What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Hepatobiliary Cancers

Friday, April 28, 2023
6:00 AM – 7:30 AM

Faculty

Ahmed Omar Kaseb, MD, CMQ
Blanca Ledezma, MSN, NP, AOCNP
Daneng Li, MD
Amanda K Wagner, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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Faculty

Ahmed Omar Kaseb, MD, CMQ
John E and Dorothy J Harris Professor in
Gastrointestinal Cancer Research
Member, National Hepatobiliary Task Force, NCI, USA
Tenured Professor and Director, Hepatocellular
Carcinoma Program
Director, MD Anderson HCC SPORE
Editor-in-Chief, *Journal of Hepatocellular Carcinoma*
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Nurse Practitioner III
UCLA Santa Monica Hematology/Oncology
UCLA Health
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Daneng Li, MD
Associate Professor
Department of Medical Oncology
and Therapeutics Research
City of Hope Comprehensive Cancer Center
Duarte, California

Amanda K Wagner, APRN-CNP, AOCNP
GI Malignancies
The James Cancer Hospital
The Ohio State University
Columbus, Ohio

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Dr Kaseb — Disclosures

Advisory Committee, Consulting Agreements and Contracted Research	AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Eisai Inc, Exelixis Inc, Genentech, a member of the Roche Group, Merck

Ms Ledezma — Disclosures

Speakers Bureau	Amgen Inc, AstraZeneca Pharmaceuticals LP, Eisai Inc, Lilly

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Dr Li — Disclosures

Consulting Agreements	Coherus BioSciences, Delcath Systems Inc, Eisai Inc, Exelixis Inc, Genentech, a member of the Roche Group, Ipsen Biopharmaceuticals Inc, Merck, Servier Pharmaceuticals LLC, TerSera Therapeutics LLC
Contracted Research	AstraZeneca Pharmaceuticals LP, Brooklyn ImmunoTherapeutics

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Ms Wagner — Disclosures

No relevant conflicts of interest to disclose

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Eisai Inc, Incyte Corporation, Merck, and Taiho Oncology Inc.

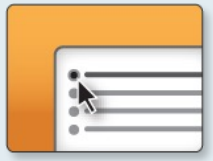
Research To Practice NCPD Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the NCPD Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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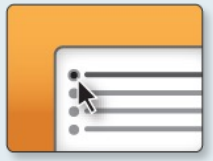
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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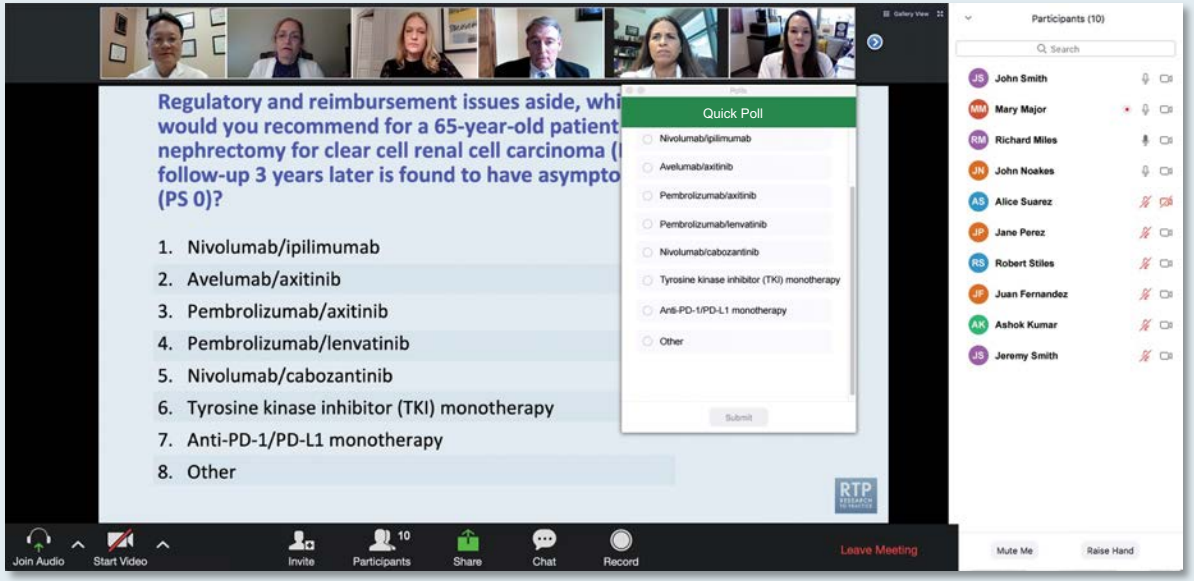
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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“What I Tell My Patients”
Fifteenth Annual RTP-ONS NCPD Symposium Series
ONS Congress, San Antonio, Texas — April 26 to 29, 2023

Wednesday April 26	**Cervical and Endometrial Cancer** 11:15 AM – 12:45 PM CT (12:15 PM – 1:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Thursday April 27	**Diffuse Large B-Cell Lymphoma** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	HER2-Targeted Antibody-Drug Conjugates 6:00 PM – 7:30 PM CT (7:00 PM – 8:30 PM ET)
Friday April 28	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	Lung Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Saturday April 29	**Acute Myeloid Leukemia, Myelodysplastic Syndromes and Myelofibrosis** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Prostate Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

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What I Tell My Patients

2023 ONS Congress

San Antonio, Texas

Symposia Themes

- New agents and therapies; ongoing trials related to specific clinical scenarios
- Patient education: Preparing to receive new therapies
- The bond that heals
- THANKS! (Great job)

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How was it different to take care of this patient versus another patient in the same oncologic setting?

What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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The James Cancer Hospital
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Miami, Florida

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Agenda

Module 1: Overview of Hepatocellular Carcinoma (HCC)

Module 2: First-Line Systemic Therapy for HCC

Module 3: Therapy for Relapsed HCC

Module 4: Overview of Biliary Tract Cancers

Module 5: First-Line Systemic Therapy for Biliary Tract Cancers

Module 6: Targeted Treatment for Biliary Tract Cancers

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Module 6: Targeted Treatment for Biliary Tract Cancers

Blanca Ledezma, MSN, NP, AOCNP

68-year-old man with PMH of hepatitis C s/p local therapies for HCC receives first-line atezolizumab/bevacizumab

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Dr Kaseb
Houston, Texas

Clinical Research Background

Dr Li
Duarte, California

- **Overview of HCC**
  - **Local therapies**
  - **Cirrhosis**

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Agenda

Module 1: Overview of Hepatocellular Carcinoma (HCC)

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Amanda K Wagner, APRN-CNP, AOCNP

A 79-year-old man with HCC and NASH cirrhosis who received first-line atezolizumab/bevacizumab → second-line lenvatinib

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Dr Kaseb
Houston, Texas

Clinical Research Background

Dr Li
Duarte, California

- **First-line systemic therapy**
  - **Atezolizumab/bevacizumab**
  - **Durvalumab/tremelimumab**
  - **TKI monotherapy**

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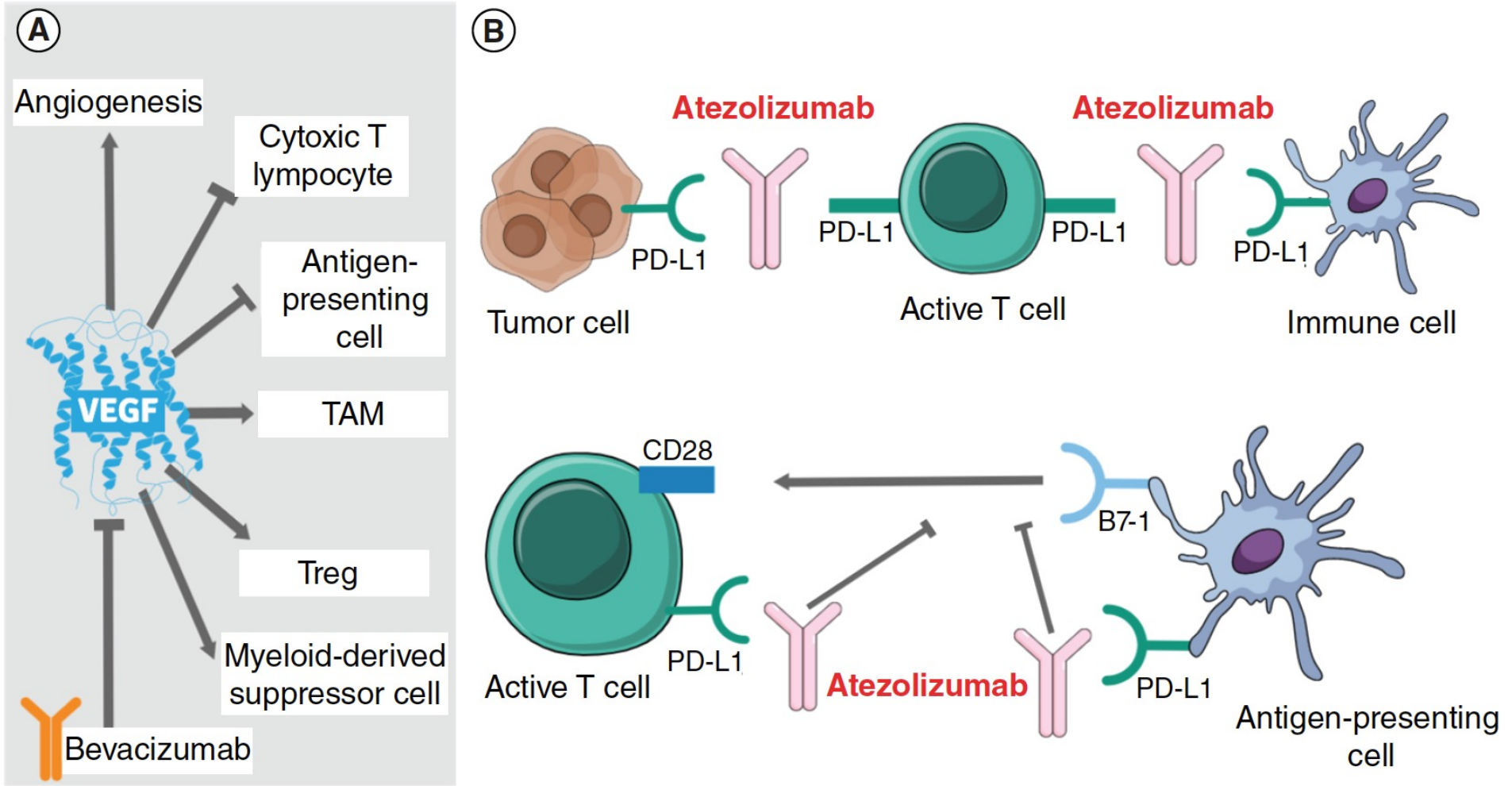
Mechanism of Action of Atezolizumab and Bevacizumab



Liu X et al. *Future Oncol* 2021;17(17):2243-56.

Atezolizumab/Bevacizumab Regimen

Mechanism of action

- PD-L1 inhibitor
- Anti-VEGF monoclonal antibody

Indication

- For patients with unresectable or metastatic HCC who have not received prior systemic therapy

Recommended dose

- Atezolizumab: 840 mg q2wk, 1,200 mg q3wk or 1,680 mg q4wk
- Bevacizumab: 15 mg/kg q3wk

Key issues

- Screening for esophageal varices

Atezolizumab package insert, 12/2022.

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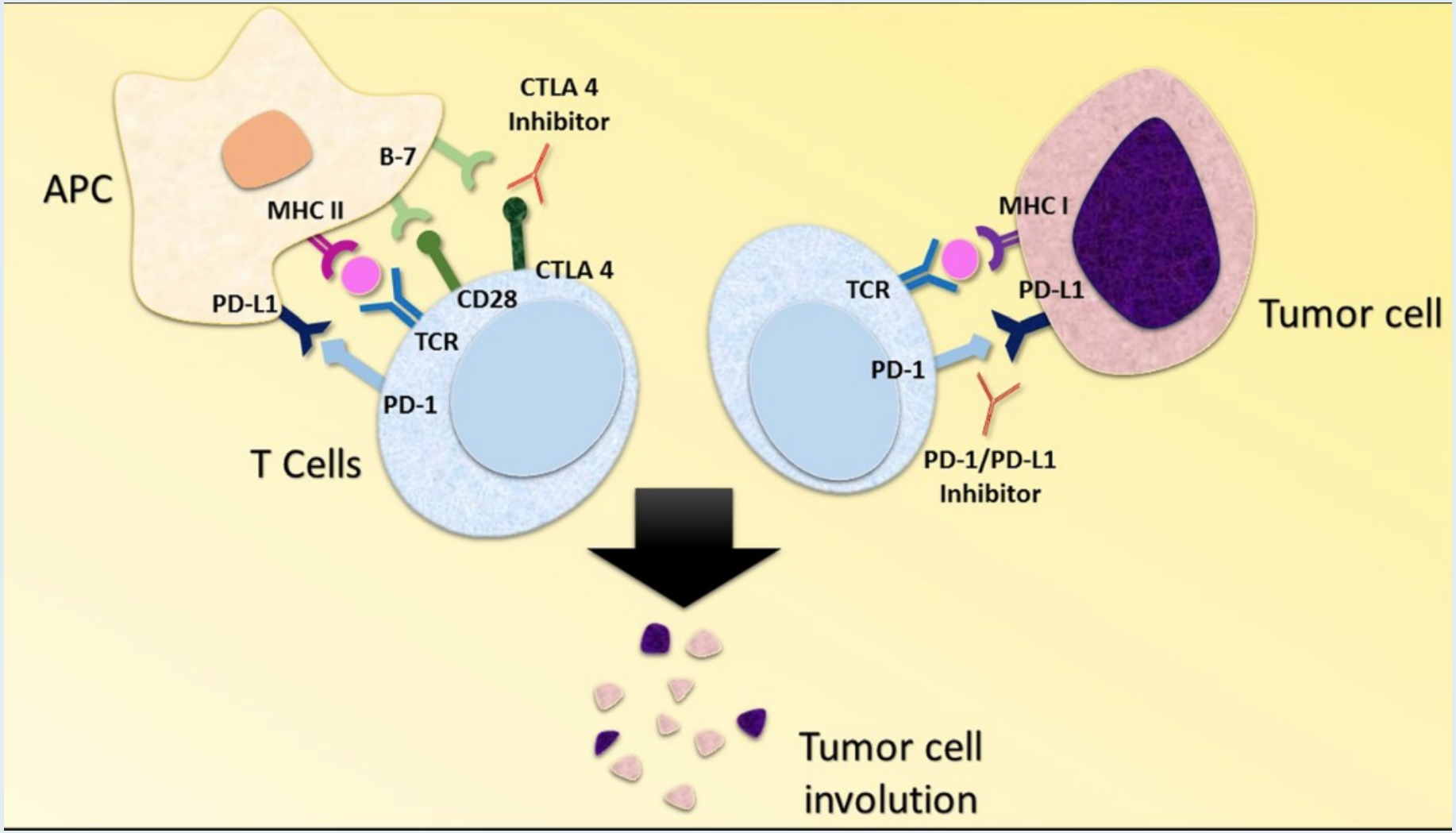
Mechanism of Action of Combined PD-1/PD-L1 and CTLA-4 Inhibitors



Chae YK et al. *J Immuno Ther* 2018;6(1):39.

Durvalumab/Tremelimumab Regimen

Mechanism of action

- PD-L1 inhibitor
- CTLA-4 inhibitor

Indication

- For adult patients with unresectable HCC who have not received prior systemic therapy

Recommended dose

- Tremelimumab: Single priming dose of 300 mg
- Durvalumab: 1,500 mg cycle 1/day 1 followed by 1,500 mg every 4 weeks

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tremelimumab-combination-durvalumab-unresectable-hepatocellular-carcinoma.

FDA Approves Tremelimumab in Combination with Durvalumab for Unresectable Hepatocellular Carcinoma

Press Release: October 21, 2022

"The Food and Drug Administration approved tremelimumab in combination with durvalumab for adult patients with unresectable hepatocellular carcinoma (uHCC).

Efficacy was evaluated in HIMALAYA (NCT03298451), a randomized (1:1:1), open-label, multicenter study in patients with confirmed uHCC who had not received prior systemic treatment for HCC. Patients were randomized to one of three arms: tremelimumab 300 mg as a one-time single intravenous (IV) infusion plus durvalumab 1500 mg IV on the same day, followed by durvalumab 1500 mg IV every 4 weeks; durvalumab 1500 mg IV every 4 weeks; or sorafenib 400 mg orally twice daily until disease progression or unacceptable toxicity. This approval is based on a comparison of the 782 patients randomized to tremelimumab plus durvalumab to sorafenib."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tremelimumab-combination-durvalumab-unresectable-hepatocellular-carcinoma

NEJM Evidence

Published June 6, 2022

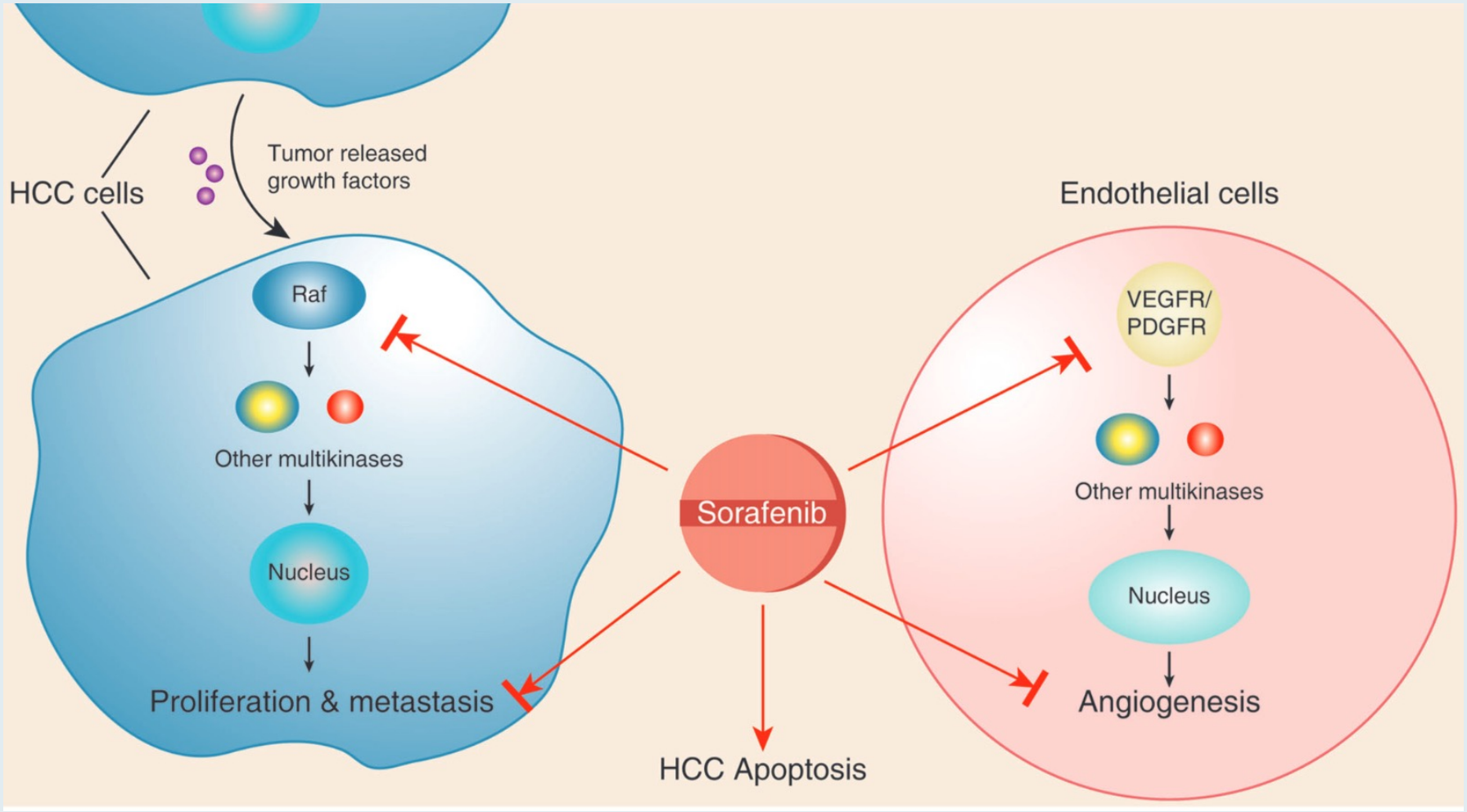
DOI: 10.1056/EVIDoa2100070

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]

Mechanism of Action of Sorafenib



Daher S et al. *J Clin Transl Hepatol* 2018; 6(1):69-78.

Sorafenib

Mechanism of action

- Oral multikinase inhibitor

Indication

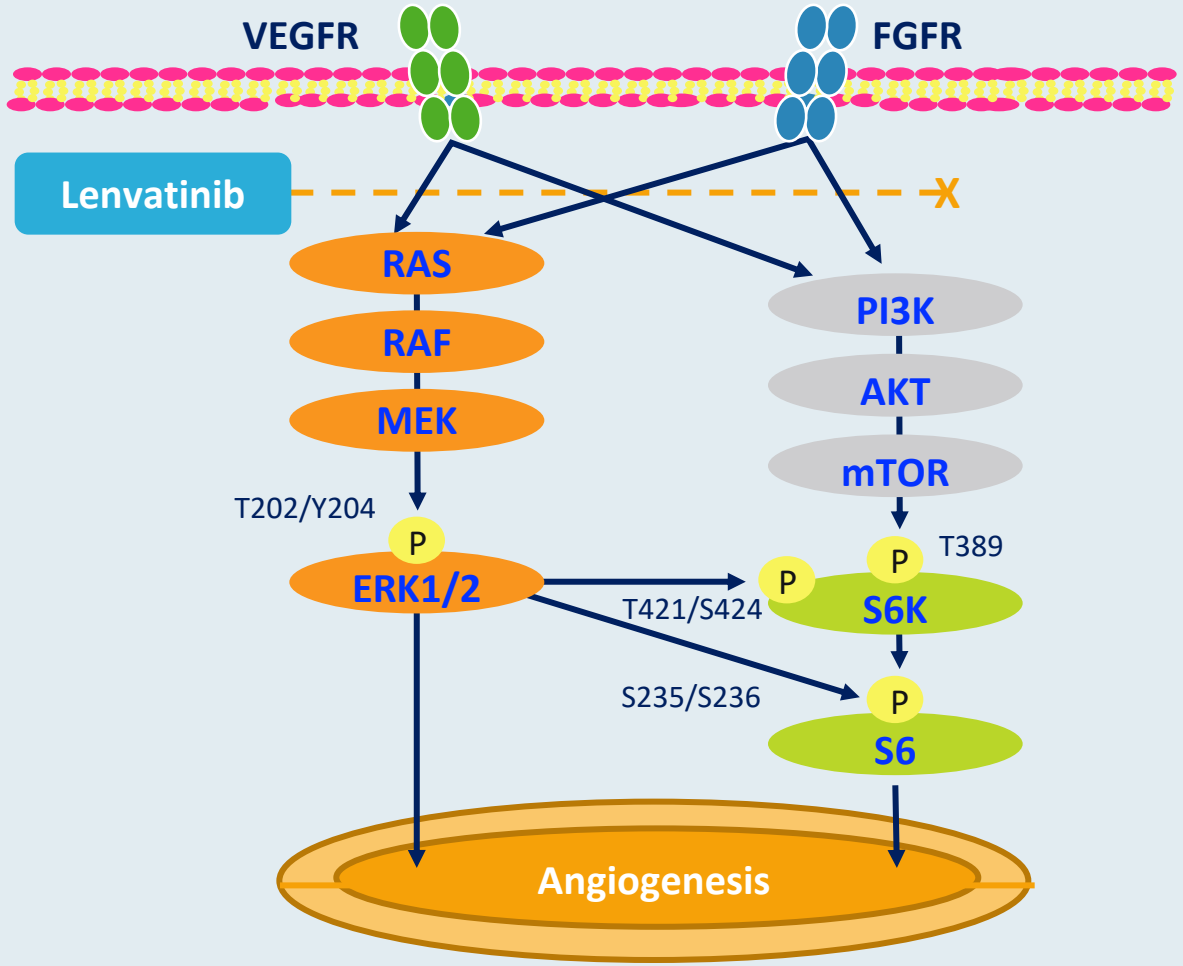
- For patients with unresectable hepatocellular carcinoma

Recommended dose

- 400 mg po BID without food

Sorafenib package insert, 7/2020.

Mechanism of Action of Lenvatinib



- Orally available inhibitor of multiple tyrosine kinases, including VEGF receptors, FGFR, RET, PDGFR and KIT
- Demonstrated promising radiographic response rates and survival results in Phase II and III trials in HCC

Finn RS et al. ASCO 2014;Abstract TPS4153; Stjepanovic N et al. *Biologics* 2014;8:129-39; Cheng AL et al. ASCO 2017;Abstract 4001; Ikeda K et al. *J Gastroenterol* 2017;52(4):512-9.

Lenvatinib

Mechanism of action

- Oral multikinase inhibitor

Indication

- As first-line therapy for patients with unresectable hepatocellular carcinoma

Recommended dose

- 12 mg orally once daily for patients of 60 kg or greater actual body weight
- 8 mg orally once daily for patients of less than 60 kg actual body weight

Lenvatinib package insert, 11/2022.

Agenda

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Blanca Ledezma, MSN, NP, AOCNP

A man in his early 70s with recurrent HCC who has experienced an extended response to nivolumab monotherapy

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Dr Kaseb
Houston, Texas

Clinical Research Background

Dr Li
Duarte, California

- **Therapy for relapsed disease: New treatments**

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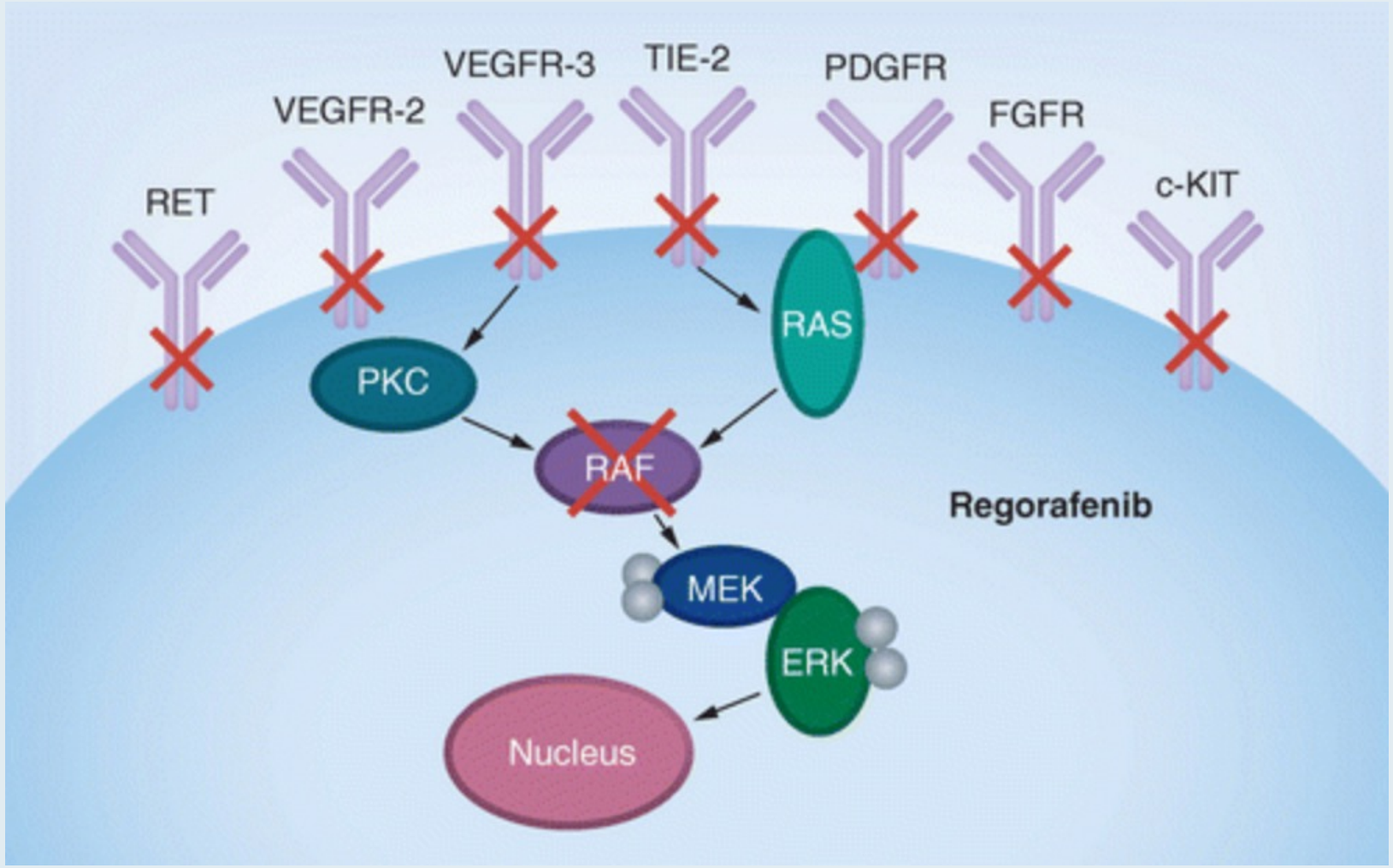
Mechanism of Action of Regorafenib



Cremolini C et al. *Future Med* 2013;2(5):411-17.

Regorafenib

Mechanism of action

- **Oral multikinase inhibitor**

Indication

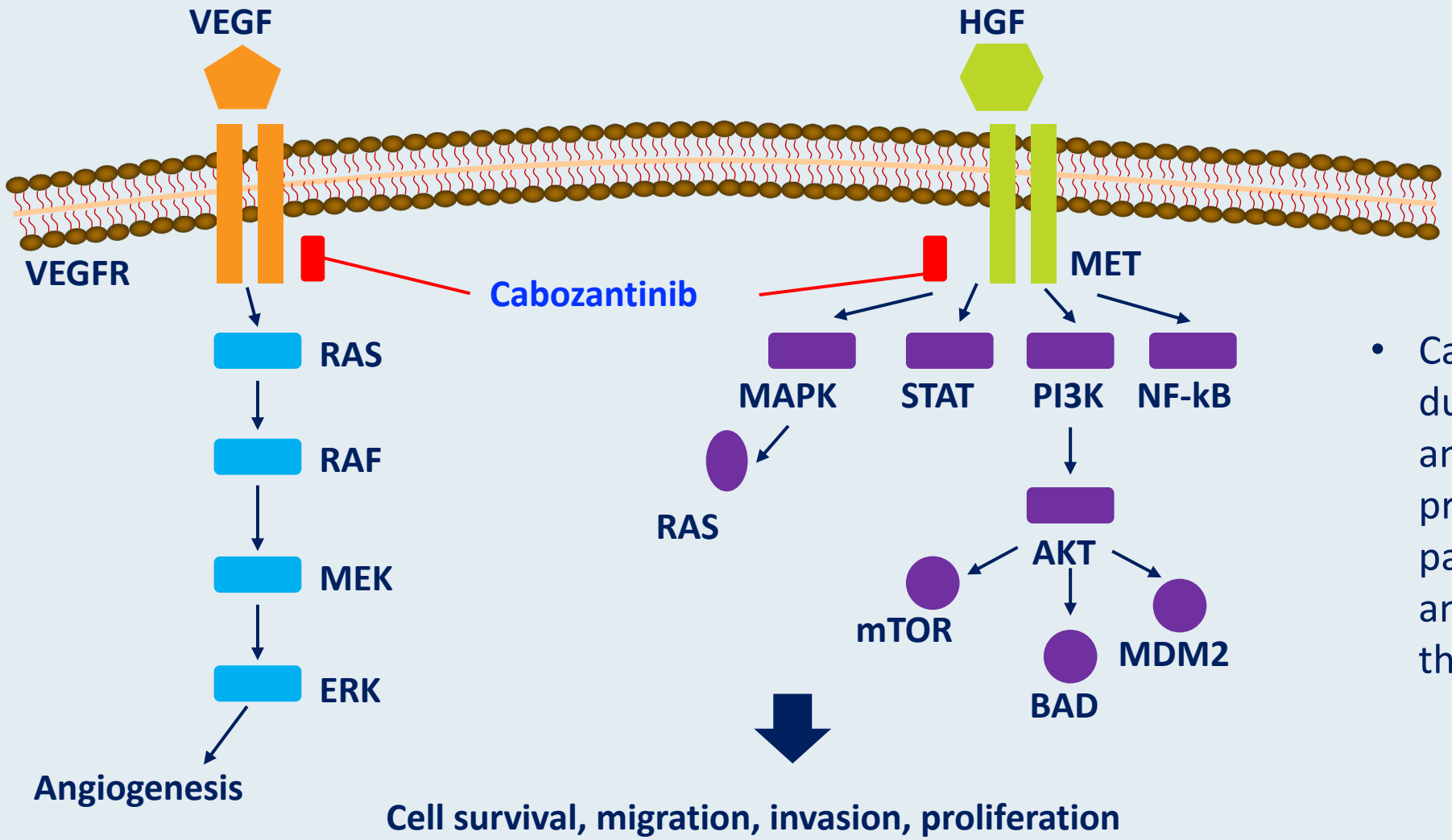
- **For patients with hepatocellular carcinoma who have previously received sorafenib**

Recommended dose

- **160 mg po once daily for the first 21 days of each 28-day cycle**

Regorafenib package insert, 12/2020.

Mechanism of Action of Cabozantinib



- Cabozantinib provides dual inhibition of MET and VEGFR-2, thereby preventing the MET pathway from acting as an alternative pathway in the development of VEGF

Cabozantinib

Mechanism of action

- Oral multikinase inhibitor

Indication

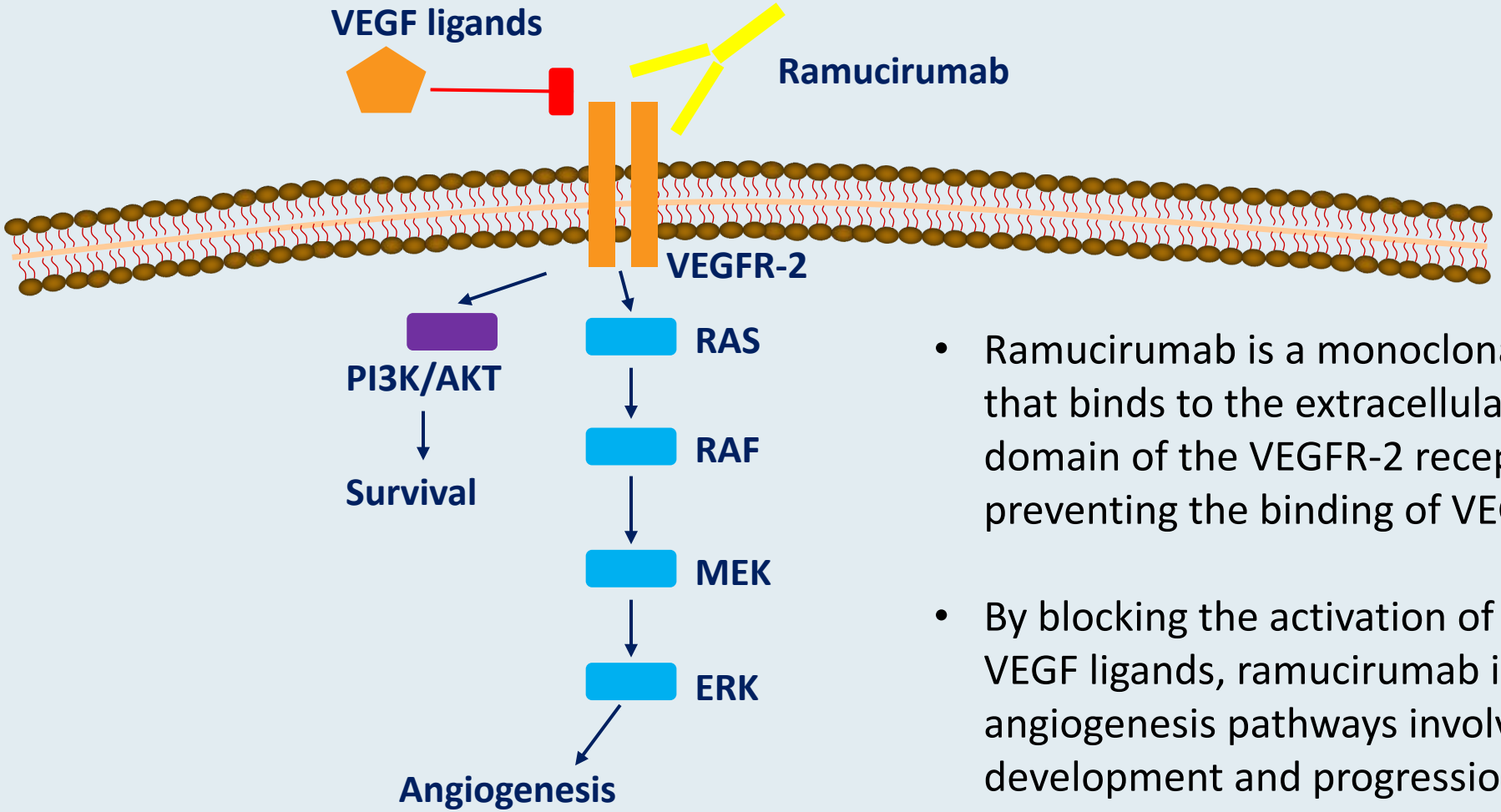
- For patients with hepatocellular carcinoma who have previously received sorafenib

Recommended dose

- 60 mg once daily without food until disease progression or unacceptable toxicity

Cabozantinib prescribing information, 1/2021.

Mechanism of Action of Ramucirumab



- Ramucirumab is a monoclonal antibody that binds to the extracellular binding domain of the VEGFR-2 receptor, preventing the binding of VEGF ligands
- By blocking the activation of VEGFR-2 by VEGF ligands, ramucirumab inhibits the angiogenesis pathways involved in the development and progression of cancer

Ramucirumab

Mechanism of action

- **Anti-VEGFR-2 monoclonal antibody**

Indication

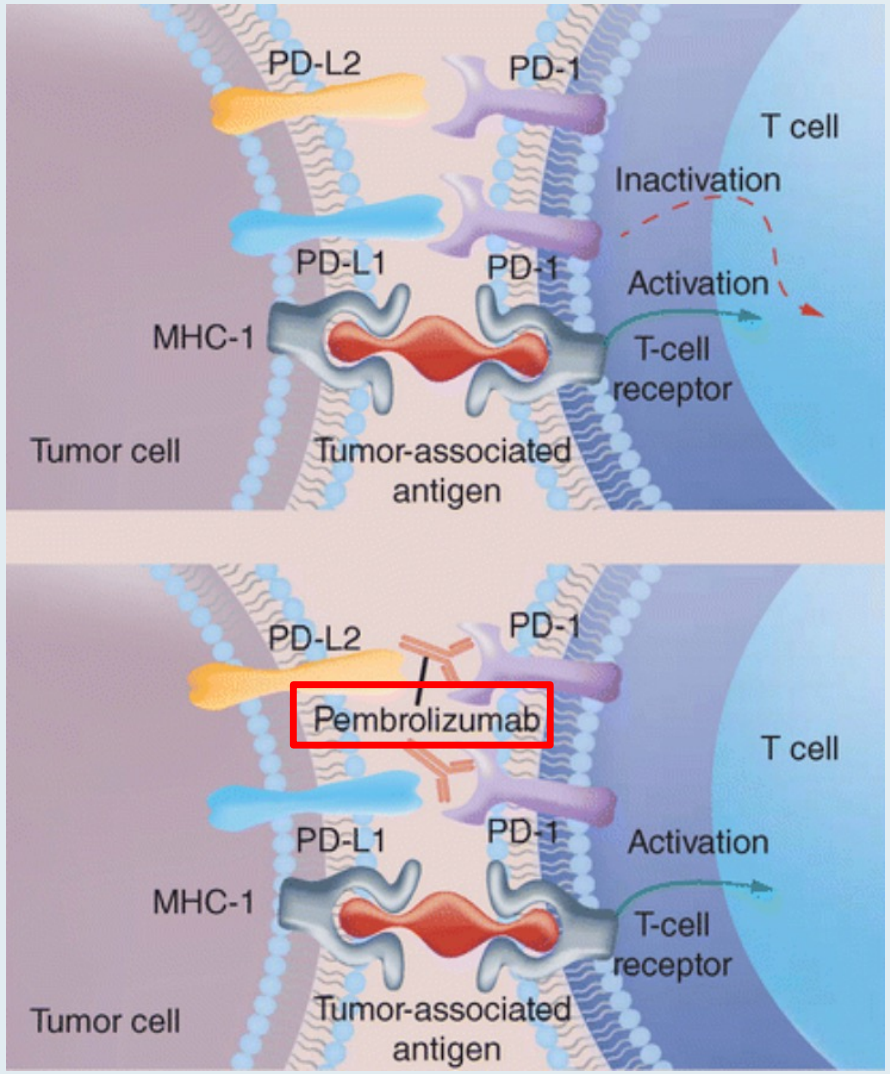
- **For patients with hepatocellular carcinoma who have an alpha fetoprotein level of ≥400 ng/mL and have previously received sorafenib**

Recommended dose

- **8 mg/kg IV infusion every 2 weeks**

Ramucirumab package insert, 3/2022.

Pembrolizumab Mechanism of Action



Reck M. *Immunotherapy* 2017;10(2):93-105.

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Pembrolizumab

Mechanism of action

- **PD-1 inhibitor**

Indication

- **For patients with hepatocellular carcinoma who have previously received sorafenib**

Recommended dose

- **200 mg every 3 weeks or 400 mg every 6 weeks**

Pembrolizumab package insert, 4/2023.

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Module 6: Targeted Treatment for Biliary Tract Cancers

Amanda K Wagner, APRN-CNP, AOCNP

72-year-old man with cholangiocarcinoma and an IDH1 mutation receives first-line gemcitabine/cisplatin/durvalumab with poor tolerance → second-line ivosidenib

Dr Kaseb
Houston, Texas

Clinical Research Background

Dr Li
Duarte, California

- **Overview of biliary tract cancers**
  - **Local therapies**
  - **Classification**

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Blanca Ledezma, MSN, NP, AOCNP

43-year-old woman with cholangiocarcinoma and an FGFR2 alteration who began pemigatinib after disease progression on gemcitabine/cisplatin

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Dr Kaseb
Houston, Texas

Clinical Research Background

Dr Li
Duarte, California

- **First-line systemic therapy**

Durvalumab

Mechanism of action

- **PD-L1 inhibitor**

Indication

- **In combination with gemcitabine and cisplatin for locally advanced or metastatic biliary tract cancer**

Recommended dose

- **Durvalumab: 1,500 mg every 3 weeks in combination with chemotherapy, and then 1,500 mg every 4 weeks as a single agent**

Durvalumab package insert, 9/2022

FDA Approves Durvalumab for Locally Advanced or Metastatic Biliary Tract Cancer

Press Release – September 2, 2022

"The Food and Drug Administration approved durvalumab in combination with gemcitabine and cisplatin for adult patients with locally advanced or metastatic biliary tract cancer (BTC).

Efficacy was evaluated in TOPAZ-1 (NCT03875235), a randomized, double-blind, placebo-controlled, multiregional trial that enrolled 685 patients with histologically confirmed locally advanced unresectable or metastatic BTC who had not previously received systemic therapy for advanced disease.

Patients were randomized 1:1 to receive:

- durvalumab 1,500 mg on Day 1 + gemcitabine 1,000 mg/m^2 and cisplatin 25 mg/m^2 on Days 1 and 8 of each 21-day cycle up to 8 cycles, followed by durvalumab 1,500 mg every 4 weeks, or
- placebo on Day 1 + gemcitabine 1,000 mg/m^2 and cisplatin 25 mg/m^2 on Days 1 and 8 of each 21-day cycle up to 8 cycles, followed by placebo every 4 weeks.

Durvalumab or placebo were continued until disease progression or unacceptable toxicity. Treatment was permitted beyond disease progression if the patient was clinically stable and deriving clinical benefit, as determined by the investigator."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-durvalumab-locally-advanced-or-metastatic-biliary-tract-cancer

Poster 56P

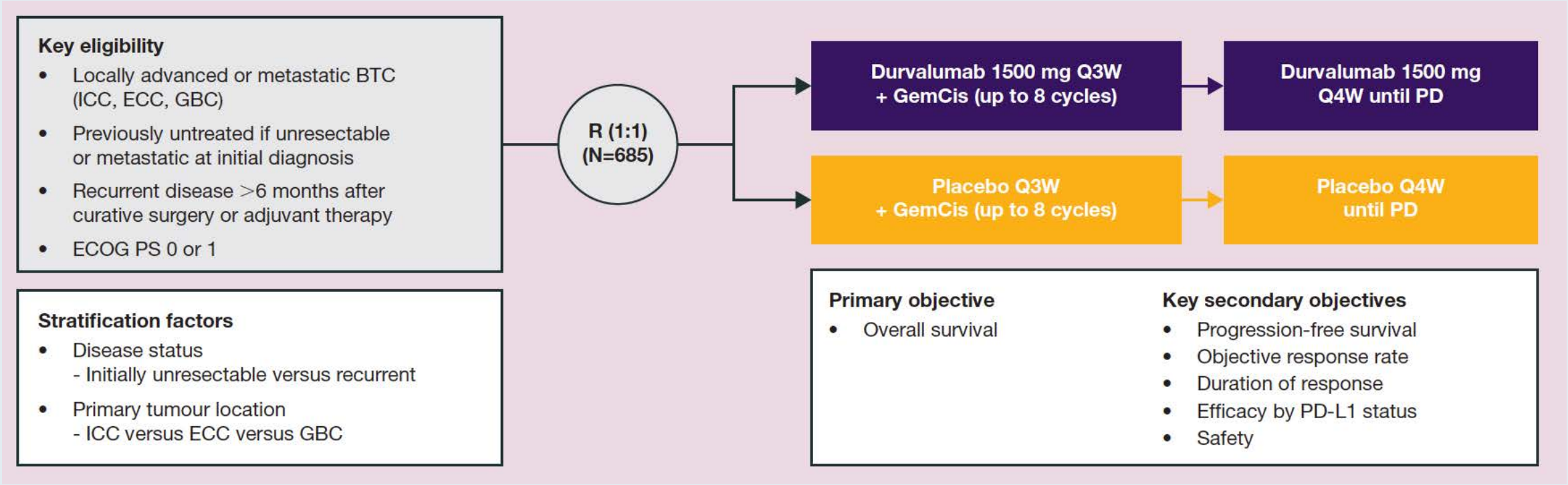
ESMO 2022

Updated overall survival from the Phase 3 TOPAZ-1 study of durvalumab or placebo plus gemcitabine and cisplatin in patients with advanced biliary tract cancer

Do-Youn Oh,[1] Aiwu Ruth He,[2] Shukui Qin,[3] Li-Tzong Chen,[4] Takuji Okusaka,[5] Arndt Vogel,[6] Jin Won Kim,[7] Thatthan Suksomboon charoen,[8] Myung Ah Lee,[9] Masayuki Kitano,[10] Howard Burris,[11] Mohamed Bouattour,[12] Suebpong Tanasanvimon,[13] Renata Zaucha,[14] Antonio Avallone,[15] Juan Cundom,[16] Benjamin Tan,[17] Nana Rokutanda,[18] Magdalena Watras,[19] Gordon Cohen,[18] Juan W. Valle[20]

[1]Division of Medical Oncology, Department of Internal Medicine, Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea; [2]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [3]Cancer Center of Nanjing, Jinling Hospital, Nanjing, China; [4]National Institute of Cancer Research, National Health Research Institutes, Zhunan, Taiwan; [5]National Cancer Center Hospital, Tokyo, Japan; [6]Hanover Medical School, Hanover, Germany; [7]Division of Medical Oncology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; [8]Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [9]Seoul St. Mary's Hospital, Catholic University, Seoul, South Korea; [10]Second Department of Internal Medicine, Wakayama Medical University, Wakayama, Japan; [11]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN, USA; [12]AP-HP Hôpital Beaujon, Paris, France; [13]Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand; [14]Department of Oncology and Radiotherapy, Medical University of Gdańsk, Gdańsk, Poland; [15]Istituto Nazionale Tumori-IRCCS Fondazione G. Pascale, Naples, Italy; [16]Instituto de Investigaciones Metabólicas, Buenos Aires, Argentina; [17]Department of Medicine, Washington University School of Medicine, St. Louis, MO, USA; [18]AstraZeneca, Gaithersburg, MD, USA; [19]AstraZeneca, Warsaw, Poland; [20]University of Manchester and the Christie NHS Foundation Trust, Manchester, UK

TOPAZ-1 Phase III Trial Schema

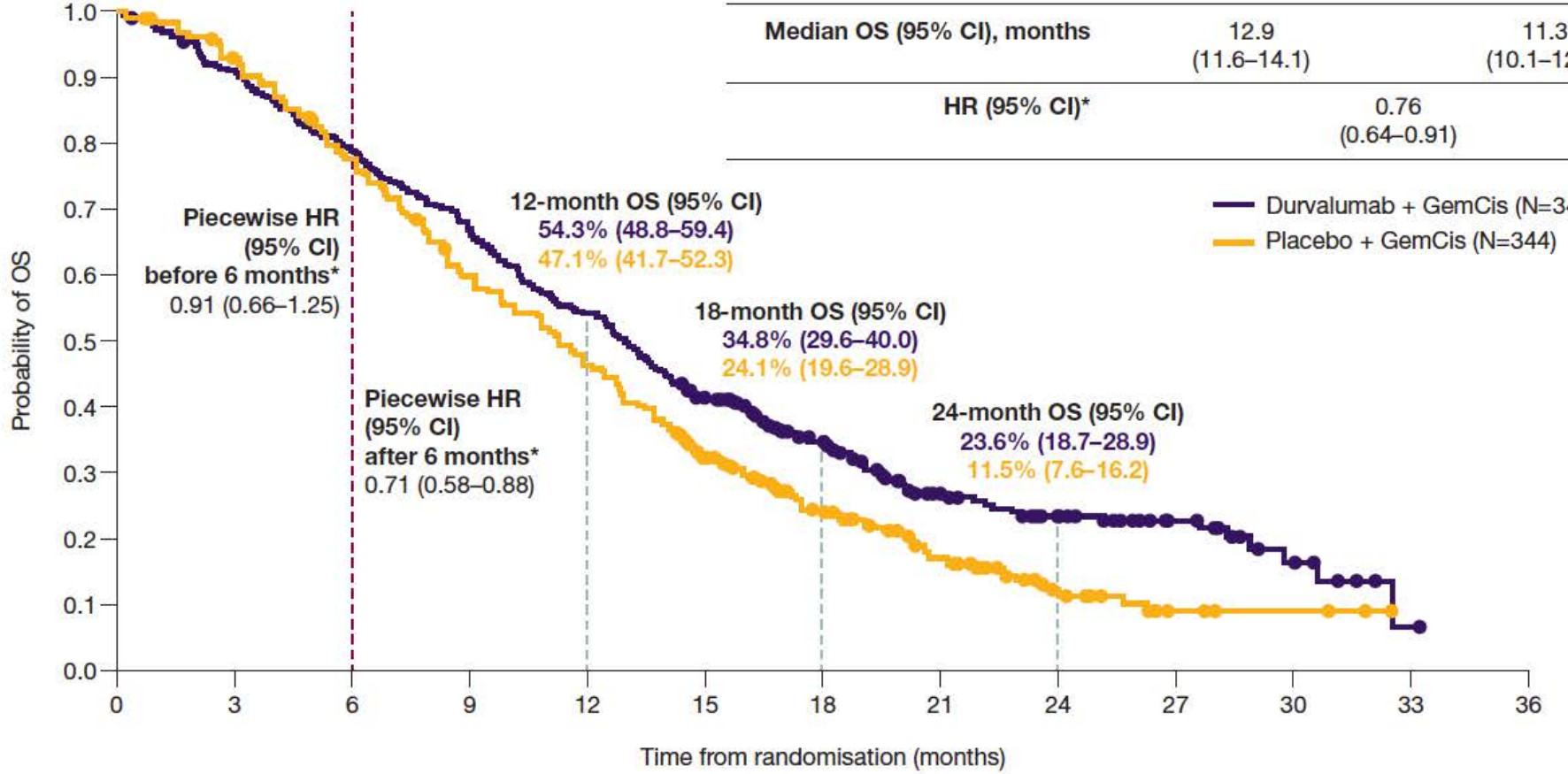


BTC = biliary tract cancer

Oh D-Y et al. ESMO 2022;Abstract 56P.

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

	Durvalumab + GemCis (N=341)	Placebo + GemCis (N=344)
Median OS (95% CI), months	12.9 (11.6–14.1)	11.3 (10.1–12.5)
HR (95% CI)*	0.76 (0.64–0.91)	



Oh D-Y et al. ESMO 2022;Abstract 56P.

Addition of Pembrolizumab to First-Line Chemotherapy Significantly Improved Overall Survival for Patients with Advanced or Unresectable Biliary Tract Cancer in the KEYNOTE-966 Trial

Press Release – January 25, 2023

Positive results from the Phase 3 KEYNOTE-966 trial were announced. In the final analysis of this trial, pembrolizumab in combination with standard of care chemotherapy (gemcitabine and cisplatin) demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS) versus chemotherapy alone for the first-line treatment of patients with advanced or unresectable biliary tract cancer (BTC). The safety profile of pembrolizumab in this trial was consistent with that observed in previously reported studies.

Results will be presented at an upcoming medical meeting and will be submitted to regulatory authorities. unresectable or metastatic BTC who had not previously received systemic therapy for advanced disease.

https://www.merck.com/news/mercks-keytruda-pembrolizumab-plus-chemotherapy-significantly-improved-overall-survival-versus-chemotherapy-in-first-line-advanced-or-unresectable-biliary-tract-cancer-in-keynote-966/

Agenda

Module 1: Overview of Hepatocellular Carcinoma (HCC)

Module 2: First-Line Systemic Therapy for HCC

Module 3: Therapy for Relapsed HCC

Module 4: Overview of Biliary Tract Cancers

Module 5: First-Line Systemic Therapy for Biliary Tract Cancers

Module 6: Targeted Treatment for Biliary Tract Cancers

Amanda K Wagner, APRN-CNP, AOCNP

A 70-year-old man with cholangiocarcinoma who received durvalumab in combination with gemcitabine/cisplatin and developed myocarditis and pneumonitis

Dr Kaseb
Houston, Texas

Clinical Research Background

Dr Li
Duarte, California

- **Targeted treatment**
  - **FGFR inhibitors**
  - **IDH inhibitors**
  - **HER2-targeted therapy**

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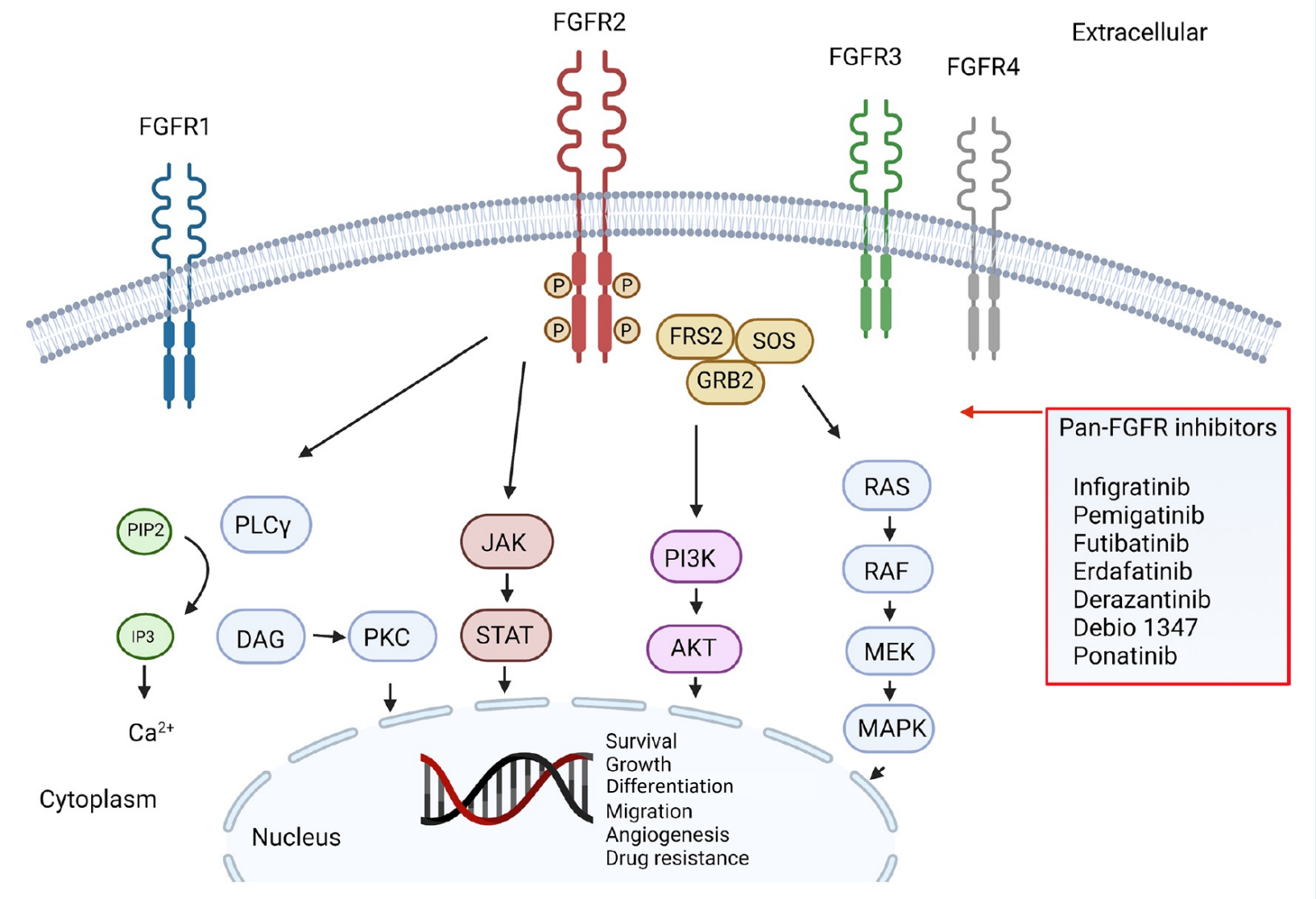
FGFR Inhibitors Mechanism of Action



Zugman M et al. *Front Oncol* 2022;12:860453.

Futibatinib

Mechanism of action

- **FGFR inhibitor**

Indication

- **For patients with previously treated, unresectable locally advanced or metastatic intrahepatic cholangiocarcinoma harboring FGFR2 gene fusions or other rearrangement**

Recommended dose

- **20 mg orally (five 4-mg tablets) once daily until disease progression or unacceptable toxicity**

Futibatinib package insert, 9/2022.

Pemigatinib

Mechanism of action

- **FGFR inhibitor**

Indication

- **For patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma harboring FGFR2 fusions or other rearrangements**

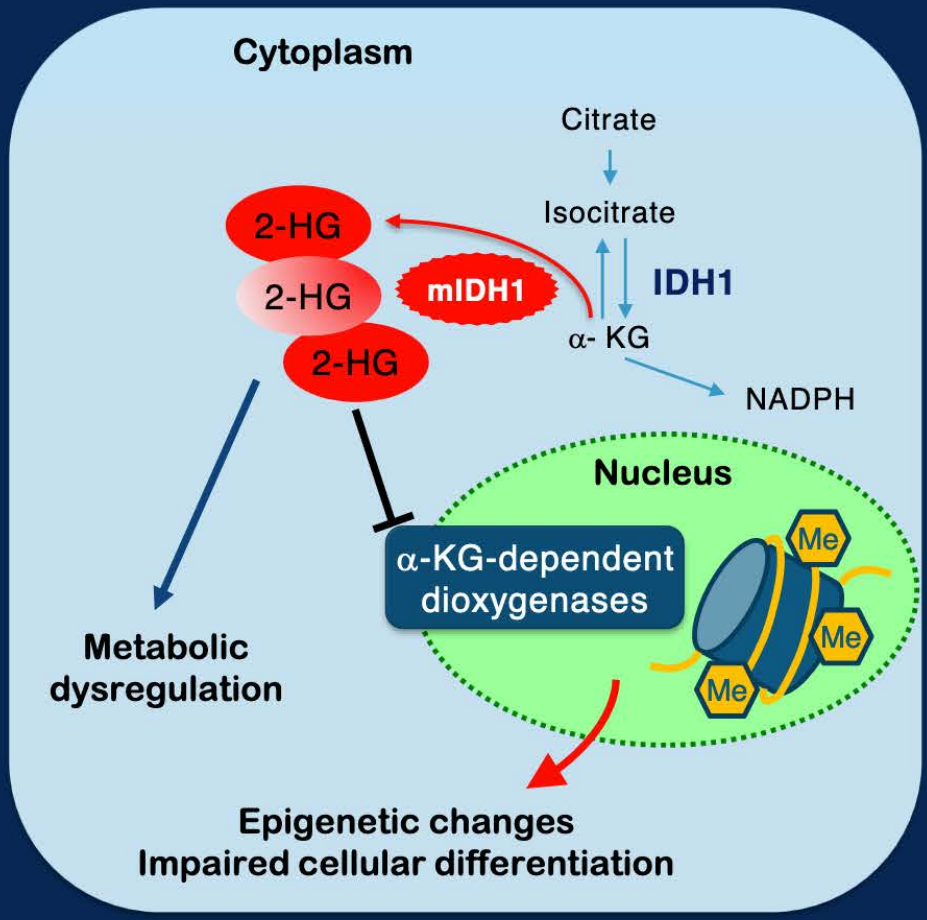
Recommended dose

- **13.5 mg po once daily for 14 consecutive days followed by 7 days off therapy in 21-day cycles until disease progression or unacceptable toxicity**

Pemigatinib package insert, 8/2022.

IDH1 Mutations in Advanced Cholangiocarcinoma

- CCA is a rare cancer for which there are limited effective therapies
- *IDH1* mutations occur in up to 20% of intrahepatic CCAs,[1] resulting in production of the oncometabolite D-2-hydroxyglutarate (2-HG), which promotes oncogenesis
  - *IDH1* mutations in CCA are not associated with prognosis[1]
- Ivosidenib (AG-120) is a first-in-class, oral, small-molecule inhibitor of mutant IDH1 (mIDH1)[2]
- The phase 3 ClarIDHy study aimed to demonstrate the efficacy of ivosidenib vs placebo in patients with unresectable or metastatic m*IDH1* CCA[3]



α-KG = alpha-ketoglutarate; Me = methyl groups; NADPH = nicotinamide adenine dinucleotide phosphate hydrogen

1. Boscoe AN, et al. *J Gastrointest Oncol.* 2019;10:751-765. **2.** Popovici-Muller J, et al. *ACS Med Chem Lett.* 2018;9:300-305.
3. Abou-Alfa GK et al. *Lancet Oncol.* 2020;21:796-807.

Zhu A et al. Gastrointestinal Cancers Symposium 2021;Abstract 266.

Ivosidenib

Mechanism of action

- **IDH1 inhibitor**

Indication

- **For patients with previously treated locally advanced or metastatic cholangiocarcinoma with a susceptible IDH1 mutation**

Recommended dose

- **500 mg po daily with or without food until disease progression or unacceptable toxicity**

Ivosidenib package insert, 5/2022.

2022 ASCO ANNUAL MEETING

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

APPENDIX

HCC

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 HBV-associated HCC (~48%)	Asian HBV-associated HCC (94%)	Global 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%

HCC = hepatocellular cancer; 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 (Continued)

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 HBV-associated HCC (~48%)	Asian HBV-associated HCC (94%)	Global 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%

HCC = hepatocellular cancer; bev = bevacizumab; HBV = hepatitis B virus; PFS = progression-free survival; OS = overall survival; ORR = objective response rate

* **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].

Research Article
Hepatic and Biliary Cancer

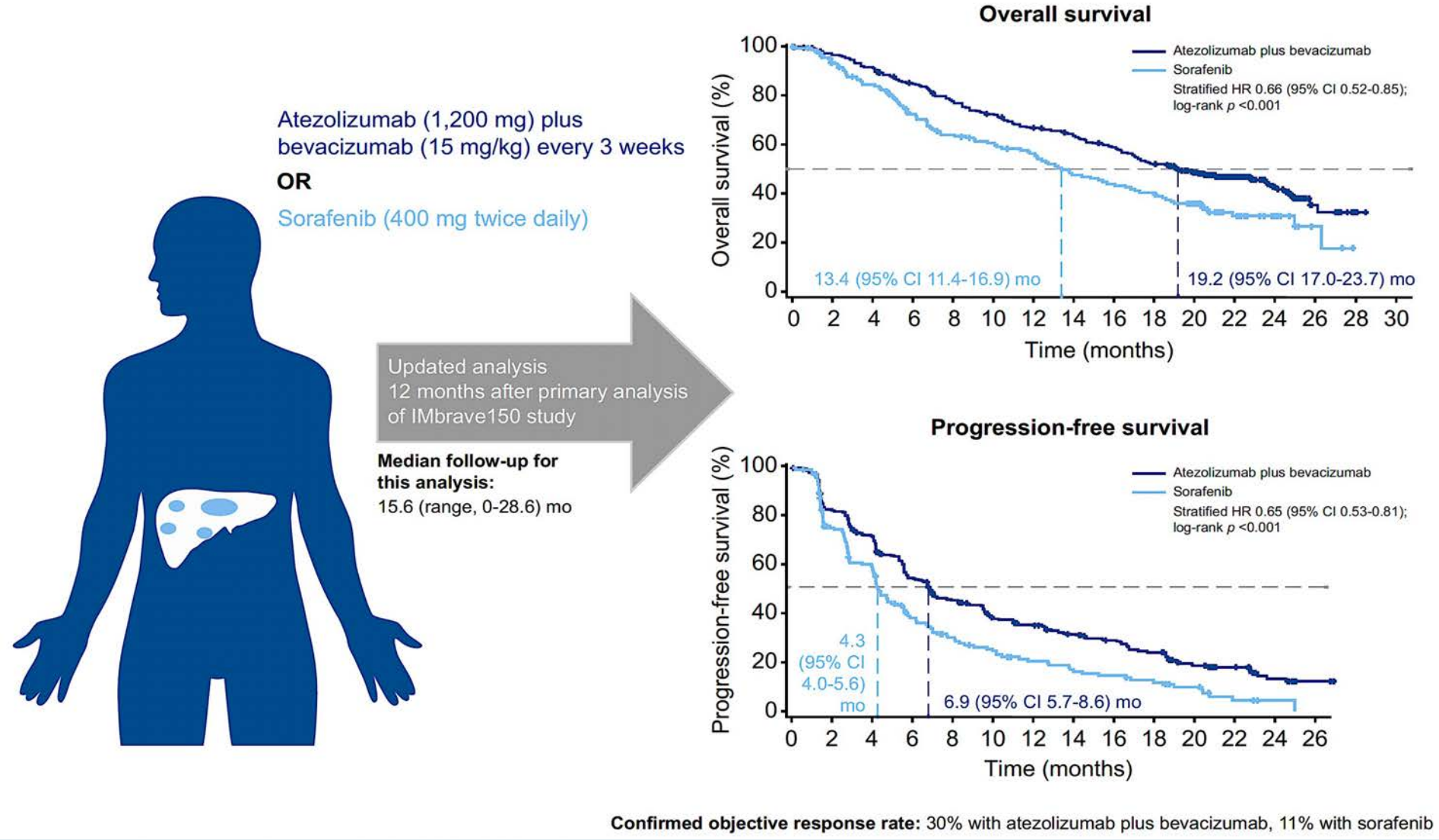
JOURNAL
OF HEPATOLOGY

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,*]

2022;76(4):862-73.

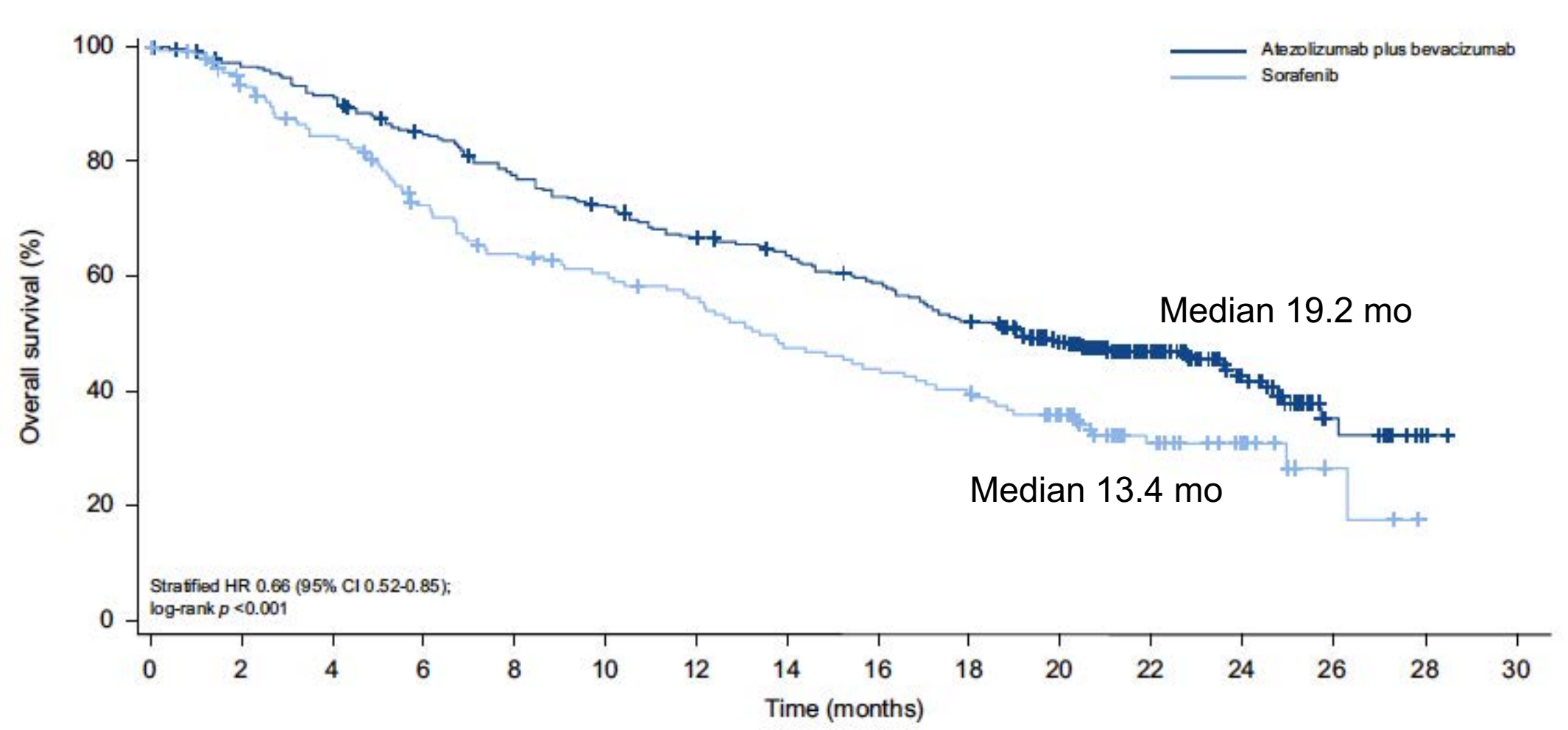
IMbrave150: Updated OS and PFS with Atezolizumab and Bevacizumab (Median Follow-Up 15.6 Months)



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

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

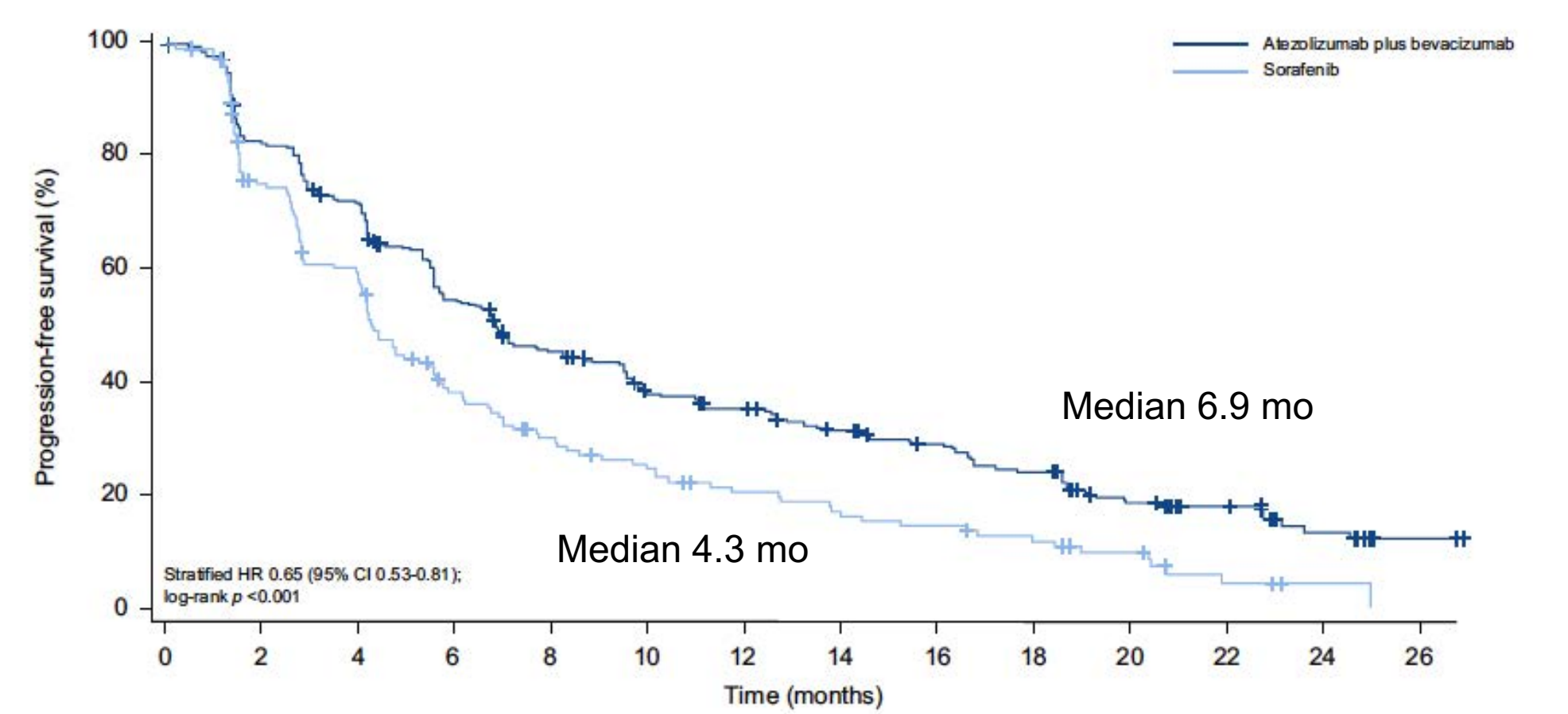
IMbrave150: Updated OS with Atezolizumab and Bevacizumab (Median Follow-Up 15.6 Months)



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

RTP RESEARCH TO PRACTICE

IMbrave150: Updated 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

FDA Approves Tremelimumab in Combination with Durvalumab for Unresectable Hepatocellular Carcinoma

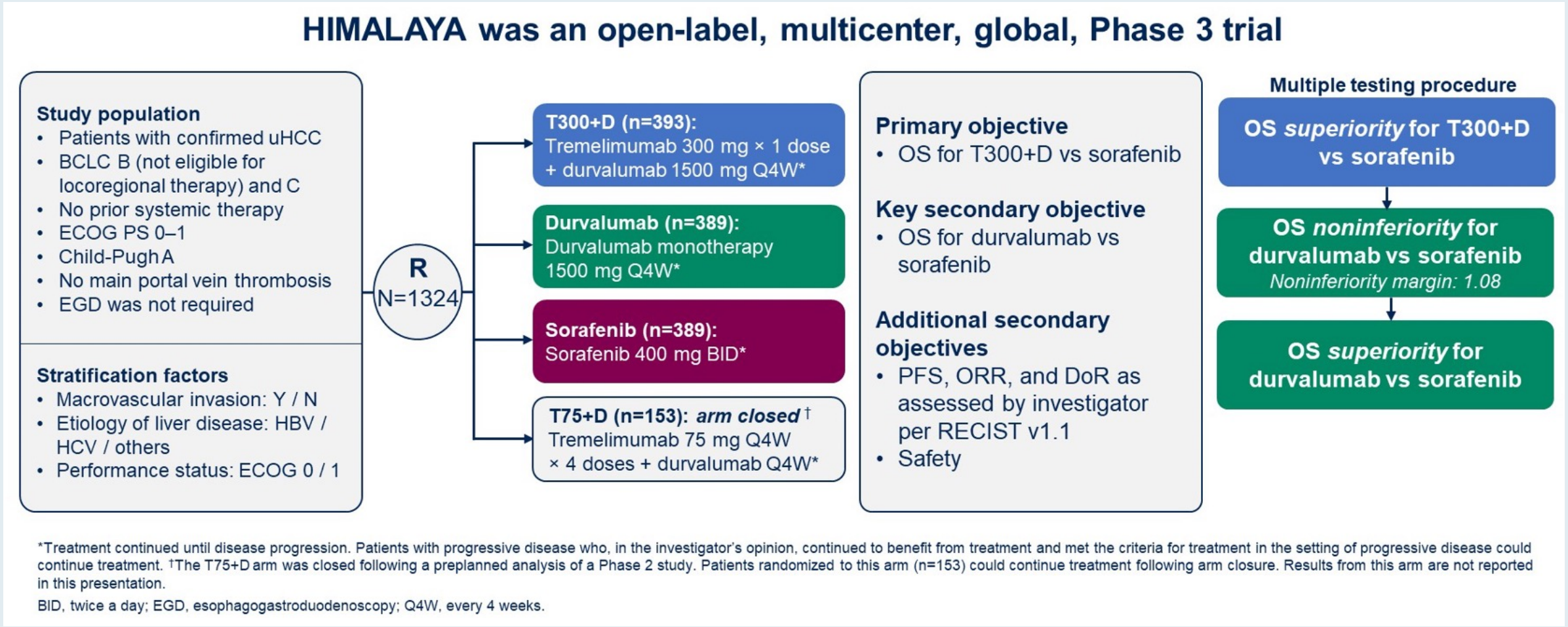
Press Release – October 21, 2022

"The Food and Drug Administration approved tremelimumab in combination with durvalumab for adult patients with unresectable hepatocellular carcinoma (uHCC).

Efficacy was evaluated in HIMALAYA (NCT03298451), a randomized (1:1:1), open-label, multicenter study in patients with confirmed uHCC who had not received prior systemic treatment for HCC. Patients were randomized to one of three arms: tremelimumab 300 mg as a one-time single intravenous (IV) infusion plus durvalumab 1500 mg IV on the same day, followed by durvalumab 1500 mg IV every 4 weeks; durvalumab 1500 mg IV every 4 weeks; or sorafenib 400 mg orally twice daily until disease progression or unacceptable toxicity. This approval is based on a comparison of the 782 patients randomized to tremelimumab plus durvalumab to sorafenib."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tremelimumab-combination-durvalumab-unresectable-hepatocellular-carcinoma

HIMALAYA Phase III Trial Schema

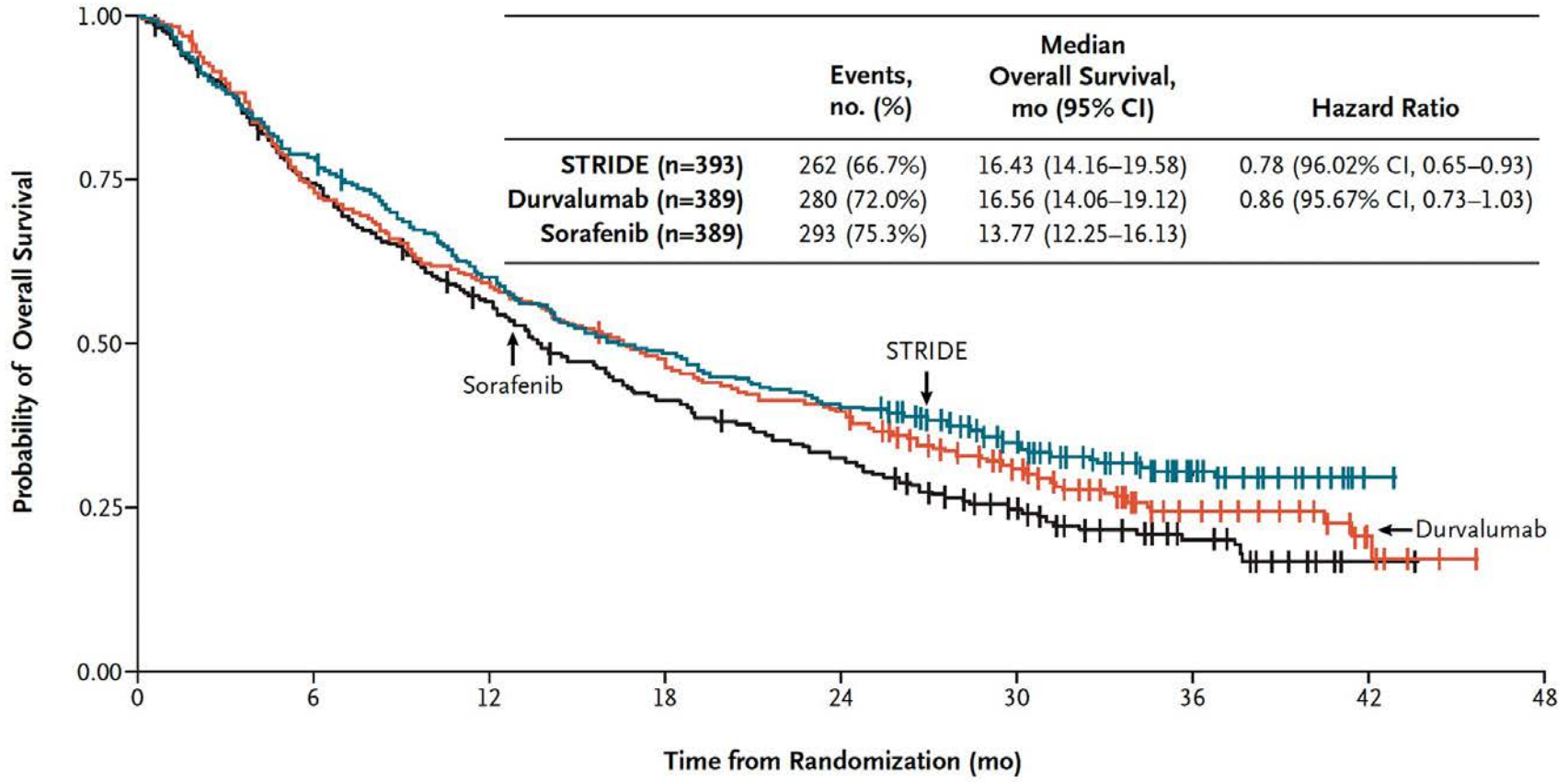


*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned 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

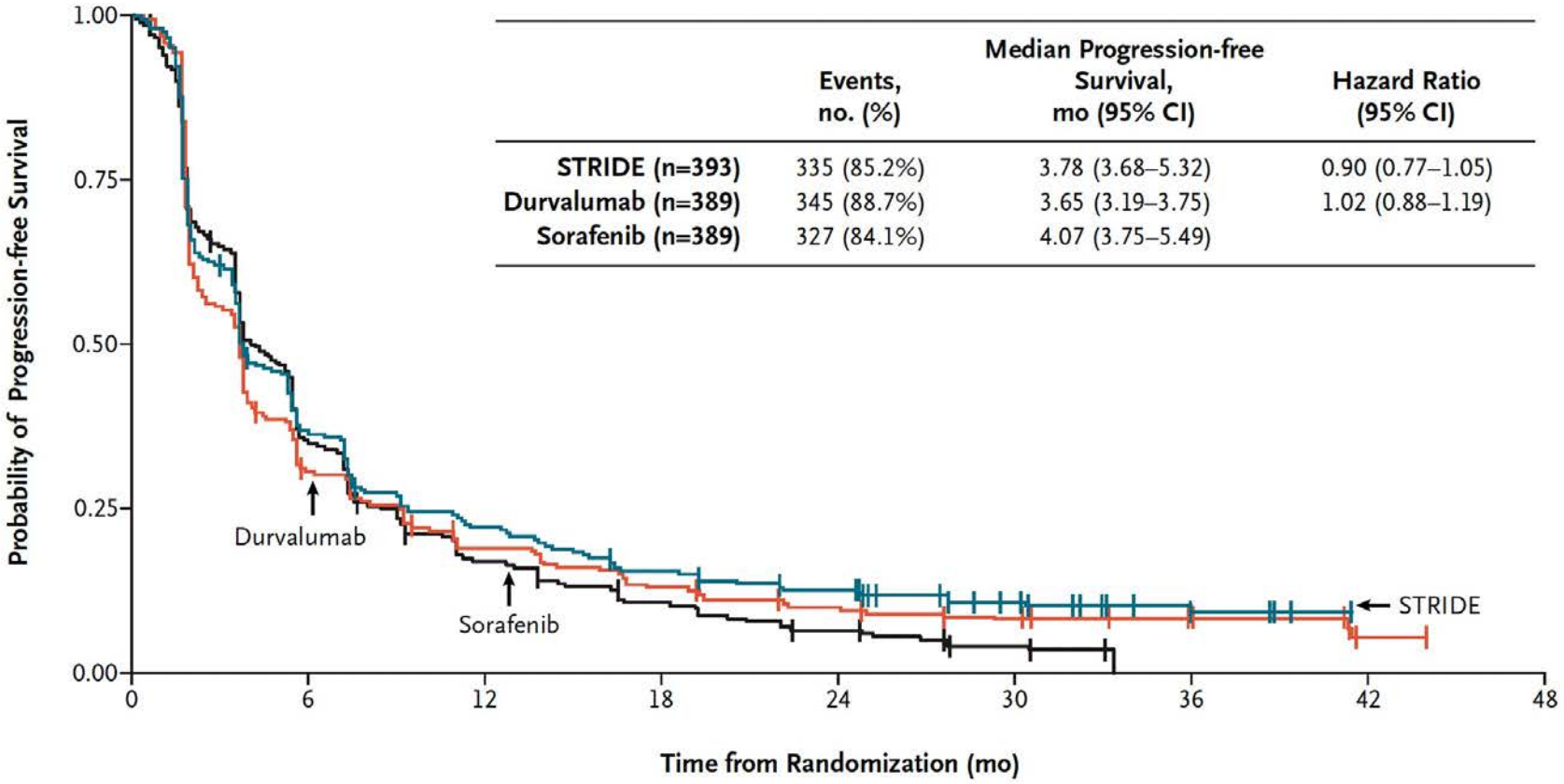


	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

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 GK et al. *NEJM Evid* 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 GK et al. *NEJM Evid* 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 GK et al. *NEJM Evid* June 6, 2022.

HIMALAYA: Treatment-Emergent Adverse Events (Safety Population)

Event	STRIDE (n=388)	Durvalumab (n=388)	Sorafenib (n=374)	T75+D (n=152)
Treatment-emergent adverse events of any cause				
Any	378 (97.4)	345 (88.9)	357 (95.5)	145 (95.4)
Any serious	157 (40.5)	115 (29.6)	111 (29.7)	52 (34.2)
Any grade 3 or 4	196 (50.5)	144 (37.1)	196 (52.4)	60 (39.5)
Leading to discontinuation	53 (13.7)	32 (8.2)	63 (16.8)	23 (15.1)
Leading to dose delay	134 (34.5)	95 (24.5)	178 (47.6)	58 (38.2)
Leading to death	30 (7.7)	26 (6.7)	27 (7.2)	12 (7.9)
Immune-mediated requiring high-dose steroids	78 (20.1)	37 (9.5)	7 (1.9)	29 (19.1)
Any grade 3 or 4 immune-mediated	49 (12.6)	25 (6.4)	9 (2.4)	19 (12.5)
Immune-mediated leading to death	6 (1.5)	0	0	0
Any grade 3 or 4 hepatic SMQ	54 (13.9)	54 (13.9)	39 (10.4)	26 (17.1)

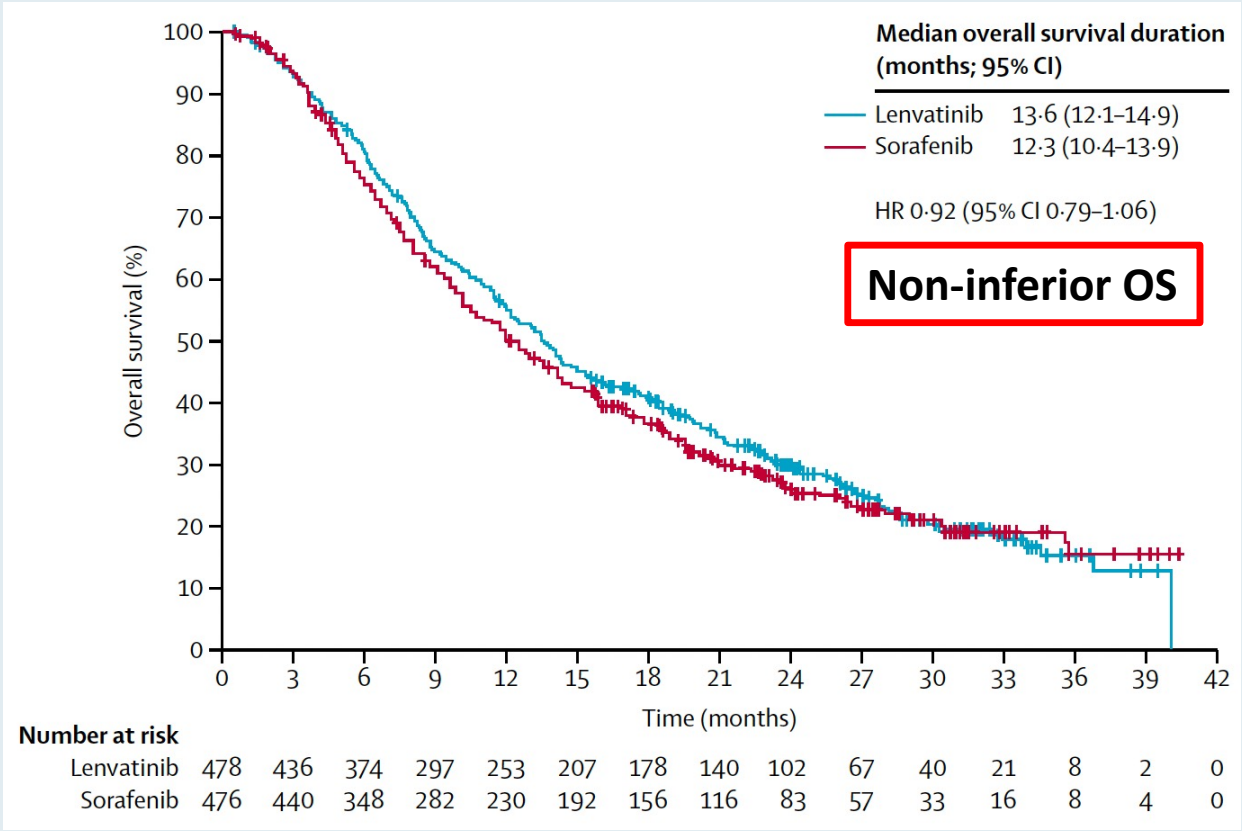
Abou-Alfa GK et al. *NEJM Evid* June 6, 2022.

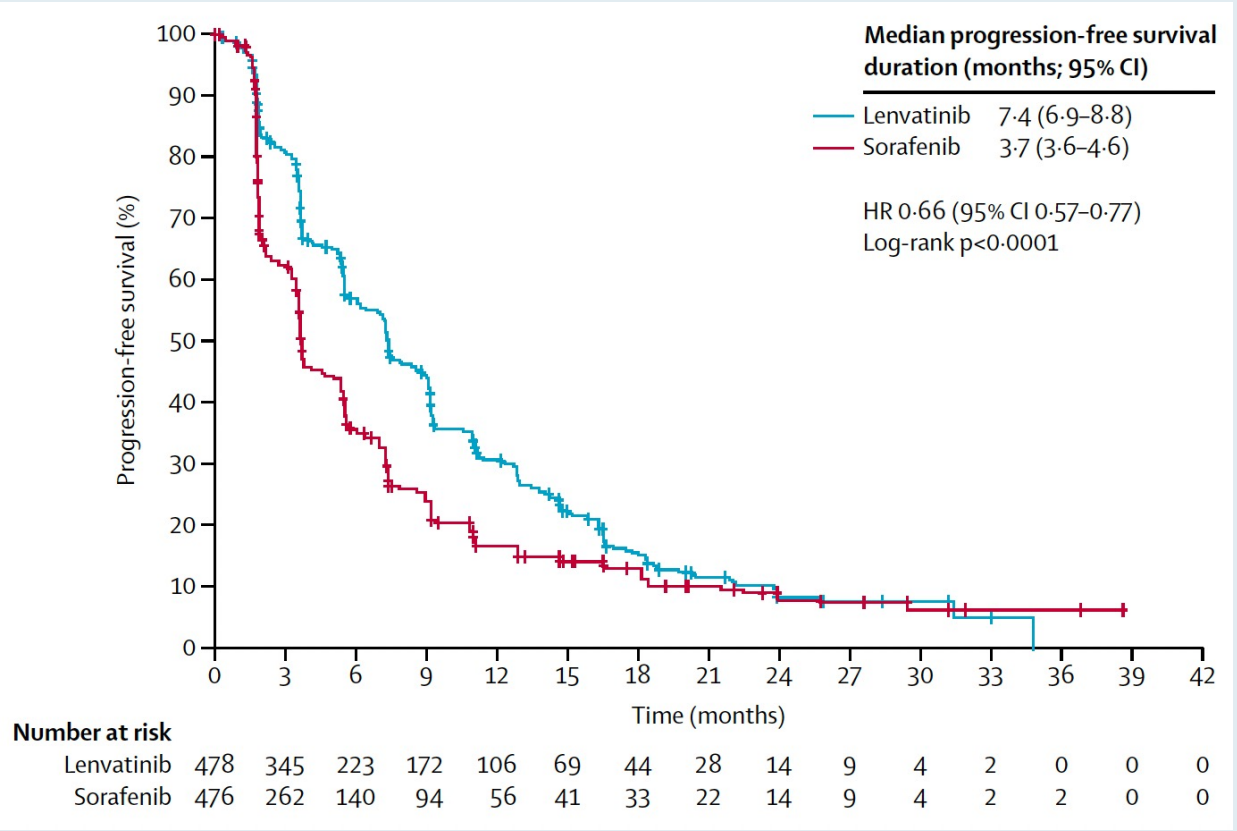
Lancet 2018;391:1163-73

Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial

Masatoshi Kudo, Richard S Finn, Shukui Qin, Kwang-Hyub Han, Kenji Ikeda, Fabio Piscaglia, Ari Baron, Joong-Won Park*, Guohong Han*, Jacek Jassem, Jean Frederic Blanc, Arndt Vogel, Dmitry Komov, T R Jeffry Evans, Carlos Lopez, Corina Dutcus, Matthew Guo, Kenichi Saito, Silvija Kraljevic, Toshiyuki Tamai, Min Ren, Ann-Lii Cheng*

REFLECT Trial: Overall and Progression-Free Survival





Kudo M et al. *Lancet* 2018;391:1163-73.

REFLECT: Common Treatment-Emergent Adverse Events

	Lenvatinib (n=476)	Sorafenib (n=475)
Palmar-plantar erythrodysaesthesia		
Any grade	128 (27%)	249 (52%)
Grade ≥3	14 (3%)	54 (11%)
Diarrhoea		
Any grade	184 (39%)	220 (46%)
Grade ≥3	20 (4%)	20 (4%)
Hypertension		
Any grade	201 (42%)	144 (30%)
Grade ≥3	111 (23%)	68 (14%)
Decreased appetite		
Any grade	162 (34%)	127 (27%)
Grade ≥3	22 (5%)	6 (1%)
Decreased weight		
Any grade	147 (31%)	106 (22%)
Grade ≥3	36 (8%)	14 (3%)
Fatigue		
Any grade	141 (30%)	119 (25%)
Grade ≥3	18 (4%)	17 (4%)

	Lenvatinib (n=476)	Sorafenib (n=475)
Alopecia		
Any grade	14 (3%)	119 (25%)
Grade ≥3	0	0
Proteinuria		
Any grade	117 (25%)	54 (11%)
Grade ≥3	27 (6%)	8 (2%)
Dysphonia		
Any grade	113 (24%)	57 (12%)
Grade ≥3	1 (<1%)	0
Nausea		
Any grade	93 (20%)	68 (14%)
Grade ≥3	4 (1%)	4 (1%)
Abdominal pain		
Any grade	81 (17%)	87 (18%)
Grade ≥3	8 (2%)	13 (3%)
Decreased platelet count		
Any grade	87 (18%)	58 (12%)
Grade ≥3	26 (5%)	16 (3%)

Kudo M et al. *Lancet* 2018;391:1163-73.

RTP RESEARCH TO PRACTICE

Cholangiocarcinoma and Biliary Tract Cancers

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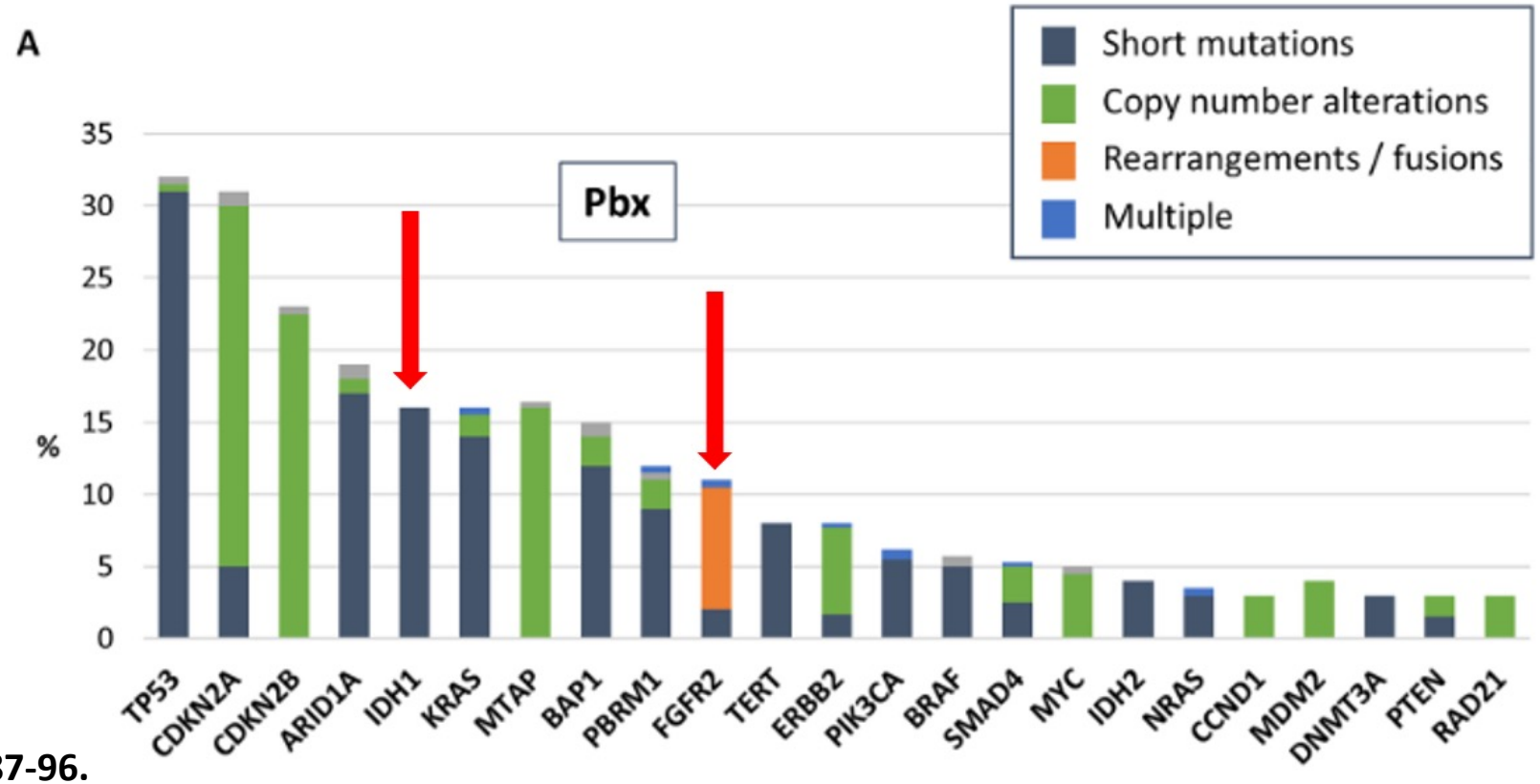
Emerging Targets in Cholangiocarcinoma: Focus on FGFR2 and IDH1

- 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.

Courtesy of Robin K Kelley, MD

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

FISH = fluorescence in situ hybridization; MSI = miscrosatellite instability; MMR = mismatch repair

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

Efficacy of FDA-Approved FGFR Inhibitors for Cholangiocarcinoma with an FGFR2 Fusion

	Pemigatinib (N = 107)	Infigratinib (N = 108)	Futibatinib (N = 67)
ORR	37.0%	23.1%	42.0%
Disease control rate	82.0%	84.3%	83.0%
Median progression-free survival	7.0 mo	7.3 mo	9.0 mo
Median overall survival	17.5 mo	12.2 mo	21.7 mo
Toxicities	Hyperphosphatemia, alopecia, diarrhea	Hyperphosphatemia, stomatitis, fatigue	Hyperphosphatemia, diarrhea, dry mouth

Vogel A et al. ESMO GI 2022;Abstract O-2; Javle M et al. *Lancet Gastroenterol* 2021;6:803-15; Goyal L et al. *N Engl J Med* 2023;388:228-39.

WORLD CONGRESS ON Gastrointestinal Cancer

O-2

#575

Presented at the 2022 ESMO World Congress on Gastrointestinal Cancer; 29 June–2 July, 2022; Barcelona, Spain

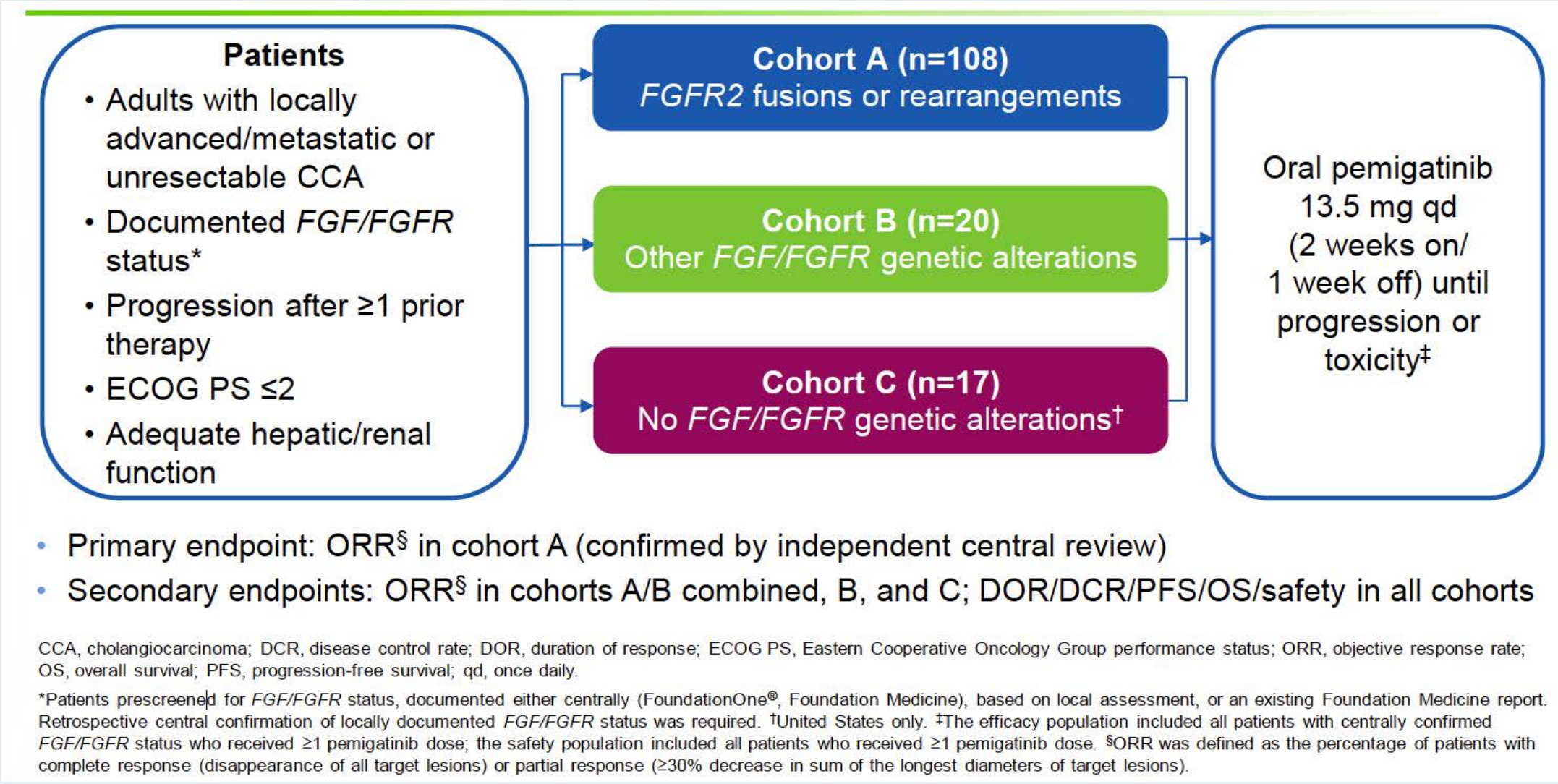
Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma: Final Results From FIGHT-202

Arndt Vogel, MD

Arndt Vogel, MD,[1] Vaibhav Sahai, MBBS, MS,[2] Antoine Hollebecque, MD,[3] Gina M. Vaccaro, MD,[4] Davide Melisi, MD, PhD,[5] Raed M. Al Rajabi, MD,[6] Andrew S. Paulson, MD,[7] Mitesh J. Borad, MD,[8] David Gallinson, DO,[9] Adrian G. Murphy, MD,[10] Do-Youn Oh, MD, PhD,[11] Efrat Dotan, MD,[12] Daniel V. Catenacci, MD,[13] Eric Van Cutsem, MD, PhD,[14] Christine F. Lihou, BS,[15] Huiling Zhen, PhD,[15] Luisa Veronese, MD,[16] Ghassan K. Abou-Alfa, MD[17]

RTP RESEARCH TO PRACTICE

FIGHT-202 Trial Schema



- Primary endpoint: ORR§ in cohort A (confirmed by independent central review)
- Secondary endpoints: ORR§ in cohorts A/B combined, B, and C; DOR/DCR/PFS/OS/safety in all cohorts

CCA, cholangiocarcinoma; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; qd, once daily.

*Patients prescreened for *FGF/FGFR* status, documented either centrally (FoundationOne®, Foundation Medicine), based on local assessment, or an existing Foundation Medicine report. Retrospective central confirmation of locally documented *FGF/FGFR* status was required. †United States only. ‡The efficacy population included all patients with centrally confirmed *FGF/FGFR* status who received ≥1 pemigatinib dose; the safety population included all patients who received ≥1 pemigatinib dose. §ORR was defined as the percentage of patients with complete response (disappearance of all target lesions) or partial response (≥30% decrease in sum of the longest diameters of target lesions).

Vogel A et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-2.

FIGHT-202 Final Results: Response to Pemigatinib

Parameter	Cohort A (n=108)	Cohort B (n=20)	Cohort C (n=17)
Duration of follow-up, median (range), mo	42.9 (19.9–52.2)	47.5 (43.7–51.1)	51.9 (49.5–53.7)
ORR,* % (95% CI)	37 (28, 47)	0 (0, 17)	0 (0, 20)
DCR,† % (95% CI)	82 (74, 89)	40 (19, 64)	18 (4, 43)
Best overall response, %			
Complete response	3	0	0
Partial response	34	0	0
Stable disease	45	40	18
Progressive disease	15	35	65
Not evaluable	3	25	18
DOR, median (95% CI), mo	9.1 (6.0, 14.5)	—	—

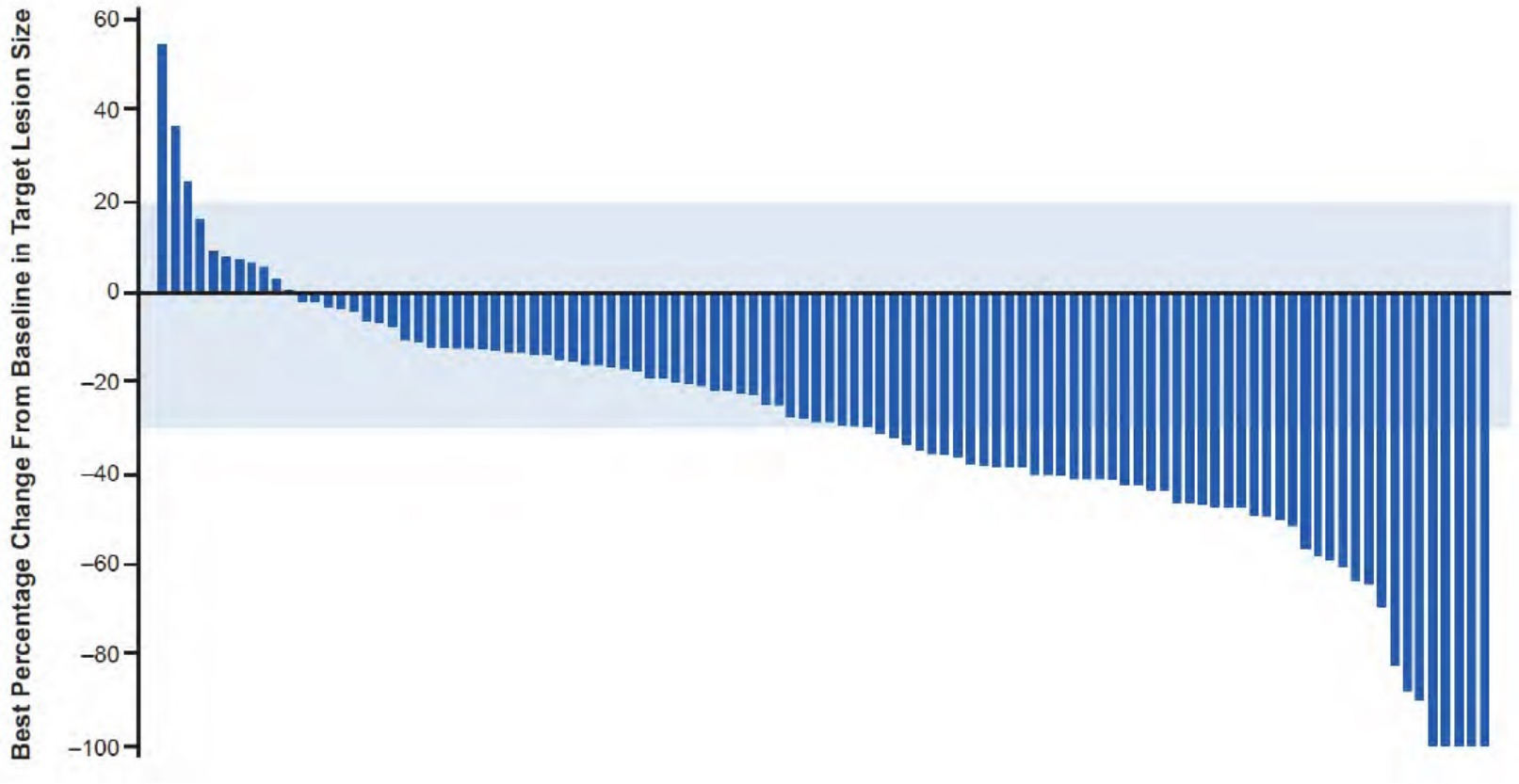
DCR, disease control rate; DOR, duration of response; ORR, objective response rate.

*ORR is complete response + partial response; †DCR is complete response + partial response + stable disease.

Vogel A et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-2.

FIGHT-202 Final Results: Best Change from Baseline in Target Lesion Size in Cohort A

- Among 104 evaluable patients, median best percentage change from baseline in the sum of target lesion diameters was –28.4% (range, –100% to +55%)

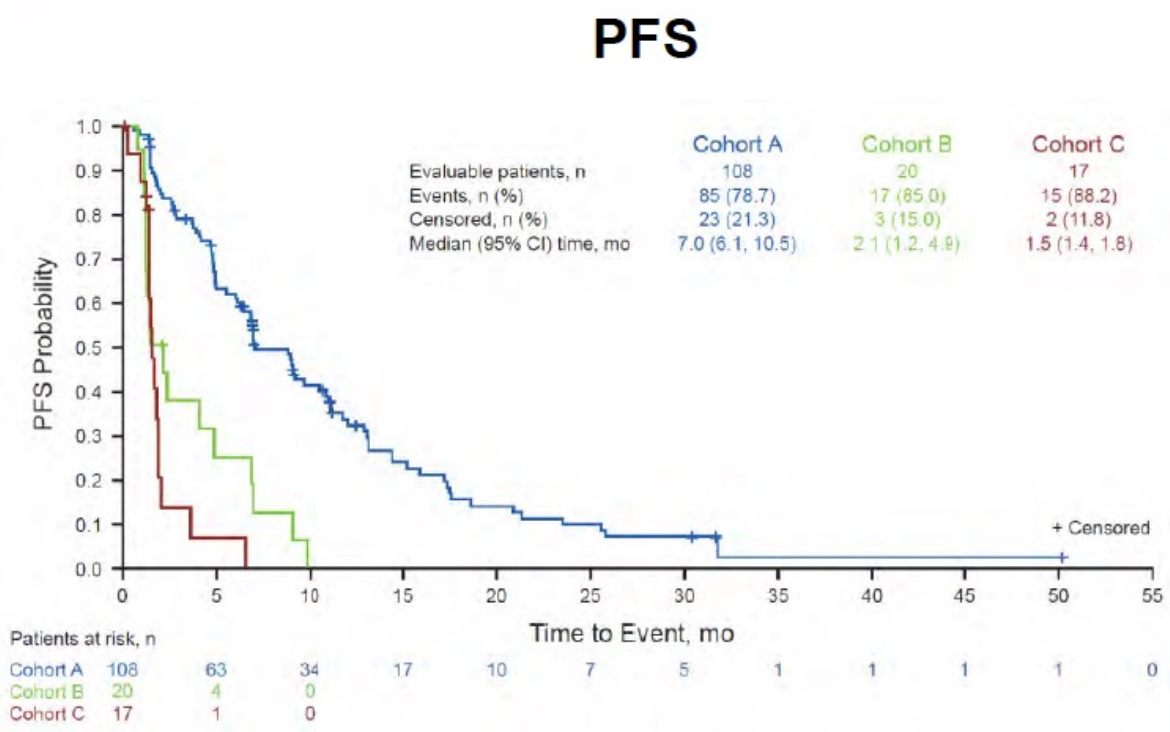


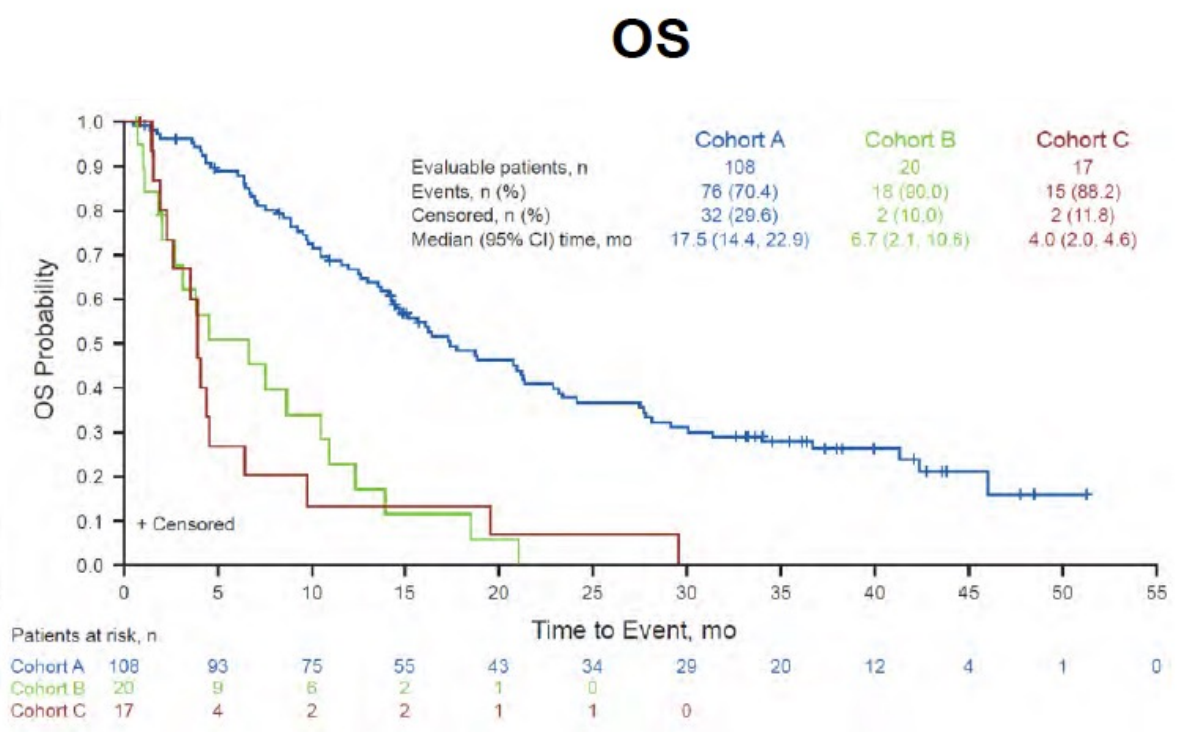
Lower limit of blue shading indicates criterion for partial response (≥30% decrease in sum of target lesion diameters).

Vogel A et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-2.

RTP RESEARCH TO PRACTICE

FIGHT-202 Final Results: PFS and OS for All Patients





- Median PFS in cohort A was 7.0 months (95% CI: 6.1, 10.5)
- Median OS in cohort A was 17.5 months (95% CI: 14.4, 22.9)

Vogel A et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-2.

RTP RESEARCH TO PRACTICE

FIGHT-202: TEAEs Occurring in ≥25% of Patients

Event	Cohort A (n=108)		Cohort B (n=20)		Cohort C (n=17)		Total (N=147)*	
	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3	All Grades	Grade ≥3
Any TEAE, %	100	67	100	75	100	76	100	69
Hyperphosphatemia	56	0	65	0	71	0	59	0
Alopecia	59	0	20	0	18	0	50	0
Diarrhoea	54	4	25	0	35	6	48	3
Fatigue	46	5	25	0	53	18	44	5
Nausea	43	3	35	0	41	0	41	2
Stomatitis	43	9	30	0	18	0	38	7
Constipation	43	1	25	0	12	0	37	1
Dysgeusia	42	0	15	0	18	0	36	0
Decreased appetite	31	1	40	5	41	6	34	2
Dry mouth	39	0	25	0	6	0	34	0
Arthralgia	34	6	25	10	12	0	30	6
Vomiting	33	2	15	0	24	0	29	1
Dry eye	35	0	5	0	6	0	28	1

- The safety profile remained consistent with the primary publication[1]; no new safety signals were observed

TEAE, treatment-emergent adverse event.

*The total includes 2 patients for whom *FGF/FGFR* status could not be centrally determined; the 2 patients were not assigned to a cohort and were evaluated for safety but not for efficacy.

1. Abou-Alfa GH, et al. *Lancet Oncol.* 2020;21(5):671-684.

Vogel A et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-2.

FDA Grants Accelerated Approval to Futibatinib for Cholangiocarcinoma

Press Release – September 30, 2022

"The Food and Drug Administration granted accelerated approval to futibatinib for adult patients with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements.

Efficacy was evaluated in TAS-120-101 (NCT02052778), a multicenter, open-label, single-arm trial that enrolled 103 patients with previously treated, unresectable, locally advanced, or metastatic intrahepatic cholangiocarcinoma harboring a FGFR2 gene fusion or other rearrangement. The presence of FGFR2 fusions or other rearrangements was determined using next generation sequencing testing. Patients received 20 mg of futibatinib orally once daily until disease progression or unacceptable toxicity.

The major efficacy outcome measures were overall response rate (ORR) and duration of response (DoR) as determined by an independent review committee according to RECIST v1.1. ORR was 42% (95% Confidence Interval [CI]: 32, 52); all 43 responders achieved partial responses. The median DoR was 9.7 months (95% CI: 7.6, 17.1)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-futibatinib-cholangiocarcinoma

The NEW ENGLAND JOURNAL of MEDICINE

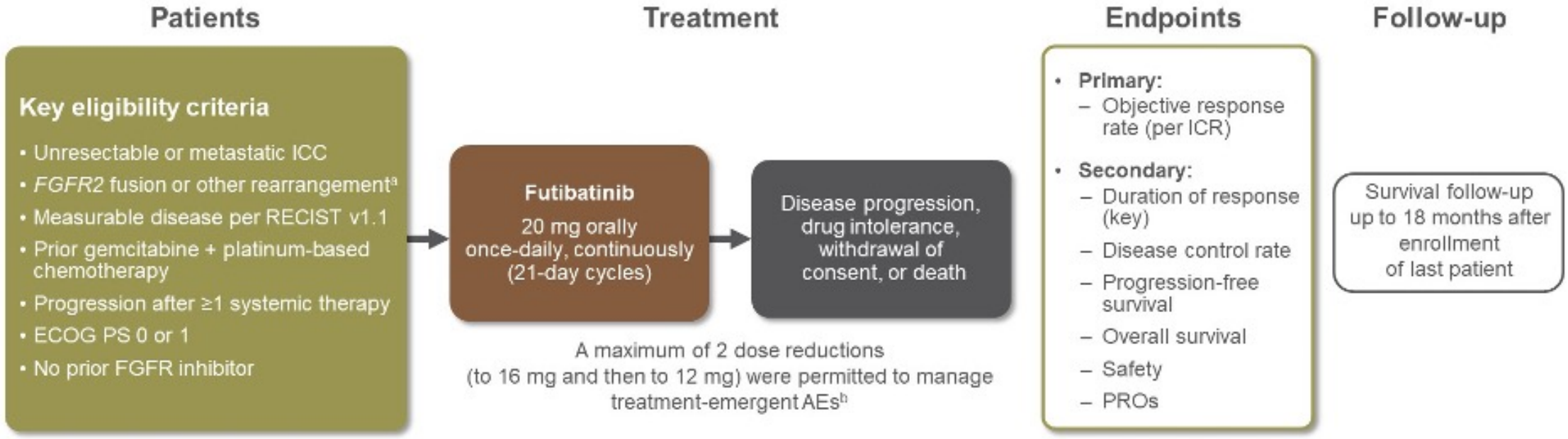
ORIGINAL ARTICLE

Futibatinib for *FGFR2*-Rearranged Intrahepatic Cholangiocarcinoma

L. Goyal, F. Meric-Bernstam, A. Hollebecque, J.W. Valle, C. Morizane, T.B. Karasic, T.A. Abrams, J. Furuse, R.K. Kelley, P.A. Cassier, H.-J. Klümpen, H.-M. Chang, L.-T. Chen, J. Tabernero, D.-Y. Oh, A. Mahipal, M. Moehler, E.P. Mitchell, Y. Komatsu, K. Masuda, D. Ahn, R.S. Epstein, A.-B. Halim, Y. Fu, T. Salimi, V. Wacheck, Y. He, M. Liu, K.A. Benhadji, and J.A. Bridgewater, for the FOENIX-CCA2 Study Investigators*

2023;388;228-39

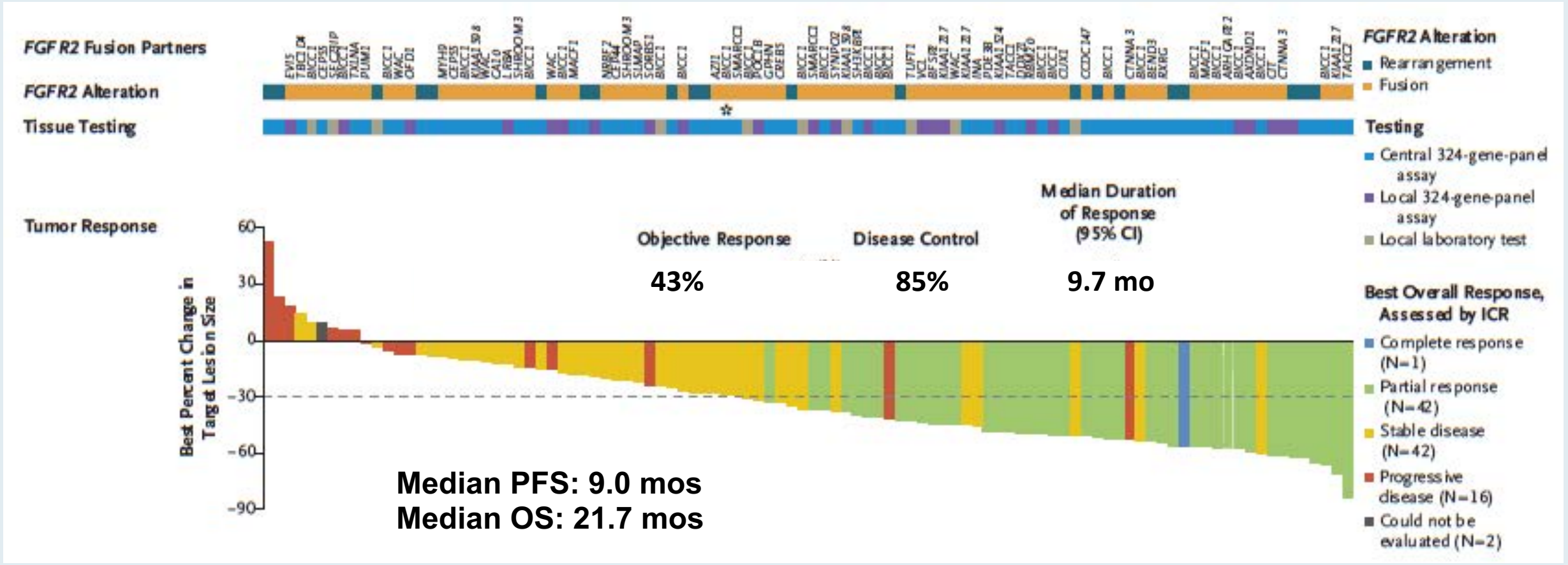
FOENIX-CCA2 (TAS-120-101): Phase II Study Design



- 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: A Phase II Study of Futibatinib for Intrahepatic Cholangiocarcinoma with FGFR2 Fusions or Rearrangements



Goyal L et al. *N Engl J Med* 2023;388;228-39.

FOENIX-CCA2: Select Treatment-Related Adverse Events with Futibatinib for Intrahepatic Cholangiocarcinoma

	All patients (N = 103)				
Event (%)	**Any grade**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Any adverse event	99	8	34	56	1
Hyperphosphatemia	85	10	46	30	0
Dry mouth	30	27	3	0	0
Palmar-plantar erythrodysesthesia syndrome	21	3	14	5	0
Increased aspartate aminotransferase level	18	11	1	7	0
Increased alanine aminotransferase level	15	5	5	4	1

Goyal L et al. *N Engl J Med* 2023;388;228-39.

FDA Approves Ivosidenib for Advanced or Metastatic Cholangiocarcinoma

Press Release – August 25, 2021

"The Food and Drug Administration approved ivosidenib for adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

Today, the FDA also approved the Oncomine Dx Target Test as a companion diagnostic device to aid in selecting patients with cholangiocarcinoma for treatment with ivosidenib.

Ivosidenib was investigated in a randomized (2:1), multicenter, double-blind, placebo-controlled clinical trial (Study AG120-C-005, NCT02989857) of 185 adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation. The patient's disease must have progressed following at least one, but not more than two prior regimens, including at least one gemcitabine- or 5-flurouracil-containing regimen. Patients were randomized to receive either ivosidenib 500 mg orally once daily or matched placebo until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ivosidenib-advanced-or-metastatic-cholangiocarcinoma

RTP RESEARCH TO PRACTICE

Research

JAMA Oncology | Original Investigation

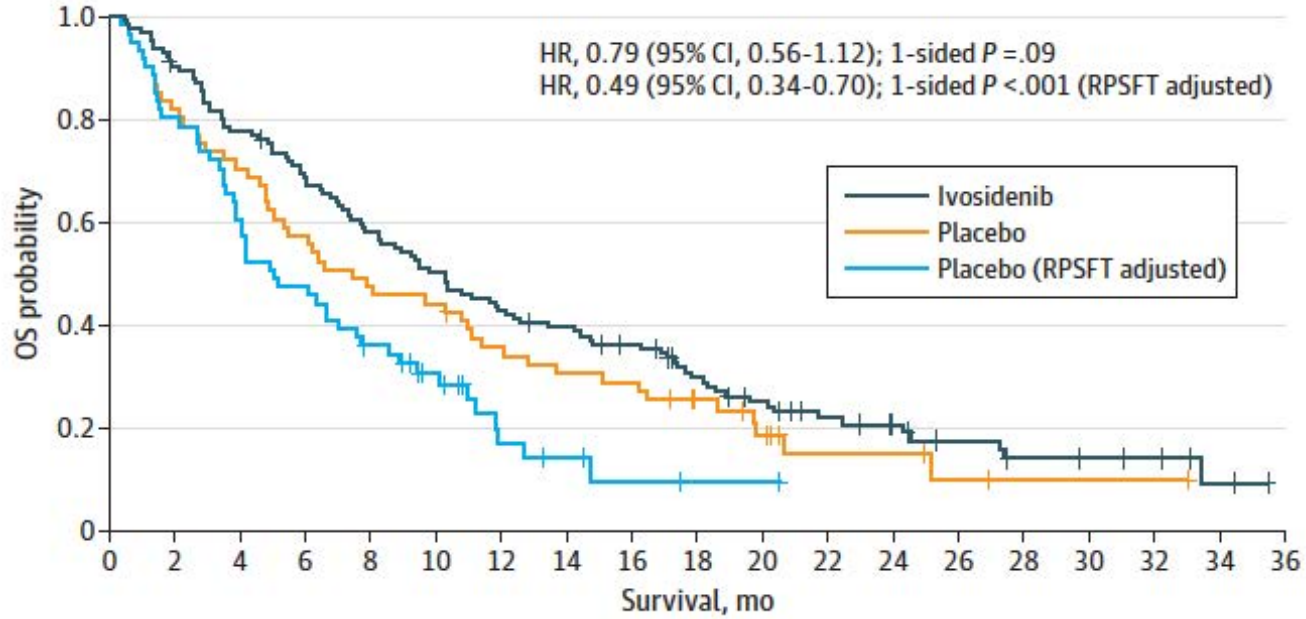
Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With *IDH1* Mutation

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

2021;7(11):1669-77

ClarIDHy: Final OS with Ivosidenib for Patients with Advanced Cholangiocarcinoma with IDH1 Mutations



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							

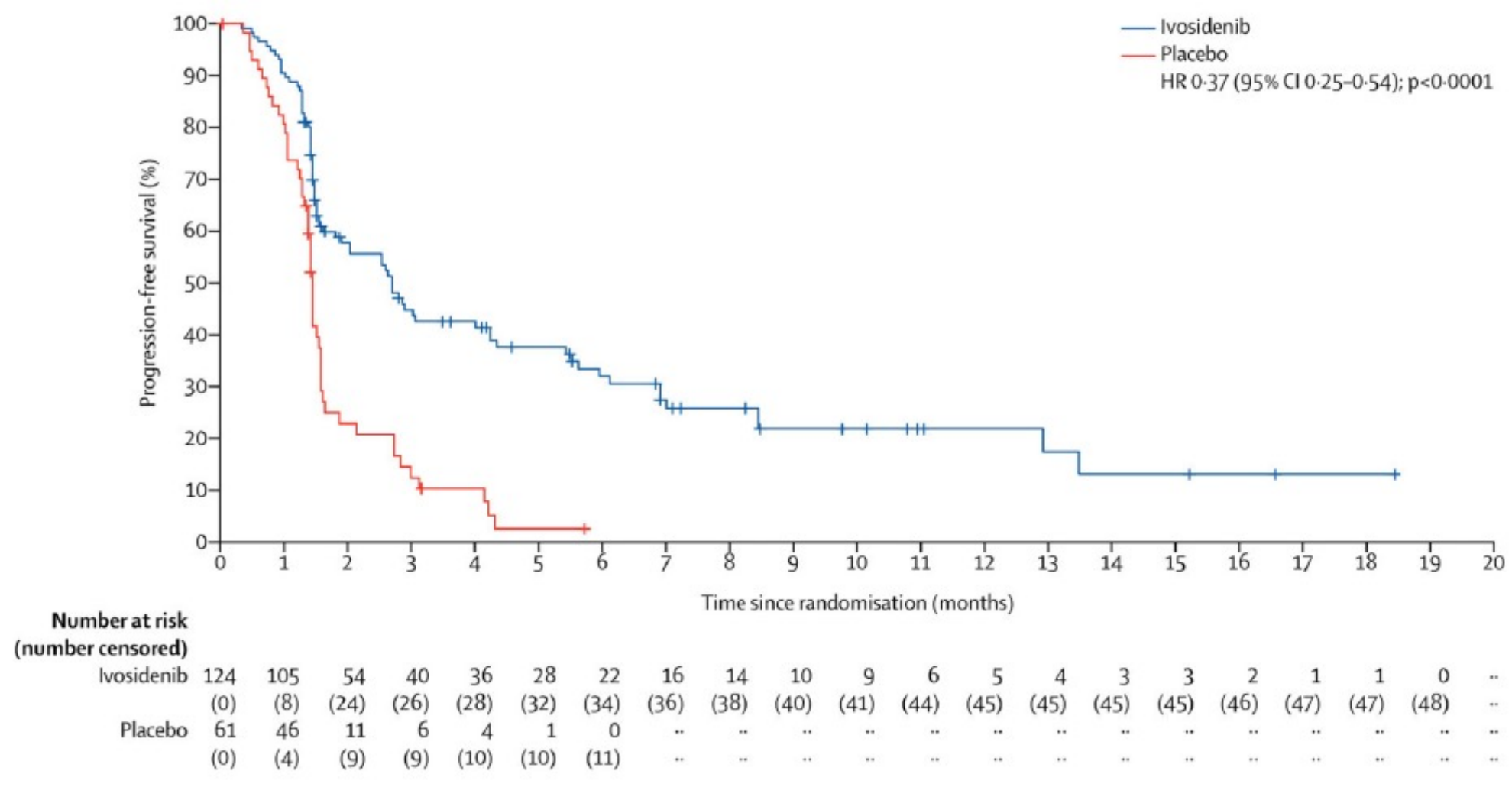
Treatment group	Events/patients, No.	OS, median (95% CI), mo
Ivosidenib	100/126	10.3 (7.8-12.4)
Placebo	50/61	7.5 (4.8-11.1)
Placebo adjusted by RPSFT	49/61	5.1 (3.8-7.6)

RPSFT = rank-preserving structural failure time

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

RTP RESEARCH TO PRACTICE

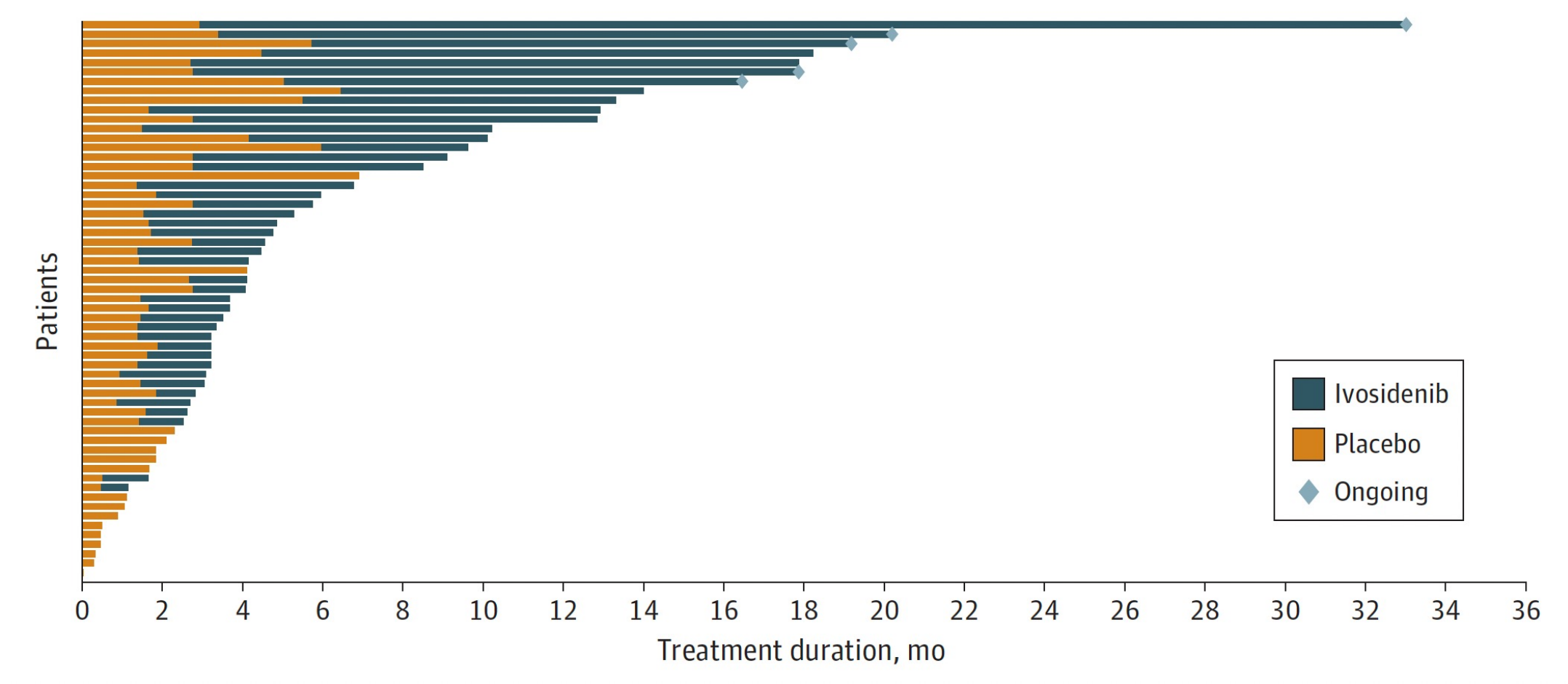
ClarIDHy: Progression-Free Survival with Ivosidenib for Advanced Cholangiocarcinoma with an IDH1 Mutation



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

RTP RESEARCH TO PRACTICE

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



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

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 prolongation	8%	1%	0	2%	0	0
ALT increase	7%	2%	0	2%	0	0
AST increase	6%	5%	0	3%	2%	0
Hyponatremia	5%	3%	2%	2%	8%	2%
Blood bilirubin increase	4%	6%	0	5%	2%	0

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

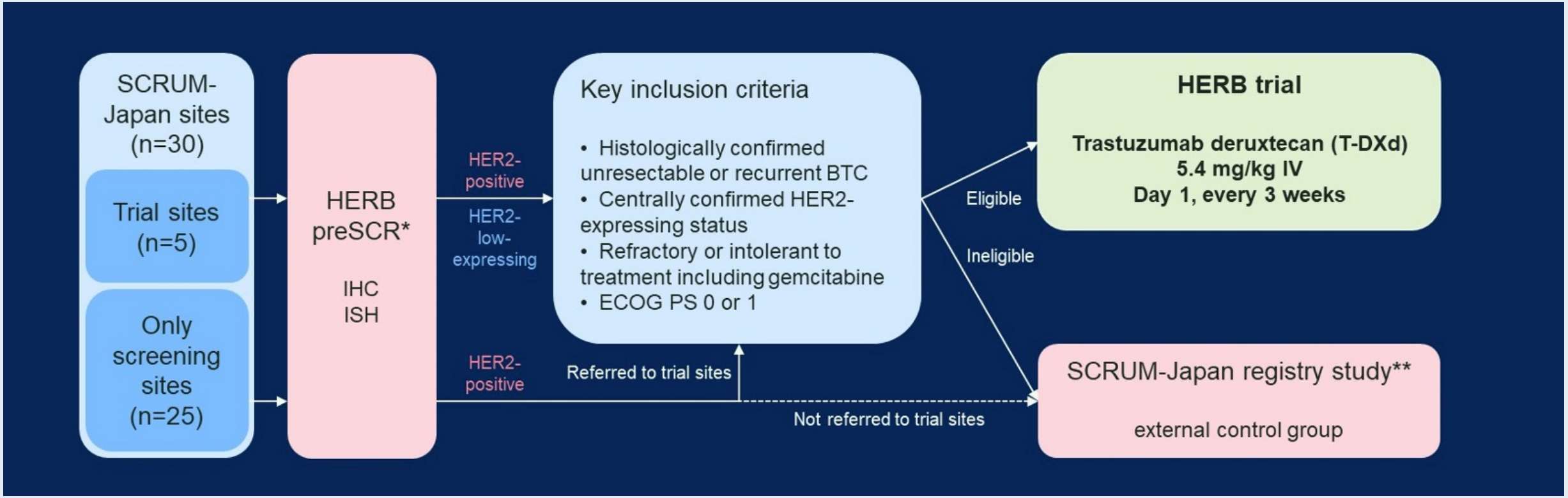
Summary of Efficacy Results from Immunotherapy Studies in Biliary Tract Cancer (BTC)

Study	Agent(s)	Line of therapy	Patients (n)	ORR	DCR	PFS	OS
KEYNOTE-158[1]	**Pembrolizumab**	**≥2L**	**104 (BTC cohort)**	**6%**	**22%**	**2.0 mo**	**9.1 mo**
Kim R et al[2]	Nivolumab	≥2L	54 (46 evaluable for response)	IR: 22% ICR: 11%	IR: 59% ICR: 50%	ITT: 3.7 mo	ITT: 14.2 mo
Kelley RK et al[3]	**Pembrolizumab + GM-CSF**	**≥2L**	**27**	**19%**	**33%**	**6-mo PFS: 35%**	**NR**
Klein O et al[4]	Nivolumab + ipilimumab	≥1L	39	23%	44%	2.9 mo	5.7 mo
Ueno M et al[5]	**Nivolumab**	**≥2L**	**30**	**3%**	**23%**	**1.4 mo**	**5.2 mo**
	Nivolumab + GemCis	**1L**	**30**	**37%**	**63%**	**4.2 mo**	**15.4 mo**
Ioka T et al[6]	Durvalumab	≥2L	42	5%	17%	1.5 mo	8.1 mo
	Tremelimumab + durvalumab		65	11%	32%	1.6 mo	10.1 mo

- 1. Ueno M et al. Presented at: ESMO Congress 2018; 19–23 October 2018; Munich, Germany. Abs 4525; 2. Kim R et al. *JAMA Oncol* 2020;6:888–894; 3. Kelley RK, et al. Presented at: ASCO Annual Meeting 2018; 1–5 June 2018; Chicago, IL. Abs 4087; 4. Klein O, et al. Poster presented at: ASCO Annual Meeting 2020; 29–31 May, 2020. Pos 196; 5. Ueno M, et al. *Lancet Gastroenterol Hepatol* 2019;4:611–621; 6. Ioka T, et al. Poster presented at: ASCO GI; 17–19 January 2019; San Francisco, CA. Poster 387 ICR, independent central review; IR, investigator review; ITT, intent-to-treat; NE, not estimable; NR, not reached

Courtesy of Tanios Bekaii-Saab, MD

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

- 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/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.

What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Hepatobiliary Cancers

Friday, April 28, 2023
6:00 AM – 7:30 AM

Faculty

Ahmed Omar Kaseb, MD, CMQ
Blanca Ledezma, MSN, NP, AOCNP
Daneng Li, MD
Amanda K Wagner, APRN-CNP, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Ovarian Cancer

Friday, April 28, 2023
12:15 PM – 1:45 PM

Faculty

Courtney Arn, CNP
David M O'Malley, MD
Richard T Penson, MD, MRCP
Jaclyn Shaver, MS, APRN, CNP, WHNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

In-person attendees can use the networked iPads® to claim NCPD credit or use the QR code as instructed in the program syllabus.

Virtual attendees: The NCPD credit link is posted in the chat room.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

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