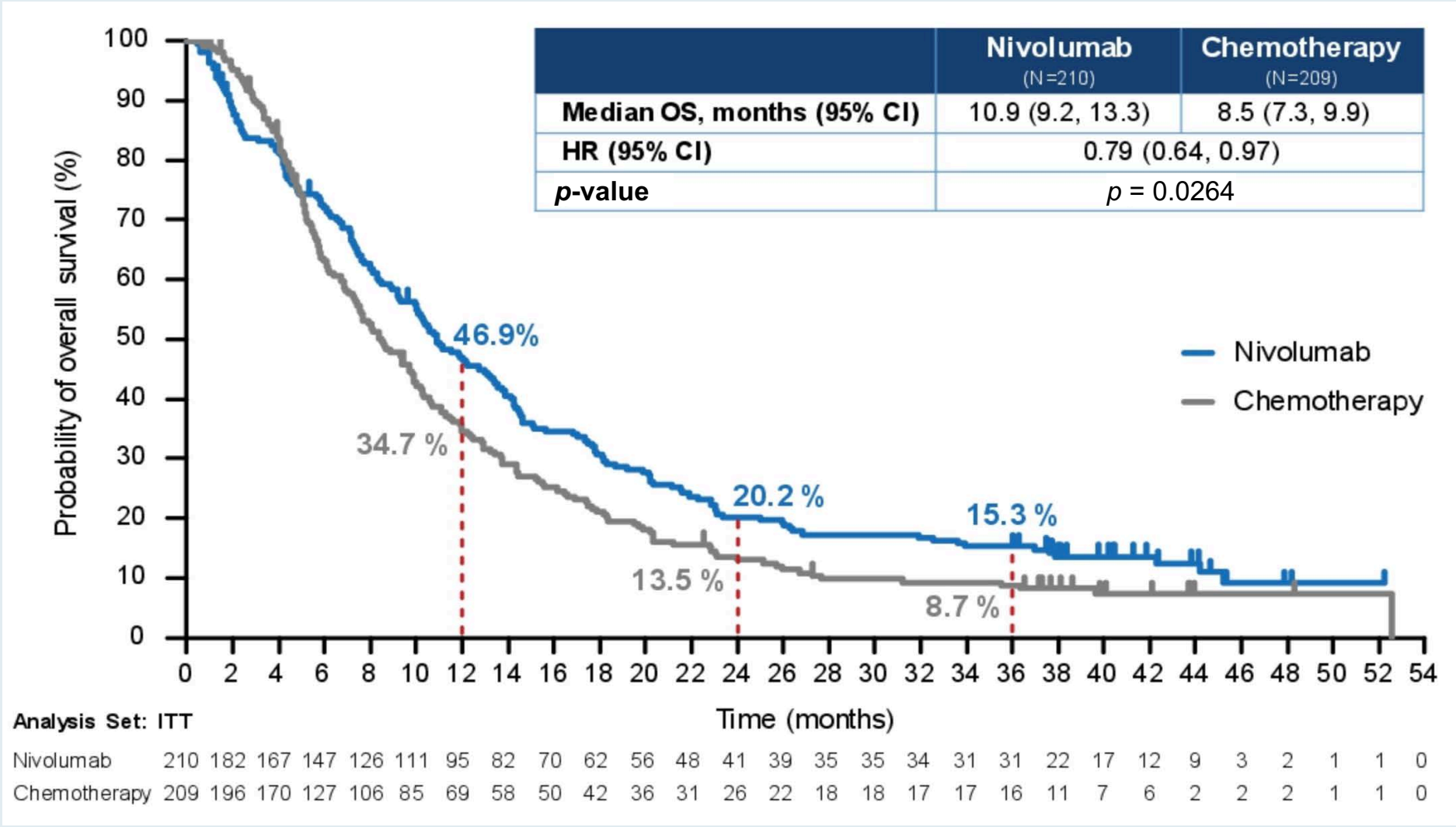
Three-year Follow-up of ATTRACTION-3: A Phase III Study of Nivolumab (Nivo) in Patients with Advanced Esophageal Squamous Cell Carcinoma (ESCC) That Is Refractory or Intolerant to Previous Chemotherapy

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

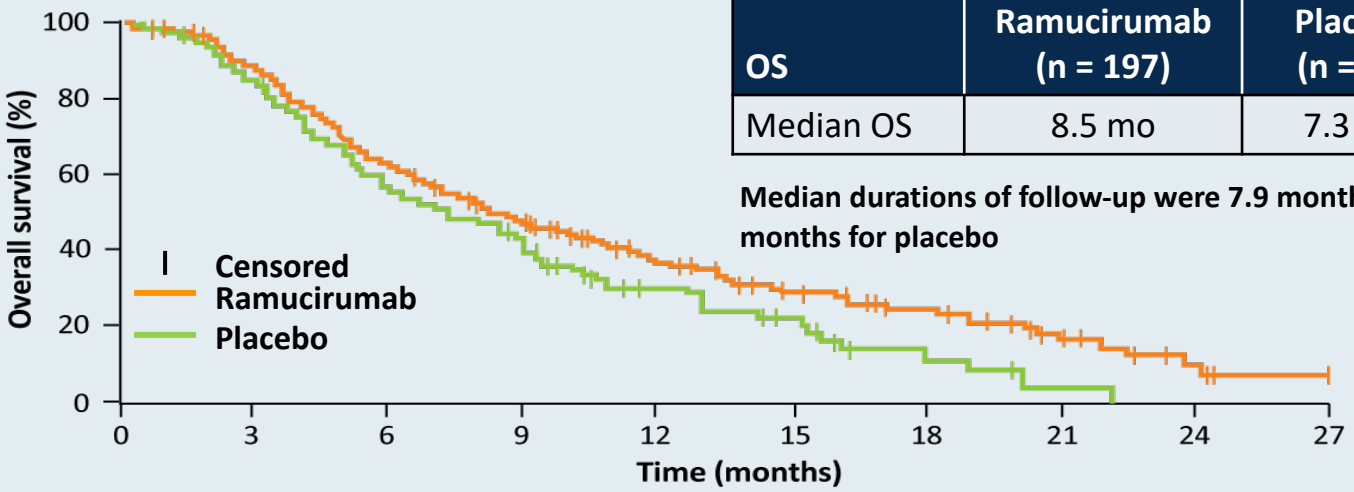
Articles

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**

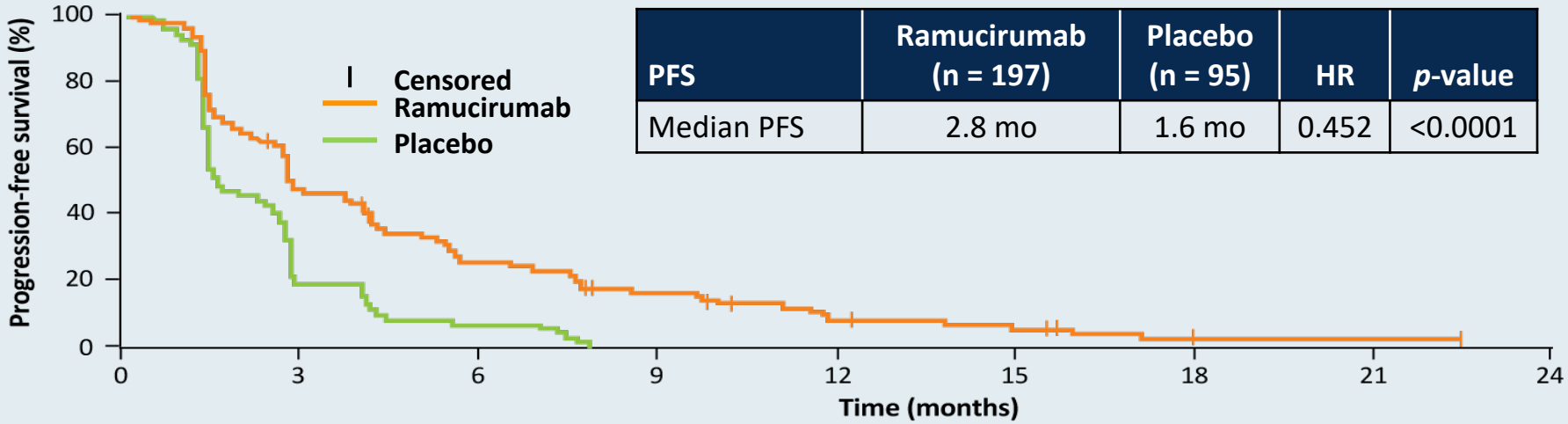
Lancet Oncol 2019;20(2):282-96.

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

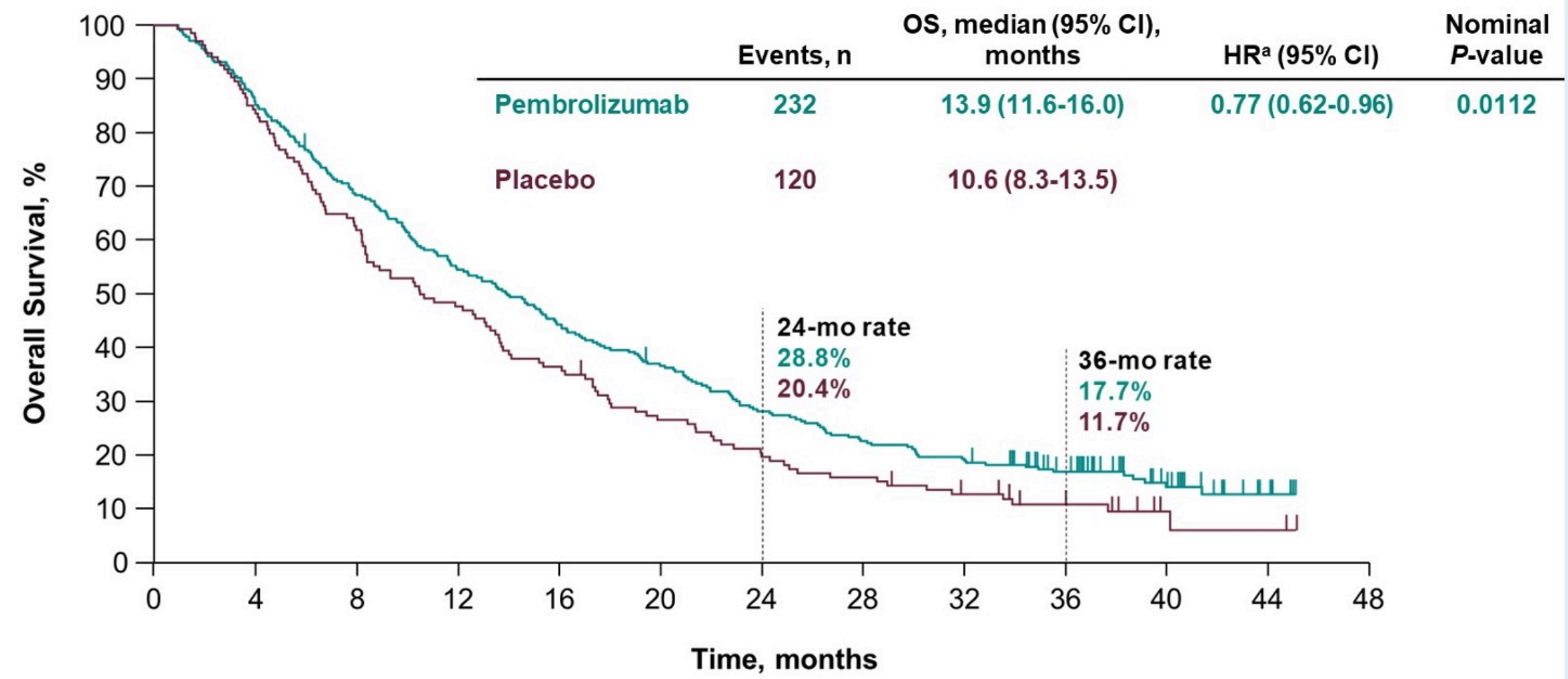
Pembrolizumab versus Placebo in Patients with Advanced Hepatocellular Carcinoma Previously Treated with Sorafenib: Updated Data from the Randomized, Phase 3 KEYNOTE-240 Study

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.

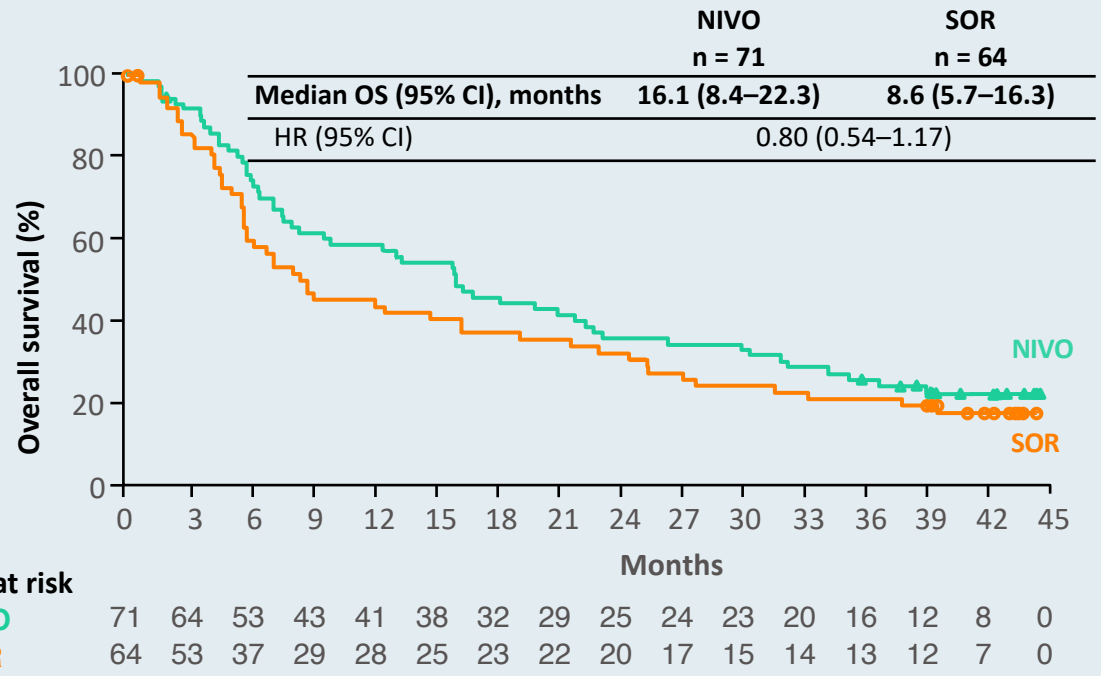
RTP RESEARCH TO PRACTICE

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

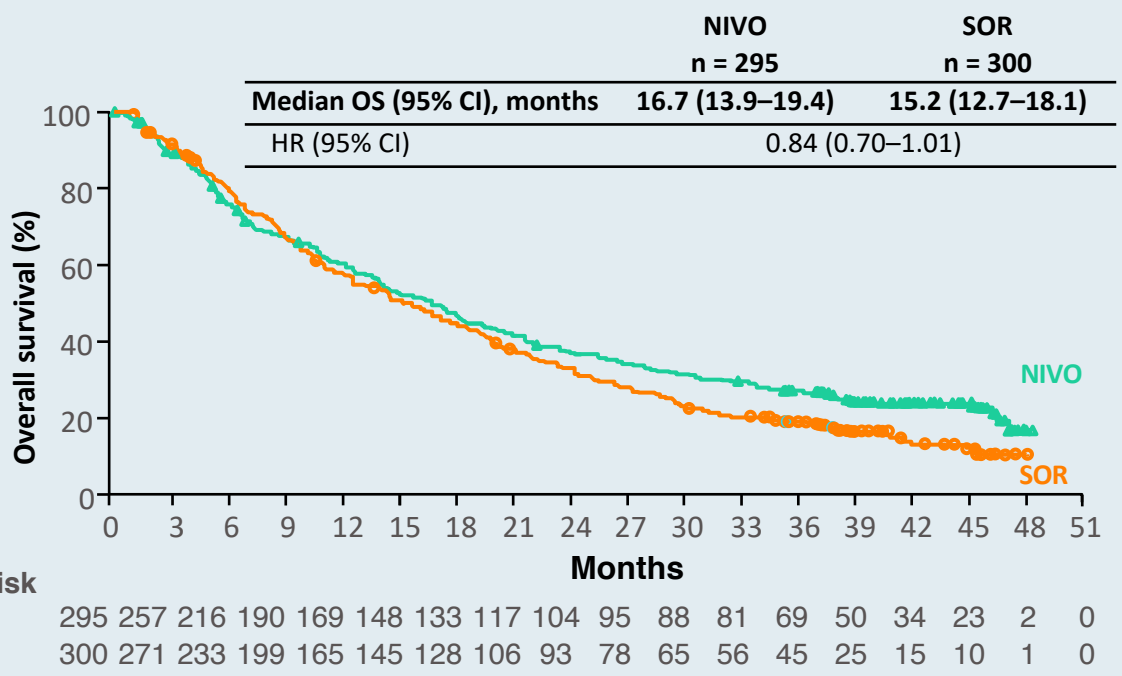
Sangro B et al.
ESMO World GI Congress 2020;Abstract LBA-3.

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

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."

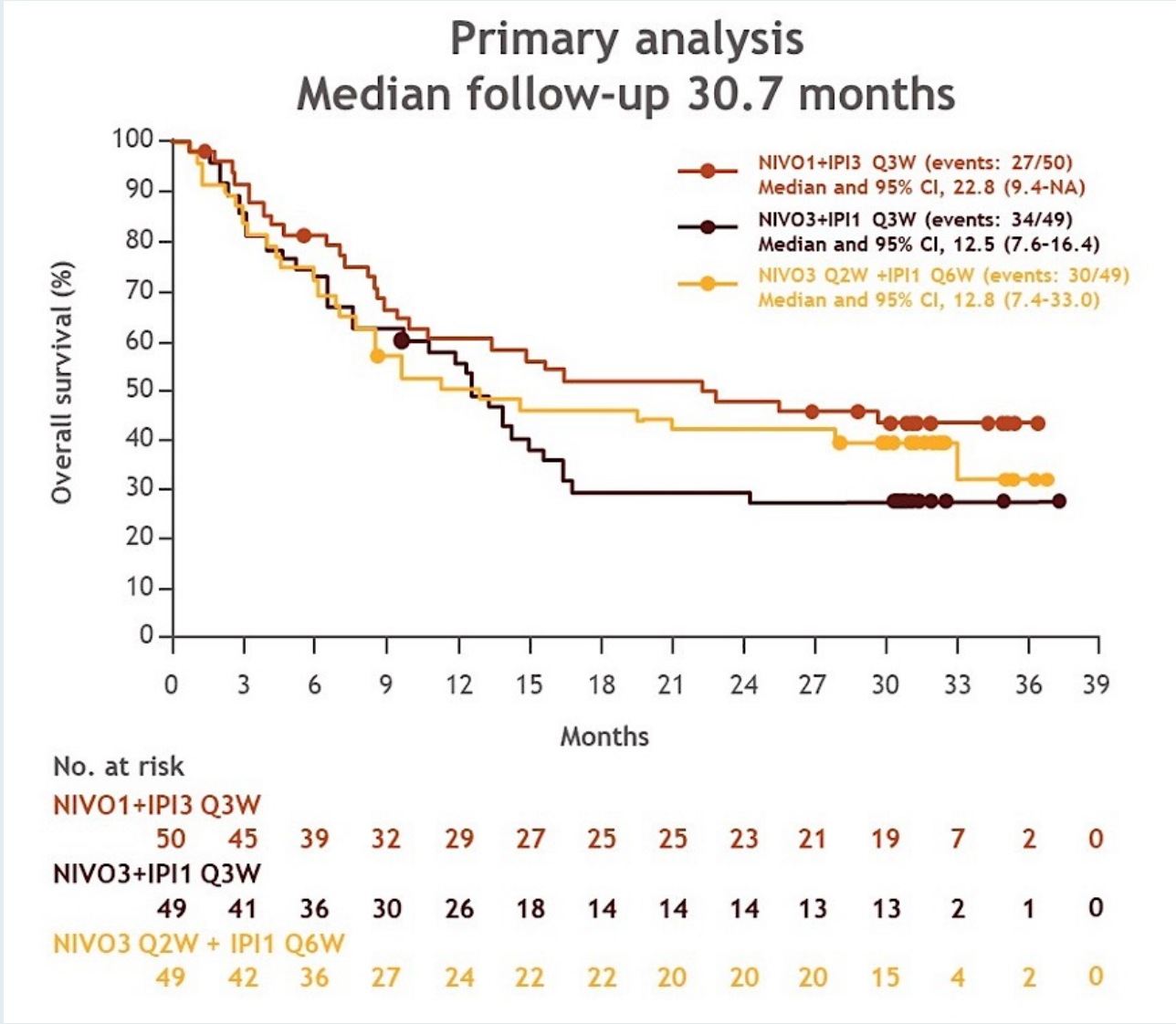
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-nivolumab-and-ipilimumab-combination-hepatocellular-carcinoma

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

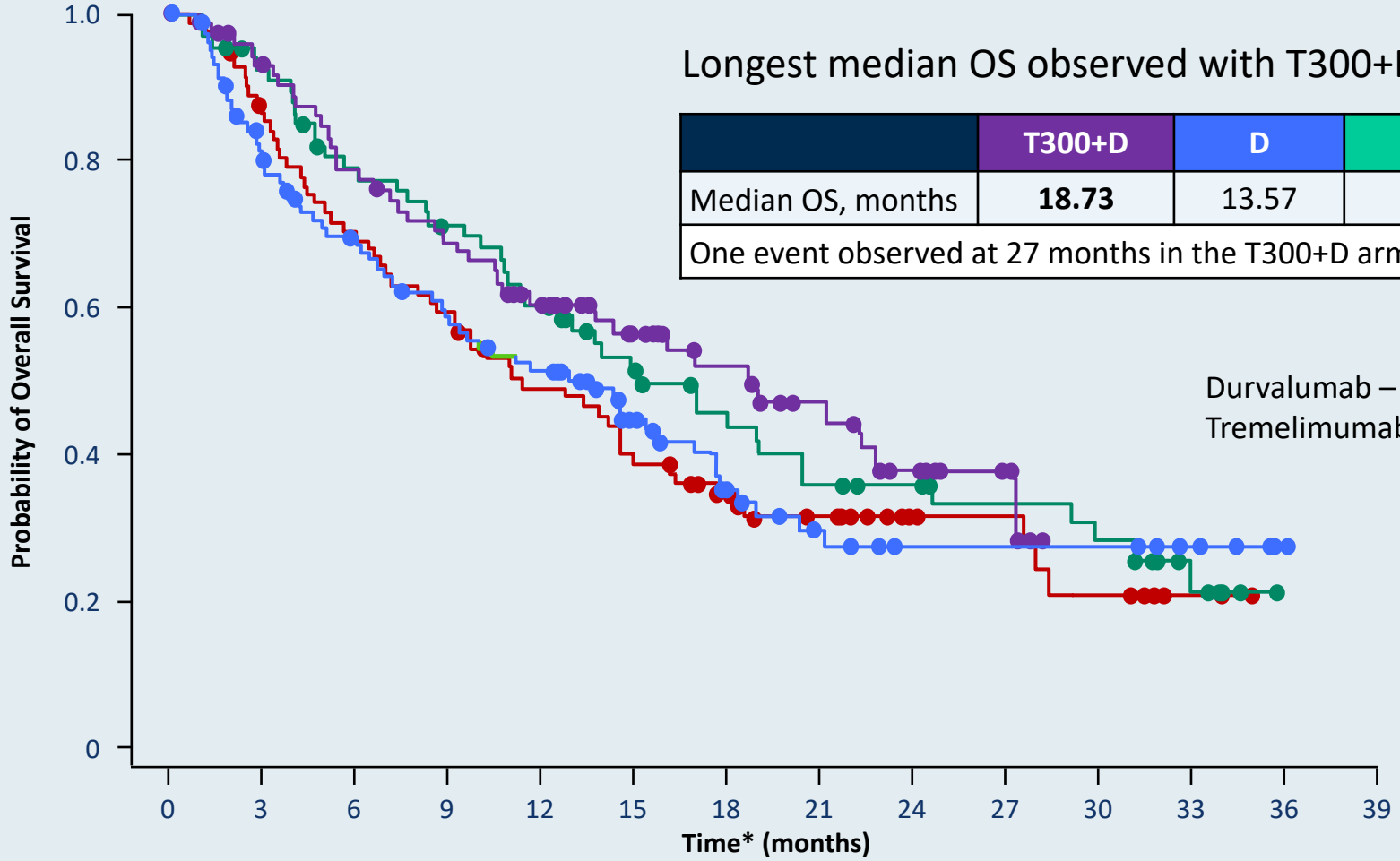
Efficacy, Tolerability, and Biologic Activity of a Novel Regimen of Tremelimumab (T) in Combination with Durvalumab (D) for Patients (pts) with Advanced Hepatocellular Carcinoma (aHCC)

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.

Dissecting the Decision: Clinical and Nursing Investigators Provide Practical Perspectives on Key Issues in Cancer Care

Part 2 — HER2-Positive Breast Cancer

Thursday, March 18, 2021
5:00 PM – 6:00 PM ET

Faculty

Jamie Carroll, APRN, MSN, CNP
Sara Hurvitz, 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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