Consensus or Controversy? Investigator Perspectives on the Current and Future Role of Immune Checkpoint Inhibitors in the Management of Hepatobiliary Cancers — A 2024 Post-ASCO Gastrointestinal Cancers Symposium Review

A CME-Accredited Virtual Event

Thursday, February 15, 2024
5:00 PM – 6:00 PM ET

Faculty

Robin (Katie) Kelley, MD
Mark Yarchoan, MD

Moderator

Neil Love, MD

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Faculty

Robin (Katie) Kelley, MD
Professor of Clinical Medicine, Division of Hematology/Oncology
Helen Diller Family Comprehensive Cancer Center
University of California, San Francisco (UCSF)
San Francisco, California

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Mark Yarchoan, MD
Associate Professor of Medical Oncology
Johns Hopkins Sidney Kimmel Cancer Center
Washington, DC

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Dr Love — Disclosures

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Nonrelevant Financial Relationship	Parker Institute for Cancer Immunotherapy

Daneng Li, MD — Disclosures
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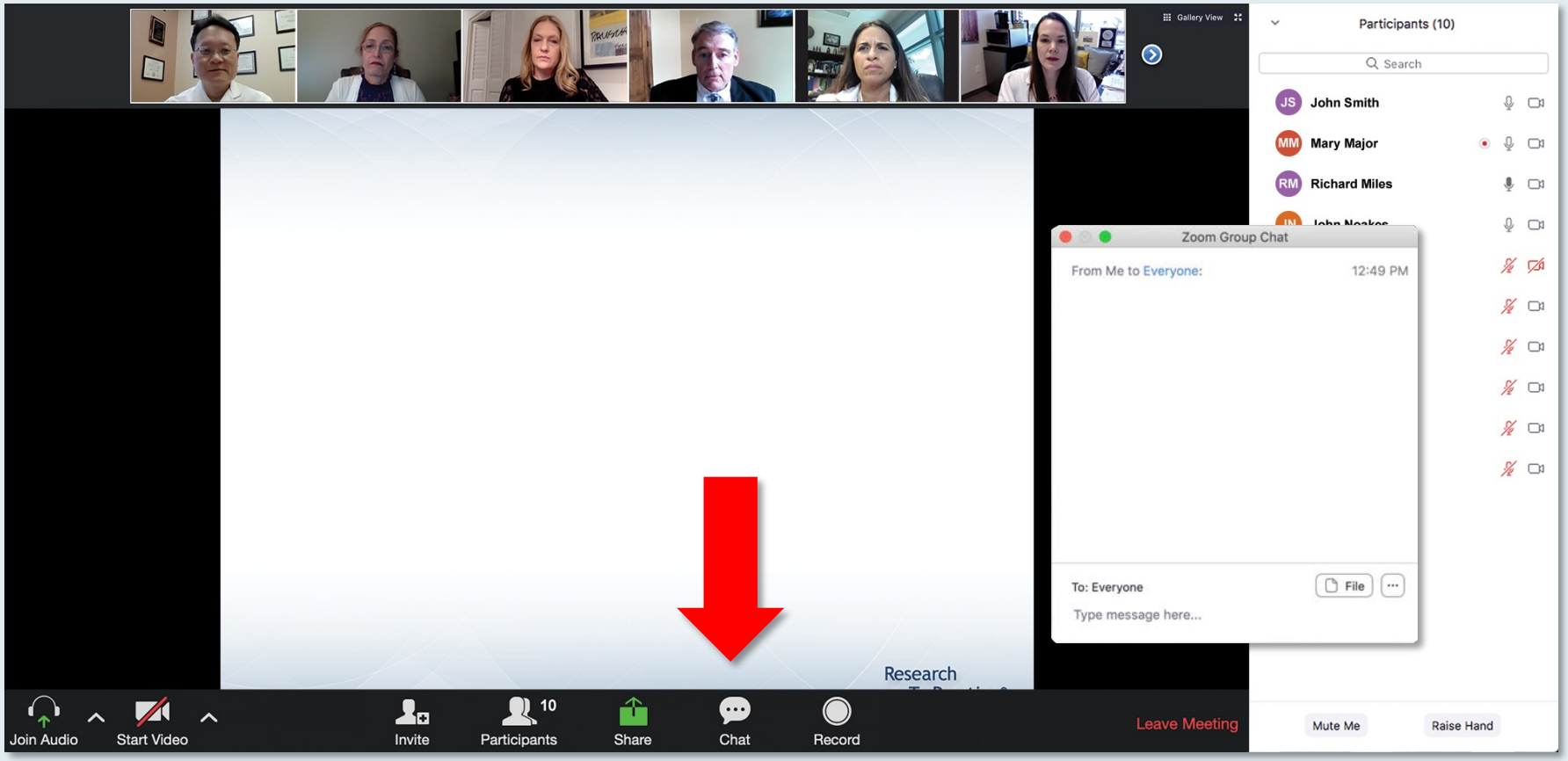

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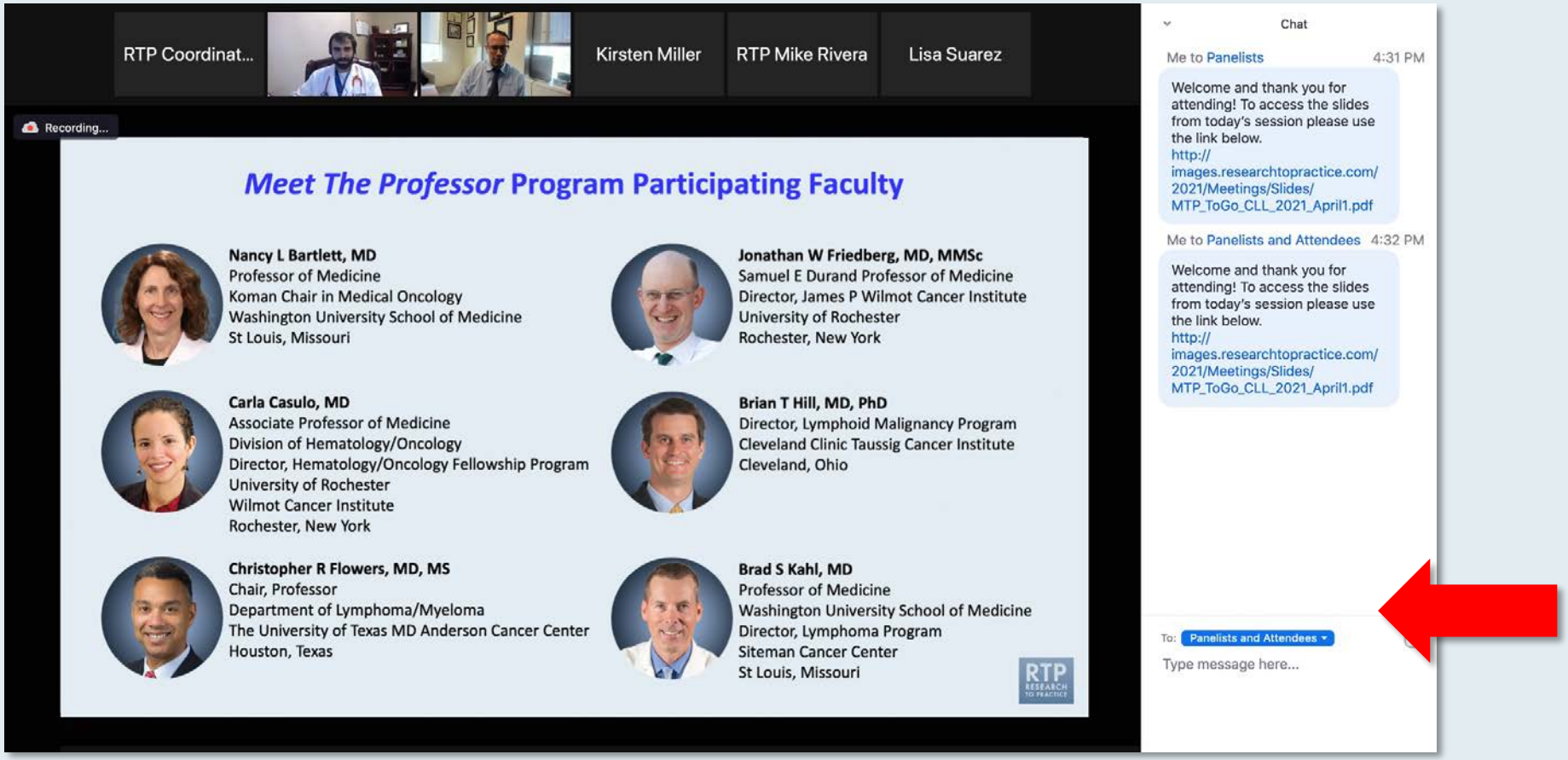

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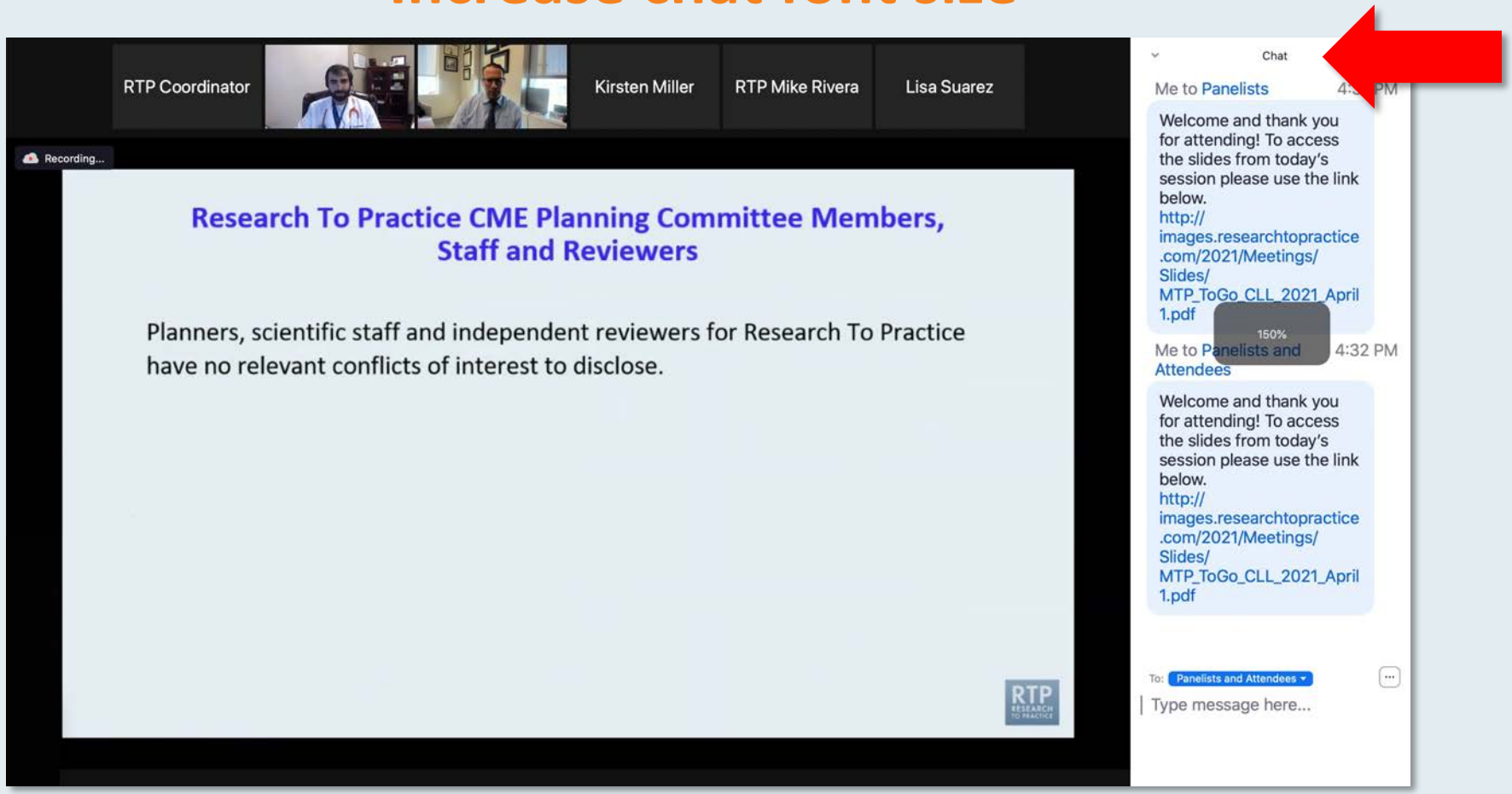

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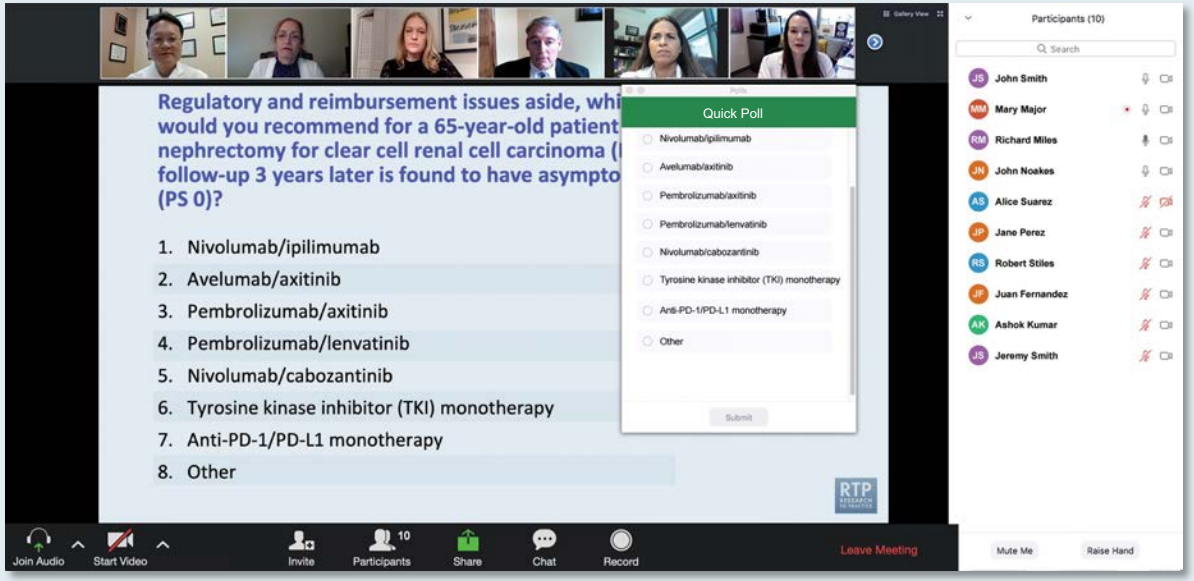

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WITH DR NEIL LOVE

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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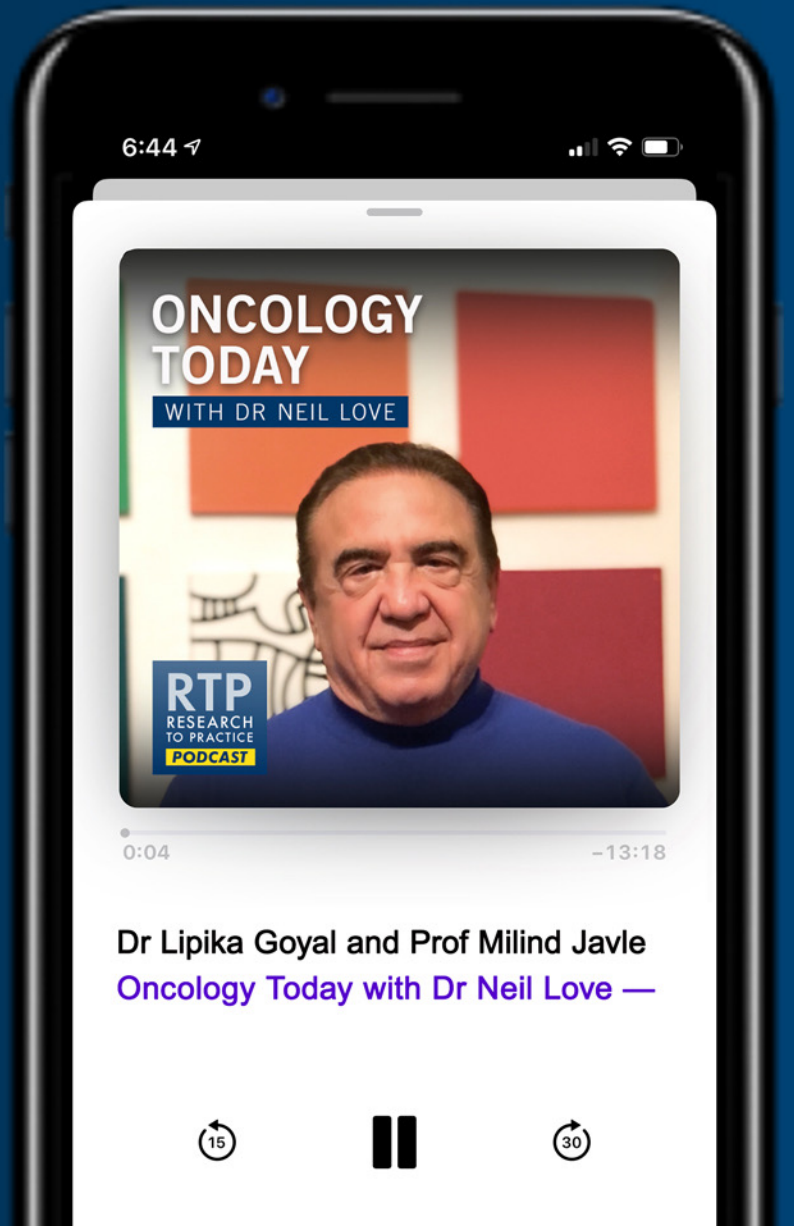

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Urothelial Bladder Cancer

Thursday, February 22, 2024
5:00 PM – 6:00 PM ET

Faculty

Shilpa Gupta, MD

Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

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

Prostate Cancer

Wednesday, February 28, 2024
5:00 PM – 6:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM

Maha Hussain, MD, FACP, FASCO

Moderator

Neil Love, MD

RTP Year in Review 2024

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A Multitumor CME/MOC-Accredited Live Webinar Series

Colorectal Cancer

Tuesday, March 5, 2024
5:00 PM – 6:00 PM ET

Faculty

Thierry Andre, MD
Arvind Dasari, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

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

Part 1 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Monday, March 18, 2024

6:30 AM – 8:00 AM PT (9:30 AM – 11:00 AM ET)

Faculty

Joyce F Liu, MD, MPH

Mansoor Raza Mirza, MD

David M O'Malley, MD

Moderator

Kathleen N Moore, MD, MS

RTP RESEARCH TO PRACTICE

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

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Monday, March 18, 2024

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Matthew A Powell, MD

Brian M Slomovitz, MD

Moderator

Shannon N Westin, MD, MPH, FASCO, FACOG

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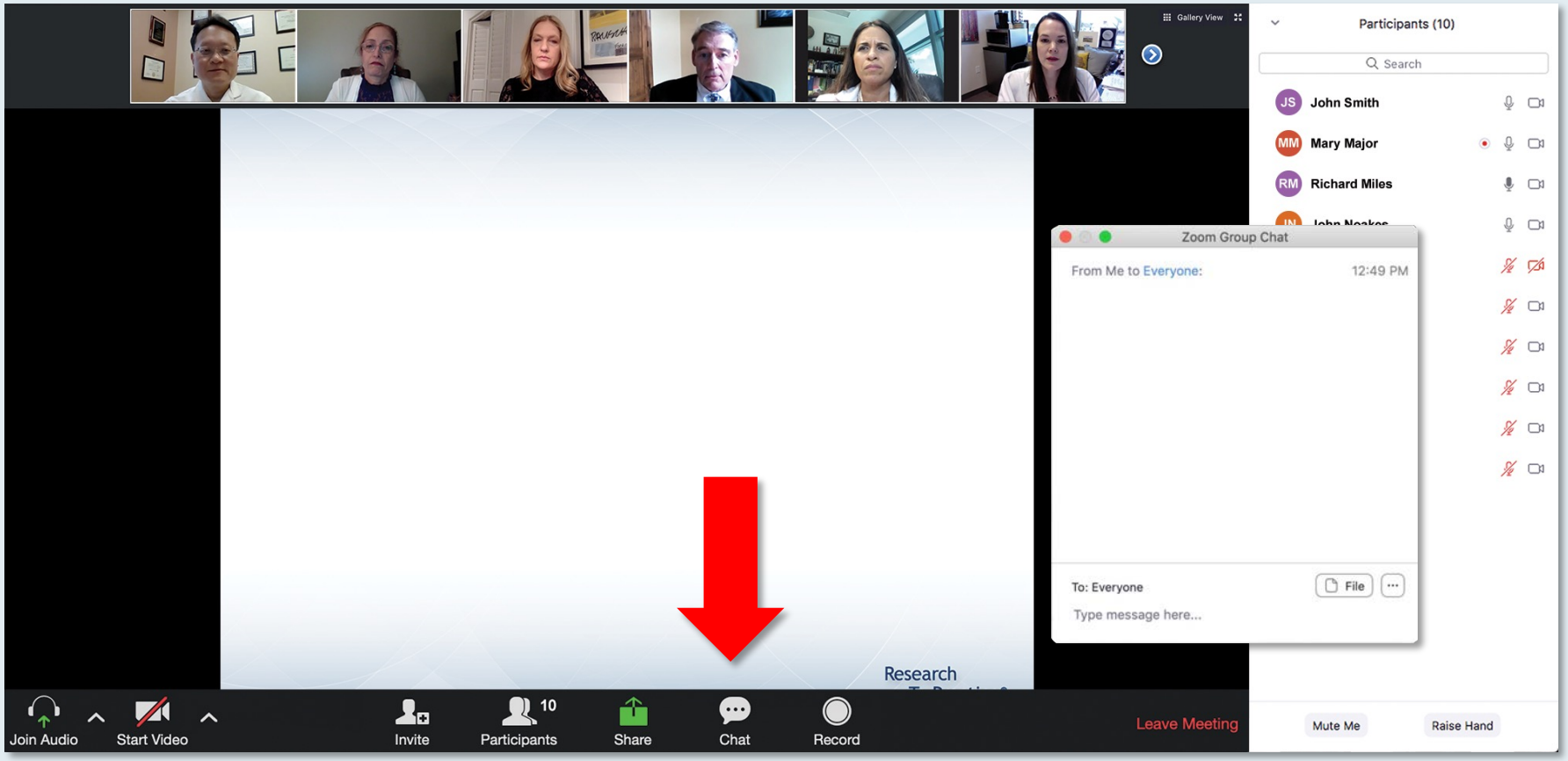

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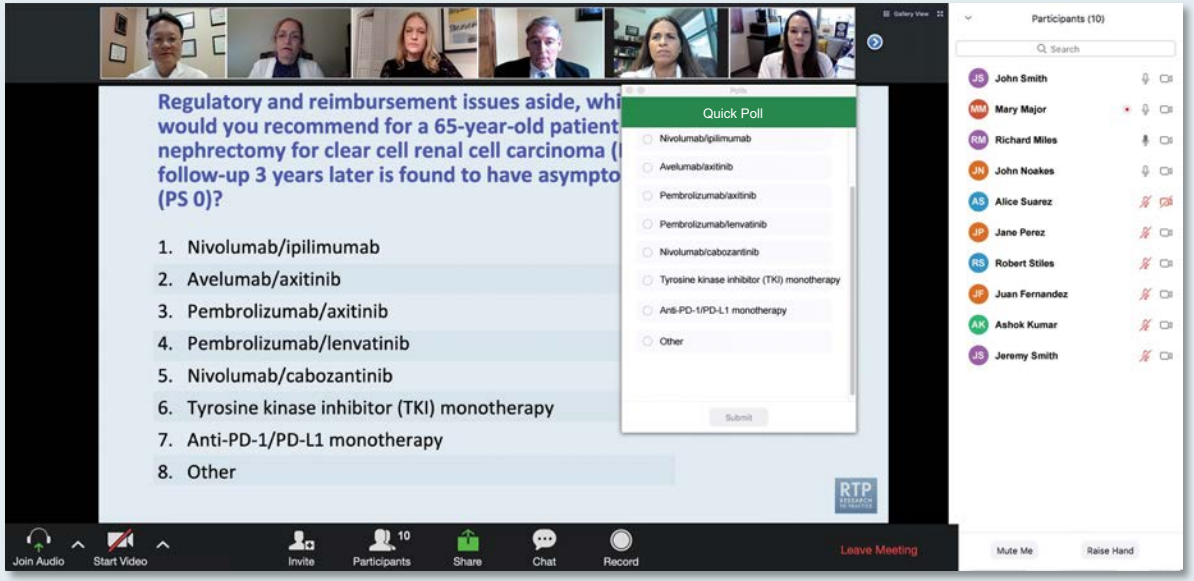

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Third Annual **National General Medical Oncology Summit**

Friday, March 22, 2024

6:30 PM – 7:00 PM

Welcome Reception

7:00 PM – 9:00 PM

Keynote Session: ER-Positive Metastatic Breast Cancer

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

Special Feature: Clinicians with Breast Cancer

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

Emmanuel 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

Pancreatic Cancer

Andrew H Ko, MD
Eileen M O'Reilly, MD

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WITH DR NEIL LOVE

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

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STANFORD CANCER CENTER

PROF MILIND JAVLE
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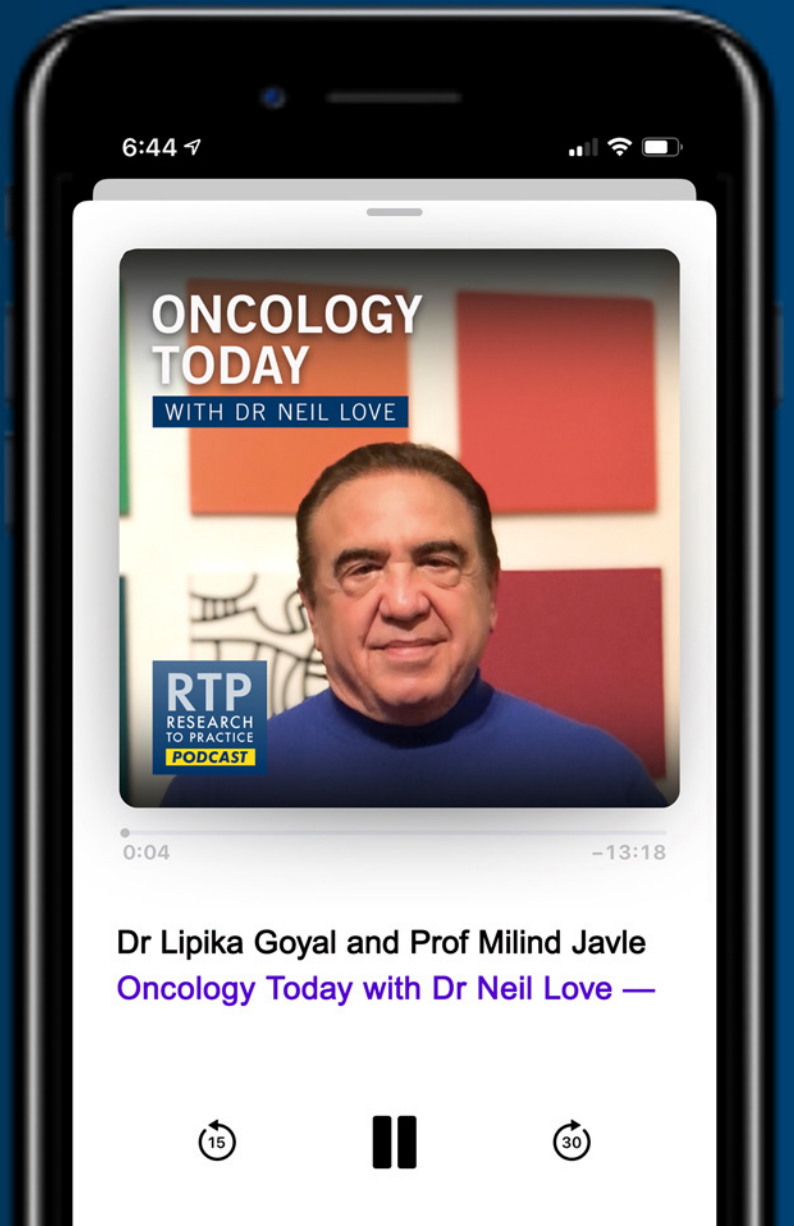

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Dr Stein — Disclosures
Video Participant

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Video Participant

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Ghassan Abou-Alfa, MD, MBA — Disclosures
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Contracted Research	AstraZeneca Pharmaceuticals LP

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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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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
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Clinical Trials Office
Yale Cancer Center
Yale School of Medicine
New Haven, Connecticut

Ahmed Omar Kaseb, MD, CMQ
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Tenured Professor and Director,
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Department of Gastrointestinal
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Division of Gastroenterology and Hepatology
Toronto General Hospital
Medical Oncology
Princess Margaret Cancer Centre
Toronto General Hospital Research Institute
Schwartz Reisman Liver Research Centre
Toronto, Ontario, Canada

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Agenda

INTRODUCTION: Interdisciplinary Management of HCC in the Community (General Medical Oncology) Setting — IR, Hepatology, Pathology Support

MODULE 1: Potential Role of Anti-PD-1/PD-L1 Antibodies in the Care of Patients with Early- and Intermediate-Stage HCC — Dr Yarchoan

MODULE 2: HCC Rounds

MODULE 3: Tolerability and Other Practical Considerations with the Use of Immune Checkpoint Inhibitors for Advanced HCC and BTCs — Dr Kelley

MODULE 4: Faculty Survey

MODULE 5: BTC Rounds

Agenda

INTRODUCTION: Interdisciplinary Management of HCC in the Community (General Medical Oncology) Setting — IR, Hepatology, Pathology Support

MODULE 1: Potential Role of Anti-PD-1/PD-L1 Antibodies in the Care of Patients with Early- and Intermediate-Stage HCC — Dr Yarchoan

MODULE 2: HCC Rounds

MODULE 3: Tolerability and Other Practical Considerations with the Use of Immune Checkpoint Inhibitors for Advanced HCC and BTCs — Dr Kelley

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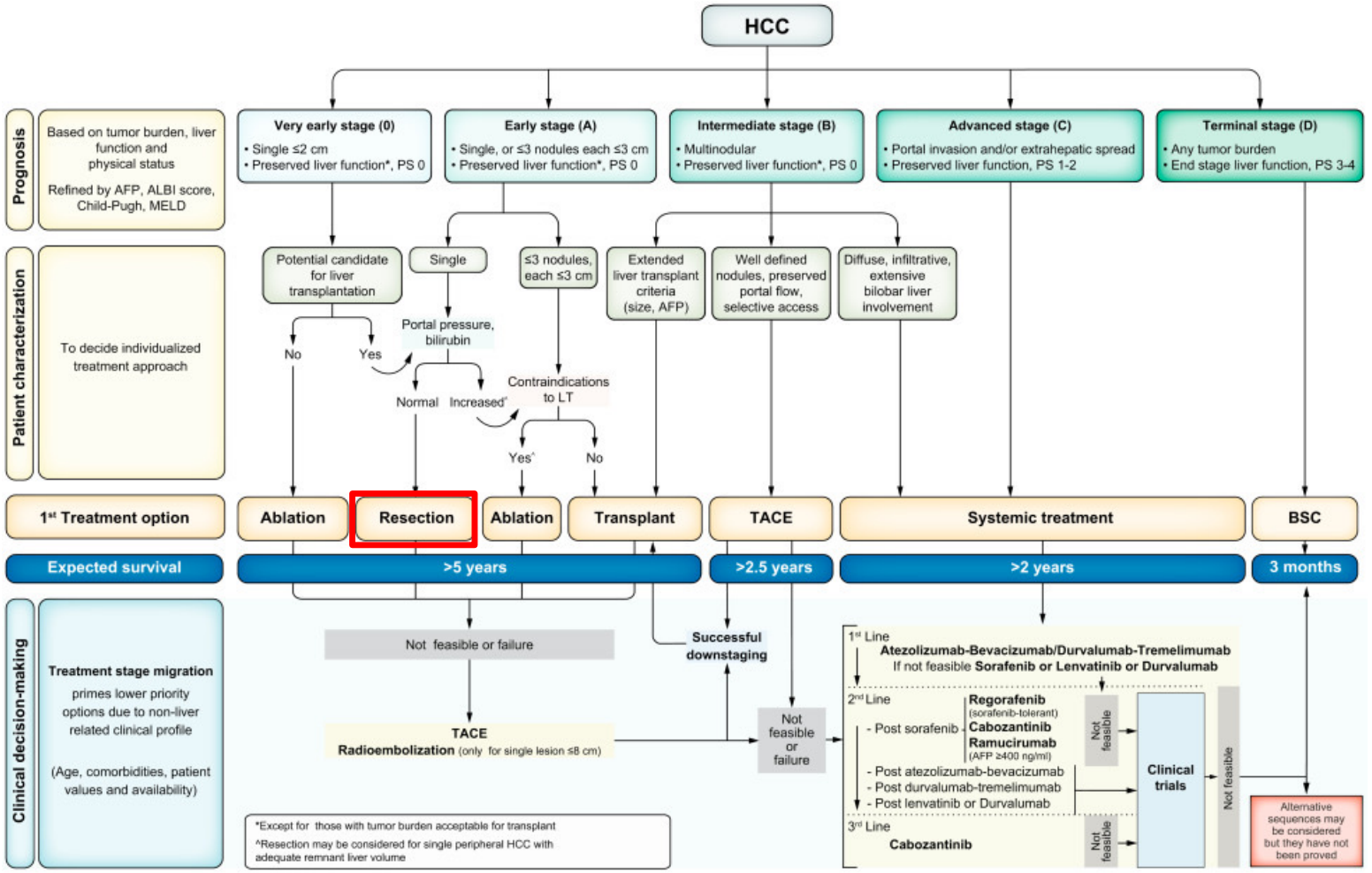
JOHNS HOPKINS
UNIVERSITY

Potential Role of Anti-PD-1/PD-L1 Antibodies in the Care of Patients with Early- and Intermediate-Stage Hepatocellular Carcinoma (HCC)

Mark Yarchoan, MD

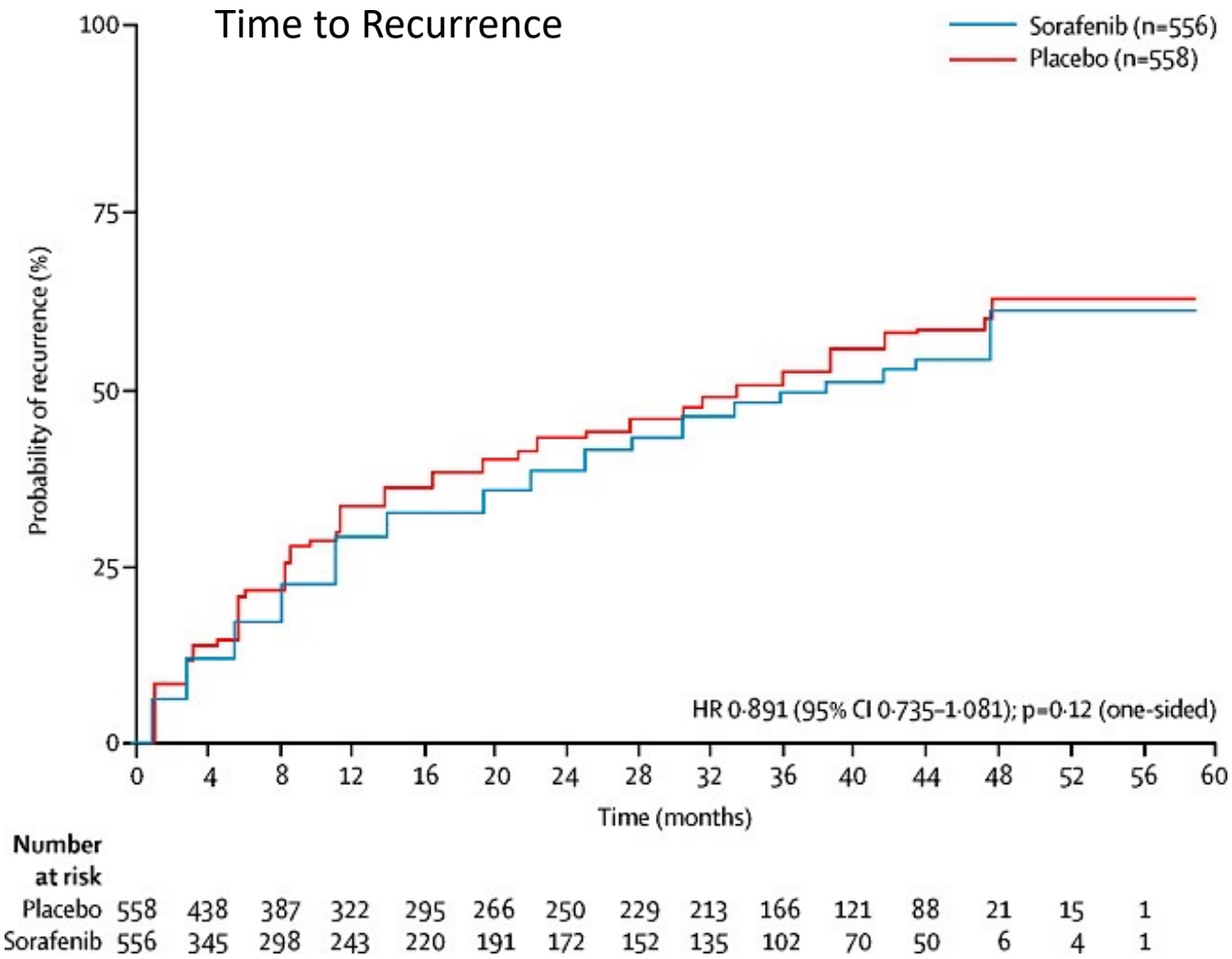
Rationale for Perioperative Systemic Therapy

- Only 15-20% of HCC is resectable
  - Recurrence after resection is common (~70-80%)
- Perioperative strategies that reduce the primary tumor and occult micrometastatic disease may improve outcomes



Reig M et al. *J Hepatol* 2022;76(3):681-93.

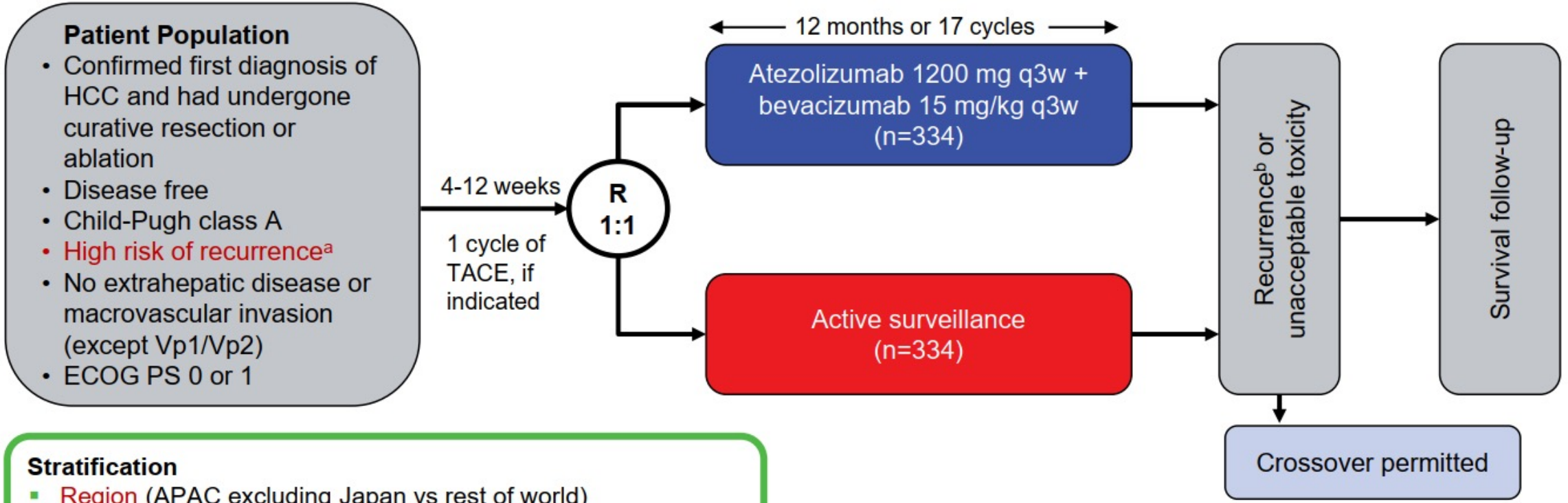
STORM Trial (Adjuvant Sorafenib)



- No difference in median RFS
  - [HR] 0.94; 95% CI 0.780–1.134; one-sided p=0.26

Bruix J et al Lancet 2015

IMbrave050



ClinicalTrials.gov, NCT04102098. ECOG PS; Eastern Cooperative Oncology Group performance status; Q3W, every three weeks; R, randomization; TACE, transarterial chemoembolization.

[a] **High-risk features** include: tumor >5 cm, >3 tumors, microvascular invasion, minor macrovascular invasion Vp1/Vp2, or Grade 3/4 pathology.

[b] Intrahepatic recurrence defined by EASL criteria. Extrahepatic recurrence defined by RECIST 1.1.

Chow et al IMbrave050
https://bit.ly/3ZPKzgM

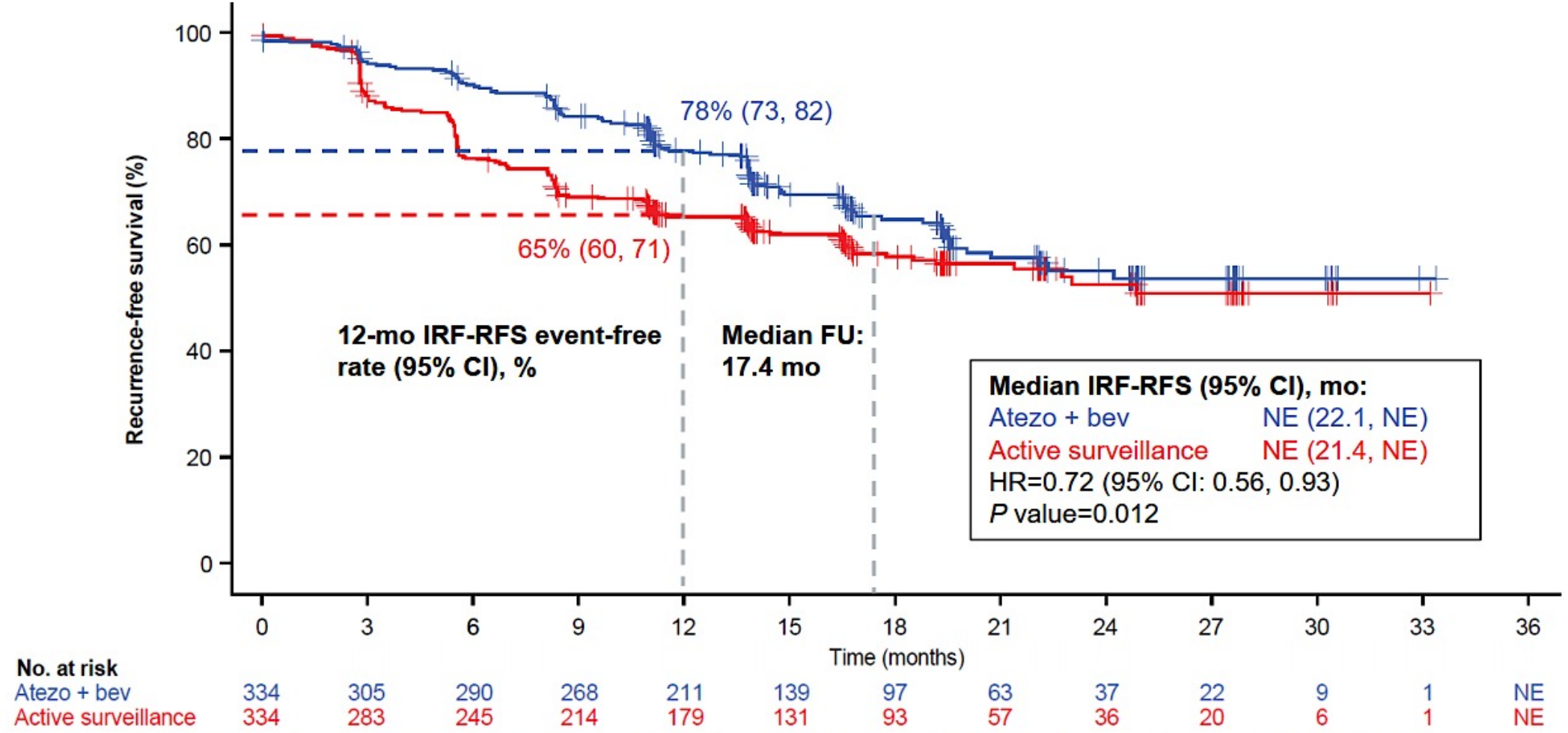
Presented by Pierce Chow, AACR 2023

IMbrave050

Curative treatment	Criteria for high risk of HCC recurrence
Resection	▪ ≤3 tumors, with **largest tumor >5 cm** regardless of vascular invasion, or poor tumor differentiation (Grade 3 or 4) ▪ **≥4 tumors**, with largest tumor ≤5 cm regardless of vascular invasion, or poor tumor differentiation (Grade 3 or 4) ▪ ≤3 tumors, with largest tumor ≤5 cm with **vascular invasion**, and/or **poor tumor differentiation** (Grade 3 or 4)
Ablation[b]	▪ 1 tumor >2 cm but ≤5 cm ▪ Multiple tumors (≤4 tumors), all ≤5 cm

Presented by Pierce Chow, AACR 2023

IMbrave050



Clinical cutoff: October 21, 2022; median follow-up duration: 17.4 mo. At clinical cutoff, 110 of 334 patients (33%) in the atezo + bev arm and 133 of 334 (40%)

Presented by Pierce Chow, AACR 2023; Qin S et al. *Lancet* 2023;402:1835-47.

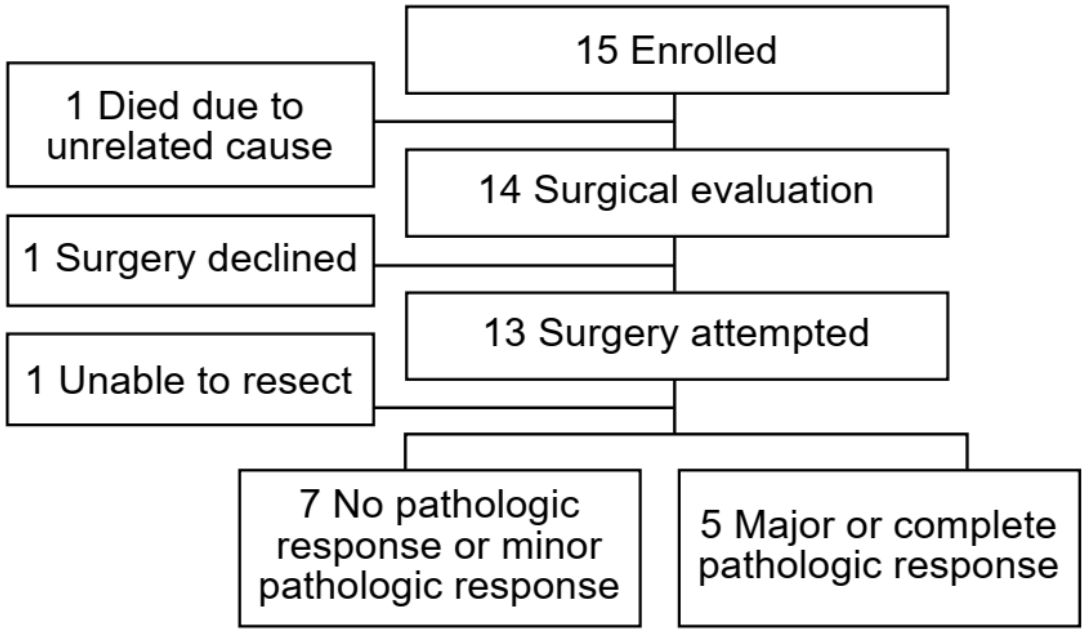
Key Unanswered Questions

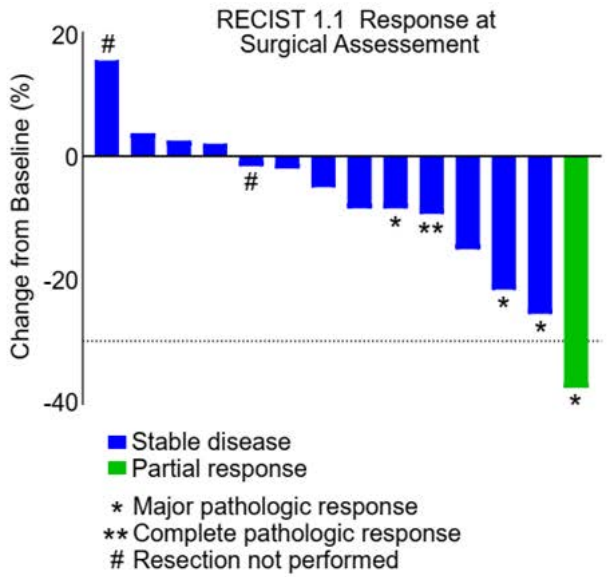
- Will RFS benefit translate into improved OS with longer follow up?
  - Did we make the scans look better, or did we cure patients?
  - Ie: Is earlier systemic treatment disease modifying, or trading later benefit for earlier benefit?
- Do we need the BEV?
  - No separation of components
- Could biomarkers (eg ctDNA, AFP) identify patients more likely to benefit?
- Optimal treatment in the setting of relapse after adjuvant BEV/ATEZO?

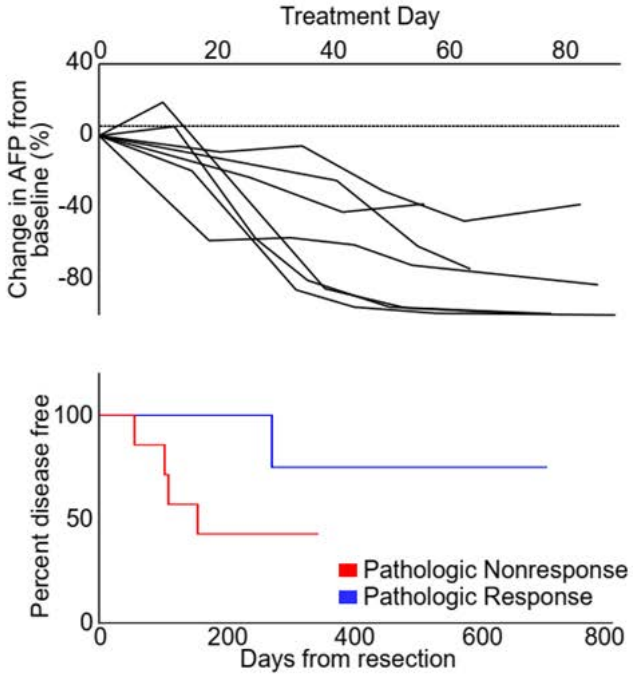
Notable Ongoing Adjuvant Clinical Trials

Trial	Key Eligibility Criteria	Treatment Arms	Primary Endpoint(s)	Current Status
KEYNOTE-937	Child-Pugh A, AFP <400 ng/mL, no prior anti–PD-(L)1 or PD-L2 therapy, no anti–CTLA-4 or stimulatory/ coinhibitory T-cell receptor therapy	Pembrolizumab vs placebo	RFS, OS	Active, not recruiting
EMERALD-2	Child-Pugh score of 5 or 6, successful resection or ablation	Durvalumab + bevacizumab vs durvalumab vs placebo	RFS	Active, not recruiting
CheckMate 9DX	Child-Pugh score of 5 or 6	Nivolumab vs placebo	RFS	Active, not recruiting
IMbrave050	Child-Pugh A, no major macrovascular invasion or extrahepatic spread, high risk of recurrence	Atezolizumab + bevacizumab vs active surveillance	RFS	COMPLETED

Neoadjuvant Therapy Is Feasible – Randomized Trials Needed



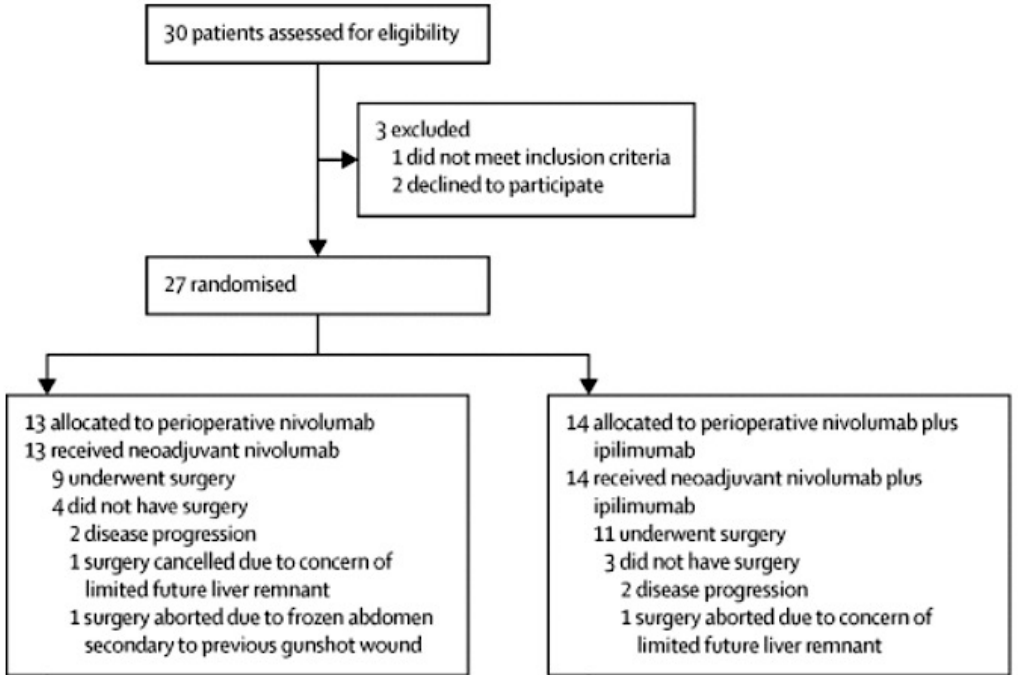




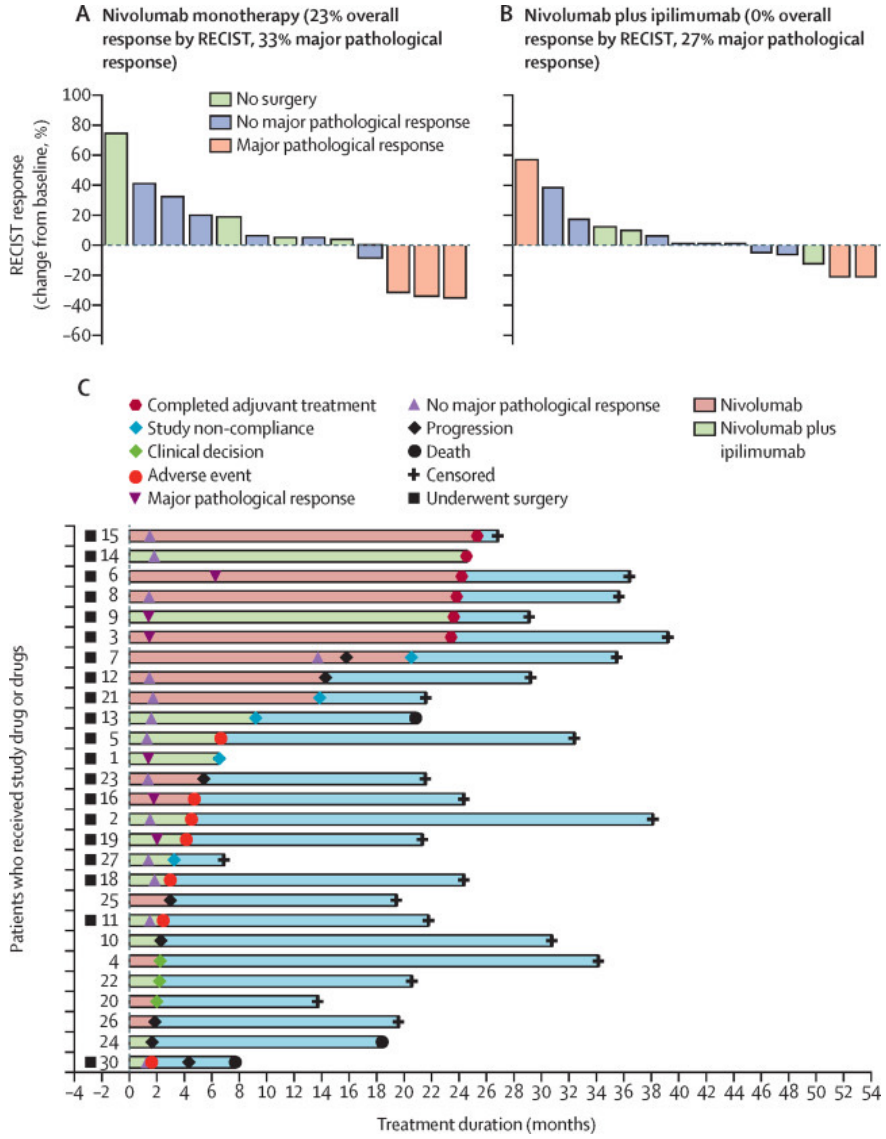
- *12 of 15 patients achieved successful margin-negative resections*
- *5/15 patients achieved major or complete pathologic responses*

Won Jin Ho et al. Nature Cancer 2021

Neoadjuvant Therapy Is Feasible – Randomized Trials Needed



- No surgical delays due to AEs, but 4 due to PD
- 20/27 treated underwent surgery
- 6/20 (30%) major pathologic response

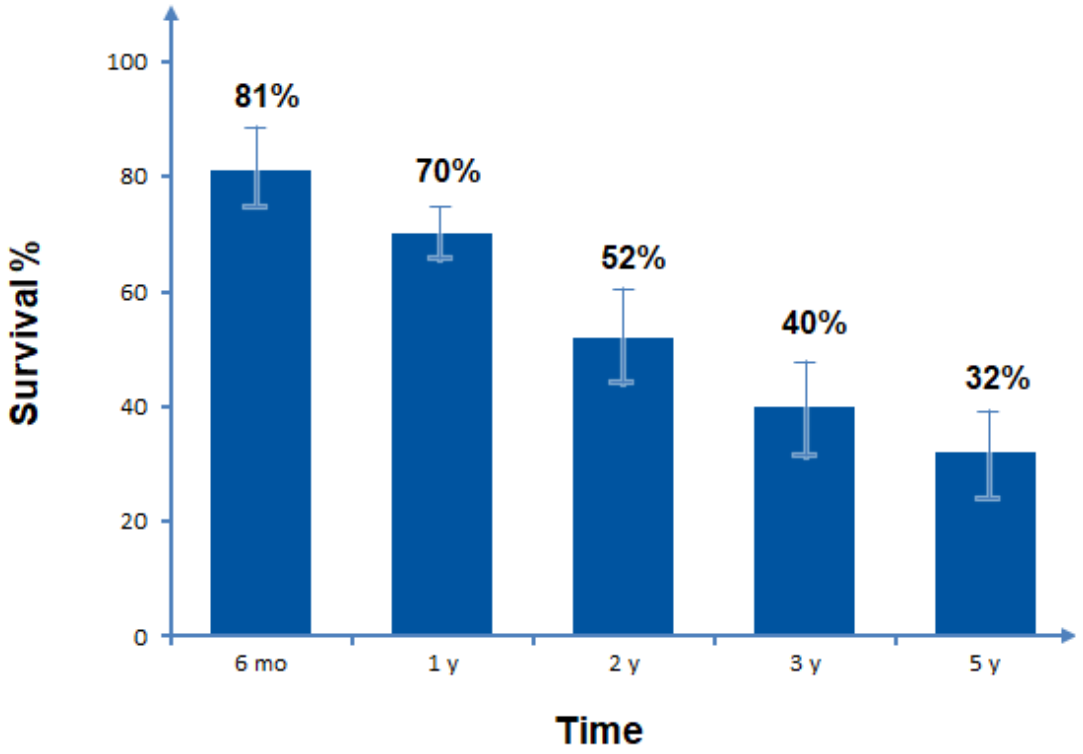


Kaseb AO, et al. Lancet Gastroenterol Hepatol. 2022

Discussion

First-line therapy for a patient who received adjuvant atezolizumab/bevacizumab and 18 months later was found to have metastatic disease?

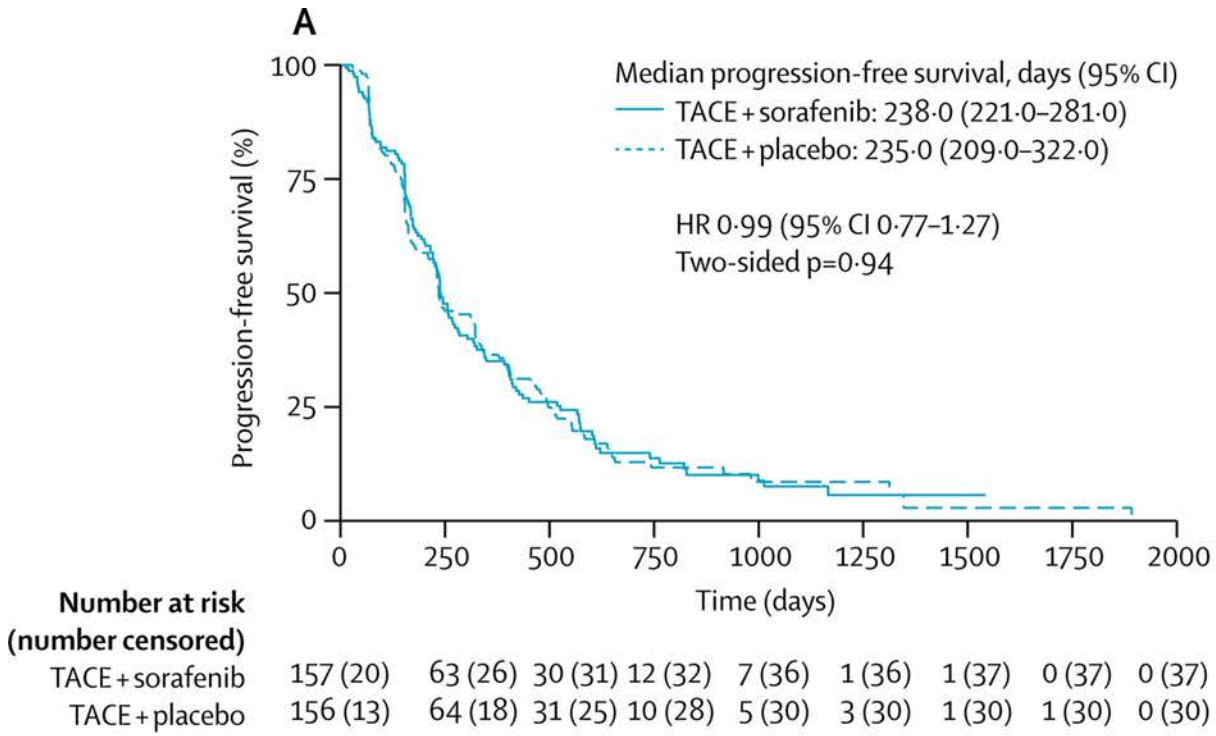
TACE Pooled ORR 52%, Median Survival ~19 Months

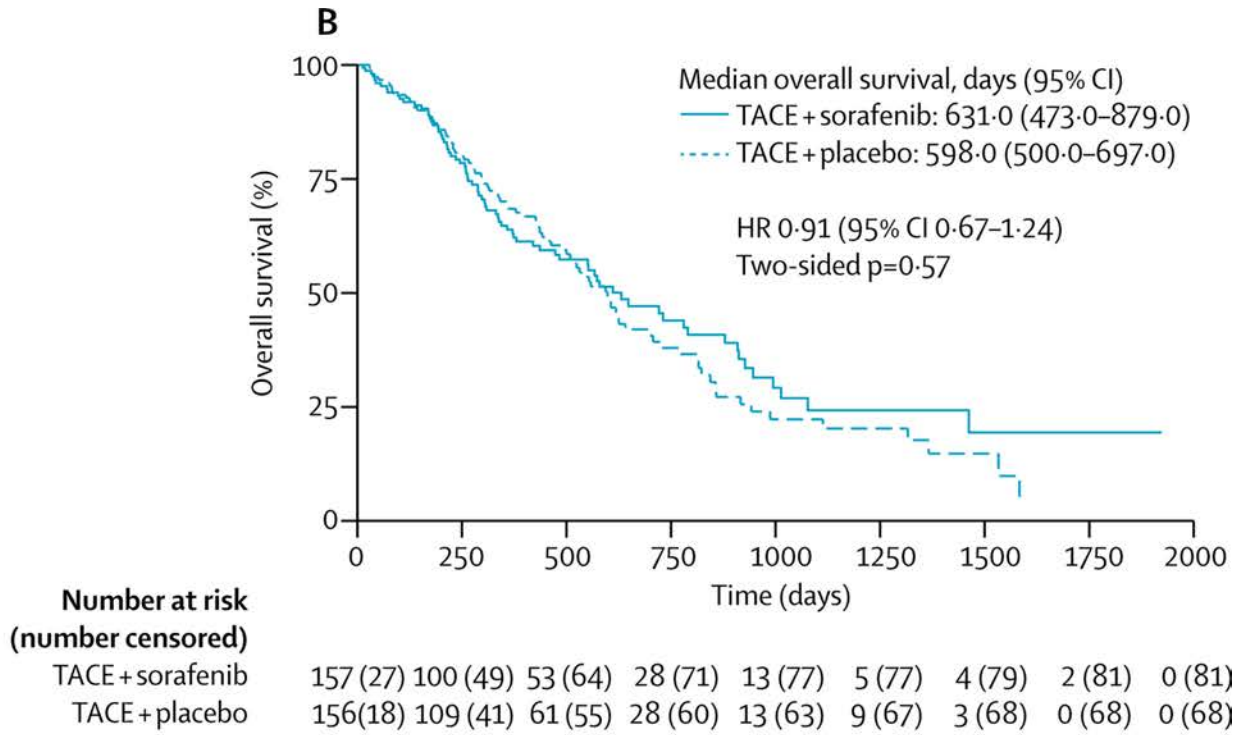


	No. of Studies	Estimate	Lower 95% CI	Upper 95% CI
Median, mo				
≤2002	19	18.5	14.6	22.4
>2002	44	19.8	15.5	24.1
1-year, %				
≤2002	19	70.7	63.2	78.3
>2002	71	70.4	65.2	75.5
2-year, %				
≤2002	21	51.1	37.1	65.1
>2002	50	52.0	43.9	60.2
3-year, %				
≤2002	13	27.8	18.3	37.4
>2002	53	43.4	34.9	51.8

Lencioni et al. Hepatology 2016

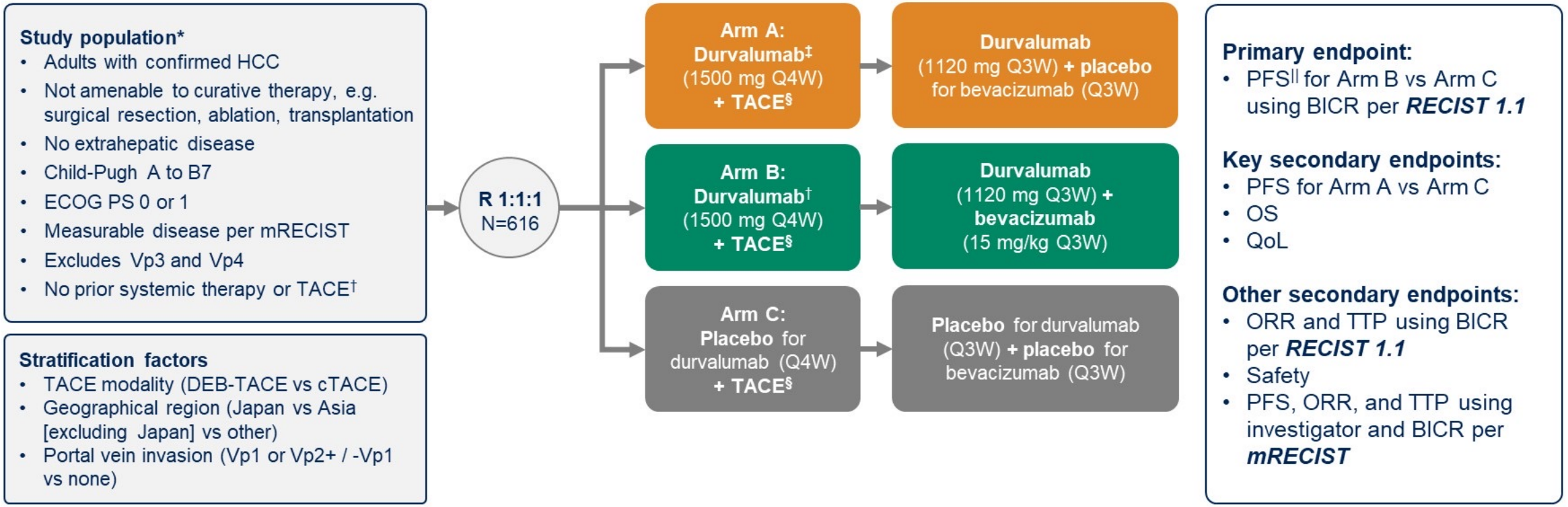
TACE + Sorafenib (TACE2 Phase 3 Trial)





Meyer T et al. *The Lancet Gastroenterology & Hepatology* 2017;2(8):565-75.

EMERALD-1



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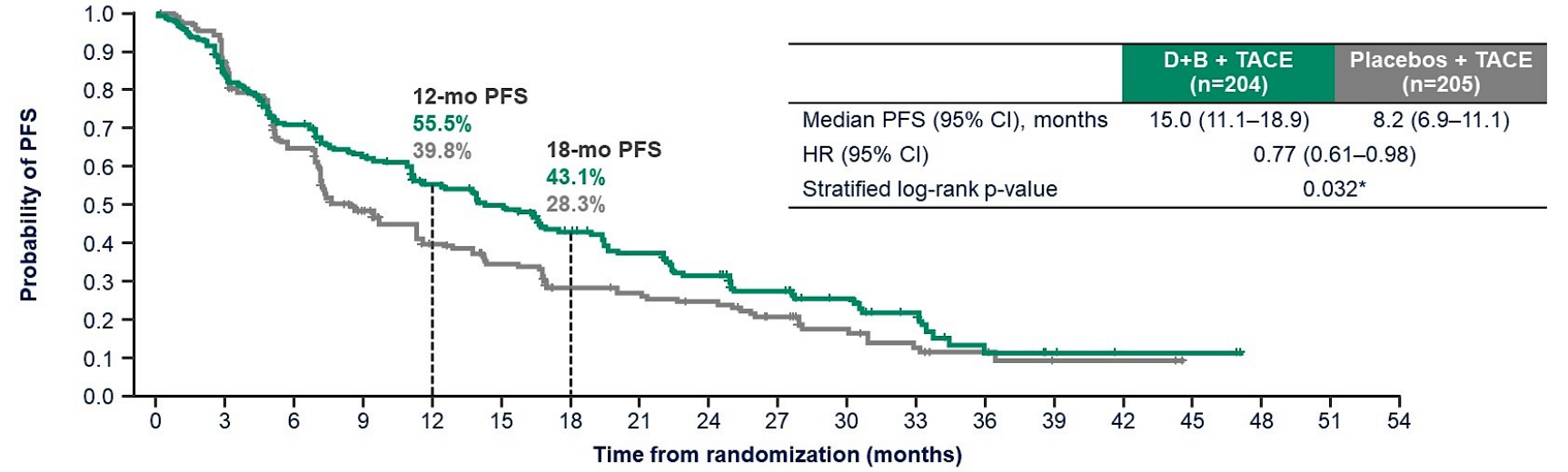
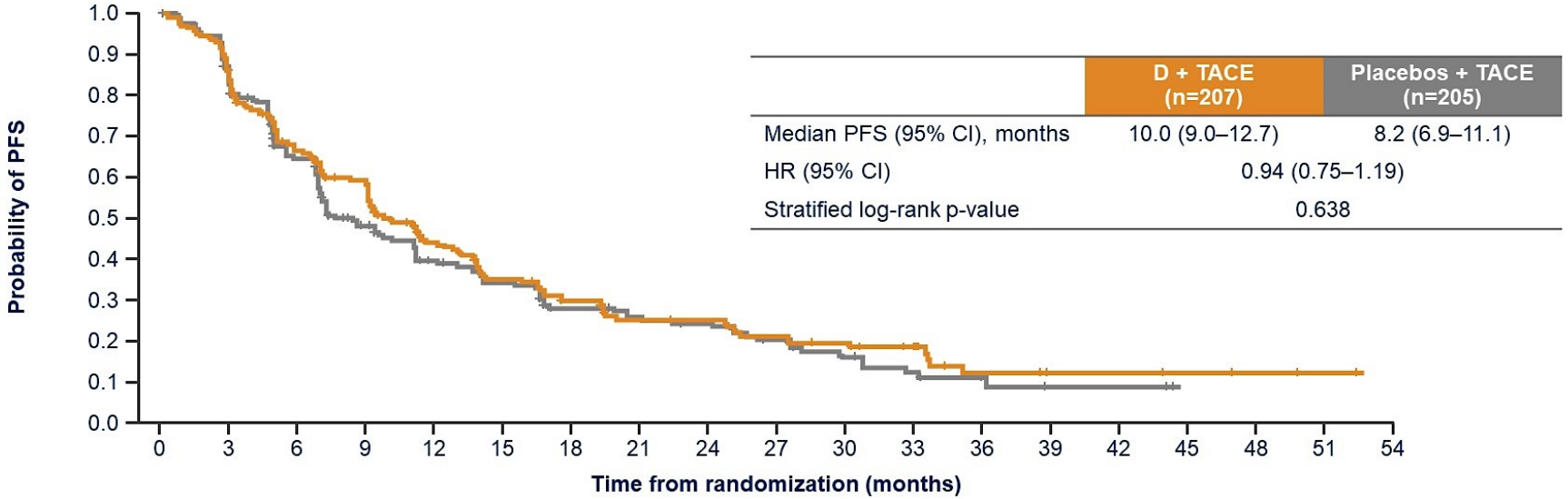
EMERALD-1



	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*	



	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	

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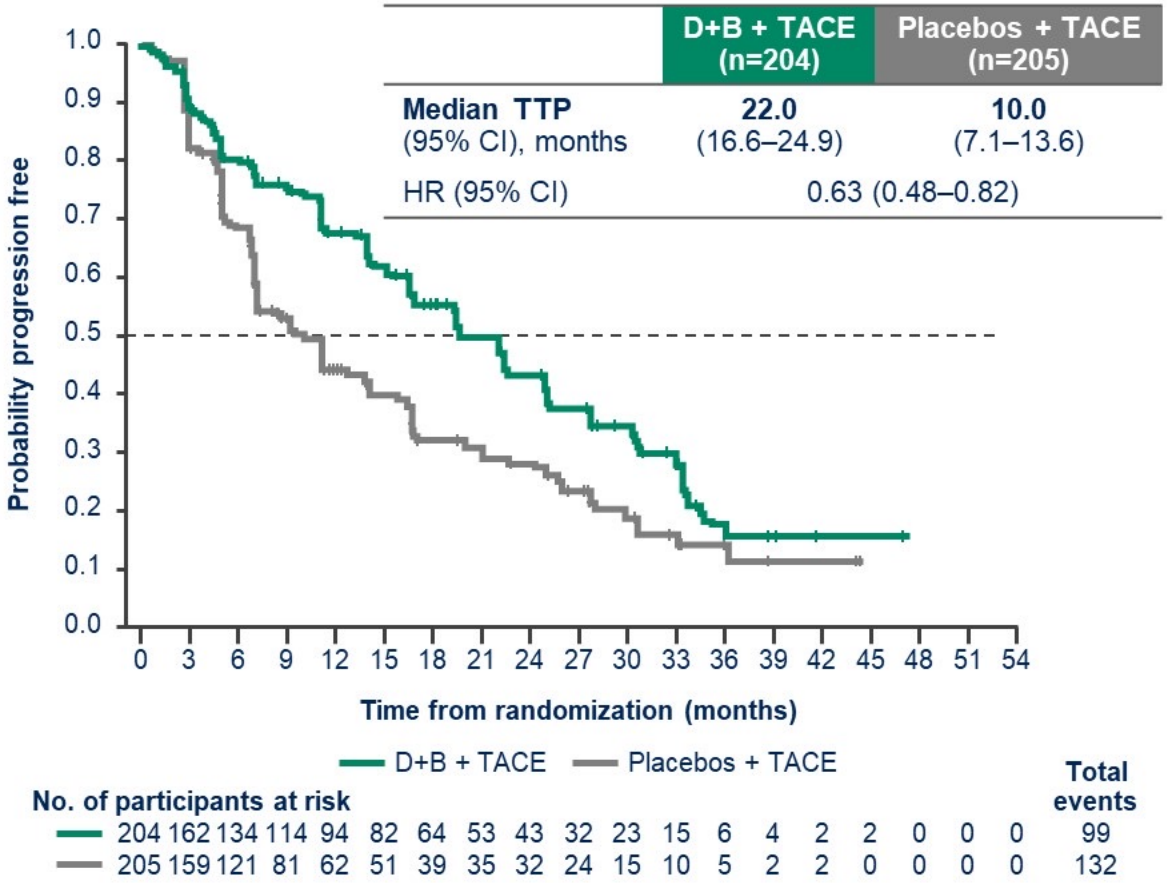
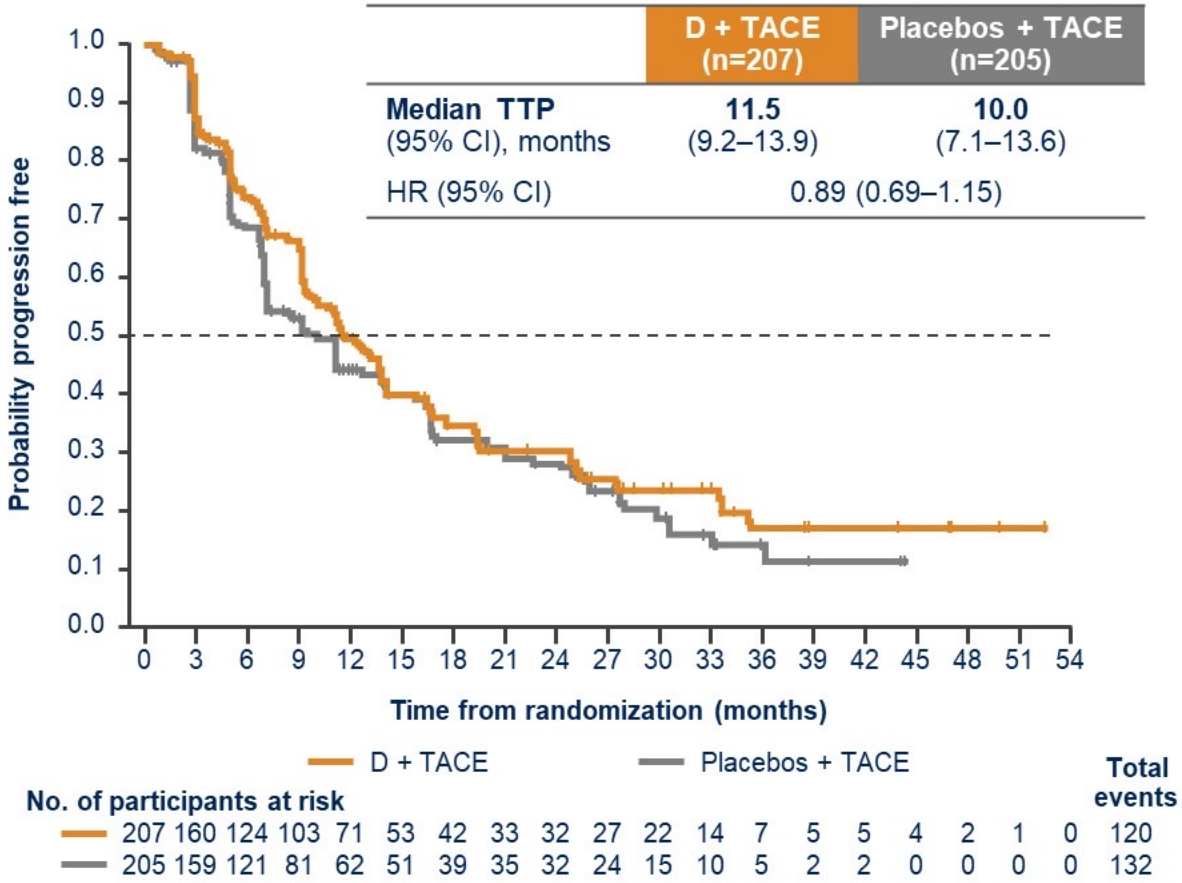
EMERALD-1

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





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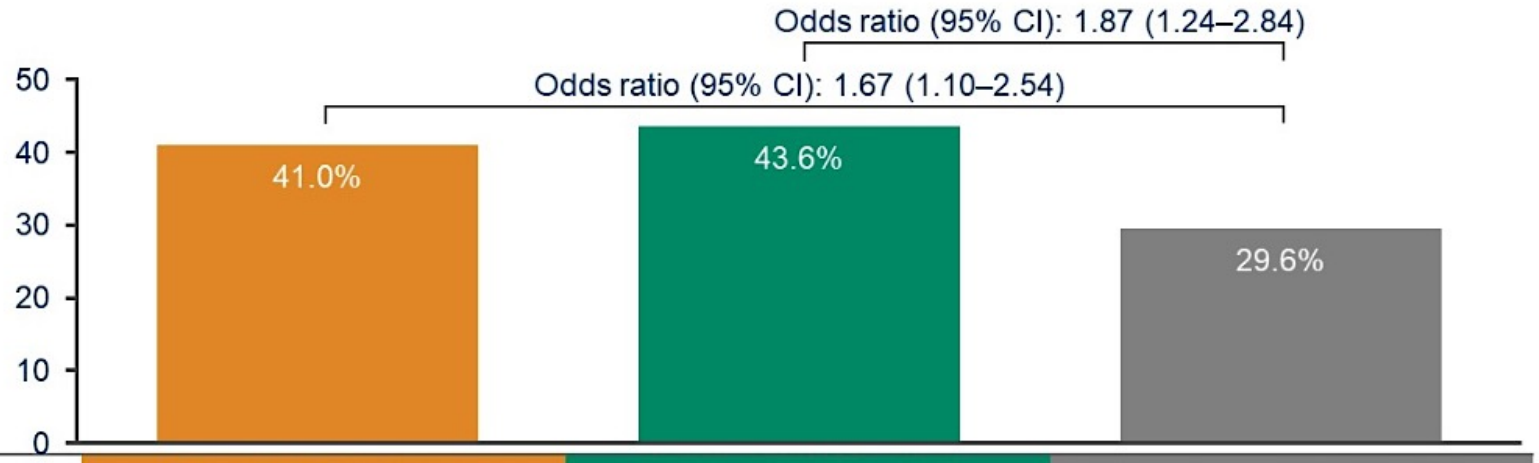
EMERALD-1



	D + TACE (n=207)	D+B + TACE (n=204)	Placebos + TACE (n=205)
Participants with measurable disease at baseline	205	202	203
Confirmed response,* n (%)	84 (41.0)	88 (43.6)	60 (29.6)
Complete response, n (%)	3 (1.5)	6 (3.0)	5 (2.5)
Partial response, n (%)	81 (39.5)	82 (40.6)	55 (27.1)
Stable disease ≥20 weeks, n (%)	42 (20.5)	45 (22.3)	63 (31.0)
Median duration of response, (LQ–UQ) months	14.0 (6.9–30.7)	22.1 (11.2–30.3)	16.4 (6.3–26.3)

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Safety Data

	D + TACE (n=232)*	D+B + TACE (n=154)*	Placebos + TACE (n=200)*
Any AE, n (%)	**215 (92.7)**	**151 (98.1)**	**186 (93.0)**
Possibly related to study treatment	117 (50.4)	124 (80.5)	90 (45.0)
Possibly provoked by TACE	101 (43.5)	78 (50.6)	95 (47.5)
SAEs (including AEs with outcome of death), n (%)	**84 (36.2)**	**74 (48.1)**	**62 (31.0)**
Possibly related to any treatment	13 (5.6)	30 (19.5)	10 (5.0)
Any AE of max CTCAE Grade 3 or 4, n (%)	**64 (27.6)**	**70 (45.5)**	**46 (23.0)**
Any AE possibly related to study treatment of max CTCAE Grade 3 or 4 , n (%)	**15 (6.5)**	**41 (26.6)**	**12 (6.0)**
Any AE possibly provoked by TACE of max CTCAE Grade 3 or 4, n (%)	**21 (9.1)**	**13 (8.4)**	**17 (8.5)**
Any AE with outcome of death, n (%)	**21 (9.1)**	**16 (10.4)**	**11 (5.5)**
Possibly related to study treatment	3 (1.3)	0	3 (1.5)
Possibly related to durvalumab / placebo	2 (0.9)	0	1 (0.5)
Possibly related to bevacizumab / placebo	1 (0.4)	0	2 (1.0)
AE leading to discontinuation, n (%)	**28 (12.1)**	**38 (24.7)**	**14 (7.0)**
Possibly related to study treatment	8 (3.4)	13 (8.4)	6 (3.0)
Possibly related to durvalumab / placebo	6 (2.6)	7 (4.5)	3 (1.5)
Possibly related to bevacizumab / placebo	3 (1.3)	9 (5.8)	4 (2.0)
Possibly provoked by TACE	2 (0.9)	0	2 (1)

*Safety analysis set: all randomized patients who received any amount of study treatment (i.e. durvalumab, bevacizumab, or placebo) regardless of arm randomized to.
AE, adverse event; B, bevacizumab; CTCAE, Common Terminology Criteria for Adverse Events; D, durvalumab; NA, not applicable; SAE, serious adverse event; TACE, transarterial chemoembolization.

Presented by Riccardo Lencioni, Gastrointestinal Cancers Symposium 2024

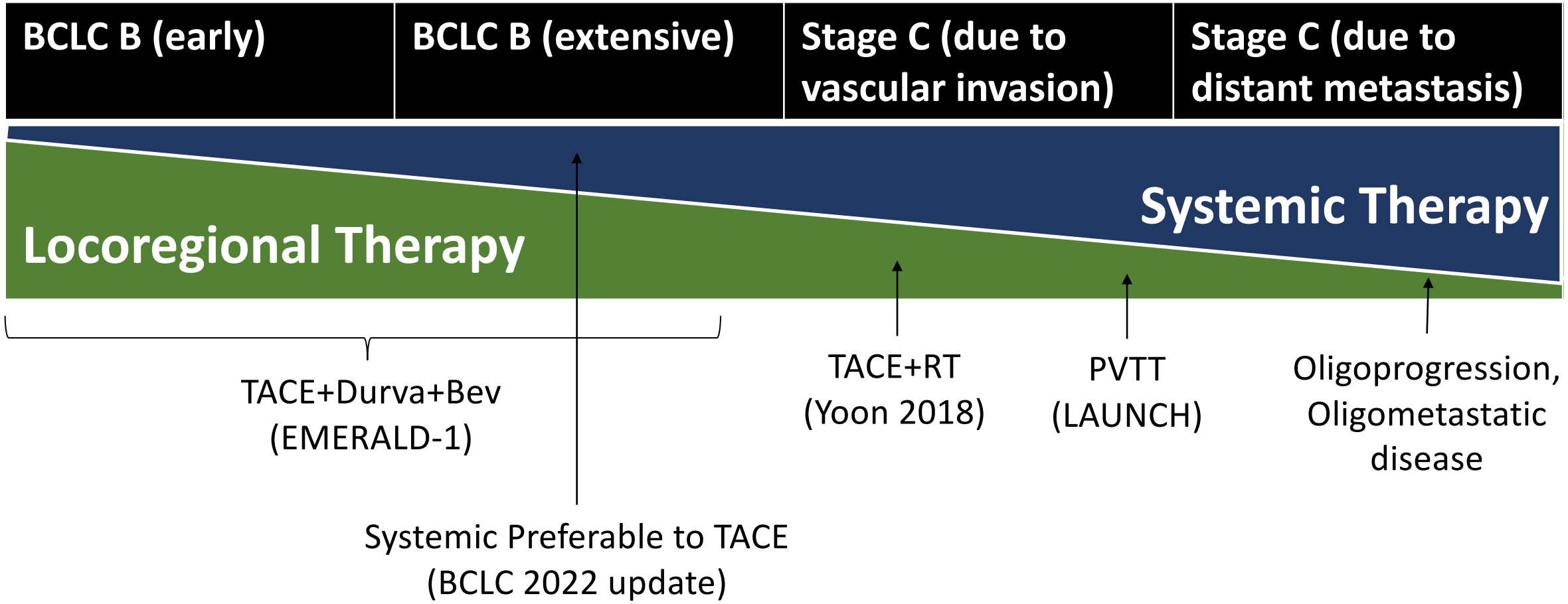
Key Unanswered Questions

- Will PFS benefit translate into improved OS?
  - Is earlier systemic treatment disease modifying, or trading later benefit for earlier benefit?
- Why is there a 7 month difference between PFS and TTP?
  - More clarity on toxicity and liver function is needed
- Do we need the TACE?
- Can this paradigm be applied to other locoregional therapies (Y90, SBRT, etc)?

Ongoing Phase 3 HCC Clinical Trials: TACE Combinations

Trial	Treatment Arms	Primary Endpoint(s)	Current Status
EMERALD-1	Durvalumab + TACE vs durvalumab + bevacizumab + TACE vs TACE + placebo	PFS	**Early Data Presented**
EMERALD-3	STRIDE+lenvatinib+TACE vs STRIDE+TACE vs TACE	PFS	Recruiting
LEAP-012	Lenvatinib + pembrolizumab + TACE vs TACE + placebo	PFS, OS	Active, not recruiting
CheckMate 74W	Nivolumab + ipilimumab + TACE vs nivolumab + TACE vs TACE	Time to TACE progression, OS	Terminated (Slow accrual)
ABC-HCC	Atezolizumab + bevacizumab vs TACE	Time to failure of treatment strategy	Recruiting
REPLACE	Regorafenib + pembrolizumab vs TACE/TARE (beyond up-to-7)	PFS	Recruiting

Locoregional and Systemic: An Evolving Gradient



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Based on the EMERALD-1 data recently presented in San Francisco, are you currently considering administering durvalumab/bevacizumab with TACE for your patients with HCC (assuming you can access this treatment)?

 Dr Kelley	Yes, I am considering using this regimen for the proper patient
 Dr Yarchoan	Yes, I am considering using this regimen for the proper patient
 Dr Abou-Alfa	Yes, and I have already identified at least one patient in my practice (65-year-old, no prior therapy, extent of disease in the liver: 7 cm seg 4/5 and 3 cm seg 8)
 Dr Abrams	Yes, I am considering using this regimen for the proper patient
 Dr Li	Yes, I am considering using this regimen for the proper patient
 Dr Stein	—

TACE = transarterial chemoembolization

RTP RESEARCH TO PRACTICE

Perspectives on EMERALD-1 data and potential integration of its treatment strategy into clinical practice

Ahmed Omar Kaseb, MD, CMQ

Arndt Vogel, MD, PhD

RTP
RESEARCH
TO PRACTICE

EMERALD-1: Differentiating between toxicity from TACE and toxicity from immunotherapy

Ahmed Omar Kaseb, MD, CMQ

RTP
RESEARCH
TO PRACTICE

First-line management of advanced HCC

Stacey Stein, MD

Thomas A Abrams, MD

Arndt Vogel, MD, PhD

RTP
RESEARCH
TO PRACTICE

Second-line treatment selection for advanced HCC; treatment options for patients with Child-Pugh C advanced disease

Thomas A Abrams, MD

RTP
RESEARCH
TO PRACTICE

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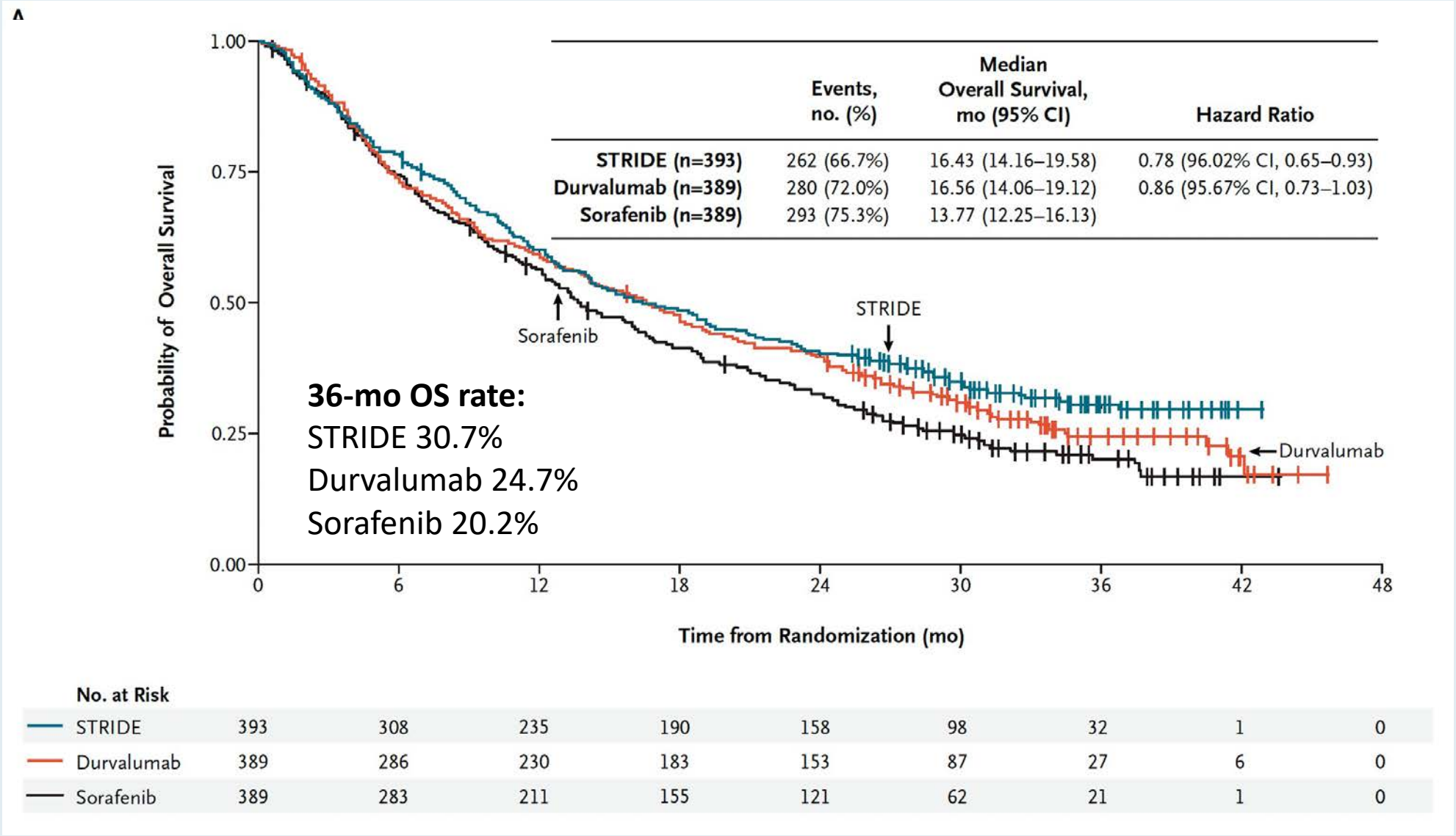
Tolerability and Other Practical Considerations with the Use of Immune Checkpoint Inhibitors for Advanced HCC and Biliary Tract Cancers (BTCs)

Katie Kelley, MD

HIMALAYA: Overall Survival



	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

No. at Risk									
STRIDE	393	308	235	190	158	98	32	1	0
Durvalumab	389	286	230	183	153	87	27	6	0
Sorafenib	389	283	211	155	121	62	21	1	0

STRIDE = single tremelimumab regular interval durvalumab

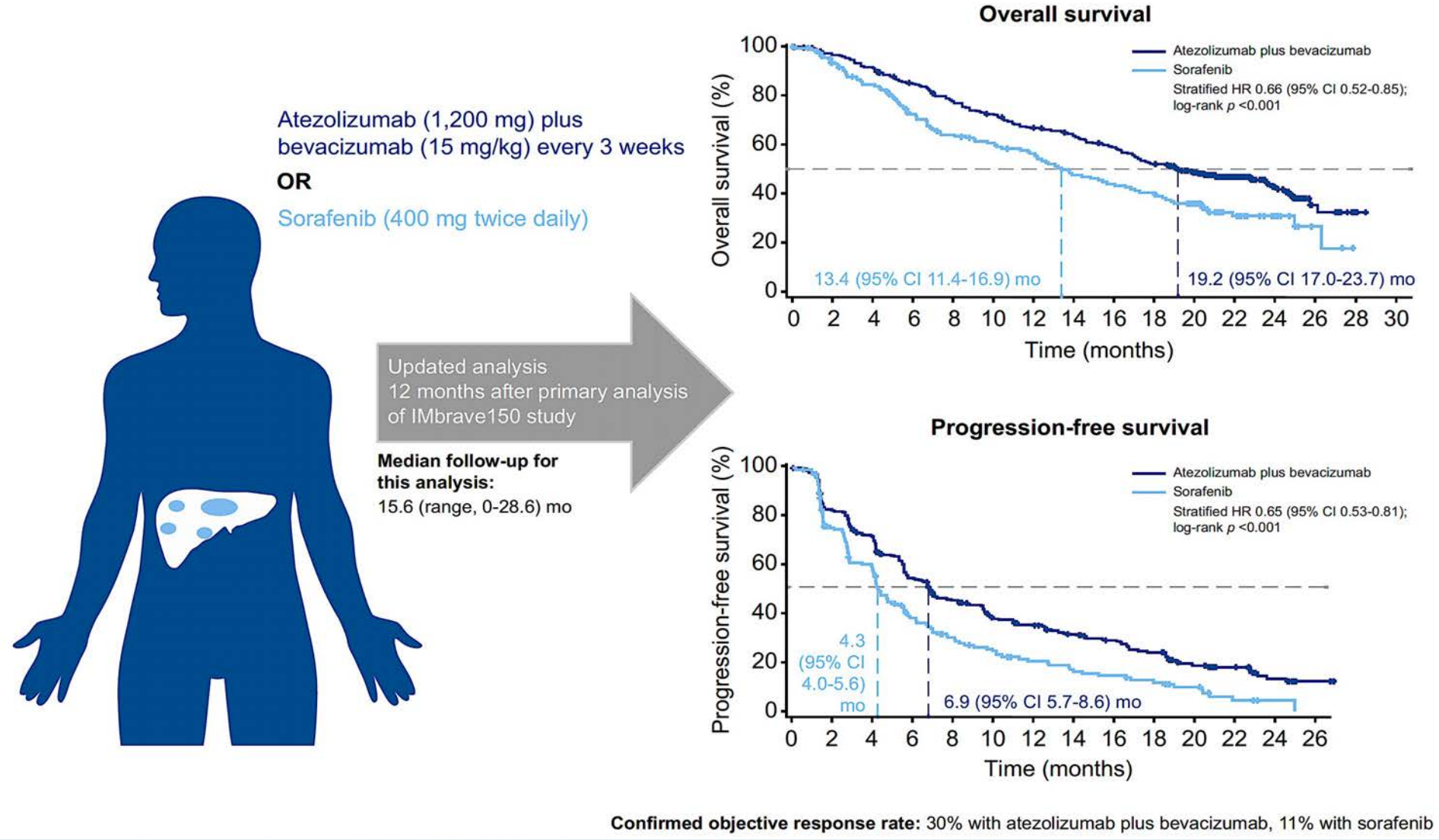
Abou-Alfa G et al. *NEJM Evid* 2022;1(8).

HIMALAYA: 4-Year Update of STRIDE Regimen versus Sorafenib

Clinical endpoint	STRIDE (durvalumab/tremelimumab) (n = 393)	Sorafenib (n = 389)
Median follow-up duration	49.12 mo	47.31 mo
Median OS	16.4 mo	13.8 mo
OS HR (*p*-value)	0.78 (0.0037)	
48-mo OS rates	25.2%	15.1%
Serious treatment-related adverse events	17.5%	9.6%

Sangro B et al. 2023 ESMO World Congress on Gastrointestinal Cancer;Abstract SO-15; Chan SL et al. ESMO Asia Congress 2023;Abstract 147P.

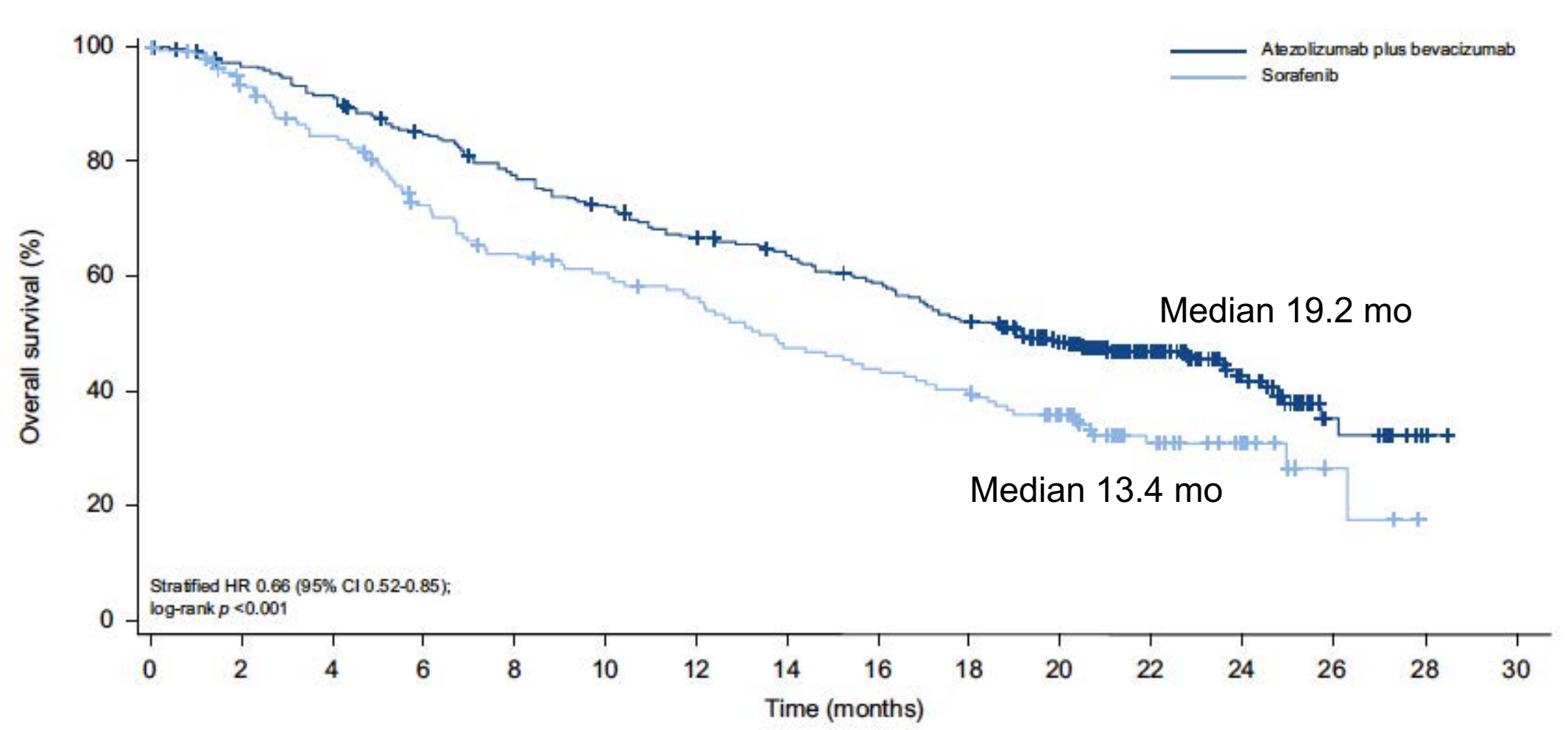
IMbrave150: Updated OS and PFS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



Confirmed objective response rate: 30% with atezolizumab plus bevacizumab, 11% with sorafenib

Cheng A-L et al. *J Hepatol* 2022;76(4):862-73.

IMbrave150: Updated OS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



Cheng A-L et al. *J Hepatol* 2022;76(4):862-73.

RTP RESEARCH TO PRACTICE

Patient characteristics

- IMbrave150
- HIMALAYA

IMbrave150

Baseline characteristics

Characteristic	Updated analysis	
	Atezo + Bev (n = 336)	Sorafenib (n = 165)
Median age (range), years	64 (26-88)	66 (33-87)
Male, n (%)	277 (82)	137 (83)
Region, n (%)		
Asia (excluding Japan[a])	133 (40)	68 (41)
Rest of world	203 (60)	97 (59)
ECOG PS 1, n (%)	127 (38)	62 (38)
Child-Pugh class, n (%)		
A / B	333 (99) / 1 (< 1)	165 (100) / 0
BCLC staging at study entry, n (%)		
A / B / C	8 (2) / 51 (15) / 277 (82)	6 (4) / 25 (15) / 134 (81)
Etiology of HCC, n (%)		
HBV / HCV / Non-viral	164 (49) / 72 (21) / 100 (30)	76 (46) / 36 (22) / 53 (32)
AFP ≥ 400 ng/mL, n (%)	126 (38)	61 (37)
EHS, n (%)	212 (63)	93 (56)
MVI, n (%)	129 (38)	71 (43)
EHS and/or MVI, n (%)	258 (77)	120 (73)
Prior TACE, n (%)	131 (39)	70 (42)
Prior radiotherapy, n (%)	34 (10)	17 (10)

Clinical cutoff: August 31, 2020; median follow-up: 15.6 mo.

[a] Japan is included in rest of world.

HIMALAYA

Baseline characteristics

Characteristic	STRIDE (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
Male sex, n (%)	327 (83.2)	323 (83.0)	337 (86.6)
Median age (range), years	65.0 (22–86)	64.0 (20–86)	64.0 (18–88)
Region, n (%) Asia (excluding Japan) Rest of world (including Japan)	 156 (39.7) 237 (60.3)	 167 (42.9) 222 (57.1)	 156 (40.1) 233 (59.9)
Viral etiology,*,† n (%) HBV HCV Nonviral	 122 (31.0) 110 (28.0) 161 (41.0)	 119 (30.6) 107 (27.5) 163 (41.9)	 119 (30.6) 104 (26.7) 166 (42.7)
ECOG PS, n (%) 0 1	 244 (62.1) 148 (37.7)	 237 (60.9) 150 (38.6)	 241 (62.0) 147 (37.8)
MVI,† n (%)	103 (26.2)	94 (24.2)	100 (25.7)
EHS,† n (%)	209 (53.2)	212 (54.5)	203 (52.2)
PD-L1 positive, n (%)	148 (37.7)	154 (39.6)	148 (38.0)
AFP ≥400 ng/ml,† n (%)	145 (36.9)	137 (35.2)	124 (31.9)

Biomarker evaluable samples were collected for all but 20 patients across all treatment arms.

*HBV: patients who tested positive for HBsAg or anti-HBc with detectable HBV DNA; HCV: patients who tested positive for HCV or had history of HCV infection; Nonviral: no active viral hepatitis identified. †Determined at screening.

AFP, alfa-fetoprotein; ECOG, Eastern Cooperative Oncology Group; EHS, extrahepatic spread; HBc, hepatitis B core; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; MVI, macrovascular invasion; PD-L1, programmed cell death ligand-1; PS, performance status; STRIDE, Single Tremelimumab Regular Interval Durvalumab.

Safety overview

- IMbrave150
- HIMALAYA

IMbrave150

Updated safety summary[a]

	Updated analysis	
	Atezo + Bev (n = 329)	Sorafenib (n = 156)
Treatment duration, median, mo	Atezo = 8.4; Bev = 7.0	2.8
All grade AE, any cause, n (%)	322 (98)	154 (99)
Treatment-related all grade AE	284 (86)	148 (95)
Grade 3-4 AE, n (%)[b]	207 (63)	89 (57)
Treatment-related Grade 3-4 AE[b]	143 (43)	72 (46)
Serious AE, n (%)	160 (49)	51 (33)
Treatment-related serious AE	76 (23)	25 (16)
Grade 5 AE, n (%)	23 (7)	9 (6)
Treatment-related Grade 5 AE	6 (2)	1 (< 1)
AE leading to withdrawal from any component, n (%)	72 (22)	18 (12)
AE leading to withdrawal from both components	34 (10)	0
AE leading to dose interruption of any study treatment, n (%)	195 (59)	68 (44)
AE leading to dose modification of sorafenib, n (%)[c]	0	58 (37)

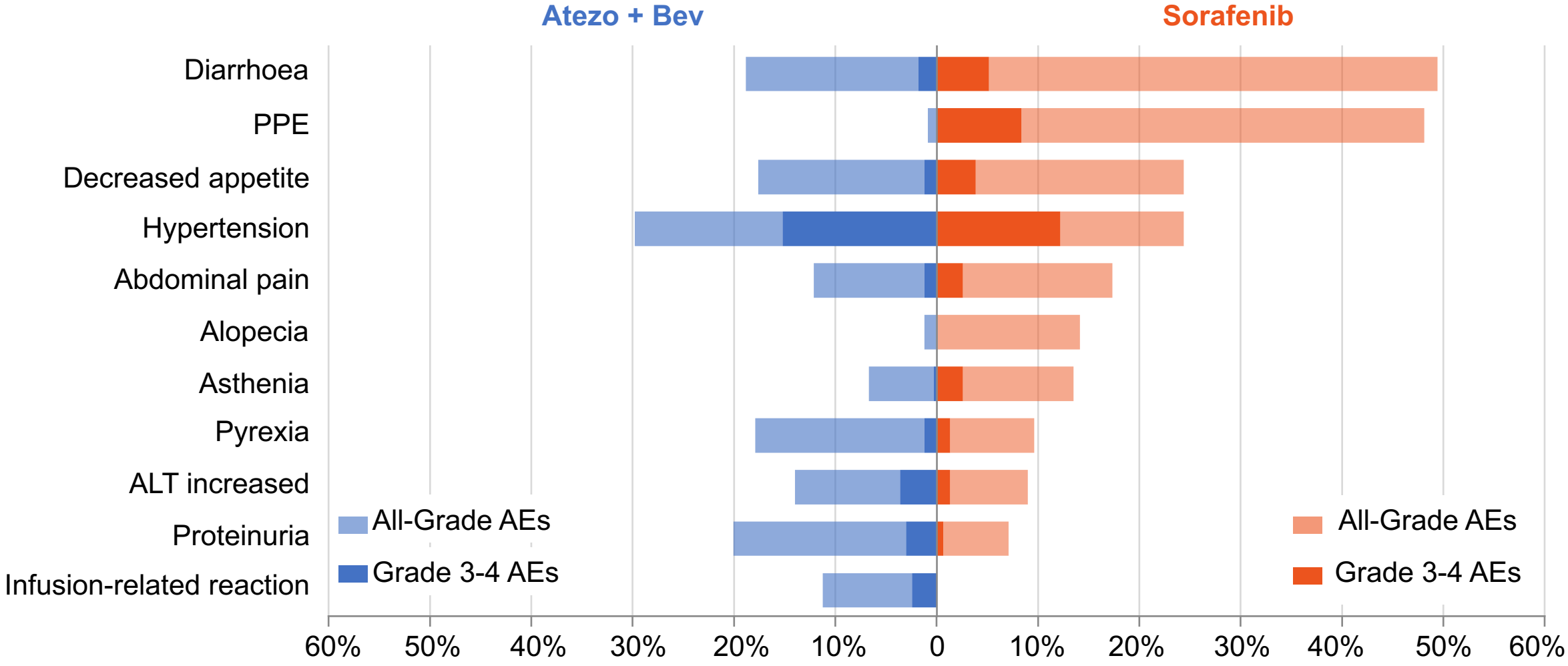
Clinical cutoff: August 31, 2020; median follow-up: 15.6 mo.

[a] Safety-evaluable population (defined as patients who received study treatment). [b] Highest grade experienced. [c] No dose modification allowed for atezo + bev arm.

IMbrave150

Safety[a]

≥ 10% frequency of AEs in either arm and > 5% difference between arms



PPE, palmar-plantar erythrodysaesthesia.
[a] Safety-evaluable population.

HIMALAYA

Safety and tolerability

Event, n (%)	STRIDE (n=388)	Durvalumab (n=388)	Sorafenib (n=374)
Any AE	378 (97.4)	345 (88.9)	357 (95.5)
Any TRAE*	294 (75.8)	202 (52.1)	317 (84.8)
Any grade 3/4 AE	196 (50.5)	144 (37.1)	196 (52.4)
Any grade 3/4 TRAE	100 (25.8)	50 (12.9)	138 (36.9)
Any serious TRAE	68 (17.5)	32 (8.2)	35 (9.4)
Any TRAE leading to death	9 (2.3)†	0	3 (0.8)‡
Any TRAE leading to discontinuation	32 (8.2)	16 (4.1)	41 (11.0)
Any grade 3/4 hepatic SMQ TRAE	23 (5.9)	20 (5.2)	17 (4.5)
Any grade 3/4 hemorrhage SMQ TRAE	2 (0.5)	0	4 (1.1)
Any grade 3/4 immune-mediated TRAE	49 (12.6)	24 (6.2)	9 (2.4)
Any immune-mediated AE requiring treatment with high-dose steroids	78 (20.1)	37 (9.5)	7 (1.9)
Any immune-mediated AE leading to discontinuation of study treatment	22 (5.7)	10 (2.6)	6 (1.6)

Includes AEs with onset or increase in severity on or after the date of the first dose through 90 days following the date of the last dose or the date of initiation of the first subsequent therapy.

*Treatment-related was as assessed by investigator. †Nervous system disorder (n=1), acute respiratory distress syndrome (n=1), hepatitis (n=1), myocarditis (n=1), immune-mediated hepatitis (n=2), pneumonitis (n=1), hepatic failure (n=1), myasthenia gravis (n=1). ‡Hematuria (n=1), cerebral hematoma (n=1), hepatic failure (n=1).

AE, adverse event; SMQ, Standardized MedDRA Query; STRIDE, Single Tremelimumab Regular Interval Durvalumab; TRAE, treatment-related adverse event.

HIMALAYA

Treatment-related hepatic or hemorrhage SMQ events

Event, n (%)	STRIDE (n=388)		Durvalumab (n=388)		Sorafenib (n=374)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Patients with hepatic SMQ TRAE	66 (17.0)	27 (7.0)	55 (14.2)	20 (5.2)	46 (12.3)	18 (4.8)
Patients with hemorrhage SMQ TRAE	7 (1.8)	2 (0.5)	3 (0.8)	0	18 (4.8)	6 (1.6)
Alanine aminotransferase increased	18 (4.6)	4 (1.0)	22 (5.7)	5 (1.3)	8 (2.1)	3 (0.8)
Aspartate aminotransferase increased	22 (5.7)	9 (2.3)	25 (6.4)	9 (2.3)	10 (2.7)	6 (1.6)
Blood bilirubin increased	6 (1.5)	1 (0.3)	6 (1.5)	0	10 (2.7)	2 (0.5)
Ascites	1 (0.3)	0	0	0	2 (0.5)	0
Hepatic encephalopathy	0	0	0	0	2 (0.5)	1 (0.3)
International normalized ratio increased	4 (1.0)	1 (0.3)	0	0	0	0
Esophageal varices hemorrhage	0	0	0	0	0	0

Includes adverse events with onset or increase in severity on or after the date of the first dose through 90 days following the date of the last dose or the date of initiation of the first subsequent therapy. Treatment-related was as assessed by investigator.

SMQ, Standardized MedDRA Query; STRIDE, Single Tremelimumab Regular Interval Durvalumab; TRAE, treatment-related adverse event.

HIMALAYA

Immune-mediated adverse events

Event, n (%)	STRIDE (n=388)				Durvalumab (n=388)			
	All grades	Grade 3 or 4	Received high-dose steroids	Leading to discontinuation	All grades	Grade 3 or 4	Received high-dose steroids	Leading to discontinuation
Patients with immune-mediated event	139 (35.8)	49 (12.6)	78 (20.1)	22 (5.7)	64 (16.5)	25 (6.4)	37 (9.5)	10 (2.6)
Pneumonitis	5 (1.3)	0	4 (1.0)	1 (0.3)	3 (0.8)	1 (0.3)	3 (0.8)	2 (0.5)
Hepatic events	29 (7.5)	16 (4.1)	29 (7.5)	9 (2.3)	26 (6.7)	17 (4.4)	25 (6.4)	5 (1.3)
Diarrhea/colitis	23 (5.9)	14 (3.6)	20 (5.2)	5 (1.3)	3 (0.8)	1 (0.3)	2 (0.5)	1 (0.3)
Adrenal insufficiency	6 (1.5)	1 (0.3)	1 (0.3)	0	6 (1.5)	3 (0.8)	3 (0.8)	0
Hyperthyroid events	18 (4.6)	1 (0.3)	2 (0.5)	0	4 (1.0)	0	0	0
Hypothyroid events	42 (10.8)	0	1 (0.3)	0	19 (4.9)	0	0	0
Renal events	4 (1.0)	2 (0.5)	3 (0.8)	2 (0.5)	0	0	0	0
Dermatitis/rash	19 (4.9)	7 (1.8)	12 (3.1)	2 (0.5)	3 (0.8)	1 (0.3)	3 (0.8)	1 (0.3)
Pancreatic events	9 (2.3)	7 (1.8)	7 (1.8)	0	2 (0.5)	1 (0.3)	2 (0.5)	0

Includes adverse events with onset or increase in severity on or after the date of the first dose through 90 days following the date of the last dose or the date of initiation of the first subsequent therapy. Patients may have had >1 event. Events include those that occurred in ≥1% of patients in either treatment arm.

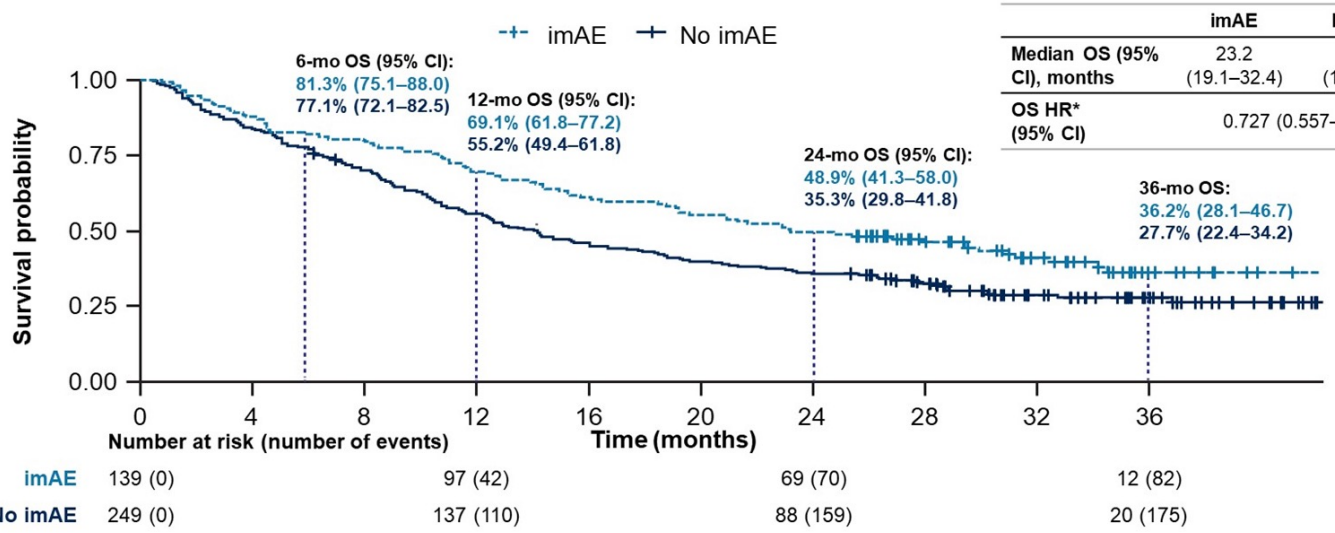
STRIDE, Single Tremelimumab Regular Interval Durvalumab.

Immune-Mediated Adverse Events (IMAE) on Durva+Treme
Correlation with Anti-Tumor Immune Response?

- Median time to IMAE onset was <90 days[1]
  - Most IMAE resolved within 60 days
  - Steroids required in 20%[2]
- Patients with IMAE had higher proportion with OS at 36 months (36.2% vs. 27.7%) on STRIDE regimen in HIMALAYA[3]
  - Both higher than sorafenib control arm

OS by imAE occurrence for STRIDE

A numerical improvement in OS was observed in participants who had an imAE versus those who did not



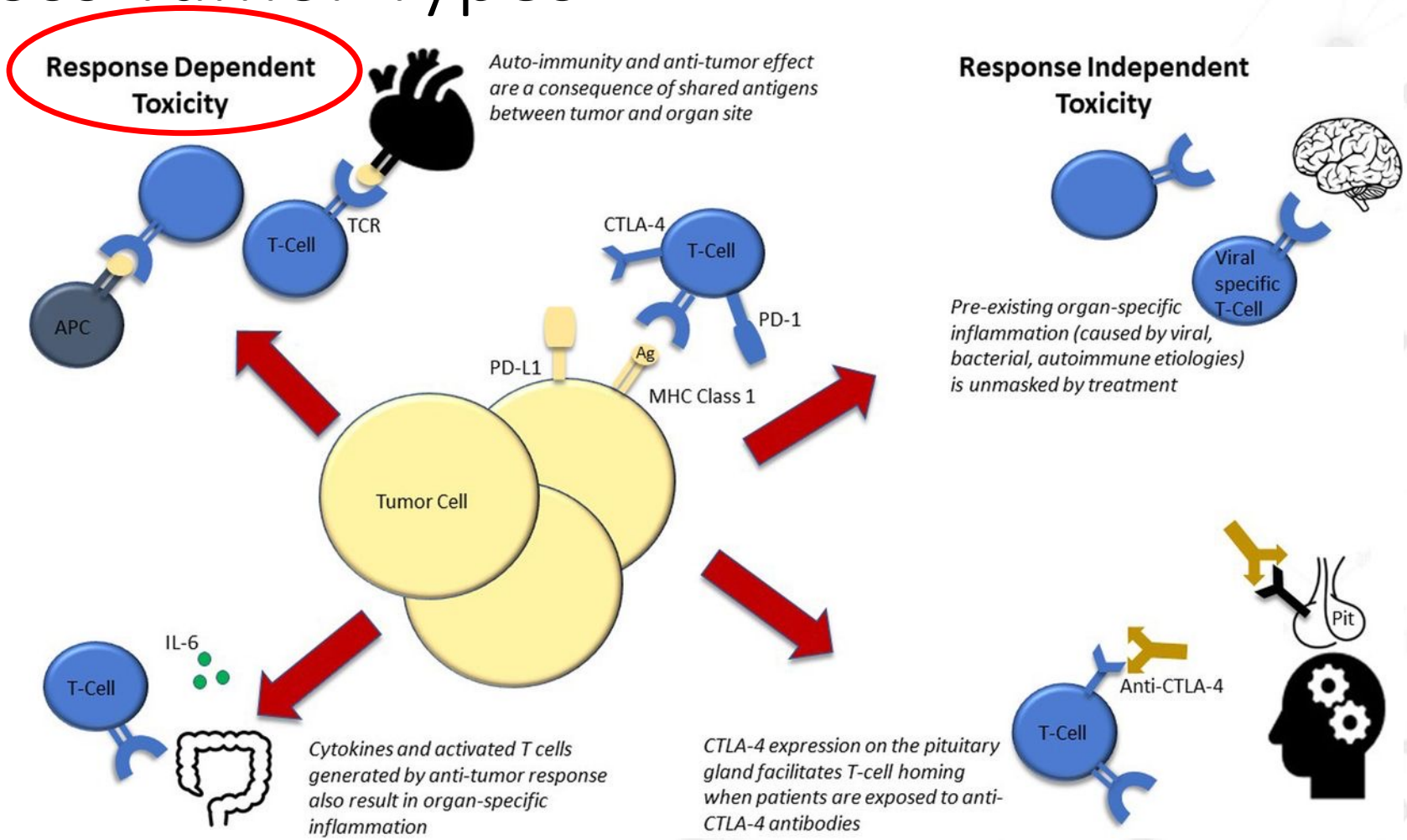
	imAE	No imAE
Median OS (95% CI), months	23.2 (19.1–32.4)	14.1 (11.6–17.9)
OS HR* (95% CI)	0.727 (0.557–0.948)	

*OS HRs and 95% CIs were calculated using Cox modeling, with imAEs as a time-varying covariate to properly account for immortal time bias and stratified by etiology, ECOG (0 / 1), and macrovascular invasion (yes / no) for participants with versus without imAEs of any grade.
CI, confidence interval; HR, hazard ratio; imAE, immune-mediated adverse event; OS, overall survival.

2023 ASCO ANNUAL MEETING #ASCO23 PRESENTED BY: George Lau, MD, FRCP, FAASLD ASCO KNOWLEDGE CONQUERS CANCE

1. Sangro et al. ILCA Annual Conference 2022, O-28; 2. Abou-Alfa et al. NEJM Evidence 2022;1(8):1-12; 3. Lau et al. ASCO Annual Meeting 2023.

Association Between IMAE and Improved Outcomes on Anti-PD1/L1 Across Tumor Types



Potential mechanisms:

- Shared Ag
- Cytokines and activated T cells causing regional organ-specific IMAE

Das and Johnson. JITC 2019;7(1):306.

IMbrave150 vs. HIMALAYA

Key Safety Parameters (All-Cause)

All-Cause AE‡	Atezo+Bev[1,2]	Durva+Treme[3]
SAE	49%	40.5%
Grade 3-4 AE	63%	50.5%
Grade 3-4 bleeding	6.4%	3.9%
Grade 3-4 A/V thrombosis	2.7%	NA (<2%)
IMAE requiring systemic steroids	NA *(expect <10% for ICI monotherapy)*	20.1%
Grade 5 AE	7%	7.7%
AE requiring discontinuation ≥ 1 drug	22%	13.7%
AE requiring interruption	59%	34.5%

- Numerically higher rates of all-cause grade 3-4 AE and bleeding/thrombotic AE with atezo+bev
- Presume higher rates imAE requiring steroid with durva+treme
- Numerically higher rates of discontinuation and interruption with atezo+bev

1. Finn et al. N Engl J Med 2020;382:1894-905; 2. Cheng et al. J Hepatol 2022;76:862-73; 3. Abou-Alfa et al. NEJM Evidence 2022;1(8):1-12. NA=not available. ‡Caution with cross-trial comparisons.

Selection Factors to Guide Choice of Atezo+Bev vs. STRIDE vs. Other in 1st Line HCC

- **In a fit, CPA patient with no significant comorbidity: I discuss both atezo+bev and STRIDE as 1st line options including ORR, PFS, OS, DOR, and landmark 4 year OS data from each regimen as well as AE profile; I believe both of these regimens are reasonable 1st line choices**
- I recommend **STRIDE** if:
  - Relative or absolute contraindications to antiangiogenic therapy: High risk varices and/or recent variceal bleed; recent venous or arterial thromboembolic event; active CAD/PVD; anticoagulation; non-healing wound; requirement for surgical/invasive procedure; high risk for cardiovascular comorbidities (e.g. elderly and/or poorly controlled DM-2, proteinuria)
- I recommend **atezo+bev** if:
  - History of autoimmune disease
  - Bulky tumor burden with high risk for complications of rapid progression
- I recommend **durvalumab** if:
  - Frailty, ECOG 2, CPB8-9, not fit for combination therapy
- I recommend **lenvatinib** if:
  - Prior transplant and/or active autoimmune disease; any other contraindications to ICI
  - Cannot receive infusional therapy for some reason (e.g. lives far away from an infusion center)
  - Low burden/indolent disease biology and wishes to avoid regular infusion treatments for a window of time (e.g. patient still working or with caregiver responsibilities)

Safety and Tolerability of Chemo-Immunotherapy for BTC

- TOPAZ-1
- KEYNOTE-966

TOPAZ-1: Safety

Table 3. Summary of Safety Data in the Safety Analysis Set.

Parameter	Durvalumab plus Gemcitabine and Cisplatin (n=338)	Placebo plus Gemcitabine and Cisplatin (n=342)
Adverse events — no. (%)		
Any grade	336 (99.4)	338 (98.8)
Serious	160 (47.3)	149 (43.6)
Grade 3 or 4	256 (75.7)	266 (77.8)
Leading to discontinuation of any study treatment	44 (13.0)	52 (15.2)
Leading to death	12 (3.6)	14 (4.1)
Treatment-related adverse events — no. (%)		
Any grade	314 (92.9)	308 (90.1)
Serious	53 (15.7)	59 (17.3)
Grade 3 or 4	212 (62.7)	222 (64.9)
Leading to discontinuation of any study treatment	30 (8.9)	39 (11.4)
Leading to death*	2 (0.6)	1 (0.3)

* Treatment-related adverse events leading to death were ischemic stroke and hepatic failure in the durvalumab treatment group and polymyositis in the placebo treatment group.

- Immune-related AE in 12.7% vs. 4.7% for durvalumab vs. placebo arms
  - Grade 3-4 immune-related AE in 2.4% vs 1.5%

Oh et al. NEJM Evidence 2022;1(8)

TOPAZ-1

Grade 3/4 AEs

Event, n (%)	Durvalumab + GemCis (n=338)	Placebo + GemCis (n=342)
Any grade 3/4 AE (≥5%)		
Anemia	80 (23.7)	77 (22.5)
Neutrophil count decreased	71 (21.0)	88 (25.7)
Neutropenia	68 (20.1)	72 (21.1)
Platelet count decreased	33 (9.8)	29 (8.5)
Cholangitis	22 (6.5)	11 (3.2)
Thrombocytopenia	16 (4.7)	18 (5.3)
White blood cell count decreased	15 (4.4)	20 (5.8)
Any grade 3/4 TRAE (≥2%)		
Neutrophil count decreased	70 (20.7)	87 (25.4)
Neutropenia	65 (19.2)	69 (20.2)
Anemia	64 (18.9)	64 (18.7)
Platelet count decreased	27 (8.0)	26 (7.6)
White blood cell count decreased	14 (4.1)	20 (5.8)
Thrombocytopenia	12 (3.6)	18 (5.3)
Fatigue	9 (2.7)	8 (2.3)
Leukopenia	7 (2.1)	2 (0.6)
Asthenia	4 (1.2)	7 (2.0)

AE, adverse event; GemCis, gemcitabine and cisplatin; TRAE, treatment-related adverse event.

Adverse Event Summary at Final Analysis

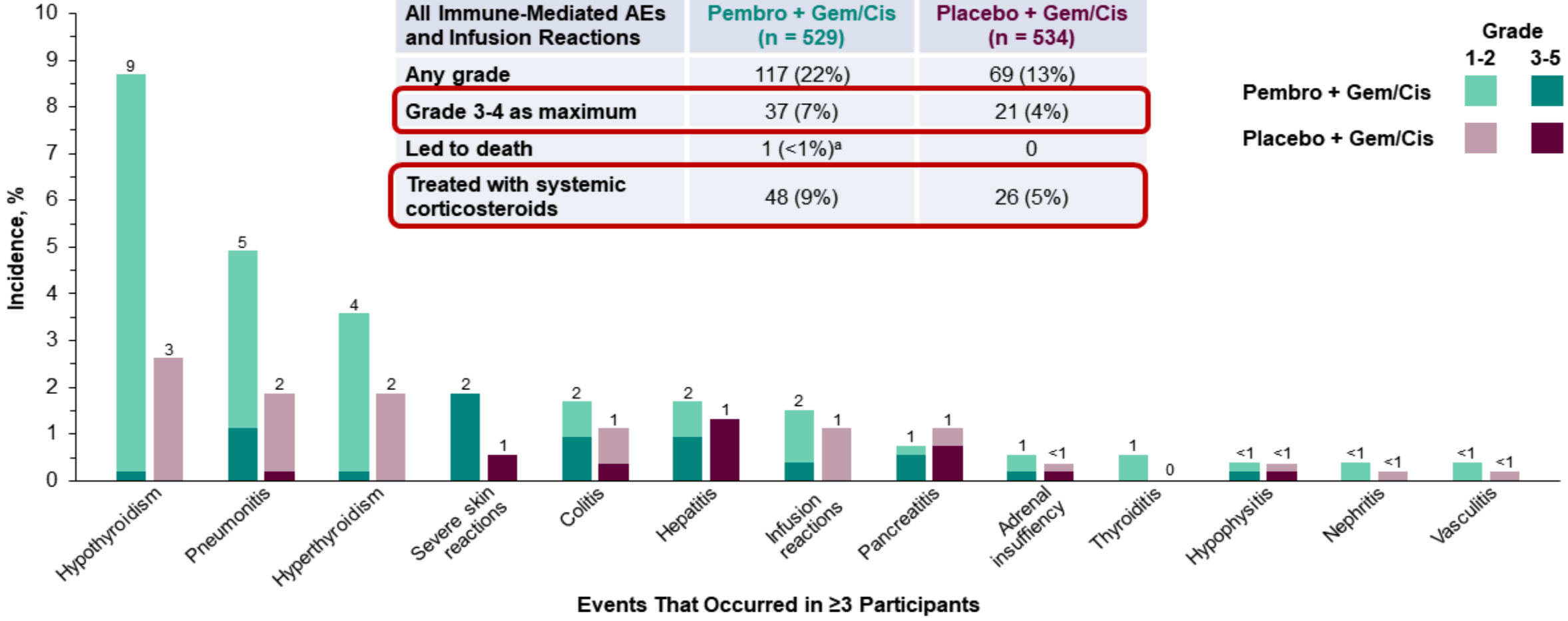
	Pembro + Gem/Cis (n = 529)	Placebo + Gem/Cis (n = 534)
Any	524 (99%)	532 (<100%)
Treatment-related	493 (93%)	500 (94%)
Grade 3-4 as maximum grade	420 (79%)	400 (75%)
Treatment-related	369 (70%)	367 (69%)
Led to death	31 (6%)	49 (9%)
Treatment-related	8 (2%)[a]	3 (1%)[b]
Led to discontinuation of ≥1 study 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%)

[a]AEs leading to death (n = 1 each): abdominal abscess, cholangitis, lower respiratory tract infection, malignant neoplasm progression, myocardial infarction, pneumonitis, septic shock, and viral pneumonia.
[b]AEs leading to death (n = 1 each): hepatorenal syndrome, sepsis, and upper gastrointestinal hemorrhage.
Data cutoff date: December 15, 2022.

KEYNOTE-966

Immune-Mediated Adverse Events and Infusion Reactions at Final Analysis

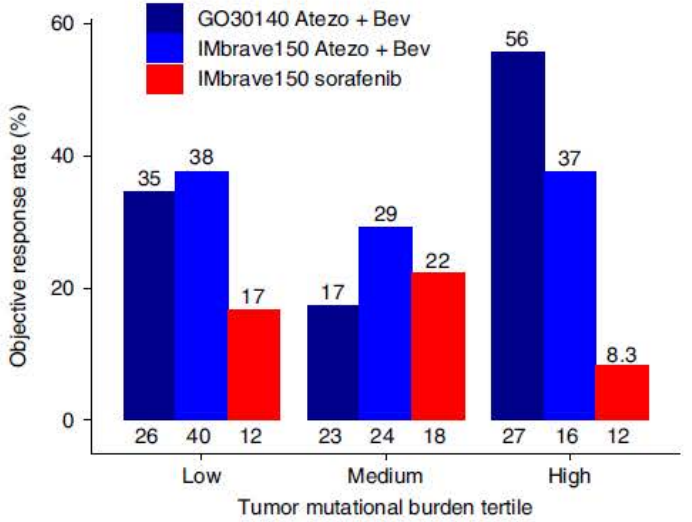
All Immune-Mediated AEs and Infusion Reactions	Pembro + Gem/Cis (n = 529)	Placebo + Gem/Cis (n = 534)
Any grade	117 (22%)	69 (13%)
Grade 3-4 as maximum	37 (7%)	21 (4%)
Led to death	1 (<1%)[a]	0
Treated with systemic corticosteroids	48 (9%)	26 (5%)

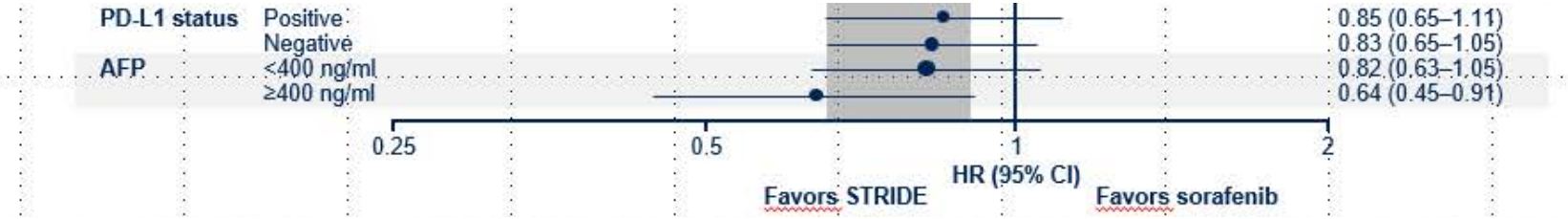


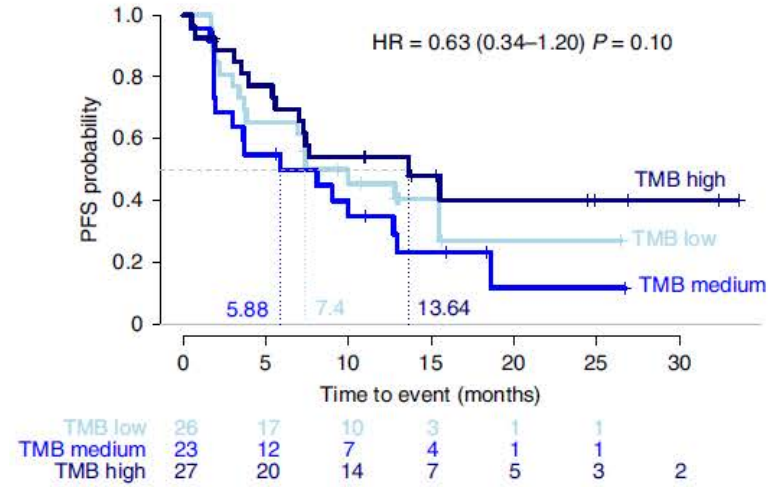
[a]Pneumonitis.
Data cutoff date: December 15, 2022.

Potential Biomarkers of Benefit from Immune Checkpoint Inhibition in HCC

- There are no established predictive biomarkers for response to ICI in HCC
  - Viral status: Does not predict ORR/PFS on ICI-based therapies; trends towards improved OS with viral status have many confounding variables
  - TMB: No significant relationship between TMB and outcomes on atezo+bev[1] or nivolumab[2] therapy
  - MSI-H patients (n=12) did not have responses in CheckMate 459[2]
  - Tumor PD-L1 expression: Non-significant trends towards greater benefit with PD-L1 expression in IMbrave150, pembrolizumab[4], and nivolumab[5]; no appreciable difference in HIMALAYA[6]



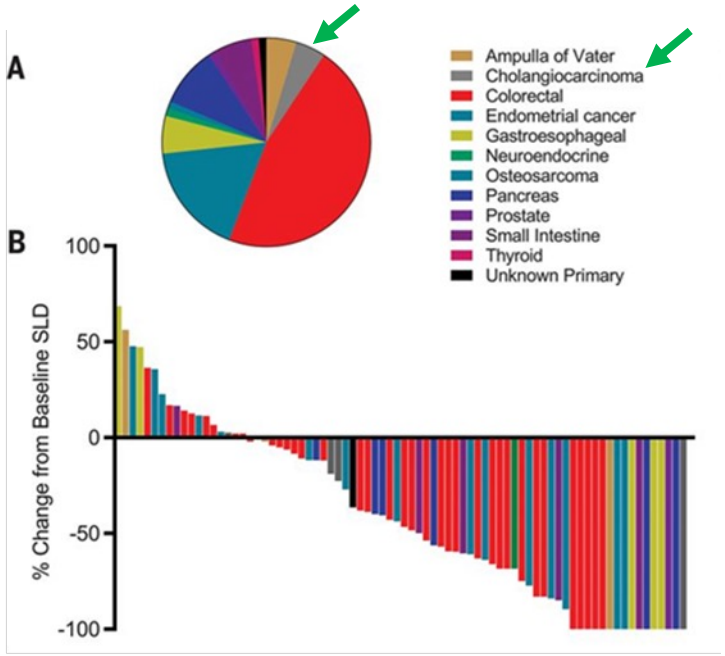




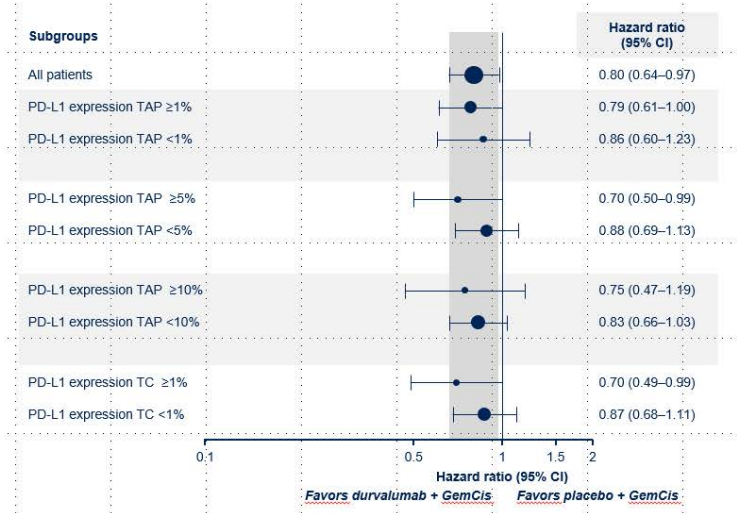
1. Zhu et al. Nat Med 2022;28:1599-1611; 2. Neely et al. AACR 2022; 3. Cheng et al. J. Hep 2022;76:862-73; 4. Zhu et al. Lancet Oncology 2018;19; 5. El-Khoueiry et al. Lancet 2017; 6. Abou-Alfa et al. NEJM Evidence 2022.

Potential Biomarkers of Benefit from Immune Checkpoint Inhibition in BTC

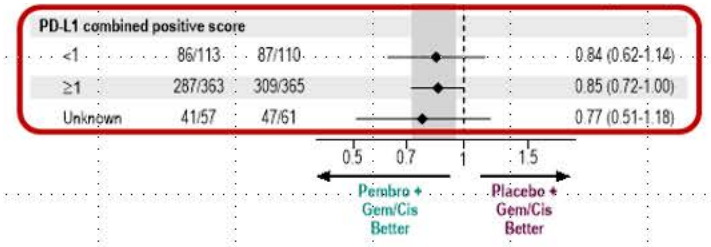
- MSI-high and/or deficient MMR is associated with high ORR on ICI as monotherapy
- High TMB may be associated with ORR but limited data specific to BTC
  - Keynote-016 and -158 showed high ORR (~40%) and prolonged DOR (>24 months) in patients with CCA with MSI-H/dMMR treated with pembrolizumab
- No significant relationship between common mutations and OS; higher ORR observed in BRCA-1/2 mutant BTC



Tumor PD-L1 status did not predict response in TOPAZ-1 or KEYNOTE-966.



Oh et al. GI ASCO 2022.



Kelley et al. AACR 2023.

1. Le et al Science 2017;357:409-13; 2. Ju et al. Am J Clin Pathol 2020153(5): 598-604; 3. Marabelle et al. J Clin Oncol 2020;38(1):1-10; 4. Marabelle et al. Lancet Oncol 2020;21(10):1353-65; 5. Oh et al. ESMO Asia 2022.

Contraindications/Cautions to ICI-Based Therapy in HCC and BTC

- Active or high-risk autoimmune disease
  - Most clinical trials have excluded patients with active or high-risk autoimmune disease
  - Retrospective studies suggest that patients with underlying autoimmune disease have higher risk for immune-related AE (IRAE)
    - History of IBD: ICI therapy associated with risk of colitis in 20%-40% of patients in retrospective case series[1,2]
    - Limited data for PSC
  - **Use of ICI in patients with active or high-risk autoimmune disease history requires multidisciplinary care and close monitoring with rheumatologist as well as counseling re: potential risk of flare/recurrence/other IRAE**
- Post organ transplant
  - Clinical trials exclude patients with prior organ transplant
  - Retrospective case series show high rates of allograft rejection when treated with ICI
    - Liver: Retrospective series report graft loss and/or death in up to ~30% of patients with prior liver transplant treated with ICI[3-5]
    - **ICI should not be used post-transplant unless under care of multidisciplinary team including liver transplant specialists and with counseling/disclosure of high risk of fatal graft loss**

1. Grover et al. JCO Oncol Practice 2020;16(9); 2. Abu-Sbeih et al. JCO 2020;38(6); 3. Runger et al. Eur J Cancer 2022;175; 4. Kayali et al. Liver Int 2023;43(1); 5. Vogel and Lleo. Liver Int 2023;43(1).

Discussion

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

Regulatory and reimbursement issues aside, what would be your preferred first-line systemic treatment for a 65-year-old patient with metastatic biliary tract cancer, no targetable mutations on NGS, PS 0 and a history of psoriasis for which they were receiving topical treatment only?

Agenda

INTRODUCTION: Interdisciplinary Management of HCC in the Community (General Medical Oncology) Setting — IR, Hepatology, Pathology Support

MODULE 1: Potential Role of Anti-PD-1/PD-L1 Antibodies in the Care of Patients with Early- and Intermediate-Stage HCC — Dr Yarchoan

MODULE 2: HCC Rounds

MODULE 3: Tolerability and Other Practical Considerations with the Use of Immune Checkpoint Inhibitors for Advanced HCC and BTCs — Dr Kelley

MODULE 4: Faculty Survey

MODULE 5: BTC Rounds

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 Kelley	Atezolizumab/bevacizumab or durvalumab/tremelimumab
 Dr Yarchoan	Atezolizumab/bevacizumab
 Dr Abou-Alfa	Durvalumab/tremelimumab
 Dr Abrams	Durvalumab/tremelimumab
 Dr Li	Atezolizumab/bevacizumab
 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 78-year-old patient with HCC, a Child-Pugh B7 score and a PS of 1?

 Dr Kelley	Durvalumab +/- tremelimumab
 Dr Yarchoan	Durvalumab/tremelimumab
 Dr Abou-Alfa	Durvalumab/tremelimumab
 Dr Abrams	Durvalumab/tremelimumab
 Dr Li	Atezolizumab/bevacizumab
 Dr Stein	Atezolizumab/bevacizumab

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 Kelley	Yes, in combination with an anti-CTLA-4 antibody
 Dr Yarchoan	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 Li	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

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 Kelley	60 years	TOPAZ-1	Some benefit
 Dr Yarchoan	46 years	TOPAZ-1	Too early to determine
 Dr Abou-Alfa	65 years	TOPAZ-1	A great deal of benefit
 Dr Abrams	34 years	TOPAZ-1	Some benefit
 Dr Li	68 years	TOPAZ-1	A great deal of 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 Kelley	Pembrolizumab + cisplatin/gemcitabine*	FOLFIRI
 Dr Yarchoan	Either durvalumab or pembrolizumab combined with cisplatin/gemcitabine	FOLFOX or FOLFIRI
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Durvalumab + nal-IRI/5-FU/LV
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Li	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Stein	Durvalumab + cisplatin/gemcitabine	FOLFIRI

LV = leucovorin

*Institutional preference for pembrolizumab

Agenda

INTRODUCTION: Interdisciplinary Management of HCC in the Community (General Medical Oncology) Setting — IR, Hepatology, Pathology Support

MODULE 1: Potential Role of Anti-PD-1/PD-L1 Antibodies in the Care of Patients with Early- and Intermediate-Stage HCC — Dr Yarchoan

MODULE 2: HCC Rounds

MODULE 3: Tolerability and Other Practical Considerations with the Use of Immune Checkpoint Inhibitors for Advanced HCC and BTCs — Dr Kelley

MODULE 4: Faculty Survey

MODULE 5: BTC Rounds

KEYNOTE-966 and TOPAZ-1: First-line therapy options for advanced BTC; managing external dwelling catheters during treatment

Stacey Stein, MD

Arndt Vogel, MD, PhD

Thomas A Abrams, MD

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TOPAZ-1: Chemotherapy dose/schedule modifications for older patients

Thomas A Abrams, MD

Ahmed Omar Kaseb, MD, CMQ

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Experience with first-line treatment of microsatellite instability-high BTC

Stacey Stein, MD

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APPENDIX

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 Kelley	About the same
 Dr Yarchoan	About the same
 Dr Abou-Alfa	Durvalumab/tremelimumab is more efficacious
 Dr Abrams	Durvalumab/tremelimumab is more efficacious
 Dr Li	Atezolizumab/bevacizumab is more efficacious
 Dr Stein	About the same

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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 Kelley	Durvalumab/tremelimumab is more tolerable
 Dr Yarchoan	About the same
 Dr Abou-Alfa	Durvalumab/tremelimumab is more tolerable
 Dr Abrams	About the same
 Dr Li	About the same
 Dr Stein	Atezolizumab/bevacizumab is more tolerable

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In general, in which situations do you use durvalumab/tremelimumab as first-line treatment for patients with 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 Yarchoan	If contraindications to bevacizumab (varices, CAD, recent bleeds), or low-volume disease likely to receive multiple lines of therapy
 Dr Abou-Alfa	All patients, except if contraindication for immune therapy
 Dr Abrams	Most first-line cases of advanced HCC
 Dr Li	If contraindication to bevacizumab
 Dr Stein	If there is a risk of bleeding

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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 Kelley	Durvalumab/tremelimumab
 Dr Yarchoan	Durvalumab/tremelimumab
 Dr Abou-Alfa	Durvalumab/tremelimumab
 Dr Abrams	Durvalumab/tremelimumab
 Dr Li	Atezolizumab/bevacizumab
 Dr Stein	Durvalumab/tremelimumab

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What was the age of the last patient in your practice with advanced hepatocellular carcinoma (HCC) who received atezolizumab/bevacizumab as first-line treatment? What was their Child-Pugh score?

	Age	Child-Pugh score
 Dr Kelley	71 years	A6
 Dr Yarchoan	44 years	A
 Dr Abou-Alfa	60 years	A
 Dr Abrams	64 years	A
 Dr Li	84 years	A6
 Dr Stein	72 years	A6

For the patient in the previous scenario with advanced HCC who received initial therapy with atezolizumab/bevacizumab, had they undergone prior local treatment? Did they undergo esophagogastroduodenoscopy (EGD)? How much benefit, if any, did the patient derive from treatment?

	Prior local Tx	EGD?	Tx benefit
 Dr Kelley	TACE, TARE, ablation	Yes	Some benefit
 Dr Yarchoan	No	Yes	Too early to determine
 Dr Abou-Alfa	No	No	Some benefit
 Dr Abrams	No	Yes	Too early to determine
 Dr Li	No	Yes	A great deal of benefit
 Dr Stein	TACE	Yes	Too early to determine

TACE = transarterial chemoembolization; TARE = transarterial radioembolization

What was the age of the last patient in your practice with advanced HCC who received durvalumab/tremelimumab as first-line treatment? What was their Child-Pugh score?

	Age	Child-Pugh score
 Dr Kelley	82 years	A6
 Dr Yarchoan	76 years	B7
 Dr Abou-Alfa	70 years	B7
 Dr Abrams	62 years	A
 Dr Li	70 years	A6
 Dr Stein	68 years	B8

For the patient in the previous scenario with advanced HCC who received initial therapy with durvalumab/tremelimumab, had they undergone prior local treatment? Did they undergo EGD? How much benefit, if any, did the patient derive from treatment?

	Prior local Tx	EGD?	Tx benefit
 Dr Kelley	No	No	A great deal of benefit
 Dr Yarchoan	No	No	Too early to determine
 Dr Abou-Alfa	No	No	A great deal of benefit
 Dr Abrams	No	No	A great deal of benefit
 Dr Li	No	Yes	Some benefit
 Dr Stein	—	Yes	Too early to determine

Do you actively screen for varices in your patients with HCC for whom you are considering treatment with atezolizumab/bevacizumab?

 Dr Kelley	Yes
 Dr Yarchoan	Yes
 Dr Abou-Alfa	Yes
 Dr Abrams	Yes
 Dr Li	Yes
 Dr Stein	Yes

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 history of transient ischemic attack 3 months ago?

 Dr Kelley	Durvalumab/tremelimumab
 Dr Yarchoan	Durvalumab/tremelimumab
 Dr Abou-Alfa	Durvalumab/tremelimumab
 Dr Abrams	Durvalumab/tremelimumab
 Dr Li	Durvalumab/tremelimumab
 Dr Stein	Durvalumab/tremelimumab

RTP RESEARCH TO PRACTICE

What is your usual first-line systemic therapy for HCC in a patient you have determined to be ineligible for an immune checkpoint inhibitor?

 Dr Kelley	Lenvatinib
 Dr Yarchoan	Lenvatinib
 Dr Abou-Alfa	Lenvatinib
 Dr Abrams	Lenvatinib
 Dr Li	Lenvatinib
 Dr Stein	Lenvatinib

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 with AFP at 2,500 ng/mL? AFP at 200 ng/mL?

	AFP 2,500 ng/mL	AFP 200 ng/mL
 Dr Kelley	Lenvatinib	Lenvatinib
 Dr Yarchoan	Lenvatinib or cabozantinib	Lenvatinib or cabozantinib
 Dr Abou-Alfa	Lenvatinib	Lenvatinib
 Dr Abrams	Lenvatinib	Lenvatinib
 Dr Li	Lenvatinib	Lenvatinib
 Dr Stein	Lenvatinib	Lenvatinib

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 durvalumab/tremelimumab with minimal toxicity, had stable disease for 14 months and then experienced disease progression with AFP at 2,500 ng/mL? AFP at 200 ng/mL?

	AFP 2,500 ng/mL	AFP 200 ng/mL
 Dr Kelley	Lenvatinib	Lenvatinib
 Dr Yarchoan	Lenvatinib	Lenvatinib
 Dr Abou-Alfa	Booster dose of tremelimumab and maintain durvalumab	Booster dose of tremelimumab and maintain durvalumab
 Dr Abrams	Lenvatinib	Lenvatinib
 Dr Li	Lenvatinib	Lenvatinib
 Dr Stein	Lenvatinib	Lenvatinib

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 with AFP at 2,500 ng/mL? AFP at 200 ng/mL?

	AFP 2,500 ng/mL	AFP 200 ng/mL
 Dr Kelley	Cabozantinib	Cabozantinib
 Dr Yarchoan	Lenvatinib or cabozantinib	Lenvatinib or cabozantinib
 Dr Abou-Alfa	Lenvatinib	Lenvatinib
 Dr Abrams	Lenvatinib	Lenvatinib
 Dr Li	Lenvatinib	Lenvatinib
 Dr Stein	Lenvatinib	Lenvatinib

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 durvalumab/tremelimumab with minimal toxicity, had stable disease for 14 months and then experienced disease progression with AFP at 2,500 ng/mL? AFP at 200 ng/mL?

	AFP 2,500 ng/mL	AFP 200 ng/mL
 Dr Kelley	Cabozantinib	Cabozantinib
 Dr Yarchoan	Lenvatinib	Lenvatinib
 Dr Abou-Alfa	Booster dose of tremelimumab and maintain durvalumab	Booster dose of tremelimumab and maintain durvalumab
 Dr Abrams	Lenvatinib	Lenvatinib
 Dr Li	Lenvatinib	Lenvatinib
 Dr Stein	Lenvatinib	Lenvatinib

Which assay or assays do you generally use to test for targetable mutations in your patients with advanced biliary tract cancer?

 Dr Kelley	DNA-based NGS, HER2 IHC/FISH
 Dr Yarchoan	Both DNA- and RNA-based NGS
 Dr Abou-Alfa	DNA-based NGS
 Dr Abrams	DNA-based NGS
 Dr Li	Both DNA- and RNA-based NGS
 Dr Stein	DNA-based NGS

NGS = next-generation sequencing

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for an 80-year-old patient with controlled hypertension and diabetes with metastatic biliary tract cancer and no targetable mutations on NGS?

	First-line Tx	Second-line Tx
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine*	FOLFIRI
 Dr Yarchoan	Either durvalumab or pembrolizumab combined with cisplatin/gemcitabine	FOLFOX or FOLFIRI
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Durvalumab + nal-IRI/5-FU/LV
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Li	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Stein	Durvalumab + cisplatin/gemcitabine	FOLFOX

*Institutional preference for pembrolizumab

What was the age of the last patient in your practice with metastatic biliary tract cancer who received targeted treatment? What specific treatment regimen did the patient receive? How much benefit, if any, did the patient derive from treatment?

	Age	Tx received	Tx benefit
 Dr Kelley	32 years	Trastuzumab deruxtecan	Some benefit
 Dr Yarchoan	68 years	Futibatinib	Too early to determine
 Dr Abou-Alfa	68 years	Ivosidenib	A great deal of benefit
 Dr Abrams	25 years	Futibatinib	Some benefit
 Dr Li	40 years	Futibatinib	A great deal of benefit
 Dr Stein	36 years	Pemigatinib	Seems to have early PD

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 Kelley	Pembrolizumab + cisplatin/gemcitabine*	Zanidatamab
 Dr Yarchoan	Would consider anti-PD-1 + anti-HER2 + gemcitabine/cisplatin	Zanidatamab
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan or zanidatamab
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	Trastuzumab/pertuzumab
 Dr Li	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan
 Dr Stein	Durvalumab + cisplatin/gemcitabine	Tucatinib/trastuzumab

*Institutional preference for pembrolizumab

Regulatory and reimbursement issues aside, for a patient with advanced biliary tract cancer and HER2 amplification, in which line of therapy would you generally administer anti-HER2 therapy?

 Dr Kelley	Second
 Dr Yarchoan	Second
 Dr Abou-Alfa	I would only administer anti-HER2 therapy as part of a clinical trial
 Dr Abrams	Second
 Dr Li	Second
 Dr Stein	Second

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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 Kelley	Pembrolizumab + cisplatin/gemcitabine*	Ivosidenib
 Dr Yarchoan	Either durvalumab or pembrolizumab combined with cisplatin/gemcitabine	Ivosidenib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Li	Durvalumab + 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 IDH2 mutation (PS 0)?

	First-line Tx	Second-line Tx
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine*	FOLFOX or FOLFIRI
 Dr Yarchoan	Either durvalumab or pembrolizumab combined with cisplatin/gemcitabine	FOLFOX or FOLFIRI (while trying to get enasidenib)
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Durvalumab + nal-IRI/5-FU/LV
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	Enasidenib
 Dr Li	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Stein	Durvalumab + cisplatin/gemcitabine	FOLFOX

*Institutional preference for pembrolizumab

Regulatory and reimbursement issues aside, for a patient with advanced biliary tract cancer and an IDH mutation, in which line of therapy would you generally administer anti-IDH therapy?

 Dr Kelley	Second
 Dr Yarchoan	Second
 Dr Abou-Alfa	Second
 Dr Abrams	Second
 Dr Li	Second
 Dr Stein	Second

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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 Kelley	Pembrolizumab + cisplatin/gemcitabine*	Futibatinib
 Dr Yarchoan	Either durvalumab or pembrolizumab combined with cisplatin/gemcitabine	Futibatinib or pemigatinib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Dr Abrams	Durvalumab + cisplatin/gemcitabine	Futibatinib
 Dr Li	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Dr Stein	Durvalumab + cisplatin/gemcitabine	Pemigatinib

*Institutional preference for pembrolizumab

Regulatory and reimbursement issues aside, for a patient with advanced biliary tract cancer and an FGFR alteration, in which line of therapy would you generally administer anti-FGFR therapy?

 Dr Kelley	Second
 Dr Yarchoan	First (in select cases) and second
 Dr Abou-Alfa	Second
 Dr Abrams	Second
 Dr Li	Second
 Dr Stein	Second

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Regulatory and reimbursement issues aside, would you consider a second FGFR inhibitor for a patient with metastatic biliary tract cancer who had previously experienced disease progression while receiving a different FGFR inhibitor?

 Dr Kelley	Yes, depends on acquired FGFR2 resistance mutation
 Dr Yarchoan	Yes, I would try futibatinib after pemigatinib
 Dr Abou-Alfa	Yes, futibatinib after pemigatinib
 Dr Abrams	Yes, I would try futibatinib after failure of pemigatinib
 Dr Li	Yes, futibatinib
 Dr Stein	Yes, futibatinib

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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

Urothelial Bladder Cancer

Thursday, February 22, 2024
5:00 PM – 6:00 PM ET

Faculty

Shilpa Gupta, MD

Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

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