Consensus or Controversy? Investigator Perspectives on the Current and Future Role of Immune Checkpoint Inhibitors in the Management of Hepatobiliary Cancers

A CME-Accredited Virtual Event Held in Conjunction with the 2024 ASCO Gastrointestinal Cancers Symposium

Saturday, January 20, 2024

8:30 AM – 9:30 AM ET (5:30 AM – 6:30 AM PT)

Faculty

Ahmed Omar Kaseb, MD, CMQ

Arndt Vogel, MD, PhD

Moderator

Neil Love, MD

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Faculty

Ahmed Omar Kaseb, MD, CMQ
John E and Dorothy J Harris Professor in Gastrointestinal Cancer Research
Member, National Hepatobiliary Task Force, NCI, USA
Tenured Professor and Director, Hepatocellular Carcinoma Program
Director, MD Anderson HCC SPORE
Editor-in-Chief, *Journal of Hepatocellular Carcinoma*
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Princess Margaret Cancer Centre
Toronto General Hospital Research Institute
Schwartz Reisman Liver Research Centre
Toronto, Ontario, Canada

MODERATOR
Neil Love, MD
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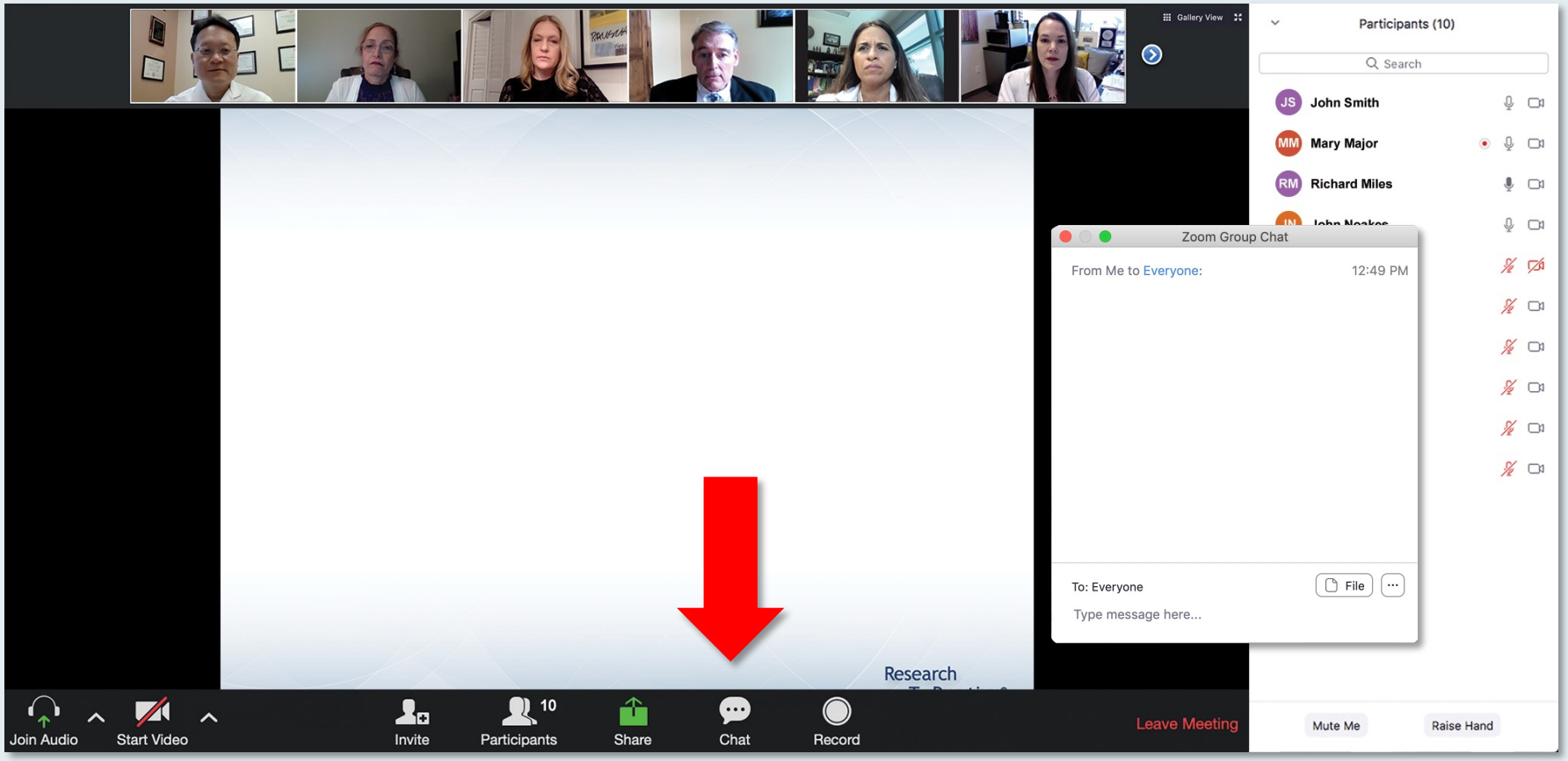

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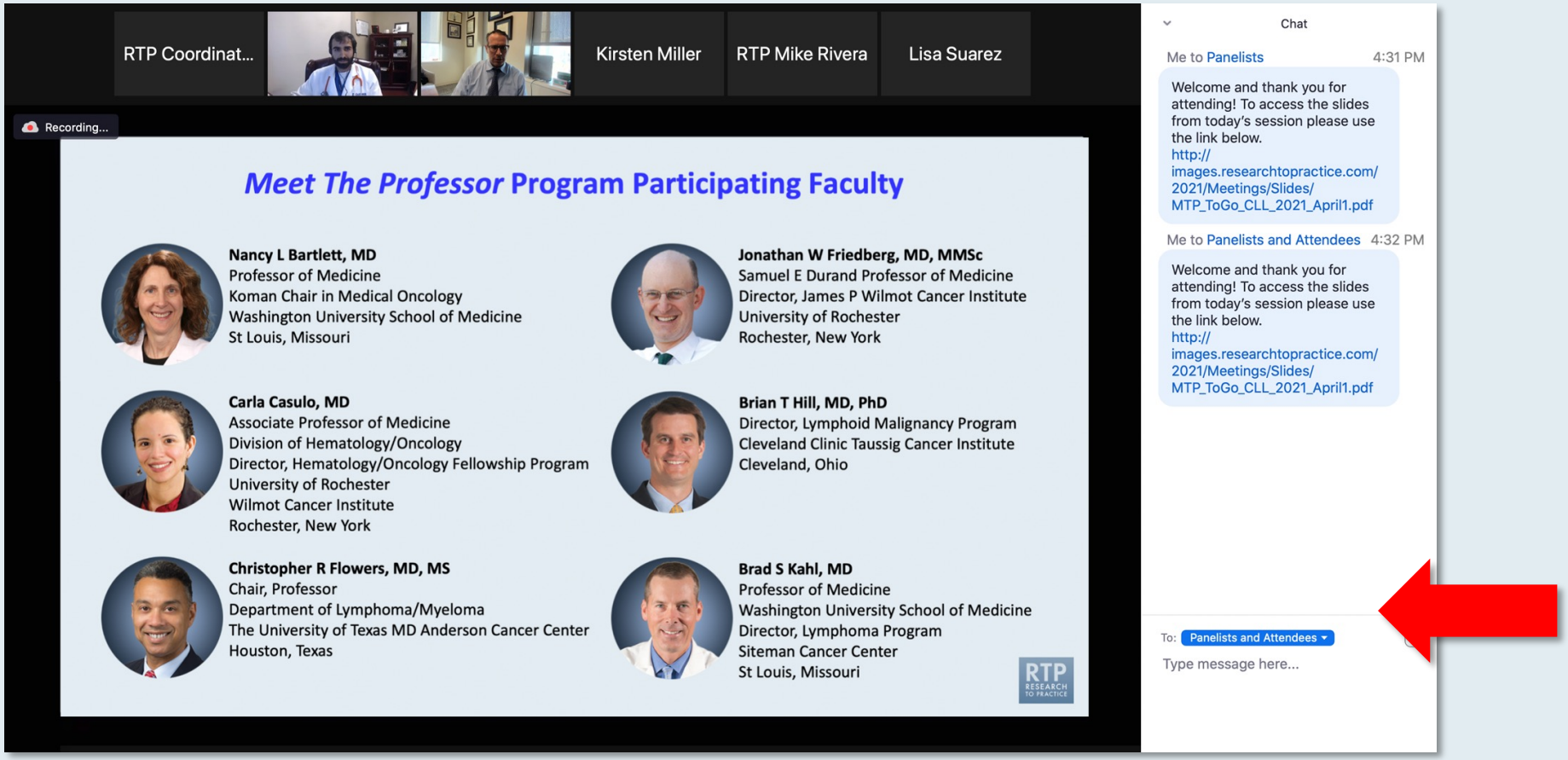

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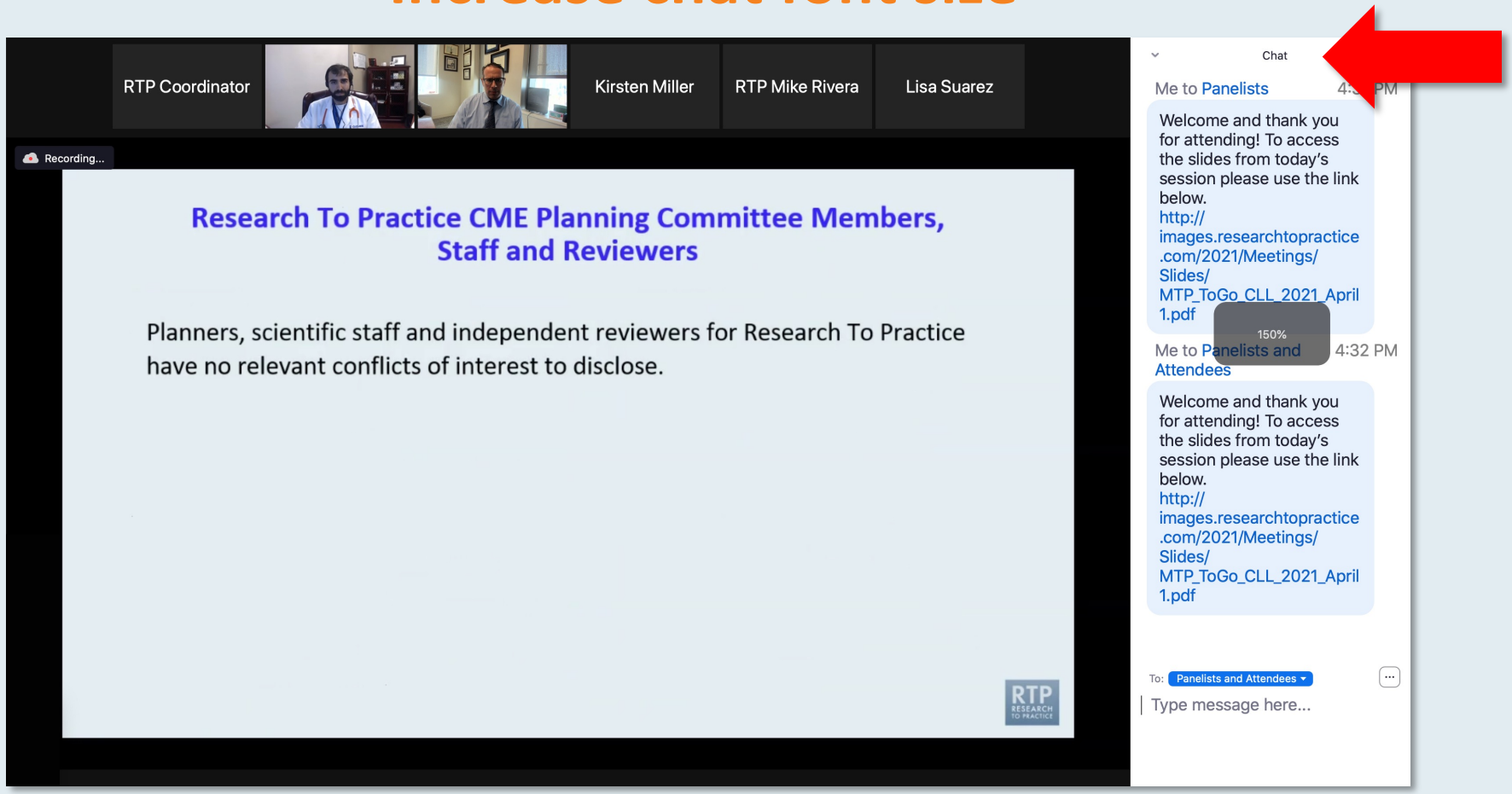

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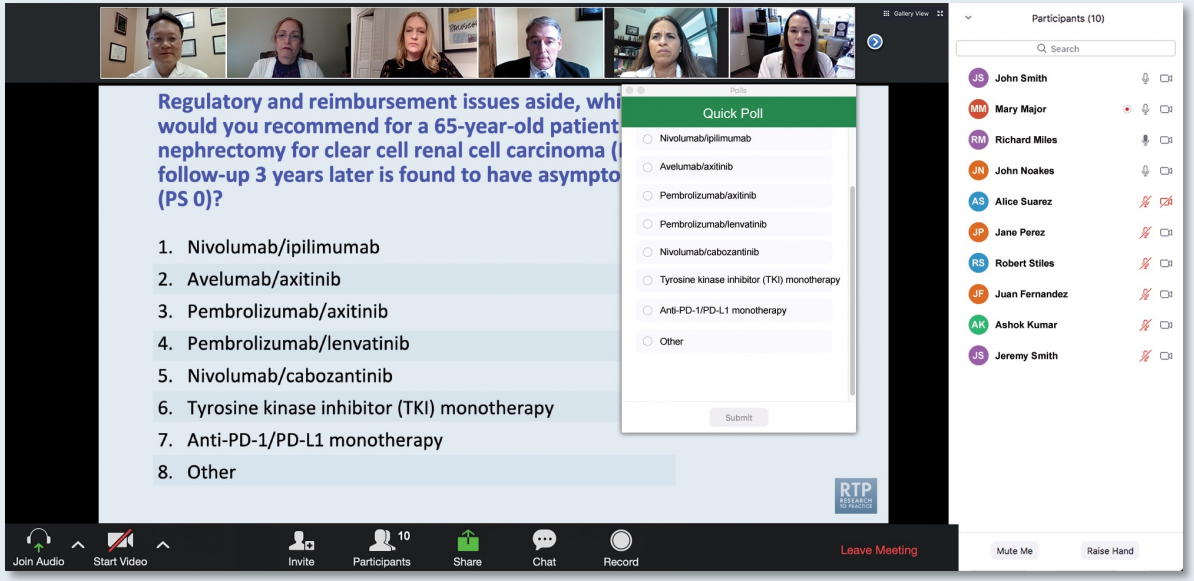

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WITH DR NEIL LOVE

Inside the Issue: Targeted and Immunotherapeutic Approaches for Biliary Tract Cancers

DR LIPIKA GOYAL
STANFORD CANCER CENTER

PROF MILIND JAVLE
THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

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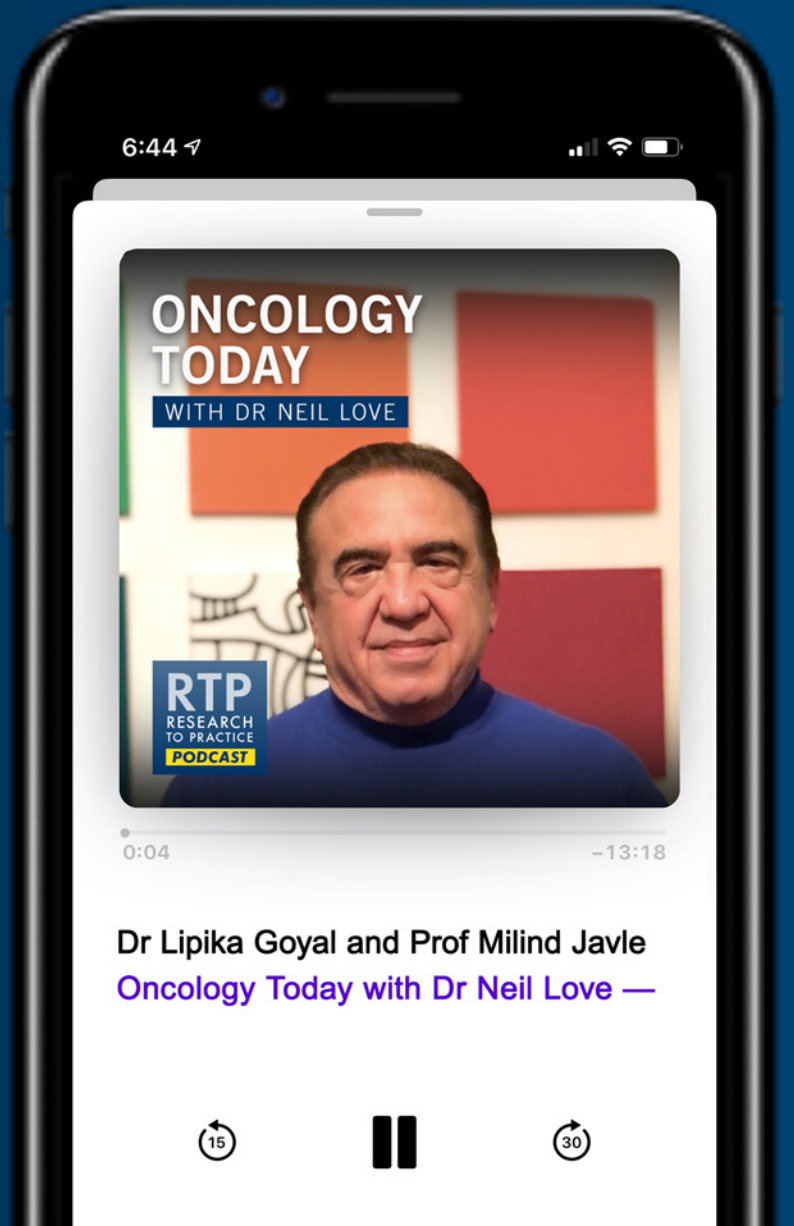

Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Prostate Cancer

Part 1 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 ASCO Genitourinary Cancers Symposium

Thursday, January 25, 2024

6:15 PM – 8:15 PM PT (9:15 PM – 11:15 PM ET)

Faculty

Rahul Aggarwal, MD

Emmanuel S Antonarakis, MD

Elisabeth I Heath, MD

A Oliver Sartor, MD

Moderator

Alan H Bryce, MD

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Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Urothelial Bladder Cancer

Part 2 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 ASCO Genitourinary Cancers Symposium

Friday, January 26, 2024

7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew Milowsky, MD, FASCO

Peter H O'Donnell, MD

Jonathan E Rosenberg, MD

Arlene Siefker-Radtke, MD

Moderator

Evan Y Yu, MD

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

HER2-Positive and Triple-Negative Breast Cancer

Tuesday, January 30, 2024
5:00 PM – 6:00 PM ET

Faculty

Ian E Krop, MD, PhD

Priyanka Sharma, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Meet The Professor

Optimizing the Management of Myelofibrosis

Thursday, February 1, 2024
5:00 PM – 6:00 PM ET

Faculty

Stephen Oh, MD, PhD

Moderator

Neil Love, MD

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A Multitumor CME/MOC- and NCPD-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

MARCH 22-24, 2024

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

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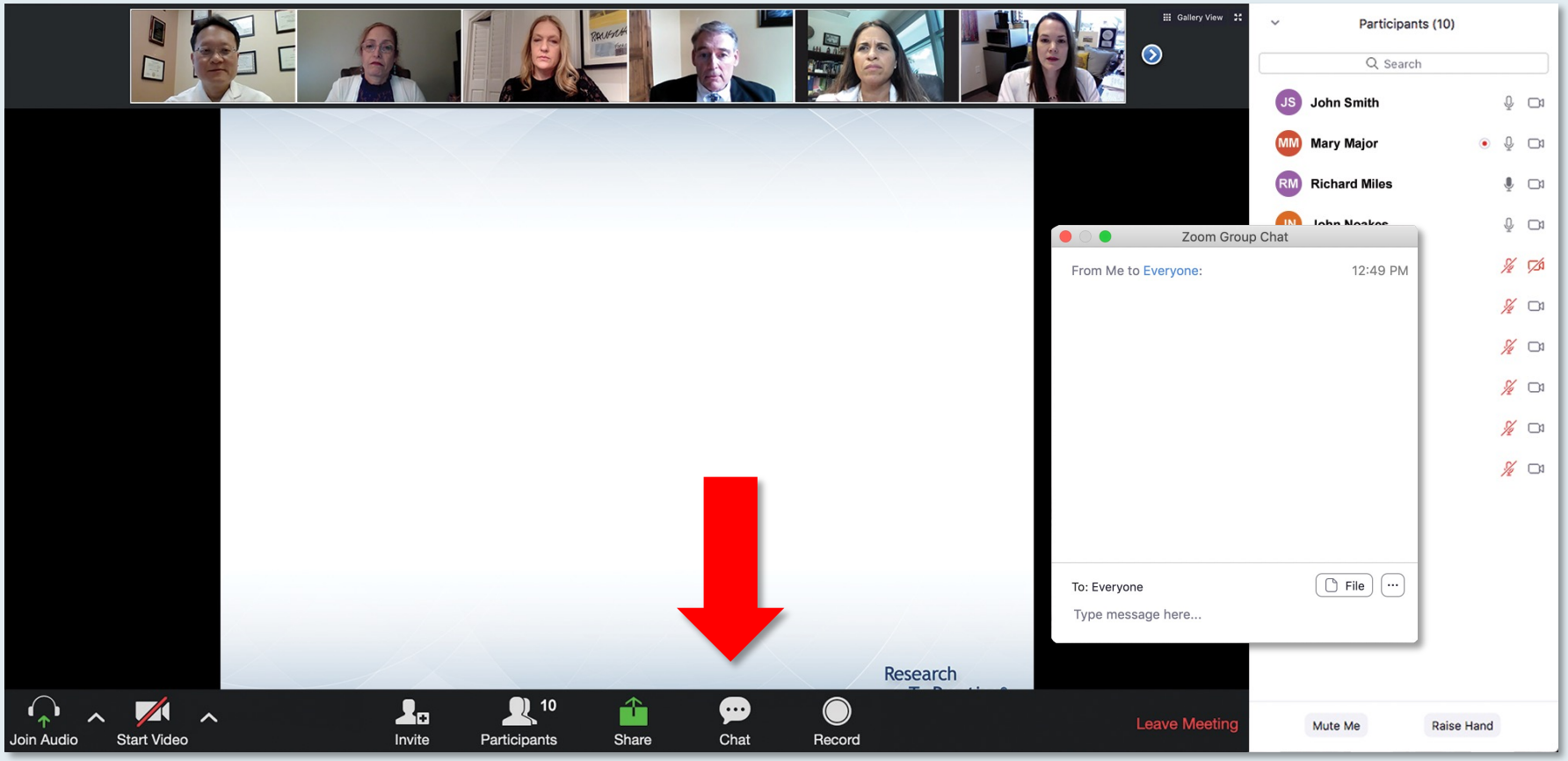

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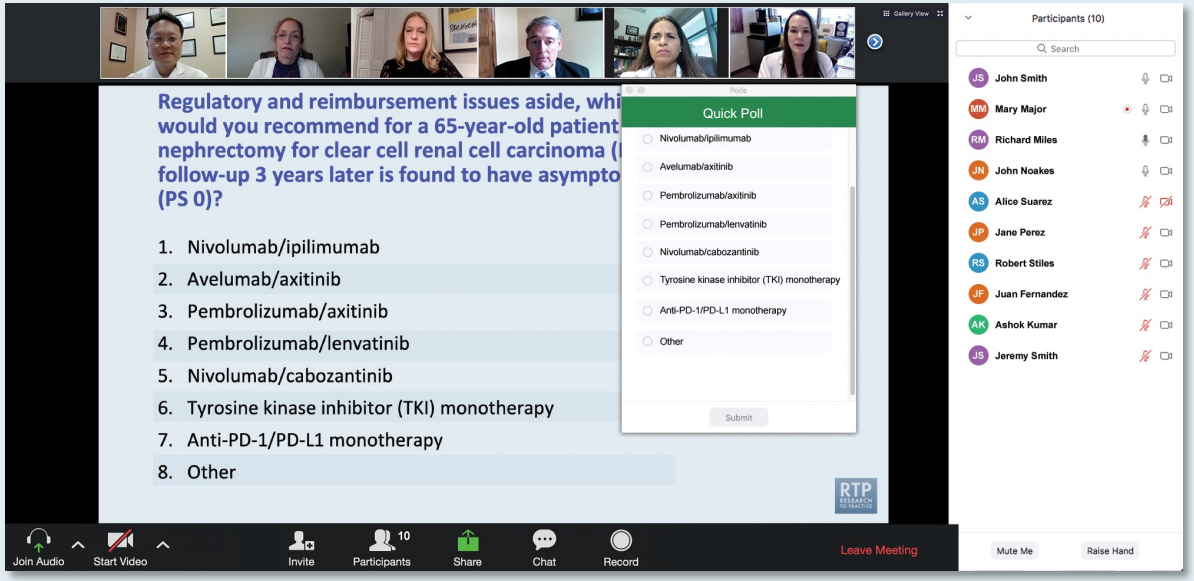

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Third Annual **National General Medical Oncology Summit**

Friday, March 22, 2024

6:00 PM – 6:30 PM

Welcome Reception

6:30 PM – 8:30 PM

Keynote Session: ER-Positive Metastatic Breast Cancer

Erika Hamilton, MD
Kevin Kalinsky, MD, MS
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Third Annual **National General Medical Oncology Summit**

Saturday, March 23, 2024

7:30 AM – 9:10 AM

Hodgkin and Non-Hodgkin Lymphoma

Ann S LaCasce, MD, MMSc
Matthew Lunning, DO
Kami Maddocks, MD
Andrew D Zelenetz, MD, PhD

9:30 AM – 10:20 AM

Gynecologic Cancers

Bradley J Monk, MD
David M O'Malley, MD

10:20 AM – 11:10 AM

Localized Breast Cancer; SABCS 2023 Review

Virginia Kaklamani, MD, DSc
Kevin Kalinsky, MD, MS
Joyce O'Shaughnessy, MD

11:10 AM – 12:00 PM

Metastatic Breast Cancer, Triple-Negative Breast Cancer, HER2-Positive Breast Cancer; SABCS 2023 Review

Erika Hamilton, MD
Virginia Kaklamani, MD, DSc
Hope S Rugo, MD

Third Annual **National General Medical Oncology Summit**

Saturday, March 23, 2024

12:30 PM – 1:20 PM

Prostate Cancer

Emanuel S Antonarakis, MD
Rana R McKay, MD

1:20 PM – 2:10 PM

Urothelial Bladder Cancer

Matthew D Galsky, MD
Jonathan E Rosenberg, MD

2:10 PM – 3:00 PM

Renal Cell Carcinoma

Eric Jonasch, MD
Brian Rini, MD

3:20 PM – 4:10 PM

Targeted Therapy for Non-Small Cell Lung Cancer

Ibiayi Dagogo-Jack, MD
Helena Yu, MD

4:10 PM – 5:00 PM

Nontargeted Treatments for Lung Cancer

Edward B Garon, MD, MS
Corey J Langer, MD

Third Annual **National General Medical Oncology Summit**

Sunday, March 24, 2024

7:30 AM – 8:20 AM

Multiple Myeloma

Natalie S Callander, MD
Paul G Richardson, MD

8:20 AM – 9:10 AM

Gastroesophageal Cancers

Yelena Y Janjigian, MD
Samuel J Klempner, MD

9:30 AM – 10:20 AM

Hepatobiliary Cancers

Ghassan Abou-Alfa, MD, MBA
Richard S Finn, MD

10:20 AM – 11:10 AM

Colorectal Cancer

Kristen K Ciombor, MD, MSCI
John Strickler, MD

11:10 AM – 12:00 PM

Topic and faculty to be announced

ONCOLOGY TODAY

WITH DR NEIL LOVE

Inside the Issue: Targeted and Immunotherapeutic Approaches for Biliary Tract Cancers

DR LIPIKA GOYAL
STANFORD CANCER CENTER

PROF MILIND JAVLE
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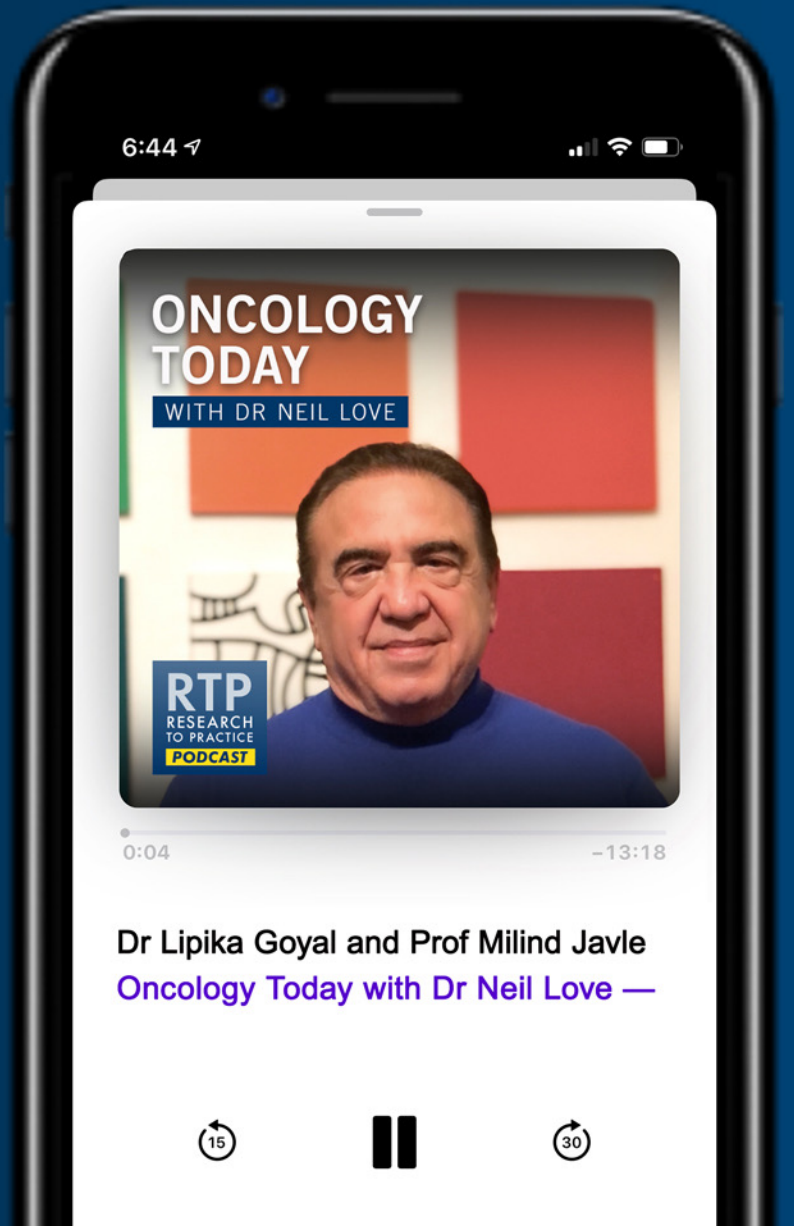

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Consulting Faculty

Thomas A Abrams, MD
Institute Physician
Dana-Farber Cancer Institute
Assistant Professor of Medicine
Harvard Medical School
Director, Liver Tumor Center
Boston, Massachusetts

Stacey Stein, MD
Associate Professor of Medicine
Assistant Medical Director of the Clinical Trials Office
Yale Cancer Center
Yale School of Medicine
New Haven, Connecticut

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Agenda

INTRODUCTION: EMERALD-1 – Immune Checkpoint Inhibitor-Based Therapy for Localized HCC Eligible for Embolization

MODULE 1: Optimal Utilization of Immune Checkpoint Inhibitors as First-Line Therapy for Advanced HCC — Dr Kaseb

MODULE 2: Incorporation of Anti-PD-1/PD-L1 Antibody-Based Approaches for Advanced Biliary Tract Cancers (BTCs) — Prof Vogel

Agenda

INTRODUCTION: EMERALD-1 – Immune Checkpoint Inhibitor-Based Therapy for Localized HCC Eligible for Embolization

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ASCO Gastrointestinal Cancers Symposium

EMERALD-1: a Phase 3, randomized, placebo-controlled study of transarterial chemoembolization combined with durvalumab with or without bevacizumab in participants with unresectable hepatocellular carcinoma eligible for embolization

Riccardo Lencioni*[1], Masatoshi Kudo[2], Joseph Erinjeri[3], Shukui Qin[4], Zhenggang Ren[5], Stephen L Chan[6], Yasuaki Arai[7], Jeong Heo[8], Anh Mai[9], Jose Escobar[10], Yamil Alonso Lopez Chuken[11], Jung-Hwan Yoon[12], Won Young Tak[13], Tanita Suttichaimongkol[14], Mohamed Bouattour[15], Shi-Ming Lin[16], Magdalena Żotkiewicz[17], Stephanie Udoye[18], Gordon J Cohen[18], **Bruno Sangro*[19]**

[1]Department of Diagnostic and Interventional Radiology, University of Pisa School of Medicine, Pisa, Italy; [2]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan; [3]Interventional Radiology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Cancer Center of Nanjing, Jinling Hospital, Nanjing, China; [5]Department of Hepatic Oncology, Liver Cancer Institute, Zhongshan Hospital, Fudan University, Shanghai, China; [6]State Key Laboratory of Translational Oncology, Department of Clinical Oncology, Sir Yue-Kong Pao Center for Cancer, The Chinese University of Hong Kong, Hong Kong SAR, China; [7]Department of Diagnostic Radiology, National Cancer Center, Chuo-ku, Tokyo, Japan; [8]Department of Internal Medicine, College of Medicine, Pusan National University and Biomedical Research Institute, Pusan National University Hospital, Busan, Republic of Korea; [9]General Surgery Department, Nhan Dan Gia Dinh Hospital, Ho Chi Minh City, Vietnam; [10]Hospital San Lucas Cardiológica del Sureste, Chiapas, Mexico; [11]I Can Oncology Centre, New León, Mexico; [12]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [13]Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Republic of Korea; [14]Division of Gastroenterology and Hepatology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand; [15]Medical Oncology, AP-HP Hôpital Beaujon, Paris, France; [16]Department of Internal Medicine, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan; [17]Oncology Biometrics, Late Oncology Statistics, AstraZeneca, Warsaw, Poland; [18]Global Medicines Development, AstraZeneca, Gaithersburg, MD, USA; [19]Liver Unit and HPB Oncology Area, Clínica Universidad de Navarra and CIBEREHD, Pamplona, Spain

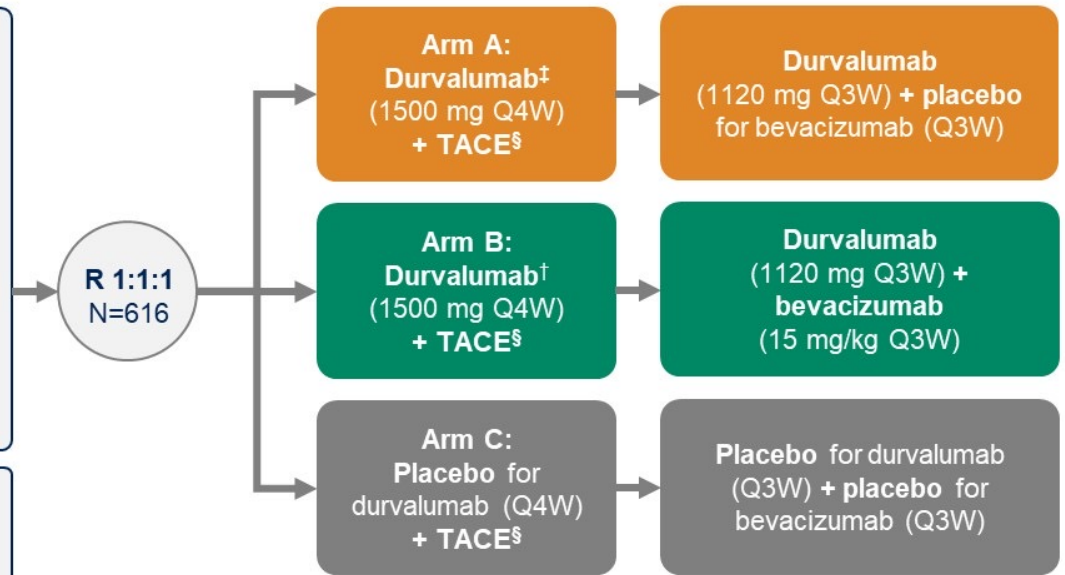
**Co-principal investigators*

EMERALD-1 study design

EMERALD-1 was a global, double-blind, placebo-controlled Phase 3 study

Study population*
- Adults with confirmed HCC
- Not amenable to curative therapy, e.g. surgical resection, ablation, transplantation
- No extrahepatic disease
- Child-Pugh A to B7
- ECOG PS 0 or 1
- Measurable disease per mRECIST
- Excludes Vp3 and Vp4
- No prior systemic therapy or TACE†

Stratification factors
- TACE modality (DEB-TACE vs cTACE)
- Geographical region (Japan vs Asia [excluding Japan] vs other)
- Portal vein invasion (Vp1 or Vp2+ / -Vp1 vs none)



Primary endpoint:
- PFS‖ for Arm B vs Arm C using BICR per ***RECIST 1.1***

Key secondary endpoints:
- PFS for Arm A vs Arm C
- OS
- QoL

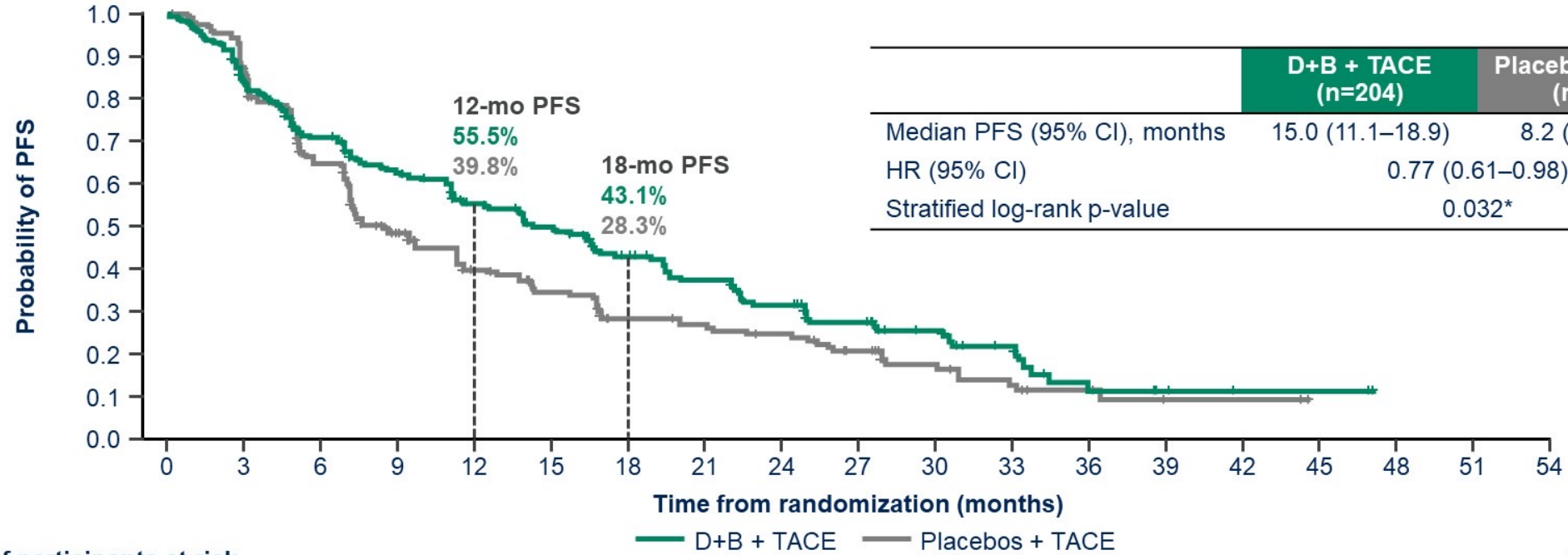
Other secondary endpoints:
- ORR and TTP using BICR per ***RECIST 1.1***
- Safety
- PFS, ORR, and TTP using investigator and BICR per ***mRECIST***

*Upper endoscopy to evaluate varices and risk of bleeding was required within 6 months of randomization. †Prior use of TACE or TAE is acceptable if it was used as part of therapy with curative intent, but not if it was used as the sole modality in curative therapy. ‡Durvalumab / placebo started ≥7 days after TACE. §DEB-TACE or cTACE. Participants will receive up to 4 TACE procedures within the 16 weeks following Day 1 of their first TACE procedure. ‖Only new lesions consistent with progression that were not eligible for TACE occurring prior to the first on study imaging at 12 weeks were considered progression events; standard mRECIST progression criteria were used after the 12-week imaging.

BICR, blinded independent central review; cTACE, conventional transarterial chemoembolization; ECOG, Eastern Cooperative Oncology Group; DEB-TACE, drug-eluting bead-transarterial chemoembolization; HCC, hepatocellular carcinoma; mRECIST, modified Response Evaluation Criteria in Solid Tumors; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; Q3W / Q4W, every 3 / 4 weeks; QoL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors; TACE, transarterial chemoembolization; TAE, transarterial embolization; TTP, time to progression.

PFS with D+B + TACE versus placebos + TACE: primary endpoint

Median PFS was improved by 6.8 months with D+B + TACE versus placebos + TACE



	D+B + TACE (n=204)	Placebos + TACE (n=205)
Median PFS (95% CI), months	15.0 (11.1–18.9)	8.2 (6.9–11.1)
HR (95% CI)	0.77 (0.61–0.98)	
Stratified log-rank p-value	0.032*	

No. of participants at risk																				Total events
D+B + TACE	204	162	134	114	94	82	64	53	43	32	23	15	6	4	2	2	0	0	0	136
Placebos + TACE	205	159	121	81	62	51	39	35	32	24	15	10	5	2	2	0	0	0	0	149

Median (range) duration of follow-up in censored participants, D+B + TACE 16.7 (0.03–47.1) months, Placebos + TACE 10.3 (0.03–44.3) months. **Median (95% CI) duration of follow-up** in all participants using the reverse Kaplan-Meier method, D+B + TACE 22.2 (16.7–27.3) months, Placebos + TACE 26.3 (16.7–30.4) months. PFS was assessed by BICR (RECIST v1.1)

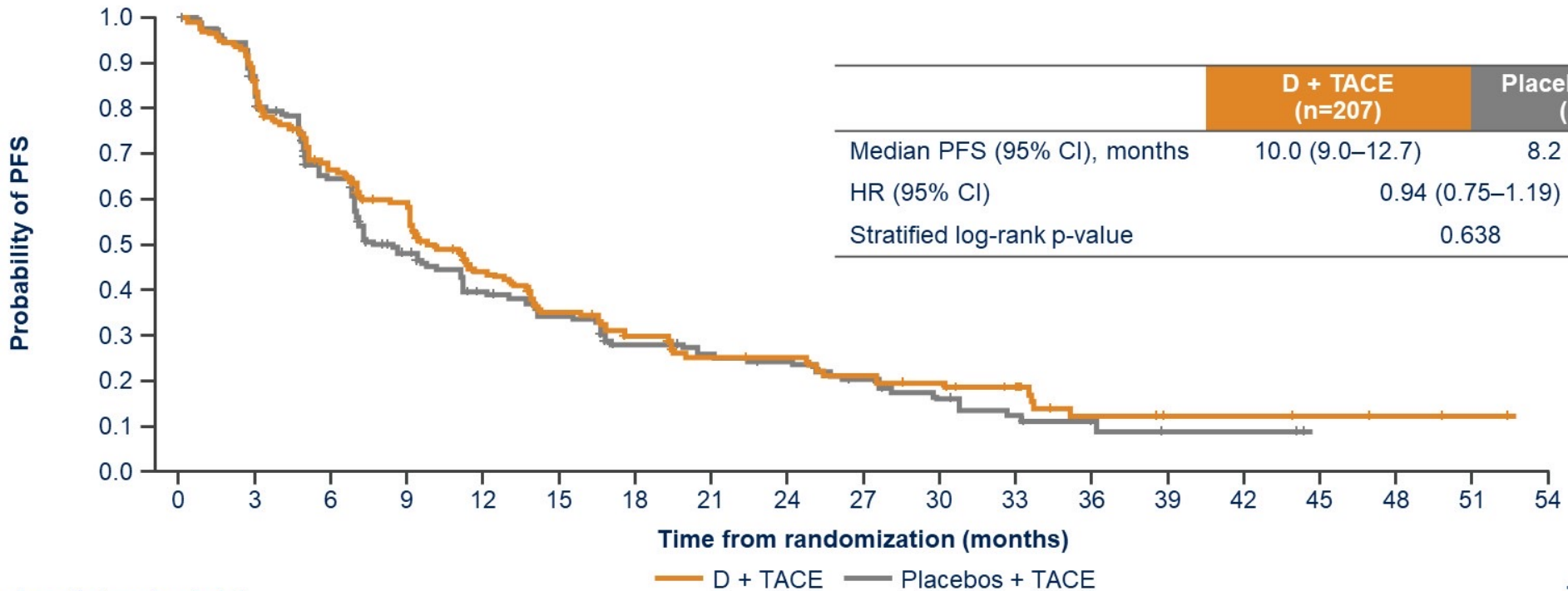
*The threshold of significance for this analysis was 0.0435 based on the α spend at the PFS interim analysis (2.27%) and the actual number of events at PFS final analysis.

B, bevacizumab; BICR, blinded independent central review; CI, confidence interval; D, durvalumab; HR, hazard ratio; mo, months, PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; TACE, transarterial chemoembolization.

PRESENTED BY: Riccardo Lencioni, MD

PFS with D + TACE versus placebos + TACE: secondary endpoint

PFS was not significantly improved with D + TACE versus placebos + TACE



	D + TACE (n=207)	Placebos + TACE (n=205)
Median PFS (95% CI), months	10.0 (9.0–12.7)	8.2 (6.9–11.1)
HR (95% CI)	0.94 (0.75–1.19)	
Stratified log-rank p-value	0.638	

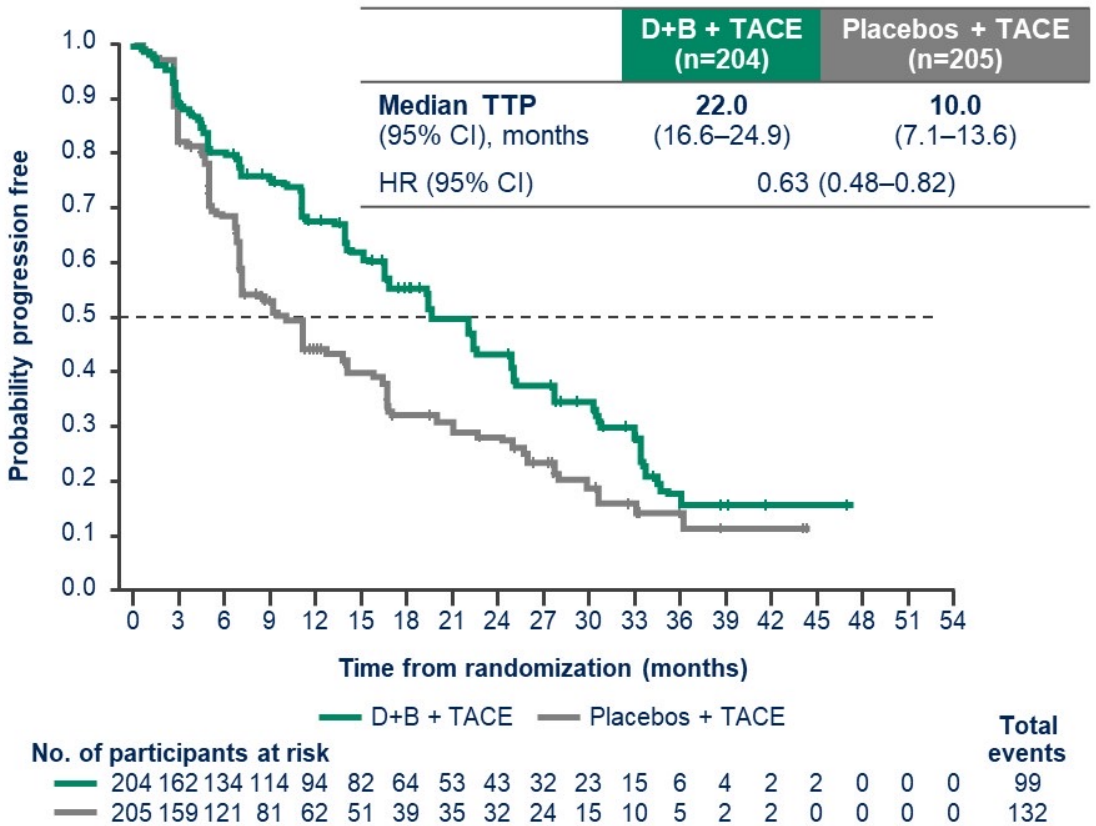
No. of participants at risk

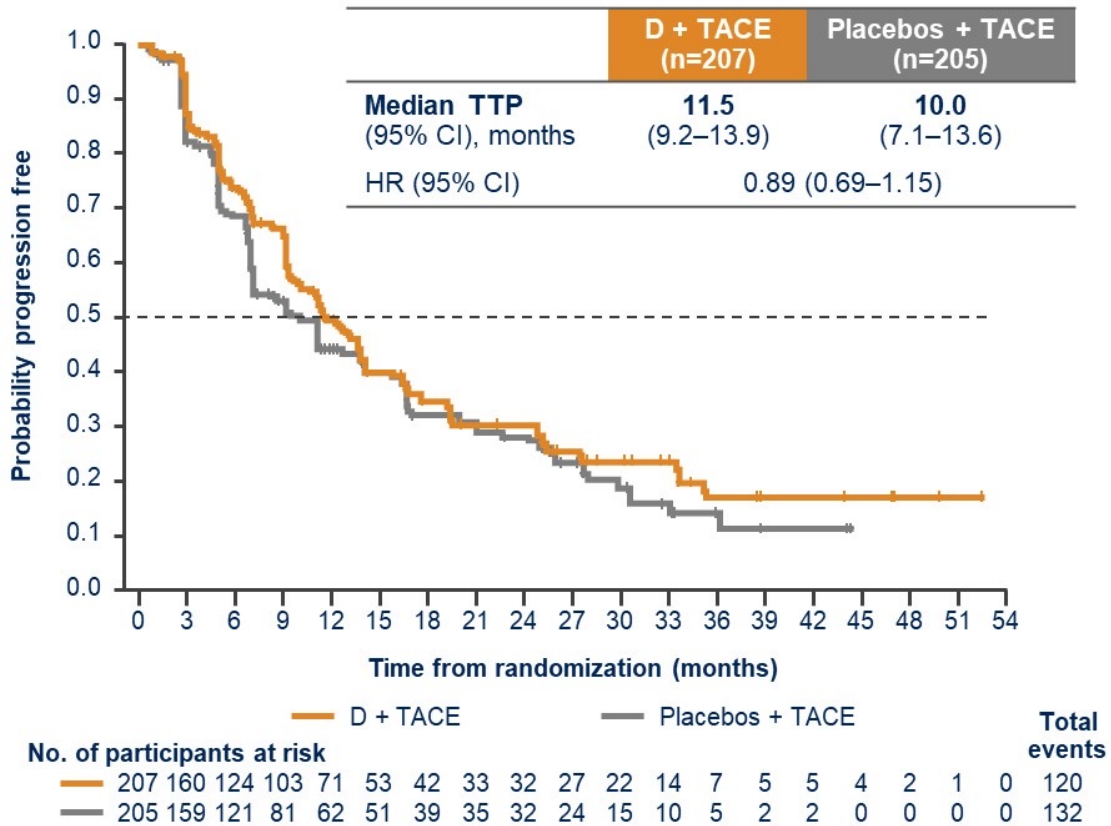
																			Total events
D + TACE	207	160	124	103	71	53	42	33	32	27	22	14	7	5	5	4	2	1	0	144
Placebos + TACE	205	159	121	81	62	51	39	35	32	24	15	10	5	2	2	0	0	0	0	149

Median (range) duration of follow-up in censored participants, D + TACE 11.5 (0.03–52.4) months, Placebos + TACE 10.3 (0.03–44.3) months. **Median (95% CI) duration of follow-up** in all participants using the reverse Kaplan-Meier method, D + TACE 27.7 (17.7–30.3) months, Placebos + TACE 26.3 (16.7–30.4) months.
PFS was assessed by BICR (RECIST v1.1)
B, bevacizumab; BICR, blinded independent central review; CI, confidence interval; D, durvalumab; HR, hazard ratio; mo, months, PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; TACE, transarterial chemoembolization.

TTP

Median TTP was improved by 12 months with D+B + TACE versus placebos + TACE





TTP was assessed by BICR (RECIST v1.1)
B, bevacizumab; BICR, blinded independent central review; CI, confidence interval; D, durvalumab; mo, months; RECIST, Response Evaluation Criteria in Solid Tumors; TACE, transarterial chemoembolization; TTP, time to progression.

Most common maximum Grade 3 or 4 TEAEs

Incidence of maximum Grade 3 or 4 AEs was low across all arms, with no unexpected safety signals

AE, n (%)	D + TACE (n=232)	D+B + TACE (n=154)	Placebos + TACE (n=200)
Hypertension	5 (2.2)	9 (5.8)	1 (0.5)
Anemia	10 (4.3)	7 (4.5)	3 (1.5)
Acute kidney injury	4 (1.7)	6 (3.9)	0
Proteinuria	0	6 (3.9)	0
Post-embolization syndrome	8 (3.4)	5 (3.2)	8 (4.0)
Hepatic encephalopathy	1 (0.4)	5 (3.2)	3 (1.5)
Ascites	4 (1.7)	4 (2.6)	3 (1.5)
Hyponatremia	1 (0.4)	4 (2.6)	0
Esophageal varices hemorrhage	0	4 (2.6)	1 (0.5)

AEs occurring in ≥2% of participants by preferred term in any arm.
AE, adverse event; B, bevacizumab; D, durvalumab; TACE, transarterial chemoembolization; TEAE, treatment-emergent adverse event.

Agenda

INTRODUCTION: EMERALD-1 – Immune Checkpoint Inhibitor-Based Therapy for Localized HCC Eligible for Embolization

MODULE 1: Optimal Utilization of Immune Checkpoint Inhibitors as First-Line Therapy for Advanced HCC — Dr Kaseb

MODULE 2: Incorporation of Anti-PD-1/PD-L1 Antibody-Based Approaches for Advanced Biliary Tract Cancers (BTCs) — Prof Vogel

Therapy for patients with viral and nonviral HCC etiology

Stacey Stein, MD

RTP
RESEARCH
TO PRACTICE

First-line management of advanced HCC

Thomas A Abrams, MD

Stacey M Stein, MD

RTP
RESEARCH
TO PRACTICE

Treatment options for patients with Child-Pugh C advanced HCC

Thomas A Abrams, MD

RTP
RESEARCH
TO PRACTICE

Transplant and other possible contraindications to immunotherapy

Stacey Stein, MD

RTP
RESEARCH
TO PRACTICE

Second-line treatment selection for advanced HCC

Thomas A Abrams, MD

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, which first-line systemic treatment would you most likely recommend for a 65-year-old patient with HCC, a Child-Pugh A score and a PS of 0?

 Dr Kaseb	Atezolizumab/bevacizumab
 Prof Vogel	Atezolizumab/bevacizumab
 Dr Abou-Alfa	Durvalumab/tremelimumab
 Dr Abrams	Durvalumab/tremelimumab
 Dr Kelley	Atezolizumab/bevacizumab or durvalumab/tremelimumab
 Dr Stein	Atezolizumab/bevacizumab

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line systemic treatment would you most likely recommend for a 65-year-old patient with HCC, a Child-Pugh A score and Grade 1 esophageal varices being managed with a beta blocker?

 Dr Kaseb	Atezolizumab/bevacizumab
 Prof Vogel	Durvalumab/tremelimumab
 Dr Abou-Alfa	Durvalumab/tremelimumab
 Dr Abrams	Durvalumab/tremelimumab
 Dr Kelley	Durvalumab/tremelimumab
 Dr Stein	Durvalumab/tremelimumab

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line systemic treatment would you most likely recommend for a 78-year-old patient with HCC, a Child-Pugh B7 score and a PS of 1?

 Dr Kaseb	Durvalumab/tremelimumab
 Prof Vogel	Durvalumab +/- tremelimumab
 Dr Abou-Alfa	Durvalumab/tremelimumab
 Dr Abrams	Durvalumab/tremelimumab
 Dr Kelley	Durvalumab +/- tremelimumab
 Dr Stein	Atezolizumab/bevacizumab

RTP RESEARCH TO PRACTICE

In general, in which situations do you use durvalumab/tremelimumab as first-line treatment for patients with advanced HCC?

 Dr Kaseb	If patient has borderline PS or borderline LFTs or large varices at risk for bleeding or just got banded
 Prof Vogel	Pts with contraindication to bev, ALBI ≥2, elderly patients, pts with history of liver decompensation
 Dr Abou-Alfa	All patients, except if contraindication for immune therapy
 Dr Abrams	Most first-line cases of advanced HCC
 Dr Kelley	Pts with peripheral vascular disease, on anticoagulation, recent/significant CAD, poorly controlled DM-2 or HTN, recent VTE, wound healing or bleeding issues
 Dr Stein	If there is a risk of bleeding

Based on current clinical trial data and/or your personal experience, how would you compare the global efficacy/treatment benefit of durvalumab/tremelimumab to that of atezolizumab/bevacizumab?

 Dr Kaseb	Atezolizumab/bevacizumab is more efficacious
 Prof Vogel	Atezolizumab/bevacizumab may be more efficacious (depending on endpoint)
 Dr Abou-Alfa	Durvalumab/tremelimumab is more efficacious
 Dr Abrams	Durvalumab/tremelimumab is more efficacious
 Dr Kelley	About the same
 Dr Stein	About the same

RTP RESEARCH TO PRACTICE

Based on current clinical trial data and/or your personal experience, how would you compare the global tolerability/toxicity of durvalumab/tremelimumab to that of atezolizumab/bevacizumab?

 Dr Kaseb	Durvalumab/tremelimumab is more tolerable
 Prof Vogel	About the same
 Dr Abou-Alfa	Durvalumab/tremelimumab is more tolerable
 Dr Abrams	About the same
 Dr Kelley	Durvalumab/tremelimumab is more tolerable
 Dr Stein	Atezolizumab/bevacizumab is more tolerable

RTP
RESEARCH
TO PRACTICE

For a patient who has received atezolizumab/bevacizumab in the up-front setting and experienced disease progression, are there any circumstances in which you will recommend an anti-PD-1/PD-L1 antibody later in the treatment course?

 Dr Kaseb	Yes, in combination with an anti-CTLA-4 antibody
 Prof Vogel	Yes, in combination with an anti-CTLA-4 antibody
 Dr Abou-Alfa	Yes, in combination with an anti-CTLA-4 antibody
 Dr Abrams	Yes, in combination with an anti-CTLA-4 antibody
 Dr Kelley	Yes, in combination with an anti-CTLA-4 antibody
 Dr Stein	Not usually — would consider if patient had long response and especially if bev could not be continued

RTP RESEARCH TO PRACTICE

Optimal Utilization of Immune Checkpoint Inhibitors as First-Line Therapy for Advanced HCC

RTP Hepatobiliary Cancers Webinar – ASCO GI
January 20th, 2024

Ahmed O Kaseb, MD

Professor and Director, HCC Program

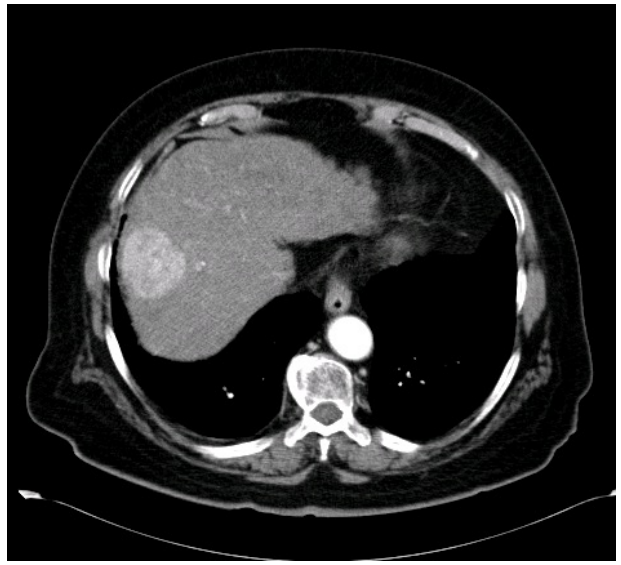
Director, MD Anderson HCC SPORE

Department of GI Medical Oncology, MD Anderson

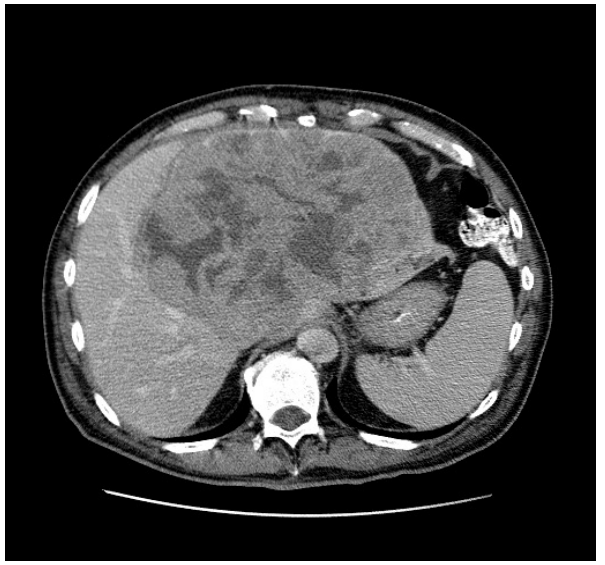
Editor-in-Chief: Journal of Hepatocellular Carcinoma

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

2 Major Pathognomonic Features in HCC call for Charting systemic therapy



HCC + Cirrhosis → Limited surgical role
→ Angiogenesis-driven & immunogenic*



HCC with no Cirrhosis → Surgical options
→ High recurrence rates

Dilemma 1: No hypothesis-driven personalized tx and CTP is the only hepatic reserve assessment tool → poor outcome in advanced HCC

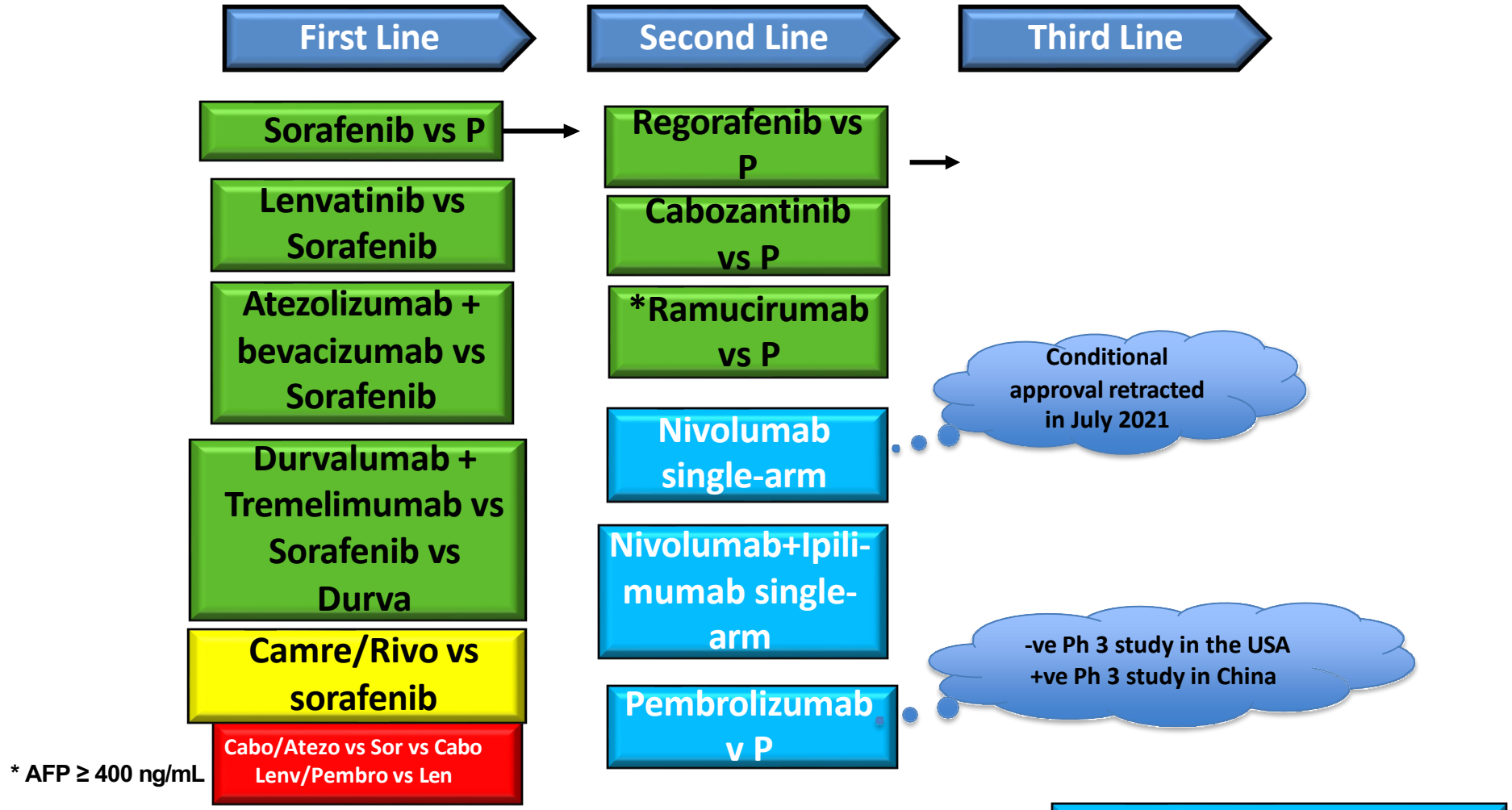
Dilemma 2: No standard neoadjuvant or adjuvant approaches → Recurrence rate is very high

* Around 30% of HCC microenvironment is immune favorable

Educational Objectives

- Learn current standard and evolving systemic therapies in HCC
- Understand key factors affecting the selection of first-line treatment for advanced HCC
- Present regimen-specific factors affecting efficacy and safety outcomes
- Discuss tx sequencing and evolving real-world data in advanced HCC
- Conclusion

The ever-changing Landscape of Systemic Therapy in HCC



Educational Objectives

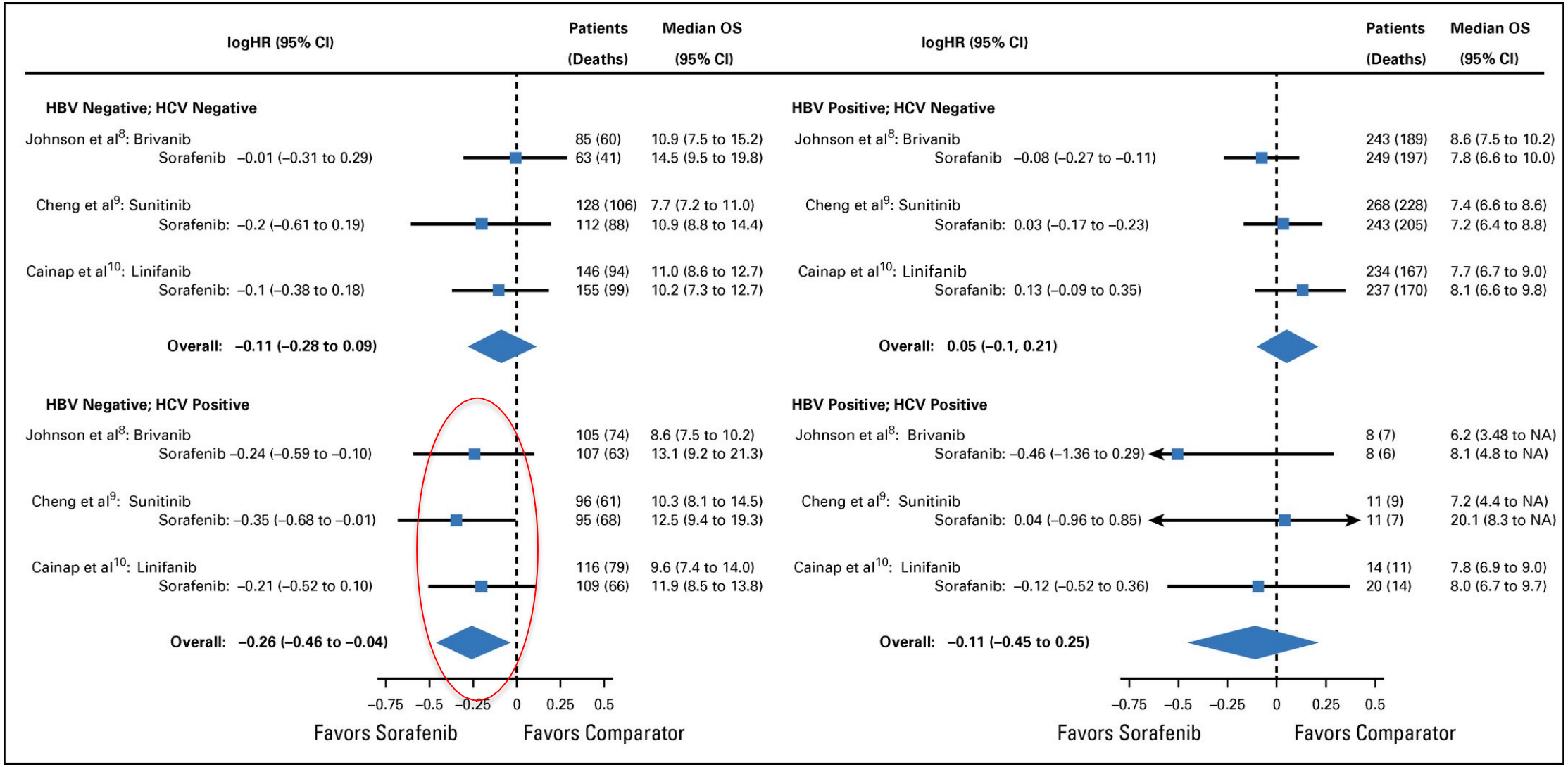
- **Learn current standard and evolving systemic therapies in HCC**
- **Understand key factors affecting the selection of first-line treatment for advanced HCC**
- **Present regimen-specific factors affecting efficacy and safety outcomes**
- **Discuss tx sequencing and evolving real-world data in advanced HCC**
- **Conclusion**

Towards Selection and Sequencing of Systemic tx in HCC

Question: do we have response predictors of systemic therapy in HCC?

… Such as biomarkers, risk factors, demographics, or liver function status?

Impact of Viral Status on Survival in Patients Receiving Sorafenib for Advanced HCC: A Meta-Analysis of Randomized Phase III Trials

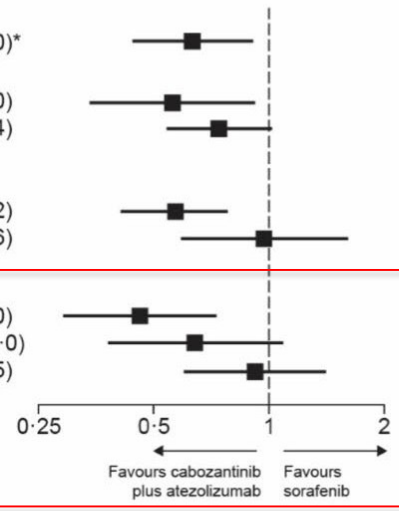


Jackson R, et al JCO 2017

Phase 3 COSMIC-312 Trial (Cabo/Atezo V sor): subset analysis[1]: Region, EHD/MVI, and Hepatitis status

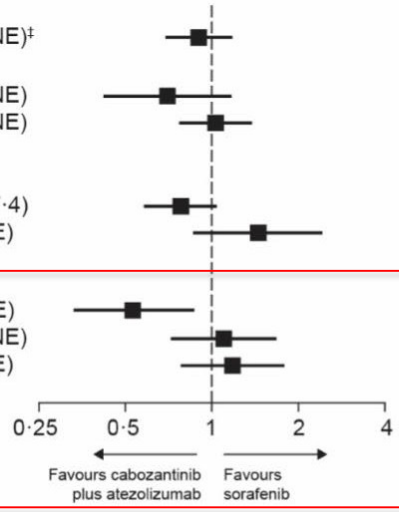
A.

	Events/n	Median (95% CI) progression-free survival, mo			HR (95% CI)
	Cabozantinib plus atezolizumab		Sorafenib		
Overall	174/250	6·8 (5·6–8·3)*	78/122	4·2 (2·8–7·0)*	0·63 (0·44–0·91)†
Region					
Asia	44/63	6·7 (4·3–8·3)	25/33	2·7 (1·4–4·0)	0·56 (0·34–0·92)
Other regions	130/187	6·9 (5·7–8·5)	53/89	5·6 (3·3–7·4)	0·74 (0·54–1·02)
EHD and/or MVI					
Yes	119/175	6·7 (5·4–8·3)	57/85	2·9 (2·6–4·2)	0·57 (0·41–0·78)
No	55/75	6·9 (5·7–9·7)	21/37	7·0 (4·3–9·6)	0·97 (0·59–1·61)
Aetiology					
HBV	52/74	6·7 (5·6–8·3)	28/35	2·7 (1·5–4·0)	0·46 (0·29–0·73)
HCV without HBV	43/71	7·9 (5·8–11·0)	21/34	5·6 (2·9–10·0)	0·64 (0·38–1·09)
Non-viral	79/105	5·8 (4·3–9·3)	29/53	7·0 (3·6–9·5)	0·92 (0·60–1·41)



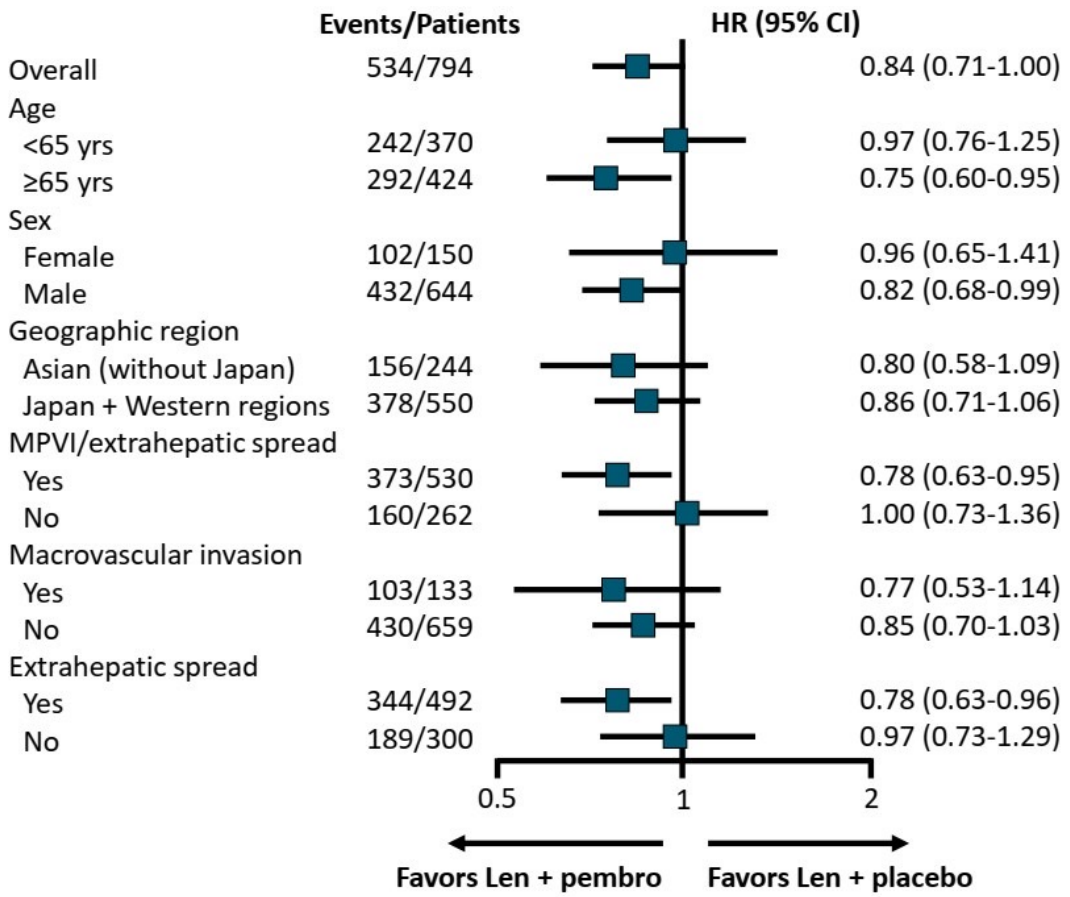
B.

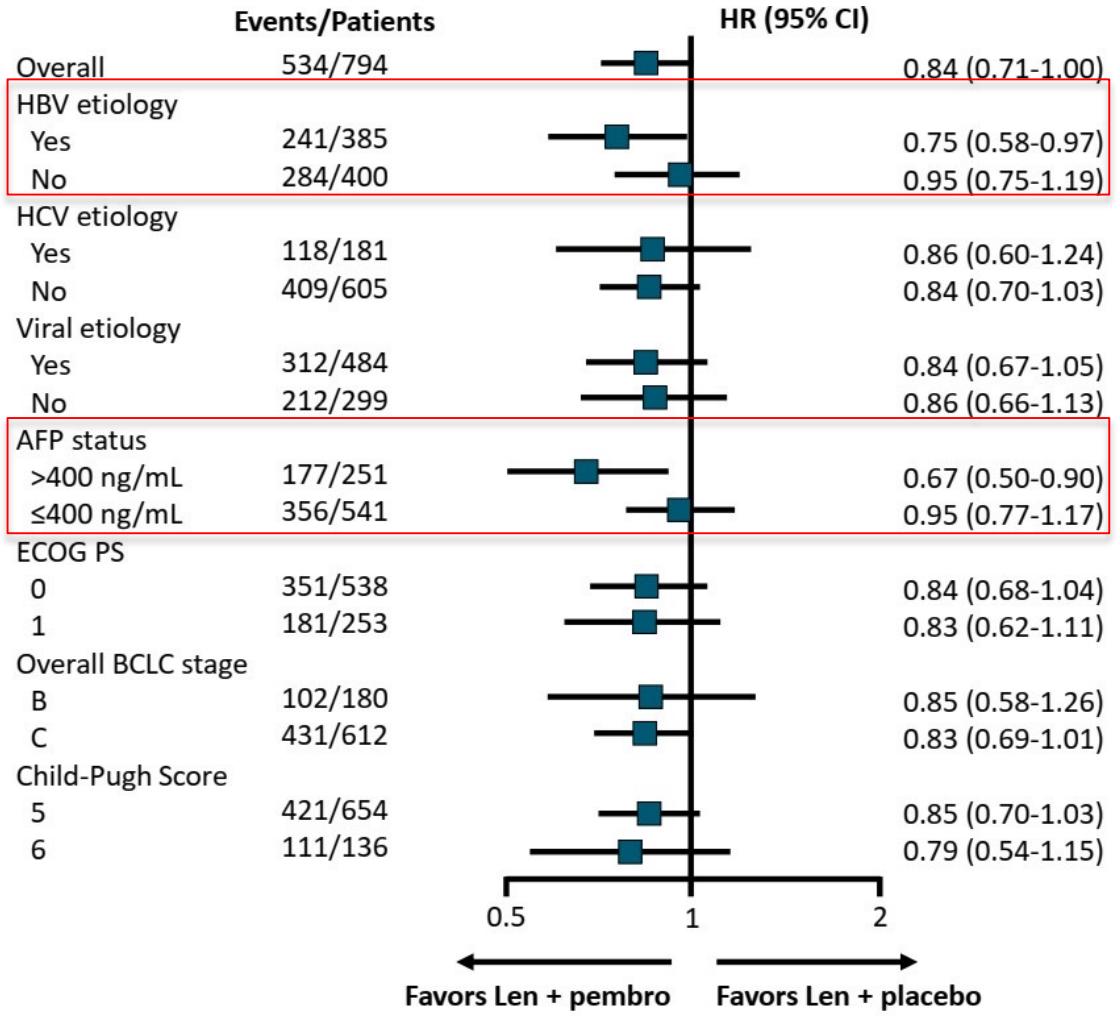
	Events/n	Median (95% CI) overall survival, mo			HR (95% CI)
	Cabozantinib plus atezolizumab		Sorafenib		
Overall	183/432	15·4 (13·7–17·7)‡	90/217	15·5 (12·1–NE)‡	0·90 (0·69–1·18)§
Region					
Asia	39/120	NE (13·7–NE)	24/63	14·9 (10·6–NE)	0·70 (0·42–1·17)
Other regions	144/312	14·9 (12·9–17·0)	66/154	15·5 (12·1–NE)	1·03 (0·77–1·38)
EHD and/or MVI					
Yes	131/298	14·9 (12·9–17·2)	70/148	12·0 (9·6–17·4)	0·78 (0·58–1·04)
No	52/134	15·8 (14·5–NE)	20/69	NE (15·0–NE)	1·45 (0·86–2·43)
Aetiology					
HBV	41/127	18·2 (15·4–NE)	28/64	14·9 (7·9–NE)	0·53 (0·33–0·87)
HCV without HBV	66/136	13·6 (10·8–17·0)	31/67	14·0 (10·6–NE)	1·10 (0·72–1·68)
Non-viral	76/169	15·2 (12·5–NE)	31/86	NE (14·9–NE)	1·18 (0·78–1·79)



Kelly, RK, et al. Lancet Oncol 2022

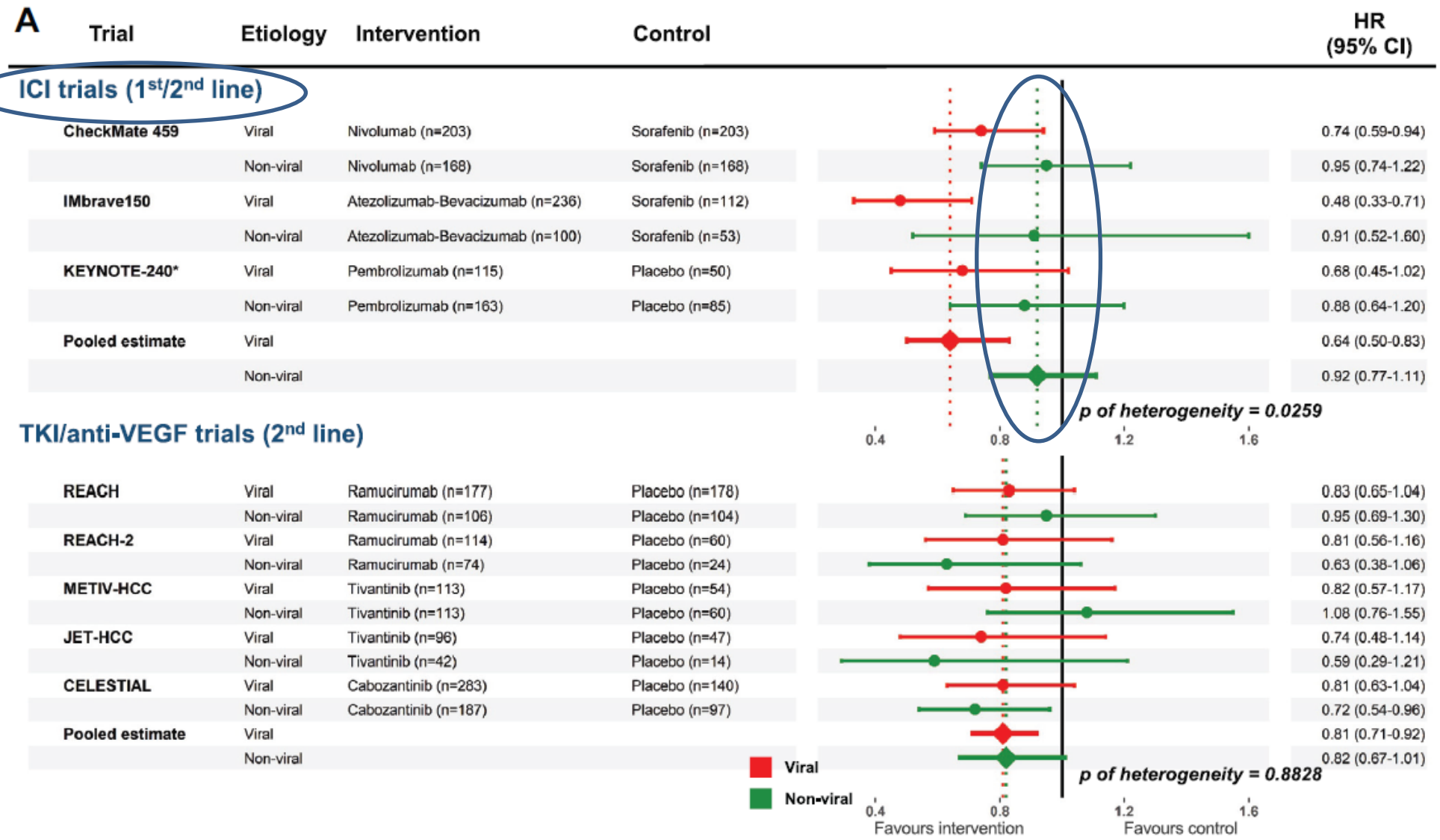
LEAP-002 (Lenvatinib plus Pembro Vs Lenvatinib) : Overall Survival Subgroup Analysis





Finn. ESMO 2022. Abstr LBA34.

Meta-analysis of Randomized Controlled Trials (2002–2020)



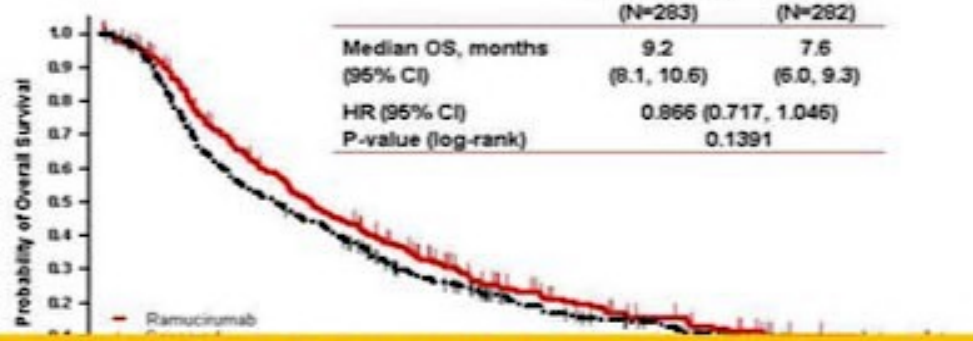
Haber PK et al. Gastroenterology 2021

REACH-1: randomized, double-blind, phase 3 trial of Ramucirumab Vs placebo as 2nd line tx in HCC "VEGF pathway"

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Overall Survival in Hepatocellular Cancer Patients
ITT Population

	Ramucirumab (N=283)	Placebo (N=282)
Median OS, months (95% CI)	9.2 (8.1, 10.6)	7.6 (6.0, 9.3)
HR (95% CI)	0.866 (0.717, 1.046)	
P-value (log-rank)	0.1391	

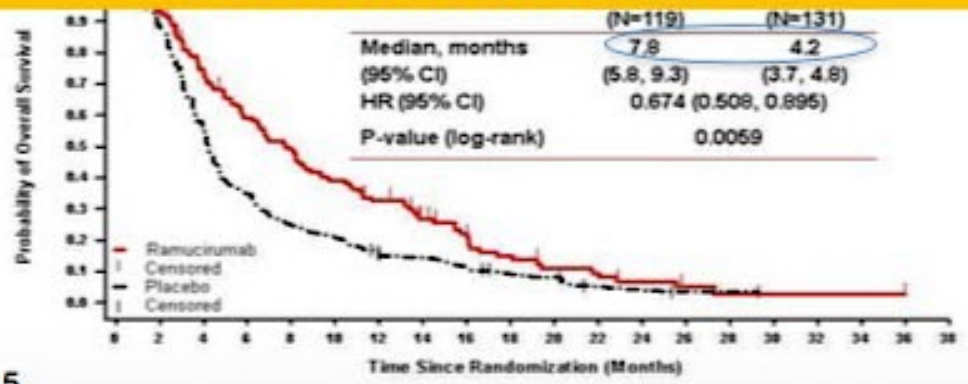


REACH-2 (AFP-high HCC: ≥400 ng/mL)

The trial met its primary endpoint: OS & secondary endpoint: PFS

Press release: April 2018

	(N=119)	(N=131)
Median, months	7.8	4.2
(95% CI)	(5.8, 9.3)	(3.7, 4.8)
HR (95% CI)	0.674 (0.508, 0.895)	
P-value (log-rank)	0.0059	



Zhu AX, et al. Lancet Oncology 2015

IMbrave150 Vs HIMALAYA pt demographics

	AB	STRIDE
Demographics		
Region (%)		
Asia (excluding Japan)	40.0	39.7
Rest of world	60.0	60.3
ECOG performance status score (%)		
0	62.0	62.1
1	38.0	37.7
Child-Pugh classification (%)		
A	100.0	98.5
B7	0	1.0
BCLC disease stage (%)		
B	15.0	19.6
C	82.0	80.4
High-risk features (%)		
AFP ≥ 400 ng/mL	38.0	36.9
Macrovascular invasion	38.0	26.2
Extrahepatic disease	63.0	53.2
Main portal vein thrombosis	15.0	0
HCC etiology (%)		
Hepatitis B	49.0	31.0
Hepatitis C	21.0	28.0
Nonviral	30.0	41.0
Prior local therapy for HCC (%)	49.0	12.2
Efficacy		
ORR (%)		
RECIST 1.1	30.0	20.1
mRECIST	35.0	N/A
Complete response rate (%)	8.0	3.1
Disease control rate (%)	74.0	60.1
mPFS (months)	6.9 (5.7, 8.6; *P* = .0001)	3.8
mOS (months)	19.2 (17, 23.7; *P* = .0009)	16.4
Safety		
TRAEs (%)		
All grades	86.0	75.8
Grades 3/4	43.0	25.8
Grade 5	2.0	2.3
Leading to dose delay/modification	59.0	21.4
Leading to treatment discontinuation	22.0	8.2

- Similar geographic region, ECOG status, baseline AFP level, and LFTs (CP-A).
- However, different **high-risk features**: IMbrave-150: higher proportions of macrovascular invasion (approximately 40% vs 25%) and extrahepatic disease (approximately 60% vs 50%).
- Furthermore, the HIMALAYA trial excluded patients with main trunk portal vein thrombosis (**Vp4 HCC**), whereas the IMbrave-150 trial did not.
- IMbrave150 mandated EGD within 6 months before tx.

https://dailynews.ascopubs.org/do/himalaya-and-imbrave-150-hepatocellular-carcinoma-critical-comparison

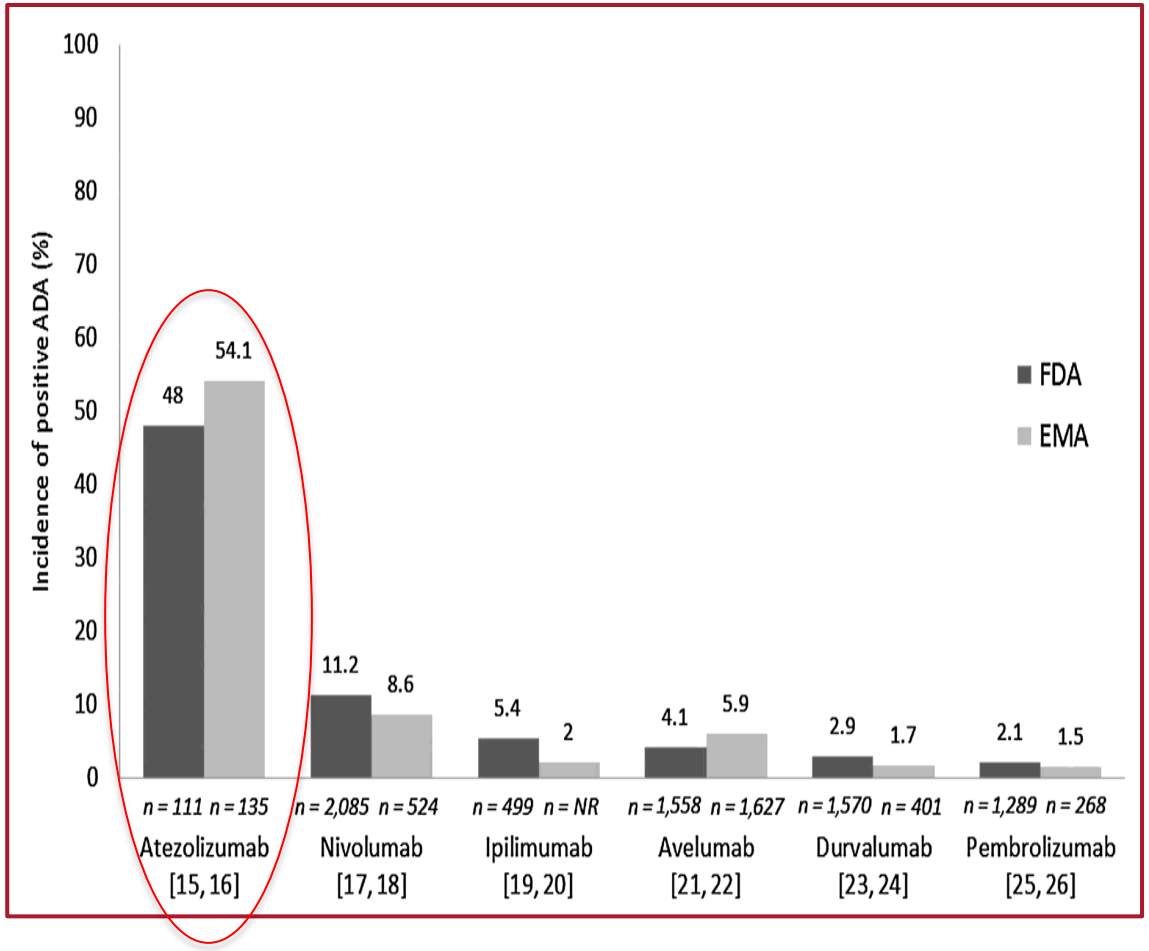
Answer:

- **AFP>400 as an indication for ramucirumab**
- **A hint of better outcome to sorafenib in HCV-HCC and immunotherapy in viral hepatitis-HCC**
- **A hint of better outcome to Cabo/Atezo, and Pembro/Len in HBV-HCC**
- **Caution in patients with borderline LFTs or overall condition (also main PVTT, tumors occupying almost entire liver, or large varices)**

Educational Objectives

- **Learn current standard and evolving systemic therapies in HCC**
- **Understand key factors affecting the selection of first-line treatment for advanced HCC**
- **Present regimen-specific factors affecting efficacy and safety outcomes**
- **Discuss tx sequencing and evolving real-world data in advanced HCC**
- **Conclusion**

Understanding the clinical implications of ADA-positive status following treatment with checkpoint inhibitors[1]



- The frequency of ADA-positive patients varies from as low as 1.5% to 54%.
- Antidrug antibodies (ADAs) can cause a decrease in the amount of drug available and may result in decreased antitumor activity.

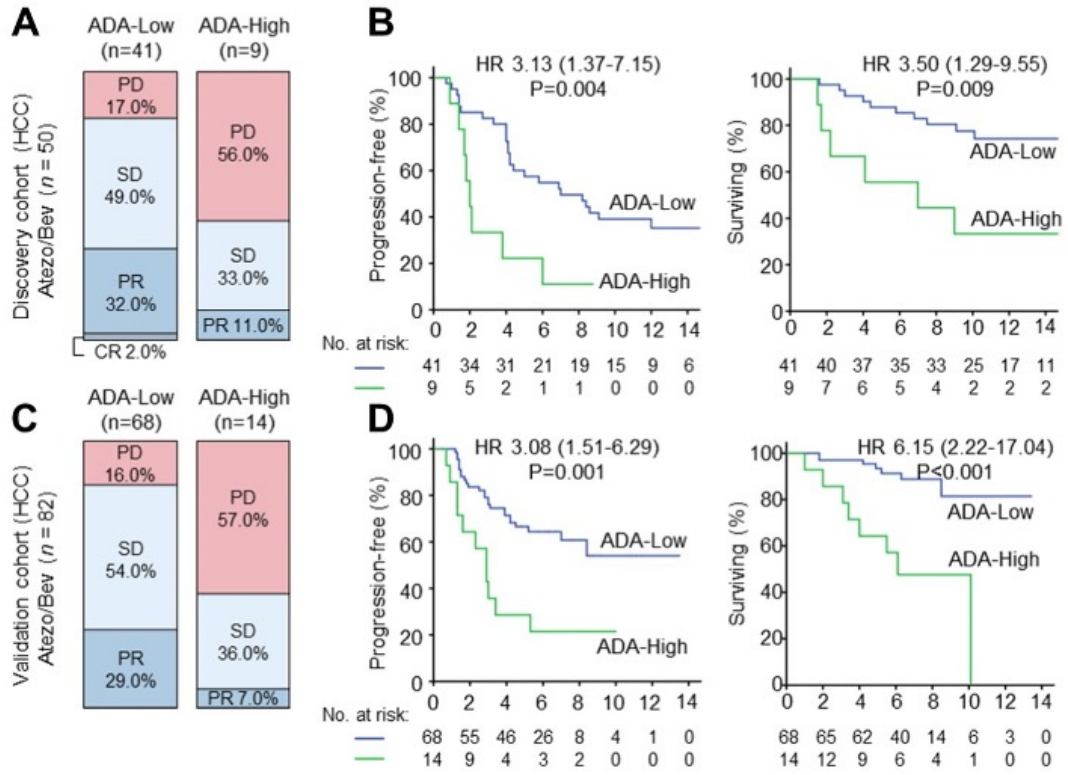
Figure Legend:
Highest published incidences of ADAs developing with different immune checkpoint inhibitors.

FDA: Food and Drug Administration; **EMA**: European Medicines Agency; **n**: Total Number of Patients Tested for ADA; **ADA**: Antidrug Antibodies; **NR**: Not Reached

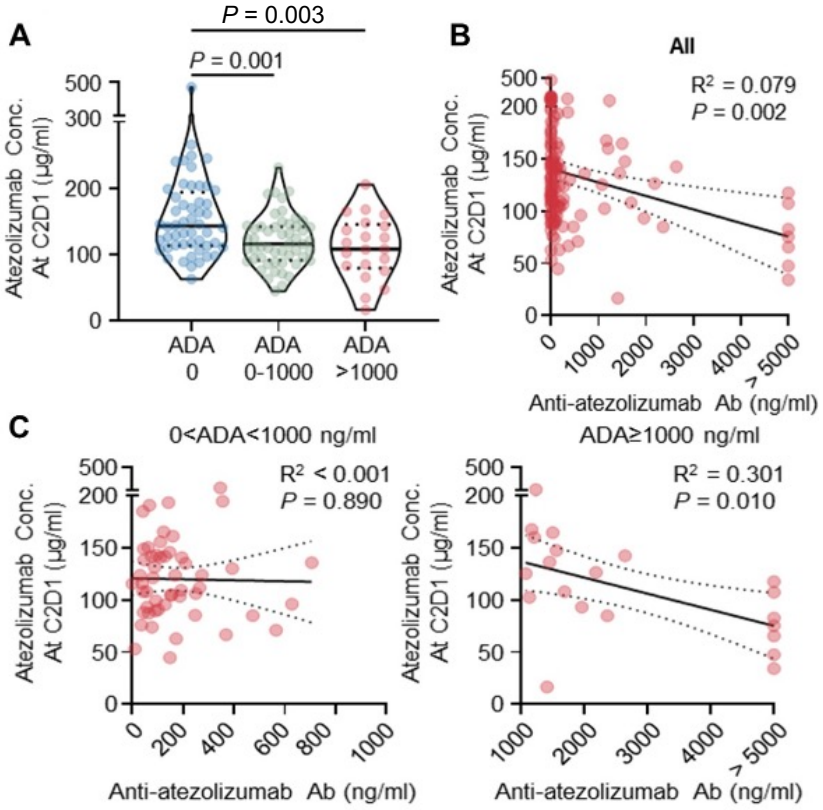
1. Enrico, D., Paci, A., Chaput, N., Karamouza, E. and Besse, B., 2019. Antidrug Antibodies Against Immune Checkpoint Blockers: Impairment of Drug Efficacy or Indication of Immune Activation?. *Clinical Cancer Research*, 26(4), pp.787-792.

Patients with high ADA levels at C2D1 found to have a decreased response rate, shorter PFS and OS, and reduced atezolizumab serum concentration vs. those with low ADA levels

ADA levels at C2D1



Atezolizumab serum concentration at varying ADA levels



Conclusions: Highly elevated ADA at C2D1 was associated with unfavourable clinical outcomes and reduced atezolizumab exposure, thereby limiting the drug's anti-cancer efficacy, in advanced HCC patients treated with atezolizumab-bevacizumab combination

ADA=anti-drug-antibody; CR=complete response; HCC=hepatocellular carcinoma; HR=hazard ratio; OS=overall survival; PD=progressive disease; PFS=progression-free survival; PR=partial response; SD=stable disease.

Jae Chon H, et al. Presented at ASCO 2022. Abstract #4105

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

CheckMate 040: Nivolumab + Ipilimumab in advanced HCC: treatment-related AEs

	Arm A n = 49		Arm B n = 49		Arm C n = 48	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Any treatment-related adverse event,[a] No. (%)	46 (94)	26 (53)	35 (71)	14 (29)	38 (79)	15 (31)
Pruritus	22 (45)	2 (4)	16 (33)	0	14 (29)	0
Rash	14 (29)	2 (4)	11 (22)	2 (4)	8 (17)	0
Diarrhea	12 (24)	2 (4)	6 (12)	1 (2)	8 (17)	1 (2)
AST increase	10 (20)	8 (16)	10 (20)	4 (8)	6 (13)	2 (4)
Hypothyroidism	10 (20)	0	4 (8)	0	4 (8)	0
Fatigue	9 (18)	1 (2)	6 (12)	0	5 (10)	0
ALT increase	8 (16)	4 (8)	7 (14)	3 (6)	4 (8)	0
Lipase increased	7 (14)	6 (12)	6 (12)	3 (6)	8 (17)	4 (8)
Adrenal insufficiency	7 (14)	1 (2)	3 (6)	0	2 (4)	0
Rash maculo-papular	7 (14)	2 (4)	4 (8)	0	3 (6)	0
Decreased appetite	6 (12)	0	4 (8)	0	3 (6)	0
Malaise	6 (12)	1 (2)	3 (6)	0	3 (6)	0
Nausea	5 (10)	0	4 (8)	0	1 (2)	0
Pyrexia	2 (4)	0	4 (8)	0	5 (10)	0
Immune-mediated adverse events requiring immune modulating medication,[b] No. (%)						
Rash	17 (35)	3 (6)	14 (29)	2 (4)	8 (17)	0
Hepatitis	10 (20)	10 (20)	6 (12)	5 (10)	3 (6)	3 (6)
Hypothyroidism	10 (20)	0	5 (10)	0	6 (13)	0
Adrenal insufficiency	9 (18)	2 (4)	3 (6)	0	3 (6)	0
Diarrhea/colitis	5 (10)	3 (6)	1 (2)	1 (2)	1 (2)	1 (2)
Pneumonitis	5 (10)	3 (6)	0	0	0	0
Hyperthyroidism	5 (10)	0	4 (8)	0	3 (6)	0
Hypophysitis	2 (4)	0	1 (2)	1 (2)	1 (2)	1 (2)

Modified from - Yau T, et al. JAMA Oncology 2020

Camrelizumab plus rivoceranib vs. sorafenib as first-line therapy for unresectable HCC: a randomized, phase 3 trial

TRAEs with Incidence of ≥20%*

Preferred term	Camrelizumab + rivoceranib (N=272)		Sorafenib (N=269)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Hypertension	189 (69.5)	102 (37.5)	116 (43.1)	40 (14.9)
AST increased	147 (54.0)	45 (16.5)	99 (36.8)	14 (5.2)
Proteinuria	134 (49.3)	16 (5.9)	72 (26.8)	5 (1.9)
ALT increased	127 (46.7)	35 (12.9)	80 (29.7)	8 (3.0)
Platelet count decreased	126 (46.3)	32 (11.8)	89 (33.1)	4 (1.5)
Blood bilirubin increased	116 (42.6)	24 (8.8)	75 (27.9)	4 (1.5)
PPE syndrome	102 (37.5)	33 (12.1)	163 (60.6)	41 (15.2)
Diarrhoea	83 (30.5)	6 (2.2)	105 (39.0)	14 (5.2)
RCEP	79 (29.0)	7 (2.6)	0	0
Neutrophil count decreased	73 (26.8)	16 (5.9)	27 (10.0)	3 (1.1)
White blood cell count decreased	73 (26.8)	7 (2.6)	38 (14.1)	3 (1.1)
GGT increased	66 (24.3)	27 (9.9)	49 (18.2)	20 (7.4)
Hypothyroidism	58 (21.3)	0	16 (5.9)	0

Data are n (%). *TRAEs of any grade occurring in ≥20% or of grade ≥3 occurring in ≥5% of patients in either group are listed. Data cutoff: Feb. 8, 2022. AST=aspartate aminotransferase; ALT=alanine aminotransferase; GGT=Gamma-glutamyl transferase; PPE=palmar-plantar erythrodysaesthesia; RCEP=reactive capillary endothelial proliferation

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IMbrave150: Adverse events of Special Interests (AESI) – focus on Atezo related

AESIs, n (%)[a]	Atezo + Bev n = 329		Sor n = 156	
	All	G3-4	All	G3-4
For atezo				
Pts with ≥ 1	226 (69)	85 (26)	128 (82)	47 (30)
Hepatic events[b]	142 (43)	70 (21)	62 (40)	26 (17)
Inc AST	64 (20)	23 (7)	26 (17)	8 (5)
Inc blood bilirubin	43 (13)	8 (2)	22 (14)	10 (6)
Inc ALT	46 (14)	12 (4)	14 (9)	2 (1)
Ascites	23 (7)	6 (2)	9 (6)	2 (1)
Rash	64 (20)	2 (1)	96 (62)	21 (14)
Hypothyroidism	36 (11)	0	4 (3)	0
Infusion-related reactions	36 (11)	8 (2)	0	0
For bev				
Pts with ≥ 1	190 (58)	76 (23)	76 (49)	29 (19)
Hypertension	102 (31)	50 (15)	40 (26)	19 (12)
Bleeding/haemorrhage	83 (25)	21 (6)	27 (17)	9 (6)
Epistaxis	34 (10)	0	7 (5)	1 (1)
Upper GI bleeding[c]	24 (7)	15 (5)	8 (5)	8 (5)
Proteinuria	70 (21)	10 (3)	13 (8)	1 (1)

Inc, increased. [a] In ≥ 5% of pts. [b] ≥ 1 category possible. [c] Grouped MedDRA PT

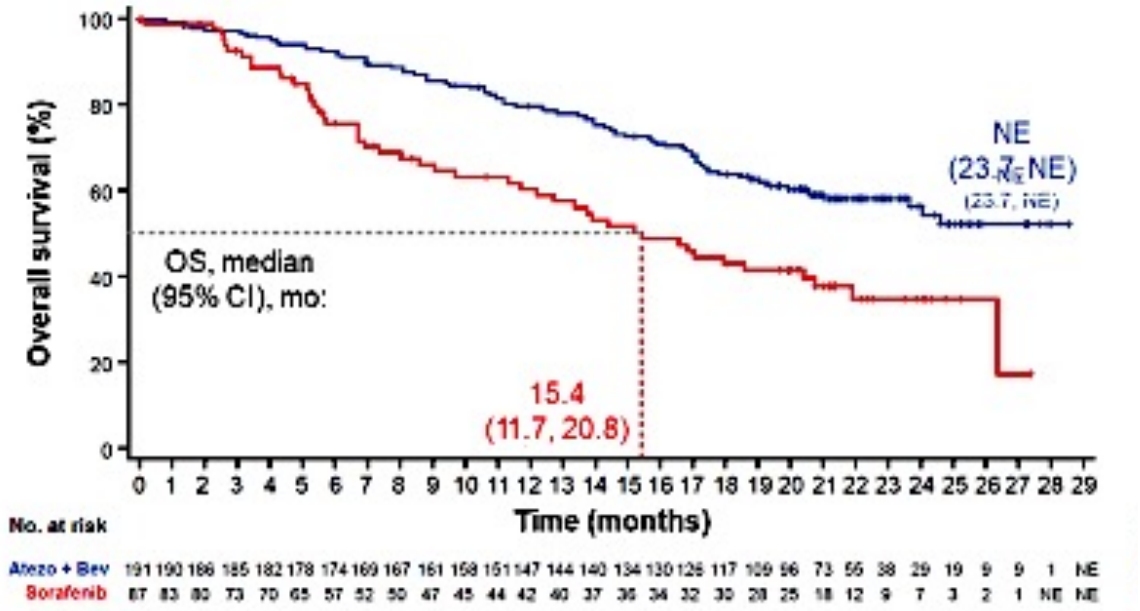
Kudo M et al, Ann of Oncol Abstract only| Volume 31, SUPPLEMENT 6, S1304-S1305, Nov 01, 2020

IMbrave150: OS for Atezo/Bev versus sorafenib by ALBI grade

OS by ALBI grade

ALBI Grade 1

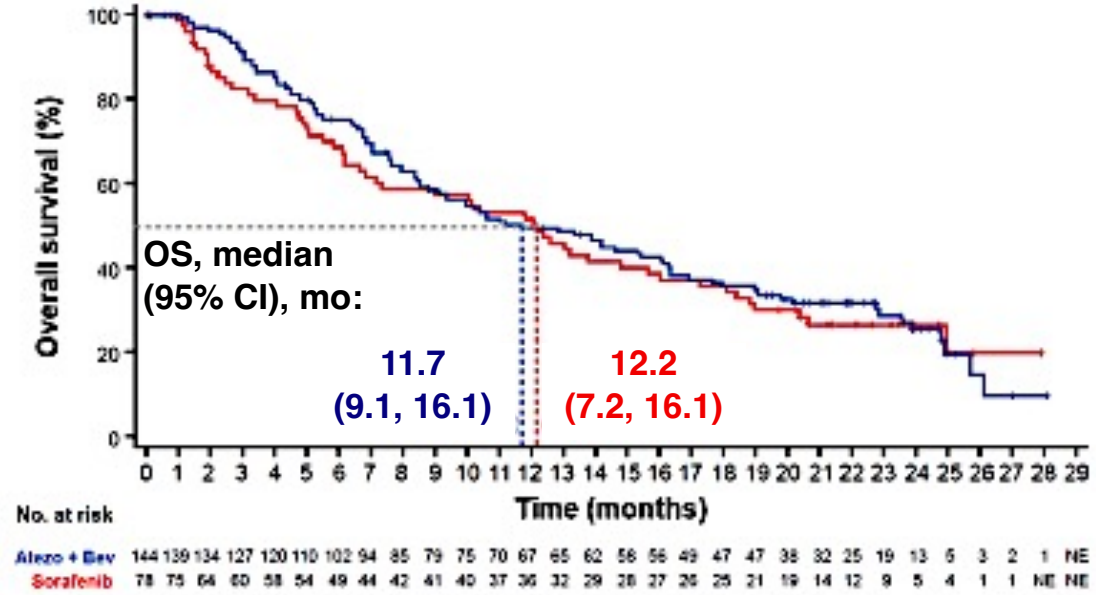
	Atezo + Bev (n=191)	Sorafenib (n=87)
OS events, n (%)	79 (41)	47 (54)
HR (95% CI)[a]	0.50 (0.35, 0.72)	



Clinical cutoff: August 31, 2020; median follow-up: 15.6 mo. NE, not estimable. [a] HR is unstratified.

ALBI Grade 2

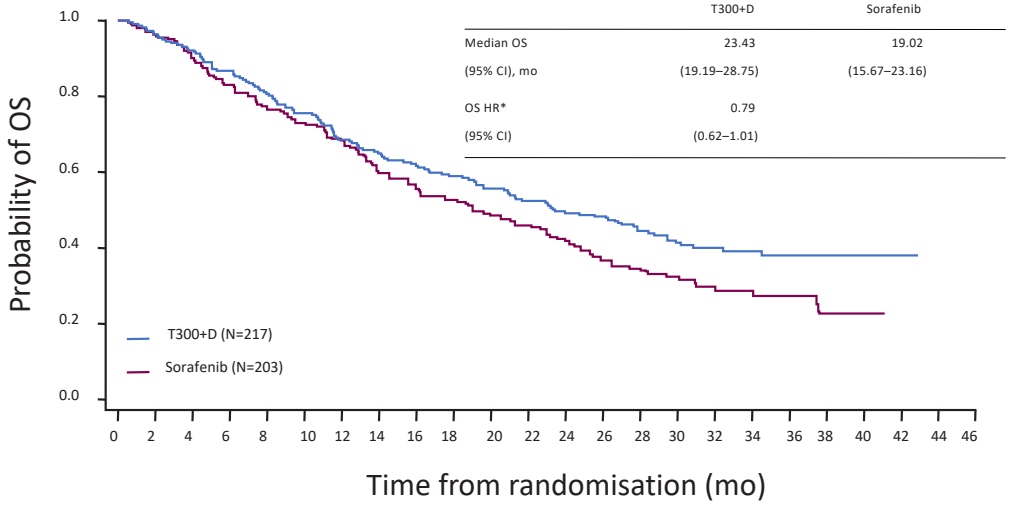
	Atezo + Bev (n=144)	Sorafenib (n=78)
OS events, n (%)	100 (69)	53 (68)
HR (95% CI)[a]	0.92 (0.66, 1.29)	



Kudo M, et al. *Liver Cancer*. 2023;12(5):479-493. Published 2023 Mar 4.

OS for HIMALAYA (Durva/Treme) versus sorafenib by ALBI grade

ALBI grade 1

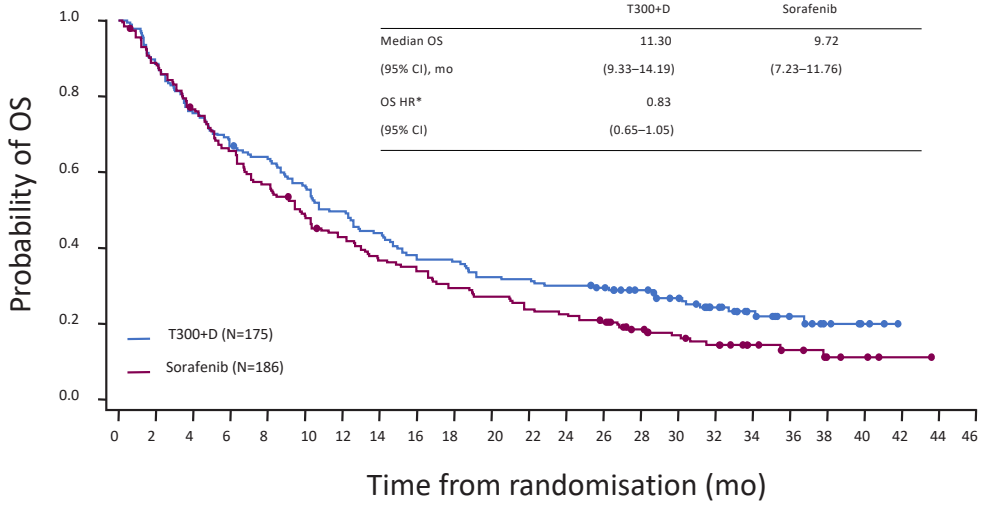


	T300+D	Sorafenib
Median OS	23.43	19.02
(95% CI), mo	(19.19–28.75)	(15.67–23.16)
OS HR*	0.79	
(95% CI)	(0.62–1.01)	

Number at risk

T300+D:	217	209	200	188	174	163	148	140	133	127	120	113	106	101	77	63	50	38	21	13	8	1	0	0
Sorafenib:	203	193	180	165	153	144	135	118	110	103	94	89	81	70	53	41	27	21	13	8	2	0	0	0

ALBI grade 2/3



	T300+D	Sorafenib
Median OS	11.30	9.72
(95% CI), mo	(9.33–14.19)	(7.23–11.76)
OS HR*	0.83	
(95% CI)	(0.65–1.05)	

Number at risk

T300+D:	175	155	132	119	110	98	86	76	64	63	56	55	52	49	42	35	25	17	11	6	3	0	0	0
Sorafenib:	186	163	139	118	102	87	76	65	60	52	48	42	40	36	26	21	17	11	8	4	3	1	0	0

- OS HRs for T300+D versus sorafenib in the ALBI grade 1 and ALBI grade 2/3 subgroups were generally consistent with the full analysis set (0.78; 96% CI, 0.65–0.93)

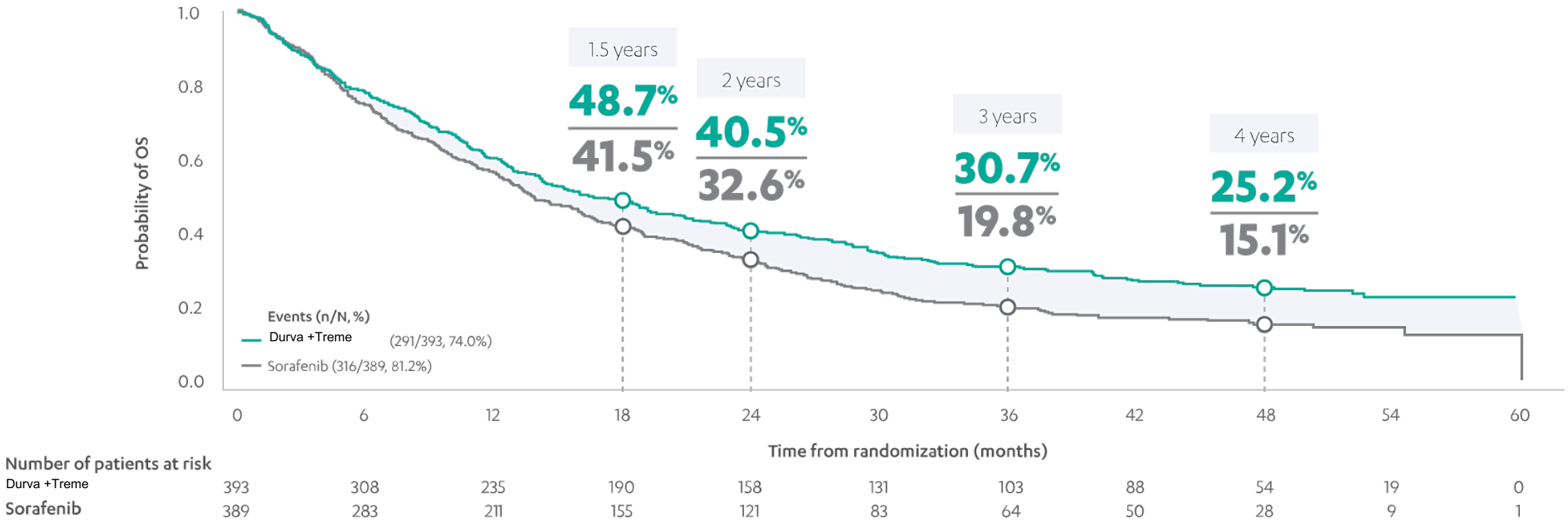
*OS HRs and 95% CIs were calculated using a Cox proportional hazards model adjusting for treatment, aetiology, ECOG performance status, and macrovascular invasion

ALBI, albumin-bilirubin; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; mo, months; OS, overall survival; T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W

1. Abou-Alfa GK, et al. NEJM Evid Published online 6 June 2022. doi:10.1056/EVIDoa2100070

*ESMO conference presentation 2022

Four-year overall survival update from the phase 3 HIMALAYA study of Durvalumab plus tremelimumab in uHCC

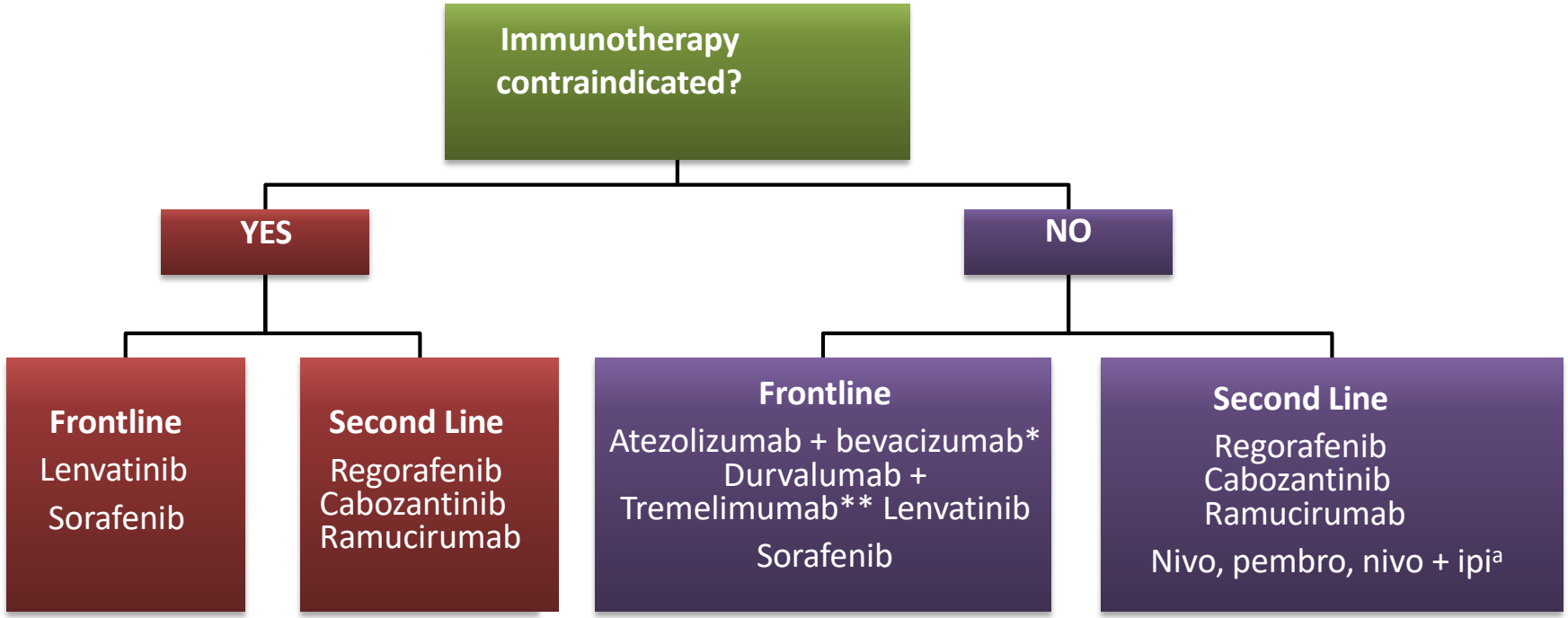


Sangro B, et al. ESMO GI 2023

Educational Objectives

- **Learn current standard and evolving systemic therapies in HCC**
- **Understand key factors affecting the selection of first-line treatment for advanced HCC**
- **Present regimen-specific factors affecting efficacy and safety outcomes**
- **Discuss tx sequencing and evolving real-world data in advanced HCC**
- **Conclusion**

Sequencing Systemic Therapy in 2024 (Approved Therapy)



- EGD within 6 months required → caution with **varices and portal HTN** (Portal vein thrombosis and/or anticoagulation)

** Trend for better tolerance with **poor hepatic reserve** (Albi score study)

General Consideration → in absence of trial options → **assess demographics and risk factors**

Patient Receives Frontline Therapy for Advanced HCC … What Happens in Real life?

After local therapy, patient progressed with the development of portal vein invasion (remained well compensated: CP-A and ECOG of 0)

After multidisciplinary evaluation → EGD recommended

EGD showed no/small varices/low bleeding risk	**EGD showed no/small varices/low bleeding risk**	**EGD showed bleeding/large varices/high bleeding risk**
Atezo/Bev Durva/Treme	Patient already on TKI (Lenvatinib or Sorafenib) or Durva/Treme	Treated with IO alone → **Treat varices**
What are the options at progression?		

TKI: e.g. Lenvatinib or Sorafenib	**Atezo/Bev Or other TKIs**	**If varices are successfully treated: <u>start using anti-angiogenesis</u> Atezo/Bev, TKI: sorafenib, Lenvatinib**

Global study of Atezo/Bev in beyond frontline therapy in HCC

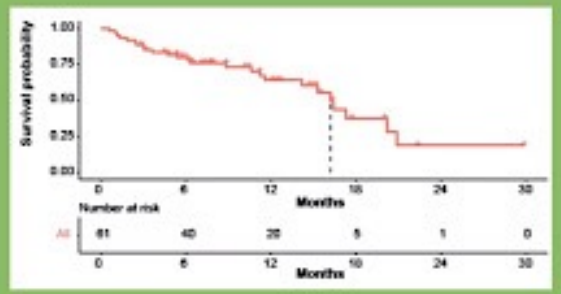
Efficacy and Safety of Atezolizumab and Bevacizumab in Patients with Hepatocellular Carcinoma After Prior Systemic Therapy

Study Population

61 patients receiving Atezolizumab and Bevacizumab after prior systemic therapy *(global, multicenter, observational)*

Created with BioRender

Outcome



Overall survival: 16.2 months

Objective response rate: 38%

Treatment-related adverse events: 42.6% (only 13.1% of CTCAE grade ≥3)

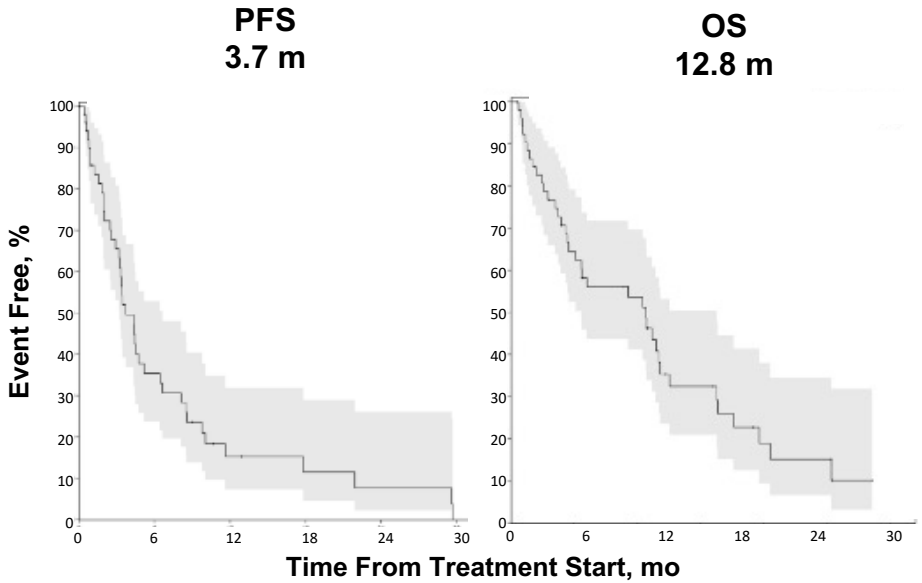
Atezolizumab and Bevacizumab appear safe and efficacious in patients with hepatocellular carcinoma previously treated with other systemic agents

Joerg, Scheiner, et al. *Hepatol Commun.* 2023.

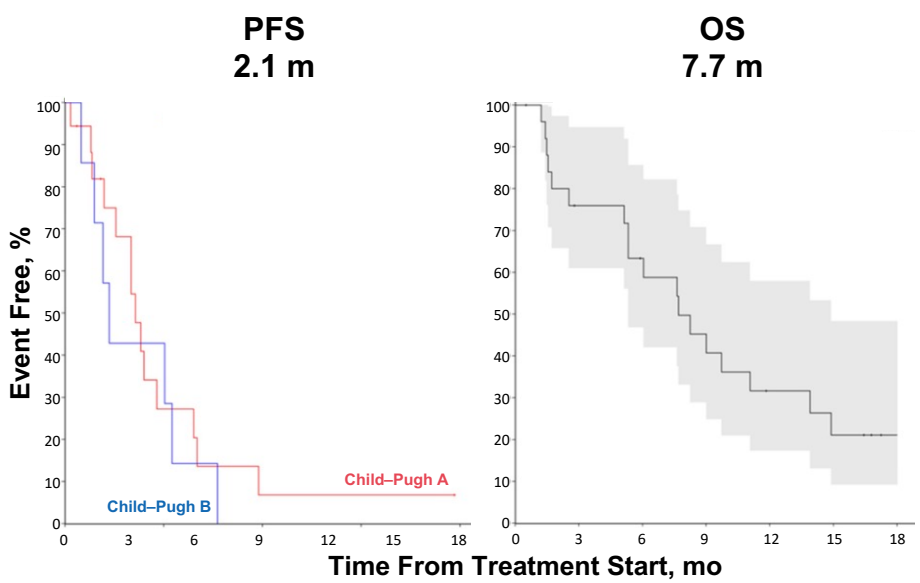
HEPATOLOGY COMMUNICATIONS
Open Access

Evolving data – post Atezo/Bev

Lenvatinib



Cabozantinib



- Lenvatinib demonstrated a PFS of 3.7 mo; mOS of 12.8 mo (N = 53)
- Cabozantinib demonstrated a PFS of 2.1 mo; mOS of 7.7 mo (N = 26)
- Other studies are currently underway to evaluate other 2L options post atezo-bev (eg, regorafenib[3])

1. Gile J et al. ASCO GI 2023. Abstract 507. 2. Palmer M et al. ASCO GI 2023. Abstract 559. 3. Cheon J et al. ASCO GI 2023. Abstract TPS634.

Real World Data of Immunotherapy Efficacy and Safety in Advanced HCC

Reference	Arm-1	Median OS/ Median PFS (Months)	Arm-2	Median OS/ Median PFS (Months)	Comments
DeCastro et al 2022[63]	IMBrave-in	15/ 8.7	IMBrave-out	6/ 3.7	IMBrave-out group showed increased risk for ascites and hepatic encephalopathy
Rimini et al, 2023[64]	IMBrave-in	16.3/ 8.3	IMBrave-out	14.3/ 6	No statistically significant difference in safety profile
Tanaka et al, 2022[65]	Atezolizumab + Bevacizumab in CP-A	NR/ 9.5	Atezolizumab + Bevacizumab in CP-B	14/ 5.1	Therapeutic efficacy correlated with worsening liver function (mALBI score grade 2b-3).
Kim et al, 2022[66]	Atezolizumab + Bevacizumab in CP-A	NR/ 6	Atezolizumab + Bevacizumab in CP-B	6/ 3	CP-B showed increase rate of grade 3 adverse effects compared to CP-A
D'Alessio et al, 2022[67]	Atezolizumab + Bevacizumab in CP-A	16.8/ 7.6	Atezolizumab + Bevacizumab in CP-B	6.7/ 3.4	
Cheon et al, 2023[68]	Atezolizumab + Bevacizumab in CP-A	NR/ 9.6	Atezolizumab + Bevacizumab in CP-B	7.7/ 3	CP-B showed increase rate of grade 3 adverse effects compared to CP-A
Rimini et al, 2023[69]	Atezolizumab + Bevacizumab in CP-B	8.2/ 6.9	Lenvatinib in CP-B	13.8/ 8.2	No statistically significant difference in PFS
Casadei-Gardini et al, 2023[70]	Atezolizumab + Bevacizumab	16.4 (OS)	Lenvatinib	16.1 (OS)	ATE/BEV improved OS in HCC patients with viral etiology. Lenvatinib improved OS in HCC patients with NASH/ NAFLD etiology.
Wong et al, 2021[71]	Single agent Nivolumab/ Pembrolizumab in CP-B	3.1 (OS)	Single agent Nivolumab/ Pembrolizumab in CP-C	1.7 (OS)	ORR for CP-B and CP-C was 6.8% and 0% respectively. TTP 2.1 and 1.4 months, respectively.
Fessas et al, 2020[72]	Nivolumab in CP-A	16.3 (OS)	Nivolumab in CP-B	7.3 (OS)	
Chapin et al, 2023[73]	Nivolumab in CP-B	5 (OS)	Sorafenib in CP-B	4 (OS)	Decreased hazard of death with nivolumab compared to sorafenib HR: 0.69

Sara A, and Pawlik T, et al. Pragmatic and Observational Research. 2023

Educational Objectives

- **Learn current standard and evolving systemic therapies in HCC**
- **Understand key factors affecting the selection of first-line treatment for advanced HCC**
- **Present regimen-specific factors affecting efficacy and safety outcomes**
- **Discuss tx sequencing and evolving real-world data in advanced HCC**
- **Conclusion**

Conclusion

- Refining 1L therapy in advanced HCC requires an understanding of benefit-risk ratio and patients' demographics and clinical features
- Despite recent approval of multiple systemic tx in HCC → prospective evidence-based medicine supporting specific sequences is lacking and is still dependent on clinical scenarios
- However, advances in combining IO+IO and IO+targeted therapies are being translated into higher response rates and longer TTP → Predictive biomarkers are needed
- Notably, designing future trials should be customized based on disease etiology, underlying liver disease, and tumor characteristics for early, intermediate and advanced stages of HCC and require global participation to address disparity in healthcare/trials access

Agenda

INTRODUCTION: EMERALD-1 – Immune Checkpoint Inhibitor-Based Therapy for Localized HCC Eligible for Embolization

MODULE 1: Optimal Utilization of Immune Checkpoint Inhibitors as First-Line Therapy for Advanced HCC — Dr Kaseb

MODULE 2: Incorporation of Anti-PD-1/PD-L1 Antibody-Based Approaches for Advanced Biliary Tract Cancers (BTCs) — Prof Vogel

KEYNOTE-966 and TOPAZ-1: Selecting first-line therapy for advanced BTC

Stacey Stein, MD

RTP
RESEARCH
TO PRACTICE

Challenges with the chemotherapy portion of the TOPAZ-1 regimen for patients with advanced BTC

Thomas A Abrams, MD

RTP
RESEARCH
TO PRACTICE

Experience with futibatinib as second-line treatment for BTC

Stacey Stein, MD

RTP
RESEARCH
TO PRACTICE

Use of targeted agents as part of up-front therapy for BTC

Thomas A Abrams, MD

RTP
RESEARCH
TO PRACTICE

Use of FGFR2 inhibitors as part of front-line therapy for BTC

Stacey Stein, MD

RTP
RESEARCH
TO PRACTICE

Prevention and management of hyperphosphatemia associated with FGFR2 inhibitors

Stacey Stein, MD

RTP
RESEARCH
TO PRACTICE

HER2-directed therapy for BTC

Thomas A Abrams, MD

RTP
RESEARCH
TO PRACTICE

What was the age of the last patient in your practice with metastatic biliary tract cancer who received durvalumab/chemotherapy as first-line treatment? What was the treatment schedule, and how much benefit, if any, did the patient derive from treatment?

	Age	Tx schedule	Tx benefit
 Dr Kaseb	69 years	Gem/cis q2wk, durvalumab q4wk	Some benefit
 Prof Vogel	65 years	TOPAZ-1	Partial response
 Dr Abou-Alfa	65 years	TOPAZ-1	A great deal of benefit
 Dr Abrams	34 years	TOPAZ-1	Some benefit
 Dr Kelley	60 years	TOPAZ-1	Some benefit
 Dr Stein	67 years	TOPAZ-1	Too early to determine

TOPAZ-1 schedule: gemcitabine/cisplatin d1 and d8, q21 days; durvalumab d1, q21 days

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic biliary tract cancer, no targetable mutations on NGS and PS 0?

	First-line Tx	Second-line Tx
 Dr Kaseb	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Prof Vogel	Durvalumab + cisplatin/gemcitabine	FOLFIRI
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Durvalumab + nal-IRI/5-FU/LV
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine*	FOLFIRI
 Dr Stein	Durvalumab + cisplatin/gemcitabine	FOLFIRI

LV = leucovorin

*Institutional preference for pembrolizumab

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic biliary tract cancer and an IDH1 mutation (PS 0)?

	First-line Tx	Second-line Tx
 Dr Kaseb	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Prof Vogel	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine*	Ivosidenib
 Dr Stein	Durvalumab + cisplatin/gemcitabine	Ivosidenib

*Institutional preference for pembrolizumab

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic biliary tract cancer and an FGFR alteration (PS 0)?

	First-line Tx	Second-line Tx
 Dr Kaseb	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Prof Vogel	Durvalumab + cisplatin/gemcitabine	Futibatinib or pemigatinib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	Futibatinib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine*	Futibatinib
 Dr Stein	Durvalumab + cisplatin/gemcitabine	Pemigatinib

*Institutional preference for pembrolizumab

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with HER2-overexpressing (IHC 3+) advanced biliary tract cancer (PS 0)?

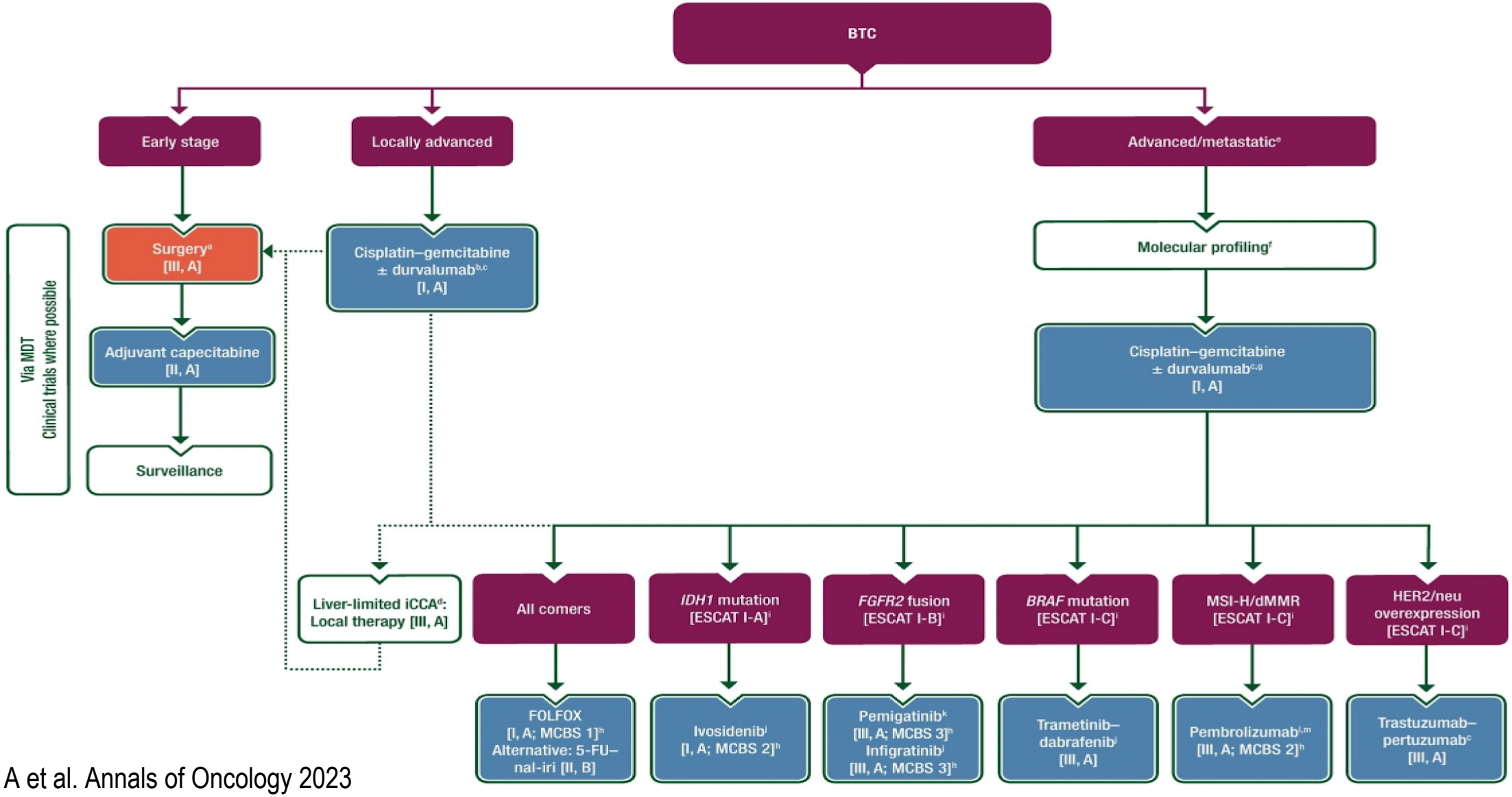
	First-line Tx	Second-line Tx
 Dr Kaseb	Durvalumab + cisplatin/gemcitabine	Trastuzumab/pertuzumab
 Prof Vogel	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan or tucatinib/trastuzumab or zanidatamab
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan or zanidatamab
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	Trastuzumab/pertuzumab
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine*	Zanidatamab
 Dr Stein	Durvalumab + cisplatin/gemcitabine	Tucatinib/trastuzumab

*Institutional preference for pembrolizumab

Incorporation of Anti-PD-1/PD-L1 Antibody-Based Approaches for Advanced Biliary Tract Cancers (BTCs)

Arndt Vogel

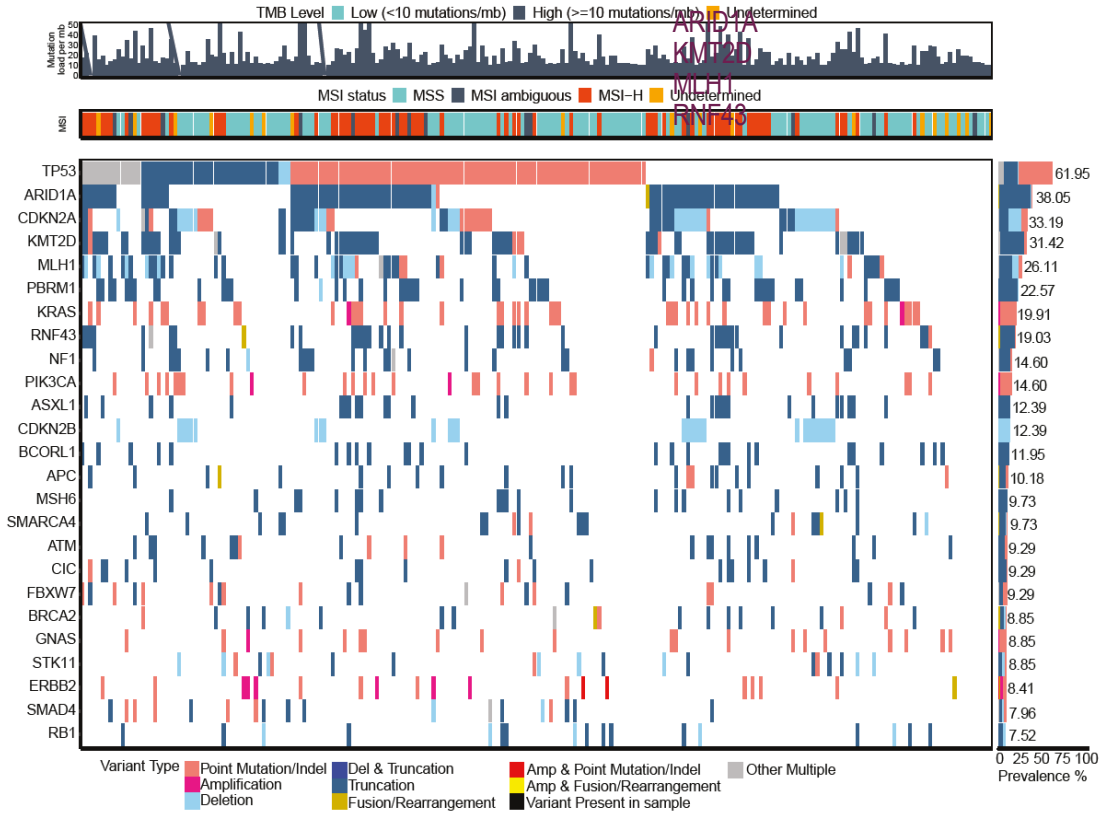
ESMO Clinical Practice Guideline 2022



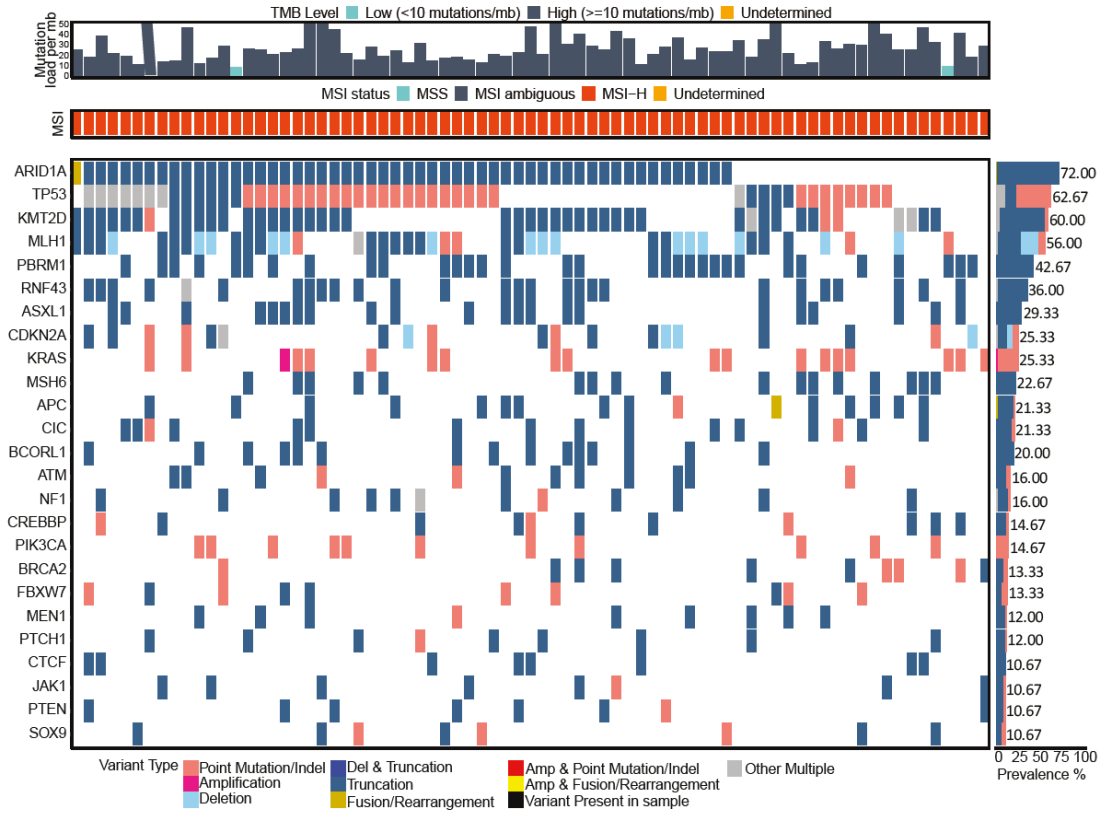
Vogel A et al. Annals of Oncology 2023

BTC: low prevalence of established IO biomarkers

TMB^{high} 226/6130 iCCAs (3.7%)



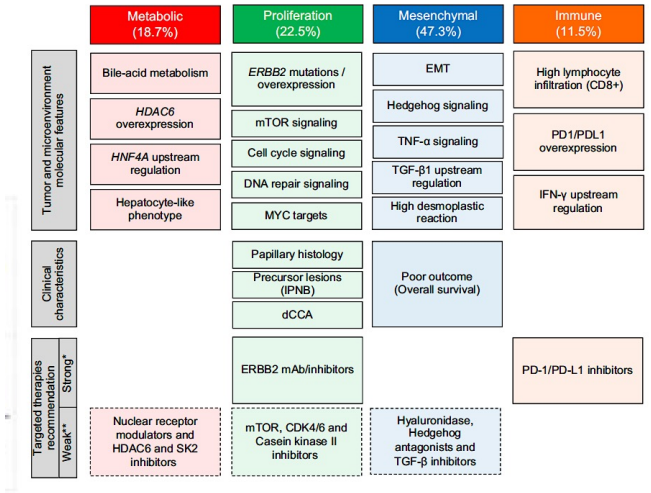
MSI^{high} 75/6130 iCCAs (1.2%)



Vogel/Saborowski Journal of Hepatology 2002

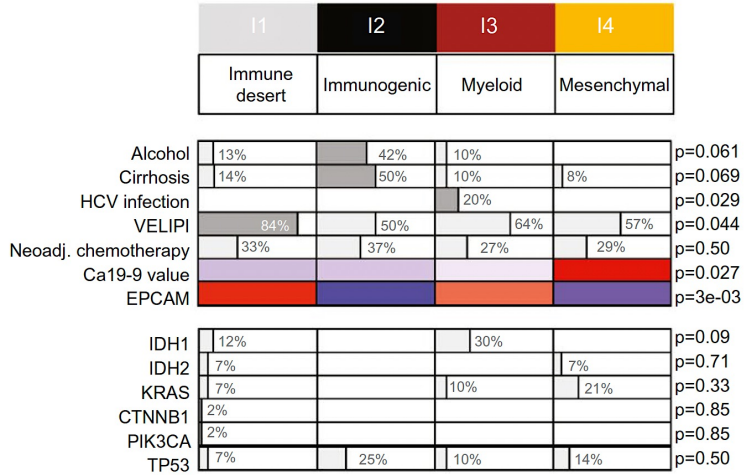
Biliary Tract Cancers: 10%-30% with “immunogenic” phenotype according to “multi-omic“ classification

Extrahepatic CCA, n= ; → 11% immune subclass



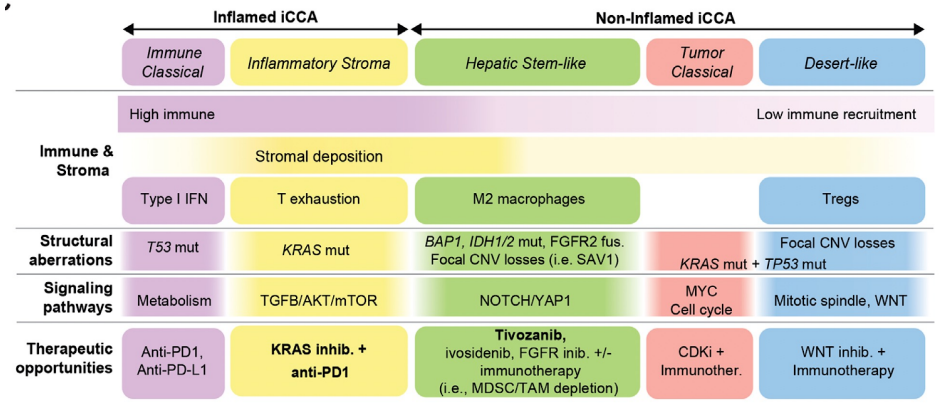
Montal et al, J. Hepatol 2020

Intrahepatic, n=566 → 13% immunogenic



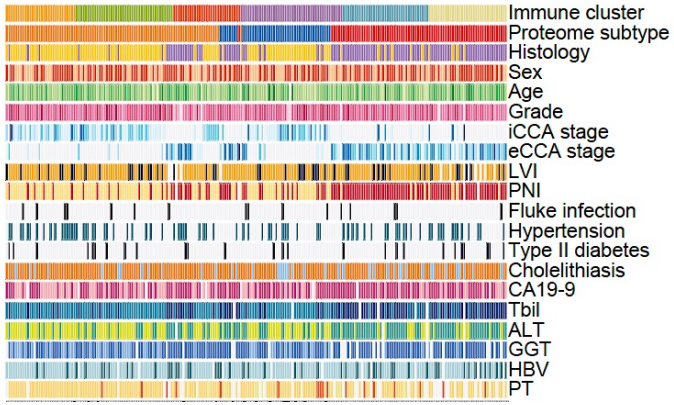
Job et al. Hepatology 2020

Intrahepatic CCA, n=900 → 10% immune classical



Martin-Serrano et al, GUT 2022

Intra- and extrahepatic, n=217 → 30% „immun-responsive“



Deng et al, Hepatology 2022

Pembrolizumab in Advanced BTC with Proficient MMR/MSS: KEYNOTE-158

N=104, multicenter basket trial biliary tract cancer (BTC) cohort with planned biomarker analyses

≥1 prior line of therapy, median 2

ICC, ECC, GBC % not reported

PD-L1+ (CPS ≥1, 22C3) 59%

99 with proficient mismatch repair (pMMR), 5 unknown

Treatment-related AE Grade 3-5 in 13.5%

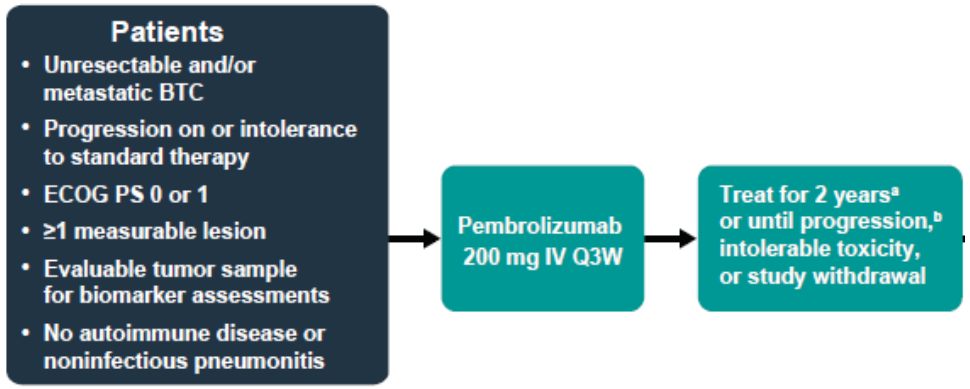
Confirmed PR (central) in 5.8% overall

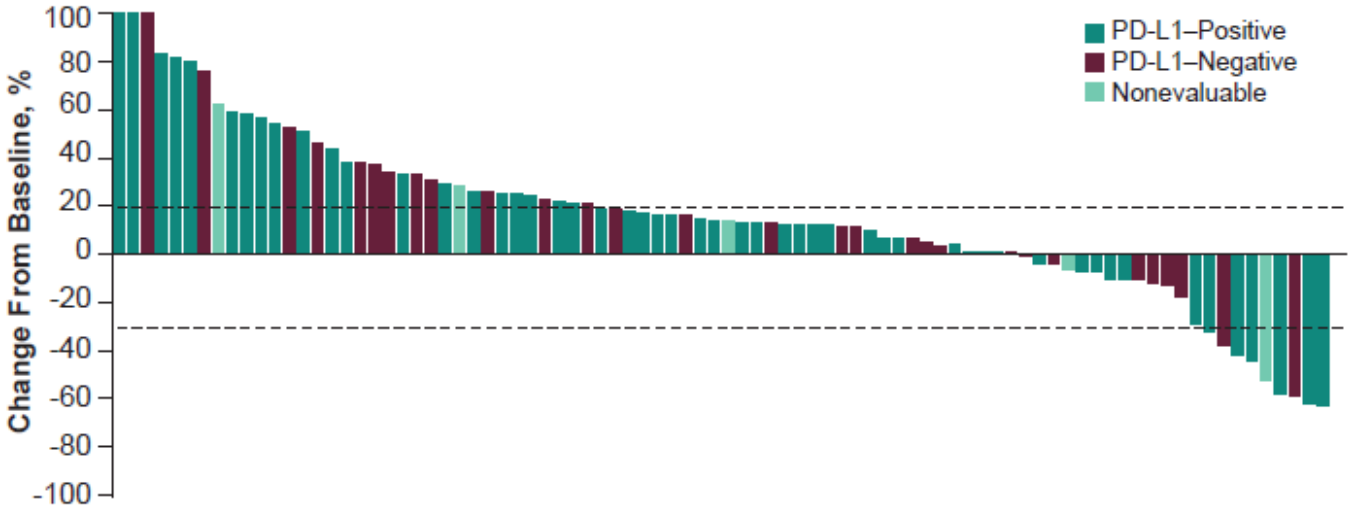
6.6% for PD-L1+

2.9% PD-L1-

mPFS 2.0 months

mOS 7.4 months

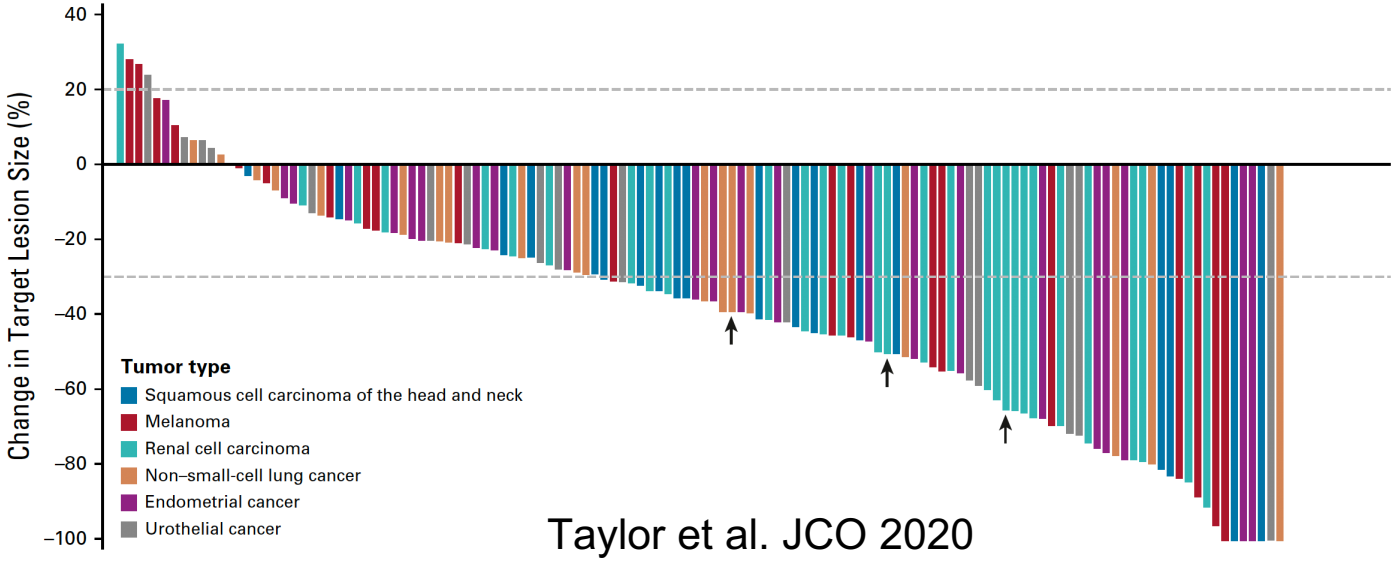




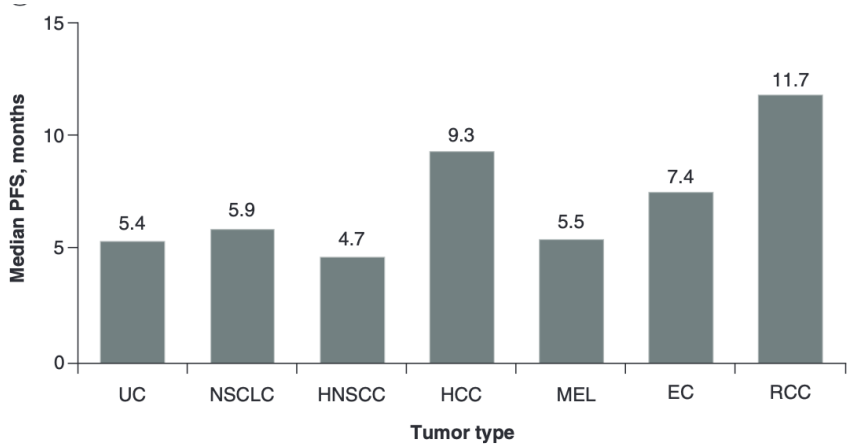
Piha-Paul et al. Int J Cancer 2020;147(8):2190-8

ICI + mTKI

Pembrolizumab and Lenvatinib



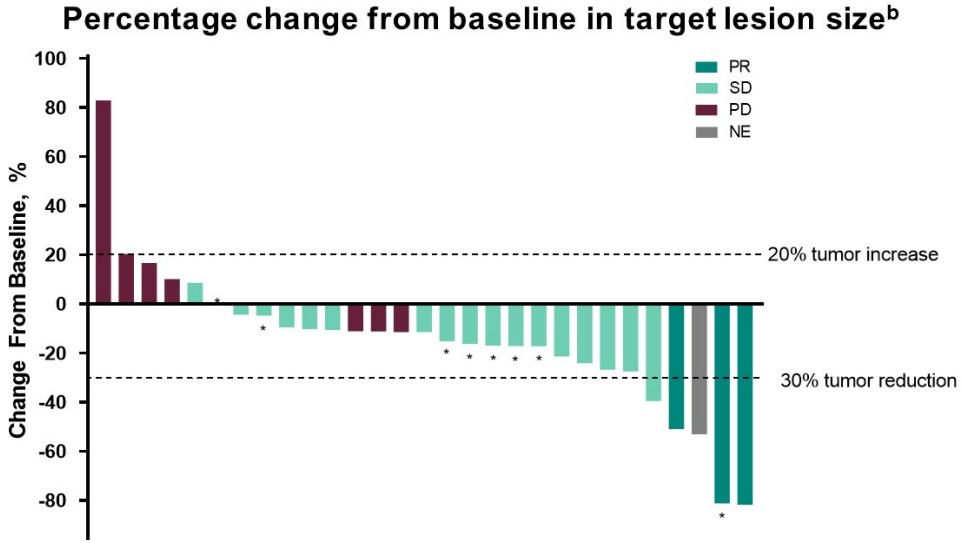
Taylor et al. JCO 2020



Biliary tract cancer: LEAP-005

n=31
ORR: 10%
DCR: 68%
PFS: 6.1 months
OS: 8.6 months

Severe AE:
Grade ≥3: 48%



Villanueva et al. ASCO 2022

Ipi + Nivo

ORR, PFS and OS

advanced BTC*
N=39

→ Nivo 3 mg/kg + Ipi 1 mg/kg Q3W for 4 doses

→ Nivo 3 mg/kg Q2W

ORR N (%)	Overall (N=39)	Gallbladder	iCCC	eCCC
ORR (CR+PR)	9 (23)	4 (31)	5 (31)	0
DCR (CR+PR+SD)	17 (44)	9 (70)	7 (44)	1 (10)
CR	0	0	0	0
PR	9 (23)	4 (31)	5 (31)	0
SD	8 (21)	5 (39)	2 (13)	1 (10)
No Assessment	9 (23)	2 (15)	3 (19)	4 (40)
Progression	13 (33)	2 (15)	6 (37)	5 (50)

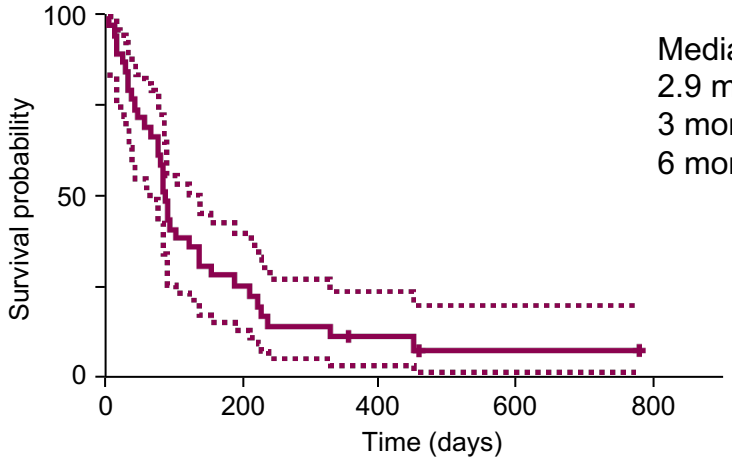
Immune-related AE:

Overall: 49%

Grade ≥3: 15%

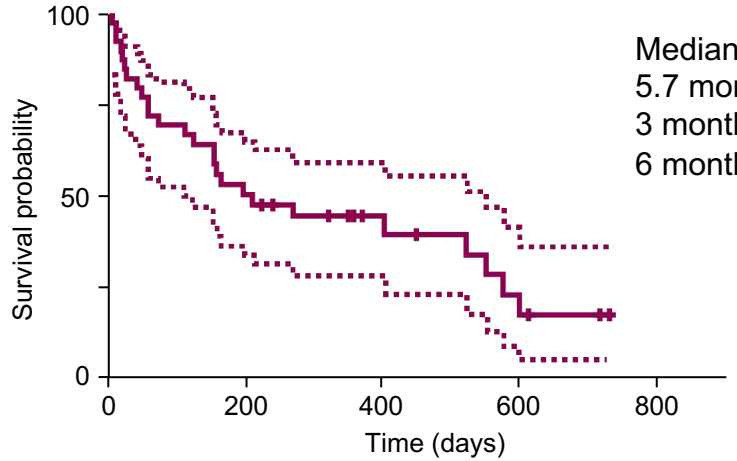
Klein et al. JAMA Oncology 2020

Progression free survival



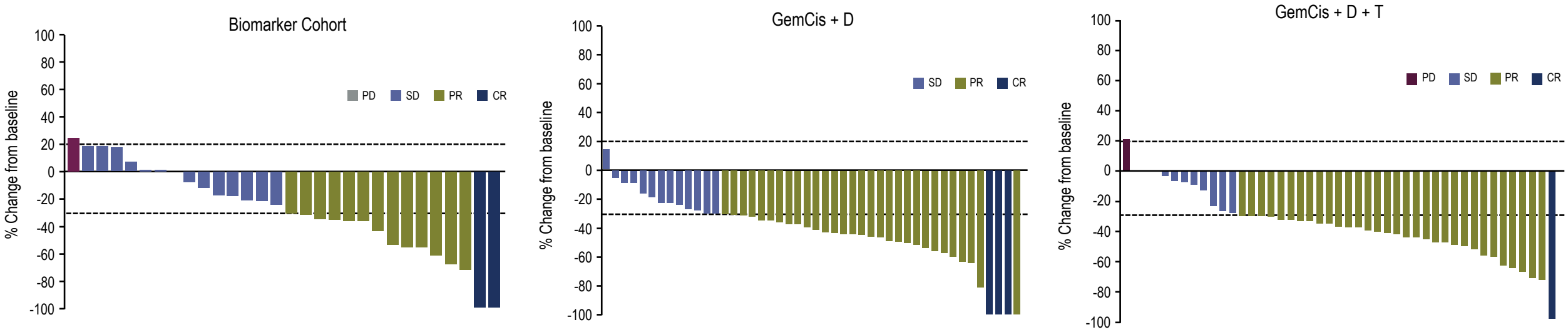
Median PFS
2.9 months (95% CI 2.2; 4.6)
3 months PFS: 51% patients
6 months PFS: 28% patients

Overall survival



Median OS
5.7 months (95% CI 2.7; 11.9)
3 months OS: 69% patients
6 months OS: 53% patients

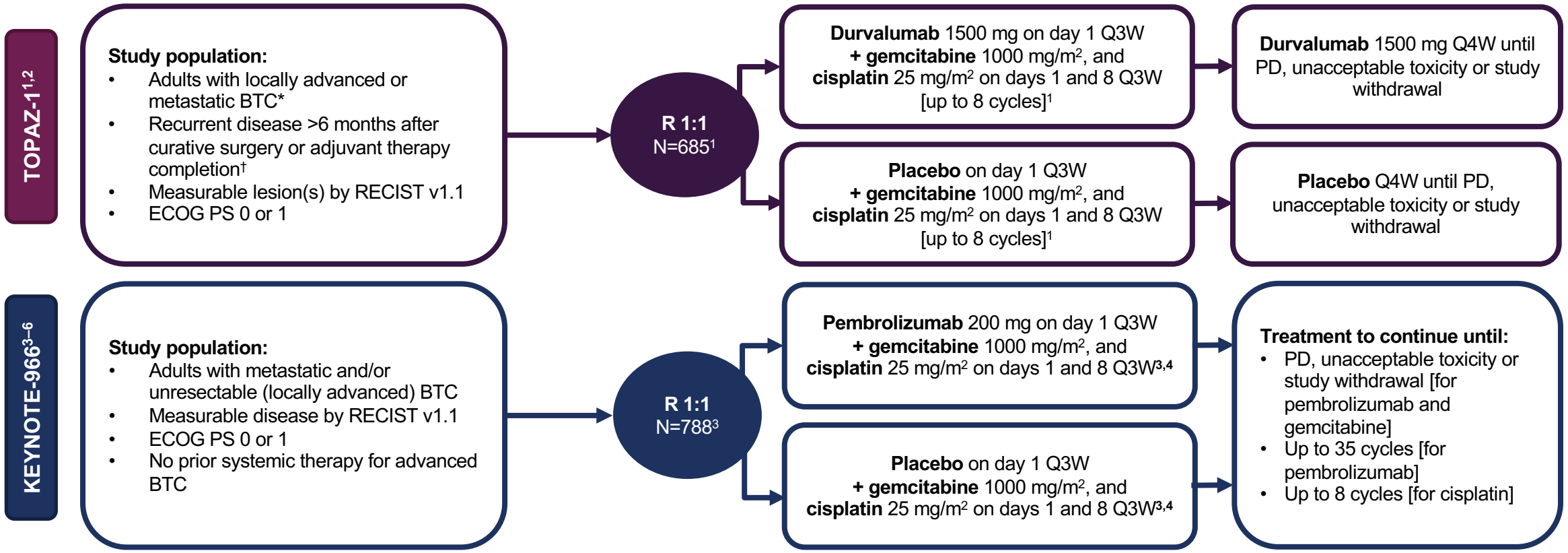
MEDITREME Study: Checkpoint Inhibition + CTx in BTC



- Objective response rates were similar in the GemCis + D cohort and GemCis + D + T cohort, and were higher compared with the BMC.
- Complete response rates were lower in GemCis + D + T cohort, whereas BMC and GemCis + D cohorts exhibited similar CR rates.
- GemCis + D + T cohort had the highest partial response rate among the three cohorts.
- The Biomarker cohort had the highest rate of stable disease among the three cohorts.
- Disease progression was not observed in the GemCis + D cohort.

Oh D-Y et al. @ASCO Virtual Annual Meeting 2020

IO-Phase-III studies in BTC: TOPAZ-1 & KEYNOTE-966



IO-Phase-III studies in BTC: TOPAZ-1 & KEYNOTE-966

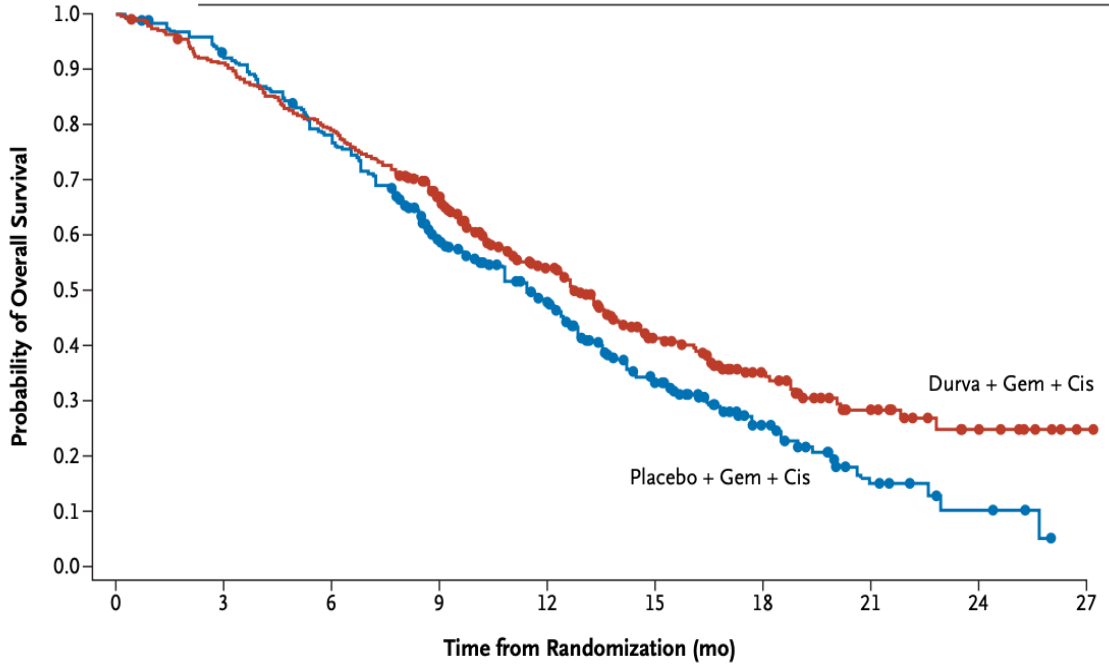
NEJM Evidence

Published June 1, 2022
NEJM Evid 2022; 1 (8)
DOI: 10.1056/EVIDoa2200015

ORIGINAL ARTICLE

Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer

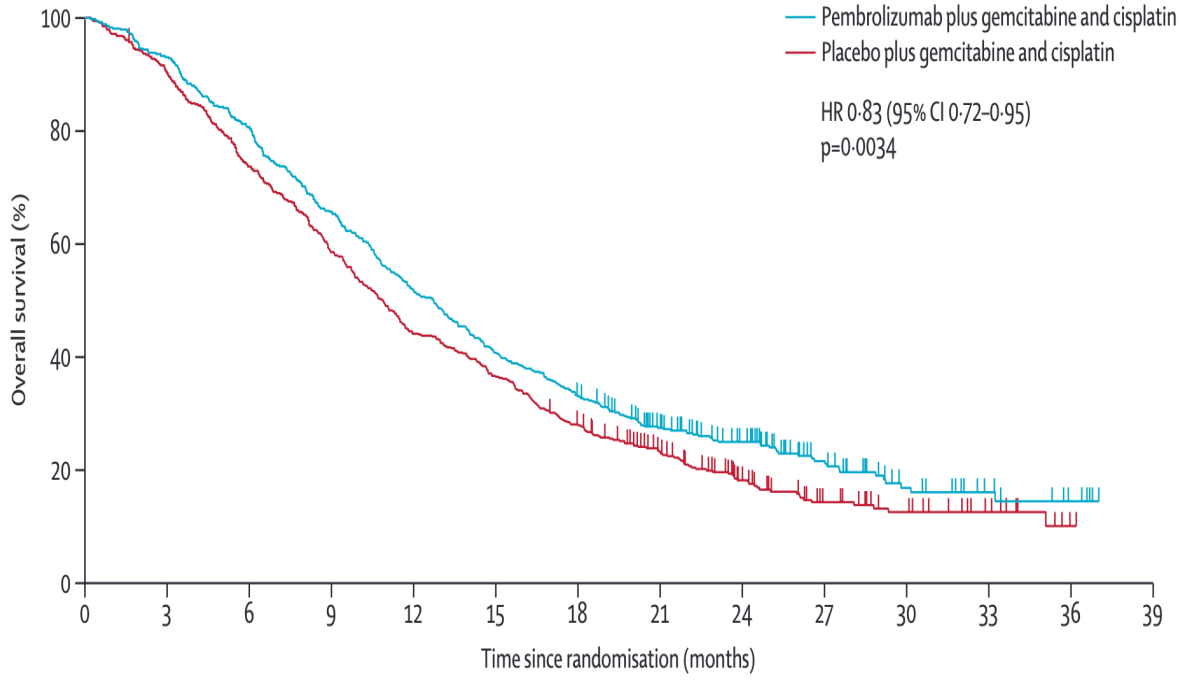
Do-Youn Oh, M.D., Ph.D.,[1] Aiwu Ruth He, M.D., Ph.D.,[2] Shukui Qin, M.D.,[3] Li-Tzong Chen, M.D., Ph.D.,[4,5,6] Takuji Okusaka, M.D., Ph.D.,[7] Arndt Vogel, M.D.,[8] Jin Won Kim, M.D., Ph.D.,[9] Thatthan Suksombooncharoen, M.D.,[10] Myung Ah Lee, M.D., Ph.D.,[11] Masayuki Kitano, M.D., Ph.D.,[12] Howard Burris, M.D.,[13] Mohamed Bouattour, M.D.,[14] Suebpong Tanasanvimon, M.D.,[15] Mairéad G. McNamara, M.B., Ph.D.,[16] Renata Zaucha, M.D., Ph.D.,[17] Antonio Avallone, M.D.,[18] Benjamin Tan, M.D.,[19] Juan Cundom, M.D.,[20] Choong-kun Lee, M.D., Ph.D.,[21] Hidenori Takahashi, M.D., Ph.D.,[22] Masafumi Ikeda, M.D., Ph.D.,[23] Jen-Shi Chen, M.D.,[24] Julie Wang, Ph.D.,[25] Mallory Makowsky, Pharm.D.,[25] Nana Rokutanda, M.D., Ph.D.,[25] Philip He, Ph.D.,[25,26] John F. Kurland, Ph.D.,[25] Gordon Cohen, M.D., M.P.H.,[25] and Juan W. Valle, M.D.,[16] for the TOPAZ-1 Investigators*



ORR: 26.7% vs 18.7%

Pembrolizumab in combination with gemcitabine and cisplatin compared with gemcitabine and cisplatin alone for patients with advanced biliary tract cancer (KEYNOTE-966): a randomised, double-blind, placebo-controlled, phase 3 trial

Robin Kate Kelley, Makoto Ueno*, Changhoon Yoo, Richard S Finn, Junji Furuse, Zhenggang Ren, Thomas Yau, Heinz-Josef Klümpen, Stephen L Chan, Masato Ozaka, Chris Verslype, Mohamed Bouattour, Joon Oh Park, Olga Barajas, Uwe Pelzer, Juan W Valle, Li Yu, Usha Malhotra, Abby B Siegel, Julien Edeline, Arndt Vogel*, on behalf of the KEYNOTE-966 Investigators†*



ORR: 29% vs 29%

Summary of Primary Results – Safety Summary

TOPAZ-1

	Durvalumab + Gem-Cis (n=338)	Placebo + Gem-Cis (n=342)
Event,[a] n (%)		
Any AE	**336 (99.4)**	**338 (98.8)**
Any Grade 3/4 AE	256 (75.7)	266 (77.8)
Any serious AE	160 (47.3)	149 (43.6)
Any AE leading to discontinuation	44 (13.0)	52 (15.2)
Any AE leading to death	12 (3.6)	14 (4.1)
Any TRAE	**314 (92.9)**	**308 (90.1)**
Any Grade 3/4 TRAE	212 (62.7)	222 (64.9)
Any serious TRAE	53 (15.7)	59 (17.3)
Any TRAE leading to discontinuation	30 (8.9)	39 (11.4)
Any TRAE leading to death	2 (0.6)	1 (0.3)
Any imAE	**43 (12.7)**	**16 (4.7)**
Any Grade 3/4 imAE	8 (2.4)	5 (1.5)

Oh D-Y et al. NEJM Evid. 2022

KEYNOTE-966

	Pembro + Gem/Cis (n = 529)	Placebo + Gem/Cis (n = 534)
Any	524 (99%)	532 (<100%)
Treatment-related	493 (93%)	500 (94%)
Grade 3-4 as maximum grade	420 (79%)	400 (75%)
Treatment-related	369 (70%)	367 (69%)
Led to death	31 (6%)	49 (9%)
Treatment-related	8 (2%)[a]	3 (1%)[b]
Led to discontinuation of ≥1 study medication	138 (26%)	122 (23%)
Treatment-related	102 (19%)	81 (15%)
Led to discontinuation of all study medication	35 (7%)	39 (7%)
Treatment-related	18 (3%)	14 (3%)

Kelley et al. AACR 2023

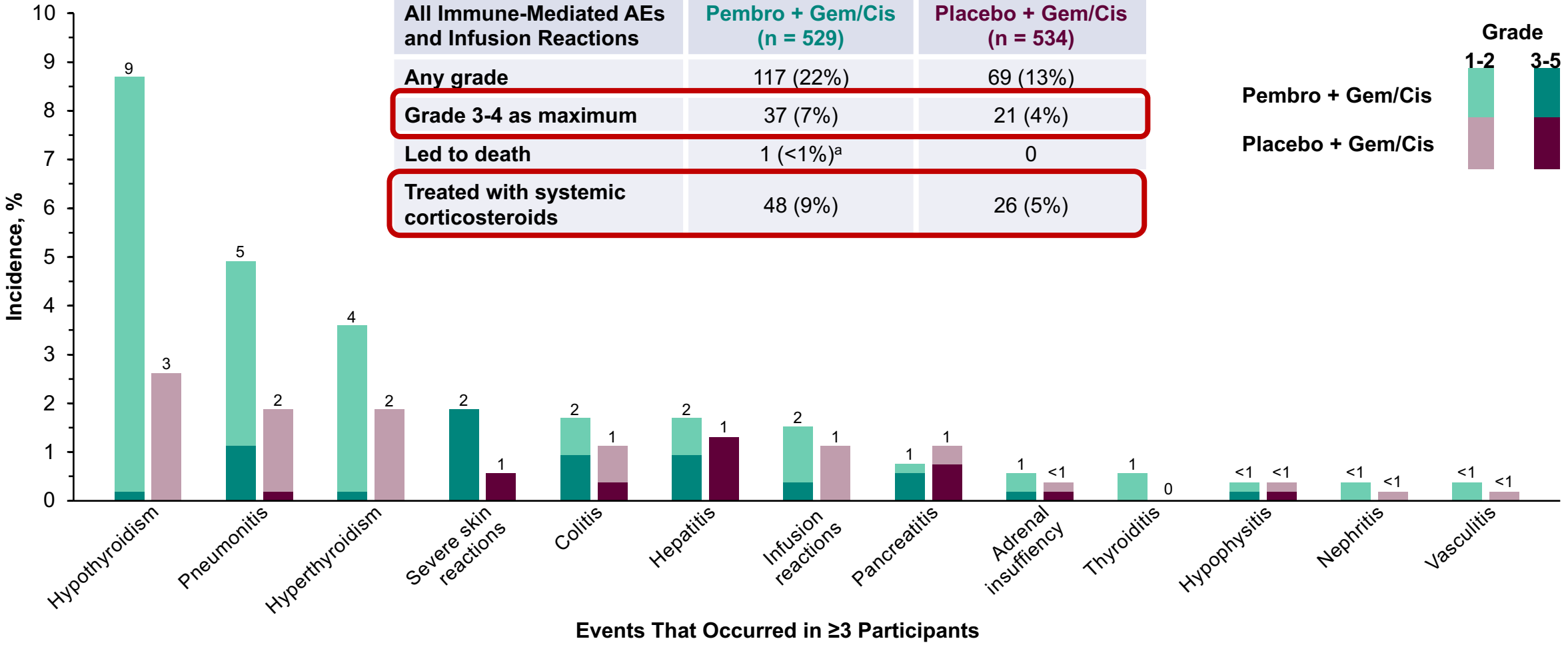
TOPAZ-1: Immune-Mediated Adverse Events

Event, n (%)	Durvalumab + GemCis (n=338)		Placebo + GemCis (n=342)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any immune-mediated AE[a]	**43 (12.7)**	**8 (2.4)**	**16 (4.7)**	**5 (1.5)**
Hypothyroid events	20 (5.9)	0	5 (1.5)	0
Dermatitis/Rash	12 (3.6)	3 (0.9)	1 (0.3)	0
Pneumonitis	3 (0.9)	1 (0.3)	2 (0.6)	1 (0.3)
Hepatic events	4 (1.2)	2 (0.6)	2 (0.6)	1 (0.3)
Adrenal insufficiency	4 (1.2)	0	1 (0.3)	0
Diarrhea/Colitis	2 (0.6)	1 (0.3)	1 (0.3)	1 (0.3)
Hyperthyroid events	2 (0.6)	0	0	0
Type 1 diabetes mellitus	1 (0.3)	1 (0.3)	0	0
Pancreatic events	1 (0.3)	0	2 (0.6)	1 (0.3)
Hypophysitis	1 (0.3)	0	0	0
Thyroiditis	1 (0.3)	0	0	0
Renal events	0	0	2 (0.6)	0
Myositis	0	0	1 (0.3)	1 (0.3)
Other rare/Miscellaneous[b]	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)

Oh D-Y et al. @ASCO-GI 2022

KEYNOTE-966: Immune-Mediated Adverse Events

All Immune-Mediated AEs and Infusion Reactions	Pembro + Gem/Cis (n = 529)	Placebo + Gem/Cis (n = 534)
Any grade	117 (22%)	69 (13%)
Grade 3-4 as maximum	37 (7%)	21 (4%)
Led to death	1 (<1%)[a]	0
Treated with systemic corticosteroids	48 (9%)	26 (5%)

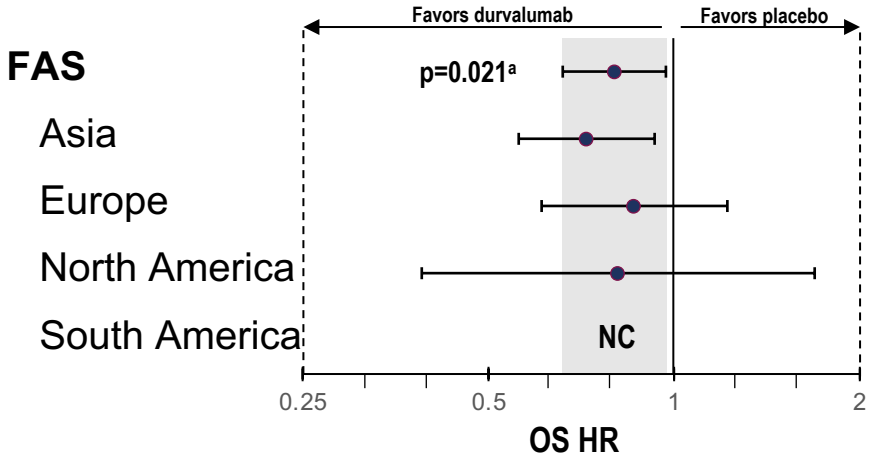


Kelley et al. AACR 2023

IO + Chemo in BTC 1st line: TOPAZ-1 Phase 3

OS in subgroups by Region

Durvalumab performed similarly across subregions; placebo performed better in South America (median OS was not reached) than in other subregions



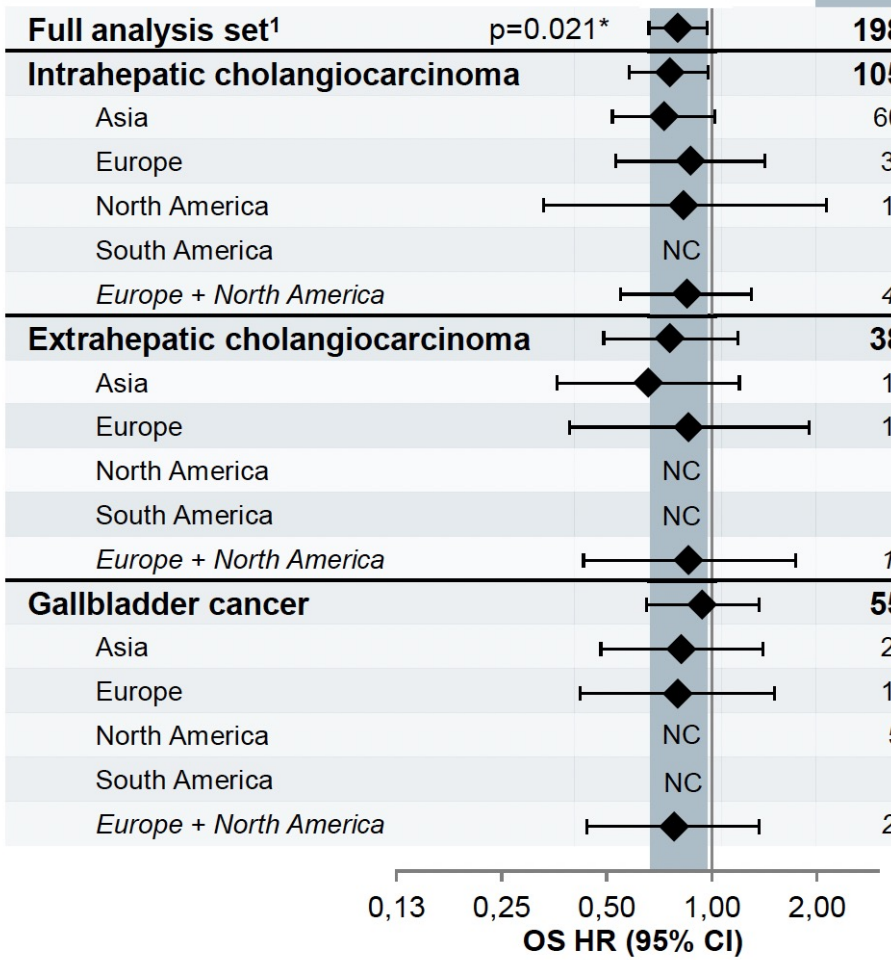
Overall Survival HR (95% CI) by Subregion

	Durvalumab + Gem-Cis		Placebo + Gem-Cis		
	Events (%)	Median OS (95% CI), months	Events (%)	Median OS (95% CI), months	OS HR (95% CI)
FAS	**198 / 341 (58.1)**	**12.8 (11.1–14.0)**	**226 / 344 (65.7)**	**11.5 (10.1–12.5)**	**0.80 (0.66–0.97)[b]**
Asia	103 / 178 (57.9)	13.6 (12.6–16.1)	137 / 196 (69.9)	11.6 (10.1–12.6)	0.72 (0.56–0.93)[b]
Europe	63 / 108 (58.3)	10.9 (9.5–14.7)	69 / 107 (64.5)	9.6 (8.0–14.0)	0.86 (0.61–1.22)[b]
North America	21 / 37 (56.8)	12.5 (10.3–17.3)	16 / 28 (57.1)	10.7 (7.1–NR)	0.81 (0.39–1.69)[b]
South America	11 / 18 (61.1)	10.3 (7.3–NR)	4 / 13 (30.8)	NR (8.0–NR)	NC

Vogel A et al. @ASCO Annual Meeting 2022

IO + Chemo in BTC 1st line: TOPAZ-1 Phase 3

OS in subgroups by Anatomic location

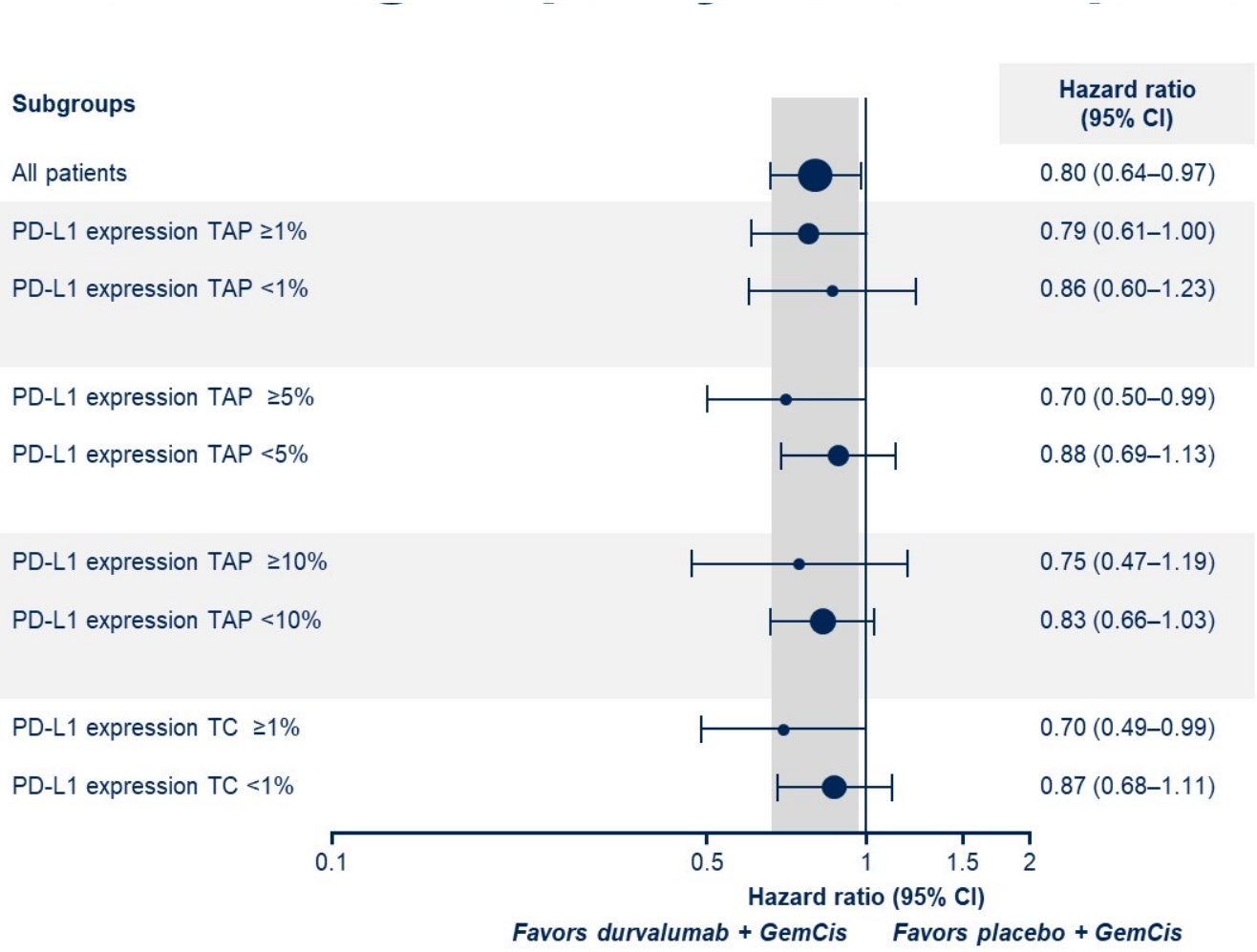


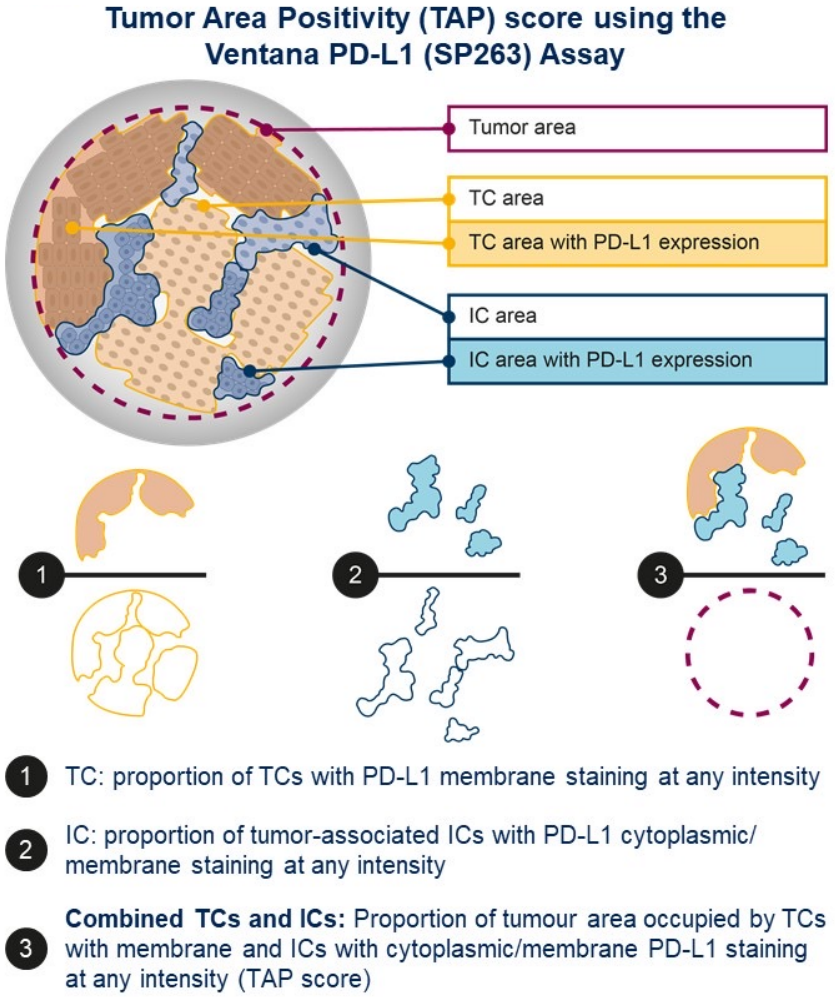
	Durvalumab + GemCis (N=341)		Placebo + GemCis (N=344)		OS HR† (95% CI)
	Events, n/N (%)	Median OS (95% CI), mo	Events, n/N (%)	Median OS (95% CI), mo	
Full analysis set[1]	**198/341 (58.1)**	**12.8 (11.1–14.0)**	**226/344 (65.7)**	**11.5 (10.1–12.5)**	**0.80 (0.66–0.97)‡**
Intrahepatic cholangiocarcinoma	**105/190 (55.3)**	**13.5 (11.9–15.1)**	**126/193 (65.3)**	**11.5 (9.8–12.8)**	**0.76 (0.58–0.98)§**
Asia	60/100 (60.0)	13.0 (9.8–14.6)	81/111 (73.0)	11.4 (9.2–12.5)	0.73 (0.52–1.02)§
Europe	31/61 (50.8)	13.5 (9.5–18.8)	35/61 (57.4)	14.0 (8.0–18.3)	0.87 (0.53–1.42)§
North America	11/21 (52.4)	15.1 (6.8–NC)	9/18 (50.0)	13.3 (5.3–NC)	0.83 (0.33–2.12)§
South America	3/8 (37.5)	NR (2.3–NC)	1/3 (33.3)	NR (8.0–NC)	NC‖
Europe + North America	*42/82 (51.2)*	*13.7 (10.9–18.1)*	*44/79 (55.7)*	*13.6 (8.5–17.7)*	*0.85 (0.55–1.30)§*
Extrahepatic cholangiocarcinoma	**38/66 (57.6)**	**12.7 (9.8–16.6)**	**42/65 (64.6)**	**12.1 (7.8–14.4)**	**0.76 (0.49–1.19)§**
Asia	18/35 (51.4)	16.6 (12.6–NC)	27/42 (65.3)	12.8 (7.7–17.3)	0.66 (0.36–1.20)§
Europe	14/23 (60.9)	9.1 (8.7–NC)	12/19 (63.2)	14.4 (7.0–NC)	0.86 (0.39–1.90)§
North America	5/6 (83.3)	11.0 (0.9–NC)	3/4 (75.0)	9.6 (3.4–NC)	NC‖
South America	1/2 (50.0)	NR (10.0–NC)	0	NC	NC‖
Europe + North America	*19/29 (65.5)*	*9.8 (8.7–16.2)*	*15/23 (65.2)*	*12.1 (7.0–14.4)*	*0.86 (0.43–1.73)§*
Gallbladder cancer	**55/85 (64.7)**	**10.7 (8.9–13.2)**	**58/86 (67.4)**	**11.0 (8.7–12.8)**	**0.94 (0.65–1.37)§**
Asia	25/43 (58.1)	13.3 (9.0–20.1)	29/43 (67.4)	12.6 (8.4-17.7)	0.82 (0.48–1.40)§
Europe	18/24 (75.0)	9.6 (5.2–11.1)	22/27 (81.5)	8.1 (4.9–11.0)	0.80 (0.42–1.51)§
North America	5/10 (50.0)	12.2 (2.6–NC)	4/6 (66.7)	10.2 (5.7–NC)	NC‖
South America	7/8 (87.5)	8.1 (0.9–NC)	3/10 (30.0)¶	NR (2.0–NC)	NC‖
Europe + North America	*23/34 (67.6)*	*10.3 (6.6–12.2)*	*26/33 (78.8)*	*8.7 (6.0–11.0)*	*0.78 (0.44–1.37)§*

He et al. @ESMO-GI 2022

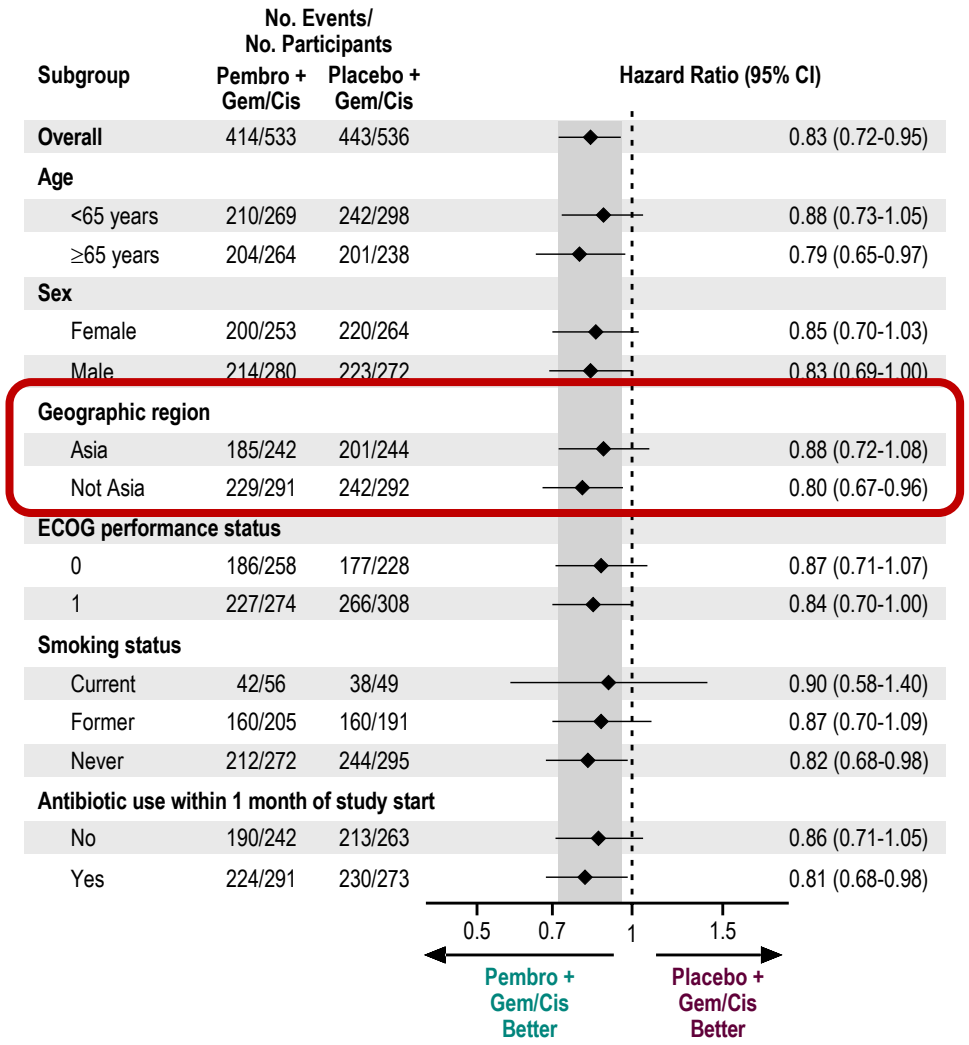
IO + Chemo in BTC 1st line: TOPAZ-1 Phase 3

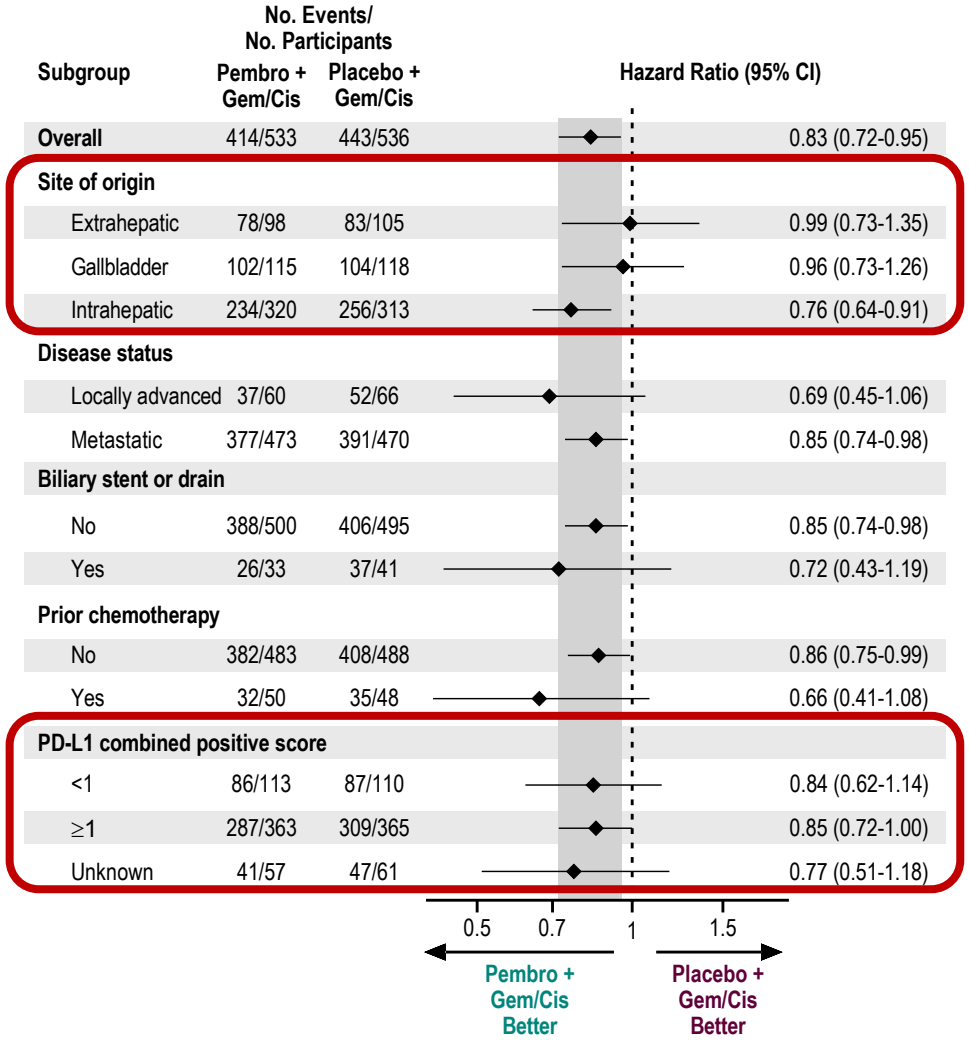
OS in subgroups by PD-L1 expression





IO + Chemo in BTC 1st line: KEYNOTE-966 Phase 3





Data cutoff date: December 15, 2022.

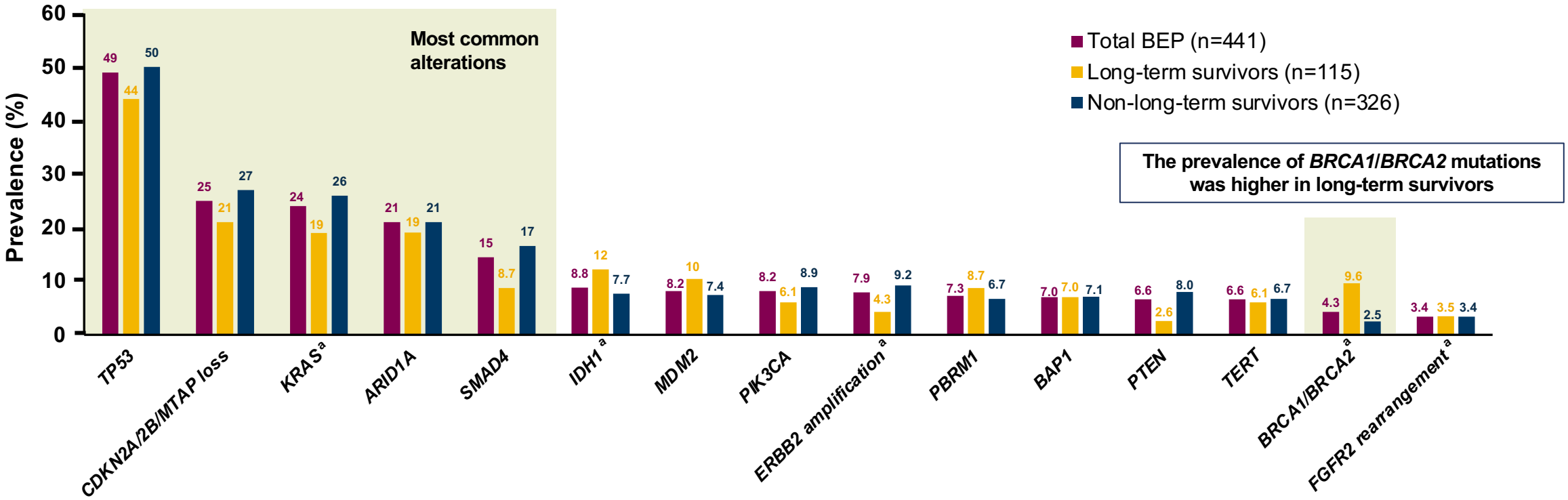
TOPAZ-1 Exploratory Analysis of Long-term Survivors:

Baseline Demographics and Disease Characteristics

Characteristic	Long-term survivors (n=153)		Full analysis set (N=685)	
	D + Gem-Cis (n=88)	P + Gem-Cis (n=65)	D + Gem-Cis (n=341)	P + Gem-Cis (n=344)
Neutrophil-to-lymphocyte ratio, n (%)[a]				
<3	45 (51.1)	43 (66.2)	131 (38.4)	138 (40.1)
≥3	41 (46.6)	21 (32.3)	205 (60.1)	200 (58.1)
Missing	2 (2.3)	1 (1.5)	5 (1.5)	6 (1.7)
Cancer antigen 19-9, n (%)[a]				
<500 U/mL	68 (77.3)	50 (76.9)	196 (57.5)	202 (58.7)
≥500 U/mL	14 (15.9)	11 (16.9)	116 (34.0)	111 (32.3)
Missing	6 (6.8)	4 (6.2)	29 (8.5)	31 (9.0)
Carcinoembryonic antigen, n (%)[a]				
<5 ng/mL	60 (68.2)	42 (64.6)	170 (49.9)	176 (51.2)
≥5 ng/mL	22 (25.0)	19 (29.2)	138 (40.5)	136 (39.5)
Missing	6 (6.8)	4 (6.2)	33 (9.7)	32 (9.3)
Subsequent anticancer therapy, n (%)	51 (58.0)	53 (81.5)	173 (50.7)	185 (53.8)
Immunotherapy	3 (3.4)	12 (18.5)	9 (2.6)	24 (7.0)
Cytotoxic chemotherapy	49 (55.7)	47 (72.3)	160 (46.9)	169 (49.1)
Targeted therapy	10 (11.4)	9 (13.8)	22 (6.5)	24 (7.0)
Taxane chemotherapy	5 (5.7)	4 (6.2)	11 (3.2)	12 (3.5)
Other	5 (5.7)	9 (13.8)	21 (6.2)	36 (10.5)
Antiangiogenic therapy	0	0	1 (0.3)	1 (0.3)
Unknown	0	0	1 (0.3)	0

- Compared with the FAS, long-term survivors more frequently (≥10% difference) had a NL ratio <3, a cancer antigen 19-9 level <500 U/mL, and a CEA level <5 ng/mL
- A higher proportion of long-term survivors in the placebo + Gem-Cis arm received subsequent anticancer therapy compared with the durvalumab + Gem-Cis arm
  - The most common subsequent anticancer therapy in the placebo + Gem-Cis arm was cytotoxic chemotherapy, followed by immunotherapy

TOPAZ-1 Exploratory Analysis of Long-term Survivors:
Genomic Profile in Biomarker-evaluable Patients



Genomic profiling was performed in the BEP in the FAS; 115/441 (26.1%) patients in the BEP were long-term survivors

- The most common alterations were *TP53* mutation, *CDKN2A/CDKN2B/MTAP* loss, *KRAS* mutation, *ARID1A* mutation and *SMAD4* mutation

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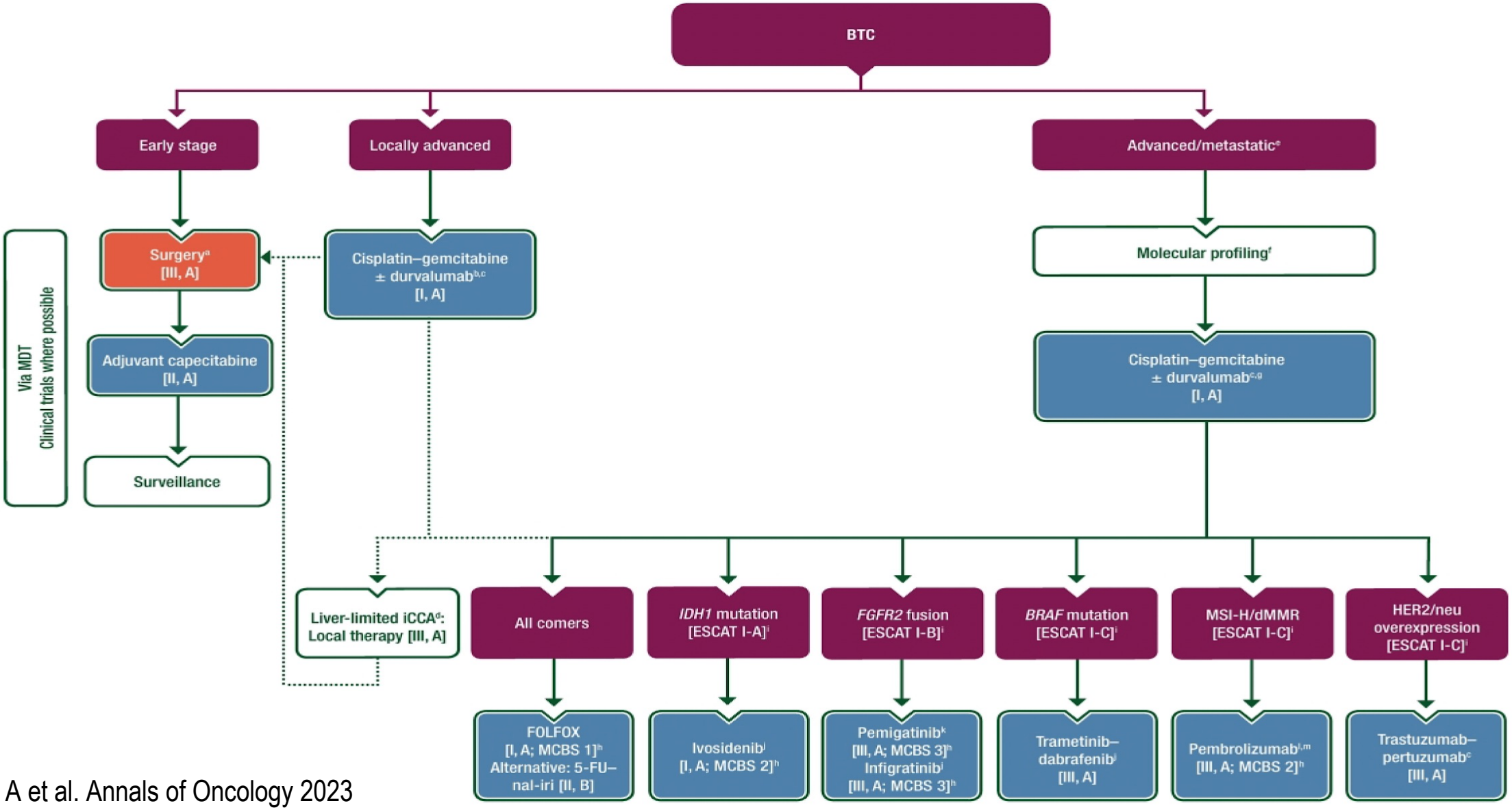

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Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Prostate Cancer

Part 1 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 ASCO Genitourinary Cancers Symposium

Thursday, January 25, 2024

6:15 PM – 8:15 PM PT (9:15 PM – 11:15 PM ET)

Faculty

Rahul Aggarwal, MD

Emmanuel S Antonarakis, MD

Elisabeth I Heath, MD

A Oliver Sartor, MD

Moderator

Alan H Bryce, MD

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