Meet The Professor
Optimizing the Management of Hepatobiliary Cancers

Ghassan Abou-Alfa, MD, MBA
Attending
Memorial Sloan Kettering Cancer Center
Professor
Weill Cornell College at Cornell University
New York, New York

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Commercial Support

This activity is supported by an educational grant from AstraZeneca Pharmaceuticals LP.

Dr Love — Disclosures

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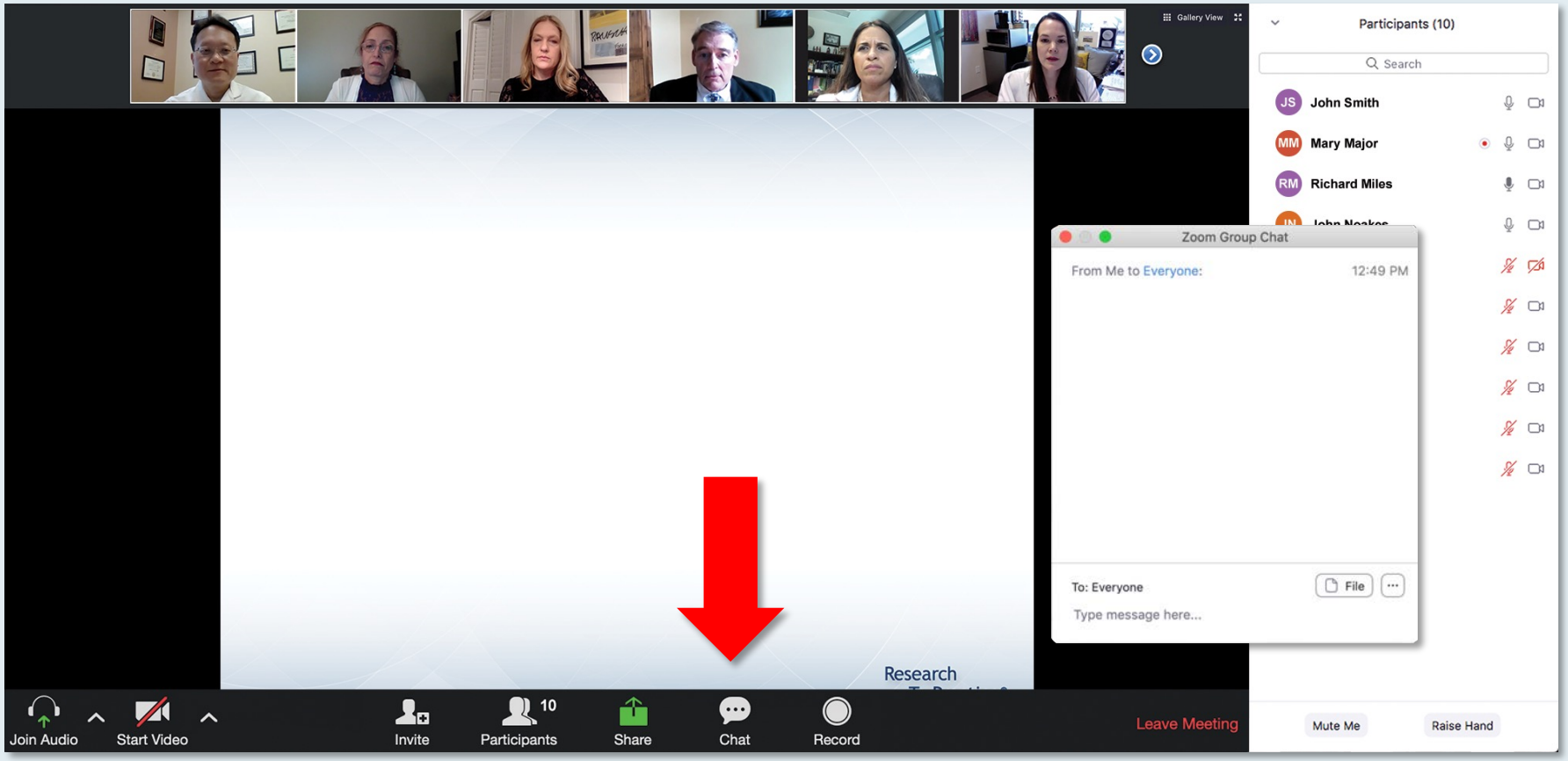
Contracted Research	Arcus Biosciences, AstraZeneca Pharmaceuticals LP, BioNTech, Bristol-Myers Squibb Company, Celgene Corporation, Flatiron Health, Genentech, a member of the Roche Group, Genoscience Pharma, Incyte Corporation, Polaris Group, Puma Biotechnology Inc, QED Therapeutics, Silenseed Ltd, Yiviva

We Encourage Clinicians in Practice to Submit Questions



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

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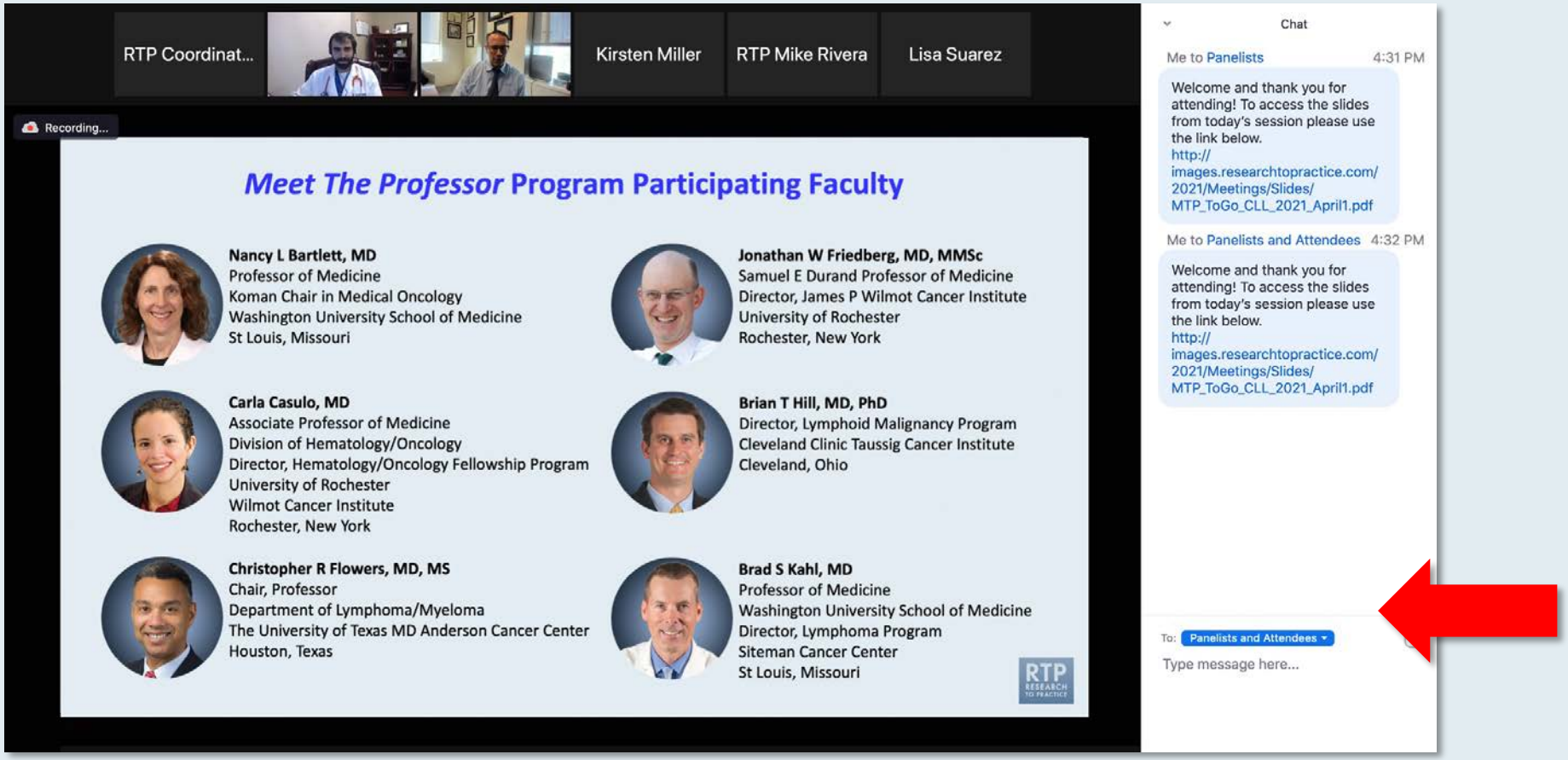
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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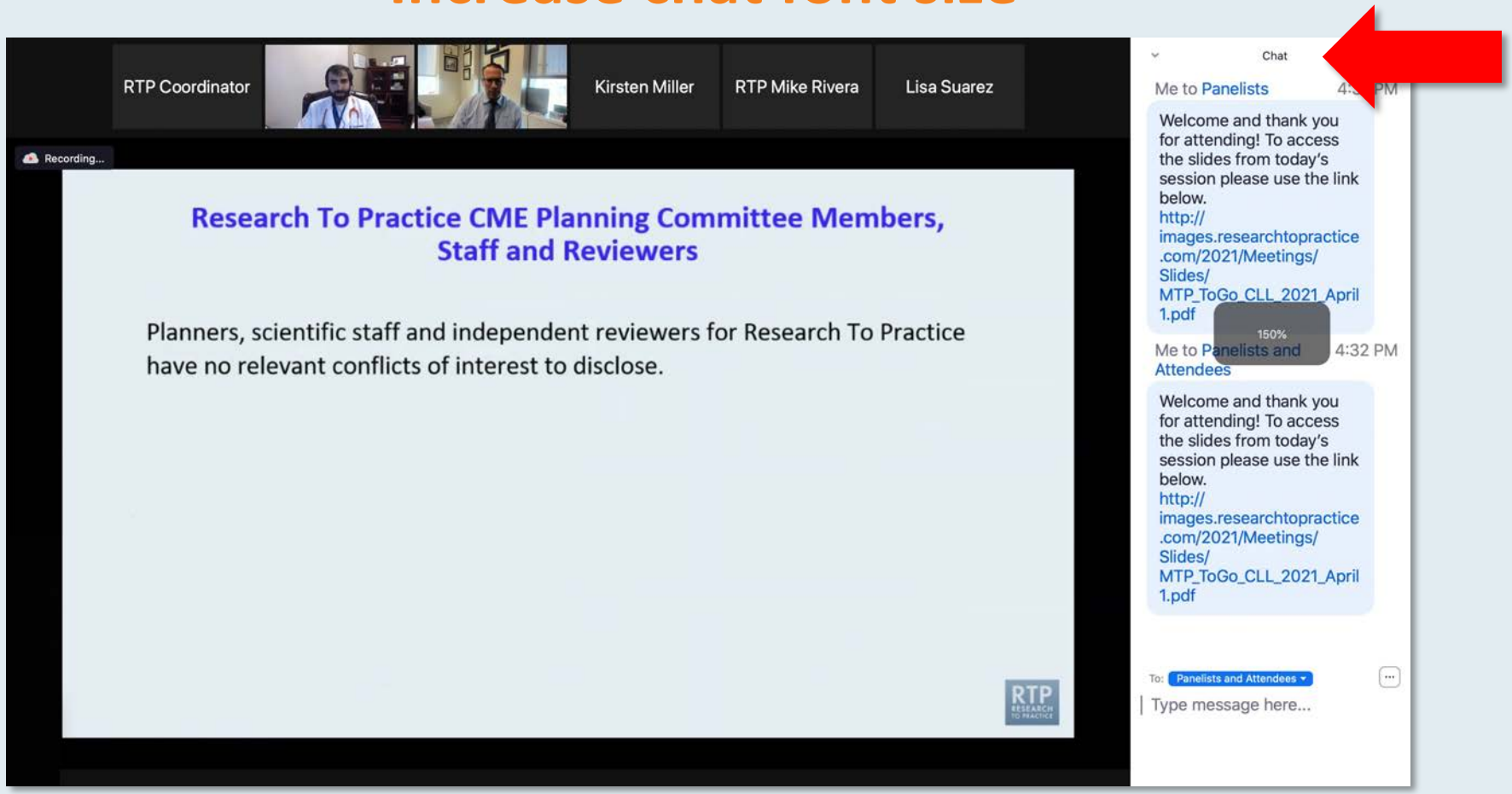

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ONCOLOGY TODAY

WITH DR NEIL LOVE

New Directions in the Management of Biliary Tract Cancers

PROF JUAN VALLE

UNIVERSITY OF MANCHESTER

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Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Tuesday, July 12, 2022
5:00 PM – 6:00 PM ET

Faculty

Samuel J Klempner, MD

Moderator

Neil Love, MD

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Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes – A Review of the 2022 ASCO Annual Meeting and EHA Congress

Wednesday, July 13, 2022
5:00 PM – 6:00 PM ET

Faculty

Richard M Stone, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Chronic Myeloid Leukemia

Tuesday, July 19, 2022
5:00 PM – 6:00 PM ET

Faculty

Daniel J DeAngelo, MD, PhD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Robin K Kelley, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Ovarian Cancer

Wednesday, August 3, 2022
5:00 PM – 6:00 PM ET

Faculty

Prof Jonathan A Ledermann

Moderator

Neil Love, MD

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TO PRACTICE

Recent Advances in Medical Oncology:
A daylong CME hybrid (live/online) event

Saturday, August 6, 2022

9:00 AM – 4:30 PM PT (12:00 PM – 7:30 PM ET)

Bellagio Las Vegas | Las Vegas, Nevada

Faculty

Neeraj Agarwal, MD
Harold J Burstein, MD, PhD
Ibiayi Dagogo-Jack, MD
Rafael Fonseca, MD
Brad S Kahl, MD
Rutika Mehta, MD, MPH
Craig Moskowitz, MD
Joyce O'Shaughnessy, MD
Krina Patel, MD, MSc
Philip A Philip, MD, PhD, FRCP
Suresh S Ramalingam, MD
Sandy Srinivas, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Meet The Professor Program Participating Faculty

Ghassan Abou-Alfa, MD, MBA
Attending
Memorial Sloan Kettering Cancer Center
Professor
Weill Cornell College at Cornell University
New York, New York

MODERATOR
Neil Love, MD
Research To Practice

Robin K (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

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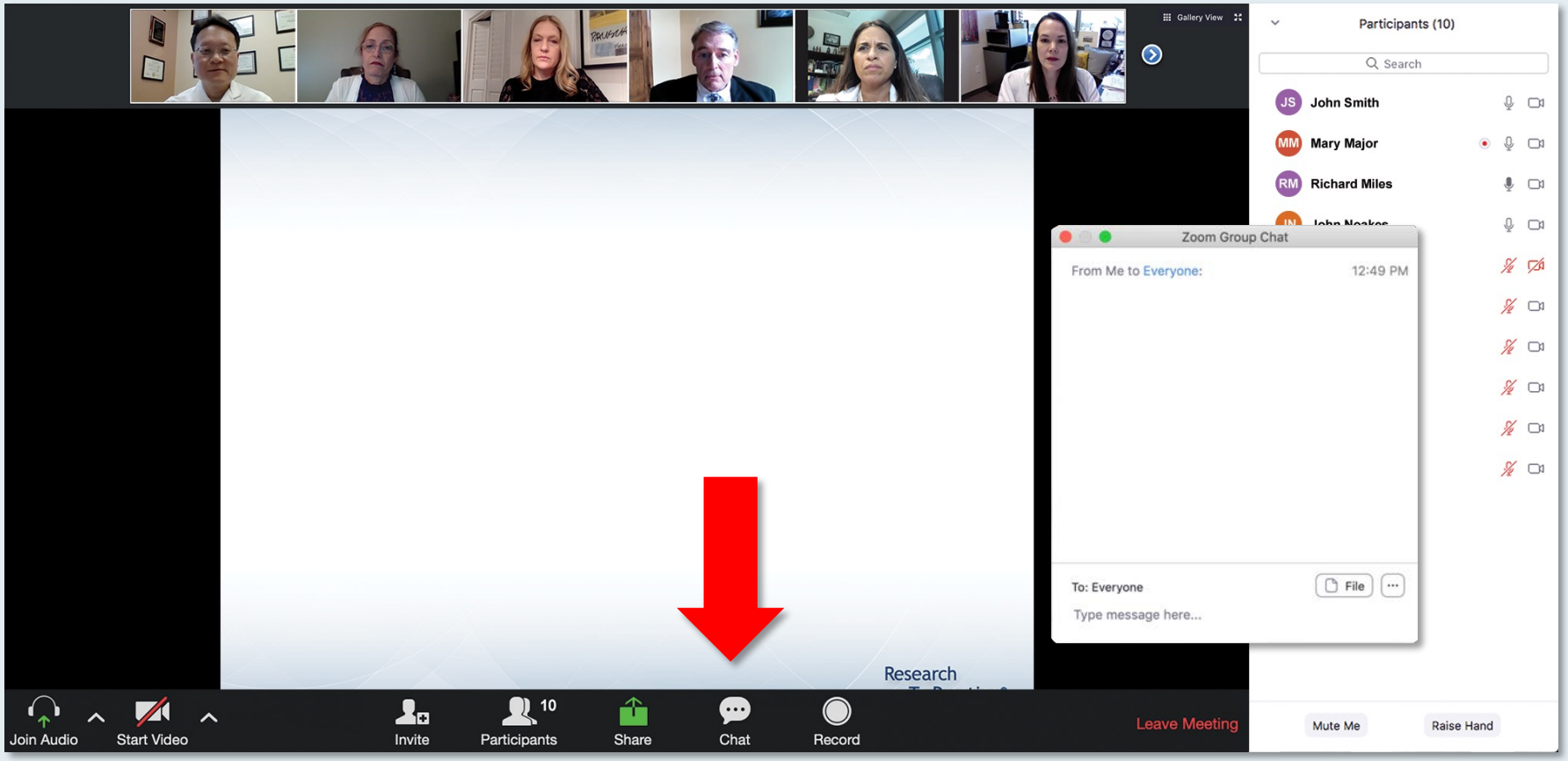

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Jennifer L Dallas, MD
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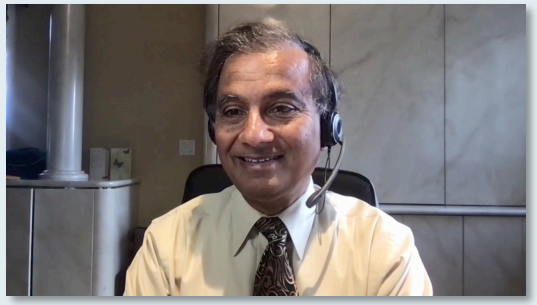
Deland, Florida



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Florida Cancer Specialists
Lecanto, Florida

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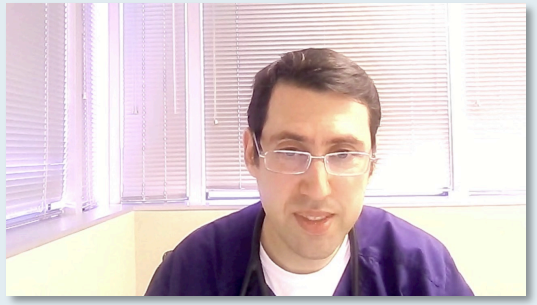
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina



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Florida Cancer Specialists
Fort Myers, Florida

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hepatobiliary Cancers (Part 3 of a 3-Part Series)

Friday, January 21, 2022
6:15 PM – 7:45 PM ET

Faculty

Ghassan Abou-Alfa, MD, MBA
Richard S Finn, MD
Robin K Kelley, MD

Moderator

Tanios Bekaii-Saab, MD

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Meet The Professor with Prof Abou-Alfa

MODULE 1: Hepatocellular Carcinoma (HCC)

- Key recent data sets
- Case presentations
- Journal Club with Prof Abou-Alfa

MODULE 2: Biliary Tract Cancers

- Key recent data set
- Case presentations
- Additional recent data sets; Journal Club with Prof Abou-Alfa

MODULE 3: Appendix of Key Publications

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- Key recent data sets
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- Journal Club with Prof Abou-Alfa

MODULE 2: Biliary Tract Cancers

- Key recent data set
- Case presentations
- Additional recent data sets; Journal Club with Prof Abou-Alfa

MODULE 3: Appendix of Key Publications

Case Presentation: A 51-year-old woman with metastatic hepatoid carcinoma of the ovary with an FGFR fusion

Dr Syed Ahmed (Libertyville, Illinois)

ASCO Gastrointestinal Cancers Symposium 2022 | Abstract 379

Phase 3 randomized, open-label, multicenter study of tremelimumab and durvalumab as first-line therapy in patients with unresectable hepatocellular carcinoma: HIMALAYA

Ghassan K Abou-Alfa,[1,2*] Stephen L Chan,[3*] Masatoshi Kudo,[4*] George Lau,[5*] Robin Kate Kelley,[6] Junji Furuse,[7] Wattana Sukeepaisarnjaroen,[8] Yoon-Koo Kang,[9] Tu V Dao,[10] Enrico N De Toni,[11] Lorenza Rimassa,[12,13] Valery Breder,[14] Alexander Vasilyev,[15] Alexandra Heurgué,[16] Vincent C Tam,[17] Kabir Mody,[18] Satheesh Chiradoni Thungappa,[19] Philip He,[20] Alejandra Negro,[20] and Bruno Sangro[21]

[1]Department of Medicine, Memorial Sloan Kettering Center, New York, NY, USA; [2]Weill Medical College, Cornell University, New York, NY, USA; [3]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, China; [4]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan; [5]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong, China; [6]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA; [7]Department of Medical Oncology, Kyorin University Faculty of Medicine, Mitaka, Japan; [8]Department of Medicine, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand; [9]Department of Oncology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea; [10]Cancer Research and Clinical Trial Center, National Cancer Hospital, Hanoi, Vietnam; [11]Department of Medicine II, University Hospital, LMU Munich, Munich, Germany; [12]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy; [13]Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy; [14]Chemotherapy Department No17, N.N. Blokhin Russian Cancer Research Center, Moscow, Russia; [15]Railway Clinical Hospital, St. Petersburg, Russia; [16]Service d'Hépato-Gastro-entérologie, Hôpital Robert-Debré, Reims, France; [17]Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada; [18]Division of Hematology/Oncology, Department of Medicine, Mayo Clinic, Jacksonville, FL, USA; [19] Sri Venkateshwara Hospital, Bangalore, India; [20]AstraZeneca, Gaithersburg, MD, USA; [21]Liver Unit and HPB Oncology Area, Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain

*Drs Ghassan K Abou-Alfa, Stephen L Chan, Masatoshi Kudo, and George Lau contributed equally to this work.

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

NEJM Evidence

Published June 6, 2022

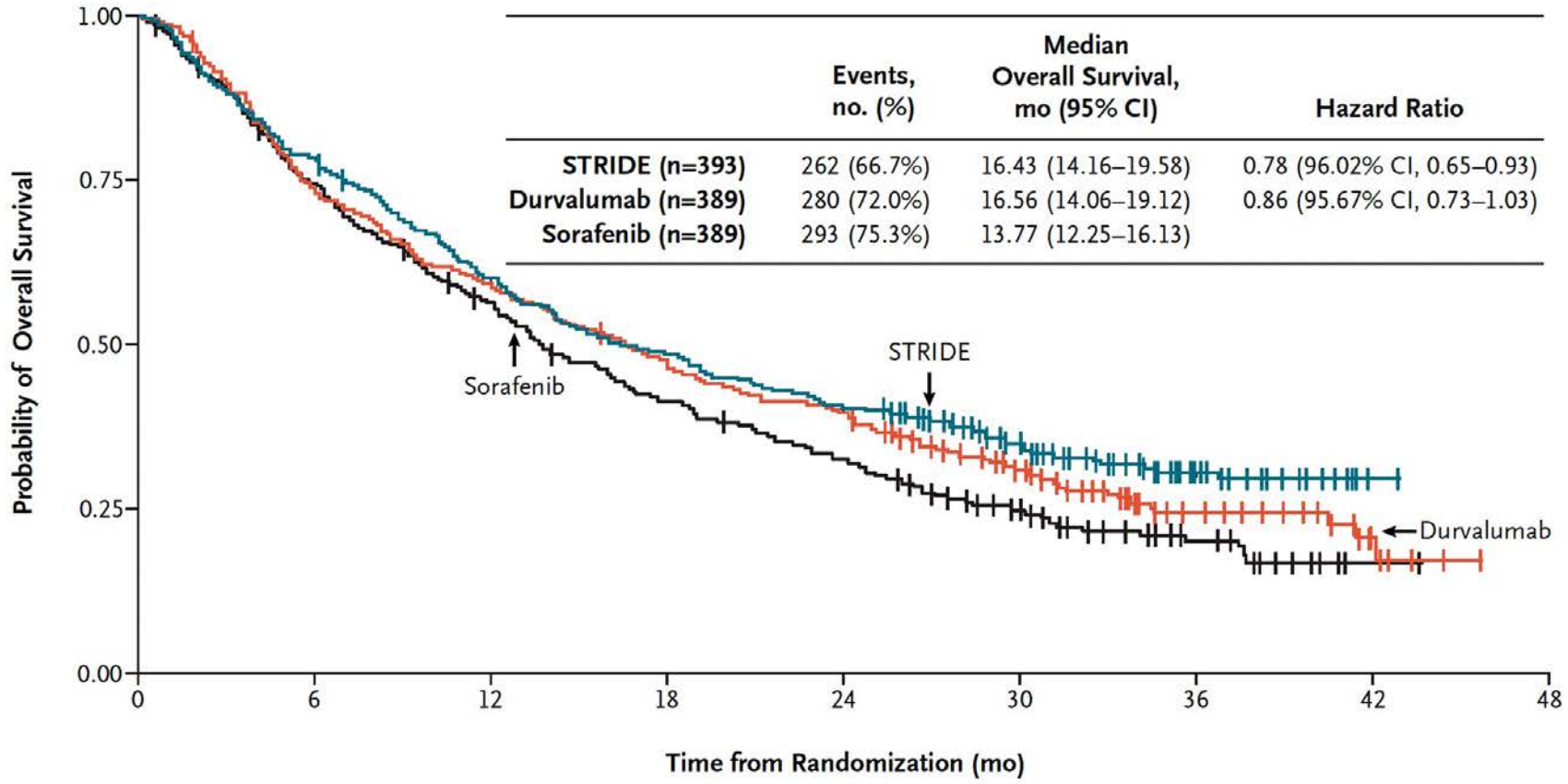
DOI: 10.1056/EVIDoa2100070

ORIGINAL ARTICLE

Tremelimumab Plus Durvalumab in Unresectable Hepatocellular Carcinoma

Ghassan K. Abou-Alfa, M.D., M.B.A.,[1,2] George Lau, M.D., F.R.C.P.,[3] Masatoshi Kudo, M.D., Ph.D.,[4] Stephen L. Chan, M.D.,[5] Robin Kate Kelley, M.D.,[6] Junji Furuse, M.D., Ph.D.,[7] Wattana Sukeepaisarnjaroen, M.D.,[8] Yoon-Koo Kang, M.D., Ph.D.,[9] Tu Van Dao, M.D., Ph.D.,[10] Enrico N. De Toni, M.D., Ph.D.,[11] Lorenza Rimassa, M.D.,[12,13] Valeriy Breder, M.D., Ph.D.,[14] Alexander Vasilyev, M.D.,[15] Alexandra Heurgué, M.D.,[16] Vincent C. Tam, M.D.,[17] Kabir Mody, M.D.,[18] Satheesh Chiradoni Thungappa, M.D.,[19] Yuriy Ostapenko, M.D.,[20] Thomas Yau, M.D.,[21] Sergio Azevedo, M.D.,[22] María Varela, M.D., Ph.D.,[23] Ann-Lii Cheng, M.D., Ph.D.,[24] Shukui Qin, M.D., Ph.D.,[25] Peter R. Galle, M.D., Ph.D.,[26] Sajid Ali, M.D.,[27] Michelle Marcovitz, Ph.D.,[27] Mallory Makowsky, Pharm.D.,[27] Philip He, Ph.D.,[27] John F. Kurland, Ph.D.,[27] Alejandra Negro, Ph.D.,[27] and Bruno Sangro, M.D., Ph.D.[28]

HIMALAYA: Overall Survival

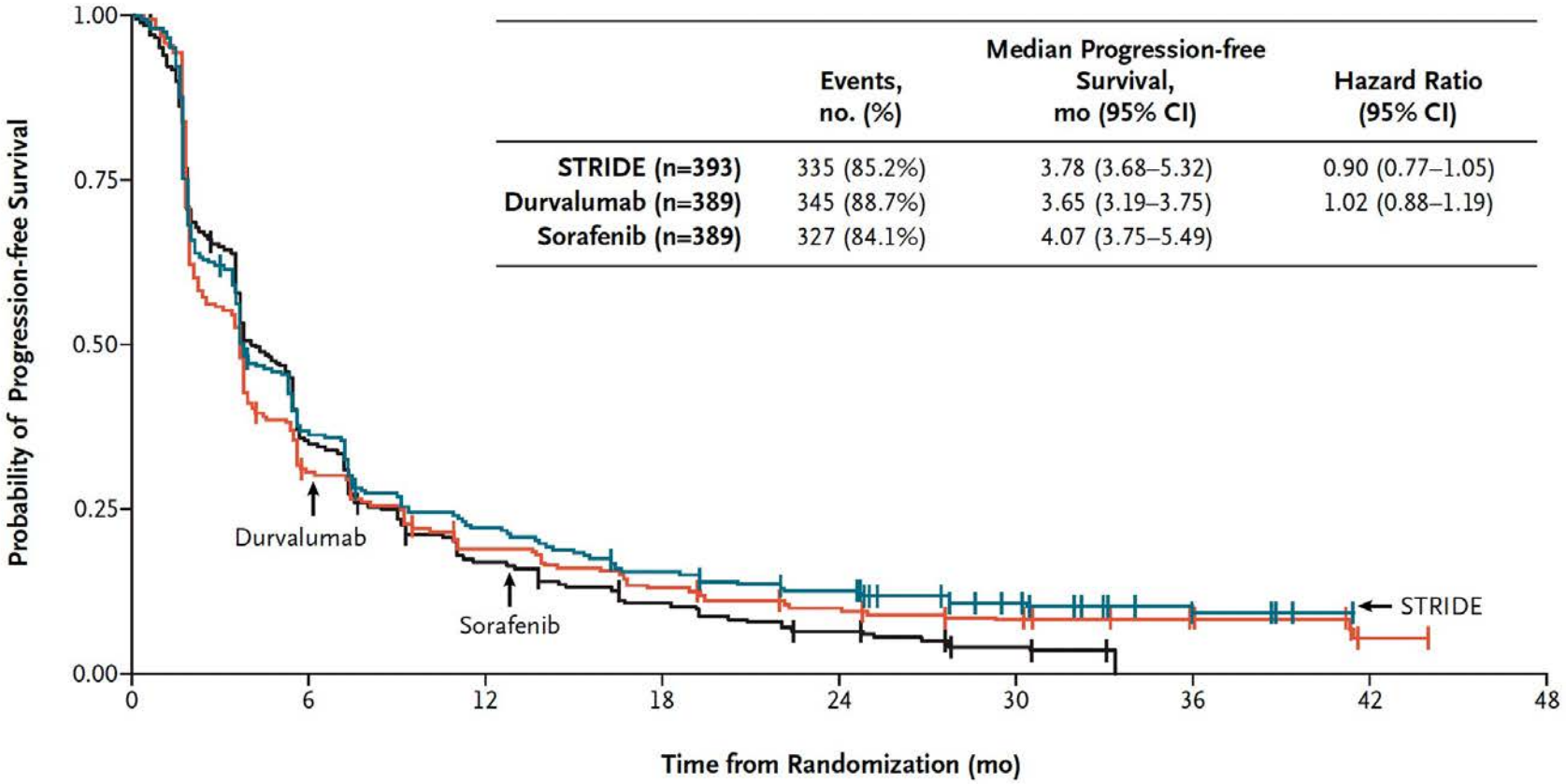


	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

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

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Progression-Free Survival



	Events, no. (%)	Median Progression-free Survival, mo (95% CI)	Hazard Ratio (95% CI)
STRIDE (n=393)	335 (85.2%)	3.78 (3.68–5.32)	0.90 (0.77–1.05)
Durvalumab (n=389)	345 (88.7%)	3.65 (3.19–3.75)	1.02 (0.88–1.19)
Sorafenib (n=389)	327 (84.1%)	4.07 (3.75–5.49)	

No. at Risk									
STRIDE	393	135	81	55	43	26	7	0	0
Durvalumab	389	115	68	47	34	20	6	1	0
Sorafenib	389	118	53	31	18	6	0	0	0

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Response Outcomes (Intent-to-Treat Population)

Parameter	STRIDE (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
Response — no. (%)			
Objective†	79 (20.1)	66 (17.0)	20 (5.1)
Complete	12 (3.1)	6 (1.5)	0
Partial	67 (17.0)	60 (15.4)	20 (5.1)
Stable disease — no. (%)	157 (39.9)	147 (37.8)	216 (55.5)
Disease control rate — %	236 (60.1)	213 (54.8)	236 (60.7)
Duration of response — mo‡			
Median	22.34	16.82	18.43
IQR	8.54–NR	7.43–NR	6.51–25.99
Time to response — mo			
Median	2.17	2.09	3.78

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

Research Article
Hepatic and Biliary Cancer

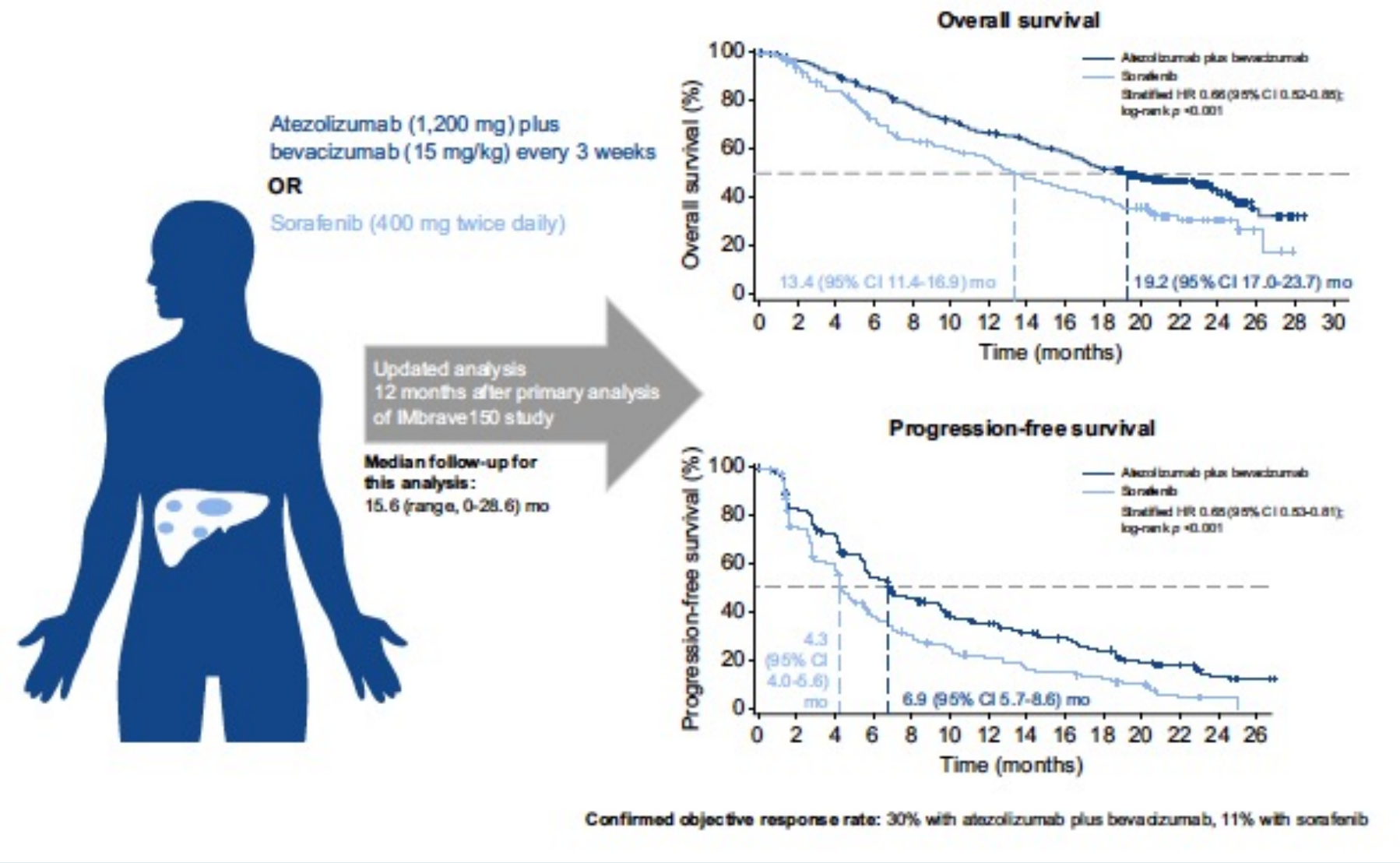
JOURNAL
OF HEPATOLOGY

Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab *vs.* sorafenib for unresectable hepatocellular carcinoma

Ann-Lii Cheng[1,*], Shukui Qin[2], Masafumi Ikeda[3], Peter R. Galle[4], Michel Ducreux[5], Tae-You Kim[6], Ho Yeong Lim[7], Masatoshi Kudo[8], Valeriy Breder[9], Philippe Merle[10], Ahmed O. Kaseb[11], Daneng Li[12], Wendy Verret[13], Ning Ma[14], Alan Nicholas[15], Yifan Wang[16], Lindong Li[17], Andrew X. Zhu[18,19], Richard S. Finn[20,*]

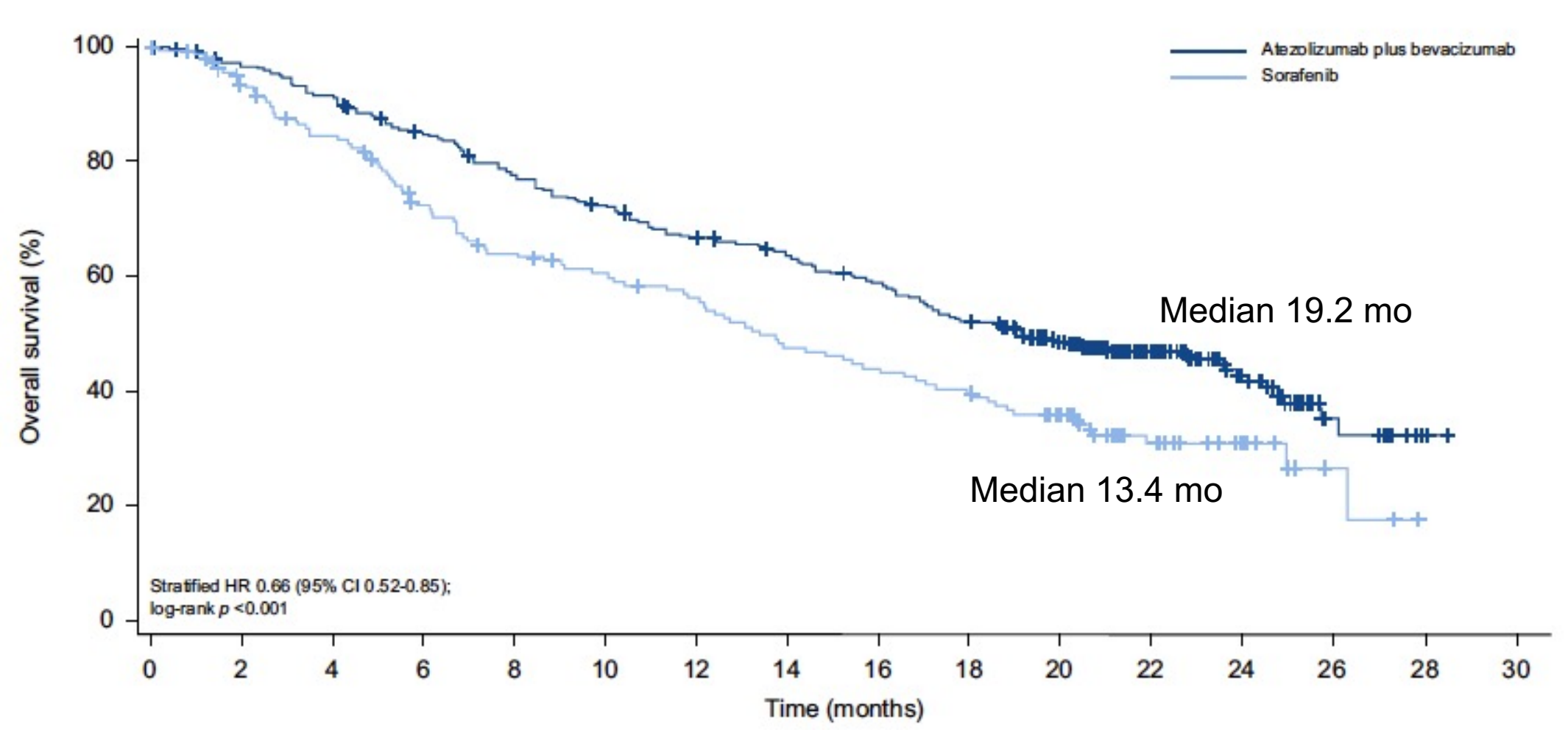
J Hepatol 2022;76(4):862-73.

IMbrave150: Updated 5-Year OS and PFS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



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

IMbrave150: Updated 5-Year OS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



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

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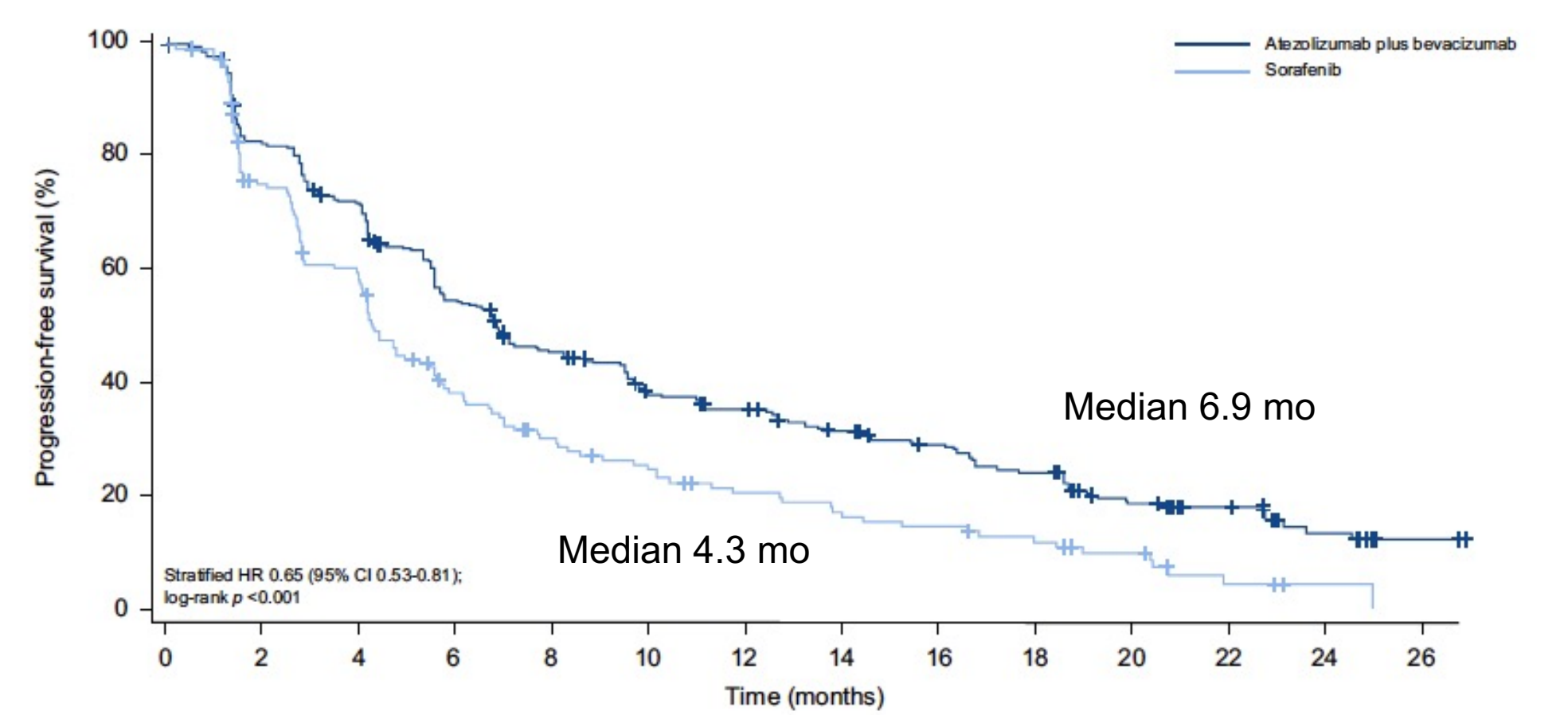

Cheng A-L et al. *J Hepatol* 2022;76(4):862-73.

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Lancet Oncol 2022;[Online ahead of print].

Cabozantinib plus atezolizumab versus sorafenib for advanced hepatocellular carcinoma (COSMIC-312): a multicentre, open-label, randomised, phase 3 trial

Robin Kate Kelley, Lorenza Rimassa*, Ann-Lii Cheng, Ahmed Kaseb, Shukui Qin, Andrew X Zhu, Stephen L Chan, Tamar Melkadze, Wattana Sukeepaisarnjaroen, Valery Breder, Gontran Verset, Edward Gane, Ivan Borbath, Jose David Gomez Rangel, Baek-Yeol Ryoo, Tamta Makharadze, Philippe Merle, Fawzi Benzaghou, Kamalika Banerjee, Saswati Hazra, Jonathan Fawcett, Thomas Yau*

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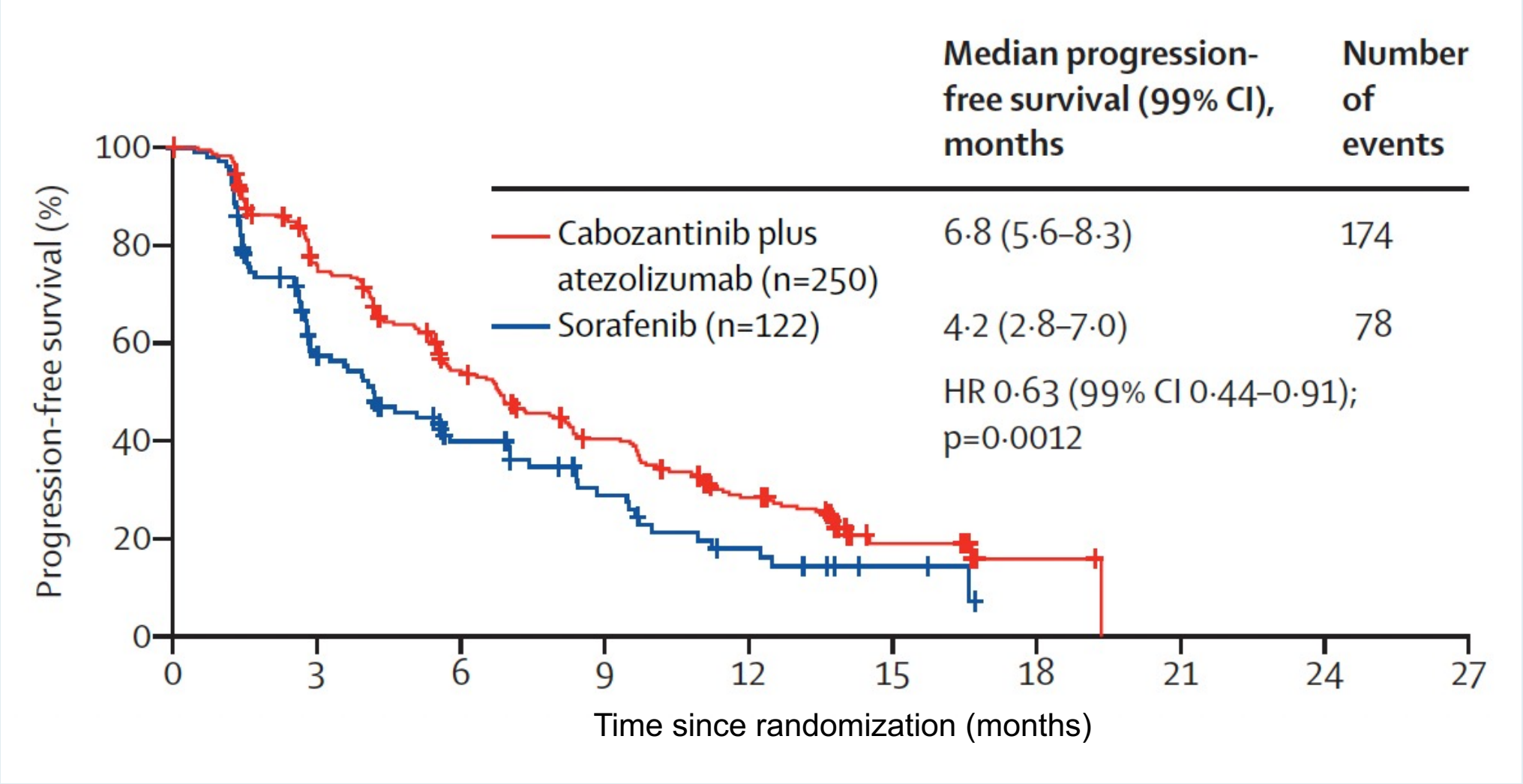
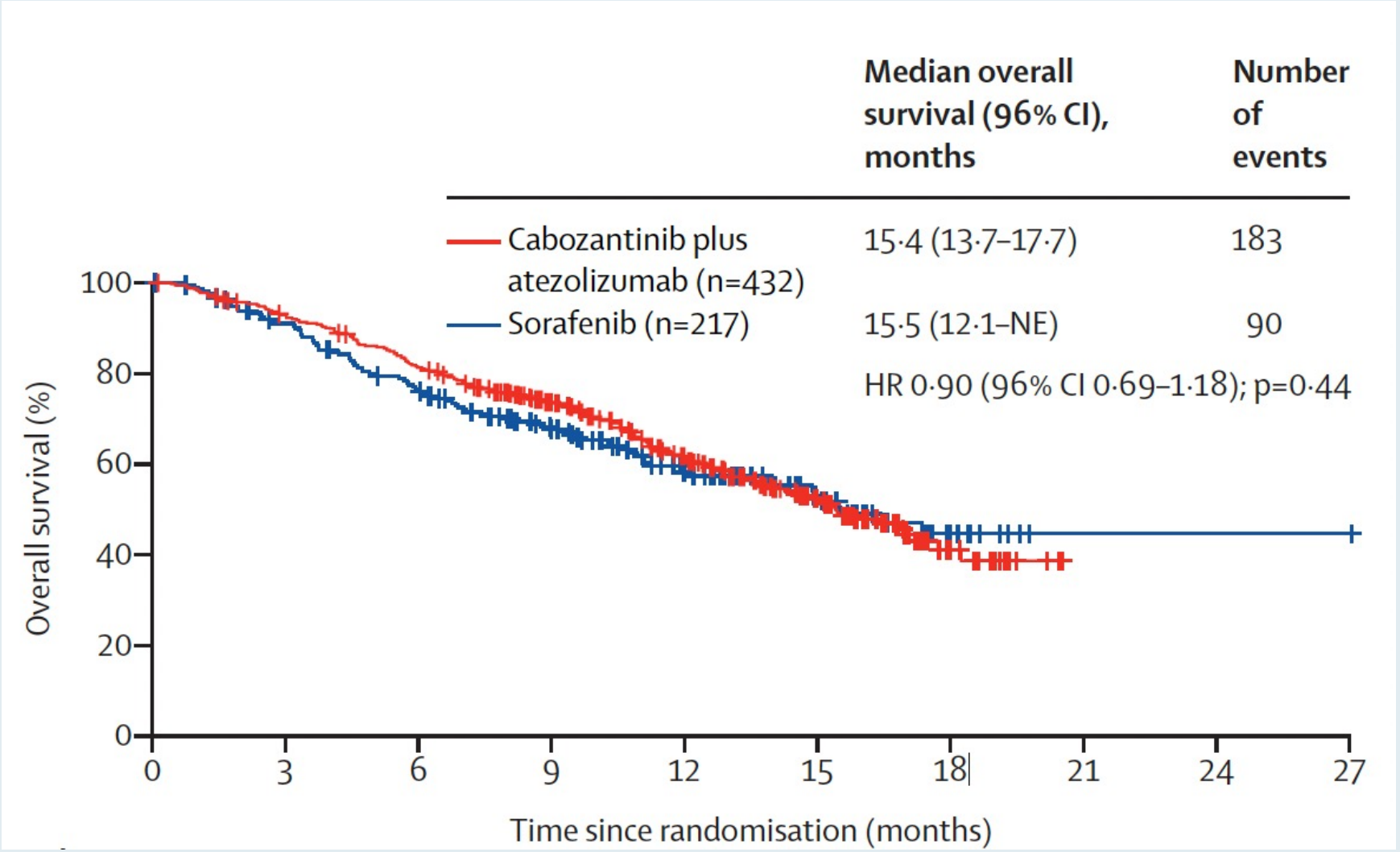
COSMIC-312: Progression-Free Survival in the ITT Population (Final Analysis)



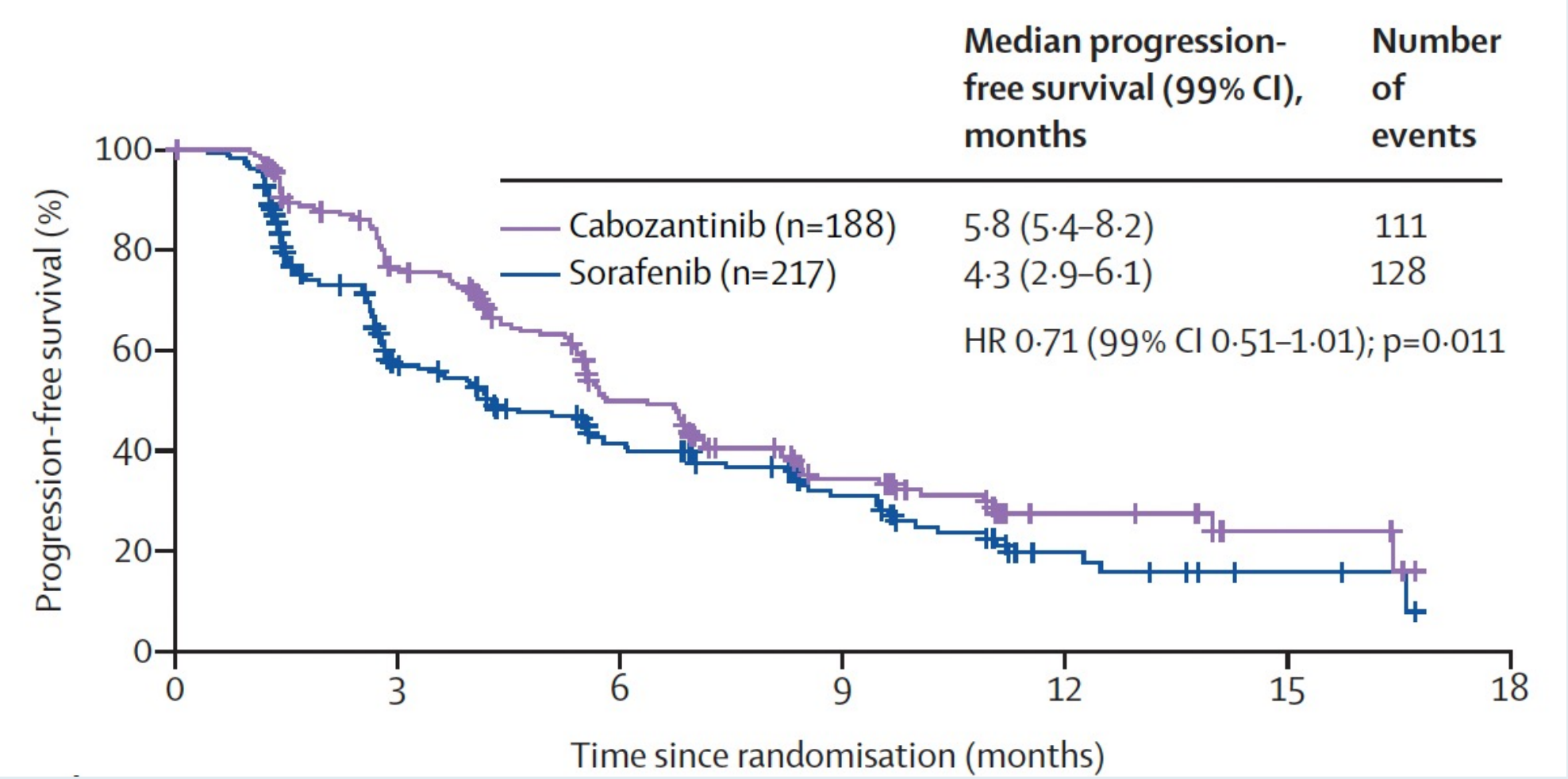
Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

COSMIC-312: Overall Survival in the ITT Population (Interim Analysis)



Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

COSMIC-312: Interim Analysis of PFS for Cabozantinib versus Sorafenib



Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

Combined Immunotherapy and VEGF Pathway-Targeted Agents as First-Line Treatment for Advanced, Unresectable HCC

Phase III Study Design	IMbrave150[a,b] (N = 501)	ORIENT-32[c] (N = 595)	COSMIC-312[d] (N = 837)
Treatment arms	Atezolizumab + bev Sorafenib	Sintilimab + bev biosimilar Sorafenib	Atezolizumab + cabozantinib* Sorafenib* Cabozantinib
Patient population	Global patient population HBV-associated HCC (~48%)	Asian patient population HBV-associated HCC (94%)	Global patient population HBV-associated HCC (~30%)
Median PFS	6.9 mo vs 4.3 mo HR: 0.65, $p < 0.001$	4.6 mo vs 2.8 mo HR: 0.56, $p < 0.0001$	6.8 mo vs 4.2 mo* HR: 0.63, $p = 0.0012$
Median OS	19.2 mo vs 13.4 mo HR: 0.66, $p < 0.001$	Not reached vs 10.4 mo HR: 0.57, $p < 0.0001$	(Combination arm vs sorafenib): 15.4 mo vs 15.5 mo HR: 0.90, $p = 0.44$
Confirmed ORR	27.3% vs 11.9%	21.0% vs 4.0%	13.0% vs 5.0% vs 11.0%

Bev = bevacizumab; HBV = hepatitis B virus; PFS = progression-free survival; OS = overall survival; ORR = objective response rate
* PFS ITT population

[a] Cheng A-L et al. *J Hepatol* 2022;76(4):862-73; [b] Finn RS et al. *N Engl J Med* 2020;382:1894-905; [c] Ren Z et al. *Lancet Oncol* 2021;22:977-90; [d] Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

Combined Immunotherapy and VEGF Pathway-Targeted Agents as First-Line Treatment for Advanced, Unresectable HCC

Phase III Study Design	IMbrave150[a,b] (N = 501)	ORIENT-32[c] (N = 595)	HIMALAYA[d,e] (N = 1,171)
Treatment arms	Atezolizumab + bev Sorafenib	Sintilimab + bev biosimilar Sorafenib	Durvalumab + tremelimumab* Durvalumab Sorafenib*
Patient population	Global patient population HBV-associated HCC (~48%)	Asian patient population HBV-associated HCC (94%)	Global patient population HBV-associated HCC (~31%)
Median PFS	6.9 mo vs 4.3 mo HR: 0.65, $p < 0.001$	4.6 mo vs 2.8 mo HR: 0.56, $p < 0.0001$	3.8 mo vs 3.7 mo vs 4.1 mo
Median OS	19.2 mo vs 13.4 mo HR: 0.66, $p < 0.001$	Not reached vs 10.4 mo HR: 0.57, $p < 0.0001$	(Combination arm vs sorafenib)*: 16.4 mo vs 13.8 mo HR: 0.78, $p = 0.0035$
Confirmed ORR	27.3% vs 11.9%	21.0% vs 4.0%	20.1% vs 17.0% vs 5.1%

* **Primary study objective:** OS for T300 + D vs sorafenib; **Secondary objective**: OS for durvalumab vs sorafenib (16.6 mo vs 13.8 mo, HR: 0.86)

[a] Cheng A-L et al. *J Hepatol* 2022;76(4):862-73; [b] Finn RS et al. *N Engl J Med* 2020;382:1894-905; [c] Ren Z et al. *Lancet Oncol* 2021;22:977-90; [d] Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379; [e] Abou-Alfa G et al. *NEJM Evidence* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

1. How would you compare the tolerability/toxicity profile of atezolizumab/bevacizumab to that of lenvatinib?

2. How would you compare the tolerability/toxicity profile of atezolizumab/bevacizumab to that of durvalumab/tremelimumab à la HIMALAYA?

3. How would you compare the efficacy/treatment benefit of atezolizumab/bevacizumab to that of durvalumab/tremelimumab à la HIMALAYA?

4. Regulatory and reimbursement issues aside, generally what do you consider the optimal first-line systemic treatment for HCC?

Meet The Professor with Prof Abou-Alfa

MODULE 1: Hepatocellular Carcinoma (HCC)

- Key recent data sets
- Case presentations
  - Dr Shameem: A 66-year-old man with a history of Child-Pugh B cirrhosis and Grade 1 esophageal varices who is receiving atezolizumab/bevacizumab for multifocal HCC
  - Dr Zafar: A 69-year-old man with previously treated HCC cirrhosis who is now diagnosed with potentially resectable HCC
  - Dr Gandhi: A 79-year-old woman receiving adjuvant anastrozole for Stage I breast cancer who is now receiving atezolizumab/bevacizumab for metastatic HCC
  - Dr Apuri: A 79-year-old man with metastatic HCC and portal vein thrombosis receiving atezolizumab/ bevacizumab – NGS with PIK3CA mutation, PD-L1 50%
- Journal Club with Prof Abou-Alfa

MODULE 2: Biliary Tract Cancers

MODULE 3: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

Case Presentation: A 66-year-old man with a history of Child-Pugh B cirrhosis and Grade 1 esophageal varices who is receiving atezolizumab/bevacizumab for multifocal HCC

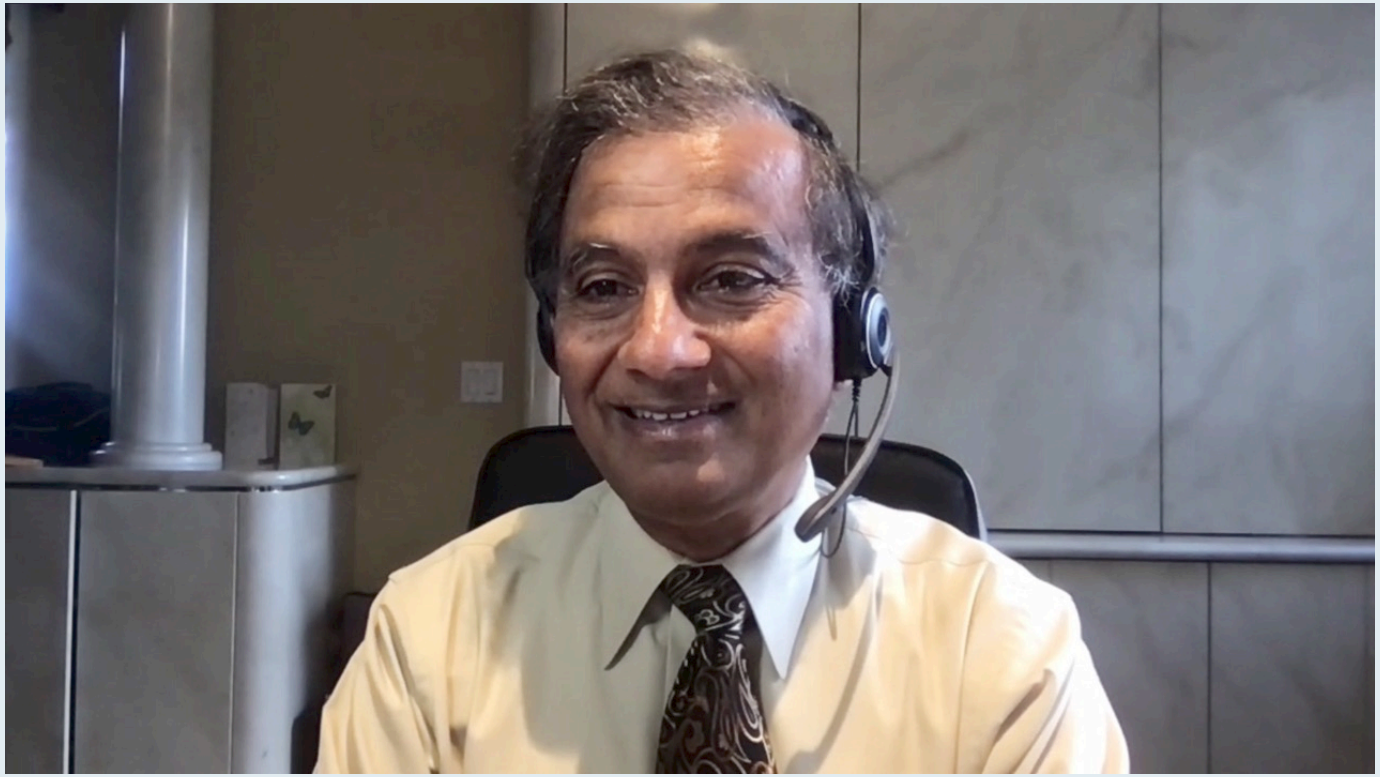
Dr Raji Shameem (Deland, Florida)

RTP RESEARCH TO PRACTICE

Case Presentation: A 69-year-old man with previously treated HCC cirrhosis who is now diagnosed with potentially resectable HCC

Dr Syed Zafar (Fort Myers, Florida)

Case Presentation: A 79-year-old woman receiving adjuvant anastrozole for Stage I breast cancer who is now receiving atezolizumab/bevacizumab for metastatic HCC



Dr Sunil Gandhi (Lecanto, Florida)

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Case Presentation: A 79-year-old man with metastatic HCC and portal vein thrombosis receiving atezolizumab/ bevacizumab – NGS (next-generation sequencing) with PIK3CA mutation, PD-L1 50%

Dr Susmitha Apuri (Lutz, Florida)

Meet The Professor with Prof Abou-Alfa

MODULE 1: Hepatocellular Carcinoma (HCC)

- Key recent data sets
- Case presentations
- Journal Club with Prof Abou-Alfa

MODULE 2: Biliary Tract Cancers

- Key recent data set
- Case presentations
- Additional recent data sets; Journal Club with Prof Abou-Alfa

MODULE 3: Appendix of Key Publications

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Hepatol Commun 2022;[Online ahead of print].

Received: 7 November 2021 | Accepted: 25 January 2022

DOI: 10.1002/hep4.1918

ORIGINAL ARTICLE

A multi-analyte cell-free DNA–based blood test for early detection of hepatocellular carcinoma

Nan Lin[1] | Yongping Lin[2] | Jianfeng Xu[3] | Dan Liu[4] | Diange Li[5] | Hongyu Meng[1] | Maxime A. Gallant[3] | Naoto Kubota[6] | Dhruvajyoti Roy[3] | Jason S. Li[7] | Emmanuel C. Gorospe[8] | Morris Sherman[9] | Robert G. Gish[10] | Ghassan K. Abou-Alfa[11] | Mindie H. Nguyen[12] | David J. Taggart[3] | Richard A. Van Etten[13] | Yujin Hoshida[6] | Wei Li[7]

Nivolumab (NIVO) and Drug Eluting Bead Transarterial Chemoembolization (deb-TACE): Updated Results from an Ongoing Phase 1 Study of Patients (pts) with Liver Limited Hepatocellular Carcinoma (HCC)

Harding J et al.

Gastrointestinal Cancers Symposium 2022;Abstract 437.

J Gastrointest Oncol 2021;12(4):1743-52.

Original Article

Ablative radiation therapy for hepatocellular carcinoma is associated with reduced treatment- and tumor-related liver failure and improved survival

Lara Hilal[1], Marsha Reyngold[1], Abraham J. Wu[1], Abdallah Araji[2], Ghassan K. Abou-Alfa[3,4], William Jarnagin[5], James J. Harding[3,4], Maya Gambarin[3,4], Imane El Dika[3,4], Paul Brady[1], John Navilio[6], Sean L. Berry[6], Jessica Flynn[7], Zhigang Zhang[7], Richard Tuli[1], Melissa Zinovoy[1], Paul B. Romesser[1], John J. Cuaron[1], Christopher H. Crane[1], Carla Hajj[1]

Editorial

J Hepatol 2021;75(4):763-4.

JOURNAL OF HEPATOLOGY

Decision making in systemic therapy of hepatocellular carcinoma: Should we pay attention to disease aetiology?

Peter R. Galle[1,*], Ghassan K. Abou-Alfa[2,3]

Research Article
Hepatic and Biliary Cancer

J Hepatol 2021;75(4):879-87.

JOURNAL OF HEPATOLOGY

Sorafenib is associated with a reduced rate of tumour growth and liver function deterioration in HCV-induced hepatocellular carcinoma

Ruwanthi Kolamunnage-Dona[1], Sarah Berhane[2,3], Harry Potts[4], Edward H. Williams[5], James Tanner[6], Tobias Janowitz[5,7,8], Matthew Hoare[5,9], Philip Johnson[10,*]

Lancet Oncol 2022;23:77-90.

Nivolumab versus sorafenib in advanced hepatocellular carcinoma (CheckMate 459): a randomised, multicentre, open-label, phase 3 trial

Thomas Yau, Joong-Won Park, Richard S Finn, Ann-Lii Cheng, Philippe Mathurin, Julien Edeline, Masatoshi Kudo, James J Harding, Philippe Merle, Olivier Rosmorduc, Lucjan Wyrwicz, Eckart Schott, Su Pin Choo, Robin Kate Kelley, Wolfgang Sieghart, Eric Assenat, Renata Zaucha, Junji Furuse, Ghassan K Abou-Alfa, Anthony B El-Khoueiry, Ignacio Melero, Damir Begic, Gong Chen, Jaclyn Neely, Tami Wisniewski, Marina Tschaika, Bruno Sangro

original reports

Safety, Efficacy, and Pharmacodynamics of Tremelimumab Plus Durvalumab for Patients With Unresectable Hepatocellular Carcinoma: Randomized Expansion of a Phase I/II Study

Robin Kate Kelley, MD[1]; Bruno Sangro, MD, PhD[2]; William Harris, MD[3]; Masafumi Ikeda, MD, PhD[4]; Takuji Okusaka, MD, PhD[5]; Yoon-Koo Kang, MD, PhD[6]; Shukui Qin, MD, PhD[7]; David W.-M. Tai, MD[8]; Ho Yeong Lim, MD[9]; Thomas Yau, MD[10]; Wei-Peng Yong, MD[11]; Ann-Lii Cheng, MD, PhD[12]; Antonio Gasbarrini, MD[13]; Silvia Damian, MD[14]; Jordi Bruix, MD[15]; Mitesh Borad, MD[16]; Johanna Bendell, MD[17]; Tae-You Kim, MD[18]; Nathan Standifer, PhD[19]; Philip He, PhD[20]; Mallory Makowsky, PharmD[20]; Alejandra Negro, PhD[20]; Masatoshi Kudo, MD, PhD[21]; and Ghassan K. Abou-Alfa, MD, MBA[22,23]

J Clin Oncol 2021;39(27):2991-3001.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Poster 436

Gastrointestinal Cancers Symposium 2022;Abstract 436.

Safety and efficacy of durvalumab plus bevacizumab in unresectable hepatocellular carcinoma: results from the Phase 2 Study 22 (NCT02519348)

Ho Yeong Lim,[1] Jeong Heo,[2] Tae-You Kim,[3] David W M Tai,[4] Yoon-Koo Kang,[5] George Lau,[6] Masatoshi Kudo,[7] Won Young Tak,[8] Magdalena Watras,[9] Sajid Ali,[10] Alejandra Negro,[11] Ghassan K Abou-Alfa,[12,13] R Kate Kelley[14*]

Exposure-Response (E-R) Efficacy and Safety (E-S) Analyses of Tremelimumab as Monotherapy or in Combination with Durvalumab in Patients (pts) with Unresectable Hepatocellular Carcinoma (uHCC)

Song X et al.

Gastrointestinal Cancers Symposium 2021;Abstract 313.

Poster 4087

ASCO 2022;Abstract 4087.

T cell receptor pharmacodynamics associated with survival and response to tremelimumab (T) in combination with durvalumab (D) in patients (pts) with unresectable hepatocellular carcinoma (uHCC)

Patricia McCoon,[1] Young S. Lee,[2] R. Kate Kelley,[3] Violeta Beleva Guthrie,[2] Song Wu,[2] Stephanie A. Bien,[4] Alejandra Negro,[5] Philip He,[5] John Kurland,[5] Carl Barrett,[1] Fernanda Pilataxi,[5] Steven Ching,[5] Ghassan K. Abou-Alfa[6]

Clin Cancer Res 2021;27(8):2200-8.

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Phase II Single-arm Study of Durvalumab and Tremelimumab with Concurrent Radiotherapy in Patients with Mismatch Repair–proficient Metastatic Colorectal Cancer

Neil H. Segal[1], Andrea Cercek[1], Geoffrey Ku[1,2], Abraham J. Wu[1], Andreas Rimner[1], Danny N. Khalil[1], Diane Reidy-Lagunes[1], John Cuaron[1], T. Jonathan Yang[1], Martin R. Weiser[1], Paul B. Romesser[1], Zsofia K. Stadler[1,2], Anna M. Varghese[1], Karuna Ganesh[1], Rona Yaeger[1], Louise C. Connell[1], David Faleck[1], Ghassan K. Abou-Alfa[1], Kathleen C. Mcauliffe[1], Pamela Vaiskauskas[1], Mark L. Solter[1], Martinique Ogle[1], Matthew J. Adamow[1], Aliya Holland[1], Pallavi Vedantam[1], Phillip Wong[1], Taha Merghoub[1], Efsevia Vakiani[1], Travis J. Hollmann[1], Krishna Juluru[1], Joanne F. Chou[1], Marinela Capanu[1], Joseph Erinjeri[1], Stephen Solomon[1], Yoshiya Yamada[1], Nancy Kemeny[1], Christopher H. Crane[1], and Leonard B. Saltz[1]

Meet The Professor with Prof Abou-Alfa

MODULE 1: Hepatocellular Carcinoma (HCC)

- Key recent data sets
- Case presentations
- Journal Club with Prof Abou-Alfa

MODULE 2: Biliary Tract Cancers

- Key recent data set
- Case presentations
- Additional recent data sets; Journal Club with Prof Abou-Alfa

MODULE 3: Appendix of Key Publications

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Meet The Professor with Prof Abou-Alfa

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MODULE 3: Appendix of Key Publications

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NEJM Evidence

Published June 1, 2022

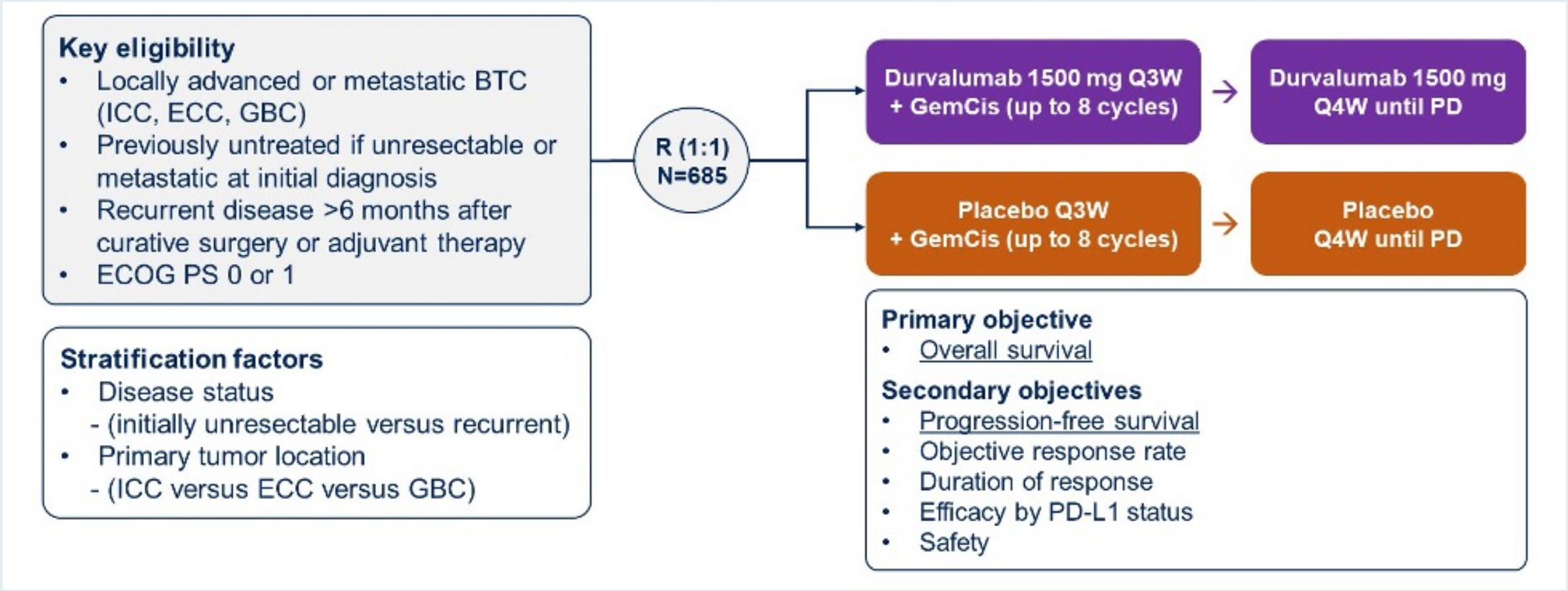
DOI: 10.1056/EVIDoa2200015

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 Suksomboon charoen, 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]

TOPAZ-1 Phase III Trial Schema

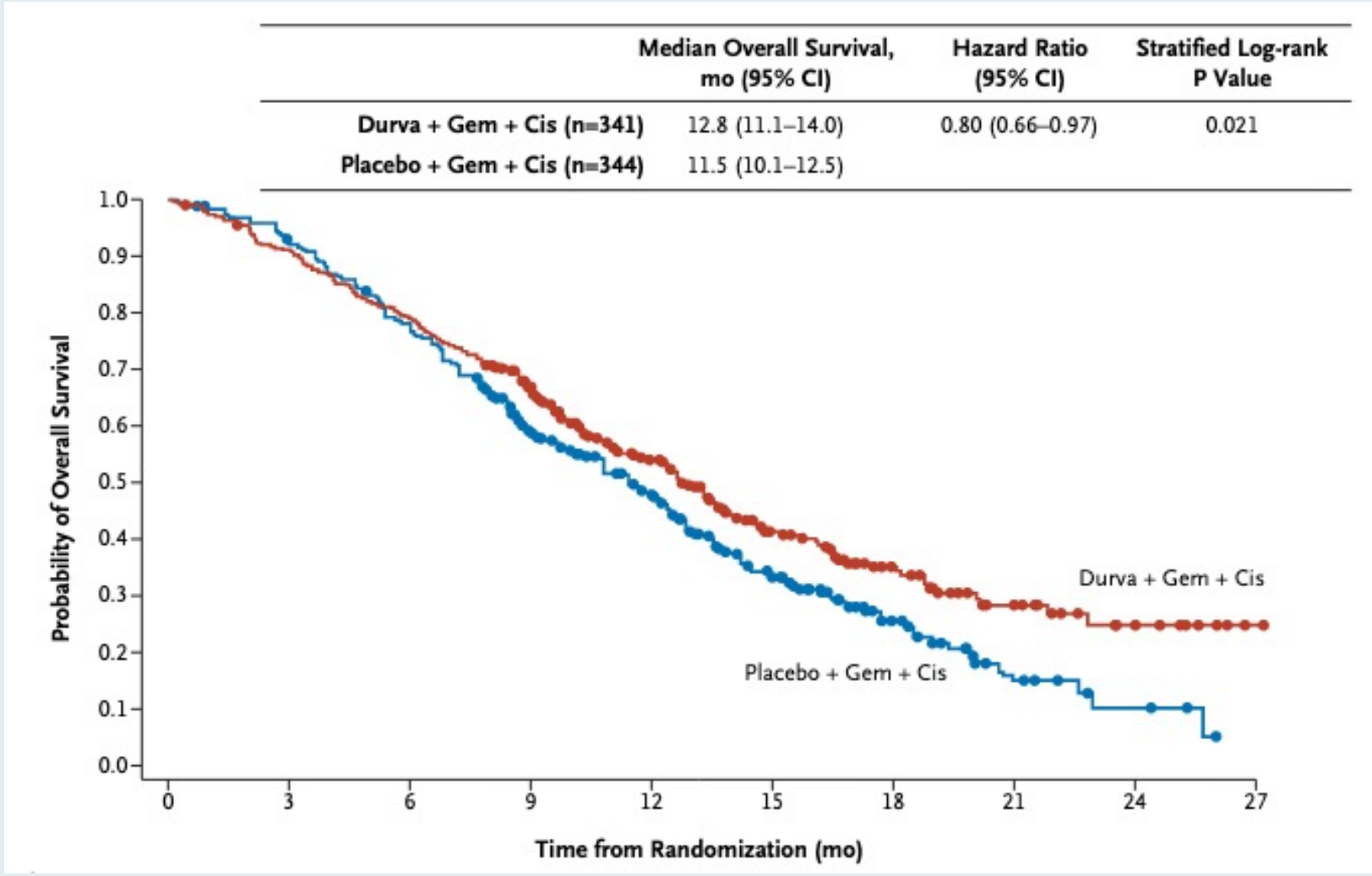


BTC = biliary tract cancer

Oh D-Y et al. Gastrointestinal Cancers Symposium 2022;Abstract 378.

TOPAZ-1: Primary Overall Survival Endpoint with Durvalumab and Gemcitabine/Cisplatin for Advanced Biliary Tract Cancer

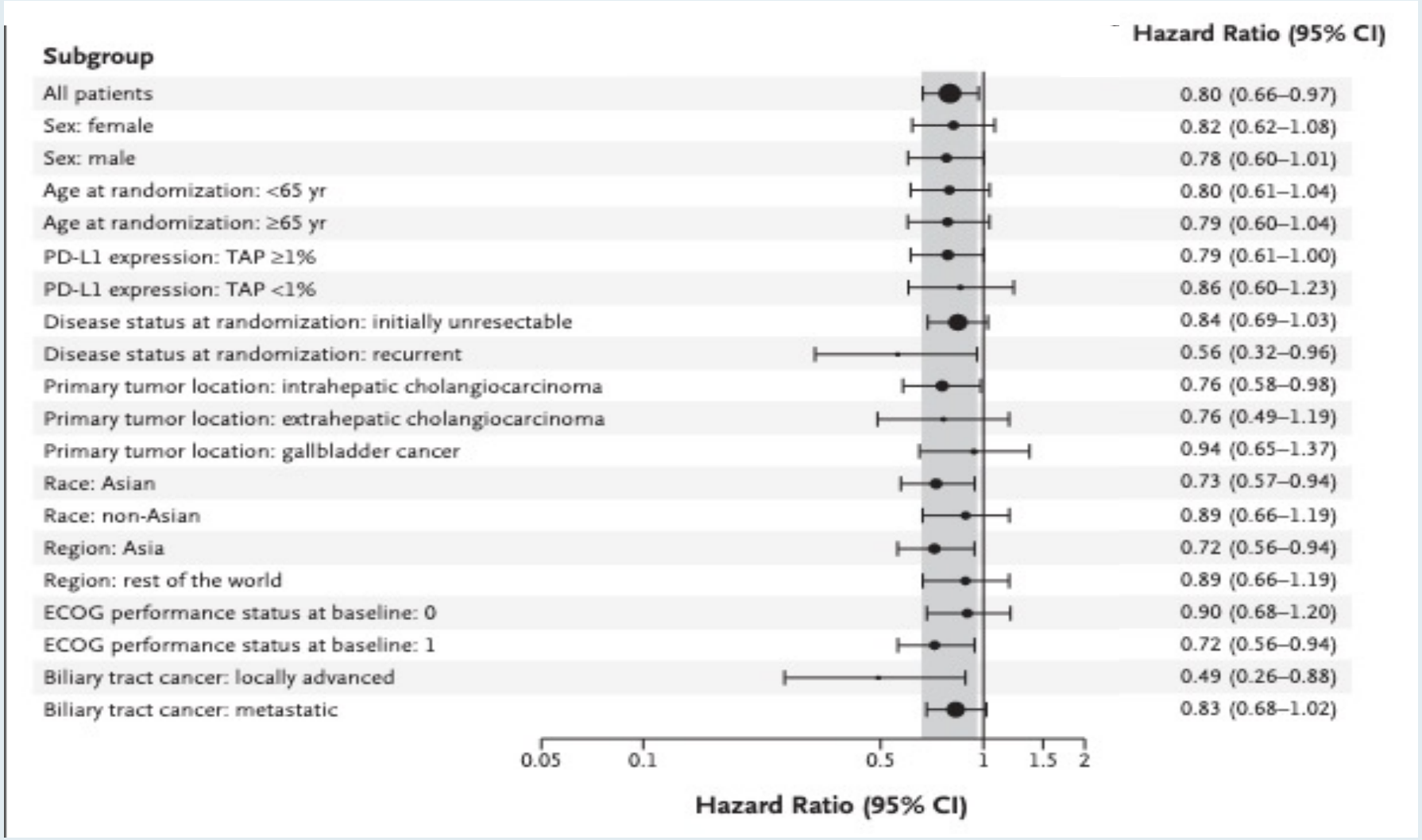
	Median Overall Survival, mo (95% CI)	Hazard Ratio (95% CI)	Stratified Log-rank P Value
Durva + Gem + Cis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + Gem + Cis (n=344)	11.5 (10.1–12.5)		



Oh D-Y et al. *NEJM Evidence*, June 1, 2022.

RTP RESEARCH TO PRACTICE

TOPAZ-1: Overall Survival Subgroup Analysis



Oh D-Y et al. *NEJM Evidence*, June 1, 2022.

TOPAZ-1: Adverse Event Summary

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)

Oh D-Y et al. *NEJM Evidence*, June 1, 2022.

RTP RESEARCH TO PRACTICE

Meet The Professor with Prof Abou-Alfa

MODULE 1: Hepatocellular Carcinoma (HCC)

MODULE 2: Biliary Tract Cancers

- Key recent data set
- Case presentations
  - Dr Shehadeh: A 57-year-old man with resected Stage IIB gall bladder cancer s/p adjuvant capecitabine who now has metastatic disease (HER2-positive) – MSS, PD-L1 0
  - Dr Metzner-Sadurski: A 43-year-old woman with a history of DCIS and family history of breast cancer, now with metastatic cholangiocarcinoma – NGS with IDH2 mutation
  - Dr Levin: A 49-year-old woman with intrahepatic cholangiocarcinoma and micrometastases in portal lymph nodes
  - Dr Dallas: A 66-year-old man with metastatic cholangiocarcinoma – NGS with PIK3CA, KRAS G12A and additional mutations
- Additional recent data sets; Journal Club with Prof Abou-Alfa

MODULE 3: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

Case Presentation: A 57-year-old man with resected Stage IIB gall bladder cancer s/p adjuvant capecitabine who now has metastatic disease (HER2-positive) – MSS, PD-L1 0

Dr Nasfat Shehadeh (Charlotte, North Carolina)

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TO PRACTICE

Lancet Oncol 2021;22:1290-300.

Pertuzumab and trastuzumab for HER2-positive, metastatic biliary tract cancer (MyPathway): a multicentre, open-label, phase 2a, multiple basket study

Milind Javle, Mitesh J Borad, Nilofer S Azad, Razelle Kurzrock, Ghassan K Abou-Alfa, Ben George, John Hainsworth, Funda Meric-Bernstam, Charles Swanton, Christopher J Sweeney, Claire F Friedman, Ron Bose, David R Spigel, Yong Wang, Jonathan Levy, Katja Schulze, Vaikunth Cuchelkar, Arisha Patel, Howard Burris

2022 ASCO® ANNUAL MEETING

Abstract 4006

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing unresectable or recurrent biliary tract cancer (BTC): An investigator-initiated multicenter phase 2 study (HERB trial)

Akihiro Ohba[1], Chigusa Morizane[1], Yasuyuki Kawamoto[2], Yoshito Komatsu[2], Makoto Ueno[3], Satoshi Kobayashi[3], Masafumi Ikeda[4], Mitsuhito Sasaki[4], Junji Furuse[5], Naohiro Okano[5], Nobuyoshi Hiraoka[1], Hiroshi Yoshida[1], Aya Kuchiba[1], Ryo Sadachi[1], Kenichi Nakamura[1], Naoko Matsui[1], Yoshiaki Nakamura[4], Wataru Okamoto[6], Takayuki Yoshino[4], Takuji Okusaka[1]

[1]National Cancer Center Hospital, [2]Hokkaido University Hospital, [3]Kanagawa Cancer Center, [4]National Cancer Center Hospital East, [5]Kyorin University Faculty of Medicine, [6]Hiroshima University Hospital

PRESENTED BY: Akihiro Ohba, MD

HERB Primary Endpoint: Confirmed Objective Response Rate (ORR) by Blinded Independent Central Review with T-DXd for Biliary Tract Cancer

- Tumor response

*: P =0.01

	HER2-positive (n=22)	HER2-low-expressing (n=8)	All pts (n=30)
Confirmed ORR (90% CI) (95% CI)	**36.4% (19.6-56.1)*** (17.2–59.3)	12.5% – (0.3–52.7)	30.0% – (14.7–49.4)
Confirmed DCR (95% CI)	81.8% (59.7–94.8)	75.0% (34.9–96.8)	80.0% (61.4–92.3)
Confirmed best response, n (%)			
CR	2 (9.1)	0 (0)	2 (6.7)
PR	6 (27.3)	1 (12.5)	7 (23.3)
SD	10 (45.5)	5 (62.5)	15 (50.0)
PD	3 (13.6)	1 (12.5)	4 (13.3)
NE	1 (4.5)	1 (12.5)	2 (6.7)

- Best percentage change

Ohba A et al. ASCO 2022;Abstract 4006.

HERB Secondary Endpoints: Progression-Free Survival (PFS) and Overall Survival (OS) with T-DXd for Biliary Tract Cancer

	HER2-positive disease (n = 22)	HER2-low expressing disease (n = 8)
Median PFS	5.1 mo	3.5 mo
6-month PFS rate	40.9%	0
Median OS	7.1 mo	8.9 mo
6-month OS rate	63.6%	75.0%

Ohba A et al. ASCO 2022;Abstract 4006.

HERB: Treatment-Emergent Adverse Events with T-DXd for Biliary Tract Cancer

Event	Any grade, n (%)	Grade ≥ 3, n (%)
Anemia	22 (68.8)	17 (53.1)
Neutrophil count decreased	18 (56.3)	10 (31.3)
White blood cell count decreased	18 (56.3)	10 (31.3)
Platelet count decreased	14 (43.8)	3 (9.4)
Nausea	14 (43.8)	0 (0)
Alopecia	13 (40.6)	0 (0)
Anorexia	12 (37.5)	1 (3.1)
Lymphocyte count decreased	11 (34.4)	7 (21.9)
Fatigue / Malaise	11 (34.4)	0 (0)
Interstitial lung disease / Pneumonitis	8 (25.0)	4 (12.5)
Hypoalbuminemia	7 (21.9)	1 (3.1)
Vomiting	7 (21.9)	0 (0)
Mucositis oral	5 (15.6)	0 (0)

Ohba A et al. ASCO 2022;Abstract 4006.

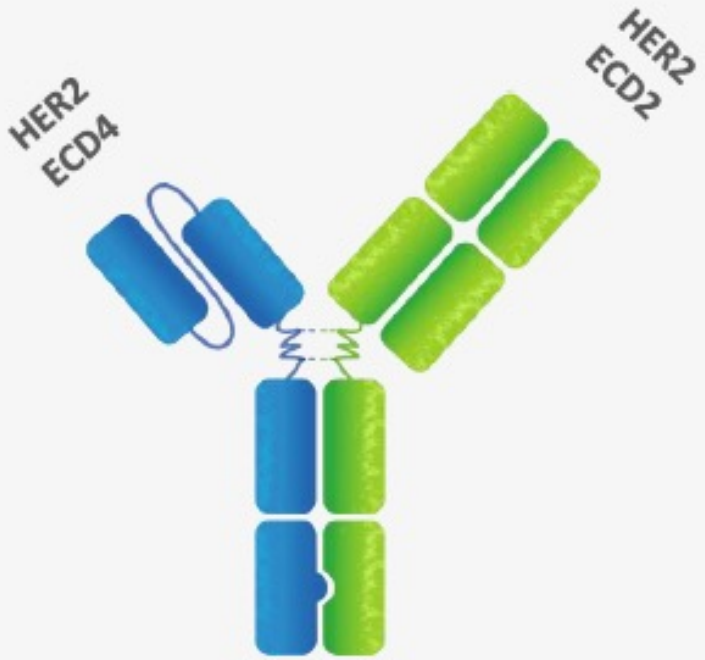
HERB: Interstitial Lung Disease (ILD)/Pneumonitis with T-DXd for Biliary Tract Cancer

	ILDs (n=8)*
Grade, n (%) 1 2 3 5	 3 (37.5) 1 (12.5) 2 (25.0) 2 (25.0)
Median time to onset (range), days	124 (35–247)**
Median Age (range), years	73 (51–75)
Sex, female, n (%)	3 (37.5)
Number of prior regimens, n (%) 1 ≥ 2	 4 (50.0) 4 (50.0)
HER2 status of IHC/ISH, n (%) 3+/+ 2+/+	 5 (62.5) 3 (37.5)
Lung metastasis, n (%)	3 (37.5)
Smoking history, n (%)	3 (37.5)
Biliary drainage, n (%)	4 (50.0)

Ohba A et al. ASCO 2022;Abstract 4006.

Zanidatamab: A Bispecific HER2-Targeted Antibody

- A biparatopic antibody that simultaneously binds two distinct sites on HER2: ECD4 (targeted by trastuzumab) and ECD2 (targeted by pertuzumab)
- Unique binding results in multiple mechanisms of action of zanidatamab that lead to improved binding, clustering, and receptor internalization and downregulation, inhibition of ligand-dependent and -independent proliferation, and potent activation of antibody-dependent cellular cytotoxicity



ECD=extracellular domain

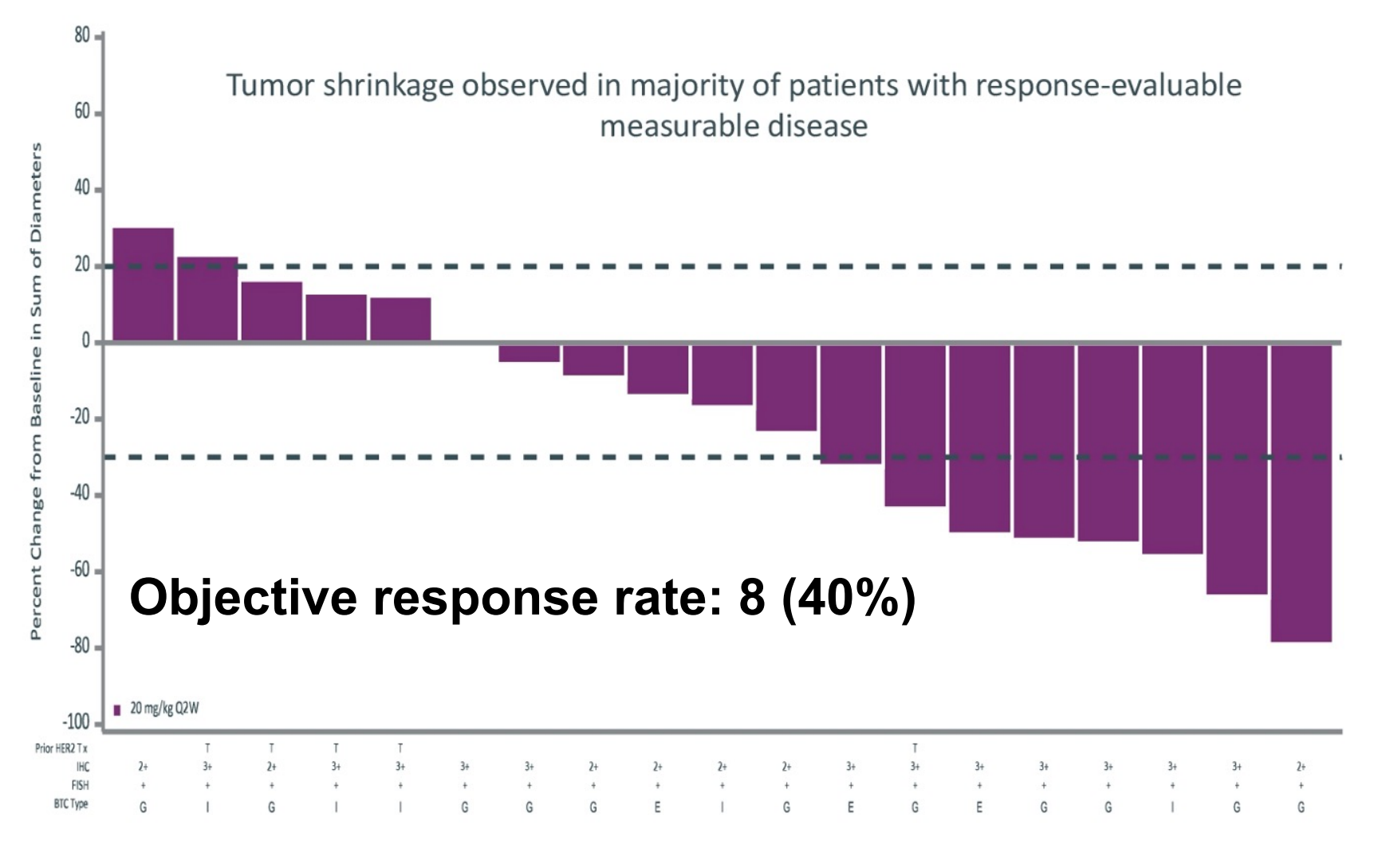
Pant S et al. Gastrointestinal Cancers Symposium 2021;Abstract TPS352.

Zanidatamab (ZW25) in HER2-Positive Biliary Tract Cancer (BTC): Results from a Phase I Study

Meric-Bernstam F et al.

Gastrointestinal Cancers Symposium 2021;Abstract 299.

Antitumor Activity of Zanidatamab in a Phase I Study for Advanced Biliary Tract Cancer



Meric-Bernstam F et al. Gastrointestinal Cancers Symposium 2021;Abstract 299.

Clinical and Genomic Characterization of ERBB2-Altered Gallbladder Cancer

Mondaca SJ et al.

ASCO 2022;Abstract 4114.

Case Presentation: A 43-year-old woman with a history of DCIS and family history of breast cancer, now with metastatic cholangiocarcinoma – NGS with IDH2 mutation

Dr Joanna Metzner-Sadurski (Greenwood, South Carolina)

RTP
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TO PRACTICE

Case Presentation: A 49-year-old woman with intrahepatic cholangiocarcinoma and micrometastases in portal lymph nodes

Dr Pavel Levin (Houston, Texas)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 66-year-old man with metastatic cholangiocarcinoma – NGS with PIK3CA, KRAS G12A and additional mutations

Dr Jennifer Dallas (Charlotte, North Carolina)

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Meet The Professor with Prof Abou-Alfa

MODULE 1: Hepatocellular Carcinoma (HCC)

- Key recent data sets
- Case presentations
- Journal Club with Prof Abou-Alfa

MODULE 2: Biliary Tract Cancers

- Key recent data set
- Case presentations
- Additional recent data sets; Journal Club with Prof Abou-Alfa

MODULE 3: Appendix of Key Publications

Therapeutic Targets and Approach to Molecular Profiling for Biliary Tract Cancers

Target	Frequency	Targeted agents	Molecular test
IDH1	***13%*** of intrahepatic cholangiocarcinomas	Ivosidenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of IDH1
FGFR pathway	**20%** of intrahepatic cholangiocarcinomas	Erdafitinib; futibatinib; infigratinib; pemigatinib	Tumor next-generation DNA sequencing including FGFR2 intronic region, targeted RNAseq or FISH testing for FGFR2 translocation
BRAF	**5%** of intrahepatic cholangiocarcinomas	Dabrafenib with trametinib; vemurafenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of BRAF
MSI-high or MMR deficiency	**2%** of biliary tract cancers	Pembrolizumab	Multiple testing modalities available: PCR, immunohistochemistry or tumor next-generation DNA sequencing
ERBB2 (HER2)	***15%-20%*** gallbladder cancer; extrahepatic cholangiocarcinomas		Multiple testing modalities available including immunohistochemistry and FISH for expression and amplification, tumor next-generation DNA sequencing for mutations

Valle JW et al. *Lancet* 2021;397(10272):428-44.

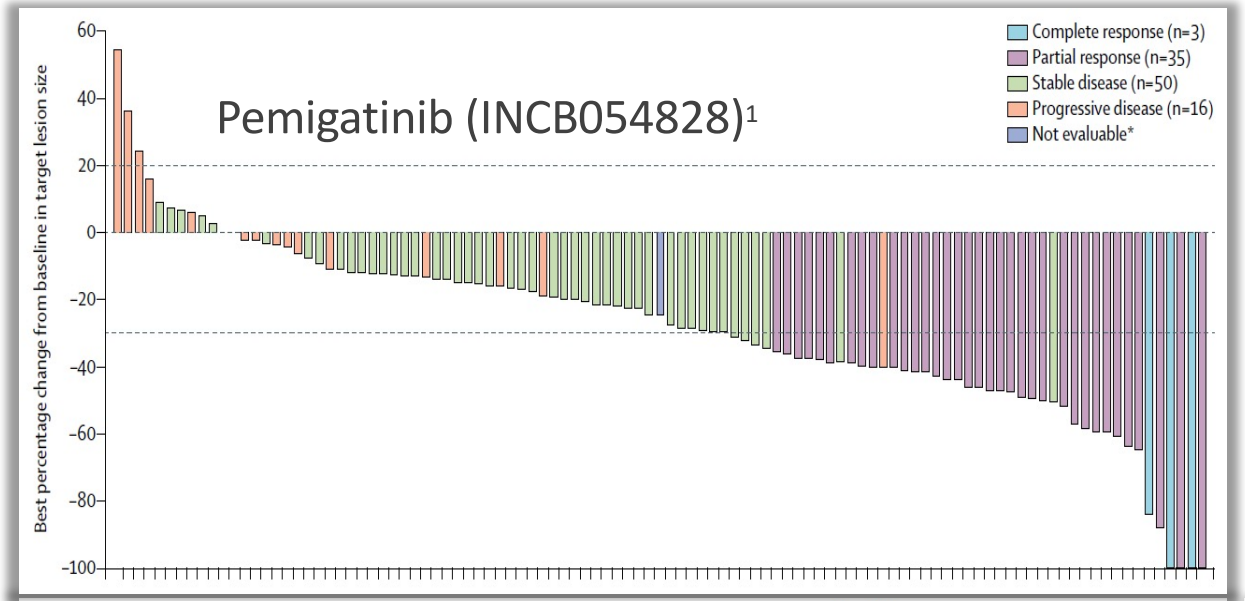
FGFR Inhibitor Efficacy in FGFR2 Fusion-Positive Cholangiocarcinoma

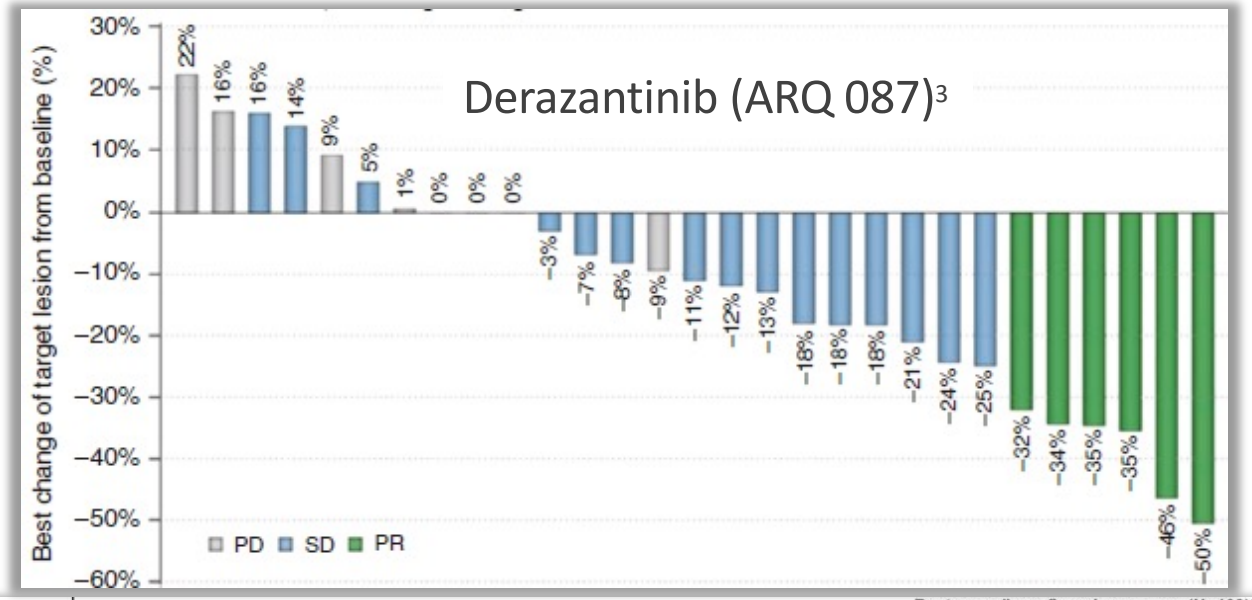
	Pemigatinib* (N = 107)	Infigratinib* (N = 108)	Futibatinib (N = 67)	Derazantinib (N = 29)
ORR	35.5%	23.1%	37.3%	20.7%
DCR	82.2%	84.3%	82.1%	82.8%
mPFS	6.9 mo	7.3 mo	7.2 mo	5.7 mo
mOS	21.1 mo	12.2 mo	NR	NR
Toxicities	Hyperphosphatemia, alopecia, diarrhea	Hyperphosphatemia, stomatitis, fatigue	Hyperphosphatemia, diarrhea, dry mouth	Hyperphosphatemia, fatigue, ocular

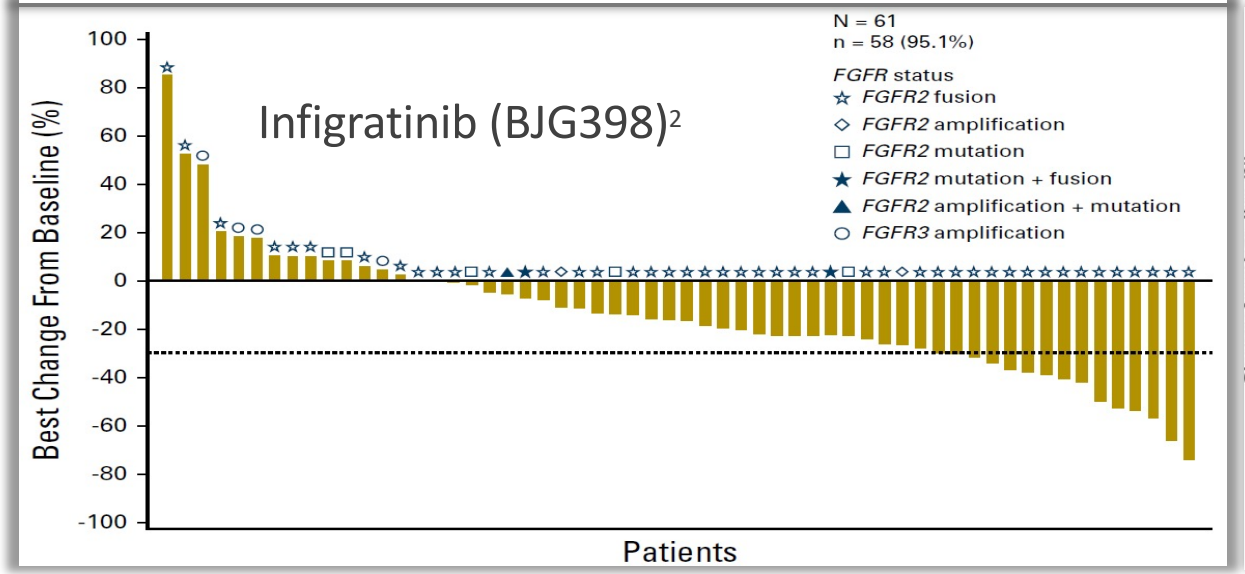
* FDA approved

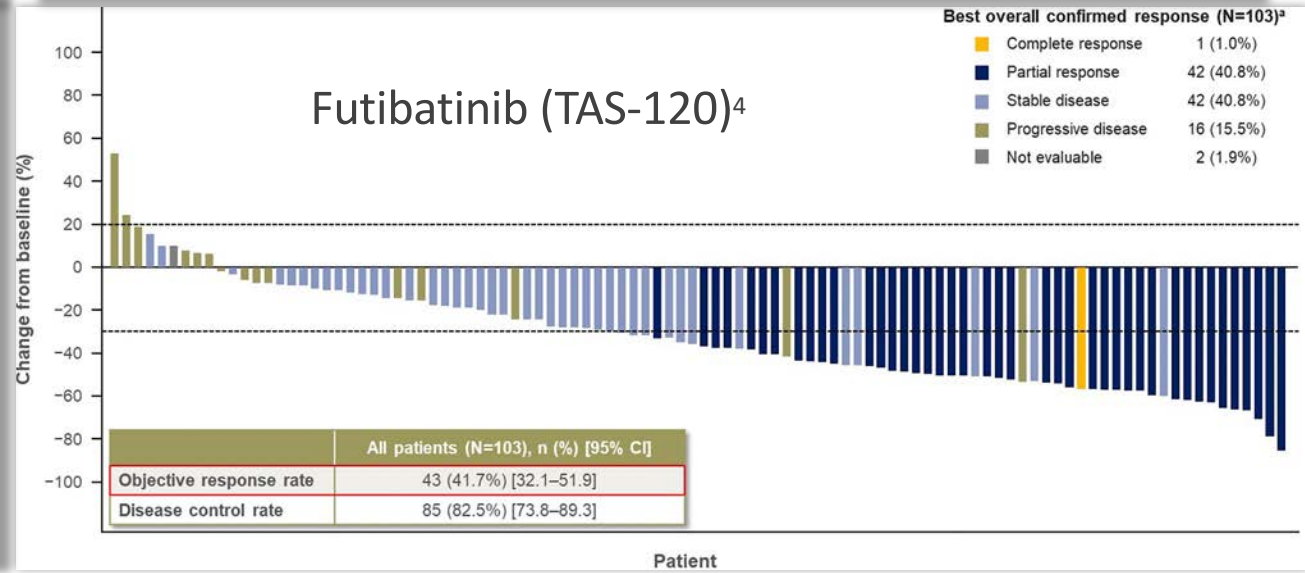
Abou-Alfa GK et al. *Lancet Oncol* 2020;21(5):671-84; Javle M et al. Gastrointestinal Cancers Symposium 2021; Goyal L et al. ASCO 2020; Mazzaferro V et al. *Br J Cancer* 2019;120(2):165-71.

Multiple FGFR2-targeted agents









1. Abou Alfa et al. *Lancet Oncol* 2020;21(5):671-684; 2. Javle et al *J Clin Oncol* 2018;36(3):276-282; 3. Mazzaferro et al *Br J Cancer* 2019;120(2):165-171; 4. Goyal et al ASCO 2022 abstr 4009

Courtesy of Professor Juan W Valle, MD

ASCO Gastrointestinal Cancers Symposium

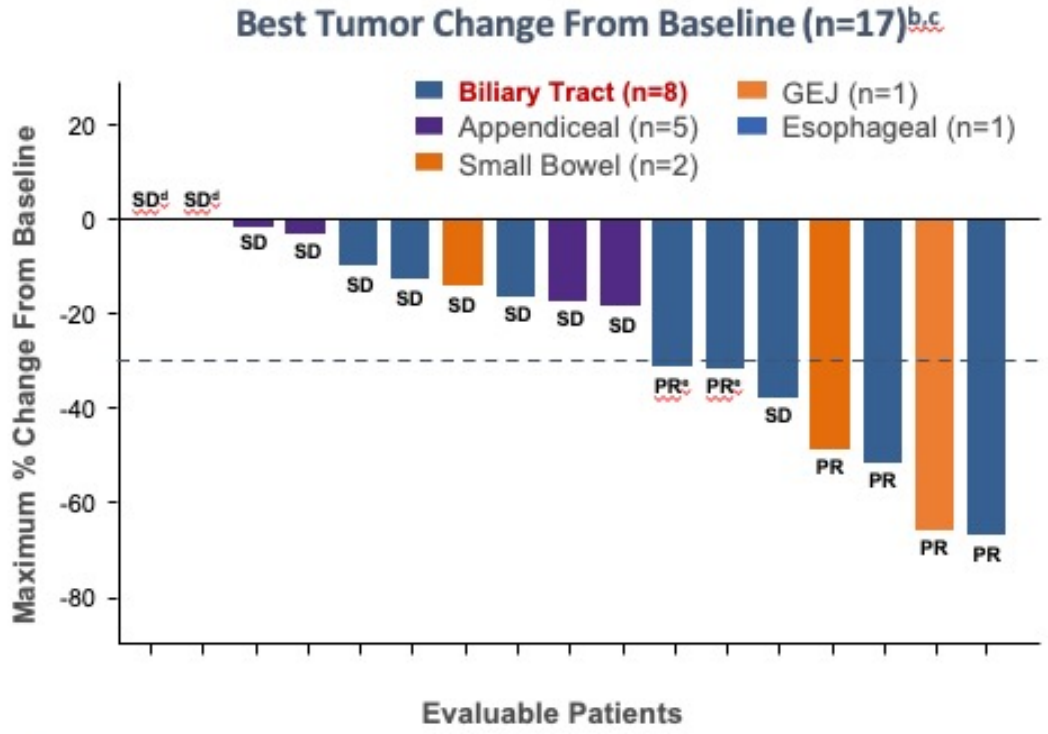
Abstract 519.

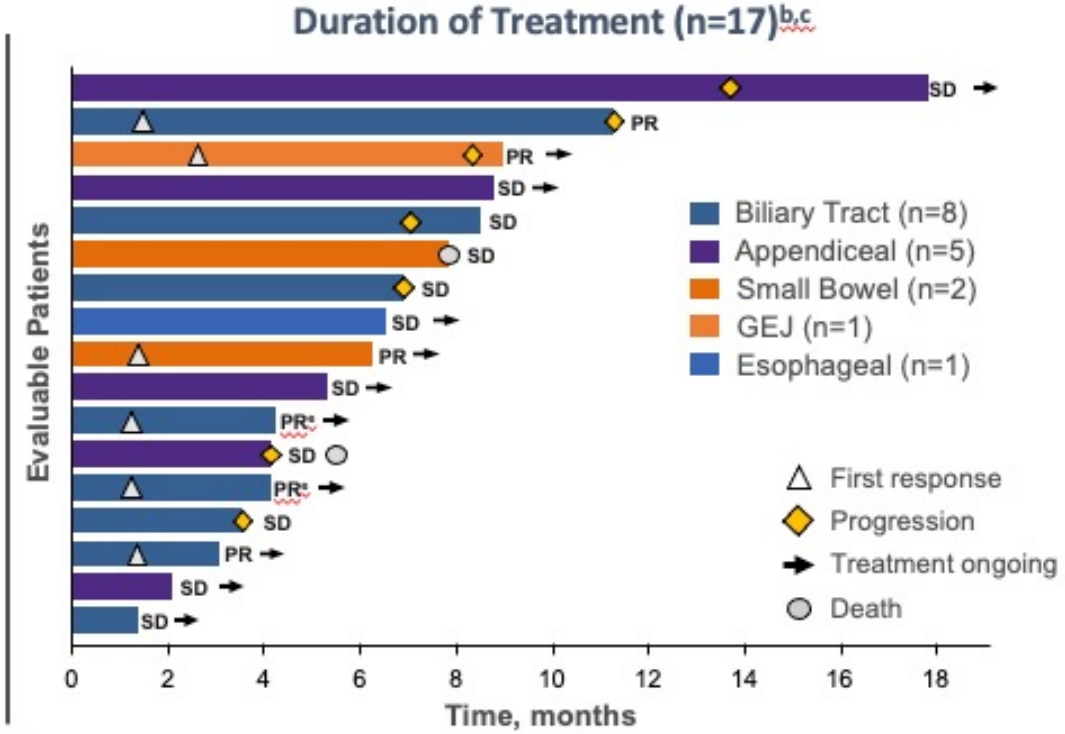
KRYSTAL-1: Updated Activity and Safety of Adagrasib (MRTX849) in Patients (Pts) With Unresectable or Metastatic Pancreatic Cancer (PDAC) and Other Gastrointestinal (GI) Tumors Harboring a KRAS^{G12C} Mutation

TS Bekaii-Saab[1], AI Spira[2], R Yaeger[3], GL Buchschacher Jr.[4], AJ McRee[5], JK Sabari[6], ML Johnson[7], M Barve[8], N Hafez[9], K Velastegui[10], JG Christensen[10], T Kheoh[10], H Der-Torossian[10], SM Gadgeel[11]

[1]Department of Medical Oncology and Hematology, Mayo Clinic, Scottsdale, Arizona, USA; [2]Virginia Cancer Specialists, Fairfax, Virginia, NEXT Oncology, Virginia, US Oncology Research, The Woodlands, Texas, USA; [3]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA; [4]Kaiser Permanente Southern California, Los Angeles, California, USA; [5]Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA; [6]Perlmutter Cancer Center, New York University Langone Health, New York, New York, USA; [7]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, Tennessee, USA; [8]Mary Crowley Cancer Research, Dallas, Texas, USA; [9]Yale Cancer Center, New Haven, Connecticut, USA; [10]Mirati Therapeutics, Inc., San Diego, California, USA; [11]Henry Ford Cancer Institute/Henry Ford Health System, Detroit, Michigan, USA

KRYSTAL-1: Best Tumor Change from Baseline and Duration of Treatment with Adagrasib for Other Gastrointestinal Tumors





- Response rate:
  - **Biliary tract cancer: 50% (4/8), including 2 unconfirmed PRs**
  - GEJ and small bowel cancer: 1 PR each
- DCR: 100% (17/17 patients)

- Median TTR: 1.3 months
- Median DOR: 7.85 months
- Median PFS: 7.85 months (95% CI 6.90–11.30)
- Treatment ongoing in 65% (11/17) of patients

Bekaii-Saab TS et al. Gastrointestinal Cancers Symposium 2022;Abstract 519.

RTP RESEARCH TO PRACTICE

JCO Precis Oncol 2022;6:e2100414.

TARGETED DRUG THERAPY

original reports

Progression-Free Survival in Patients With Cholangiocarcinoma With or Without *FGF/FGFR* Alterations: A FIGHT-202 Post Hoc Analysis of Prior Systemic Therapy Response

Kristen Bibeau, MSPH, PhD[1]; Luis Féliz, MD[2]; Christine F. Lihou, BS[1]; Haobo Ren, PhD[1]; and Ghassan K. Abou-Alfa, MD[3,4]

Lancet Gastroenterol Hepatol 2021;6:803-15.

Infigratinib (BGJ398) in previously treated patients with advanced or metastatic cholangiocarcinoma with *FGFR2* fusions or rearrangements: mature results from a multicentre, open-label, single-arm, phase 2 study

Milind Javle, Sameek Roychowdhury, Robin Kate Kelley, Saeed Sadeghi, Teresa Macarulla, Karl Heinz Weiss, Dirk-Thomas Waldschmidt, Lipika Goyal, Ivan Borbath, Anthony El-Khoueiry, Mitesh J Borad, Wei Peng Yong, Philip A Philip, Michael Bitzer, Surbpong Tanasanvimon, Ai Li, Amit Pande, Harris S Soifer, Stacie Peacock Shepherd, Susan Moran, Andrew X Zhu, Tanios S Bekaii-Saab, Ghassan K Abou-Alfa

Poster 4074

ASCO 2022;Abstract 4074.

Patient-reported outcomes from the Phase 3 HIMALAYA study of tremelimumab plus durvalumab in unresectable hepatocellular carcinoma

Bruno Sangro,[1] Peter R Galle,[2] Robin Kate Kelley,[3] Chaiyut Charoentum,[4] Enrico N De Toni,[5] Yuriy Ostapenko,[6] Jeong Heo,[7] Ann-Lii Cheng,[8] Arndt Vogel,[9] Michelle Marcovitz,[10] Jayne Abraham,[11] Nikunj Patel,[10] Alejandra Negro,[10] Ghassan K Abou-Alfa[12,13]

A phase 3, double-blind, randomized study of nivolumab and ipilimumab, nivolumab monotherapy, or placebo plus transarterial chemoembolization in patients with intermediate-stage hepatocellular carcinoma

Bruno Sangro,[1] James J. Harding,[2] Matthew Johnson,[3] Daniel Palmer,[4] Julien Edeline,[5] Ghassan K. Abou-Alfa,[2] Ann-Lii Cheng,[6] Thomas Decaens,[7] Anthony B. El-Khoueiry,[8] Richard S. Finn,[9] Peter Galle,[10] Joong-Won Park,[11] Thomas Yau,[12] Damir Begic,[13] Yun Shen,[13] Jaclyn Neely,[13] Ashwin Sama,[13] Masatoshi Kudo[14]

Gastrointestinal Cancers Symposium 2021;Abstract TPS349.

Research

JAMA Oncol 2021;7(11):1669-77.

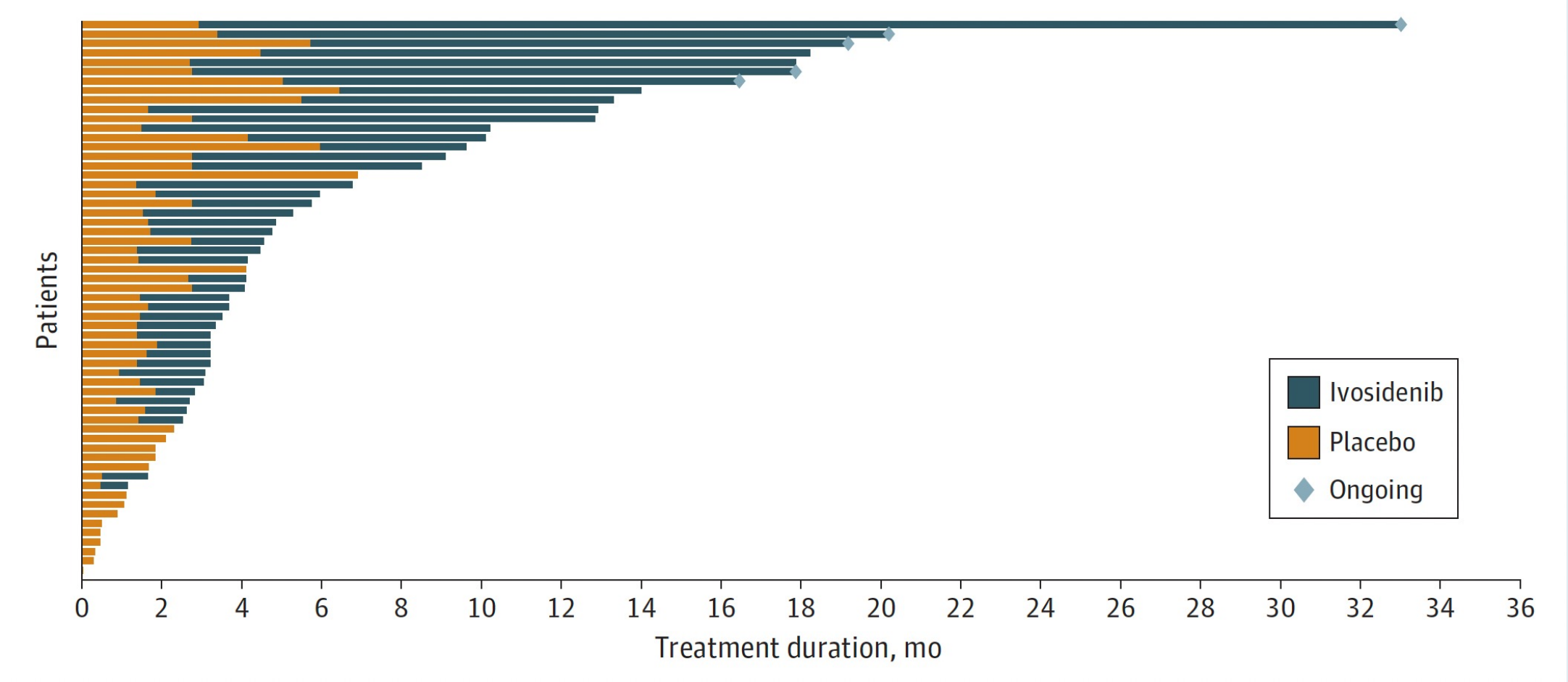
JAMA Oncology | Original Investigation

Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With *IDH1* Mutation

The Phase 3 Randomized Clinical ClarIDHy Trial

Andrew X. Zhu, MD, PhD; Teresa Macarulla, MD; Milind M. Javle, MD; R. Kate Kelley, MD; Sam J. Lubner, MD; Jorge Adeva, MD; James M. Cleary, MD; Daniel V. T. Catenacci, MD; Mitesh J. Borad, MD; John A. Bridgewater, PhD; William P. Harris, MD; Adrian G. Murphy, MD; Do-Youn Oh, MD; Jonathan R. Whisenant, MD; Maeve A. Lowery, MD; Lipika Goyal, MD; Rachna T. Shroff, MD; Anthony B. El-Khoueiry, MD; Christina X. Chamberlain, PhD; Elia Aguado-Fraile, PhD; Sung Choe, PhD; Bin Wu, PhD; Hua Liu, PhD; Camelia Gliser, BS; Shuchi S. Pandya, MD; Juan W. Valle, MD; Ghassan K. Abou-Alfa, MD

ClarIDHy: Treatment Duration for All Patients Treated with Placebo, Including Those Who Crossed Over to Ivosidenib



Zhu AX et al. *JAMA Oncol* 2021;7(11):1669-77.

Immunogenomic Characterization of Biliary Tract Cancers: Biomarker Enrichment for Benefit to Immune Checkpoint Blockade

Park W et al.

ASCO 2022;Abstract 4083.

JCO Clin Cancer Inform 2021;5:221-30.

SPECIAL SERIES: CANCER CLASSIFICATION SYSTEMS

review articles

OncoTree: A Cancer Classification System for Precision Oncology

Ritika Kundra, MS[1]; Hongxin Zhang, MS[1]; Robert Sheridan, MS[1]; Sahussapont Joseph Sirintrapun, MD[2]; Avery Wang, MS[1]; Angelica Ochoa, MS[1]; Manda Wilson, MS[1]; Benjamin Gross, MS[1]; Yichao Sun, MS[1]; Ramyasree Madupuri, MS[1]; Baby A. Satravada, MS[1]; Dalicia Reales, MPH[3]; Efsevia Vakiani, MD, PhD[1]; Hikmat A. Al-Ahmadie, MD[2]; Ahmet Dogan, MD, PhD[2]; Maria Arcila, MD[4]; Ahmet Zehir, PhD[2]; Steven Maron, MD, MSc[5]; Michael F. Berger, PhD[6,1,2]; Cristina Viaplana, MS[7]; Katherine Janeway, MD, MMSc[8]; Matthew Ducar, MS[9]; Lynette Sholl, MD[10,11]; Snjezana Dogan, MD[2]; Philippe Bedard, MD[12,13]; Lea F. Surrey, MD[14,15]; Iker Huerga Sanchez, MS[16]; Aijaz Syed, MS[2]; Anoop Balakrishnan Rema, MS[2]; Debyani Chakravarty, PhD[1]; Sarah Suehnholz, PhD[1]; Moriah Nissan, PhD[1]; Gopakumar V. Iyer, MD[5]; Rajmohan Murali, MD[2]; Nancy Bouvier, BA[17]; Robert A. Soslow, MD[2]; David Hyman, MD[18]; Anas Younes, MD[19]; Andrew Intlekofer, MD, PhD[6]; James J. Harding, MD[5,20]; Richard D. Carvajal, MD[21]; Paul J. Sabbatini, MD[5,20]; Ghassan K. Abou-Alfa, MD[5]; Luc Morris, MD, MSc[6,22,23]; Yelena Y. Janjigian, MD[5]; Meighan M. Gallagher, MPH[24]; Tara A. Soumerai, MD[25]; Ingo K. Mellinghoff, MD[5,6]; Abraham A. Hakimi, MD[26]; Matthew Fury, MD[27]; Jason T. Huse, MD, PhD[28]; Aditya Bagrodia, MD[29]; Meera Hameed, MD[2]; Stacy Thomas, MS[30]; Stuart Gardos, BA[30]; Ethan Cerami, PhD[31]; Tali Mazor, PhD[32]; Priti Kumari, MS[32]; Pichai Raman, PhD[33]; Priyanka Shivdasani, MS[34]; Suzanne MacFarland, MD[35,36]; Scott Newman, PhD[37]; Angela Waanders, MD, MPH[38]; Jianjiong Gao, PhD[1]; David Solit, MD[1,5,6,20]; and Nikolaus Schultz, PhD[1,6,39]

Cancer 2022;128(5):944-9.

Commentary

Equipoise, drug development, and biliary cancer

Tristan Y. Lee, MD [1]; Susan E. Bates, MD [1]; and Ghassan K. Abou-Alfa, MD, MBA [2,3]

Meet The Professor with Prof Abou-Alfa

MODULE 1: Hepatocellular Carcinoma (HCC)

- Key recent data sets
- Case presentations
- Journal Club with Prof Abou-Alfa

MODULE 2: Biliary Tract Cancers

- Key recent data set
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MODULE 3: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

First-Line Treatment for Advanced Hepatocellular Carcinoma (HCC)

FDA-Approved Systemic Therapy for Advanced HCC

Sorafenib

First Line

Lenvatinib

Atezolizumab + bevacizumab

Durvalumab/tremelimumab*

Second Line and Beyond

Regorafenib

Nivolumab†

Pembrolizumab‡

Cabozantinib

Ramucirumab

Nivolumab + ipilimumab‡

* Positive Phase III trial

† Accelerated approval withdrawn

‡ Accelerated approval

RTP RESEARCH TO PRACTICE

FDA-Approved Anti-VEGF-Directed Monotherapy for HCC

Approved line of therapy	Agent	Study	Primary outcomes
First line	**Sorafenib**[1]	Sorafenib vs placebo (N = 602) Phase III SHARP trial	TTP 4.1 mo vs 4.9 mo mOS 10.7 mo vs 7.9 mo
	Lenvatinib[2]	Lenvatinib vs sorafenib (N = 954) Phase III REFLECT trial	mPFS 7.4 mo vs 3.7 mo mOS 13.6 mo vs 12.3 mo
Second line	**Regorafenib**[3]	Regorafenib vs placebo (N = 573) Phase III RESORCE trial	mPFS 3.1 mo vs 1.5 mo mOS 10.7 mo vs 7.9 mo
	Cabozantinib[4]	Cabozantinib vs placebo (N = 707) Phase III CELESTIAL trial	mPFS 5.2 mo vs 1.9 mo mOS 10.2 mo vs 8.0 mo
	Ramucirumab[5]	Ramucirumab vs placebo (N = 565) Phase III REACH-2 trial	mPFS 2.8 mo vs 1.6 mo mOS 8.5 mo vs 7.3 mo

TTP = time to progression; mPFS = median progression-free survival; mOS = median overall survival

[1] Llovet JM et al. *N Engl J Med* 2008;359(4):378-90; [2] Kudo M et al. *Lancet* 2018;391(10126):1163-73; [3] Bruix J et al. *Lancet* 2017;389(10064):56-66; [4] Abou-Alfa GK et al. *N Engl J Med* 2018;379(1):54-63; [5] Zhu AX et al. *Lancet Oncol* 2019;20(2):282-96.

Research Article
Hepatic and Biliary Cancer

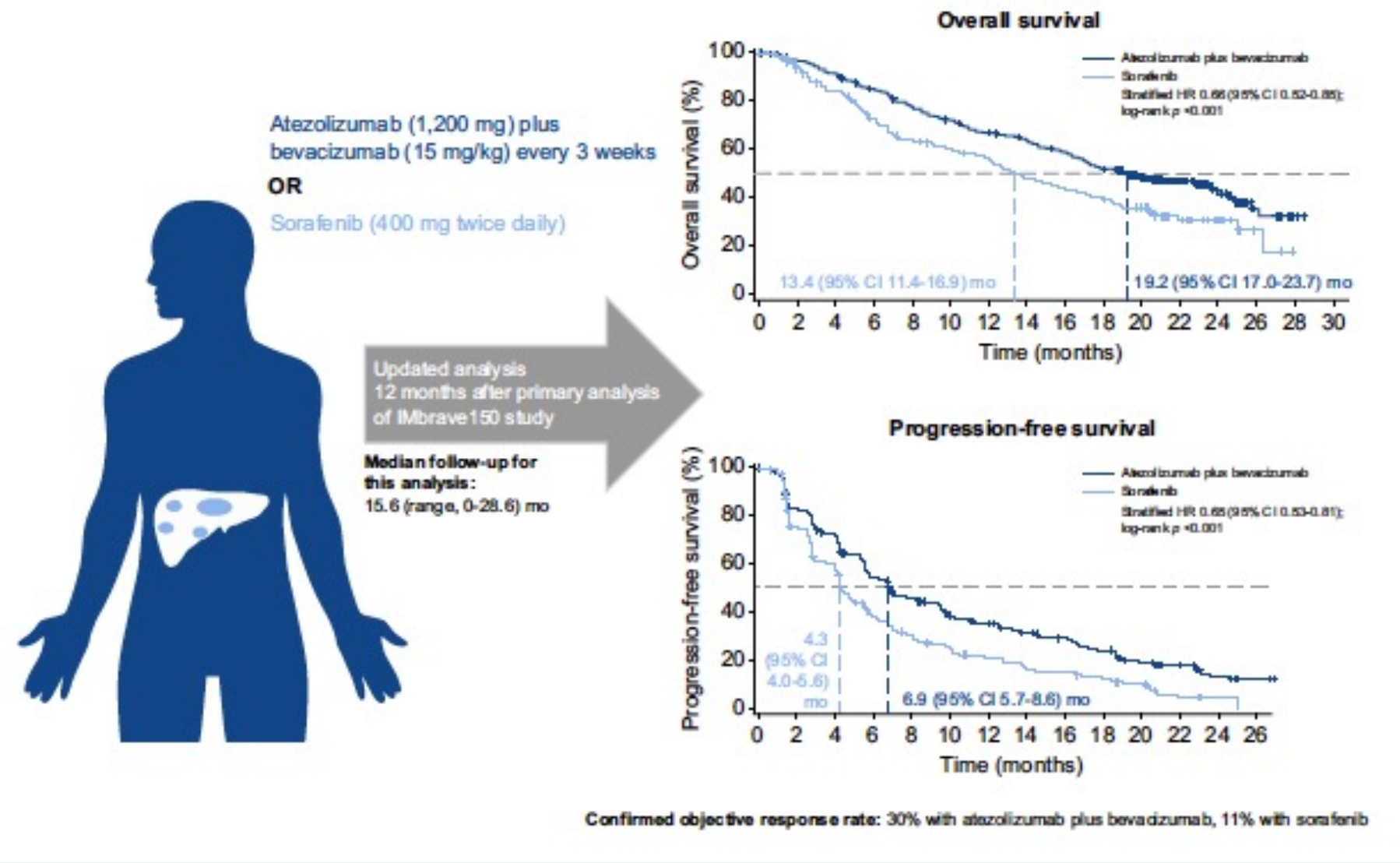
JOURNAL
OF HEPATOLOGY

Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab *vs.* sorafenib for unresectable hepatocellular carcinoma

Ann-Lii Cheng[1,*], Shukui Qin[2], Masafumi Ikeda[3], Peter R. Galle[4], Michel Ducreux[5], Tae-You Kim[6], Ho Yeong Lim[7], Masatoshi Kudo[8], Valeriy Breder[9], Philippe Merle[10], Ahmed O. Kaseb[11], Daneng Li[12], Wendy Verret[13], Ning Ma[14], Alan Nicholas[15], Yifan Wang[16], Lindong Li[17], Andrew X. Zhu[18,19], Richard S. Finn[20,*]

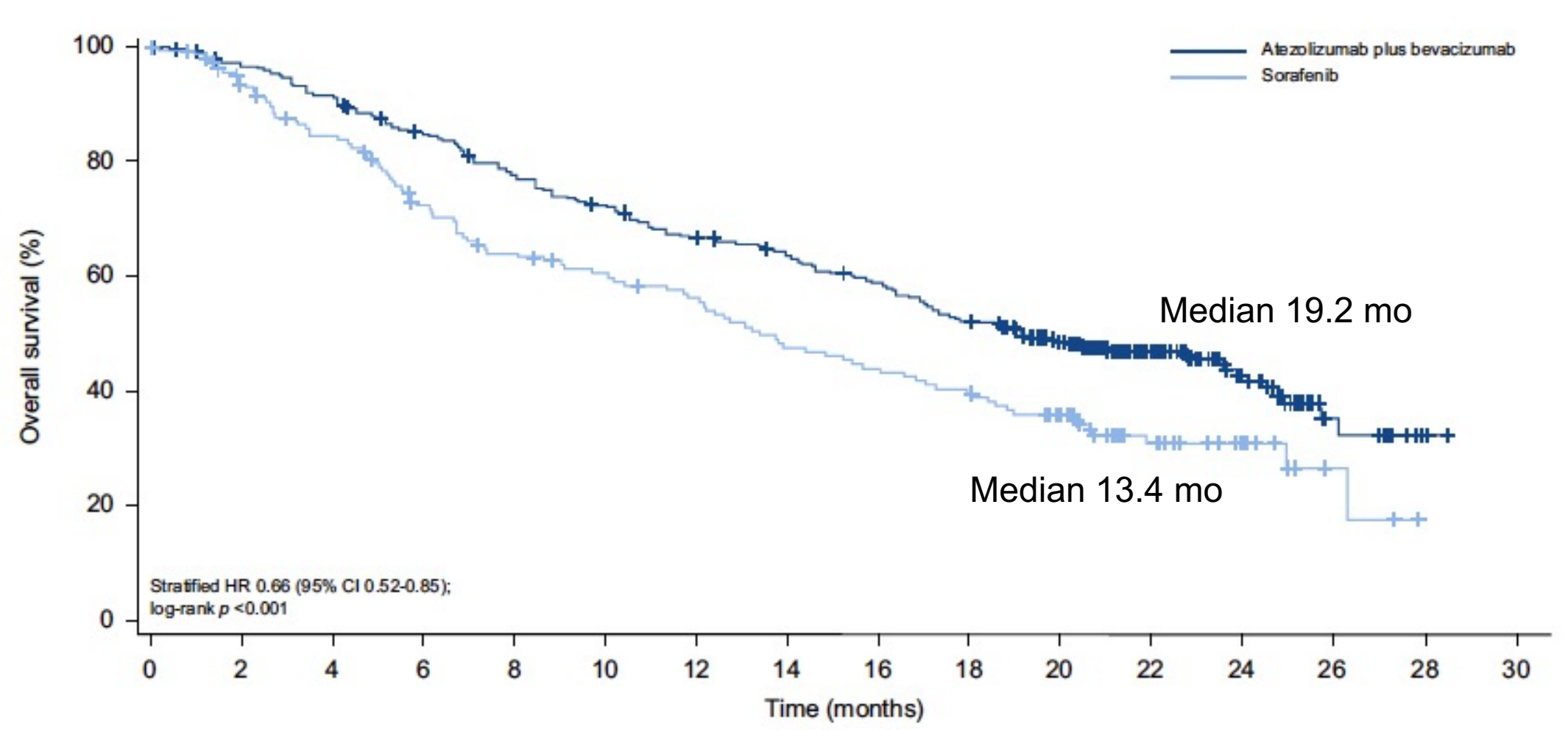
J Hepatol 2022;76(4):862-73.

IMbrave150: Updated 5-Year OS and PFS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



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

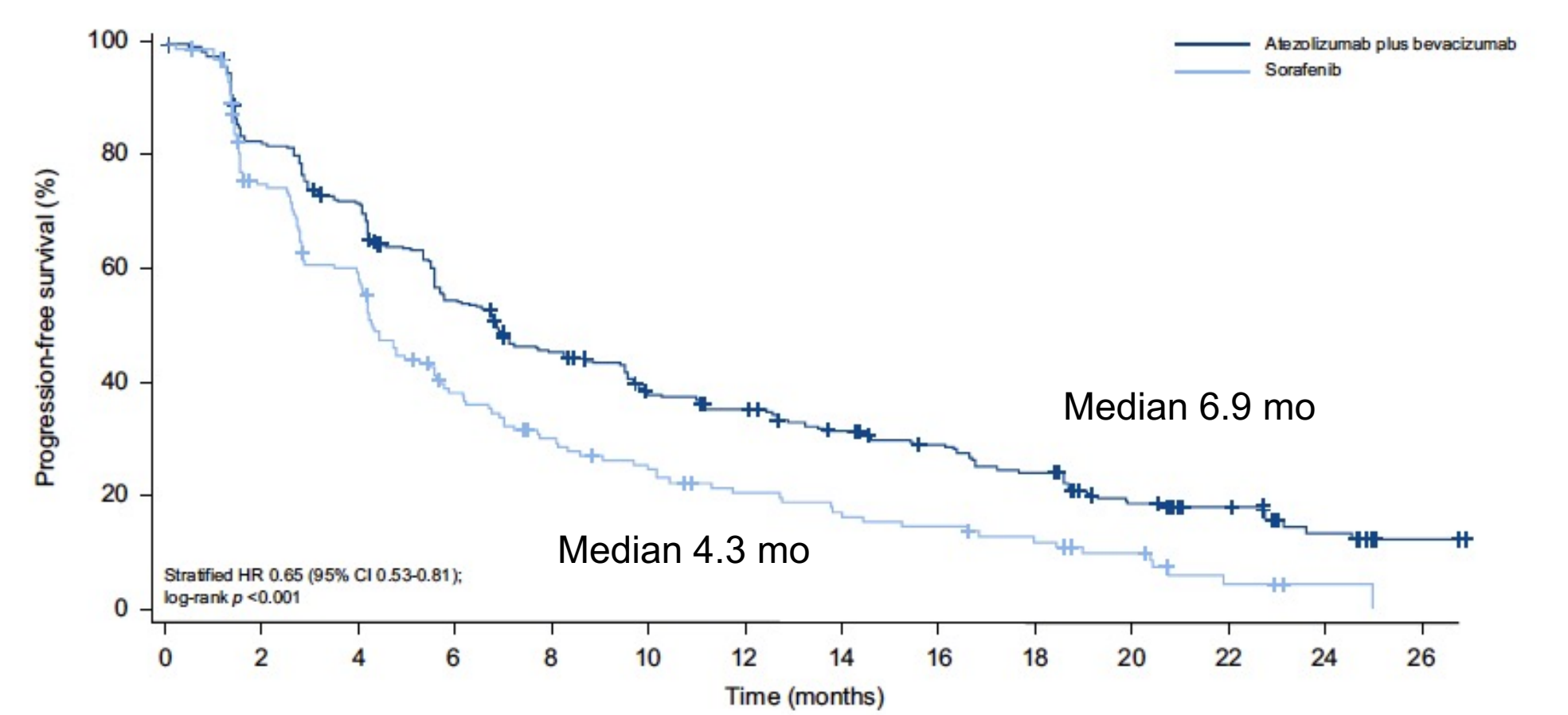
IMbrave150: Updated 5-Year OS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



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

RTP RESEARCH TO PRACTICE

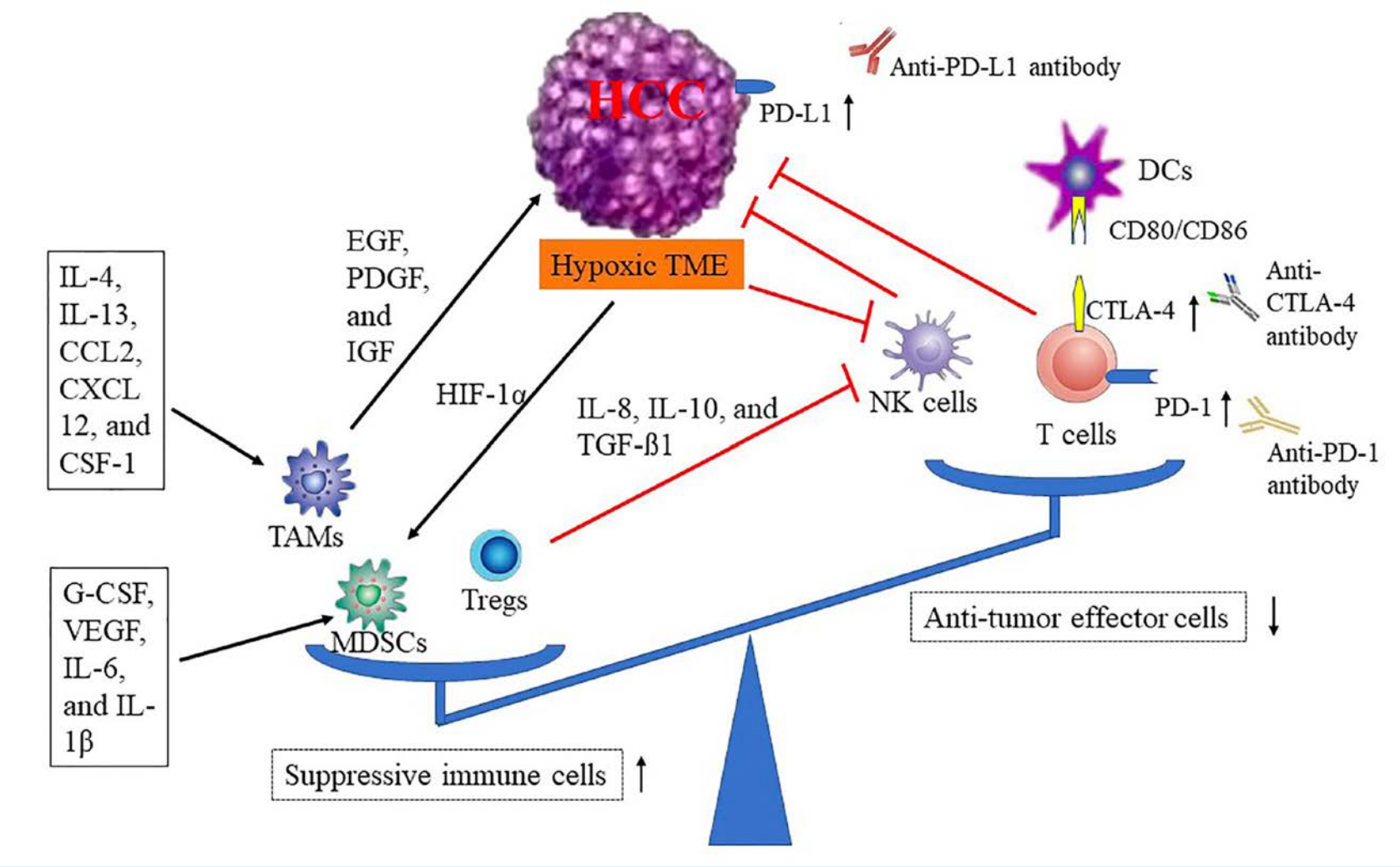
IMbrave150: Updated 5-Year PFS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



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

RTP RESEARCH TO PRACTICE

Increase in Immune Checkpoint Proteins in the Tumor Microenvironment of HCC: Rationale for Targeting PD-1/PD-L1 and CTLA-4



Due to the differences in timing, location, and nonoverlapping effects between the PD-1/PD-L1 and CTLA-4 signaling pathways, combination therapy concurrently targeting these 2 immune checkpoints may achieve synergistic effects in the treatment of HCC

Xing R et al. *Front Immunol* 2021;12:783236.

NEJM Evidence

Published June 6, 2022

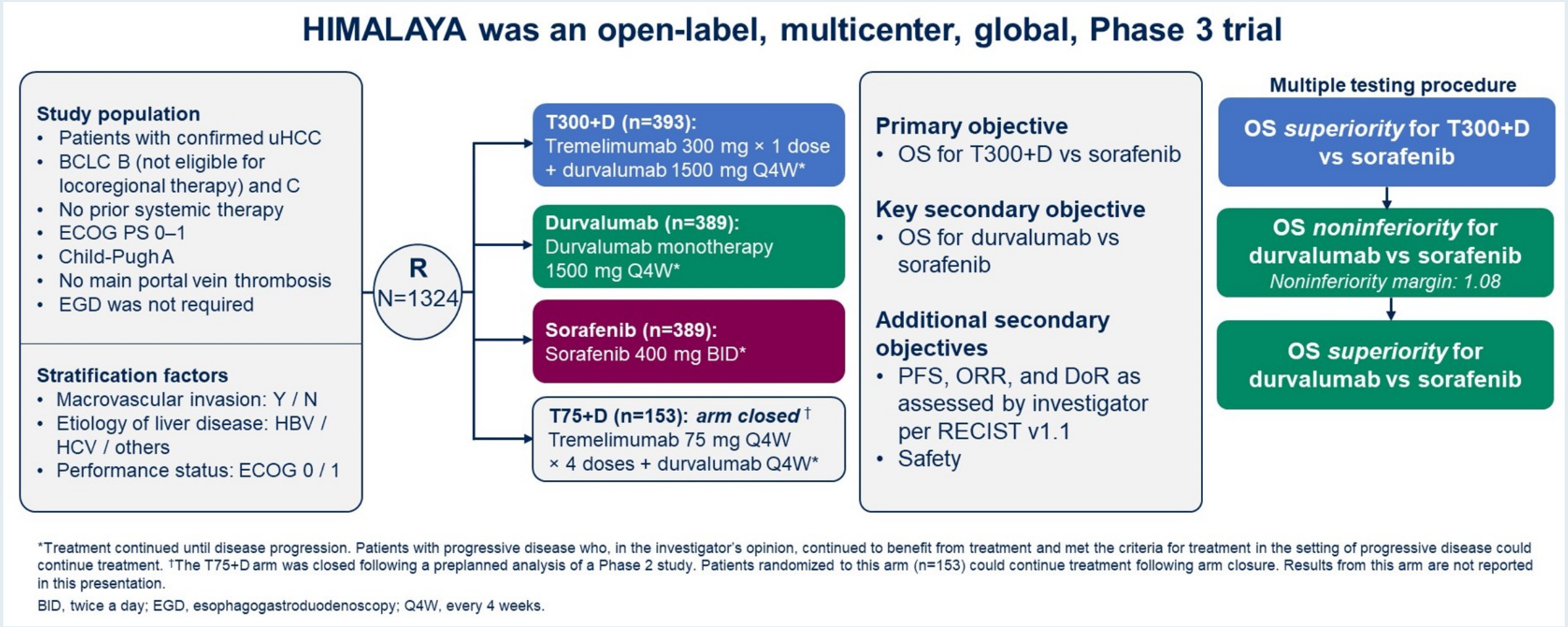
DOI: 10.1056/EVIDoa2100070

ORIGINAL ARTICLE

Tremelimumab Plus Durvalumab in Unresectable Hepatocellular Carcinoma

Ghassan K. Abou-Alfa, M.D., M.B.A.,[1,2] George Lau, M.D., F.R.C.P.,[3] Masatoshi Kudo, M.D., Ph.D.,[4] Stephen L. Chan, M.D.,[5] Robin Kate Kelley, M.D.,[6] Junji Furuse, M.D., Ph.D.,[7] Wattana Sukeepaisarnjaroen, M.D.,[8] Yoon-Koo Kang, M.D., Ph.D.,[9] Tu Van Dao, M.D., Ph.D.,[10] Enrico N. De Toni, M.D., Ph.D.,[11] Lorenza Rimassa, M.D.,[12,13] Valeriy Breder, M.D., Ph.D.,[14] Alexander Vasilyev, M.D.,[15] Alexandra Heurgué, M.D.,[16] Vincent C. Tam, M.D.,[17] Kabir Mody, M.D.,[18] Satheesh Chiradoni Thungappa, M.D.,[19] Yuriy Ostapenko, M.D.,[20] Thomas Yau, M.D.,[21] Sergio Azevedo, M.D.,[22] María Varela, M.D., Ph.D.,[23] Ann-Lii Cheng, M.D., Ph.D.,[24] Shukui Qin, M.D., Ph.D.,[25] Peter R. Galle, M.D., Ph.D.,[26] Sajid Ali, M.D.,[27] Michelle Marcovitz, Ph.D.,[27] Mallory Makowsky, Pharm.D.,[27] Philip He, Ph.D.,[27] John F. Kurland, Ph.D.,[27] Alejandra Negro, Ph.D.,[27] and Bruno Sangro, M.D., Ph.D.[28]

HIMALAYA Phase III Trial Schema

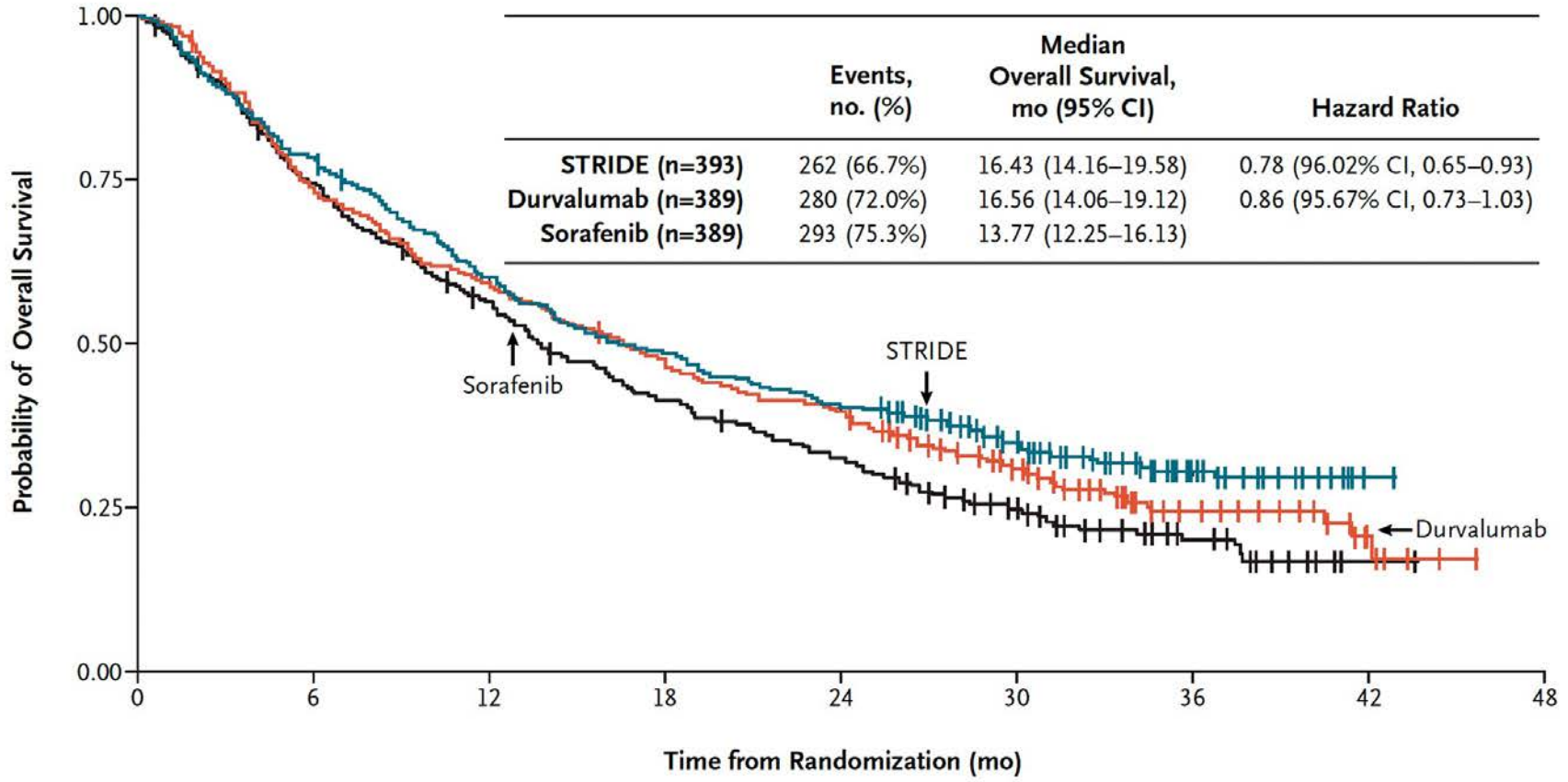


*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned analysis of a Phase 2 study. Patients randomized to this arm (n=153) could continue treatment following arm closure. Results from this arm are not reported in this presentation.

BID, twice a day; EGD, esophagogastroduodenoscopy; Q4W, every 4 weeks.

Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379.

HIMALAYA: Overall Survival

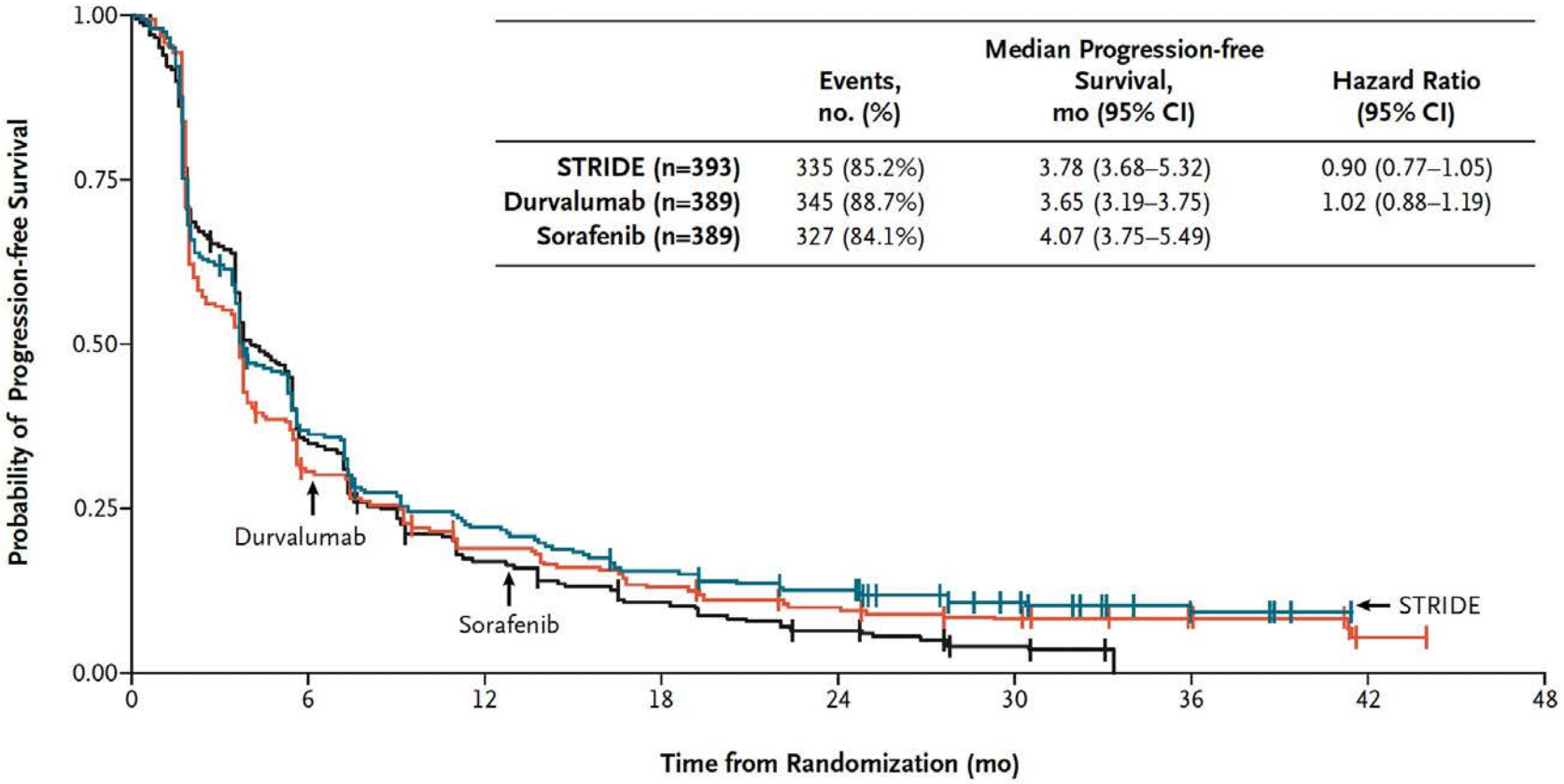


	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

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

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Progression-Free Survival



	Events, no. (%)	Median Progression-free Survival, mo (95% CI)	Hazard Ratio (95% CI)
STRIDE (n=393)	335 (85.2%)	3.78 (3.68–5.32)	0.90 (0.77–1.05)
Durvalumab (n=389)	345 (88.7%)	3.65 (3.19–3.75)	1.02 (0.88–1.19)
Sorafenib (n=389)	327 (84.1%)	4.07 (3.75–5.49)	

No. at Risk									
STRIDE	393	135	81	55	43	26	7	0	0
Durvalumab	389	115	68	47	34	20	6	1	0
Sorafenib	389	118	53	31	18	6	0	0	0

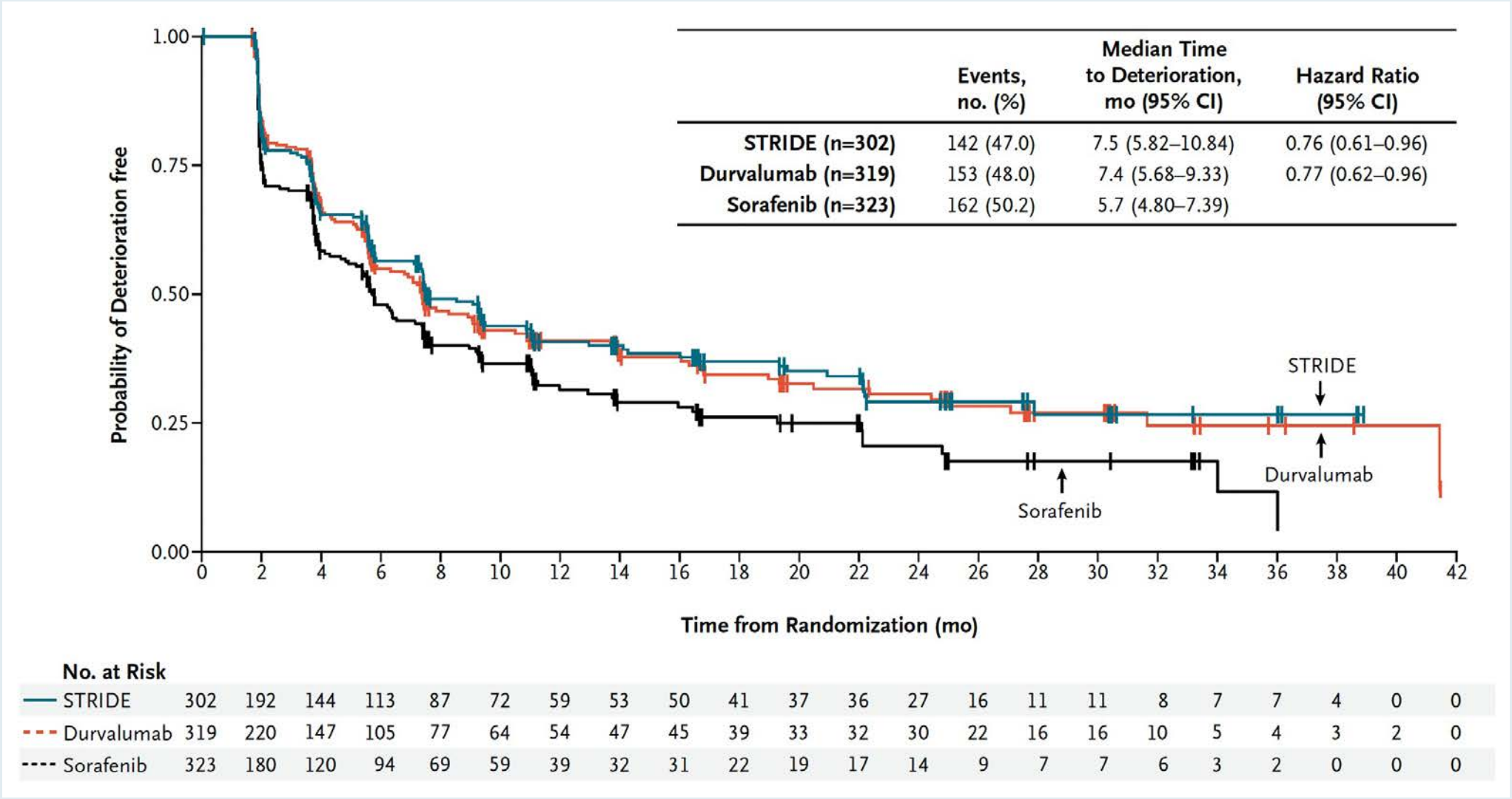
Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Response Outcomes (Intent-to-Treat Population)

Parameter	STRIDE (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
Response — no. (%)			
Objective†	79 (20.1)	66 (17.0)	20 (5.1)
Complete	12 (3.1)	6 (1.5)	0
Partial	67 (17.0)	60 (15.4)	20 (5.1)
Stable disease — no. (%)	157 (39.9)	147 (37.8)	216 (55.5)
Disease control rate — %	236 (60.1)	213 (54.8)	236 (60.7)
Duration of response — mo‡			
Median	22.34	16.82	18.43
IQR	8.54–NR	7.43–NR	6.51–25.99
Time to response — mo			
Median	2.17	2.09	3.78

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Time to Deterioration of Global Health Status or Quality of Life



	Events, no. (%)	Median Time to Deterioration, mo (95% CI)	Hazard Ratio (95% CI)
STRIDE (n=302)	142 (47.0)	7.5 (5.82–10.84)	0.76 (0.61–0.96)
Durvalumab (n=319)	153 (48.0)	7.4 (5.68–9.33)	0.77 (0.62–0.96)
Sorafenib (n=323)	162 (50.2)	5.7 (4.80–7.39)	

No. at Risk																						
STRIDE	302	192	144	113	87	72	59	53	50	41	37	36	27	16	11	11	8	7	7	4	0	0
Durvalumab	319	220	147	105	77	64	54	47	45	39	33	32	30	22	16	16	10	5	4	3	2	0
Sorafenib	323	180	120	94	69	59	39	32	31	22	19	17	14	9	7	7	6	3	2	0	0	0

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Summary of Treatment-Related Adverse Events

Event	STRIDE (n=388)	Durvalumab (n=388)	Sorafenib (n=374)	T75+D (n=152)
Any	294 (75.8)	202 (52.1)	317 (84.8)	106 (69.7)
Any serious	68 (17.5)	32 (8.2)	35 (9.4)	28 (18.4)
Grade 3 or 4	100 (25.8)	50 (12.9)	138 (36.9)	32 (21.1)
Leading to discontinuation	32 (8.2)	16 (4.1)	41 (11.0)	13 (8.6)
Leading to dose delay	83 (21.4)	54 (13.9)	144 (38.5)	42 (27.6)
Leading to death	9 (2.3)†	0	3 (0.8)‡	2 (1.3)
Grade 3 or 4 immune-mediated	49 (12.6)	24 (6.2)	9 (2.4)	18 (11.8)
Any immune-mediated leading to death	6 (1.5)§	0	0	0
Grade 3 or 4 hepatic SMQ	23 (5.9)	20 (5.2)	17 (4.5)	15 (9.9)

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

RTP RESEARCH TO PRACTICE

HIMALAYA: Select Treatment-Emergent Adverse Events

Event	STRIDE (n=388)		Durvalumab (n=388)		Sorafenib (n=374)		T75+D (N=152)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Diarrhea	103 (26.5)	17 (4.4)	58 (14.9)	6 (1.5)	167 (44.7)	16 (4.3)	32 (21.1)	4 (2.6)
Constipation	36 (9.3)	0	42 (10.8)	0	35 (9.4)	0	12 (7.9)	1 (0.7)
Abdominal pain	46 (11.9)	5 (1.3)	37 (9.5)	4 (1.0)	63 (16.8)	12 (3.2)	26 (17.1)	3 (2.0)
Nausea	47 (12.1)	0	37 (9.5)	0	53 (14.2)	0	14 (9.2)	0
Pruritus	89 (22.9)	0	56 (14.4)	0	24 (6.4)	1 (0.3)	27 (17.8)	0
Rash	87 (22.4)	6 (1.5)	40 (10.3)	1 (0.3)	51 (13.6)	4 (1.1)	27 (17.8)	0
Alopecia	2 (0.5)	0	5 (1.3)	0	53 (14.2)	0	1 (0.7)	0
Palmar-plantar erythrodysesthesia syndrome	3 (0.8)	0	1 (0.3)	0	174 (46.5)	34 (9.1)	3 (2.0)	1 (0.7)
Aspartate aminotransferase increased	48 (12.4)	20 (5.2)	56 (14.4)	26 (6.7)	24 (6.4)	12 (3.2)	16 (10.5)	10 (6.6)
Alanine aminotransferase increased	36 (9.3)	10 (2.6)	44 (11.3)	12 (3.1)	20 (5.3)	7 (1.9)	10 (6.6)	5 (3.3)

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

Select Ongoing Phase III Trials of Combination Therapy for Locoregional HCC

Study	N	Eligibility	Randomization arms	Est primary completion
EMERALD-1	724	Child-Pugh A-B7 Not amenable to curative surgery, transplant or ablation	• TACE + durvalumab • TACE + durvalumab + bevacizumab • TACE + placebo	September 2022
EMERALD-2	877	Child-Pugh score of 5-6 High risk of recurrence after curative resection or ablation	• Durvalumab + bevacizumab q3wk • Durvalumab + placebo q3wk • Durvalumab + placebo q2wk	June 2023
EMERALD-3	525	Child-Pugh A Not amenable to curative surgery, transplant or ablation	• TACE + durvalumab + tremelimumab + lenvatinib • TACE + durvalumab + tremelimumab • TACE	October 2025

TACE = transarterial chemoembolization

www.clinicaltrials.gov. Accessed June 2022.

Lancet Oncol 2022;[Online ahead of print].

Cabozantinib plus atezolizumab versus sorafenib for advanced hepatocellular carcinoma (COSMIC-312): a multicentre, open-label, randomised, phase 3 trial

Robin Kate Kelley, Lorenza Rimassa*, Ann-Lii Cheng, Ahmed Kaseb, Shukui Qin, Andrew X Zhu, Stephen L Chan, Tamar Melkadze, Wattana Sukeepaisarnjaroen, Valery Breder, Gontran Verset, Edward Gane, Ivan Borbath, Jose David Gomez Rangel, Baek-Yeol Ryoo, Tamta Makharadze, Philippe Merle, Fawzi Benzaghou, Kamalika Banerjee, Saswati Hazra, Jonathan Fawcett, Thomas Yau*

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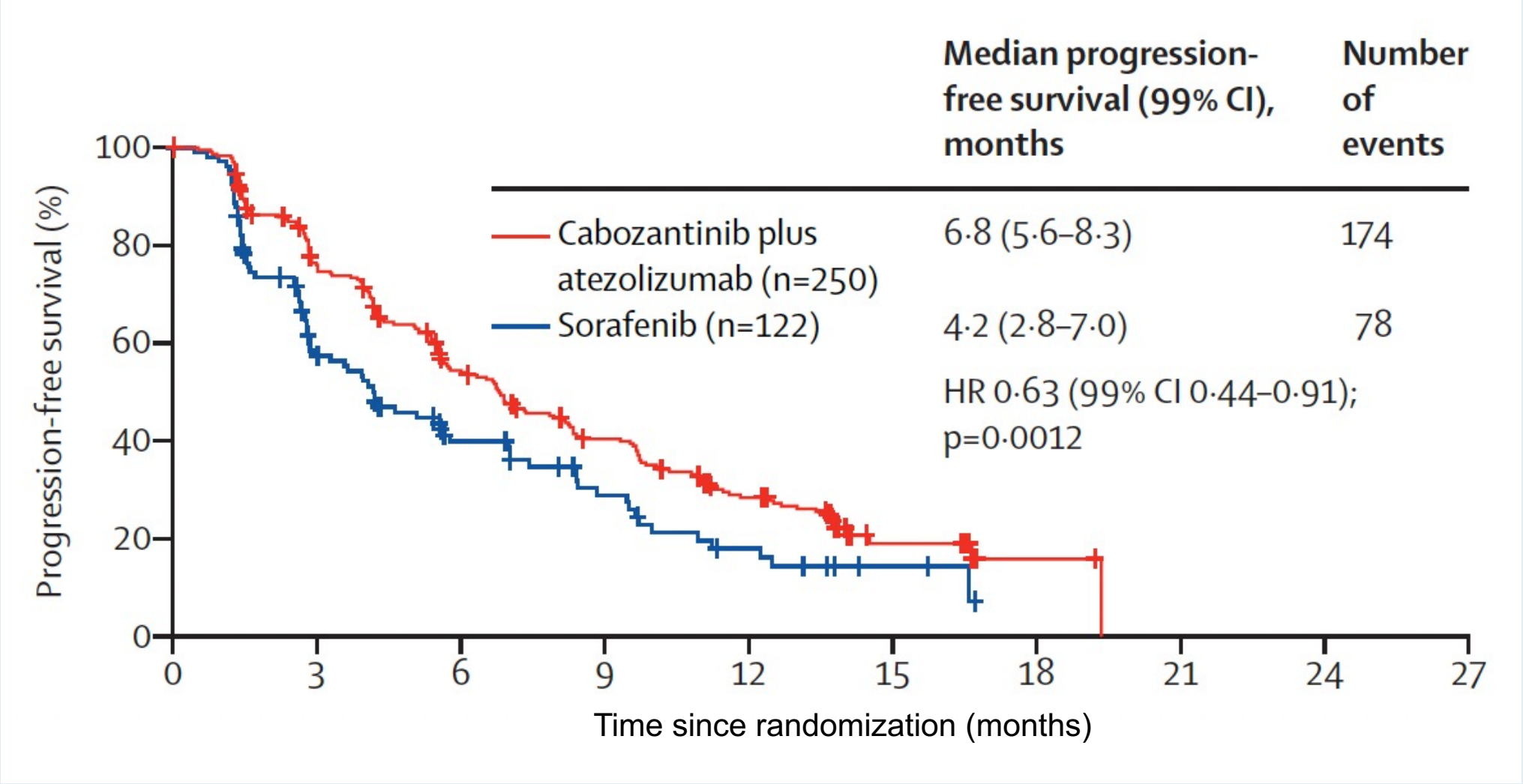
oa OPEN ACCESS

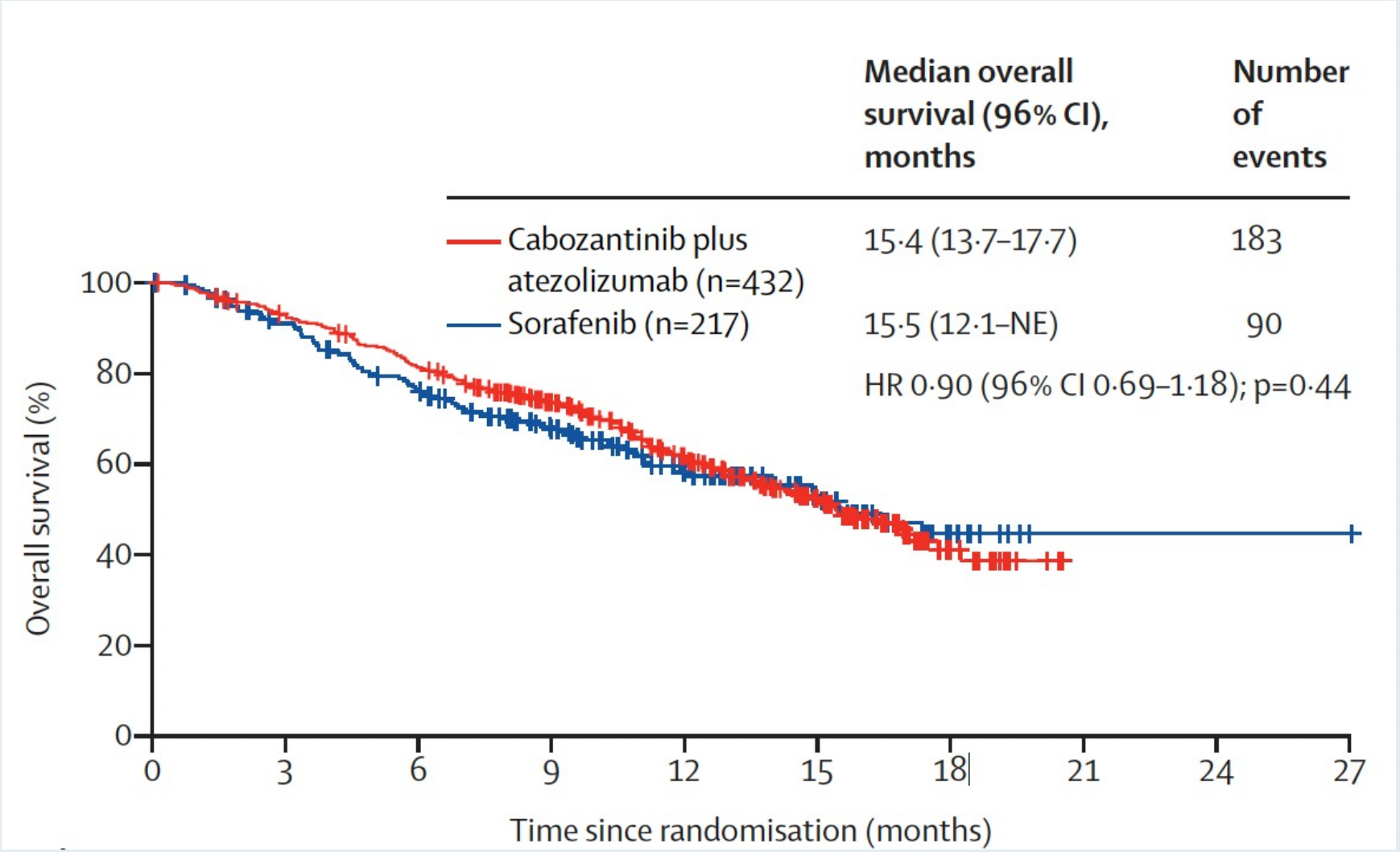
RTP RESEARCH TO PRACTICE

COSMIC-312: Progression-Free Survival in the ITT Population (Final Analysis)



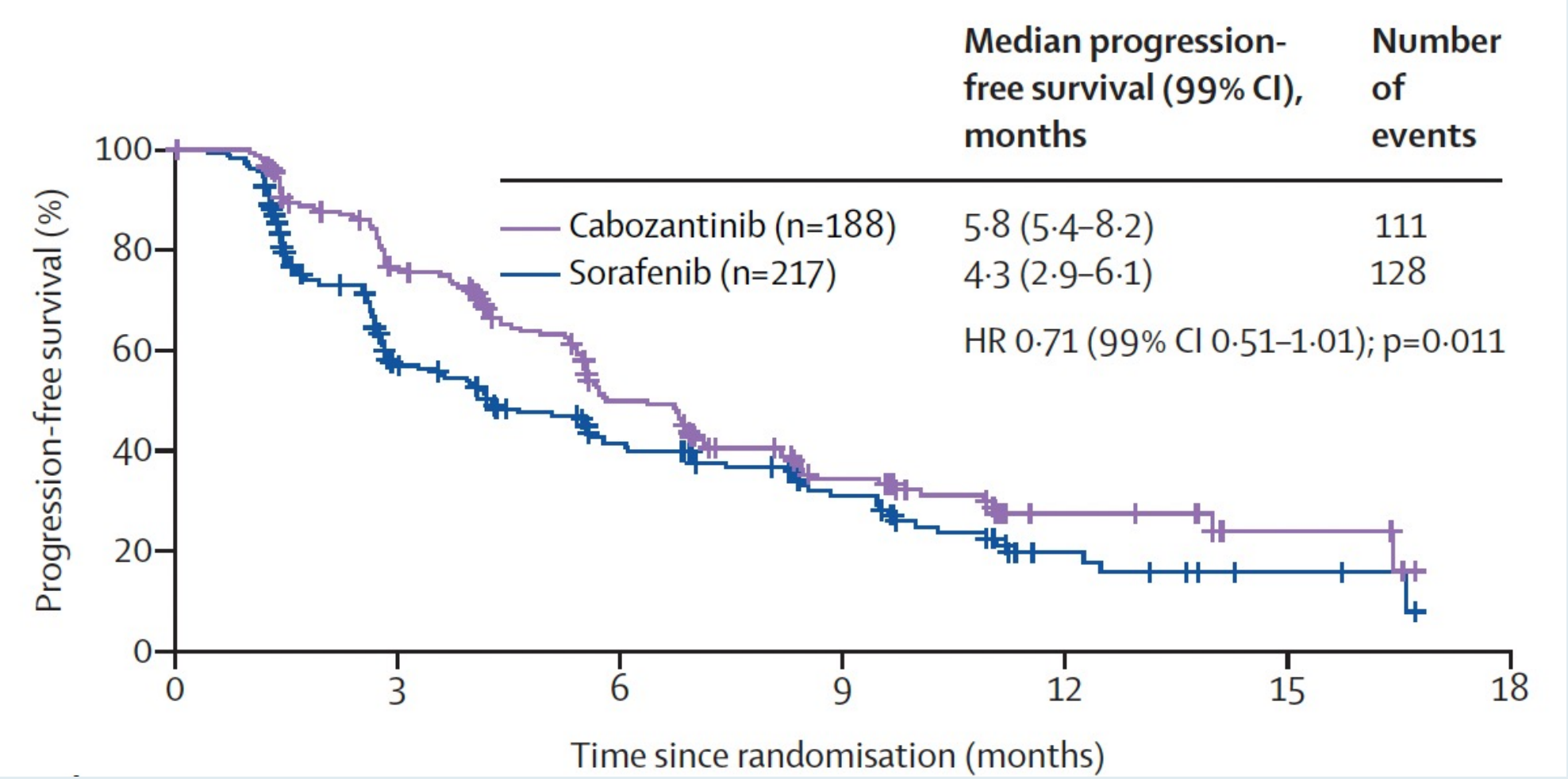
Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

COSMIC-312: Overall Survival in the ITT Population (Interim Analysis)



Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

COSMIC-312: Interim Analysis of PFS for Cabozantinib versus Sorafenib



Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

COSMIC-312: Tumor Response by Blinded Independent Review Committee

	Progression-free survival ITT population		ITT population		
	Cabozantinib plus atezolizumab (n=250)	Sorafenib (n=122)	Cabozantinib plus atezolizumab (n=432)	Sorafenib (n=217)	Cabozantinib (n=188)
Objective response, n (%, 95% CI)	32 (13%, 8·9–17·6)	6 (5%, 1·8–10·4)	47 (11%, 8·1–14·2)	8 (4%, 1·6–7·1)	12 (6%, 3·3–10·9)
Best overall response					
Complete response	1 (<1%)	0	1 (<1%)	0	0
Partial response	31 (12%)	6 (5%)	46 (11%)	8 (4%)	12 (6%)
Stable disease	172 (69%)	71 (58%)	290 (67%)	132 (61%)	145 (77%)
Progressive disease	32 (13%)	26 (21%)	61 (14%)	44 (20%)	20 (11%)
Unable to evaluate or missing	12 (5%)	19 (16%)	29 (7%)	32 (15%)	8 (4%)
No measurable disease	2 (1%)	0	5 (1%)	1 (<1%)	3 (2%)
Disease control*	204 (82%)	77 (63%)	337 (78%)	140 (65%)	157 (84%)
Median time to response (IQR), months	4·1 (2·5–8·4)	3·5 (1·5–4·5)	4·0 (2·6–8·3)	3·5 (2·1–4·4)	4·2 (2·1–5·6)
Median duration of response (95% CI), months	12·4 (9·8–NE)	8·4 (3·0–NE)	10·6 (7·1–12·7)	8·8 (3·0–NE)	15·1 (4·4–NE)
Median time to progression (95% CI), months	7·1 (6·3–8·5)	4·2 (2·9–7·0)	7·0 (6·7–8·3)	4·6 (3·6–6·1)	6·8 (5·6–8·2)

Data are n (%) unless otherwise indicated. ITT=intention-to-treat. NE=not estimable. RECIST 1.1=Response Evaluation Criteria in Solid Tumors version 1.1. *Disease control was defined as the proportion of patients with a complete response, partial response, or stable disease (post-hoc analysis). BIRC=blinded independent radiology committee.

Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

COSMIC-312: Select Adverse Events

	Cabozantinib plus atezolizumab (n=429)				Sorafenib (n=207)				Cabozantinib (n=188)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Any event	104 (24%)	245 (57%)	28 (7%)	51 (12%)	87 (42%)	84 (41%)	11 (5%)	23 (11%)	44 (23%)	101 (54%)	12 (6%)	30 (16%)
Diarrhoea	190 (44%)	18 (4%)	0	0	93 (45%)	4 (2%)	0	0	91 (48%)	12 (6%)	0	0
Palmar-plantar erythrodysaesthesia syndrome	148 (34%)	35 (8%)	0	0	75 (36%)	17 (8%)	0	0	66 (35%)	16 (9%)	0	0
Aspartate aminotransferase increased	92 (21%)	37 (9%)	0	0	22 (11%)	7 (3%)	1 (<1%)	0	43 (23%)	18 (10%)	0	0
Alanine aminotransferase increased	89 (21%)	35 (8%)	3 (1%)	0	17 (8%)	5 (2%)	1 (<1%)	0	43 (23%)	12 (6%)	0	0
Decreased appetite	109 (25%)	7 (2%)	0	0	37 (18%)	4 (2%)	0	0	69 (37%)	9 (5%)	0	0
Fatigue	91 (21%)	15 (3%)	0	0	25 (12%)	8 (4%)	0	0	52 (28%)	7 (4%)	0	0
Hypertension	63 (15%)	37 (9%)	0	0	21 (10%)	17 (8%)	0	0	32 (17%)	23 (12%)	0	0

Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

Selection and Sequencing of Therapies for Relapsed/Refractory HCC

FDA-Approved Anti-VEGF-Directed Monotherapy for HCC

Approved line of therapy	Agent	Study	Primary outcomes
First line	Sorafenib[1]	Sorafenib vs placebo (N = 602) Phase III SHARP trial	TTP 4.1 mo vs 4.9 mo mOS 10.7 mo vs 7.9 mo
	Lenvatinib[2]	Lenvatinib vs sorafenib (N = 954) Phase III REFLECT trial	mPFS 7.4 mo vs 3.7 mo mOS 13.6 mo vs 12.3 mo
Second line	**Regorafenib[3]**	Regorafenib vs placebo (N = 573) Phase III RESORCE trial	mPFS 3.1 mo vs 1.5 mo mOS 10.7 mo vs 7.9 mo
	Cabozantinib[4]	Cabozantinib vs placebo (N = 707) Phase III CELESTIAL trial	mPFS 5.2 mo vs 1.9 mo mOS 10.2 mo vs 8.0 mo
	Ramucirumab[5]	Ramucirumab vs placebo (N = 565) Phase III REACH-2 trial	mPFS 2.8 mo vs 1.6 mo mOS 8.5 mo vs 7.3 mo

TTP = time to progression; mPFS = median progression-free survival ; mOS = median overall survival

[1] Llovet JM et al. *N Engl J Med* 2008;359(4):378-90; [2] Kudo M et al. *Lancet* 2018;391(10126):1163-73; [3] Bruix J et al. *Lancet* 2017;389(10064):56-66; [4] Abou-Alfa GK et al. *N Engl J Med* 2018;379(1):54-63; [5] Zhu AX et al. *Lancet Oncol* 2019;20(2):282-96.

Research

JAMA Oncology | Original Investigation

Efficacy and Safety of Nivolumab Plus Ipilimumab in Patients With Advanced Hepatocellular Carcinoma Previously Treated With Sorafenib

The CheckMate 040 Randomized Clinical Trial

Thomas Yau, MD; Yoon-Koo Kang, MD; Tae-You Kim, MD; Anthony B. El-Khoueiry, MD; Armando Santoro, MD; Bruno Sangro, MD; Ignacio Melero, MD; Masatoshi Kudo, MD; Ming-Mo Hou, MD; Ana Matilla, MD; Francesco Tovoli, MD; Jennifer J. Knox, MD; Aiwu Ruth He, MD; Bassel F. El-Rayes, MD; Mirelis Acosta-Rivera, MD; Ho-Yeong Lim, MD; Jaclyn Neely, PhD; Yun Shen, PhD; Tami Wisniewski, MPH; Jeffrey Anderson, MD; Chiun Hsu, MD, PhD

JAMA Oncol 2020;6(11):e204564.

CheckMate 040: Summary

RCT Nivolumab Plus Ipilimumab in Advanced Hepatocellular Carcinoma Previously Treated With Sorafenib

POPULATION

120 Men
28 Women

Adults with histologically confirmed advanced hepatocellular carcinoma previously treated with sorafenib

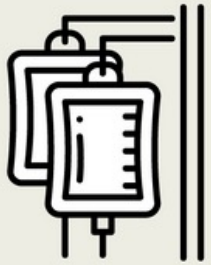
Median 60 (IQR 52.5-66.5) y

SETTINGS / LOCATIONS

31 Medical centers across 10 countries in Asia, Europe, and North America

INTERVENTION

148 Patients randomized



50 Nivolumab 1 mg/kg + ipilimumab 3 mg/kg

Arm A: NIVO1+IPI3 intravenously every 3 weeks for a total of 4 doses, then nivolumab 240 mg intravenously every 2 weeks

49 Nivolumab 3 mg/kg + ipilimumab 1 mg/kg

Arm B: NIVO3+IPI1 intravenously every 3 weeks for a total of 4 doses, then nivolumab 240 mg intravenously every 2 weeks

49 Nivolumab 3 mg/kg + ipilimumab 1 mg/kg

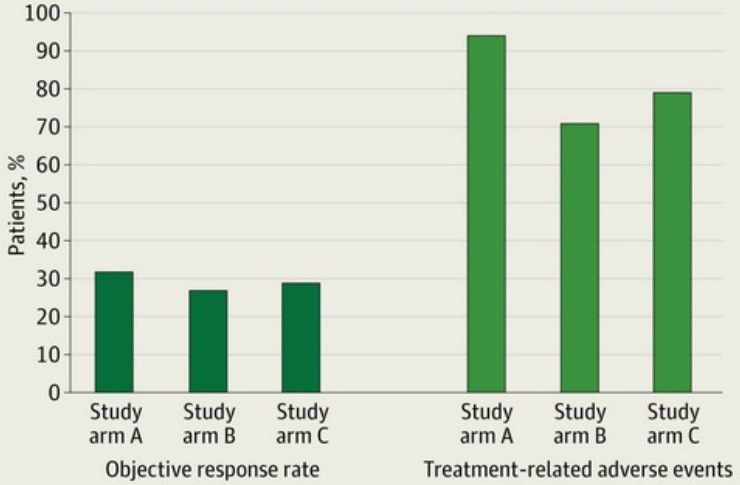
Arm C: NIVO3 intravenously every 2 weeks + IPI1 intravenously every 6 weeks

PRIMARY OUTCOME

Primary end points were treatment-related adverse events (TRAEs) and the objective response rate (ORR); proportion of patients with complete response or partial response per Response Evaluation Criteria In Solid Tumors v1.1 criteria

FINDINGS

Nivolumab plus ipilimumab had manageable safety and durable responses in patients with advanced HCC. The study was not powered to detect statistical differences between treatment arms.



A: ORR (95% CI): 32% (20%-47%); TRAEs: 46/49 pts (94%)
B: ORR (95% CI): 27% (15%-41%); TRAEs: 35/49 pts (71%)
C: ORR (95% CI): 29% (17%-43%); TRAEs: 38/48 pts (79%)

Yau T et al. *JAMA Oncol* 2020;6(11):e204564.

RTP RESEARCH TO PRACTICE

original reports

Safety, Efficacy, and Pharmacodynamics of Tremelimumab Plus Durvalumab for Patients With Unresectable Hepatocellular Carcinoma: Randomized Expansion of a Phase I/II Study

Robin Kate Kelley, MD[1]; Bruno Sangro, MD, PhD[2]; William Harris, MD[3]; Masafumi Ikeda, MD, PhD[4]; Takuji Okusaka, MD, PhD[5]; Yoon-Koo Kang, MD, PhD[6]; Shukui Qin, MD, PhD[7]; David W.-M. Tai, MD[8]; Ho Yeong Lim, MD[9]; Thomas Yau, MD[10]; Wei-Peng Yong, MD[11]; Ann-Lii Cheng, MD, PhD[12]; Antonio Gasbarrini, MD[13]; Silvia Damian, MD[14]; Jordi Bruix, MD[15]; Mitesh Borad, MD[16]; Johanna Bendell, MD[17]; Tae-You Kim, MD[18]; Nathan Standifer, PhD[19]; Philip He, PhD[20]; Mallory Makowsky, PharmD[20]; Alejandra Negro, PhD[20]; Masatoshi Kudo, MD, PhD[21]; and Ghassan K. Abou-Alfa, MD, MBA[22,23]

J Clin Oncol 2021;39(27):2991-3001.

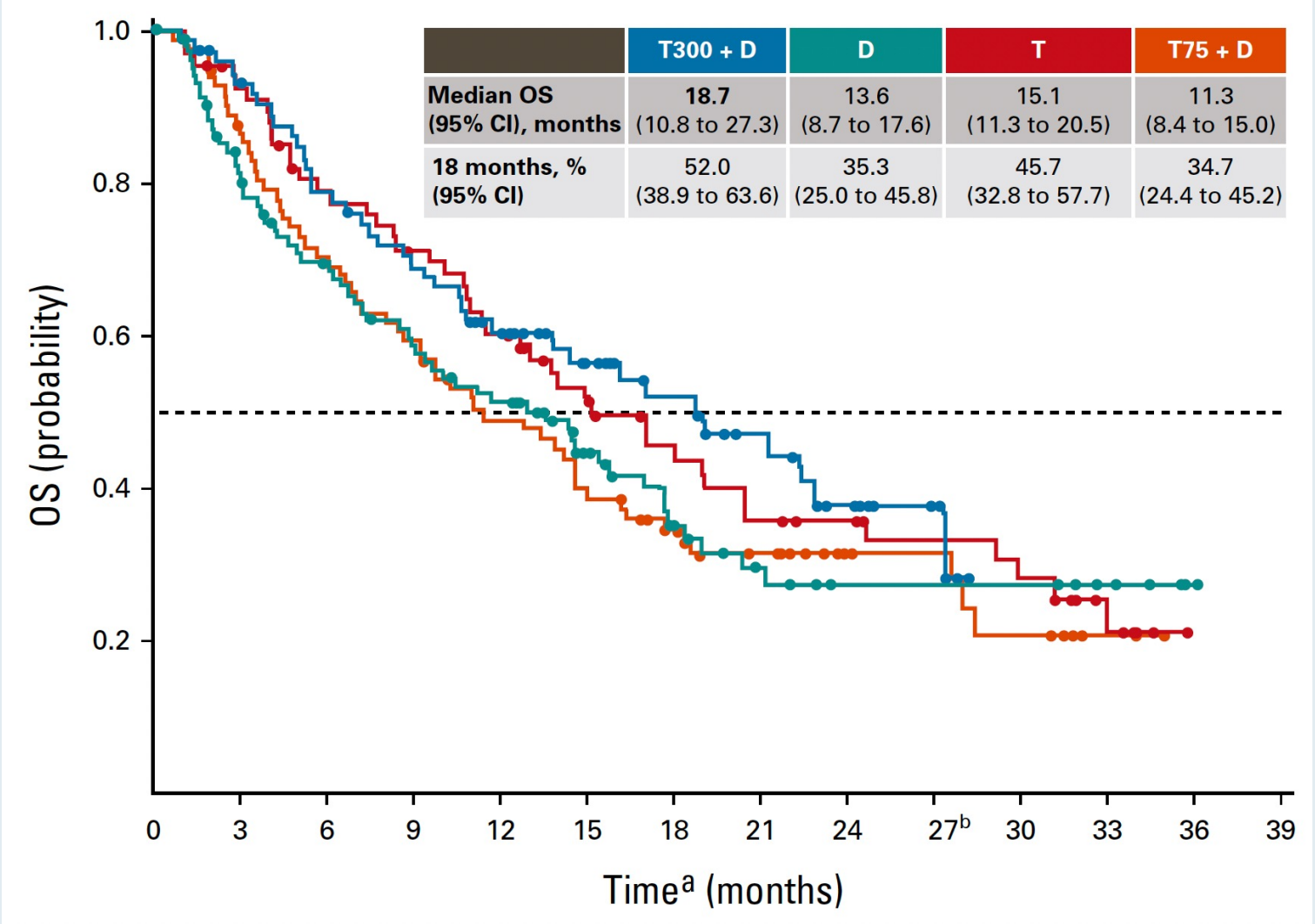
Durvalumab and Tremelimumab Alone or in Combination for Progressive HCC After Prior Sorafenib: Response Outcomes

Outcome	T300 + D (n = 75)	Durvalumab (n = 104)	Tremelimumab (n = 69)	T75 + D (n = 84)
ORR	24%	11%	7%	10%
CR	1%	0	0	2%
PR	17%	11%	5%	6%
SD	16%	28%	29%	23%
Disease control rate	34%	39%	34%	31%
Median DoR	Not reached	11 mo	24 mo	13 mo
Median PFS	2.2 mo	2.1 mo	2.7 mo	1.9 mo

ORR = objective response rate; CR = complete response; PR = partial response; SD = stable disease; DoR = duration of response; PFS = progression-free survival

Kelley RK et al. *J Clin Oncol* 2021;39(27):2991-3001.

Durvalumab and Tremelimumab Alone or in Combination for Progressive HCC After Prior Sorafenib: Overall Survival



Kelley RK et al. *J Clin Oncol* 2021;39(27):2991-3001.

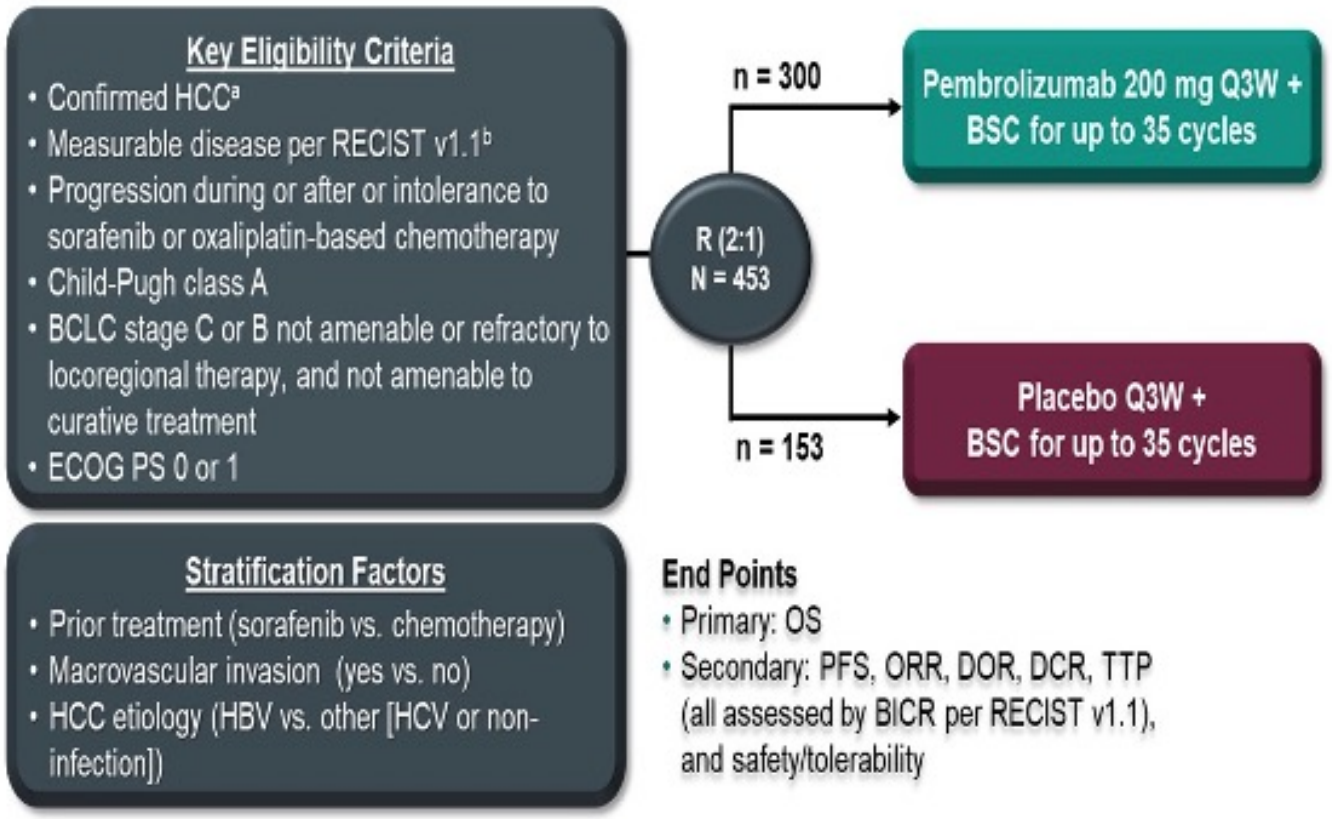
RTP RESEARCH TO PRACTICE

Pembrolizumab Plus Best Supportive Care Versus Placebo Plus Best Supportive Care as Second-line Therapy in Patients in Asia With Advanced Hepatocellular Carcinoma: Phase 3 KEYNOTE-394 Study

Shukui Qin, MD[1]; Zhendong Chen, MD[2]; Weijia Fang, MD[3]; Zhenggang Ren, MD[4]; Ruocai Xu, MD[5]; Baek-Yeol Ryoo, MD[6]; Zhiqiang Meng, MD[7]; Yuxian Bai, MD[8]; Xiaoming Chen, MD[9,10]; Xiufeng Liu, MD[1]; Juxiang Xiao, MD[11]; Gwo Fuang Ho, MRCP, MBChB[12]; Yimin Mao, MD[13]; Xin Wang, MD[14]; Jieer Ying, MD[15]; Jianfeng Li, MD[16]; Wen Yan Zhong, PhD[17]; Yu Zhou, MD[17]; Abby B. Siegel, MD[18]; Chunyi Hao, MD[19]

Gastrointestinal Cancers Symposium 2022;Abstract 383.

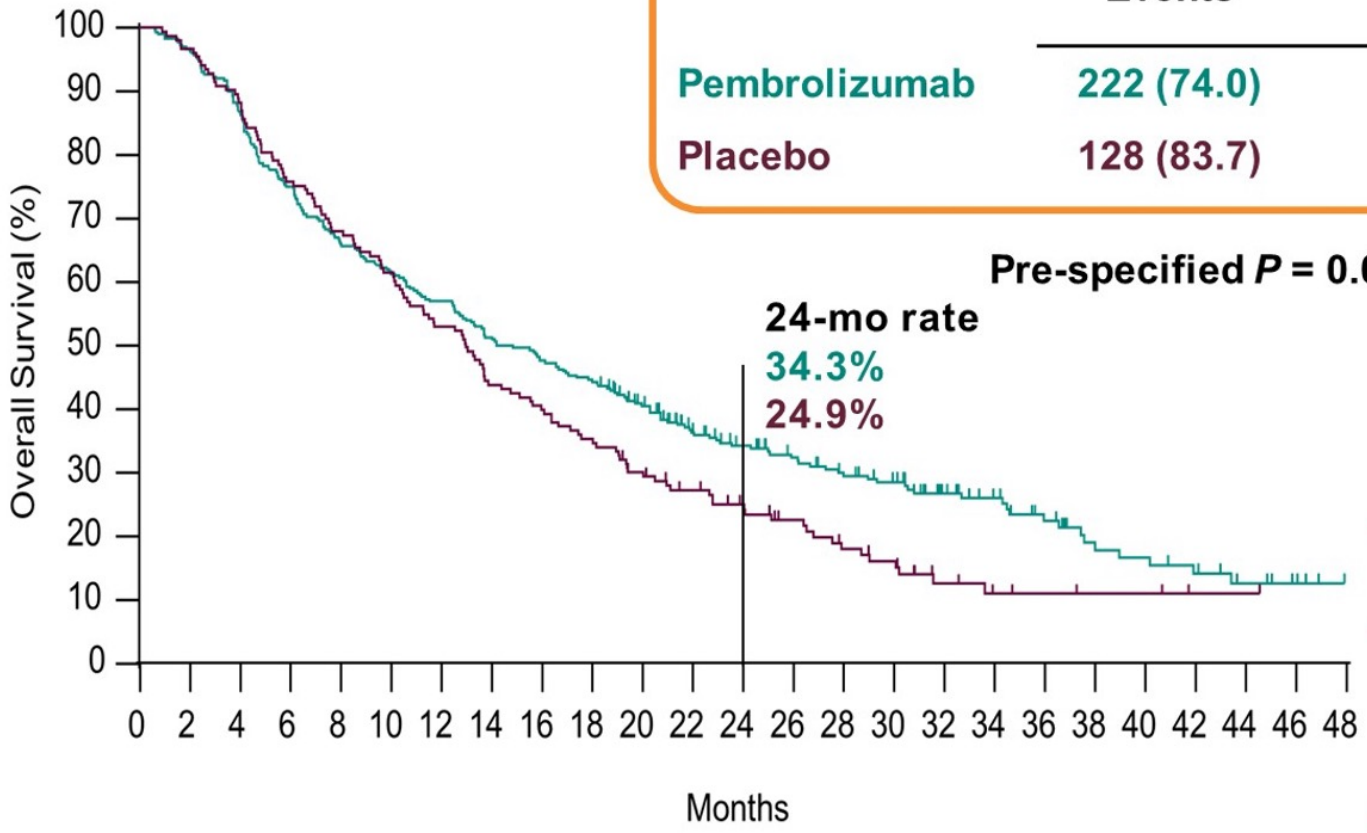
KEYNOTE-394 Study Design and Statistical Considerations



- Overall Type I error = 0.025 controlled across testing of OS, PFS, and ORR[1]
  - Initial allocation PFS = 0.002; OS = 0.023
  - Re-allocated per multiplicity strategy specified in the protocol among 3 endpoints above
- Per protocol, there were 2 interim and 1 final analysis for OS and 1 interim and 1 final analysis for PFS and ORR
  - Interim analysis for PFS and ORR at the time of OS 1st interim analysis
  - Final analysis at the time of OS 2nd interim analysis
- Efficacy boundaries
  - *P* = 0.0193 for OS (final analysis cutoff, June 30, 2021, based on 350 observed events)
  - *P* = 0.0134 for PFS and *P* = 0.0091 for ORR (at 2nd interim cutoff, June 30, 2020; only if OS criteria met)

Qin S et al. Gastrointestinal Cancers Symposium 2022;Abstract 383.

KEYNOTE-394: Overall Survival



	Events	OS, median (95% CI), mo	HR (95% CI)	*P*[a]
Pembrolizumab	222 (74.0)	14.6 (12.6-18.0)	0.79 (0.63-0.99)	*0.0180*
Placebo	128 (83.7)	13.0 (10.5-15.1)		

Pre-specified *P* = 0.0193 required for statistical significance

Post-Study Systemic Anticancer Therapy

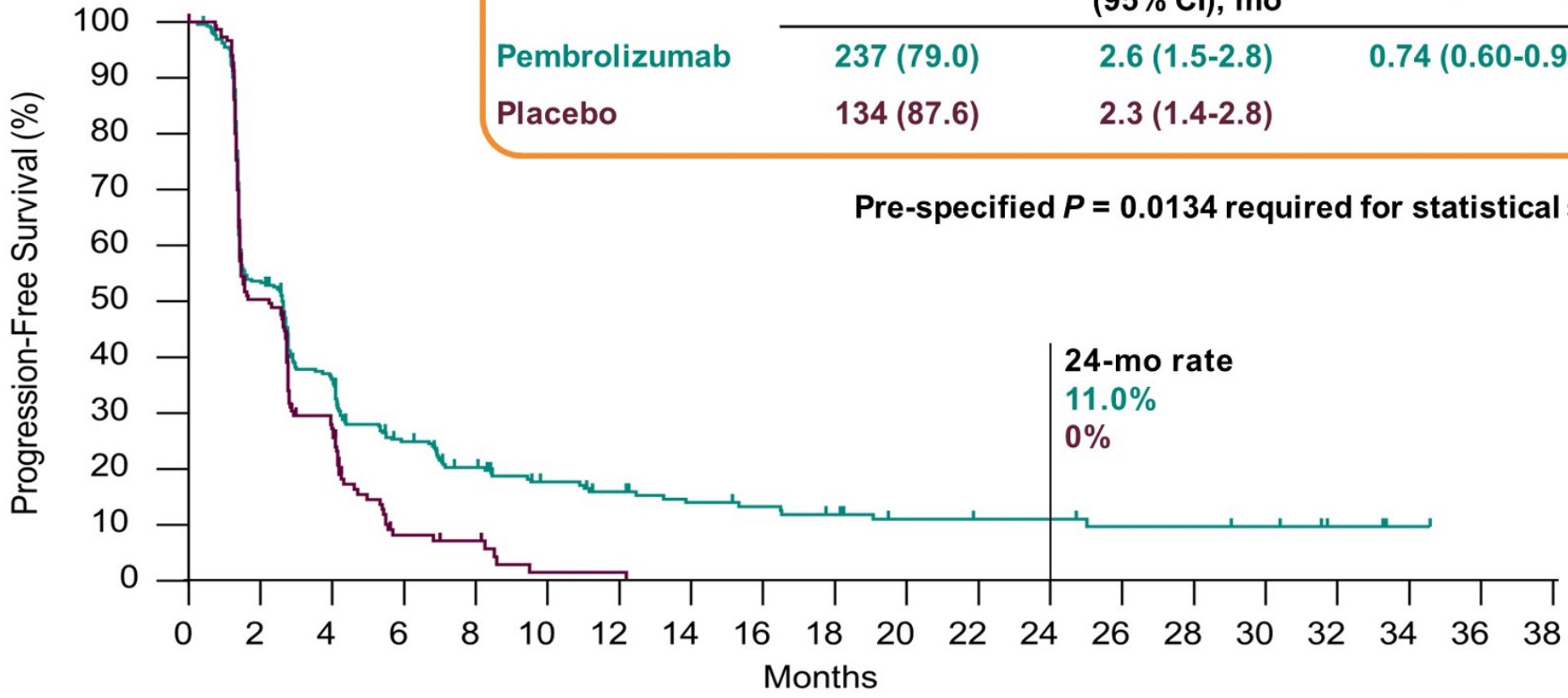
	Pembrolizumab n = 300	Placebo n = 153
Any post-study systemic anticancer therapy	152 (50.7)	102 (66.7)
PD-1 inhibitor or PD-L1 inhibitor[b]	62 (20.7)	43 (28.1)

Qin S et al. Gastrointestinal Cancers Symposium 2022;Abstract 383.

KEYNOTE-394: Progression-Free Survival

	Events	PFS, median (95% CI), mo	HR (95% CI)	*P*[a]
Pembrolizumab	237 (79.0)	2.6 (1.5-2.8)	0.74 (0.60-0.92)	*0.0032*
Placebo	134 (87.6)	2.3 (1.4-2.8)		

Pre-specified *P* = 0.0134 required for statistical significance



Qin S et al. Gastrointestinal Cancers Symposium 2022;Abstract 383.

RTP RESEARCH TO PRACTICE

KEYNOTE-394: Objective Response

	Pembrolizumab n = 300	Placebo n = 153
ORR (CR + PR), % (95% CI)	12.7 (9.1-17.0)	1.3 (0.2-4.6)
Estimated treatment difference, (95% CI; *P*[a])	11.4 (6.7-16.0); *<0.0001*	
Best overall response, n (%)		
CR	6 (2.0)	1 (0.7)
PR	32 (10.7)	1 (0.7)
SD	115 (38.3)	70 (45.8)
Sustained SD[b]	26 (8.7)	8 (5.2)
PD	129 (43.0)	72 (47.1)
Not evaluable	10 (3.3)	1 (0.7)
Not assessable[c]	8 (2.7)	8 (5.2)
DOR,[d] median (range), mo	23.9 (2.8 to 32.0+)	5.6 (3.0+ to 5.6)

Pre-specified *P* = 0.0091 required for statistical significance

Qin S et al. Gastrointestinal Cancers Symposium 2022;Abstract 383.

KEYNOTE-394: Adverse Event (AE) Summary

n (%)	Pembrolizumab n = 299	Placebo n = 153
All-cause AEs		
Any	283 (94.6)	147 (96.1)
Grade 3-5	157 (52.5)	50 (32.7)
Led to discontinuation	38 (12.7)	12 (7.8)
Led to death	10 (3.3)	2 (1.3)
Treatment-related AEs		
Any	200 (66.9)	76 (49.7)
Grade 3-5[a]	43 (14.4)	9 (5.9)
Led to discontinuation	12 (4.0)	1 (0.7)
Led to death	3 (1.0)	0

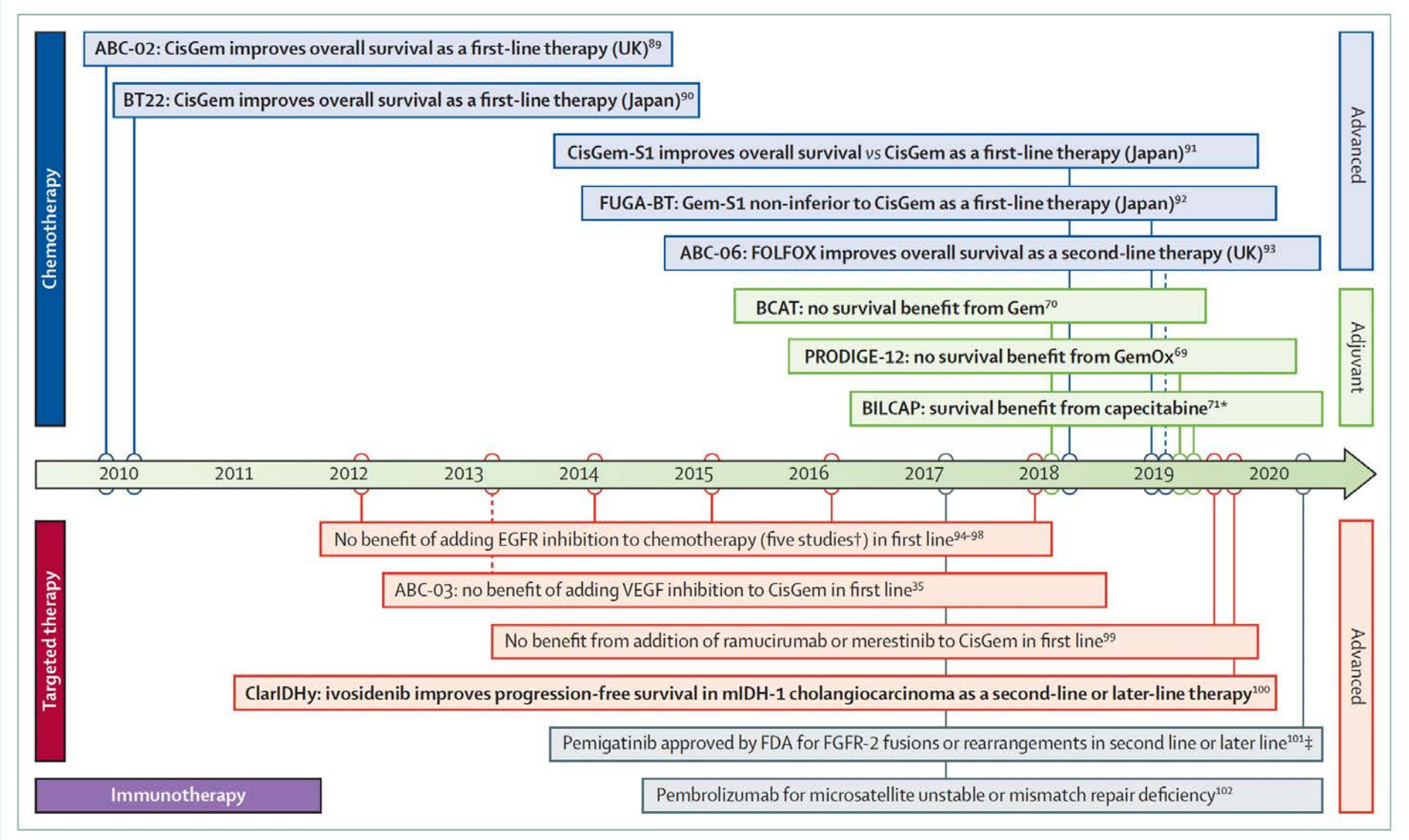
n (%)	Pembrolizumab n = 299	Placebo n = 153
Immune-mediated AEs[b]		
Any	54 (18.1)	16 (10.5)
Grade 3-5	9 (3.0)	0
Led to discontinuation	5 (1.7)	0
Led to death[c]	1 (0.3)	0
Immune-mediated hepatitis[c,d]	5 (1.7)	0

Qin S et al. Gastrointestinal Cancers Symposium 2022;Abstract 383.

Current Treatment Strategies for Advanced Biliary Tract Cancers

RTP
RESEARCH
TO PRACTICE

Timeline of Developments in Systemic Therapy of Biliary Tract Cancer



Valle JW et al. *Lancet* 2021;397(10272):428-44.

RTP RESEARCH TO PRACTICE

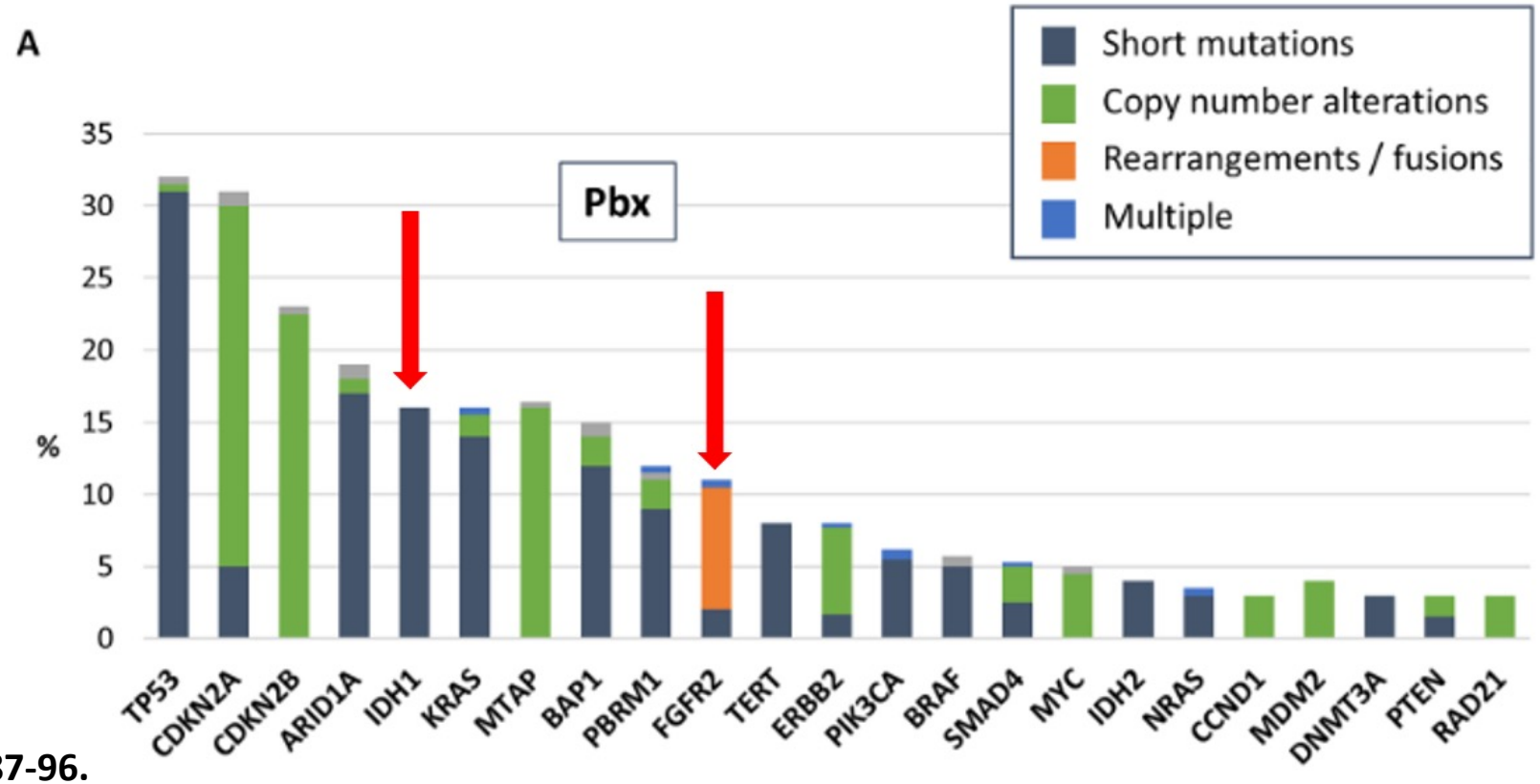
Therapeutic Targets and Approach to Molecular Profiling for Biliary Tract Cancers

Target	Frequency	Targeted agents	Molecular test
IDH1	***13%*** of intrahepatic cholangiocarcinomas	Ivosidenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of IDH1
FGFR pathway	**20%** of intrahepatic cholangiocarcinomas	Erdafitinib; futibatinib; infigratinib; pemigatinib	Tumor next-generation DNA sequencing including FGFR2 intronic region, targeted RNAseq or FISH testing for FGFR2 translocation
BRAF	**5%** of intrahepatic cholangiocarcinomas	Dabrafenib with trametinib; vemurafenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of BRAF
MSI-high or MMR deficiency	**2%** of biliary tract cancers	Pembrolizumab	Multiple testing modalities available: PCR, immunohistochemistry or tumor next-generation DNA sequencing
ERBB2 (HER2)	***15%-20%*** gallbladder cancer; extrahepatic cholangiocarcinomas		Multiple testing modalities available including immunohistochemistry and FISH for expression and amplification, tumor next-generation DNA sequencing for mutations

Valle JW et al. *Lancet* 2021;397(10272):428-44.

Emerging Targets in Cholangiocarcinoma: Focus on FGFR2 and IDH1

- Mutation profiling of N=1632 iCCA using Foundation Medicine panel
  - n=1048 with primary tumor biopsy (PbX)
  - *FGFR2* fusion or rearrangement: 9%
  - *IDH1* mutation: 16%



Israel MA et al. *Oncologist* 2021;26(9):787-96.

RTP RESEARCH TO PRACTICE

FGFR Inhibitor Efficacy in FGFR2 Fusion-Positive Cholangiocarcinoma

	Pemigatinib* (N = 107)	Infigratinib* (N = 108)	Futibatinib (N = 67)	Derazantinib (N = 29)
ORR	35.5%	23.1%	37.3%	20.7%
DCR	82.2%	84.3%	82.1%	82.8%
mPFS	6.9 mo	7.3 mo	7.2 mo	5.7 mo
mOS	21.1 mo	12.2 mo	NR	NR
Toxicities	Hyperphosphatemia, alopecia, diarrhea	Hyperphosphatemia, stomatitis, fatigue	Hyperphosphatemia, diarrhea, dry mouth	Hyperphosphatemia, fatigue, ocular

* FDA approved

Abou-Alfa GK et al. *Lancet Oncol* 2020;21(5):671-84; Javle M et al. Gastrointestinal Cancers Symposium 2021; Goyal L et al. ASCO 2020; Mazzaferro V et al. *Br J Cancer* 2019;120(2):165-71.

Lancet Gasteroenterol Hepatol 2021;6(10):803-15.

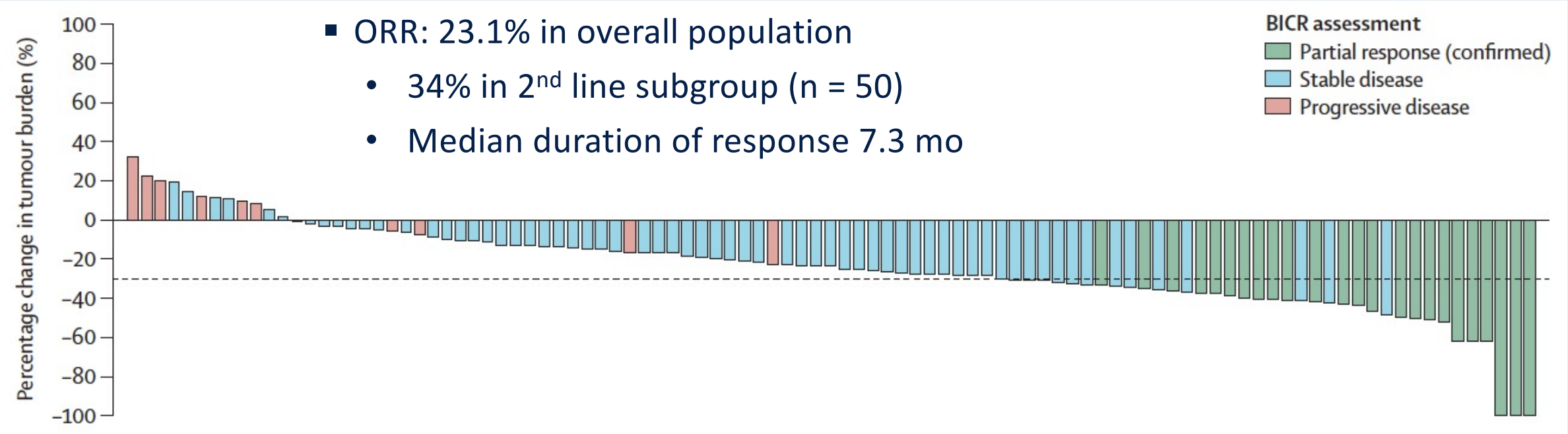
Articles

Infigratinib (BGJ398) in previously treated patients with advanced or metastatic cholangiocarcinoma with *FGFR2* fusions or rearrangements: mature results from a multicentre, open-label, single-arm, phase 2 study

Milind Javle, Sameek Roychowdhury, Robin Kate Kelley, Saeed Sadeghi, Teresa Macarulla, Karl Heinz Weiss, Dirk-Thomas Waldschmidt, Lipika Goyal, Ivan Borbath, Anthony El-Khoueiry, Mitesh J Borad, Wei Peng Yong, Philip A Philip, Michael Bitzer, Surbpong Tanasanvimon, Ai Li, Amit Pande, Harris S Soifer, Stacie Peacock Shepherd, Susan Moran, Andrew X Zhu, Tanios S Bekaii-Saab, Ghassan K Abou-Alfa

Phase II Study of Infigratinib for Advanced or Metastatic Cholangiocarcinoma Harboring FGFR2 Fusions or Rearrangements

- ORR: 23.1% in overall population
  - 34% in 2nd line subgroup (n = 50)
  - Median duration of response 7.3 mo



Javle M et al. *Lancet Gasteroenterol Hepatol* 2021;6(10):803-15.

RTP RESEARCH TO PRACTICE

Infigratinib for Advanced or Metastatic Cholangiocarcinoma: Adverse Events in ≥20% of Patients

	Treatment-emergent adverse events					Treatment-related adverse events of any grade
	Grade 1	Grade 2	Grade 3	Grade 4	Any grade	
Any adverse event	8 (7%)	29 (27%)	61 (56%)	9 (8%)	107 (99%)	104 (96%)
Hyperphosphataemia	37 (34%)	35 (32%)	11 (10%)	0	83 (77%)	80 (74%)
Stomatitis	29 (27%)	14 (13%)	16 (15%)	0	59 (55%)	55 (51%)
Fatigue	21 (19%)	18 (17%)	4 (4%)	0	43 (40%)	31 (29%)
Alopecia	34 (31%)	7 (6%)	0	0	41 (38%)	35 (32%)
Dry eye	25 (23%)	11 (10%)	1 (1%)	0	37 (34%)	34 (31%)
Palmar-plantar erythrodysaesthesia syndrome	11 (10%)	18 (17%)	7 (6%)	0	36 (33%)	35 (32%)
Arthralgia	22 (20%)	12 (11%)	0	0	34 (31%)	31 (29%)
Dysgeusia	27 (25%)	7 (6%)	0	0	34 (31%)	28 (26%)
Constipation	22 (20%)	9 (8%)	1 (1%)	0	32 (30%)	10 (9%)
Dry mouth	24 (22%)	3 (3%)	0	0	27 (25%)	23 (21%)
Hypercalcaemia	13 (12%)	8 (7%)	5 (5%)	1 (1%)	27 (25%)	17 (16%)
Blood creatinine concentration increased	19 (18%)	7 (6%)	0	0	26 (24%)	17 (16%)
Diarrhoea	17 (16%)	6 (6%)	3 (3%)	0	26 (24%)	19 (18%)
Dry skin	23 (21%)	2 (2%)	0	0	25 (23%)	22 (20%)
Decreased appetite	16 (15%)	7 (6%)	1 (1%)	0	24 (22%)	16 (15%)
Hypophosphataemia	6 (6%)	4 (4%)	13 (12%)	1 (1%)	24 (22%)	10 (9%)
Blurred vision	13 (12%)	10 (9%)	0	0	23 (21%)	20 (19%)
AST concentration increased	18 (17%)	3 (3%)	2 (2%)	0	23 (21%)	10 (9%)
Vomiting	16 (15%)	6 (6%)	1 (1%)	0	23 (21%)	14 (13%)

Javle M et al. *Lancet Gasteroenterol Hepatol* 2021;6(10):803-15.

Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma: Update of FIGHT-202

Abou-Alfa GK,[1,2] Sahai V,[3] Hollebecque A,[4] Vaccaro G,[5] Melisi D,[6] Al-Rajabi R,[7] Paulson AS,[8] Borad MJ,[9] Gallinson D,[10] Murphy AG,[11] Oh D-Y,[12] Dotan E,[13] Catenacci DV,[14] Van Cutsem E,[15] Lihou C,[16] Zhen H,[16] Féliz L,[17] Vogel A[18]

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Weill Medical College at Cornell University, New York, NY, USA; [3]Division of Hematology and Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA; [4]Department of Adult Medicine, Gustave Roussy, Villejuif, France; [5]Providence Cancer Center Oncology and Hematology Care Clinic, Portland, OR, USA; [6]Digestive Molecular Clinical Oncology Research Unit, Department of Medicine, Università degli studi di Verona, Verona, Italy; [7]Department of Internal Medicine, Division of Hematology/Oncology, University of Kansas Cancer Center, Kansas City, KS, USA; [8]Baylor Charles A. Sammons Cancer Center, Baylor University Medical Center, Dallas, TX, USA; [9]Department of Internal Medicine, Mayo Clinic Cancer Center, Scottsdale, AZ, USA; [10]Department of Hematology/Oncology, Morristown Memorial Hospital, Carol Cancer Center, Morristown, NJ, USA; [11]Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [12]Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea; [13]Department of Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA; [14]Department of Medicine, University of Chicago Medicine, Chicago, IL, USA; [15]Department of Digestive Oncology, University Hospitals Leuven and KU Leuven, Leuven, Belgium; [16]Incyte Corporation, Wilmington, DE, USA; [17]Incyte Biosciences International Sàrl, Morges, Switzerland; [18]Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Niedersachsen, Germany

2021 American Society of Clinical Oncology (ASCO) Annual Meeting, June 4–8, 2021: Poster 4086

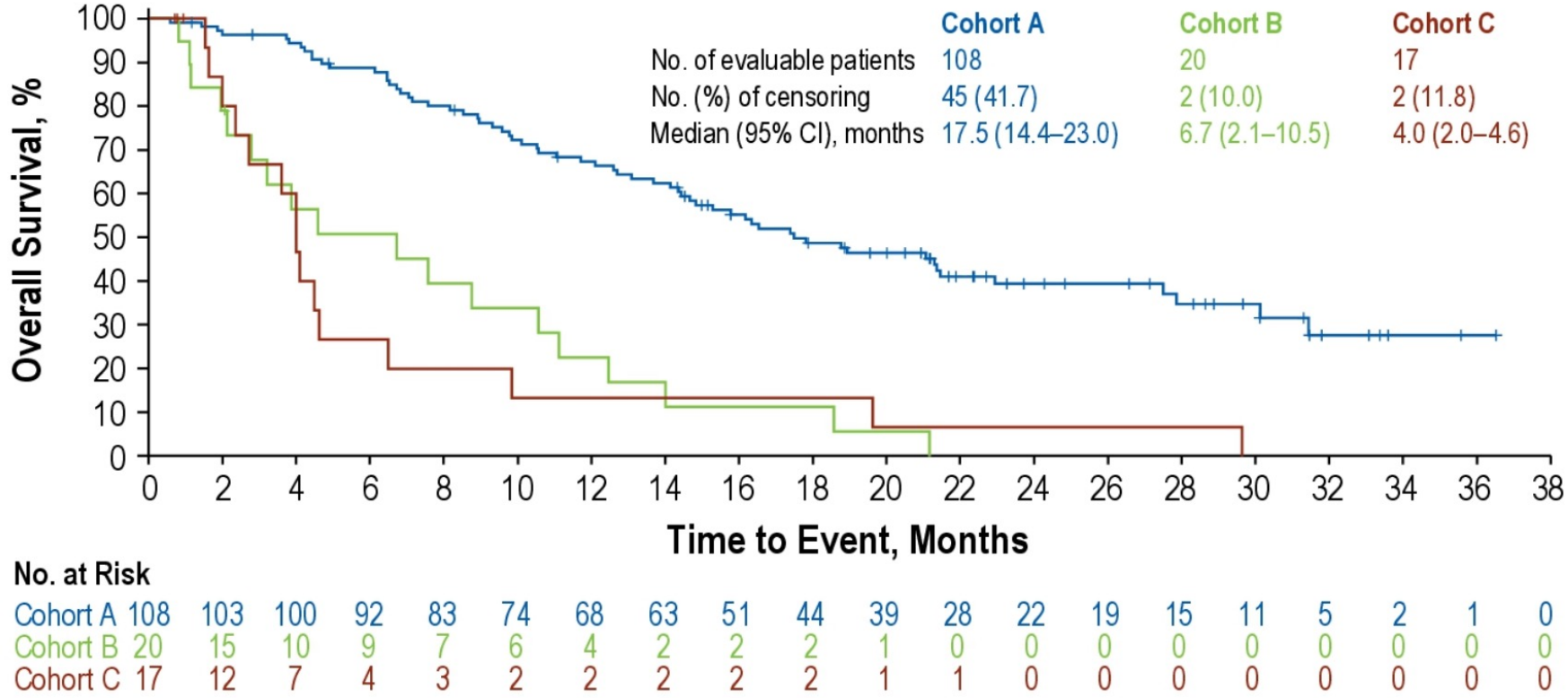
FIGHT-202: Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma

Outcome	Cohort A (N = 108)
Overall response rate	37%
Disease control rate	83%
Median duration of response	8.1 months
Median PFS	7.0 months
Median OS	17.5 months
Median OS in responders	30.1 months
Median OS in nonresponders	13.7 months

About-Alfa GK et al. ASCO 2021;Abstract 4086.

FIGHT-202: Overall Survival (OS) with Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma

- Median OS for patients with *FGFR2* fusions or rearrangements (cohort A) was 17.5 months
  - The median OS for patients who responded to pemigatinib with either a complete or partial response was 30.1 months; median OS for patients who did not respond to pemigatinib was 13.7 months



About-Alfa GK et al. ASCO 2021;Abstract 4086.

RTP RESEARCH TO PRACTICE

FIGHT-202: Adverse Events with Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma

- The most common treatment-emergent adverse events of any grade and of grade ≥3 are summarized in **Table 2**
  - Overall, the safety profile observed in the current analysis was consistent with the primary analysis[1] and no new safety signals were observed

Table 2. TEAEs Occurring in ≥25% of Overall Patient Population

	Cohort A (n = 108)* *FGFR2* Fusions or Rearrangements		Cohort B (n = 20) Other *FGF/FGFR* Genetic Alterations		Cohort C (n = 17) No *FGF/FGFR* Genetic Alterations		Total (N=147)†	
Adverse Event, n (%)	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Hyperphosphatemia	60 (55.6)	0	13 (65.0)	0	12 (70.6)	0	86 (58.5)	0
Alopecia	64 (59.3)	0	4 (20.0)	0	3 (17.6)	0	73 (49.7)	0
Diarrhea	57 (52.8)	4 (3.7)	5 (25.0)	0	6 (35.3)	1 (5.9)	69 (46.9)	5 (3.4)
Fatigue	50 (46.3)	5 (4.6)	5 (25.0)	0	9 (52.9)	3 (17.6)	64 (43.5)	8 (5.4)
Nausea	46 (42.6)	3 (2.8)	7 (35.0)	0	7 (41.2)	0	61 (41.5)	3 (2.0)
Dysgeusia	52 (48.1)	0	3 (15.0)	0	3 (17.6)	0	60 (40.8)	0
Stomatitis	45 (41.7)	9 (8.3)	6 (30.0)	0	3 (17.6)	0	55 (37.4)	9 (6.1)
Constipation	46 (42.6)	1 (0.9)	5 (25.0)	0	2 (11.8)	0	54 (36.7)	1 (0.7)
Decreased appetite	34 (31.5)	1 (0.9)	8 (40.0)	1 (5.0)	7 (41.2)	1 (5.9)	50 (34.0)	3 (2.0)
Dry mouth	42 (38.9)	0	5 (25.0)	0	1 (5.9)	0	50 (34.0)	0
Vomiting	36 (33.3)	2 (1.9)	3 (15.0)	0	4 (23.5)	0	43 (29.3)	2 (1.4)
Dry eye	38 (35.2)	0	1 (5.0)	0	1 (5.9)	0	41 (27.9)	1 (0.7)
Arthralgia	33 (30.6)	7 (6.5)	4 (20.0)	2 (10.0)	1 (5.9)	0	38 (25.9)	9 (6.1)

Includes 1 patient from Japan who was enrolled in cohort A after the primary cutoff date (enrollment was held open in Japan for this patient because they were already in screening). †The total includes 2 patients for whom *FGF/FGFR* status could not be centrally determined, 1 of whom was reassigned from cohort C after the primary cutoff date (March 22, 2019). TEAE, treatment-emergent adverse event.

About-Alfa GK et al. ASCO 2021;Abstract 4086.

FDA Accepts for Priority Review Futibanib's New Drug Application for Cholangiocarcinoma

Press Release: March 30, 2022

"The US Food and Drug Administration (FDA) has accepted for priority review the New Drug Application (NDA) for futibatinib in the treatment of patients with previously treated locally advanced or metastatic cholangiocarcinoma (CCA) harboring FGFR2 gene rearrangements, including gene fusions. Futibatinib is an investigational, oral, potent, selective and irreversible small-molecule inhibitor of FGFR1, 2, 3 and 4. The FDA provided an anticipated Prescription Drug User Fee Act (PDUFA) action date of September 30, 2022.

The NDA is based on data from the pivotal Phase 2b FOENIX-CCA2 trial in 103 patients with locally advanced or metastatic unresectable intrahepatic (inside the liver) CCA, harboring FGFR2 gene rearrangements including fusions who had received one or more prior lines of systemic therapy. Patients in the trial received futibatinib 20 mg once daily until disease progression or unacceptable toxicity. The trial's primary endpoint was an objective response rate (ORR), which was 41.7% as assessed by independent central review. The key secondary endpoint of duration of response (DOR) demonstrated a median of 9.7 months (72% of responses ≥6 months). Common treatment-related adverse events (TRAEs) in the trial were hyperphosphatemia (85%), alopecia (33%) and dry mouth (30%). The only serious adverse reaction reported in more than one patient enrolled in the FOENIX-CCA2 trial was migraine (1.9%)."

https://www.prnewswire.com/news-releases/us-food-and-drug-administration-fda-accepts-for-priority-review-taiho-oncologys-new-drug-application-for-futibatinib-for-cholangiocarcinoma-301513278.html?tc=eml_cleartime

RTP RESEARCH TO PRACTICE

Updated Results of the FOENIX-CCA2 Trial: Efficacy and Safety of Futibatinib in Intrahepatic Cholangiocarcinoma Harboring *FGFR2* Fusions/Rearrangements

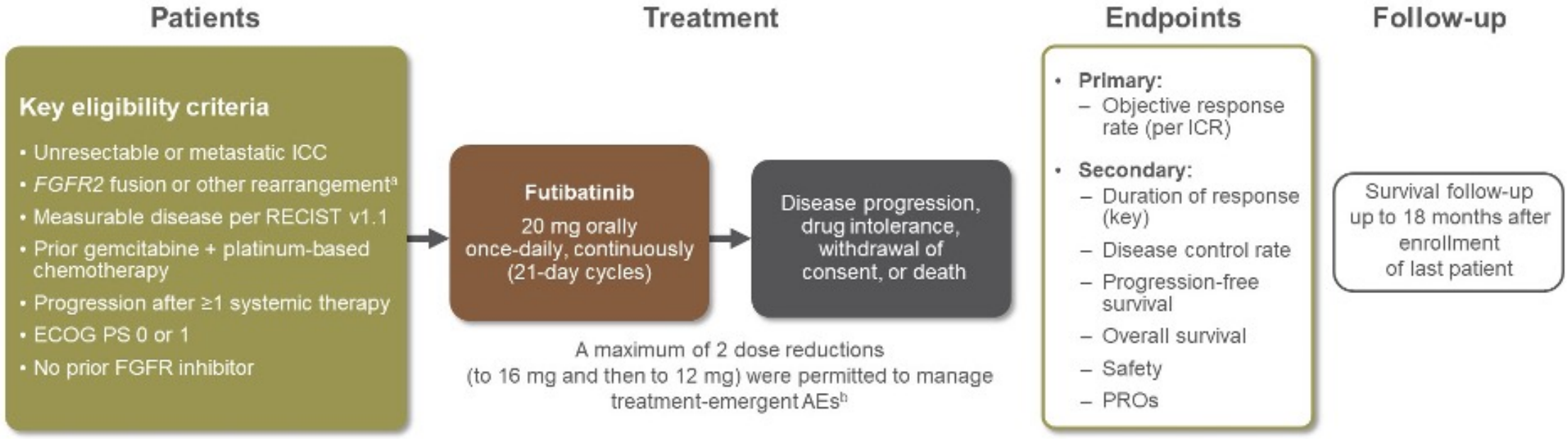
Lipika Goyal,[1] Funda Meric-Bernstam,[2] Antoine Hollebecque,[3] Chigusa Morizane,[4] Juan W. Valle,[5] Thomas B. Karasic,[6] Thomas A. Abrams,[7] Robin Kate Kelley,[8] Philippe Cassier,[9] Junji Furuse,[10] Heinz-Josef Klümpen,[11] Heung-Moon Chang,[12] Li-Tzong Chen,[13] Yoshito Komatsu,[14] Kunihiro Masuda,[15] Daniel Ahn,[16] Kate Li,[17] Karim A. Benhadji,[17] Volker Wacheck,[17] John A. Bridgewater[18]

[1]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [2]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Gustave Roussy, Drug Development Department (DITEP), F-94805, Villejuif, France; [4]National Cancer Center Hospital, Tokyo, Japan; [5]University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [6]Hospital of the University of Pennsylvania, Philadelphia, PA, USA; [7]Dana-Farber Cancer Institute, Boston, MA, USA; [8]University of California, San Francisco, CA, USA; [9]Centre Léon-Bérard, Lyon, France; [10]Kyorin University, Faculty of Medicine, Tokyo, Japan; [11]Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands; [12]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [13]National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan; [14]Hokkaido University Hospital Cancer Center, Hokkaido, Japan; [15]Tohoku University Graduate School of Medicine, Miyagi, Japan; [16]Mayo Clinic, Phoenix, AZ, USA; [17]Taiho Oncology, Inc., Princeton, NJ, USA; [18]UCL Cancer Institute, London, UK

ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

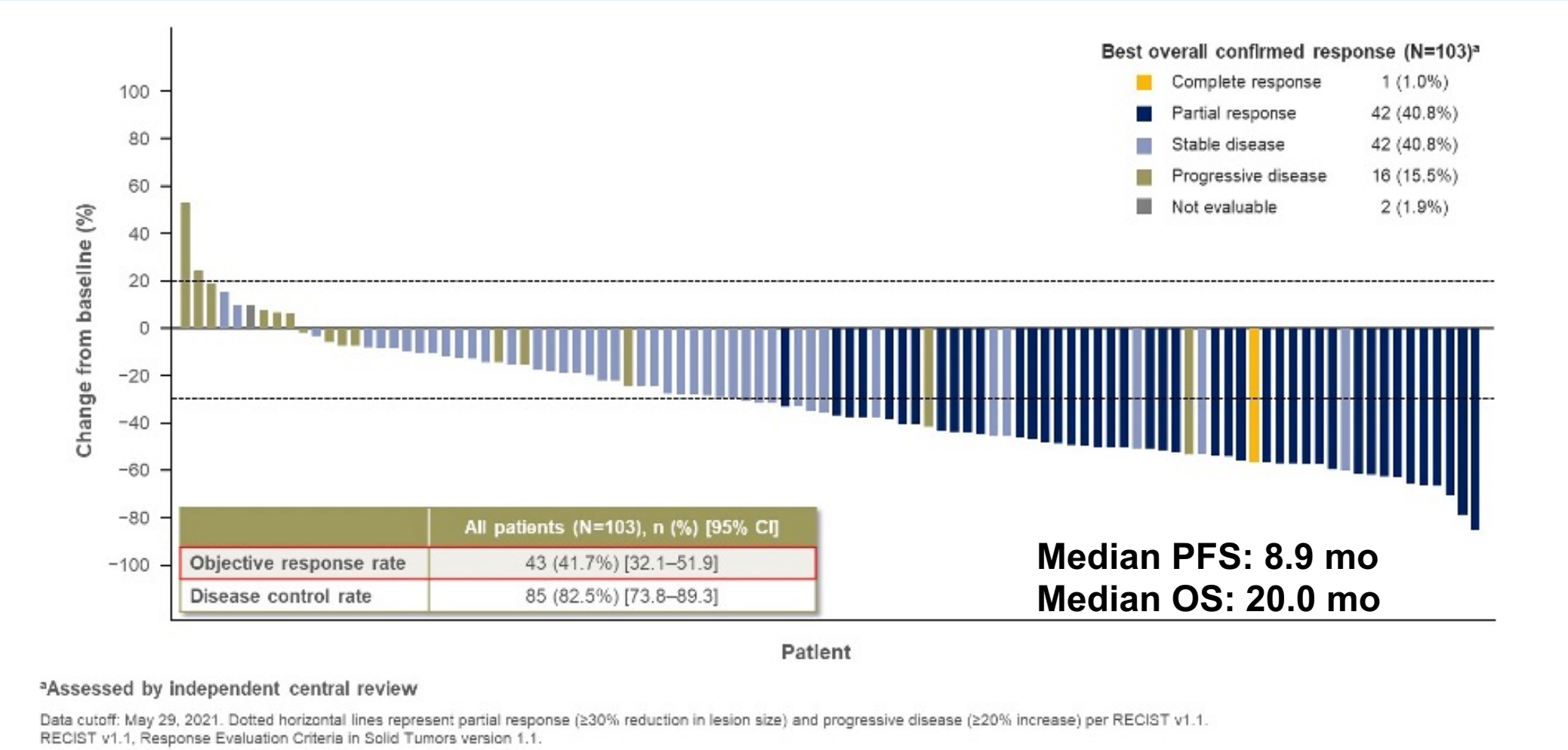
FOENIX-CCA2: Phase II Study Design



- At the time of the final data cutoff (May 29, 2021), median follow-up was 25.0 months, and 96/103 patients (93%) had discontinued treatment
- The median number of treatment cycles was 13.0, for a median treatment duration of 9.1 months

Goyal L et al. ASCO 2022;Abstract 4009.

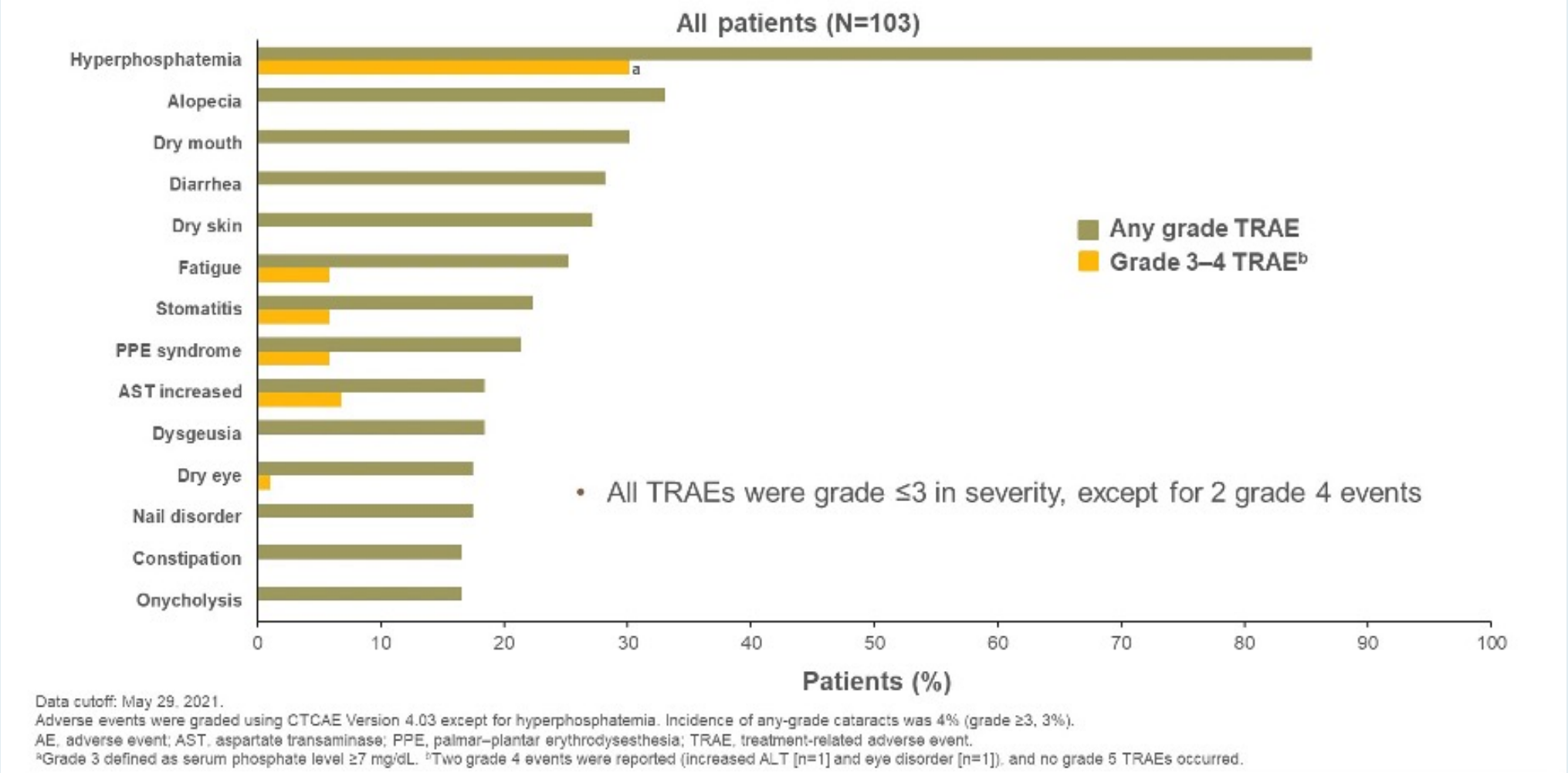
FOENIX-CCA2: Phase II Study of Futibatinib for Intrahepatic Cholangiocarcinoma with FGFR2 Fusions/Rearrangements



Goyal L et al. ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

FOENIX-CCA2: Most Common (≥15%) Treatment-Related Adverse Events (TRAEs) with Futibatinib for Intrahepatic Cholangiocarcinoma



Goyal L et al. ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

FOENIX-CCA2: Adverse Events (AEs) of Special Interest with Futibatinib for Intrahepatic Cholangiocarcinoma

AE of special interest by group term	Safety population (N=103), n (%)		
	Any grade[a]	Grade 3	Grade 4
Hyperphosphatemia[b]	94 (91)	32 (31)	0
Nail toxicities[c]	54 (52)	2 (2)	0
Increased ALT and AST[d]	28 (27)	12 (12)	1 (1)
Palmar–plantar erythrodysesthesia (PPE) syndrome	23 (22)	6 (6)	0
Rash[e]	9 (9)	0	0
Retinal disorders[f]	8 (8)	0	0

- One AE of special interest led to treatment discontinuation (PPE syndrome, grade 1)
- Hyperphosphatemia was manageable with phosphate-lowering therapy and dose modification
  - Median time to resolution of grade 3 hyperphosphatemia was 7.0 days (range, 2.0–26.0 days)

Goyal L et al. ASCO 2022;Abstract 4009.

Ongoing Phase III Studies of FGFR Inhibitors for Advanced Cholangiocarcinoma

Study	N	Eligibility	Randomization arms	Est primary completion
FIGHT-302	434	• Previously untreated • Unresectable and/or metastatic • FGFR2 rearrangement	• Pemigatinib • Gemcitabine + cisplatin	March 2027
PROOF	300	• Previously untreated • Unresectable and/or metastatic • FGFR2 fusion/translocation	• Infigratinib • Gemcitabine + cisplatin	January 2026
FOENIX-CCA3	216	• Previously untreated • Unresectable and/or metastatic • FGFR2 rearrangement	• Futibatinib • Gemcitabine + cisplatin	April 2025

www.clinicaltrials.gov. Accessed June 2022.

Research

JAMA Oncology | Original Investigation

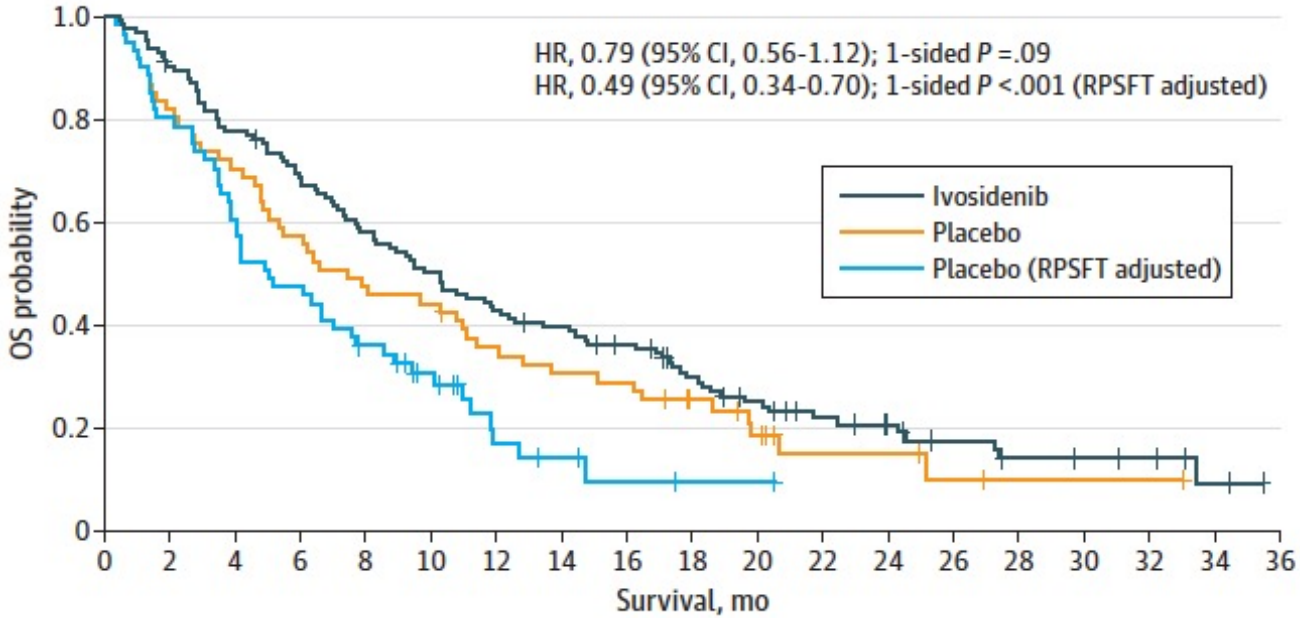
Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With *IDH1* Mutation

The Phase 3 Randomized Clinical ClarIDHy Trial

Andrew X. Zhu, MD, PhD; Teresa Macarulla, MD; Milind M. Javle, MD; R. Kate Kelley, MD; Sam J. Lubner, MD; Jorge Adeva, MD; James M. Cleary, MD; Daniel V. T. Catenacci, MD; Mitesh J. Borad, MD; John A. Bridgewater, PhD; William P. Harris, MD; Adrian G. Murphy, MD; Do-Youn Oh, MD; Jonathan R. Whisenant, MD; Maeve A. Lowery, MD; Lipika Goyal, MD; Rachna T. Shroff, MD; Anthony B. El-Khoueiry, MD; Christina X. Chamberlain, PhD; Elia Aguado-Fraile, PhD; Sung Choe, PhD; Bin Wu, PhD; Hua Liu, PhD; Camelia Gliser, BS; Shuchi S. Pandya, MD; Juan W. Valle, MD; Ghassan K. Abou-Alfa, MD

JAMA Oncol 2021;7(11):1669-77.

ClarIDHy: Final Overall Survival (OS) with Ivosidenib for Advanced Cholangiocarcinoma with an IDH1 Mutation



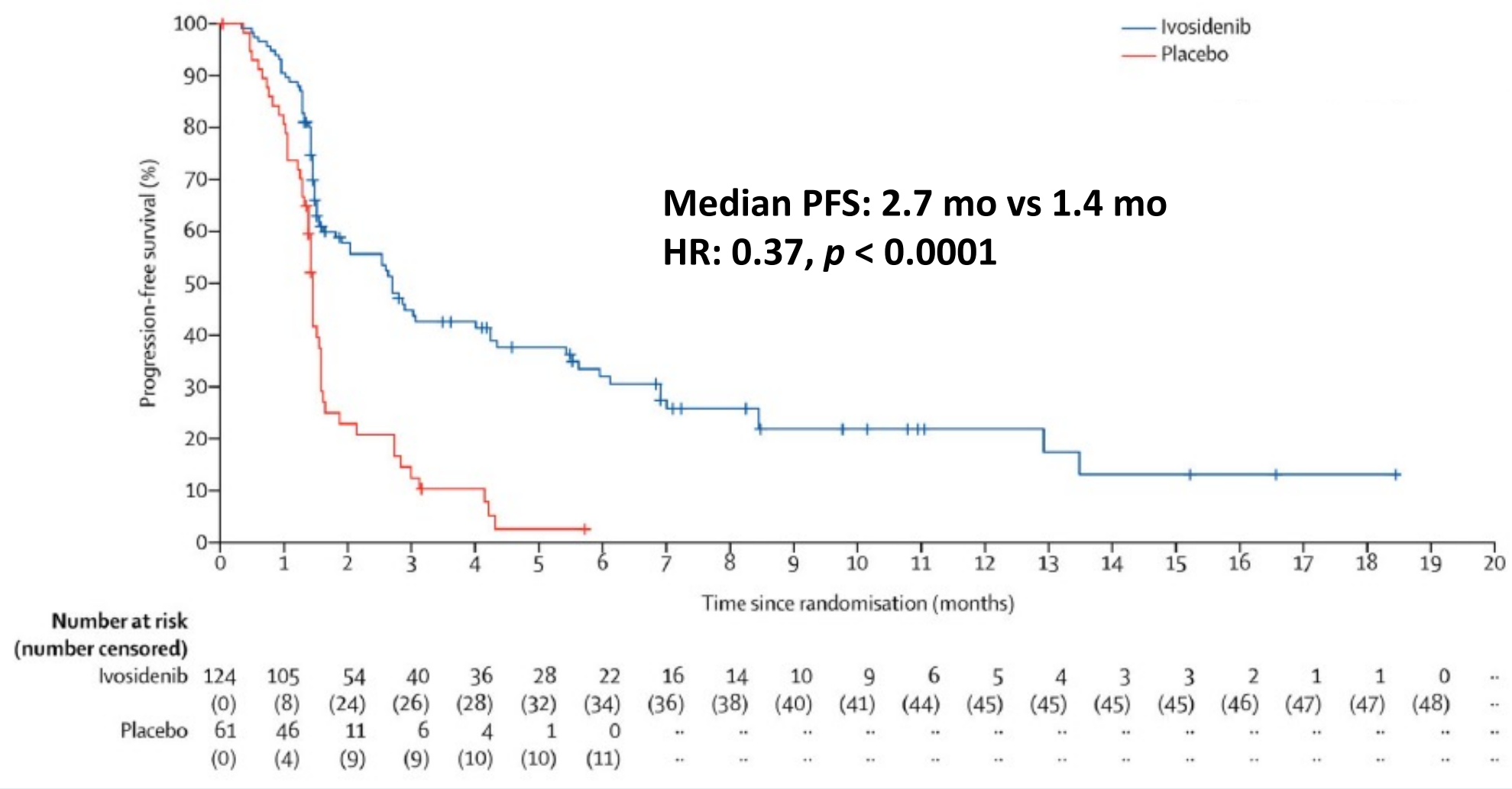
No. at risk

Ivosidenib	126	113	97	85	72	62	53	48	42	32	25	18	14	10	7	6	5	2
Placebo	61	50	43	35	29	27	21	18	17	12	8	4	4	2	1	1	1	
Placebo (RPSFT adjusted)	61	49	37	29	21	14	6	4	2	1	1							

Treatment group	Events/patients, No.	OS, median (95% CI), mo
Ivosidenib	100/126	10.3 (7.8-12.4)
Placebo	50/61	7.5 (4.8-11.1)
Placebo adjusted by RPSFT	49/61	5.1 (3.8-7.6)

Zhu AX et al. *JAMA Oncol* 2021;7(1):1669-77.

ClarIDHy: Progression-Free Survival (PFS) with Ivosidenib for Advanced Cholangiocarcinoma with an IDH1 Mutation



Abou-Alfa GK et al. *Lancet Oncol* 2020;21(6):796-807.

RTP RESEARCH TO PRACTICE

ClarIDHy: Select Adverse Events

Adverse Event	Ivosidenib (n = 121)			Placebo (n = 59)		
	Grade 1-2	Grade 3	Grade 4	Grade 1-2	Grade 3	Grade 4
Diarrhea	33%	2%	0	24%	2%	0
Fatigue	23%	3%	0	15%	0	0
Ascites	13%	7%	0	8%	7%	0
Electrocardiogram QT prolonged	8%	1%	0	2%	0	0
ALT increased	7%	2%	0	2%	0	0
AST increased	6%	5%	0	3%	2%	0
Hyponatremia	5%	3%	2%	2%	8%	2%
Blood bilirubin increased	4%	6%	0	5%	2%	0

Abou-Alfa GK et al. *Lancet Oncol* 2020;21(6):796-807.

Dabrafenib/Trametinib Combination Granted Accelerated Approval for a Tumor-Agnostic Indication for Solid Tumors with BRAF V600E Mutation

Press Release: June 23, 2022

"The US Food and Drug Administration (FDA) granted accelerated approval for dabrafenib + trametinib for the treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options. In accordance with the Accelerated Approval Program, continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

The FDA approval was based on clinical efficacy and safety demonstrated in three clinical trials. In the Phase II ROAR (Rare Oncology Agnostic Research) basket study and the NCI-MATCH Subprotocol H study, dabrafenib + trametinib resulted in overall response rates of up to 80% in patients with BRAF V600E solid tumors, including high- and low-grade glioma, biliary tract cancer and certain gynecological and gastrointestinal cancers. An additional study (Study X2101) demonstrated the clinical benefit and acceptable safety profile of dabrafenib + trametinib in pediatric patients.

The safety profile of dabrafenib + trametinib observed in these studies was consistent with the known safety profile in other approved indications."

https://www.novartis.com/news/media-releases/novartis-tafinlar-mekinist-receives-fda-approval-first-tumor-agnostic-indication-braf-v600e-solid-tumors

RTP RESEARCH TO PRACTICE

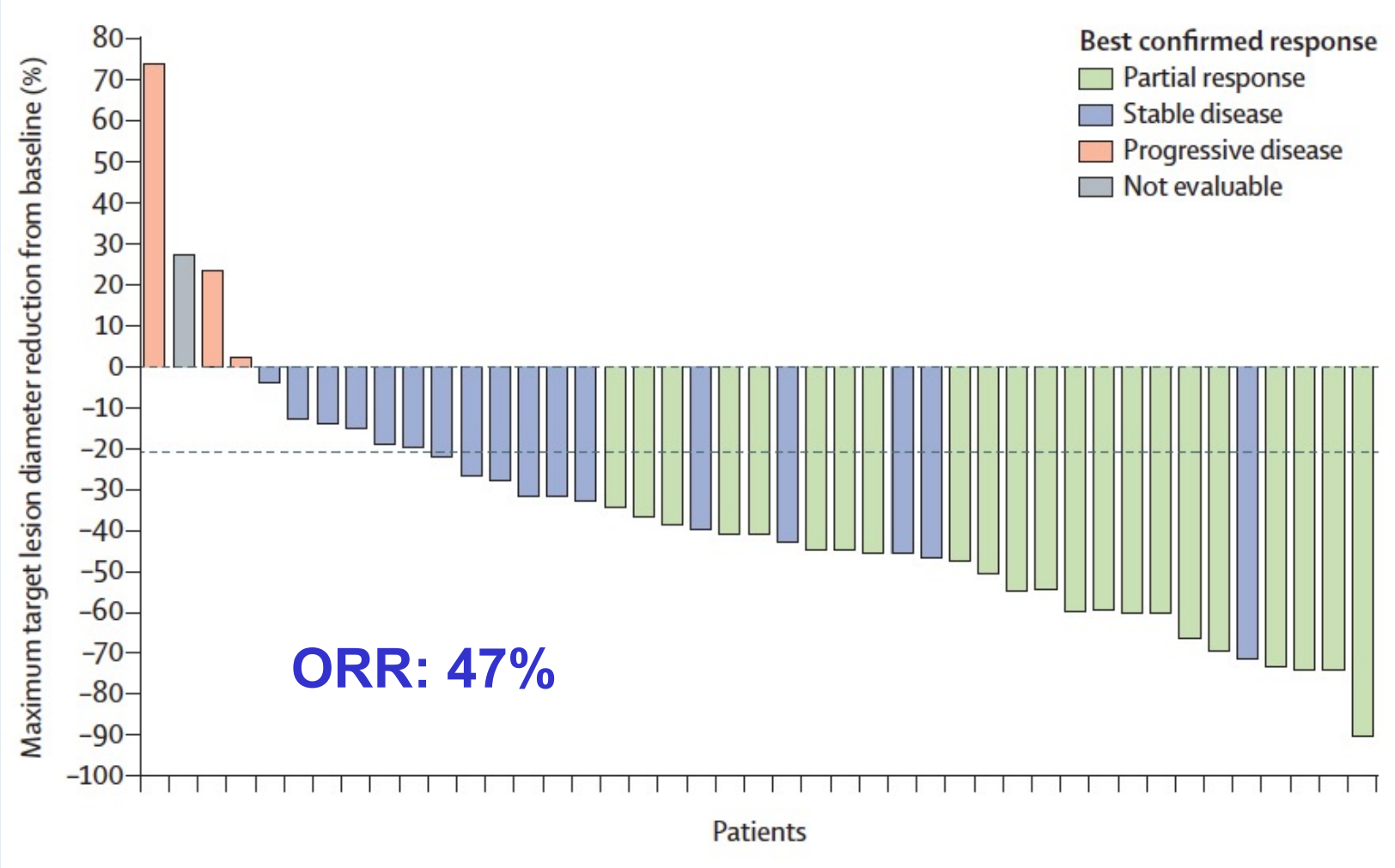
Articles

Dabrafenib plus trametinib in patients with *BRAF*^{V600E}-mutated biliary tract cancer (ROAR): a phase 2, open-label, single-arm, multicentre basket trial

Vivek Subbiah, Ulrik Lassen, Elena Élez, Antoine Italiano, Giuseppe Curigliano, Milind Javle, Filippo de Braud, Gerald W Prager, Richard Greil, Alexander Stein, Angelica Fasolo, Jan H M Schellens, Patrick Y Wen, Kert Viele, Aislyn D Boran, Eduard Gasal, Paul Burgess, Palanichamy Ilankumaran, Zev A Wainberg

***Lancet Oncol* 2020;21(9):1234-43.**

ROAR Phase II Basket Trial: Dabrafenib/Trametinib Combination for Cholangiocarcinoma with a BRAF V600E Mutation



Subbiah V et al. *Lancet Oncol* 2020;21(9):1234-43.

RTP RESEARCH TO PRACTICE

ROAR Phase II Basket Trial: Select Adverse Events with Dabrafenib/Trametinib for Cholangiocarcinoma with a BRAF V600E Mutation

	Grade 1-2	Grade 3	Grade 4
Increased gamma-glutamyltransferase	7 (16%)	5 (12%)	0
Pyrexia	26 (60%)	3 (7%)	0
Decreased WBC count	7 (16%)	3 (7%)	0
Hypertension	2 (5%)	3 (7%)	0
Hyperglycemia	6 (14%)	2 (5%)	0

Subbiah V et al. *Lancet Oncol* 2020;21(9):1234-43.

RTP RESEARCH TO PRACTICE

Future Directions in the Management of Biliary Tract Cancers

NEJM Evidence

Published June 1, 2022

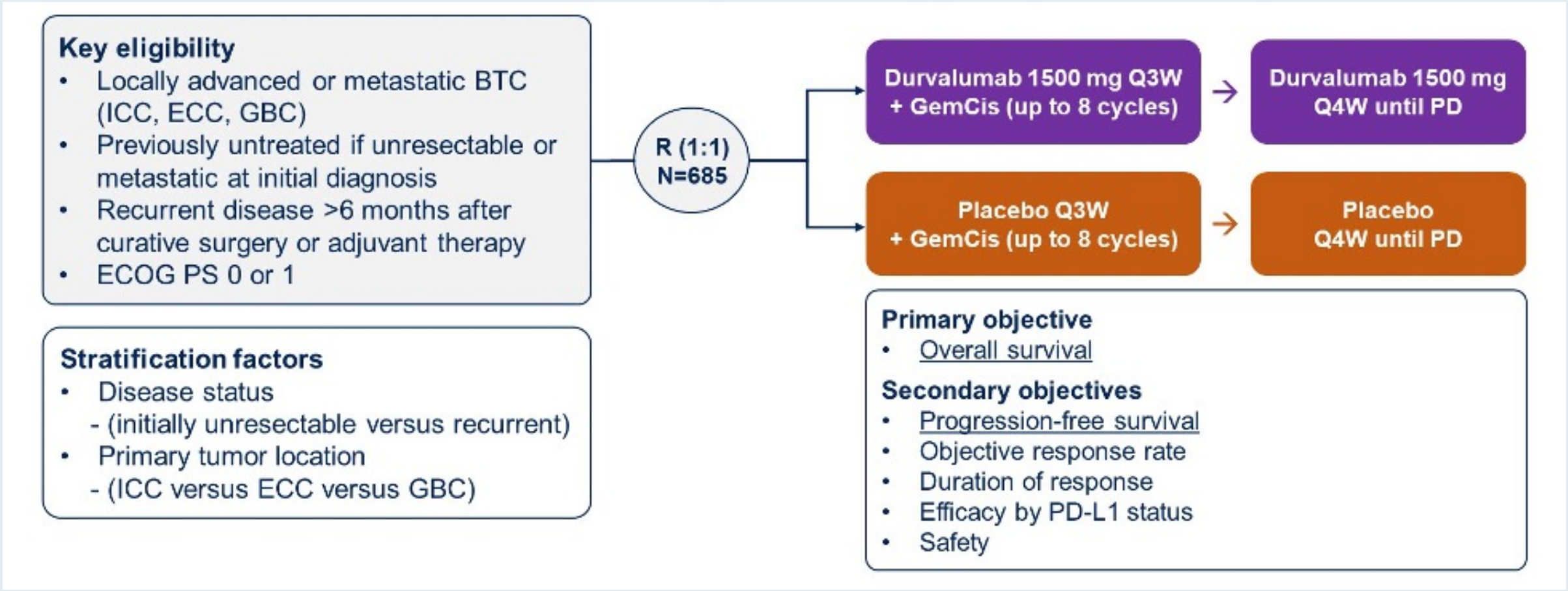
DOI: 10.1056/EVIDoa2200015

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 Suksomboon charoen, 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]

TOPAZ-1 Phase III Trial Schema

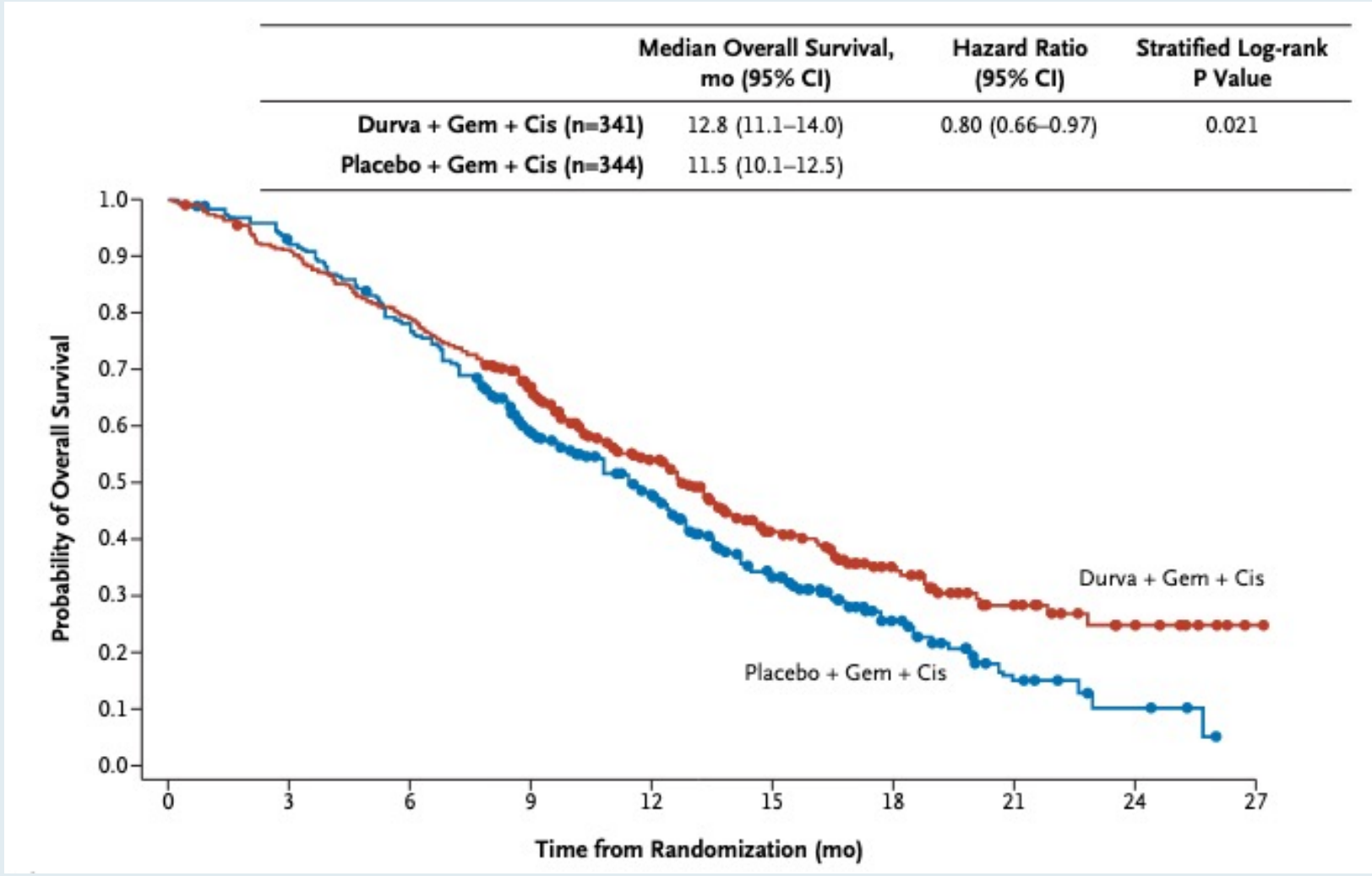


BTC = biliary tract cancer

Oh D-Y et al. Gastrointestinal Cancers Symposium 2022;Abstract 378.

TOPAZ-1: Primary Overall Survival Endpoint with Durvalumab and Gemcitabine/Cisplatin for Advanced Biliary Tract Cancer

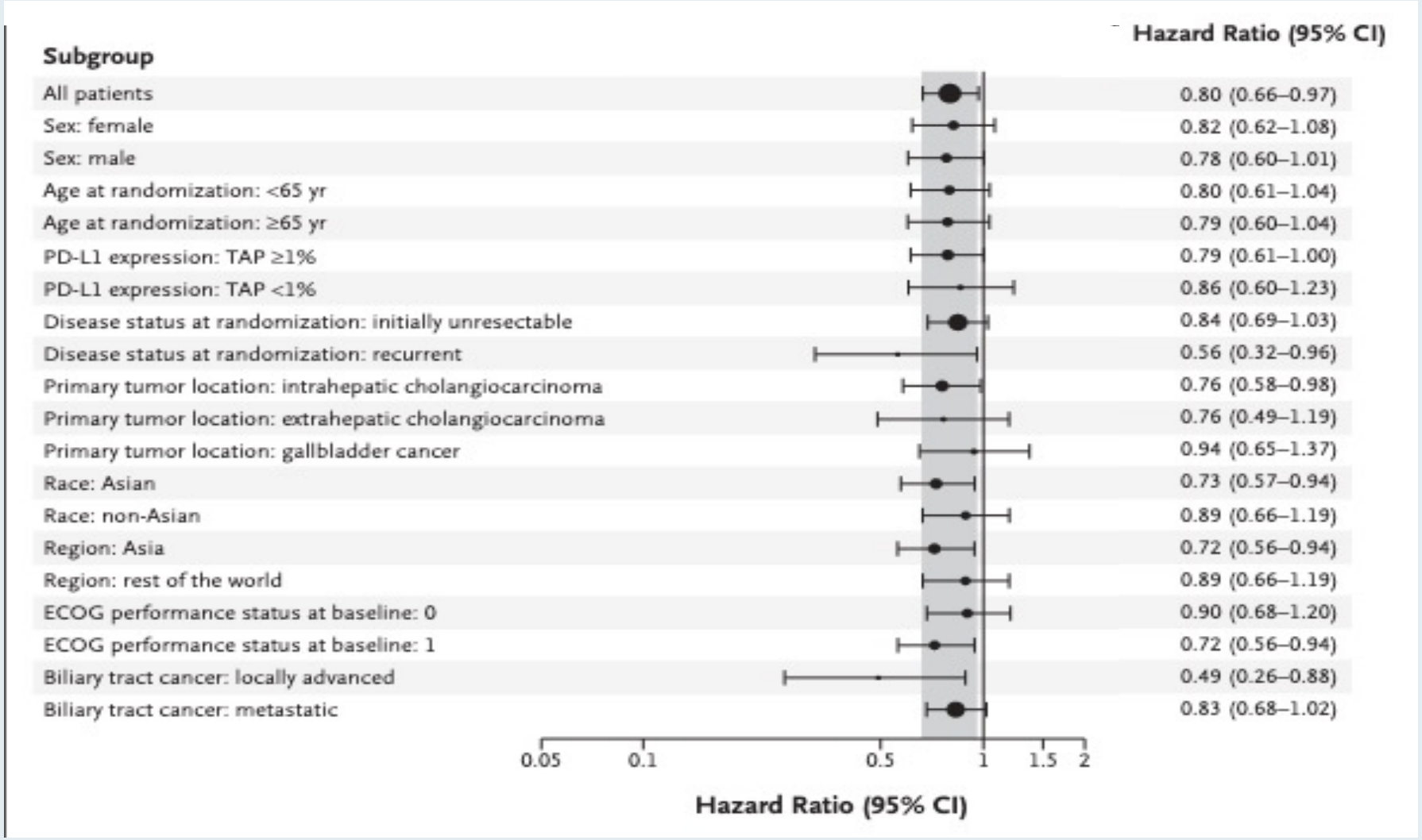
	Median Overall Survival, mo (95% CI)	Hazard Ratio (95% CI)	Stratified Log-rank P Value
Durva + Gem + Cis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + Gem + Cis (n=344)	11.5 (10.1–12.5)		



Oh D-Y et al. *NEJM Evidence*, June 1, 2022

RTP RESEARCH TO PRACTICE

TOPAZ-1: Overall Survival Subgroup Analysis



Oh D-Y et al. *NEJM Evidence*, June 1, 2022

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TOPAZ-1: Adverse Event Summary

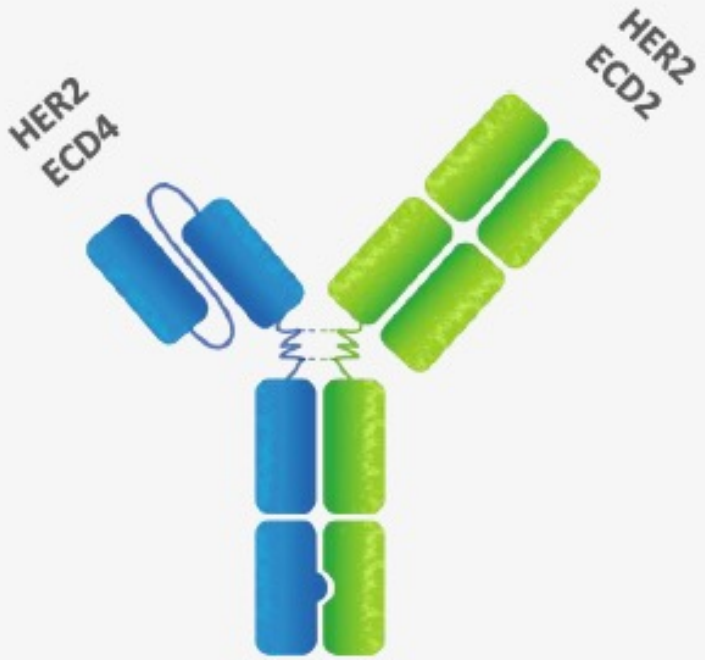
Parameter	Durvalumab plus Gemcitabine and Cisplatin (n=338)	Placebo plus Gemcitabine and Cisplatin (n=342)
Adverse events — no. (%)		
Any grade	336 (99.4)	338 (98.8)
Serious	160 (47.3)	149 (43.6)
Grade 3 or 4	256 (75.7)	266 (77.8)
Leading to discontinuation of any study treatment	44 (13.0)	52 (15.2)
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)

Oh D-Y et al. *NEJM Evidence*, June 1, 2022

RTP RESEARCH TO PRACTICE

Zanidatamab: A Bispecific HER2-Targeted Antibody

- A biparatopic antibody that simultaneously binds two distinct sites on HER2: ECD4 (targeted by trastuzumab) and ECD2 (targeted by pertuzumab)
- Unique binding results in multiple mechanisms of action of zanidatamab that lead to improved binding, clustering, and receptor internalization and downregulation, inhibition of ligand-dependent and -independent proliferation, and potent activation of antibody-dependent cellular cytotoxicity



ECD=extracellular domain

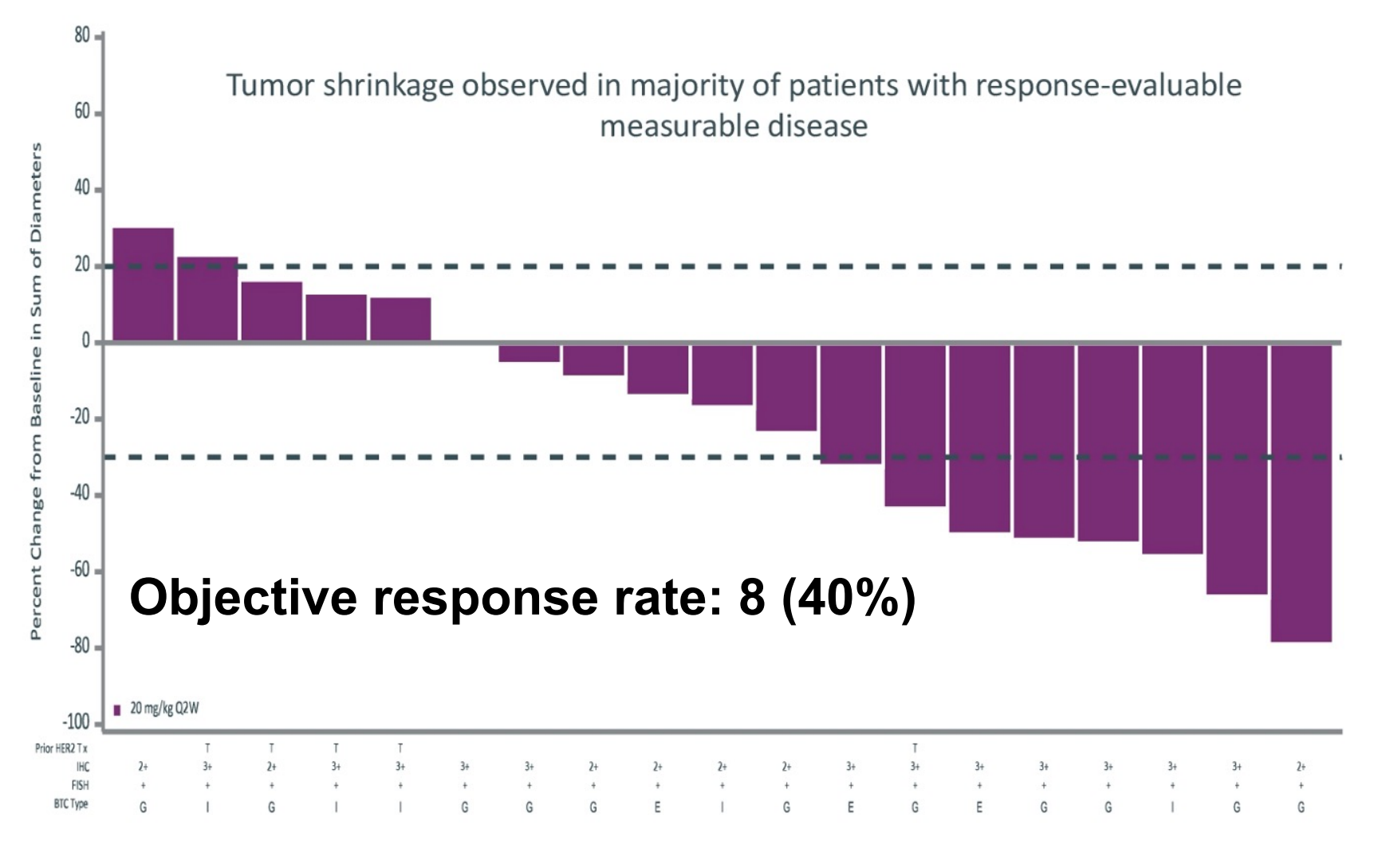
Pant S et al. Gastrointestinal Cancers Symposium 2021;Abstract TPS352.

Zanidatamab (ZW25) in HER2-Positive Biliary Tract Cancer (BTC): Results from a Phase I Study

Meric-Bernstam F et al.

Gastrointestinal Cancers Symposium 2021;Abstract 299.

Antitumor Activity of Zanidatamab in a Phase I Study for Advanced Biliary Tract Cancer



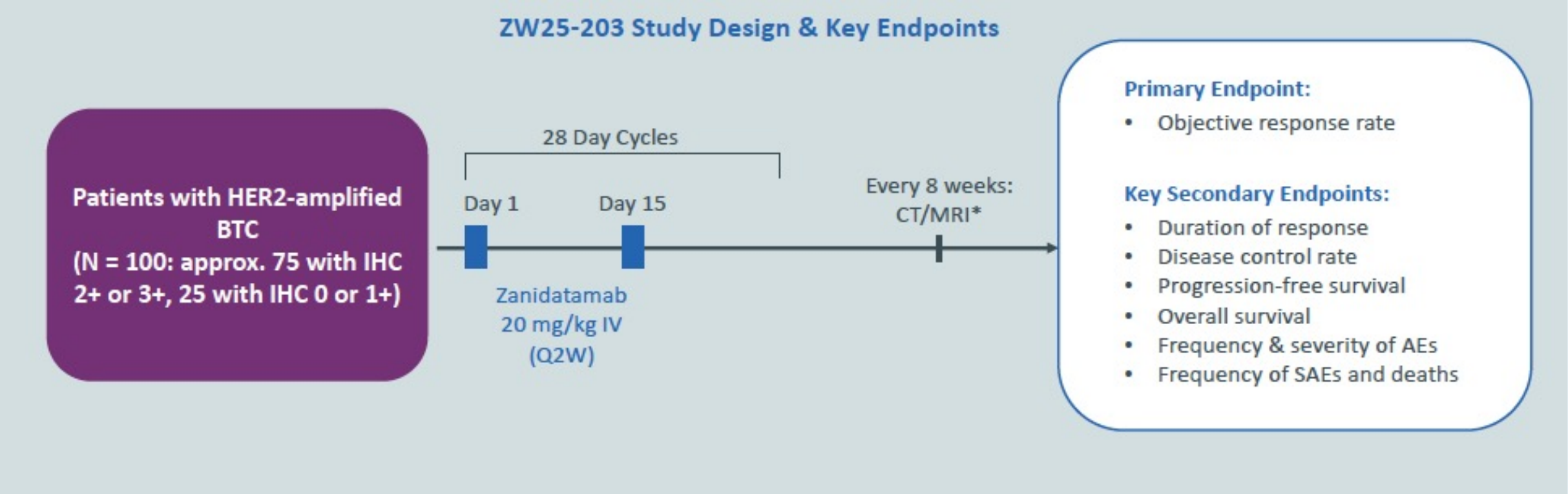
Meric-Bernstam F et al. Gastrointestinal Cancers Symposium 2021;Abstract 299.

Adverse Events (AEs) Associated with Zanidatamab in a Phase I Study for Advanced Biliary Tract Cancer

	N = 21
Patients with treatment-emergent AEs	21 (100%)
Patients with zanidatamab-related AEs (≥15% of patients)	
Any AE	15 (71%)
Diarrhea	9 (43%)
Infusion-related reaction	7 (33%)

Meric-Bernstam F et al. Gastrointestinal Cancers Symposium 2021;Abstract 299.

HERIZON-BTC-01 (ZW25-203): Phase IIb Study of Zanidatamab Monotherapy for Advanced or Metastatic HER2-Amplified Biliary Tract Cancer



Pant S et al. Gastrointestinal Cancers Symposium 2021;Abstract TPS352.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

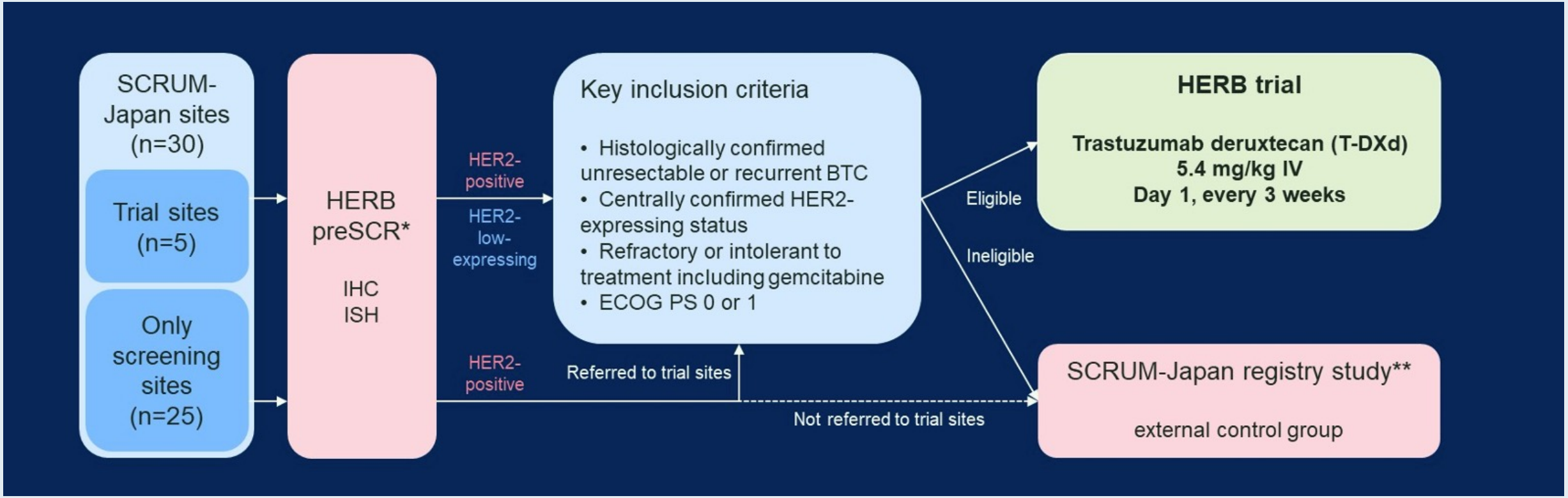
Abstract 4006.

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing unresectable or recurrent biliary tract cancer (BTC): An investigator-initiated multicenter phase 2 study (HERB trial)

Akihiro Ohba[1], Chigusa Morizane[1], Yasuyuki Kawamoto[2], Yoshito Komatsu[2], Makoto Ueno[3], Satoshi Kobayashi[3], Masafumi Ikeda[4], Mitsuhito Sasaki[4], Junji Furuse[5], Naohiro Okano[5], Nobuyoshi Hiraoka[1], Hiroshi Yoshida[1], Aya Kuchiba[1], Ryo Sadachi[1], Kenichi Nakamura[1], Naoko Matsui[1], Yoshiaki Nakamura[4], Wataru Okamoto[6], Takayuki Yoshino[4], Takuji Okusaka[1]

[1]National Cancer Center Hospital, [2]Hokkaido University Hospital, [3]Kanagawa Cancer Center, [4]National Cancer Center Hospital East, [5]Kyorin University Faculty of Medicine, [6]Hiroshima University Hospital

HERB: A Phase II Study of Trastuzumab Deruxtecan (T-DXd) for HER2-Expressing Biliary Tract Cancer



Ohba A et al. ASCO 2022;Abstract 4006.

HERB Primary Endpoint: Confirmed Objective Response Rate (ORR) by Blinded Independent Central Review with T-DXd for Biliary Tract Cancer

- Tumor response

*: P =0.01

	HER2-positive (n=22)	HER2-low-expressing (n=8)	All pts (n=30)
Confirmed ORR (90% CI) (95% CI)	**36.4% (19.6-56.1)*** (17.2–59.3)	12.5% – (0.3–52.7)	30.0% – (14.7–49.4)
Confirmed DCR (95% CI)	81.8% (59.7–94.8)	75.0% (34.9–96.8)	80.0% (61.4–92.3)
Confirmed best response, n (%)			
CR	2 (9.1)	0 (0)	2 (6.7)
PR	6 (27.3)	1 (12.5)	7 (23.3)
SD	10 (45.5)	5 (62.5)	15 (50.0)
PD	3 (13.6)	1 (12.5)	4 (13.3)
NE	1 (4.5)	1 (12.5)	2 (6.7)

- Best percentage change

Ohba A et al. ASCO 2022;Abstract 4006.

HERB Secondary Endpoints: Progression-Free Survival (PFS) and Overall Survival (OS) with T-DXd for Biliary Tract Cancer

	HER2-positive disease (n = 22)	HER2-low expressing disease (n = 8)
Median PFS	5.1 mo	3.5 mo
6-month PFS rate	40.9%	0
Median OS	7.1 mo	8.9 mo
6-month OS rate	63.6%	75.0%

Ohba A et al. ASCO 2022;Abstract 4006.

HERB: Treatment-Emergent Adverse Events with T-DXd for Biliary Tract Cancer

Event	Any grade, n (%)	Grade ≥ 3, n (%)
Anemia	22 (68.8)	17 (53.1)
Neutrophil count decreased	18 (56.3)	10 (31.3)
White blood cell count decreased	18 (56.3)	10 (31.3)
Platelet count decreased	14 (43.8)	3 (9.4)
Nausea	14 (43.8)	0 (0)
Alopecia	13 (40.6)	0 (0)
Anorexia	12 (37.5)	1 (3.1)
Lymphocyte count decreased	11 (34.4)	7 (21.9)
Fatigue / Malaise	11 (34.4)	0 (0)
Interstitial lung disease / Pneumonitis	8 (25.0)	4 (12.5)
Hypoalbuminemia	7 (21.9)	1 (3.1)
Vomiting	7 (21.9)	0 (0)
Mucositis oral	5 (15.6)	0 (0)

Ohba A et al. ASCO 2022;Abstract 4006.

HERB: Interstitial Lung Disease (ILD)/Pneumonitis with T-DXd for Biliary Tract Cancer

	ILDs (n=8)*
Grade, n (%) 1 2 3 5	 3 (37.5) 1 (12.5) 2 (25.0) 2 (25.0)
Median time to onset (range), days	124 (35–247)**
Median Age (range), years	73 (51–75)
Sex, female, n (%)	3 (37.5)
Number of prior regimens, n (%) 1 ≥ 2	 4 (50.0) 4 (50.0)
HER2 status of IHC/ISH, n (%) 3+/+ 2+/+	 5 (62.5) 3 (37.5)
Lung metastasis, n (%)	3 (37.5)
Smoking history, n (%)	3 (37.5)
Biliary drainage, n (%)	4 (50.0)

Ohba A et al. ASCO 2022;Abstract 4006.

ASCO Gastrointestinal Cancers Symposium

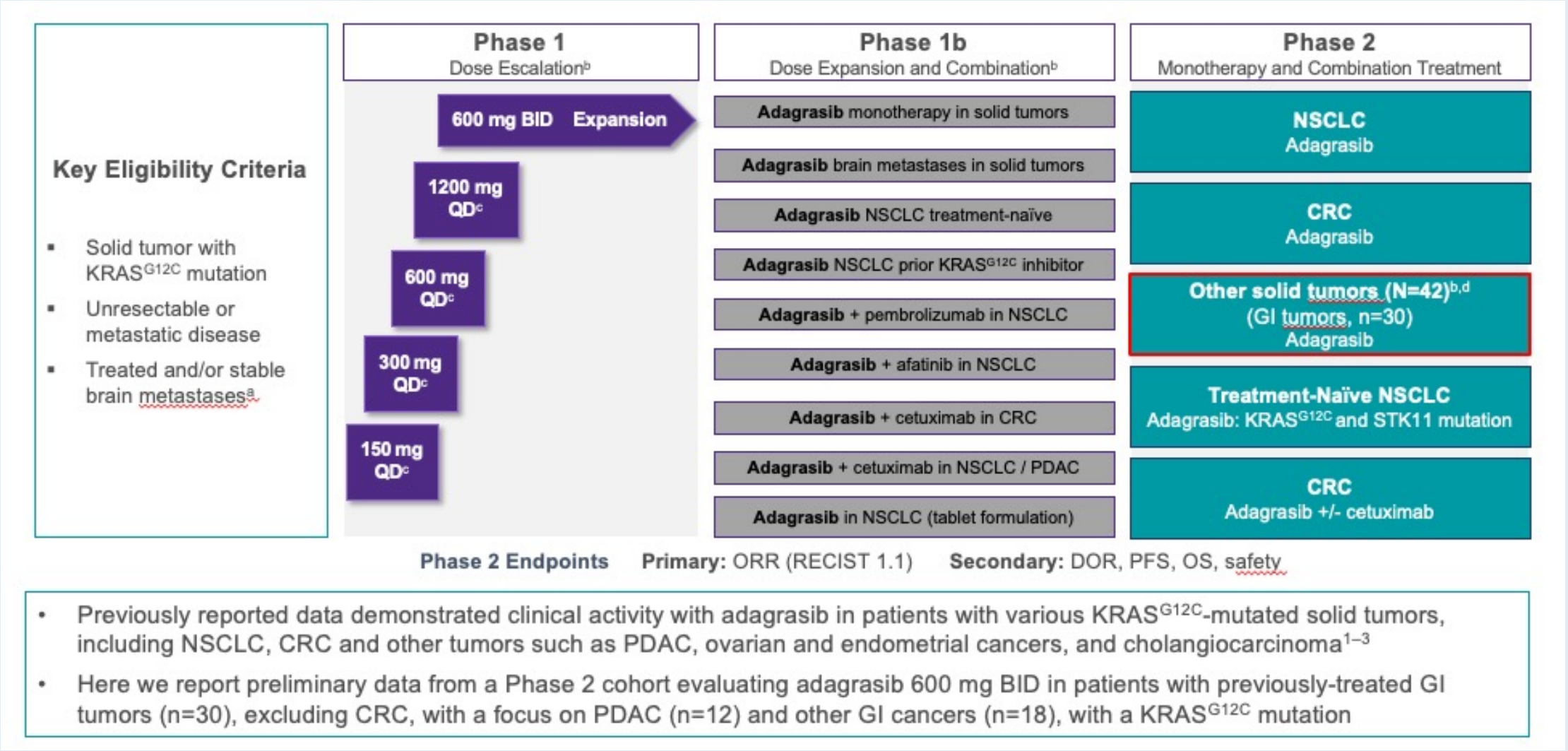
Abstract 519.

KRYSTAL-1: Updated Activity and Safety of Adagrasib (MRTX849) in Patients (Pts) With Unresectable or Metastatic Pancreatic Cancer (PDAC) and Other Gastrointestinal (GI) Tumors Harboring a KRAS^{G12C} Mutation

TS Bekaii-Saab[1], AI Spira[2], R Yaeger[3], GL Buchschacher Jr.[4], AJ McRee[5], JK Sabari[6], ML Johnson[7], M Barve[8], N Hafez[9], K Velastegui[10], JG Christensen[10], T Kheoh[10], H Der-Torossian[10], SM Gadgeel[11]

[1]Department of Medical Oncology and Hematology, Mayo Clinic, Scottsdale, Arizona, USA; [2]Virginia Cancer Specialists, Fairfax, Virginia, NEXT Oncology, Virginia, US Oncology Research, The Woodlands, Texas, USA; [3]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA; [4]Kaiser Permanente Southern California, Los Angeles, California, USA; [5]Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA; [6]Perlmutter Cancer Center, New York University Langone Health, New York, New York, USA; [7]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, Tennessee, USA; [8]Mary Crowley Cancer Research, Dallas, Texas, USA; [9]Yale Cancer Center, New Haven, Connecticut, USA; [10]Mirati Therapeutics, Inc., San Diego, California, USA; [11]Henry Ford Cancer Institute/Henry Ford Health System, Detroit, Michigan, USA

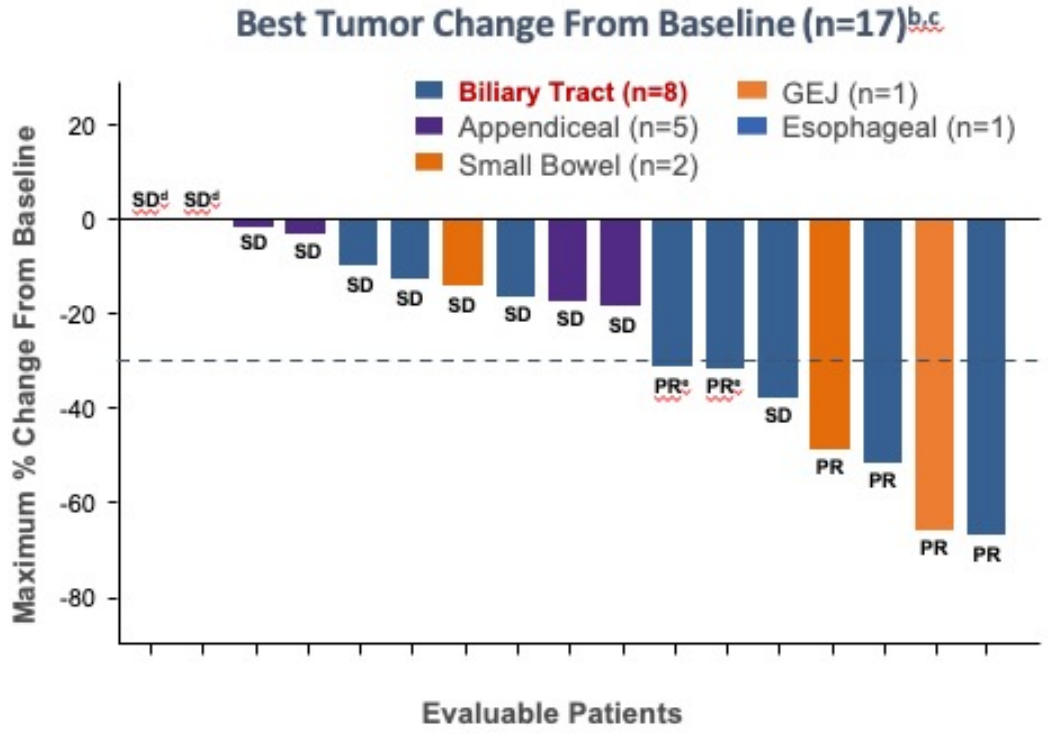
KRYSTAL-1: Trial Schema

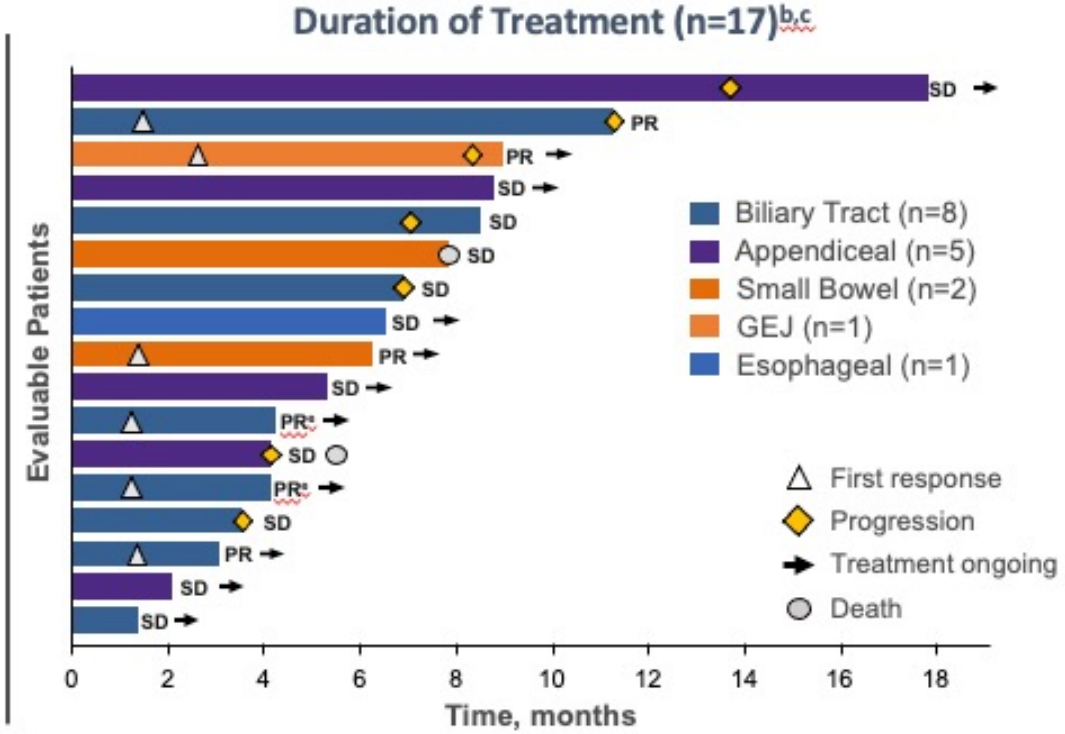


- Previously reported data demonstrated clinical activity with adagrasib in patients with various KRAS^{G12C}-mutated solid tumors, including NSCLC, CRC and other tumors such as PDAC, ovarian and endometrial cancers, and cholangiocarcinoma[1–3]
- Here we report preliminary data from a Phase 2 cohort evaluating adagrasib 600 mg BID in patients with previously-treated GI tumors (n=30), excluding CRC, with a focus on PDAC (n=12) and other GI cancers (n=18), with a KRAS^{G12C} mutation

Bekaii-Saab TS et al. Gastrointestinal Cancers Symposium 2022;Abstract 519.

KRYSTAL-1: Best Tumor Change from Baseline and Duration of Treatment with Adagrasib for Other Gastrointestinal Tumors





- Response rate:
  - **Biliary tract cancer: 50% (4/8), including 2 unconfirmed PRs**
  - GEJ and small bowel cancer: 1 PR each
- DCR: 100% (17/17 patients)

- Median TTR: 1.3 months
- Median DOR: 7.85 months
- Median PFS: 7.85 months (95% CI 6.90–11.30)
- Treatment ongoing in 65% (11/17) of patients

Bekaii-Saab TS et al. Gastrointestinal Cancers Symposium 2022;Abstract 519.

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Tuesday, July 12, 2022
5:00 PM – 6:00 PM ET

Faculty

Samuel J Klempner, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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