What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Hepatobiliary Cancers

Thursday, April 28, 2022
8:20 PM – 9:20 PM PT

Faculty

Richard S Finn, MD
Amanda K Wagner, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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TO PRACTICE

Faculty

Richard S Finn, MD
Professor, Department of Medicine, Division of Hematology/Oncology
David Geffen School of Medicine at UCLA
Director, Signal Transduction and Therapeutics Program
Jonsson Comprehensive Cancer Center at UCLA
Los Angeles, 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 Finn — Disclosures

Advisory Committee	CStone Pharmaceuticals
Consulting Agreements	Adaptimmune, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, CStone Pharmaceuticals, Eisai Inc, Exelixis Inc, Genentech, a member of the Roche Group, Lilly, Merck, Pfizer Inc
Contracted Research (to UCLA)	Adaptimmune, Bayer HealthCare Pharmaceuticals, Eisai Inc, Genentech, a member of the Roche Group, Lilly, Merck, Pfizer Inc
Data and Safety Monitoring Board/Committee	AstraZeneca Pharmaceuticals LP, Hengrui Therapeutics Inc

Ms Wagner — Disclosures

No relevant conflicts of interest to disclose

Commercial Support

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

Research To Practice CME 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 premeeting survey before the meeting. Survey results will be presented and 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 CME 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 premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

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

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

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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"
14th Annual RTP-ONS NCPD Symposium Series
ONS Congress, Anaheim, California — April 27 - May 1, 2022

Thursday April 28	**Prostate Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Non–Small Cell Lung Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Hepatobiliary Cancers 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Friday April 29	**Small Cell Lung Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Acute Myeloid Leukemia and Myelodysplastic Syndromes 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Saturday April 30	**Cervical and Endometrial Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Bladder Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

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What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

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Prostate Cancer

Thursday, April 28, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Kathy D Burns, RN, MSN, AGACNP-BC, OCN
Robert Dreicer, MD, MS
Sandy Srinivas, MD
Ronald Stein, JD, MSN, NP-C, AOCNP

Non-Small Cell Lung Cancer

Thursday, April 28, 2022
6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty
Edward B Garon, MD, MS
Kelly EH Goodwin, MSN, RN, ANP-BC
Tara Plues, APRN, MSN
Anne S Tsao, MD, MBA

Ovarian Cancer

Thursday, April 28, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Jennifer Filipi, MSN, NP
Kathleen N Moore, MD, MS
Krishnansu S Tewari, MD
Deborah Wright, MSN, APRN, AGCNS-BC

Hepatobiliary Cancers

Thursday, April 28, 2022
8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty
Richard S Finn, MD
Amanda K Wagner, APRN-CNP, AOCNP

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

An NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Small Cell Lung Cancer

Friday, April 29, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Marianne J Davies, DNP, MSN, RN, APRN
Matthew Gubens, MD, MS
Lowell L Hart, MD
Chaely J Medley, MSN, AGNP

Breast Cancer

Friday, April 29, 2022
6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty
Jamie Carroll, APRN, MSN, CNP
Sara A Hurvitz, MD
Kelly Leonard, MSN, FNP-BC
Hope S Rugo, MD

Chronic Lymphocytic Leukemia

Friday, April 29, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Lesley Camille Ballance, MSN, FNP-BC
Amy Goodrich, CRNP
Anthony R Mato, MD, MSCE
Susan O'Brien, MD

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Friday, April 29, 2022
8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty
Ilene Galinsky, NP
Eunice S Wang, MD

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

An NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Cervical and Endometrial Cancer

Saturday, April 30, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Paula J Anastasia, MN, RN, AOCN
Robert L Coleman, MD
David M O'Malley, MD
Jaclyn Shaver, MS, APRN, CNP, WHNP

Bladder Cancer

Saturday, April 30, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Monica Averia, MSN, AOCNP, NP-C
Shilpa Gupta, MD
Brenda Martone, MSN, NP-BC, AOCNP
Sumanta Kumar Pal, MD

Join Us After ONS for Our Series Continuation

What I Tell My Patients —
A 2-Part NCPD Webinar Series

Hodgkin and Non-Hodgkin Lymphomas

Date and time to be announced

Gastroesophageal Cancers

Wednesday, May 18, 2022

5:00 PM – 6:00 PM ET

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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?

How often do you feel frustrated by your work?

1. Never
2. A few times per year
3. Once a month
4. A few times per month
5. Once a week
6. A few times per week
7. Every day

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Faculty

Richard S Finn, MD
Professor, Department of Medicine, Division of Hematology/Oncology
David Geffen School of Medicine at UCLA
Director, Signal Transduction and Therapeutics Program
Jonsson Comprehensive Cancer Center at UCLA
Los Angeles, California

Amanda K Wagner, APRN-CNP, AOCNP
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The James Cancer Hospital
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Agenda

Module 1 – First-line Treatment of Hepatocellular Cancer (HCC)

Module 2 – Management of Recurrent HCC

Module 3 – Biliary Tract Cancers

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Agenda

Module 1 – First-line Treatment of Hepatocellular Cancer (HCC)

Module 2 – Management of Recurrent HCC

Module 3 – Biliary Tract Cancers

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SELF-ASSESSMENT QUIZ

Currently, what is the most commonly used first-line treatment for patients with HCC?

1. Sorafenib
2. Lenvatinib
3. Atezolizumab/bevacizumab
4. I don’t know

SELF-ASSESSMENT QUIZ

Which of the following is considered a contraindication to atezolizumab/bevacizumab treatment?

1. Esophageal varices
2. Multiple sclerosis
3. Both 1 and 2
4. Neither 1 nor 2
5. I don’t know

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SELF-ASSESSMENT QUIZ

Patients with HCC caused by hepatitis B or hepatitis C respond as well to treatment as those whose disease was not caused by the virus.

1. Agree
2. Disagree
3. I don’t know

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SELF-ASSESSMENT QUIZ

Which of the following is a common side effect of lenvatinib?

1. Hypertension
2. Peripheral neuropathy
3. Cardiac failure
4. I don’t know

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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*

*Accelerated approval

*#Accelerated approval withdrawn

^^ positive phase 3 trial

RTP RESEARCH TO PRACTICE

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

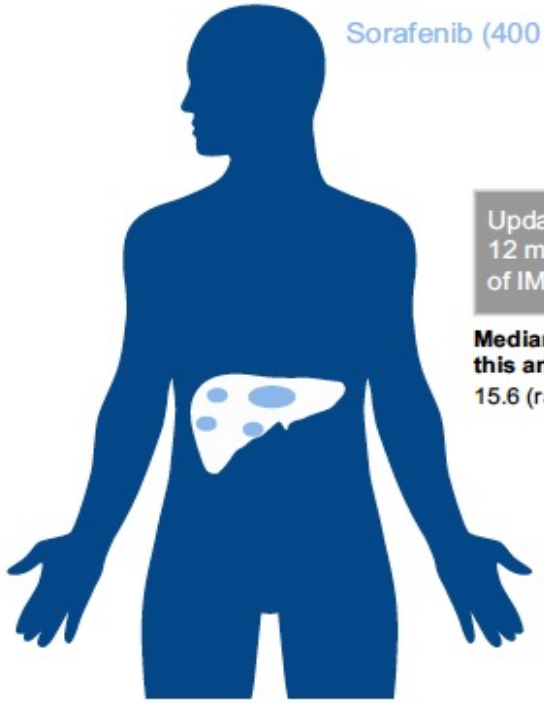
Research Article
Hepatic and Biliary Cancer

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,*]

IMbrave150: Updated Survival Outcomes with Atezolizumab and Bevacizumab as First-Line Treatment for Unresectable Metastatic HCC



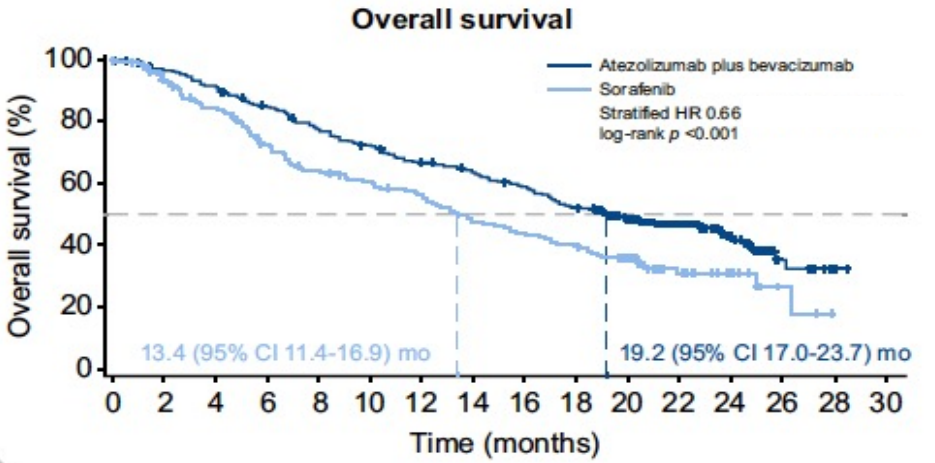
Atezolizumab (1,200 mg) plus bevacizumab (15 mg/kg) every 3 weeks

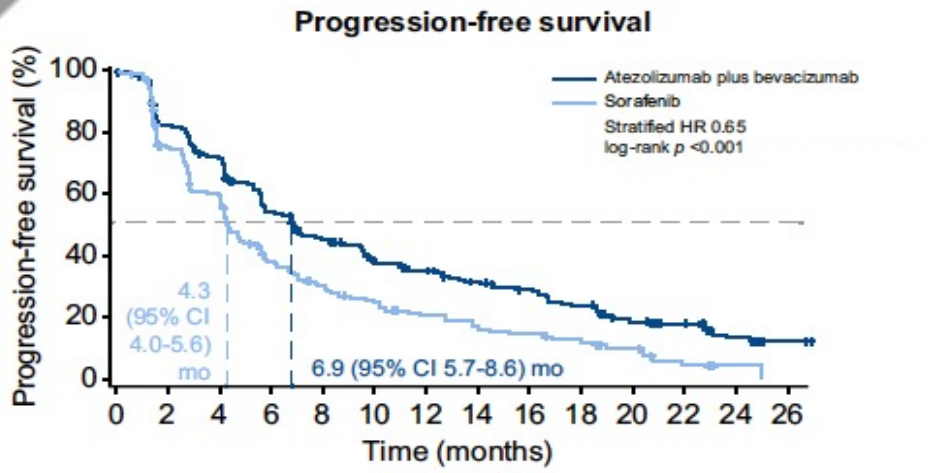
OR

Sorafenib (400 mg twice daily)

Updated analysis
12 months after primary analysis of IMbrave150 study

Median follow-up for this analysis:
15.6 (range, 0-28.6) mo





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

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

SELF-ASSESSMENT QUIZ

Which of the following was demonstrated in a clinical trial to be more efficacious than sorafenib as first-line therapy for patients with advanced HCC?

1. Durvalumab/tremelimumab
2. Ipilimumab/nivolumab
3. Pembrolizumab
4. Dostarlimab
5. I don’t know

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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

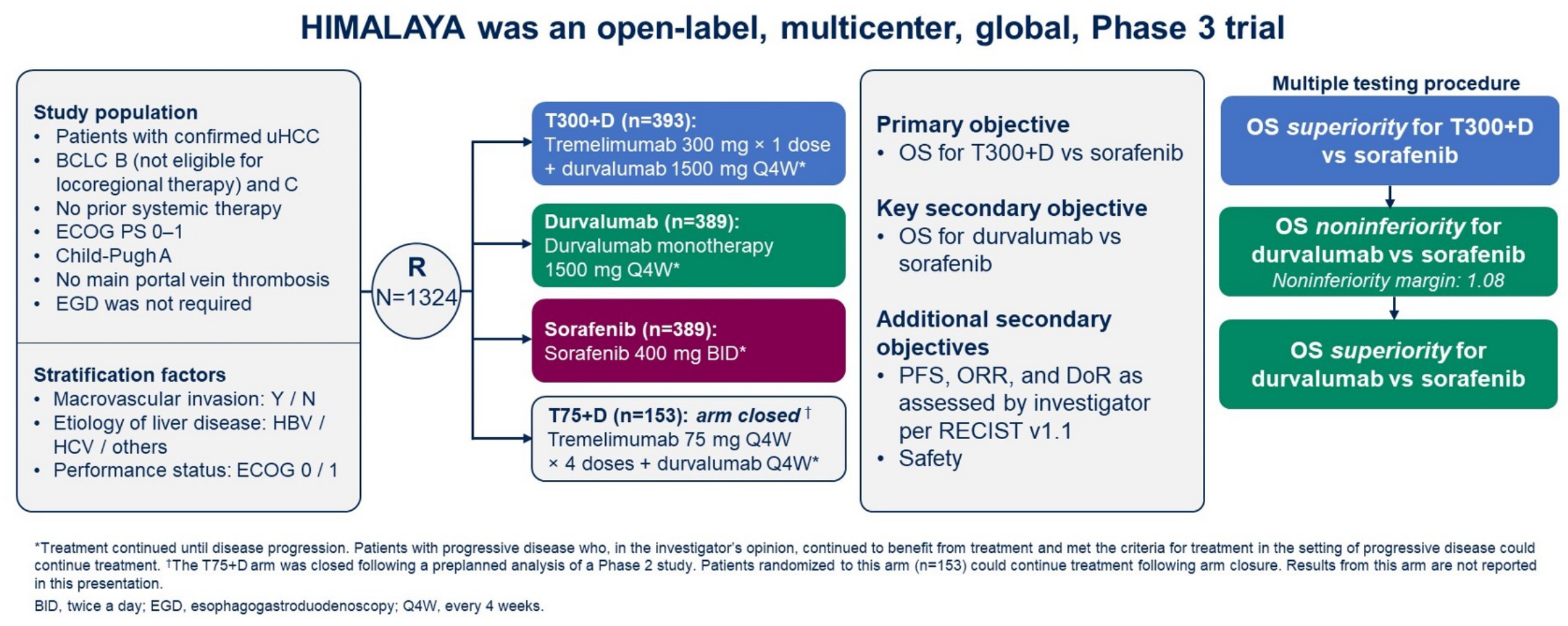
Ghassan K Abou-Alfa,[1,2*] Stephen L Chan,[3*] Masatoshi Kudo,[4*] George Lau,[5*] Robin Kate Kelley,[6] Junji Furuse,[7] Wattana Sukeepaisarnjaroen,[8] Yoon-Koo Kang,[9] Tu V Dao,[10] Enrico N De Toni,[11] Lorenza Rimassa,[12,13] Valery Breder,[14] Alexander Vasilyev,[15] Alexandra Heurgué,[16] Vincent 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

HIMALAYA: Phase III Trial of Durvalumab and Tremelimumab as First-Line Therapy for Advanced HCC



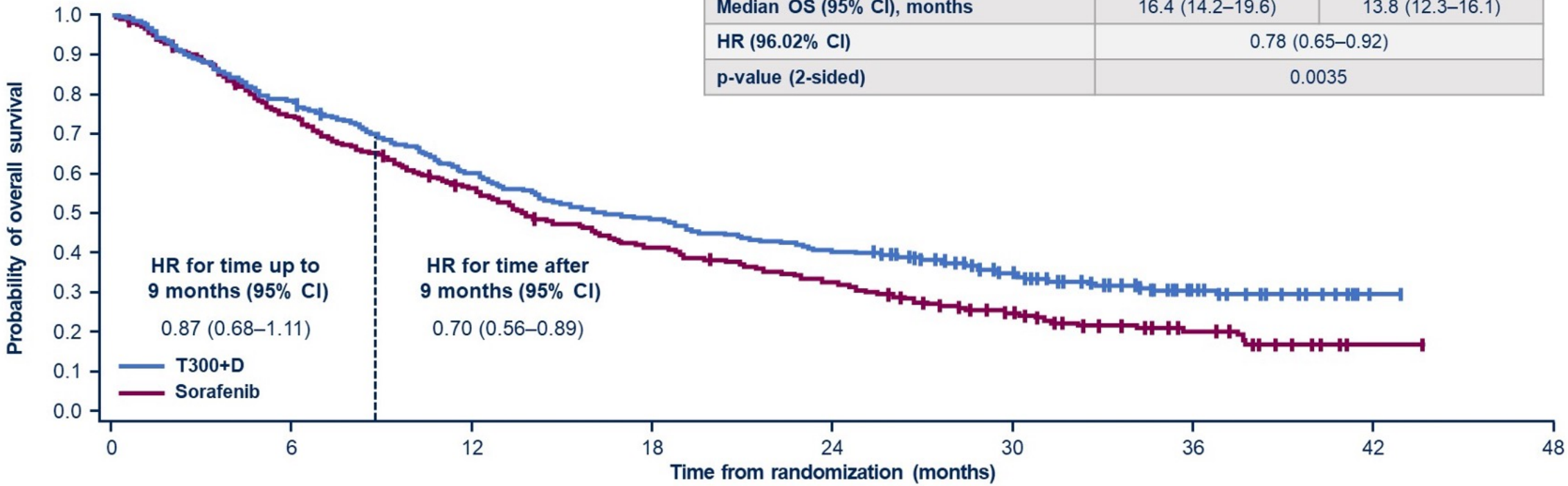
*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned 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 Primary Endpoint: OS for Tremelimumab 300 and Durvalumab as First-Line Therapy for Unresectable HCC

	T300+D (n=393)	Sorafenib (n=389)
OS events, n (%)	262 (66.7)	293 (75.3)
Median OS (95% CI), months	16.4 (14.2–19.6)	13.8 (12.3–16.1)
HR (96.02% CI)	0.78 (0.65–0.92)	
p-value (2-sided)	0.0035	



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

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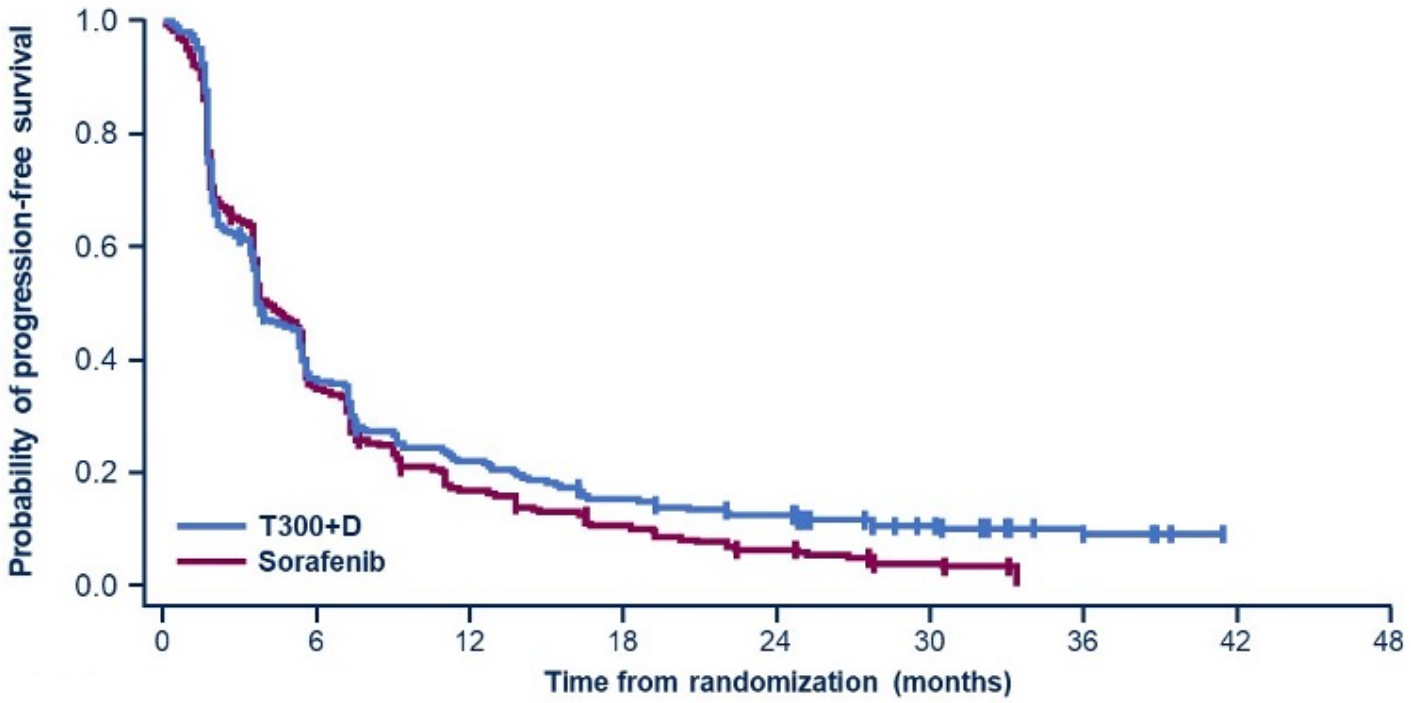
HIMALAYA: Progression-Free Survival



	T300+D (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
PFS events, n (%)	335 (85.2)	345 (88.7)	327 (84.1)
Median PFS (95% CI), months	3.78 (3.68–5.32)	3.65 (3.19–3.75)	4.07 (3.75–5.49)
PFS HR* (95% CI)	0.90 (0.77–1.05)	1.02 (0.88–1.19)	–
Progression-free at DCO, n (%)	49 (12.5)	32 (8.2)	19 (4.9)
Median TTP (95% CI), months	5.42 (3.81–5.62)	3.75 (3.68–5.42)	5.55 (5.13–5.75)
Treated ≥1 cycle beyond progression, n (%)†	182 (46.9)	188 (48.5)	134 (34.4)

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

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HIMALAYA: Safety and Tolerability

Event, n (%)	T300+D (n=388)	Durvalumab (n=388)	Sorafenib (n=374)
Any AE	378 (97.4)	345 (88.9)	357 (95.5)
Any TRAE*	294 (75.8)	202 (52.1)	317 (84.8)
Any grade 3/4 AE	196 (50.5)	144 (37.1)	196 (52.4)
Any grade 3/4 TRAE	100 (25.8)	50 (12.9)	138 (36.9)
Any serious TRAE	68 (17.5)	32 (8.2)	35 (9.4)
Any TRAE leading to death	9 (2.3)†	0	3 (0.8)‡
Any TRAE leading to discontinuation	32 (8.2)	16 (4.1)	41 (11.0)

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

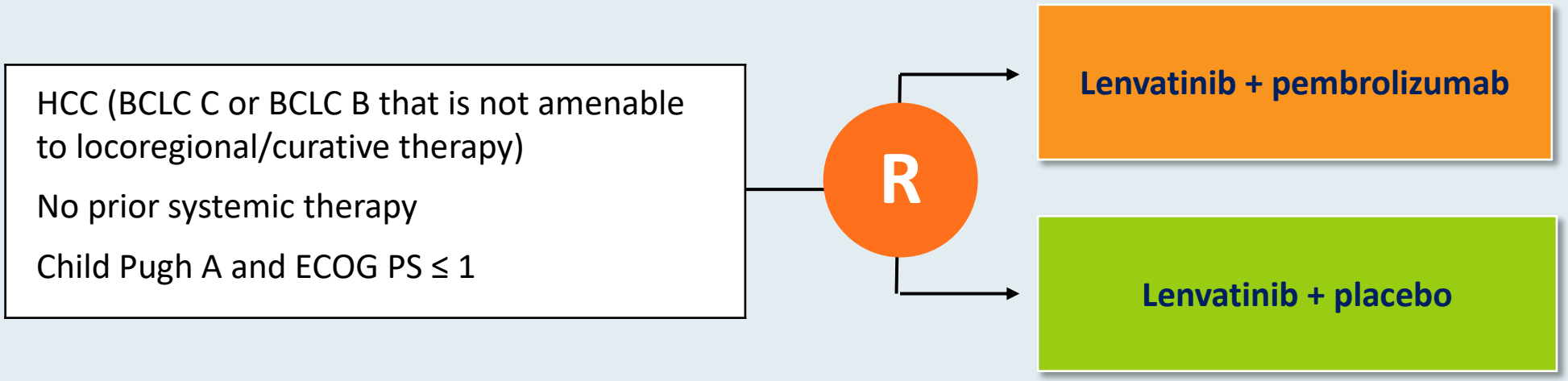
*Treatment-related was as assessed by investigator. †Nervous system disorder (n=1), acute respiratory distress syndrome (n=1), hepatitis (n=1), myocarditis (n=1), immune-mediated hepatitis (n=2), pneumonitis (n=1), hepatic failure (n=1), myasthenia gravis (n=1). ‡Hematuria (n=1), cerebral hematoma (n=1),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

AE, adverse event; SMQ, Standardized MedDRA Query; T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W; TRAE, treatment-related adverse event.

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

LEAP-002: A Phase III Trial of Pembrolizumab/Lenvatinib as First-Line Therapy for Advanced HCC

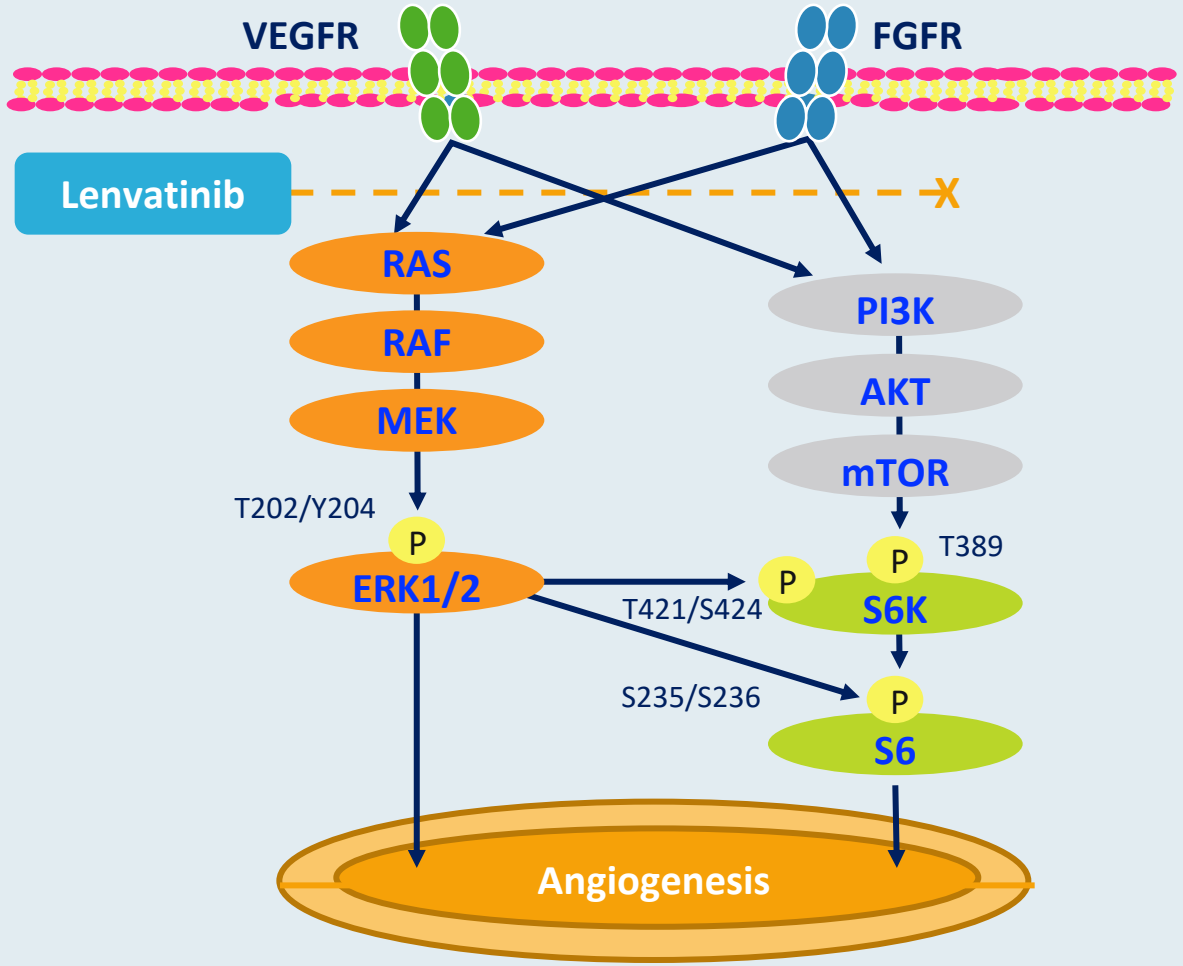
Trial Identifier: NCT03713593 (Closed)



Primary Endpoints: Progression-free survival, overall survival
Secondary Endpoints: Objective response rate, duration of response, disease control rate, time-to-progression, safety

Llovet JM et al. ASCO 2019;Abst TPS4152; www.clinicaltrials.gov, Accessed April 2022.

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

Lenvatinib

Mechanism of action

- Oral multikinase inhibitor

Indication

- For patients with unresectable hepatocellular carcinoma as first-line therapy

Recommended dose

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

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

Questions — Richard S Finn, MD

Patients with newly diagnosed metastatic HCC

- **What therapies are used in this setting, and how is treatment selected?**

Commentary — Richard S Finn, MD

Patients with newly diagnosed metastatic HCC

- **Who is appropriate for systemic therapy?**
  - **Tumor factors**
  - **Physiology factors**
- **Choice of therapy**
  - **Side effects vs Efficacy**
  - **Most active: atezolizumab and bevacizumab**
    - **Contraindications:**
      - **Bevacizumab: high risk bleeding (need EGD), significant ischemia**
      - **Atezolizumab (IO): significant autoimmune disease, chronic steroid use**
  - **Alternatives to atezo-bev**
    - **Lenvatinib or sorafenib (TKIs)**
    - **If no contraindication to IO**
      - **when approved: durvalumab-tremelimumab or single-agent durvalumab**

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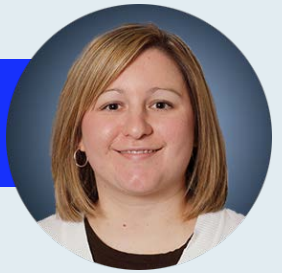
Questions — Amanda K Wagner, APRN-CNP, AOCNP



Patients with newly diagnosed metastatic HCC

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are the key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities?**
- **What are some of the psychosocial issues that arise in this situation?**

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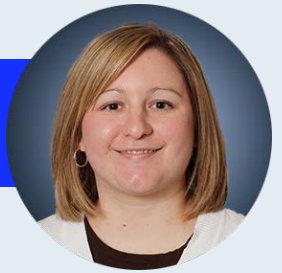
Commentary — Amanda K Wagner, APRN-CNP, AOCNP



Patients with newly diagnosed metastatic HCC

- **CANCER RELATED SYMPTOMS**
  - **Pain, anorexia, weight loss, fatigue, jaundice, nausea/vomiting, change in bowel habits**
  - **What is their performance status?**
- **CIRRHOSIS RELATED SYMPTOMS**
  - **Ascites, edema, hepatic encephalopathy, esophageal varices, hx of GI bleed**
  - **Child-Pugh score (total bilirubin, albumin, PT/INR, ascites, encephalopathy)**
- **What else is pertinent in the patient's past medical history?**
  - **Any prior history of uncontrolled HTN, recent CVA/MI?**
  - **History of transplant, autoimmune problems**
  - **Unhealed wounds**

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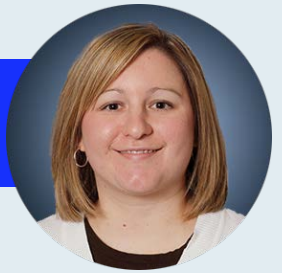
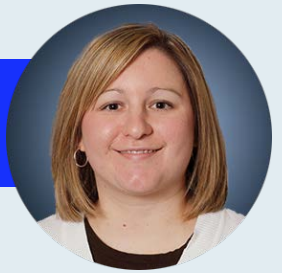
Commentary — Amanda K Wagner, APRN-CNP, AOCNP



- Atezolizumab is an antibody used to block PD-L1
- PD-L1 shuts down the immune response to infection or cancer
- An antibody to PD-L1 can stop it from turning off the immune system's response and may boost it to fight the cancer
- Since we are boosting the immune system, we may boost its ability to attack normal, healthy organs and tissue
- Bevacizumab is a monoclonal antibody used to interfere with the process of angiogenesis by targeting VEGF
- Goal of cancer therapy is to slow cancer growth to improve quality of life and lengthen life
- IV infusion q3 weeks
- Common Side Effects
  - Fatigue
  - Decreased appetite
  - Headache
  - Nausea/vomiting
  - Joint aches/pains
  - Rash
  - Hypertension
  - Proteinuria
- More Serious Complications
  - Immune mediated side effects
  - Hypertensive crisis
  - Bowel perforation
  - Poor wound healing

RTP RESEARCH TO PRACTICE

Commentary — Amanda K Wagner, APRN-CNP, AOCNP



Patient Case #1

- **77 yo male with history of HTN, no known history of cirrhosis**
- **Presented with a cough, incidentally found to have a large right liver mass, biopsy + HCC. No evidence of metastatic disease. Underwent right hepatectomy**
- **Developed progression in the liver, underwent y90**
- **After six months, had rising AFP, imaging revealed new adrenal metastases and progression in the liver, adrenal biopsy +HCC**
- **Child-Pugh A. PS 0, still working full time as a pastor. EGD completed, small EV treated**
- **Started on treatment with Atezo/Bev**
- **Tolerated treatment well, noted mild arthralgias after treatment, relieved with OTC analgesics. Hypertension well controlled on losartan**
- **Developed progression of disease with new bone mets after 9 months of therapy**

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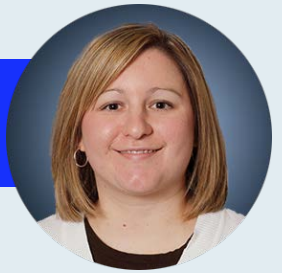
Commentary — Amanda K Wagner, APRN-CNP, AOCNP

Patient Case #2

71 yo male with hx of cirrhosis secondary to NASH, Child-Pugh A

- **Presented with epigastric pain, found to have right liver mass with extension into the portal vein, underwent biopsy, pathology consistent with HCC**
- **Initially treated with y90 for local control**
- **After 1 year, developed progression of disease within the liver as well as new lung metastases**
- **Discussed treatment with Atezo/Bev. EGD prior to starting negative**
- **Has received 8 cycles of therapy with partial response noted on imaging, decrease in AFP. Abdominal pain resolved**
- **Recently developed sudden onset diabetes, felt to likely be secondary to immunotherapy. Very rapid onset. Insulin dependent, hasn't responded well to oral agents.**

Commentary — Amanda K Wagner, APRN-CNP, AOCNP



- **Psychosocial concerns**
- **PRIOR or CURRENT ALCOHOL/DRUG USE**
  - **Lack of social support**
  - **Socioeconomic concerns — lack of resources, transportation**
  - **Issues with compliance with treatment, including adherence to oral medications**
- **MENTAL HEALTH PROBLEMS**
  - **Anxiety, Depression**

Agenda

Module 1 – First-line Treatment of Hepatocellular Cancer (HCC)

Module 2 – Management of Recurrent HCC

Module 3 – Biliary Tract Cancers

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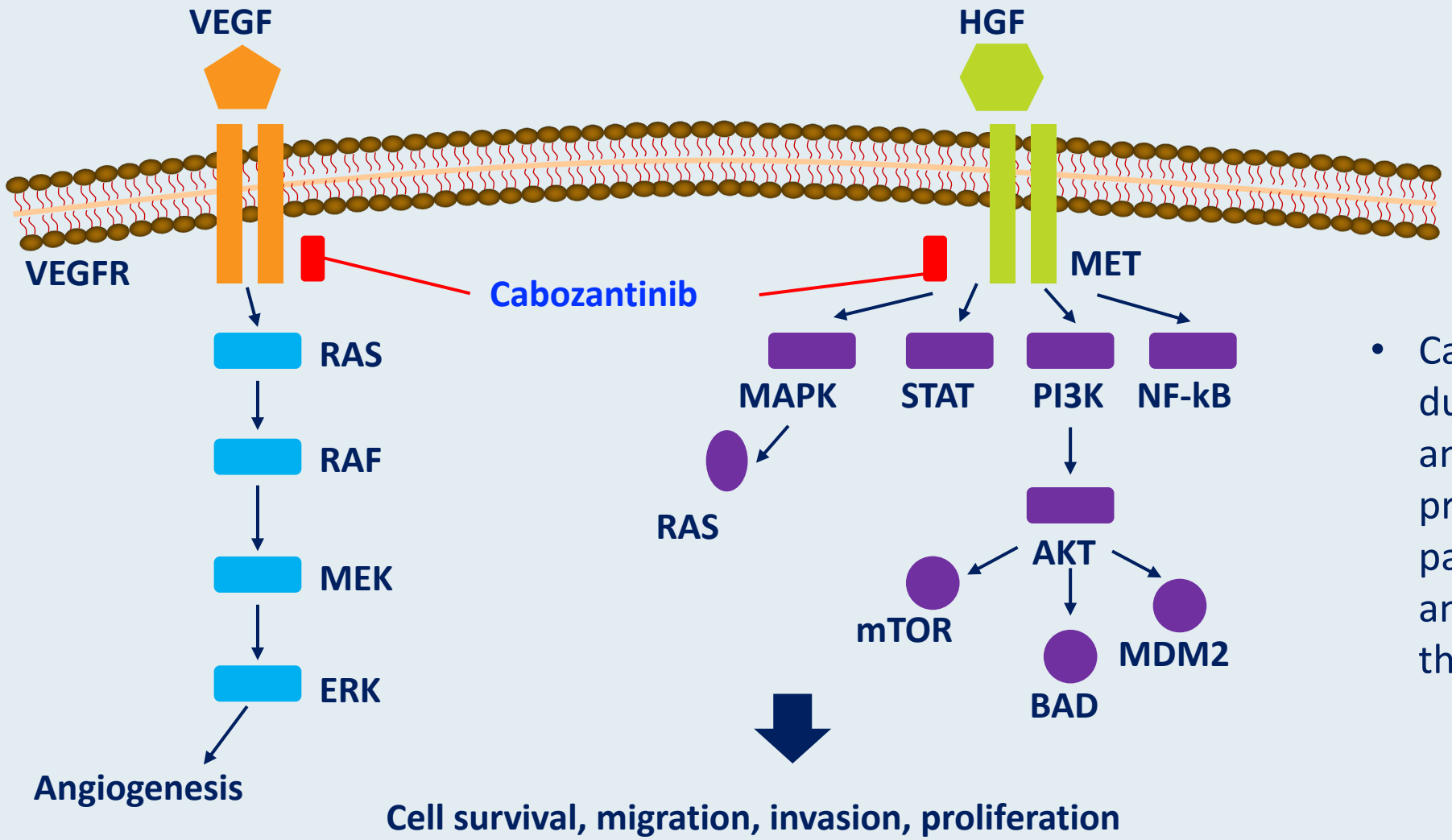
NCCN Category 1 Treatment Options for Metastatic HCC After Progression on First-Line Therapy

NCCN Category 1 option	Clinical trial	Setting	Median overall survival
Regorafenib	RESORCE *(Bruix J et al. Lancet Oncol 2017)*	Postsorafenib Child-Pugh A	10.6 mo vs 7.8 mo (placebo)
Cabozantinib	CELESTIAL *(Abou-Alfa GK et al. N Engl J Med 2018)*	Postsorafenib Child-Pugh A	10.2 mo vs 8.0 mo (placebo)
Ramucirumab	REACH, REACH-2 *(Zhu AX et al. Lancet Oncol 2019)*	Postsorafenib Child-Pugh A AFP ≥ 400 ng/mL	Pooled analysis: 8.1 mo vs 5.0 mo (placebo)

NCCN Guidelines in Oncology – Hepatobiliary Cancers. Version 1.2022

Mechanism of Action of Cabozantinib



- Cabozantinib provides dual inhibition of MET and VEFGR2, thereby preventing the MET pathway from acting as an alternative pathway in the development of VEGF

Cabozantinib

Mechanism of action

- **Oral multikinase inhibitor**

Indication

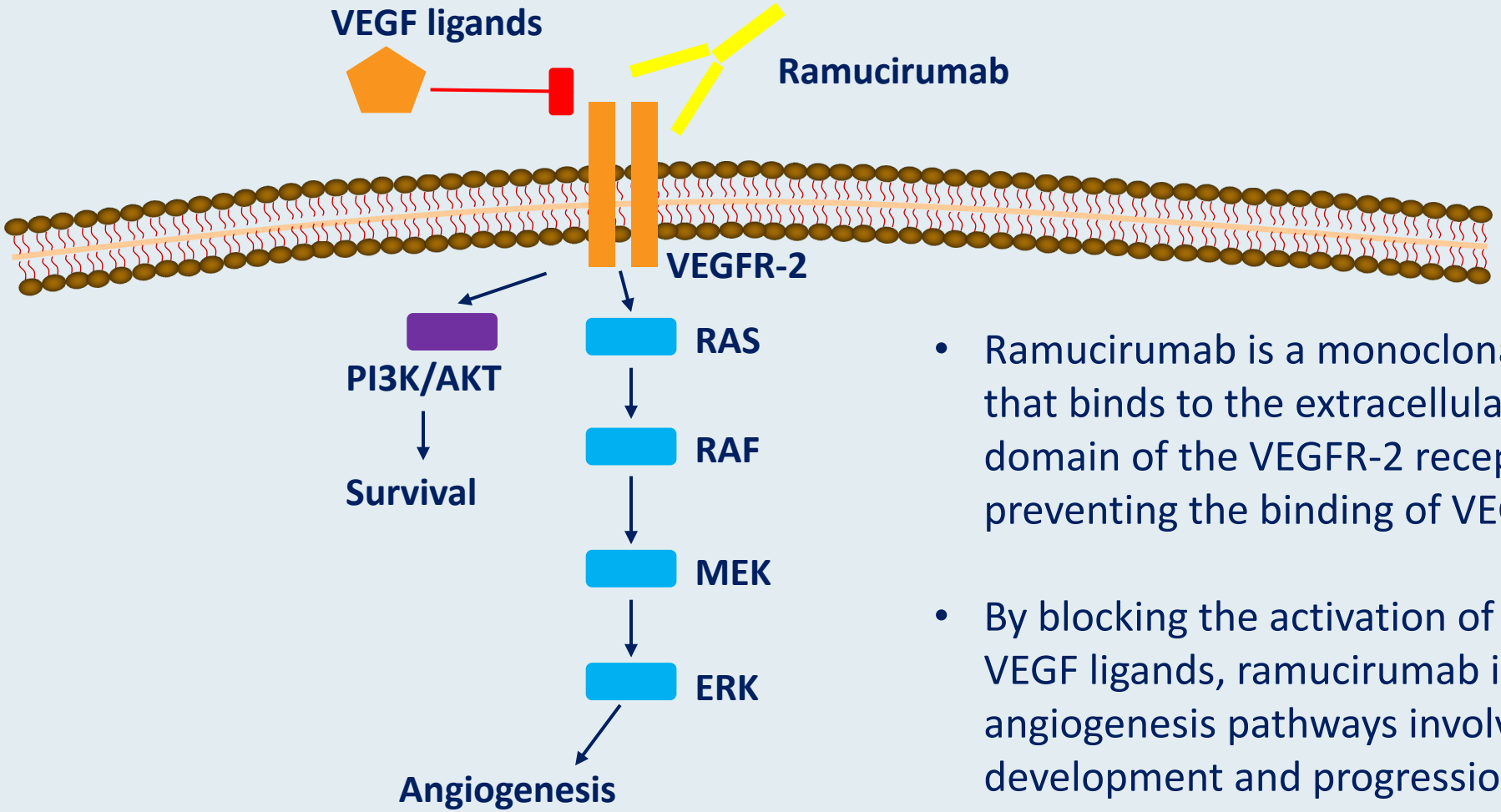
- **For patients with hepatocellular carcinoma who have previously been treated with sorafenib**

Recommended dose

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

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

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-VEGFR2 monoclonal antibody**

Indication

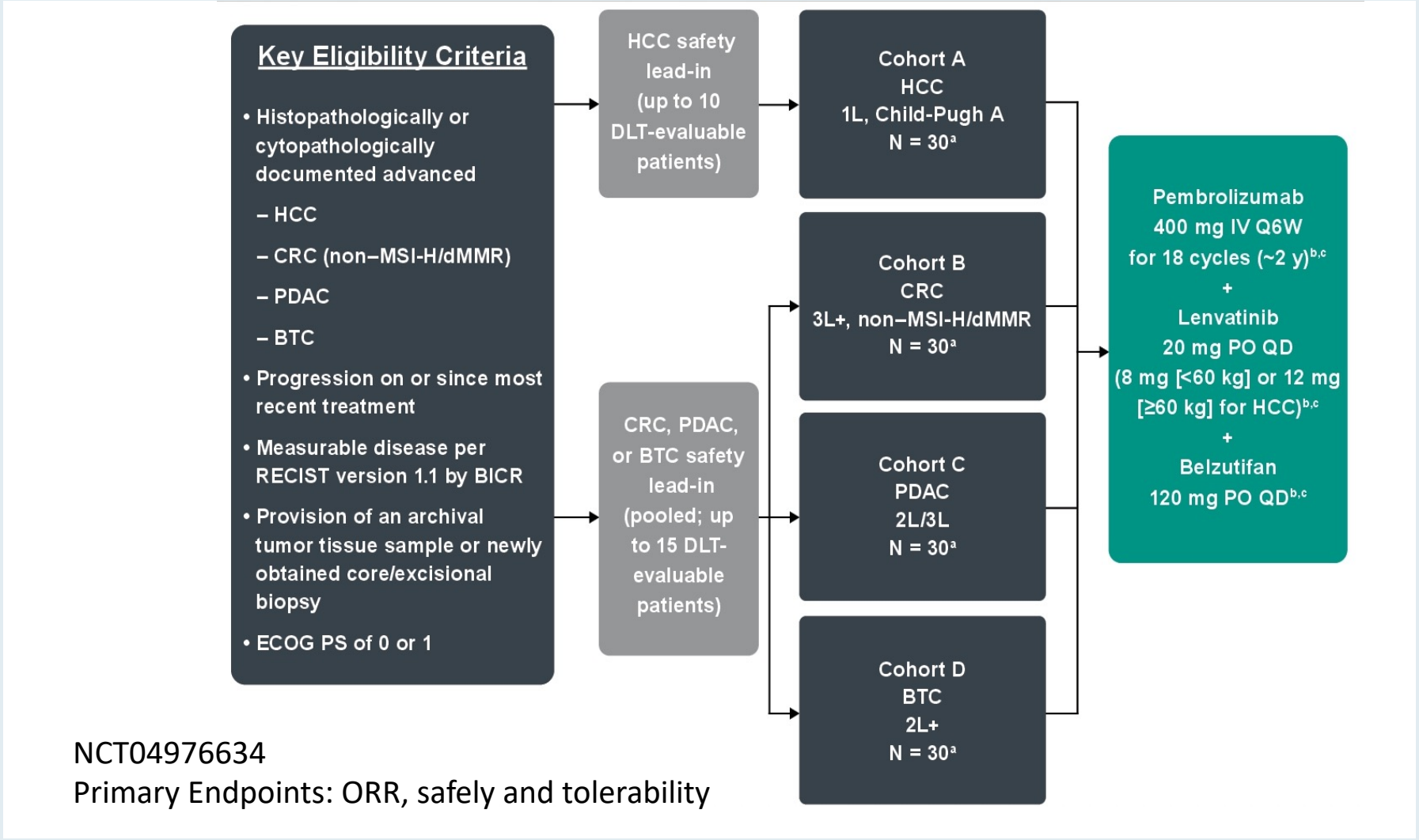
- **For patients with hepatocellular carcinoma who have an alpha fetoprotein of ≥400 ng/mL and have previously been treated with sorafenib**

Dose/schedule

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

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125477s029lbl.pdf; Ramucirumab package insert.

Ongoing Phase II Study of Pembrolizumab with Lenvatinib and Belzutifan for Advanced Solid Tumors



NCT04976634
Primary Endpoints: ORR, safely and tolerability

Kelley RK et al. Gastrointestinal Cancers Symposium 2022;Abstract TPS669.

Questions — Richard S Finn, MD

Patients with metastatic HCC who have experienced disease progression on atezolizumab/bevacizumab

- **What therapies are used in this setting, and how is treatment selected?**

Commentary — Richard S Finn, MD

Patients with metastatic HCC who have experienced disease progression on atezolizumab/bevacizumab

- **Considerations after progression on atezolizumab and bevacizumab**
  - **Best response (PR, SD, PD)**
  - **Duration of response**
  - **Toxicity**
- **Sequence existing drugs**
  - **1st line TKIs: lenvatinib, sorafenib**
  - **2nd line and beyond: regorafenib, cabozantinib, ramucirumab**
- **Role of IO post IO?**
  - **lenvatinib (+ pembrolizumab)**
  - **ipilimumab + nivolumab**
- **If never had IO in front line**
  - **single agent pembrolizumab**

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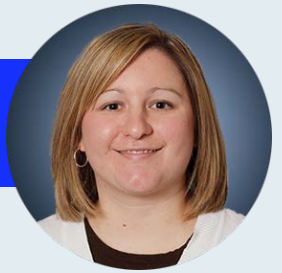
Questions — Amanda K Wagner, APRN-CNP, AOCNP



Patients with metastatic HCC who have experienced disease progression on atezolizumab/bevacizumab

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are the key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities?**
- **What are some of the psychosocial issues that arise in this situation?**

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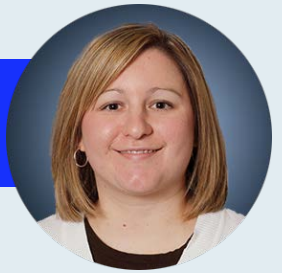
Commentary — Amanda K Wagner, APRN-CNP, AOCNP



Patients with metastatic HCC who have experienced disease progression on atezolizumab/bevacizumab

- **CANCER RELATED SYMPTOMS**
  - **Are symptoms related to cancer worsening?**
    - **How is their performance status?**
    - **Cancer related pain**
    - **Anorexia/weight loss**
    - **Nausea/vomiting**
    - **Worsening ascites**
  - **How is their liver function? Has Child-Pugh score changed?**
  - **CBC (thrombocytopenia?)**
  - **Do they have any residual side effects from first line treatment?**
- **PSYCHOSOCIAL CONCERNS**
  - **Anxiety, depression. Lack of support, End of life discussions**

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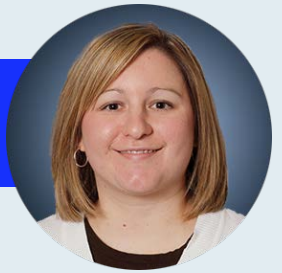
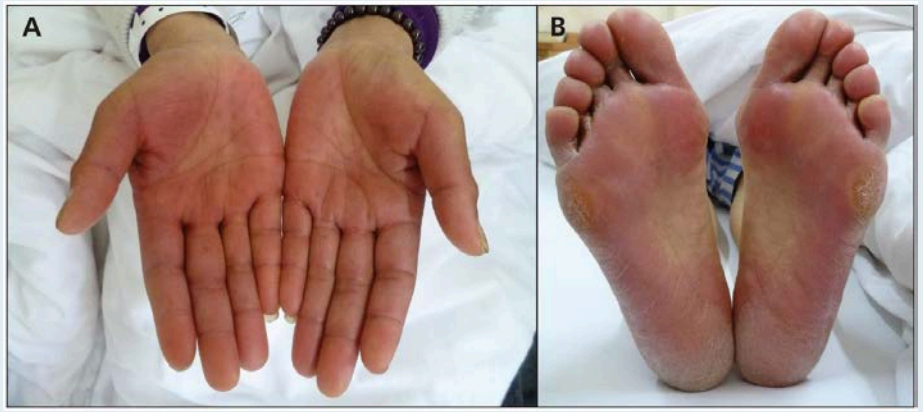
Commentary — Amanda K Wagner, APRN-CNP, AOCNP



- **Lenvatinib (CP A only)**
  - **Hypertension, diarrhea, anorexia, weight loss, fatigue**
- **Sorafenib (CP A or B7)**
  - **Diarrhea, hand foot syndrome, hypertension, fatigue**
- **Regorafenib (CP A only)**
  - **Hypertension, anorexia, hepatotoxicity, hand foot syndrome, fatigue and diarrhea**
- **Cabozantinib (CP A only)**
  - **Hand foot skin reaction, hypertension, elevated AST, fatigue, and diarrhea**
- **Ramucirumab (CP A only, AFP >400)**
  - **Hypertension, diarrhea, headache, bleeding**



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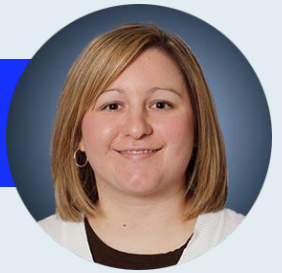
Commentary — Amanda K Wagner, APRN-CNP, AOCNP

Back to patient case #1

- **Patient had progression of disease on Atezo/Bev with new spinal mets, increase in size of liver lesions and adrenal mets**
- **Labs: wbc 4.5, hgb 14, plts 104K, total bili 1.4, albumin 3.7, other LFTs within normal limits**
- **No ascites, encephalopathy. CP score remains 5 A**
- **BP 130s/70s at home on Losartan 100 mg**
- **More fatigued, but still working. PS=1**
- **Denies pain, n/v**
- **Discussed treatment with Lenvatinib, plan to start at 8 mg daily, escalate as tolerated to 12 mg dose**
- **Start bisphosphonate for bone metastases**

Commentary — Amanda K Wagner, APRN-CNP, AOCNP



Case #3

- 69 yo male with history of Hep C cirrhosis and metastatic HCC
  - Child-Pugh A, PS=0. Received front line therapy with Atezo/Bev
  - Received ~11 months of therapy before he had progression of disease
  - Imaging with progression in the liver, new lung metastases
  - Patient was hospitalized with infection, treated with antibiotics
  - After discharge, was seen in the clinic. PS=3, new anorexia/weight loss, abdominal pain, nausea/vomiting
  - Labs significant for new hyperbilirubinemia, t. bili=3.7
  - Discussed 2nd line therapy with Lenvatinib, however, wanted patient's PS/LFTs to improve
  - Unfortunately, liver function continued to decline despite PTC drain. Clinically declined as well, best supportive care recommended

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Agenda

Module 1 – First-line Treatment of Hepatocellular Cancer (HCC)

Module 2 – Management of Recurrent HCC

Module 3 – Biliary Tract Cancers

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SELF-ASSESSMENT QUIZ

First-line systemic treatment of metastatic biliary tract cancers in the next year is likely to be…

1. Chemotherapy
2. Chemotherapy with bevacizumab
3. Chemotherapy with immunotherapy
4. Chemotherapy followed by PARP inhibitor maintenance
5. None of the above
6. I don’t know

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SELF-ASSESSMENT QUIZ

Which of the following is a targetable mutation observed in biliary cancer?

1. IDH
2. FGFR
3. Both 1 and 2
4. Neither 1 nor 2
5. I don’t know

RTP RESEARCH TO PRACTICE

ASCO Gastrointestinal Cancers Symposium 2022;Abstract 378.

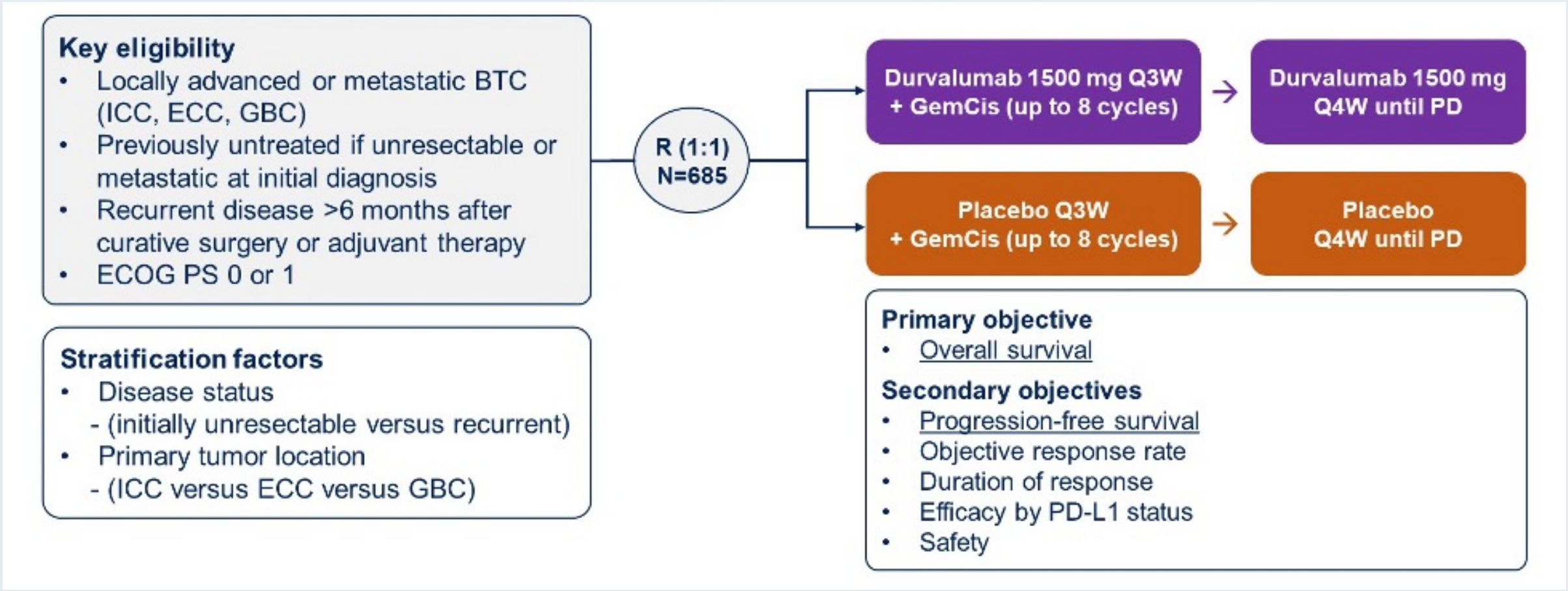
A Phase 3 randomized, double-blind, placebo-controlled study of durvalumab in combination with gemcitabine plus cisplatin in patients with advanced biliary tract cancer: TOPAZ-1

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] Nana Rokutanda,[17] Julia Xiong,[17] Gordon Cohen,[17] Juan W. Valle[18]

[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]Division of Hematology and Oncology, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [3]Cancer Center of Nanjing, Jinling Hospital, Nanjing, China; [4]Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, and National Institute of Cancer Research, Tainan, and National Cheng Kung University Hospital, National Cheng Kung University, Tainan, Taiwan; [5]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, Tokyo, Japan; [6]Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany; [7]Division of Medical Oncology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul, South Korea; [8]Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [9]Division of Medical Oncology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The 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]Department of Liver Cancer Unit, AP-HP Hôpital Beaujon, Paris, France; [13]Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, 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]AstraZeneca, Gaithersburg, MD, USA; [18]Division of Cancer Sciences, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK

PRESENTED BY: Do-Youn Oh, MD, PhD

TOPAZ-1 Phase III Trial Schema

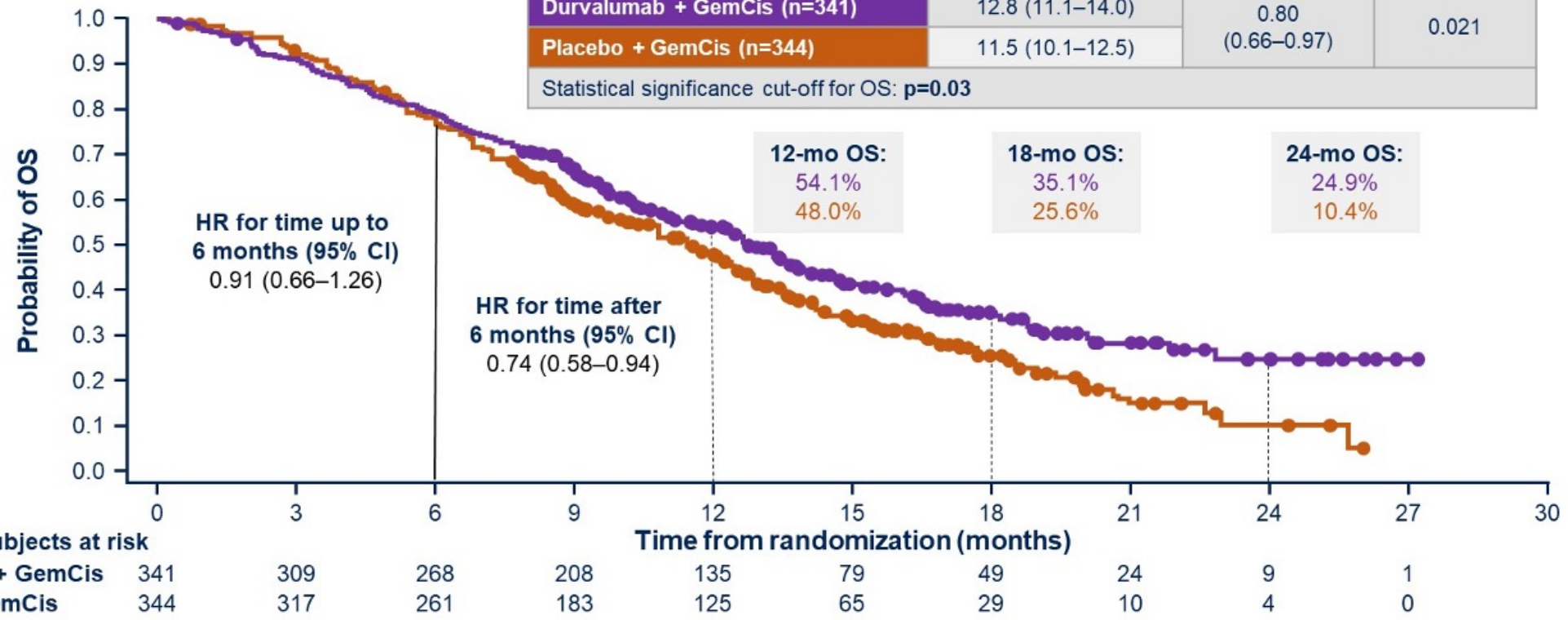


BTC = biliary tract cancer

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

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

	Median OS (95% CI), months	Hazard ratio (95% CI)	p-value
Durvalumab + GemCis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + GemCis (n=344)	11.5 (10.1–12.5)		
Statistical significance cut-off for OS: **p=0.03**			

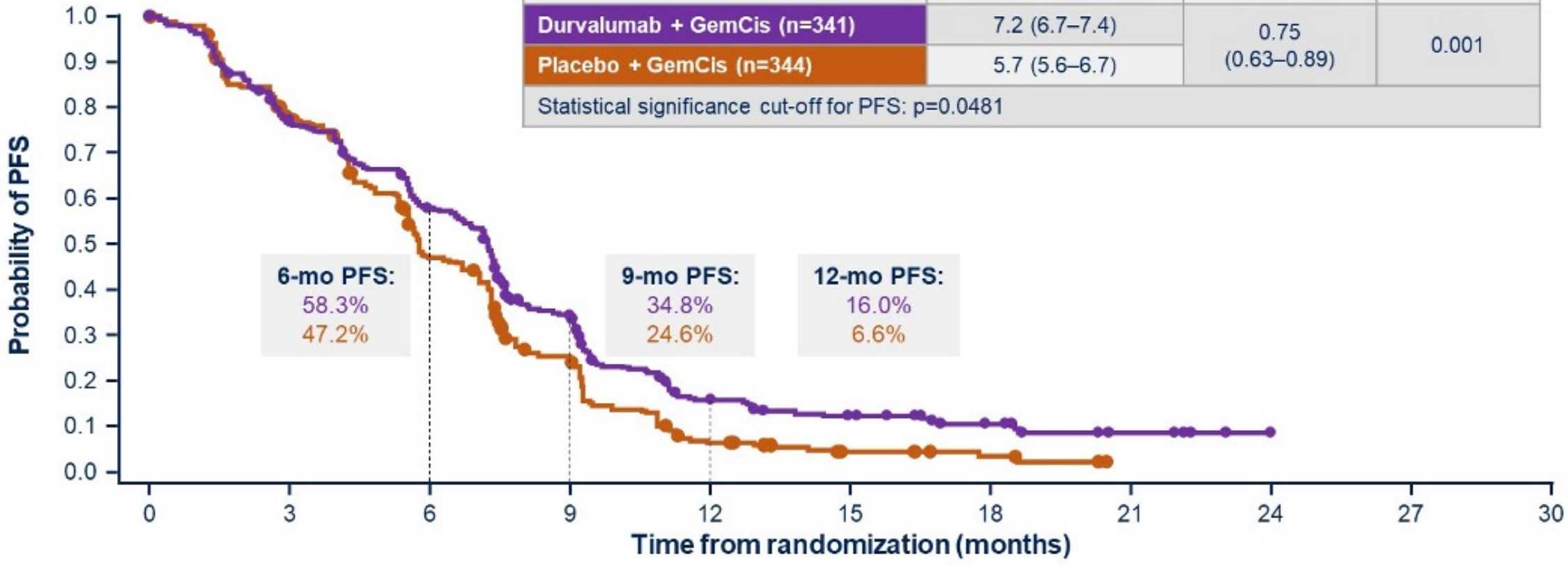


Median duration of follow-up (95% CI) was 16.8 (14.8–17.7) months with durvalumab + GemCis and 15.9 (14.9–16.9) months with placebo + GemCis.
CI, confidence interval; GemCis, gemcitabine and cisplatin; HR, hazard ratio; mo, month; OS, overall survival.

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

TOPAZ-1: Progression-Free Survival

	Median PFS (95% CI), months	Hazard ratio (95% CI)	p-value
Durvalumab + GemCis (n=341)	7.2 (6.7–7.4)	0.75 (0.63–0.89)	0.001
Placebo + GemCis (n=344)	5.7 (5.6–6.7)		
Statistical significance cut-off for PFS: p=0.0481			



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

TOPAZ-1: Immune-Mediated Adverse Events

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

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

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

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

Research

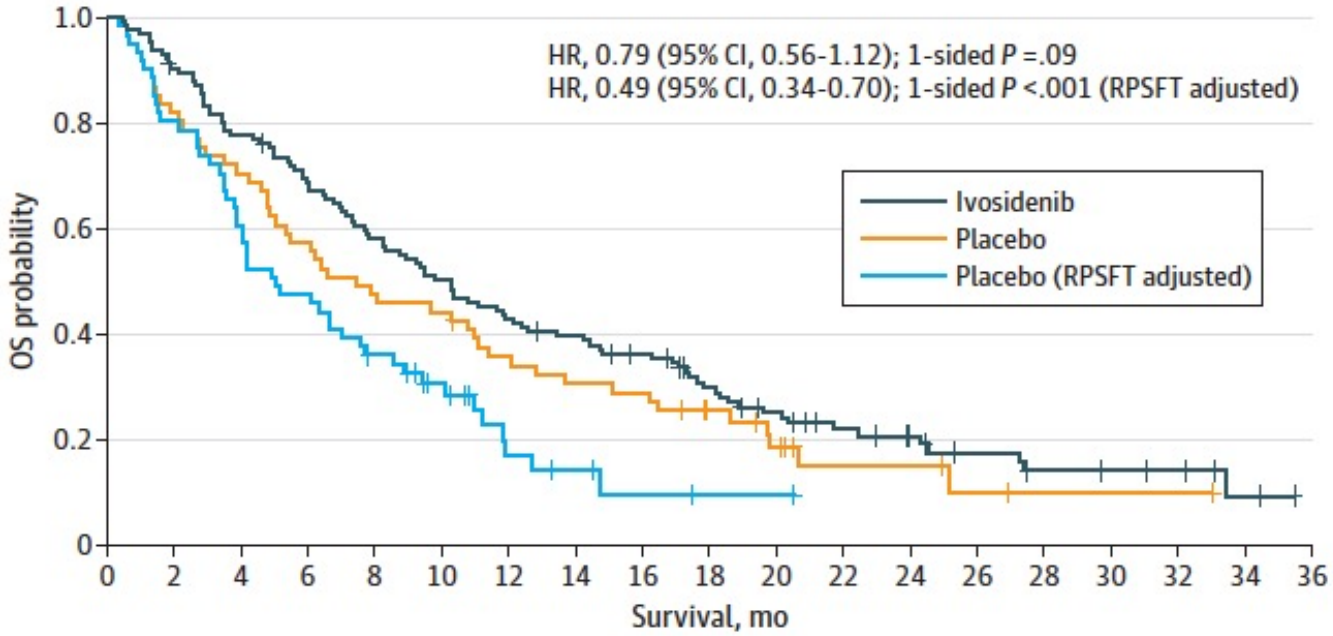
JAMA Oncology | Original Investigation

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

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



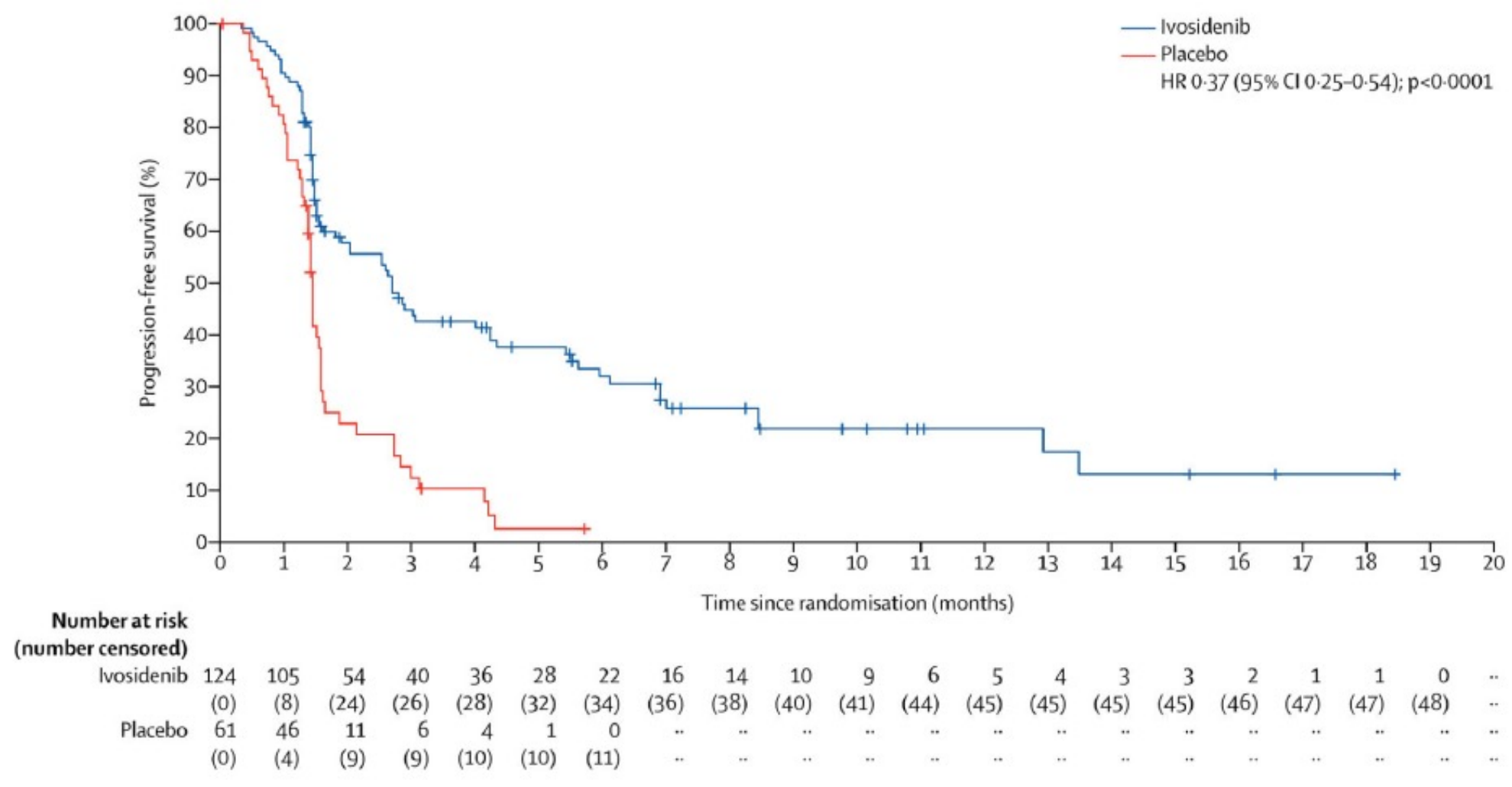
No. at risk

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(11):1669-77.

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

FDA Grants Accelerated Approval to Infigratinib for Metastatic Cholangiocarcinoma

Press Release – May 28, 2021

"The Food and Drug Administration granted accelerated approval to infigratinib, a kinase inhibitor for adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.

The FDA also approved FoundationOne® CDx for selection of patients with FGFR2 fusion or other rearrangement as a companion diagnostic device for treatment with infigratinib.

Efficacy was demonstrated in CBGJ398X2204 (NCT02150967), a multicenter open-label single-arm trial, that enrolled 108 patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement as determined by local or central testing. Patients received infigratinib 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles until disease progression or unacceptable toxicity."

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

THE LANCET
Gastroenterology & Hepatology
Volume 6, Issue 10, October 2021, Pages 803-815

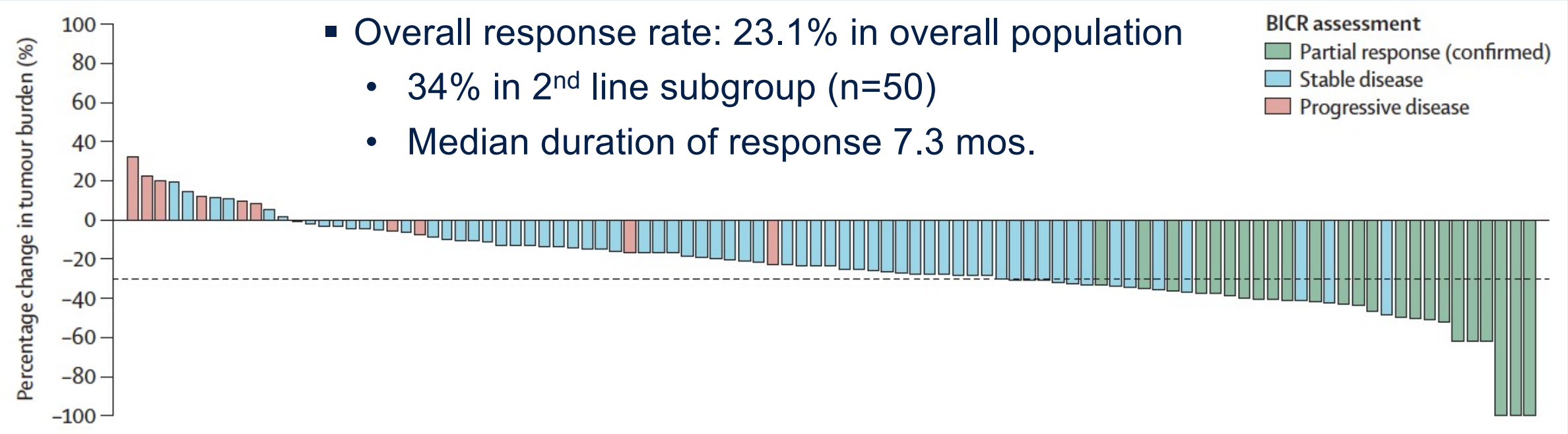
Articles

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

Prof Milind Javle MD [a], Sameek Roychowdhury MD [b, c], Robin Kate Kelley MD [d], Saeed Sadeghi MD [e], Teresa Macarulla MD [f], Prof Karl Heinz Weiss MD [g, h], Dirk-Thomas Waldschmidt MD [i], Lipika Goyal MD [j], Prof Ivan Borbath MD [l], Anthony El-Khoueiry MD [m], Mitesh J Borad MD [o], Wei Peng Yong MBChB [p, q], Philip A Philip MD [r], Michael Bitzer MD [s, t], Surbpong Tanasanvimon MD [u], Ai Li PhD [v], Amit Pande MD [w], Harris S Soifer PhD [x] ... Prof Ghassan K Abou-Alfa MD [z, aa]

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

- Overall response rate: 23.1% in overall population
  - 34% in 2nd line subgroup (n=50)
  - Median duration of response 7.3 mos.



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

RTP RESEARCH TO PRACTICE

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

- The ORR for cohort A was 37.0% in this updated analysis with 4 complete responses (CRs) and 36 partial responses (PRs), and a median duration of response of 8.1 months (**Table 1**)
- The updated median PFS was 7.0 months, and the updated median OS was 17.5 months (**Table 1**)
- No changes in the numbers of patients with CR or PR occurred in cohorts B and C in the current vs the primary analysis

Table 1. Efficacy Outcomes in Patients With *FGFR2* Fusions or Rearrangements (Cohort A)

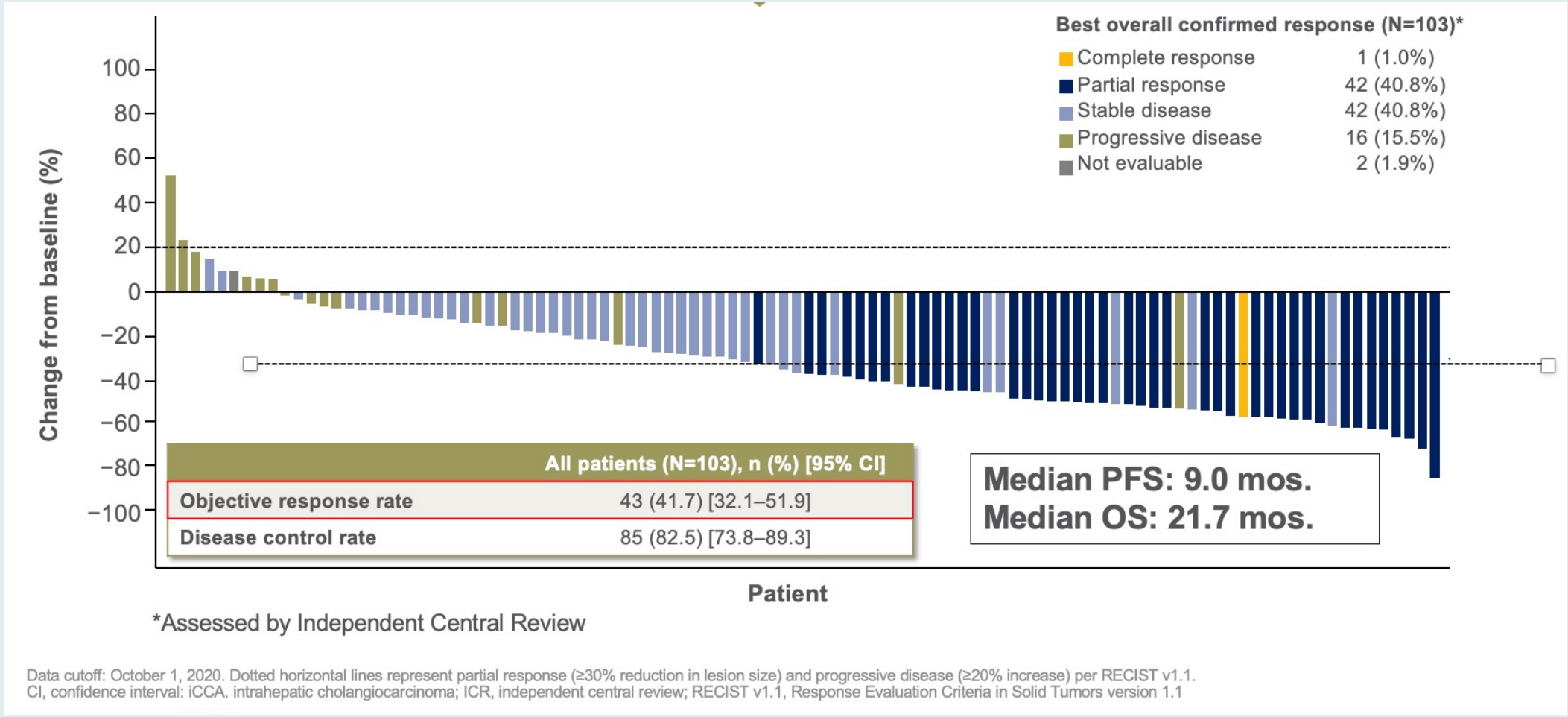
Variable	Primary Analysis[1] (n = 107)	Current Analysis (n = 108)*
ORR (95% CI), %	35.5 (26.5–45.4)	**37.0 (27.9–46.9)**
Best OR, † n (%)		
CR	3 (2.8)	4 (3.7)
PR	35 (32.7)	36 (33.3)
SD	50 (46.7)	49 (45.4)
PD	16 (14.9)	16 (14.8)
Not evaluable‡	3 (2.8)	3 (2.8)
DCR (95% CI), %	82 (74–89)	82.4 (73.9–89.1)
mDOR (95% CI), mo	7.5 (5.7–14.5)	8.1 (5.7–13.1)
mPFS (95% CI), mo	6.9 (6.2–9.6)	7.0 (6.1–10.5)
mOS (95% CI), mo	21.1 (14·8–NE)§	17.5 (14.4–23.0)
Responders	–	30.1 (21.5–NE)
Nonresponders	–	13.7 (9.6–16.2)

*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). †Assessed and confirmed by independent central review. ‡Postbaseline tumor assessment was not performed owing to study discontinuation (2 participants in cohort A, 4 participants in cohort B, 3 participants in cohort C) or was performed prior to the minimum interval of 39 days for an assessment of SD (1 patient in cohort A, 1 patient in cohort B). §OS not mature at data cutoff used for the primary analysis (March 22, 2019).
mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; NE, not estimable; OR, objective response; PD, progressive disease; SD, stable disease.

1. Abou-Alfa GK, et al. *Lancet Oncol.* 2020;21:671–668.

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

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



Data cutoff: October 1, 2020. Dotted horizontal lines represent partial response (≥30% reduction in lesion size) and progressive disease (≥20% increase) per RECIST v1.1.
CI, confidence interval: iCCA. intrahepatic cholangiocarcinoma; ICR, independent central review; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Goyal L et al. AACR 2021;Abstract CT010.

RTP RESEARCH TO PRACTICE

Questions — Richard S Finn, MD

Patients with metastatic cholangiocarcinoma

- **What therapies are used in this setting, and how is treatment selected?**

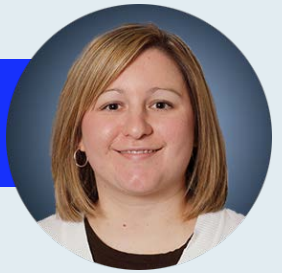
Commentary — Richard S Finn, MD

Patients with metastatic cholangiocarcinoma

- **Not “one disease”**
  - **Molecular profiling is standard of care**
- **Front line**
  - **Gemcitabine and cisplatin (historical)**
  - **Gemcitabine and cisplatin + durvalumab (new SOC, TOPAZ study)**
- **Second line**
  - **Mutation driven: IDH, FGFR translocations, HER2, BRAF**
  - **Chemotherapy: FOLFOX, FOLFIRI**
  - **Lenvatinib + pembrolizumab, single agent nivo or pembro**

RTP RESEARCH TO PRACTICE

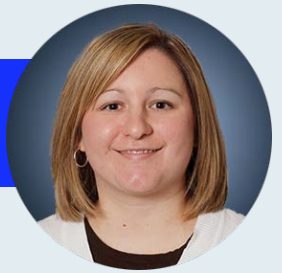
Questions — Amanda K Wagner, APRN-CNP, AOCNP



Patients with metastatic cholangiocarcinoma

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are the key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities?**
- **What are some of the psychosocial issues that arise in this situation?**

Commentary — Amanda K Wagner, APRN-CNP, AOCNP

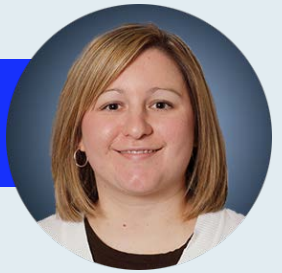


Patients with metastatic cholangiocarcinoma

- **DISEASE RELATED COMPLICATIONS**
  - **Obstructive jaundice**
    - **ERCP with stent vs PTC biliary drain**
  - **Liver cirrhosis/failure with associated ascites/edema**
    - **Paracentesis, diuretics**
  - **Cholangitis**
  - **Anorexia and weight loss**
    - **Dietician referral, nutritional supplements, consider appetite stimulants**
  - **Cancer related pain**
    - **Analgesics, consider referral to palliative medicine**
  - **Fatigue**

RTP RESEARCH TO PRACTICE

Commentary — Amanda K Wagner, APRN-CNP, AOCNP



TREATMENT RELATED SIDE EFFECTS

- **Fatigue**
- **Anorexia/weight loss**
- **Nausea/vomiting**
- **Diarrhea**
- **Neuropathy**
- **Myelosuppression**
- **Infection**

- **PSYCHOSOCIAL CONCERNS**
- **Anxiety/depression**
- **Pharmacologic and nonpharmacologic management**
- **Difficulty coping, poor prognosis**
- **End of life discussions**

RTP
RESEARCH
TO PRACTICE

Appendix

Atezolizumab/Bevacizumab Regimen

Mechanism of action

- PD-L1 inhibitor
- Anti-VEGF monoclonal antibody

Indication

- Investigational

Phase III study dose

- Atezolizumab: 1,200 mg every 3 weeks
- Bevacizumab: 15 mg/kg every 3 weeks

Key Toxicities

- Grade 3/4 hypertension: 15%

Finn RS et al. *N Engl J Med* 2020;382(20):1894-905.

IMbrave150: Updated Safety Outcomes

- After longer follow-up, the safety profile of atezolizumab combined with bevacizumab was consistent with the primary analysis

- The most common treatment-related adverse events with atezolizumab/bevacizumab were:
  - Proteinuria 29%
  - Hypertension 28%
  - Increased AST 16%
  - Fatigue 16%

- Treatment-related Grade 5 events occurred in 6 (2%) patients in the atezolizumab/bevacizumab study arm
  - Gastrointestinal hemorrhage, gastric ulcer perforation, subarachnoid hemorrhage, pneumonia, abnormal hepatic function and liver injury

- Treatment-related Grade 5 events occurred in 1 (<1%) patient in the sorafenib study arm (hepatic cirrhosis)

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

ESMO ASIA VIRTUAL ONCOLOGY WEEK

ESMO VIRTUAL PLENARY

ABSTRACT VP10-2021

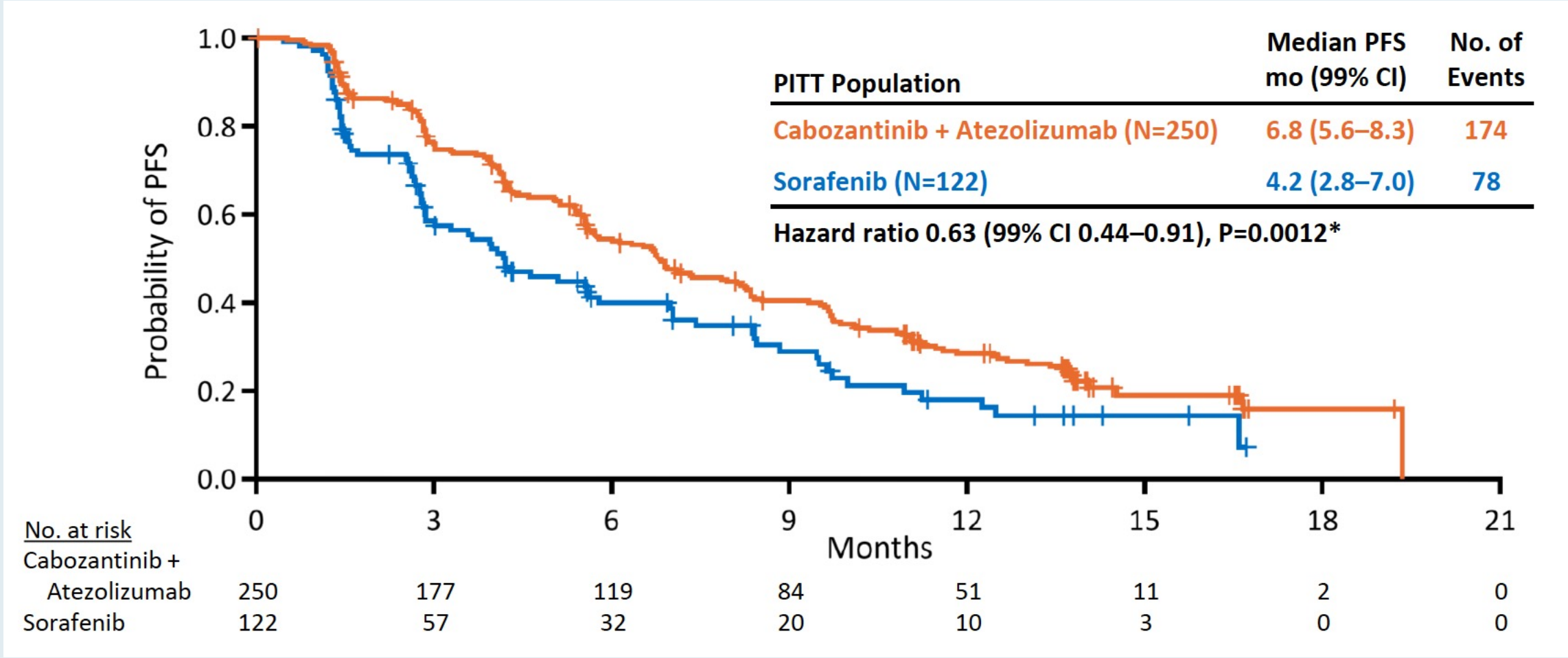
Cabozantinib plus atezolizumab versus sorafenib as first-line systemic treatment for advanced hepatocellular carcinoma: results from the randomized phase 3 COSMIC-312 trial

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

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

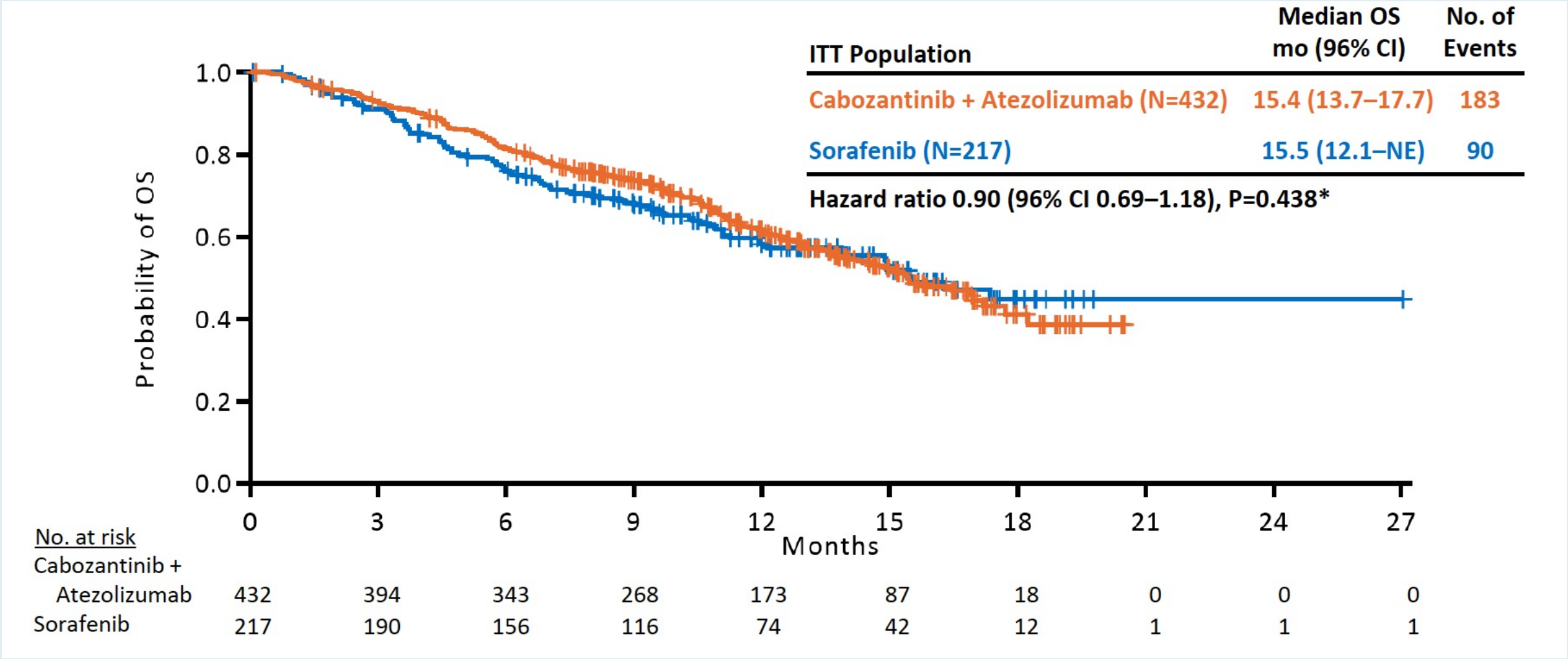
RTP RESEARCH TO PRACTICE

COSMIC-312: Final Analysis of the Primary Progression-Free Survival (PFS) Endpoint with Cabozantinib and Atezolizumab as First-Line Treatment for Advanced HCC



Kelley RK et al. ESMO Asia Virtual Oncology Week 2021;Abstract VP10-2021.

COSMIC-312 Primary Endpoint of OS: Interim Analysis



Kelley RK et al. ESMO Asia Virtual Oncology Week 2021;Abstract VP10-2021.

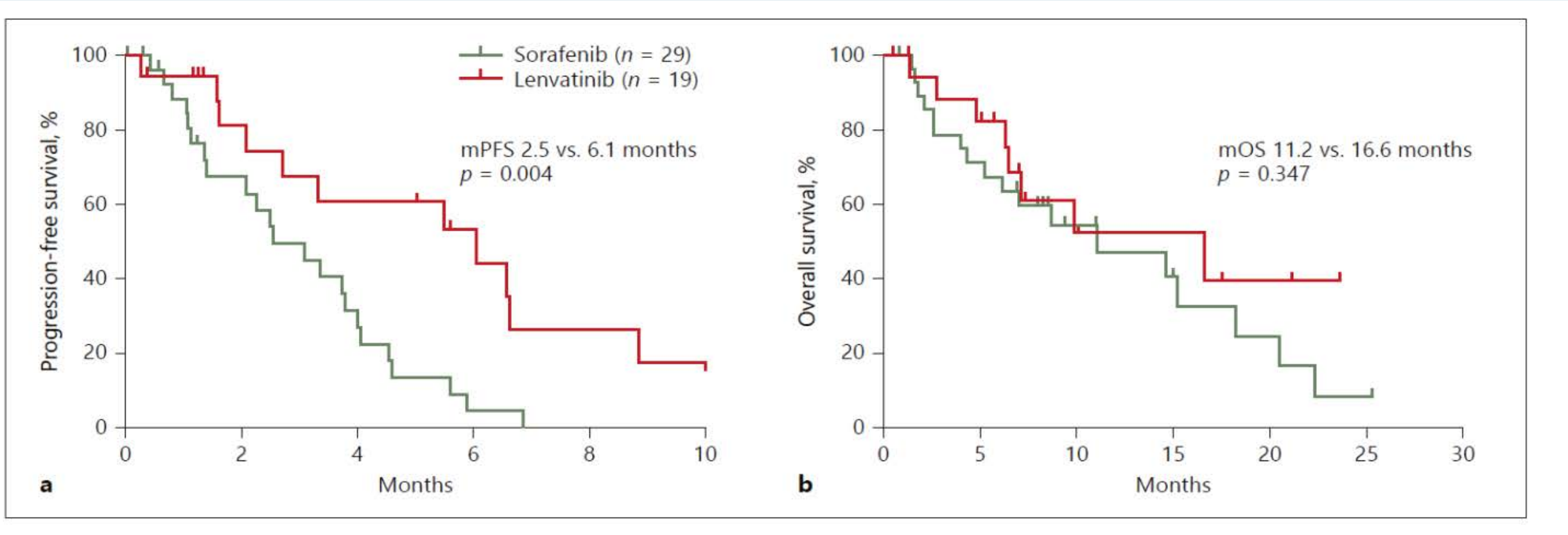
COSMIC-312 Summary of Adverse Events

	Cabozantinib + Atezolizumab (N=429)		Sorafenib (N=207)		Cabozantinib (N=188)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Treatment-related adverse events*						
Any adverse event, %	93	55	90	33	95	55
Diarrhea	42	3.5	42	1.0	48	5.3
Palmar-plantar erythrodysesthesia	42	7.9	44	8.2	44	8.5
ALT increased	22	6.3	5.8	1.9	22	5.9
AST increased	21	6.5	8.2	2.4	22	5.3
Decreased appetite	21	0.9	16	1.9	30	3.2
Fatigue	20	2.6	14	3.4	27	3.2
Hypertension	19	7.0	15	6.3	26	11
Adverse events of interest (all-cause)						
Any hemorrhage, %	17	2.8	14	4.8	15	3.2
Any immune-mediated adverse event leading to systemic steroid use,† %	7.2	4.4	1.0	0.5	0	0

*Treatment-related AEs occurring in ≥20% of patients in any treatment arm
†Treatment-emergent AEs of special interest leading to initiation of systemic immune-modulating medication

Kelley RK et al. ESMO Asia Virtual Oncology Week 2021;Abstract VP10-2021.

Activity of Multikinase Inhibitors in Patients with Advanced HCC After Disease Progression on First-Line Atezolizumab/Bevacizumab



Yoo C et al. *Liver Cancer* 2021;10(2):107-14.

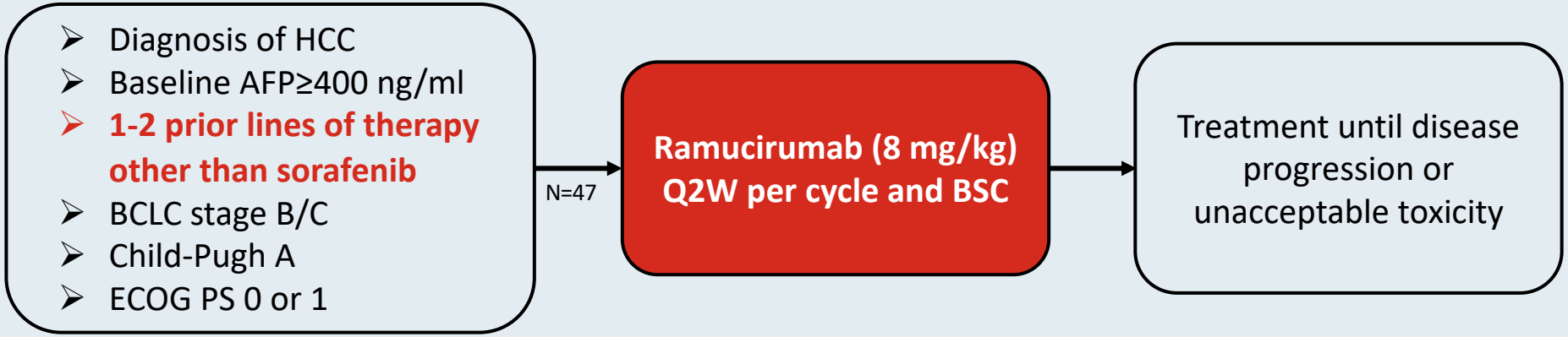
RTP RESEARCH TO PRACTICE

Ramucirumab for Patients with Advanced Hepatocellular Carcinoma and Elevated α-Fetoprotein Following a Non-Sorafenib Based First-Line Therapy: Final Results from an Expansion Cohort of REACH-2

Finn RS et al

Gastrointestinal Cancers Symposium 2022;Abstract 423

REACH-2 Trial: Open Label Expansion



- **Primary endpoint:** Safety
- **Secondary endpoints:** OS, PFS (RECIST v1.1), TTP, ORR, PK, patient-reported outcomes, immunogenicity
- **Pooled analysis:** open-label cohort was indirectly compared to patients from REACH (AFP ≥400 ng/mL) and REACH-2 who received prior sorafenib using individual patient data meta-analysis

Analysis of single arm Open-Label Expansion Cohort will be independent of Main Cohort. The final analysis of the primary and secondary endpoints will occur after all patients enrolled in the OLE cohort have completed at least 3 cycles of ramucirumab or discontinued for any reason.

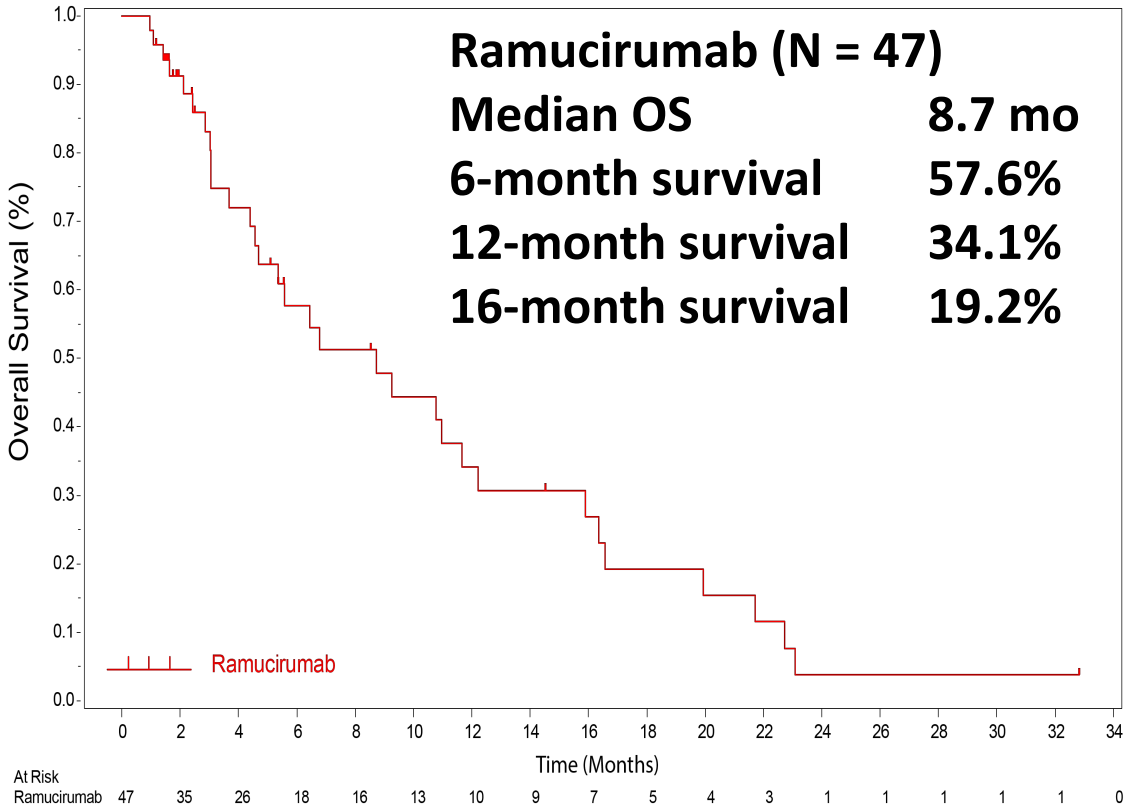
AFP = alpha-fetoprotein; BCLC = Barcelona Clinic Liver Cancer; BSC = best supportive care; ECOG PS = Eastern Cooperative Oncology Group Performance Status; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PK = pharmacokinetics; Q2W = every 2 weeks; TTP = time-to-progression

Data cut-off date was May 11, 2021

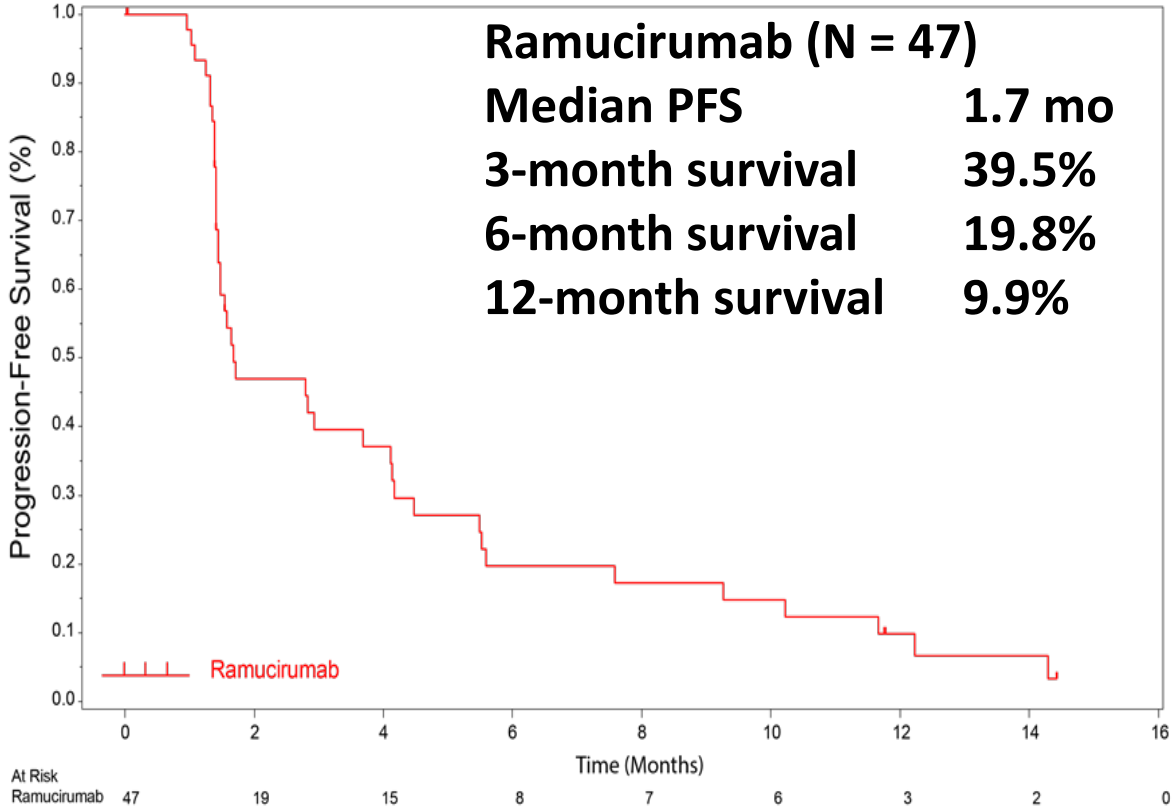
Finn RS et al. Gastrointestinal Cancers Symposium 2022;Abstract 423.

REACH-2 Trial: Survival Summary

Overall Survival (OS)



Progression-Free Survival (PFS)



Finn RS et al. Gastrointestinal Cancers Symposium 2022;Abstract 423.

RTP RESEARCH TO PRACTICE

Side Effect Teaching Points

- Tyrosine Kinase Inhibitor (TKI) drugs commonly cause **fatigue, diarrhea, hand-foot reaction, nausea, vomiting, anorexia, weight loss, hypertension**
  - Early/frequent intervention and good provider communication KEY to overall tolerance
    - Daily blood pressure logging
    - Skin care education
    - Nutritional counseling
    - Proactive antiemetic use

Courtesy of: Jessica Mitchell, APRN, CNP, MPH

Side Effect Teaching Points

- **Ramucirumab**
  - **Increased risk of bleeding,** careful monitoring especially in HCC patient with decreased liver function
  - **Hypertension,** maintain daily blood pressure records from home monitoring, watch for other signs of increased blood pressure such as headache, dizziness

Courtesy of: Jessica Mitchell, APRN, CNP, MPH

Psychosocial Aspects

- Hand-foot syndrome caused difficulty walking/pain, decreasing patient's ability to be independent/active, which was a very important component of his life. Additional physical changes (temporal wasting, cachexia, abdominal distention due to ascites) impacted his desire of continuing to be social.
- However, patient very active in Alcoholics Anonymous community, doing public speaking about his situation/taking responsibility for life choices. Very focused on cultivating forgiveness/peace/mending broken relationships from prior alcoholism before death.

Courtesy of: Jessica Mitchell, APRN, CNP, MPH

TOPAZ-1: Grade 3/4 Adverse Events

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

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

What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Small Cell Lung Cancer

Friday, April 29, 2022
6:00 AM – 7:30 AM PT

Faculty

Marianne J Davies, DNP, MSN, RN, APRN, CNS-BC, ACNP-BC, AOCNP, FAAN
Matthew Gubens, MD, MS
Lowell L Hart, MD
Chaely J Medley, MSN, AGNP

Moderator

Neil Love, MD

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Thank you for joining us!

In-person attendees: Please fill out your Educational Assessment and NCPD Credit Form.

Online attendees: NCPD credit information will be emailed to each participant within 3 business days.

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