Practical Perspectives: Experts Review Actual Cases of Patients with Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

Thursday, January 30, 2025
5:00 PM – 6:00 PM ET

Faculty

John Bridgewater, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

John Bridgewater, MD, PhD
Chair, National Cancer Research Institute Upper Gastrointestinal Group
Senior Lecturer, Medical Oncology
UCL Cancer Institute
London, United Kingdom

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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Commercial Support

This activity is supported by an educational grant from Jazz Pharmaceuticals Inc.

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Dr Love — Disclosures

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Dr Bridgewater — Disclosures
Faculty

No relevant conflicts of interest to disclose.

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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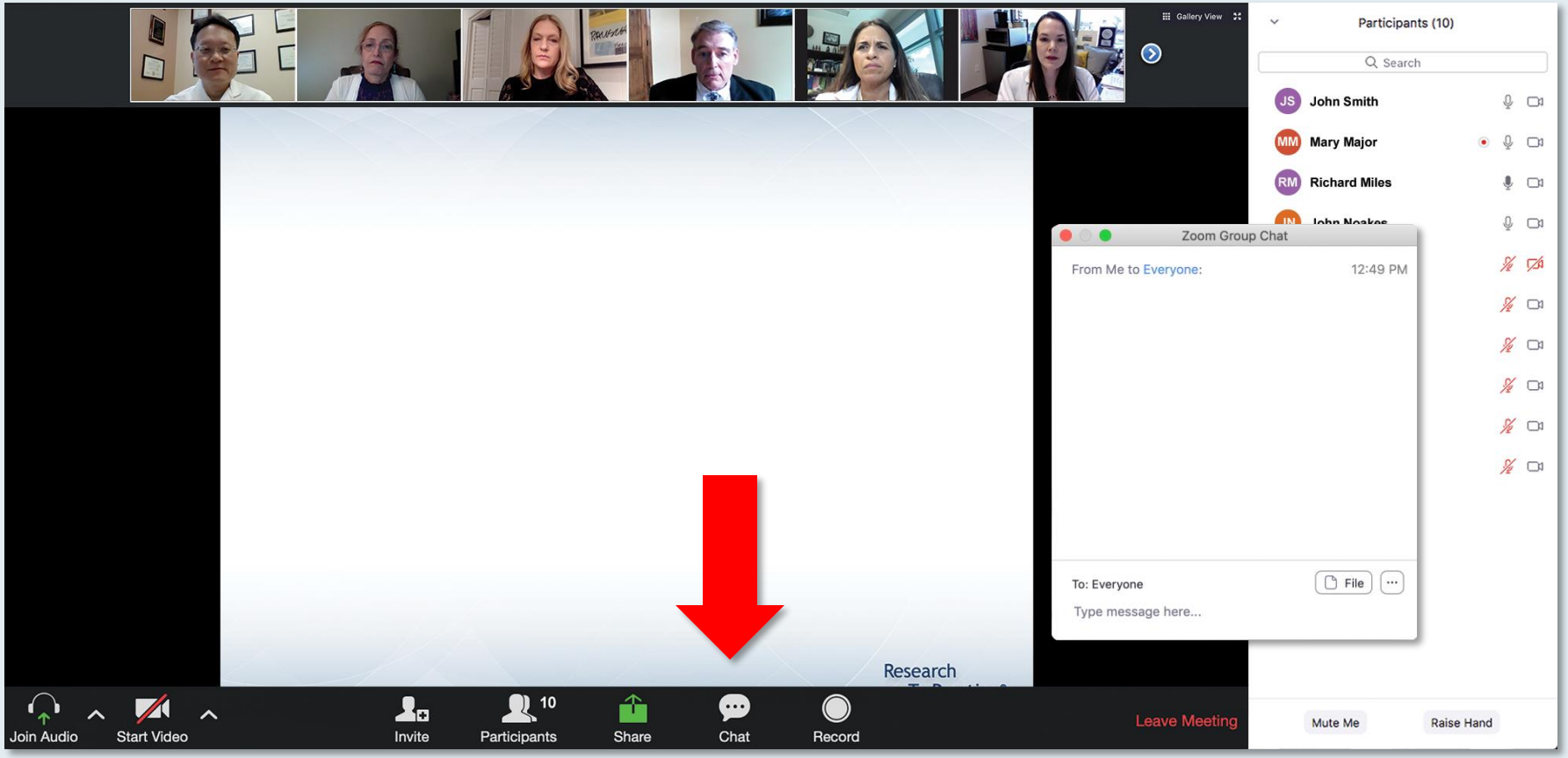
We Encourage Clinicians in Practice to Submit Questions



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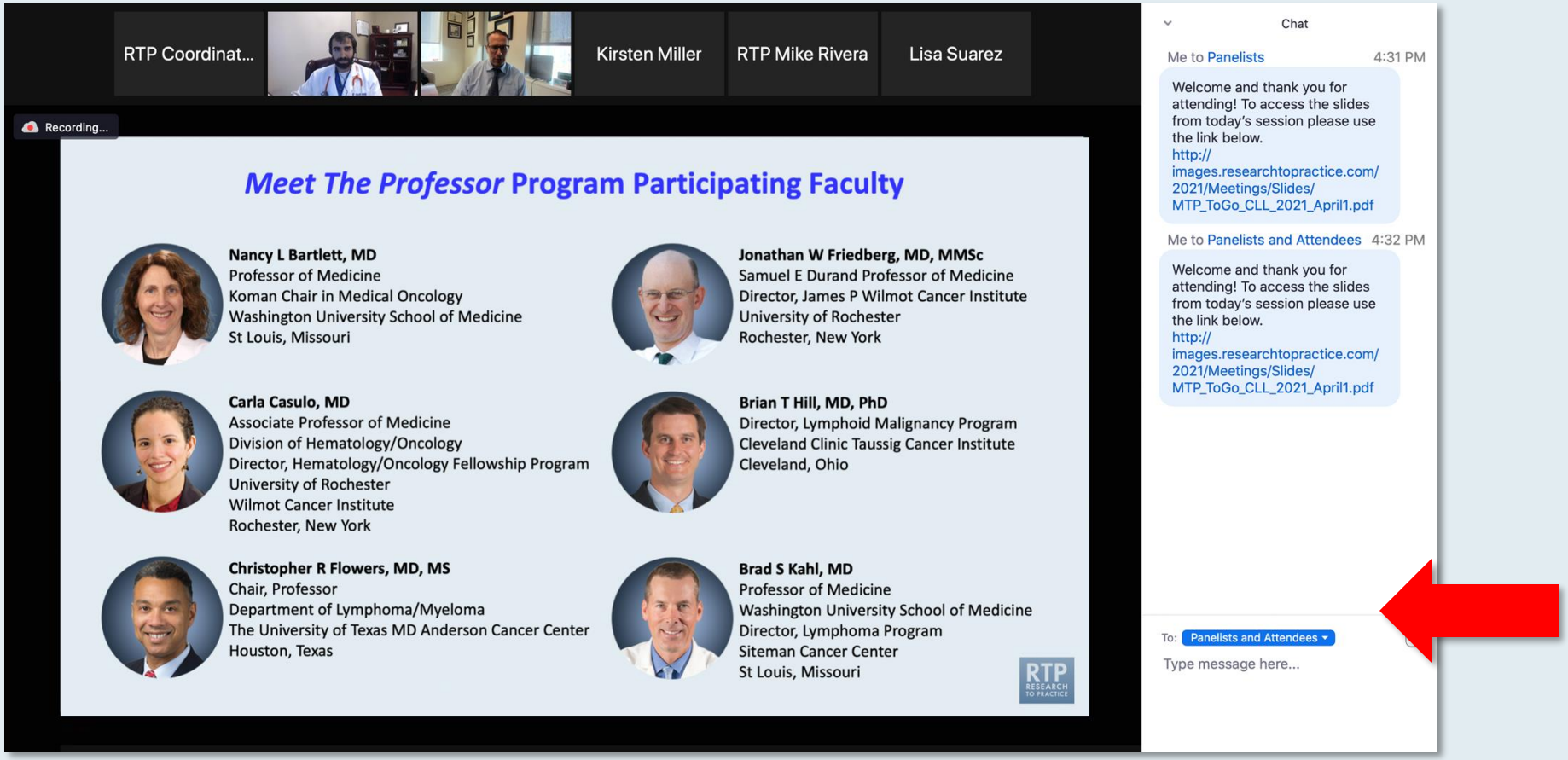
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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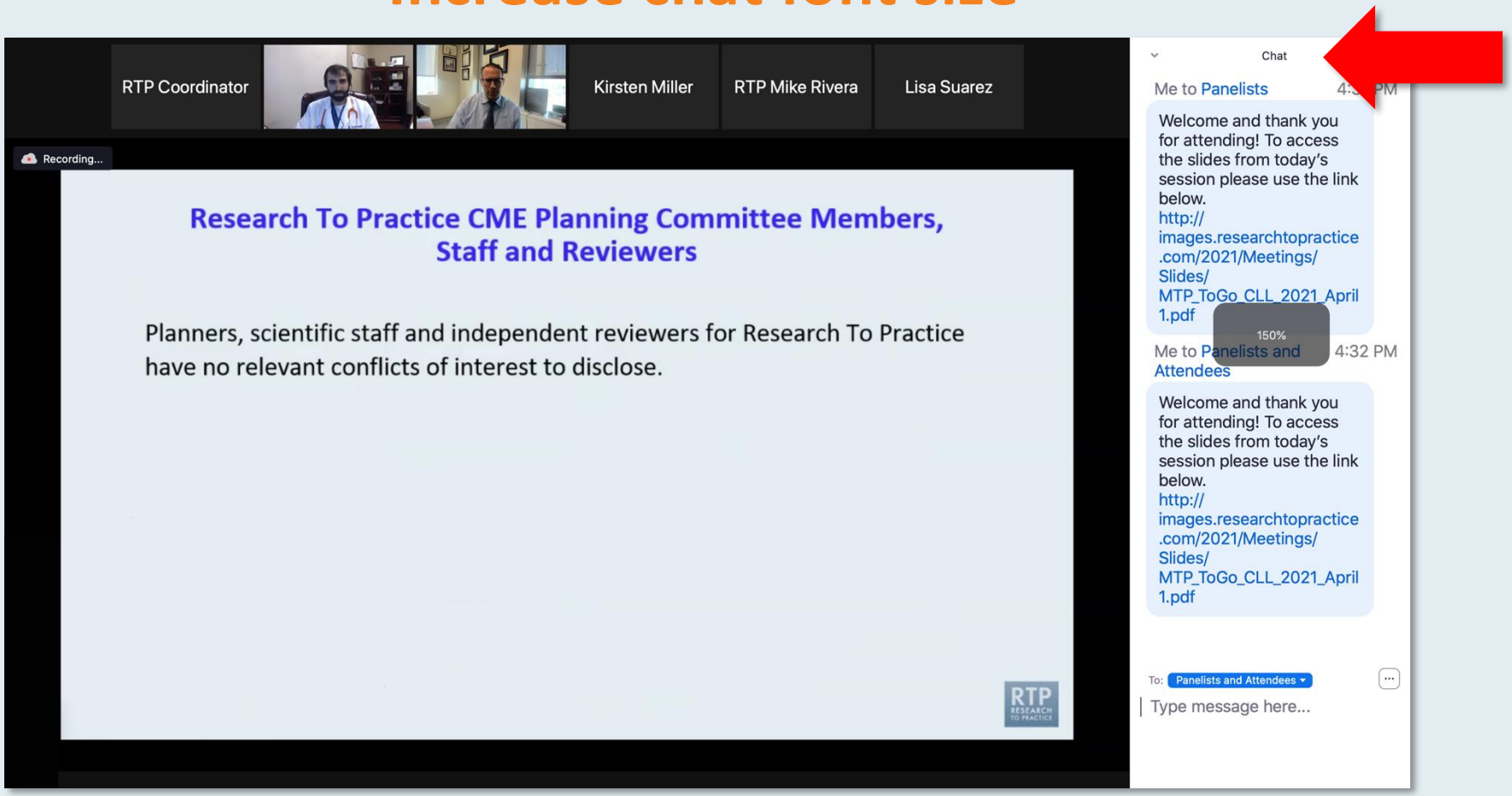
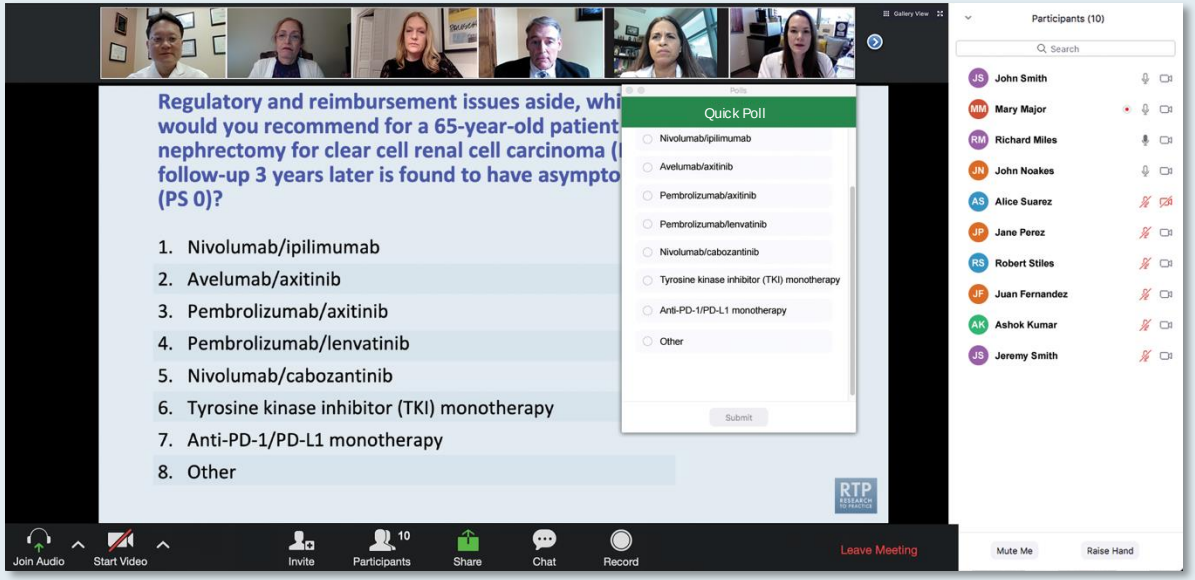
Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



ONCOLOGY TODAY

WITH DR NEIL LOVE

Striving for Consensus: Optimizing the Current and Future Management of Biliary Tract Cancers

DR LIPIKA GOYAL
STANFORD CANCER CENTER

MILIND JAVLE, MD
THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

JAMES J HARDING, MD
MEMORIAL SLOAN KETTERING CANCER CENTER

ROBIN K (KATIE) KELLEY, MD
UCSF HELEN DILLER FAMILY COMPREHENSIVE CANCER CENTER

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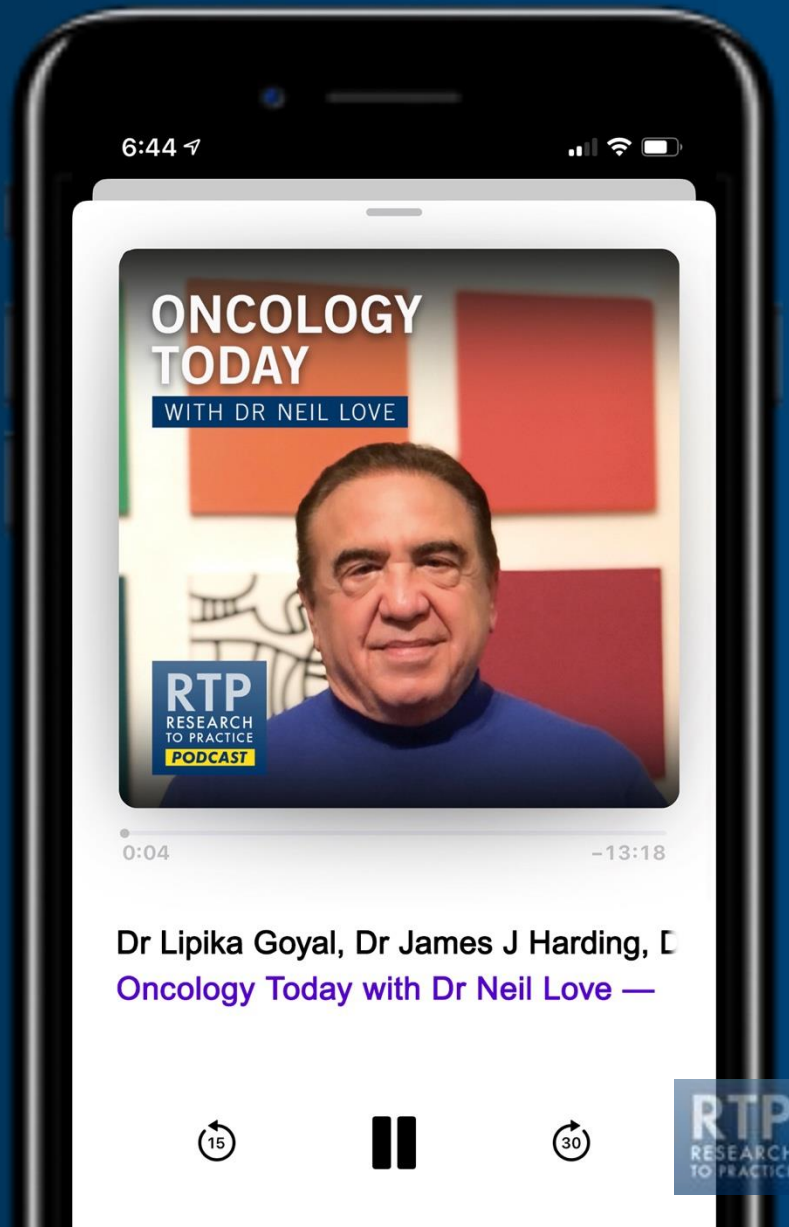

What Clinicians Want to Know: Addressing Current Questions Related to Novel Treatment Approaches for Urothelial Bladder Cancer and Prostate Cancer

A CME Symposium Held in Conjunction with the 2025 ASCO® Genitourinary Cancers Symposium

Thursday, February 13, 2025
7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty (Bladder Cancer)

Terence Friedlander, MD
Matthew D Galsky, MD

Faculty (Prostate Cancer)

Neeraj Agarwal, MD, FASCO
Andrew J Armstrong, MD, ScM

Moderator

Elisabeth I Heath, MD

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What Clinicians Want to Know: Addressing Current Questions Related to the Management of Renal Cell Carcinoma

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Thomas E Hutson, DO, PharmD, PhD

Rana R McKay, MD

Tian Zhang, MD, MHS

Moderator

Sumanta Kumar Pal, MD

RTP RESEARCH TO PRACTICE

Patterns of Care: Examining the Current Use of Genetic Testing and Related Clinical Management for Patients with Localized Breast Cancer

A CME/MOC-Accredited Webinar in Partnership with the American Society of Breast Surgeons

Thursday, February 20, 2025

5:00 PM – 6:00 PM ET

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Kevin S Hughes, MD

Mark Robson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Save The Date

Fourth Annual
National General Medical Oncology Summit

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

Friday to Sunday, February 28 to March 2, 2025

Fontainebleau Hotel, Miami Beach, Florida

Moderated by Neil Love, MD

Thank you for joining us!

Information on how to obtain CME, ABIM MOC and ABS credit will be provided at the conclusion of the activity in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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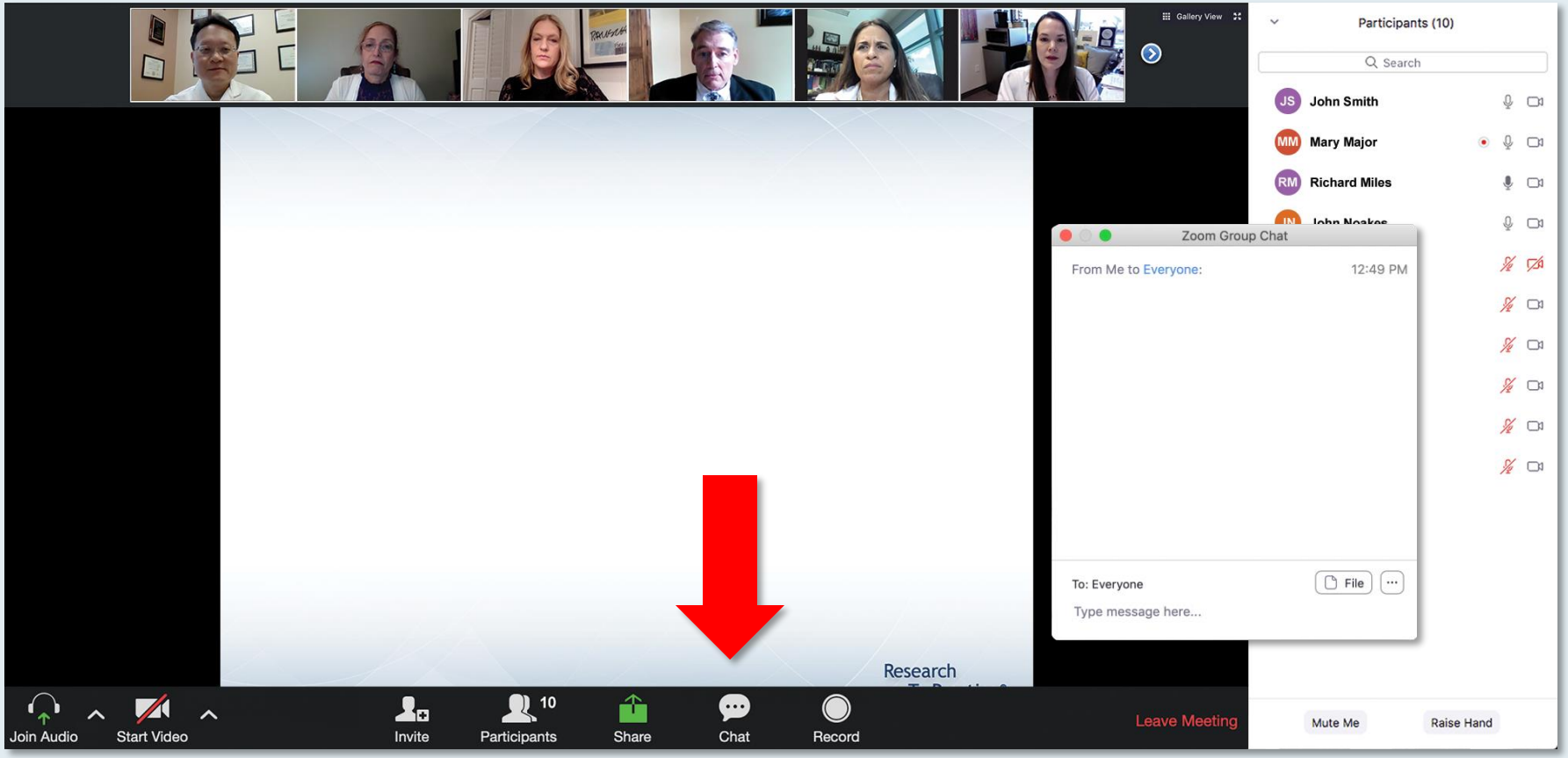

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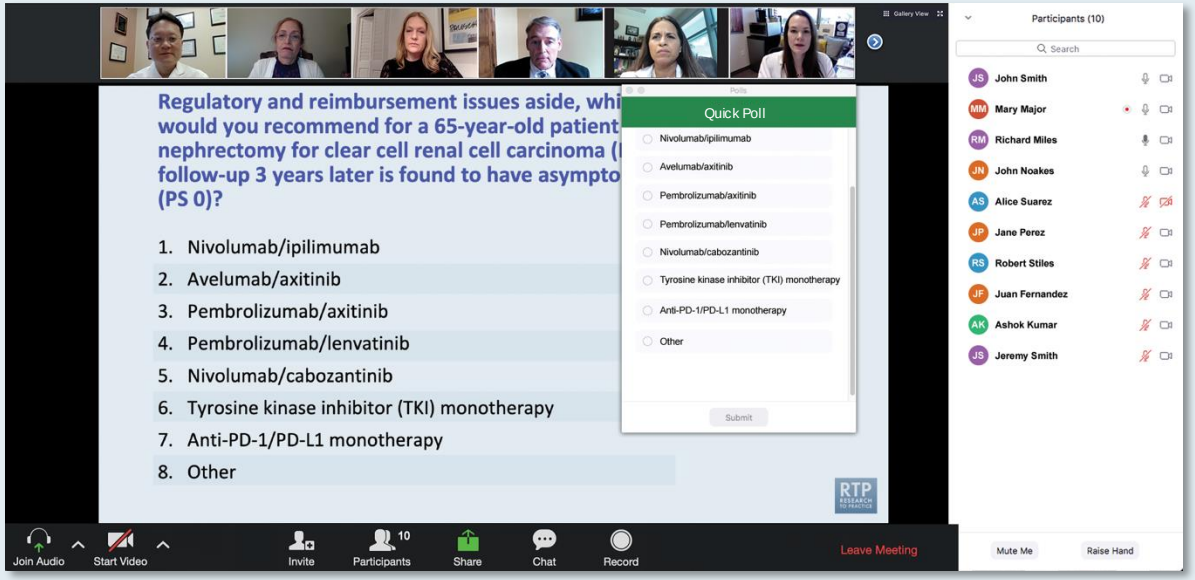

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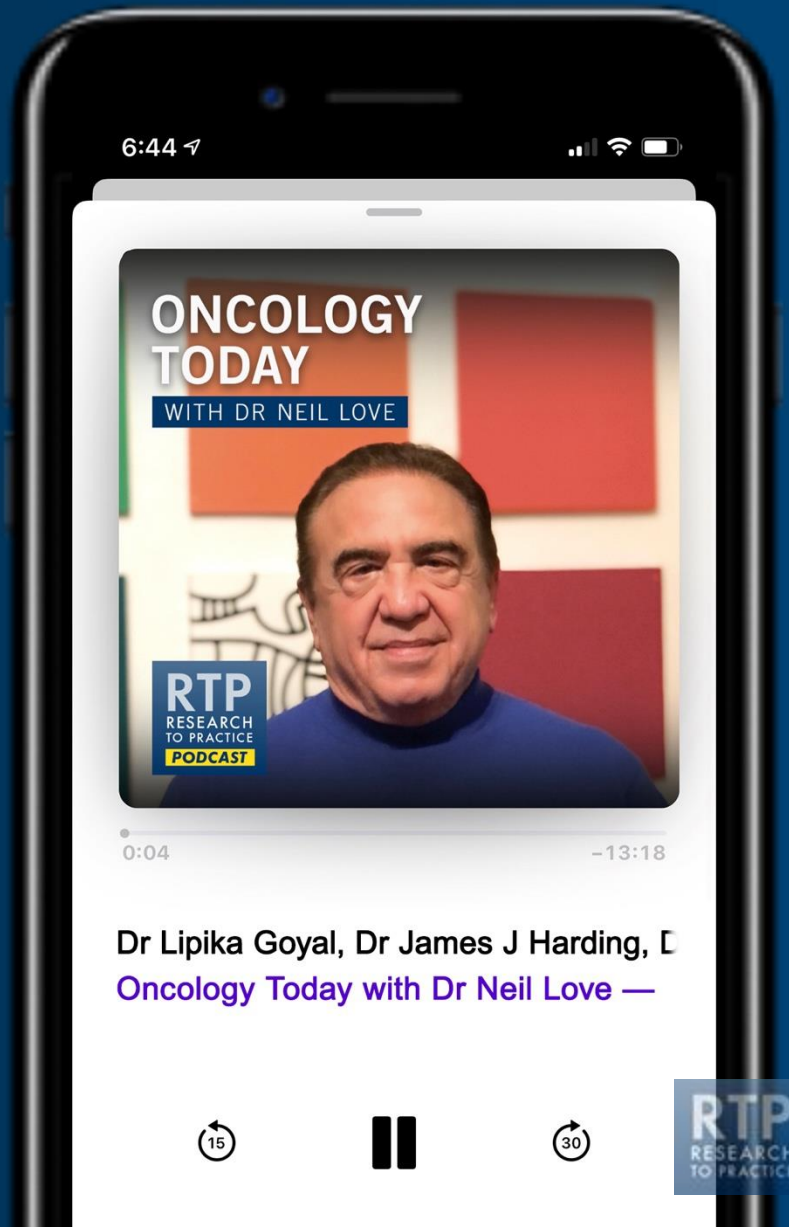

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Faculty

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Dr Love — Disclosures

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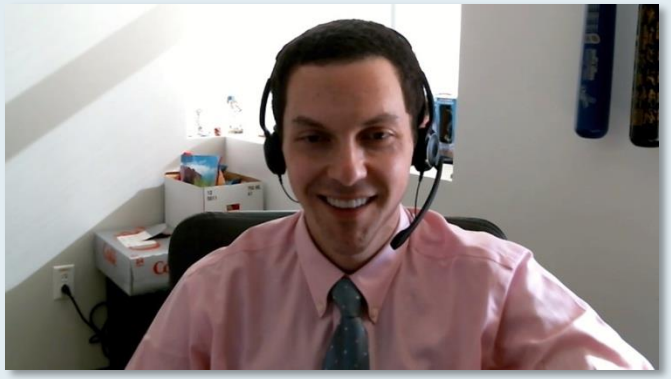
Contributing General Medical Oncologists

Jennifer L Dallas, MD
Oncology Specialists of Charlotte
Charlotte, North Carolina



Jeremy Lorber, MD
Cedars-Sinai Medical Center
Beverly Hills, California

Victoria Giffi, MD
Meritus Hematology and Oncology Specialists
Hagerstown, Maryland

Henna Malik, MD
Texas Oncology
Houston, Texas

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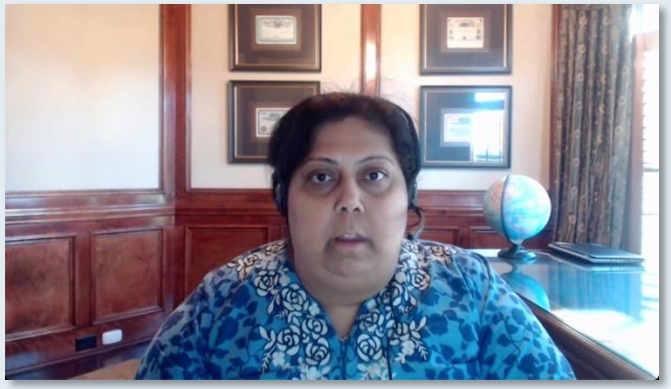
Contributing General Medical Oncologists

Brian P Mulherin, MD
American Oncology Network
Indianapolis, Indiana

Sean Warsch, MD
Messino Cancer Centers
Asheville, North Carolina



Niyati A Nathwani, MD
Carolina Blood and Cancer Care Associates
Charlotte, North Carolina

RTP RESEARCH TO PRACTICE

Agenda

Introduction: Biology and Epidemiology; Classification

Module 1: Localized Biliary Tract Cancers (BTCs)

Module 2: First-Line Treatment of Metastatic BTC

Module 3: HER2-Positive Advanced BTC

Module 4: Management of Mixed Hepatocellular Carcinoma (HCC)/BTC Tumors

Module 5: Advanced Cholangiocarcinoma with an FGFR2 Fusion

Module 6: Other Important Issues in BTC

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Guideline

OPEN ACCESS

British Society of Gastroenterology guidelines for the diagnosis and management of cholangiocarcinoma

Simon M Rushbrook,[1] Timothy James Kendall ,[2,3] Yoh Zen,[4] Raneem Albazaz,[5] Prakash Manoharan,[6] Stephen P Pereira,[7] Richard Sturgess,[8] Brian R Davidson,[9] Hassan Z Malik,[10] Derek Manas,[11] Nigel Heaton,[12] K Raj Prasad,[13] John Bridgewater,[14] Juan W Valle,[15] Rebecca Goody,[16] Maria Hawkins,[17] Wendy Prentice,[18] Helen Morement,[19] Martine Walmsley,[20] Shahid A Khan [21,22]

***Gut* 2023 December 7;73(1):16-46**

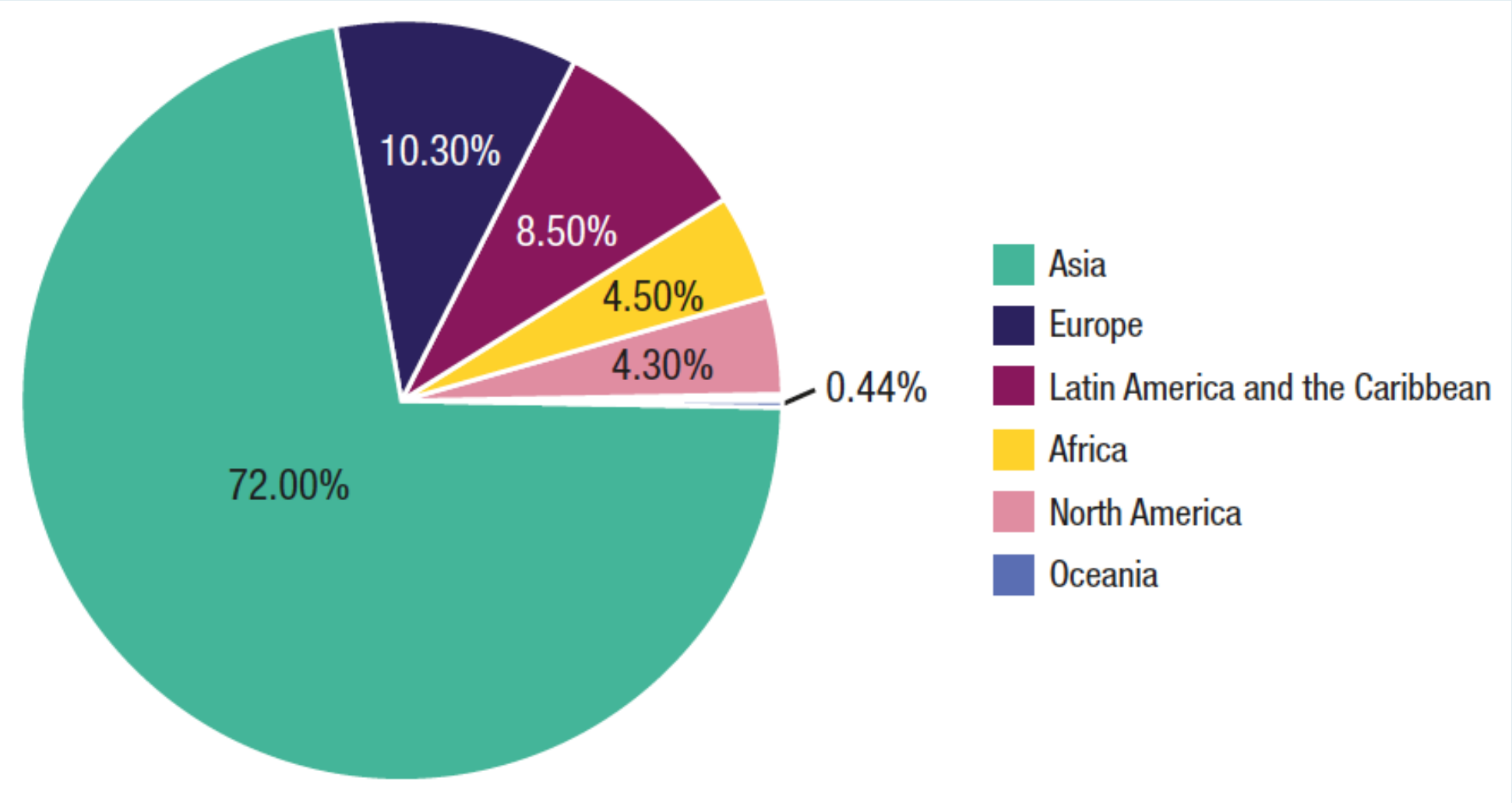
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Global Epidemiology Trends in Biliary Tract Cancer: A Targeted Literature Review

Bridgewater JA et al.

ESMO GI 2024;Abstract 290P.

Global Incidence of Gallbladder Cancer Cases in 2022



Bridgewater JA et al. EMSO GI 2024;Abstract 290P.

Real-World Treatment Patterns in Patients with Biliary Tract Cancer (BTC): Retrospective Chart Review Survey in Europe (GARNET-2)

Bridgewater JA et al.

ESMO 2023;Abstract 125P.

Obesity and Biliary Tract Cancers: Changing Epidemiology

Al Mahmasani L et al.

Gastrointestinal Cancers Symposium 2025;Abstract TPS643.

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THERAPEUTIC ADVANCES in
Medical Oncology

Review

Adjuvant therapy of biliary tract cancers

Joanna Kefas, John Bridgewater, Arndt Vogel, Alexander Stein and John Primrose

***Ther Adv Med Oncol* 2023 March 28;15**

Case Presentation: 61-year-old woman with extrahepatic cholangiocarcinoma (T3N1) receives preoperative cisplatin/ gemcitabine with durvalumab

Dr Victoria Giffi (Hagerstown, Maryland)

Case Presentation: 64-year-old woman with cholangiocarcinoma with an IDH1 mutation receives chemoradiation therapy

Dr Niyati Nathwani (Charlotte, North Carolina)

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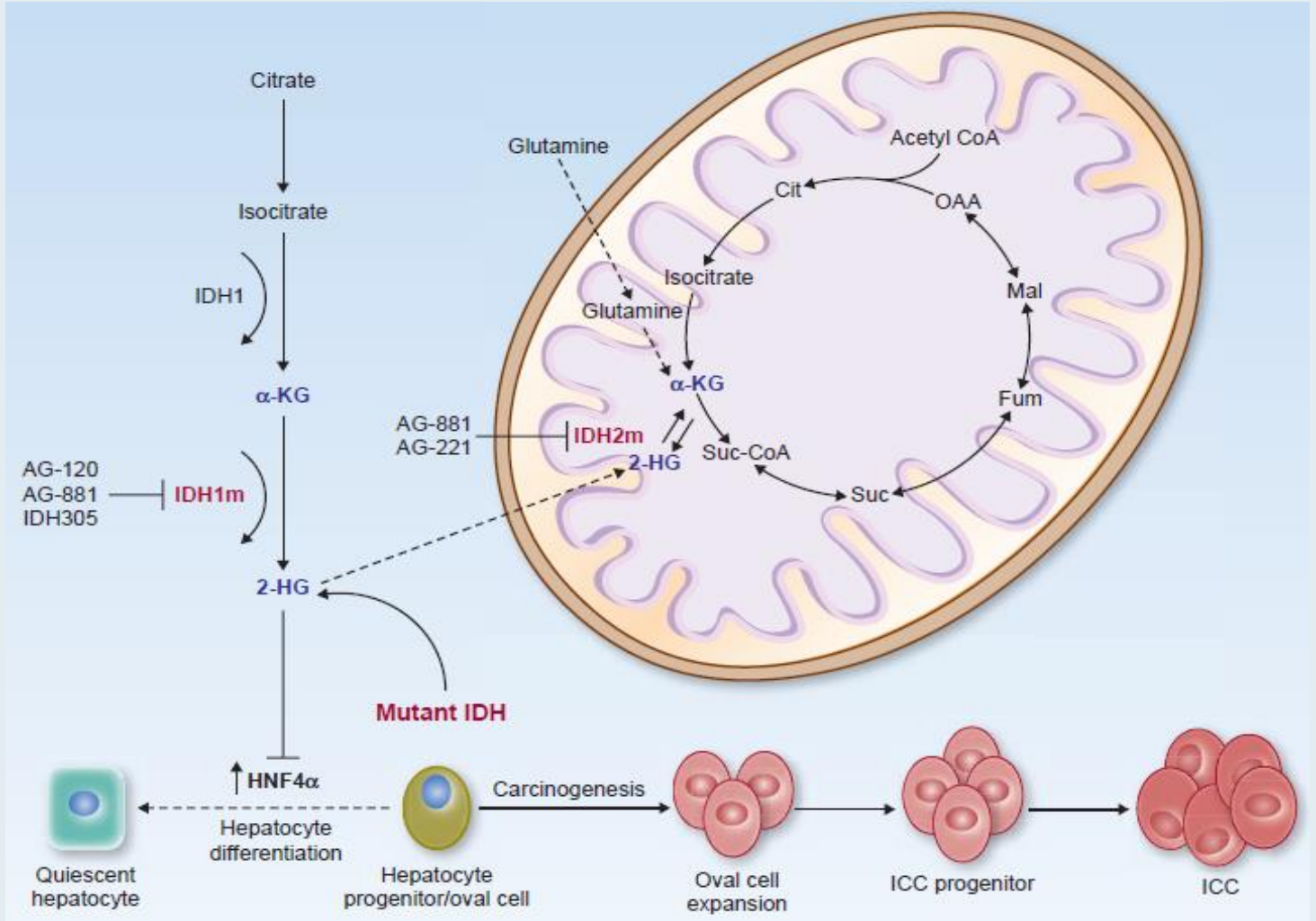
IDH Mutations as a Therapeutic Target

- IDH exists as 3 isoforms
- IDH-1 and -2 have cancer-associated mutations which happen early in tumor development
- These mutations result in novel gain-of-function enzyme activity that
  - blocks normal cell differentiation
  - promotes tumorigenesis



Valle JW et al. *Cancer Discov* 2017;7:943-62; Cairns RA et al. *Nat Rev Cancer* 2011;11:85-95.

Research

JAMA Oncology | Original Investigation

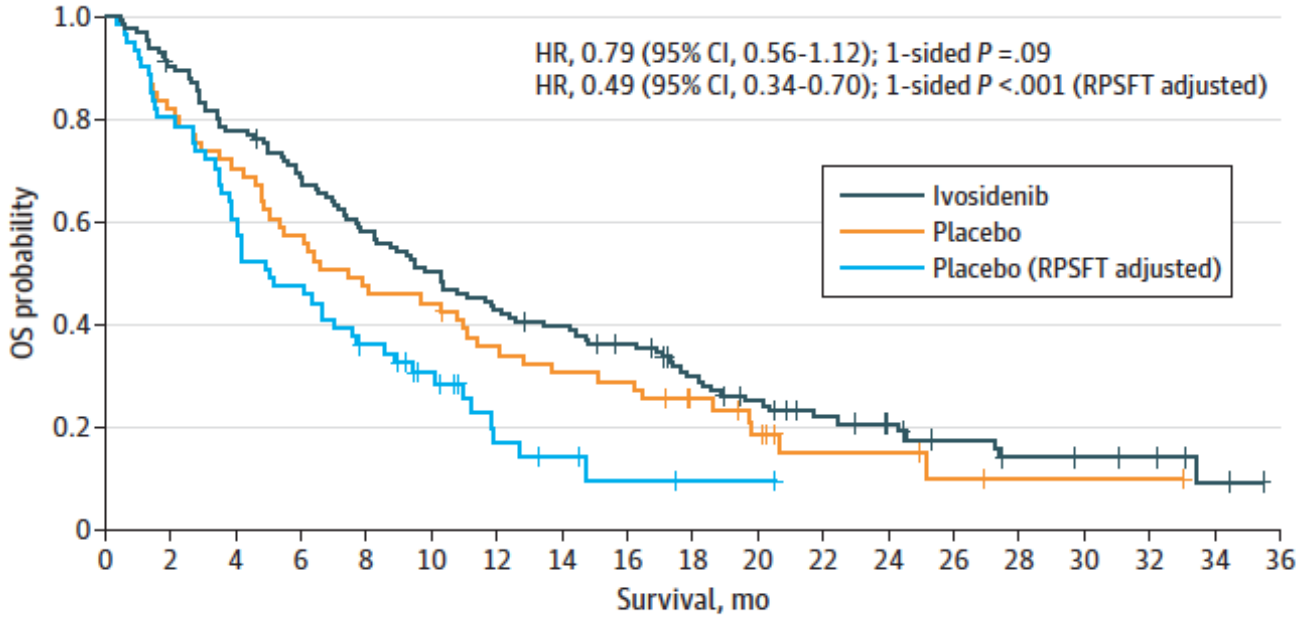
Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With *IDH1* Mutation

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 an IDH1 Mutation



No. at risk

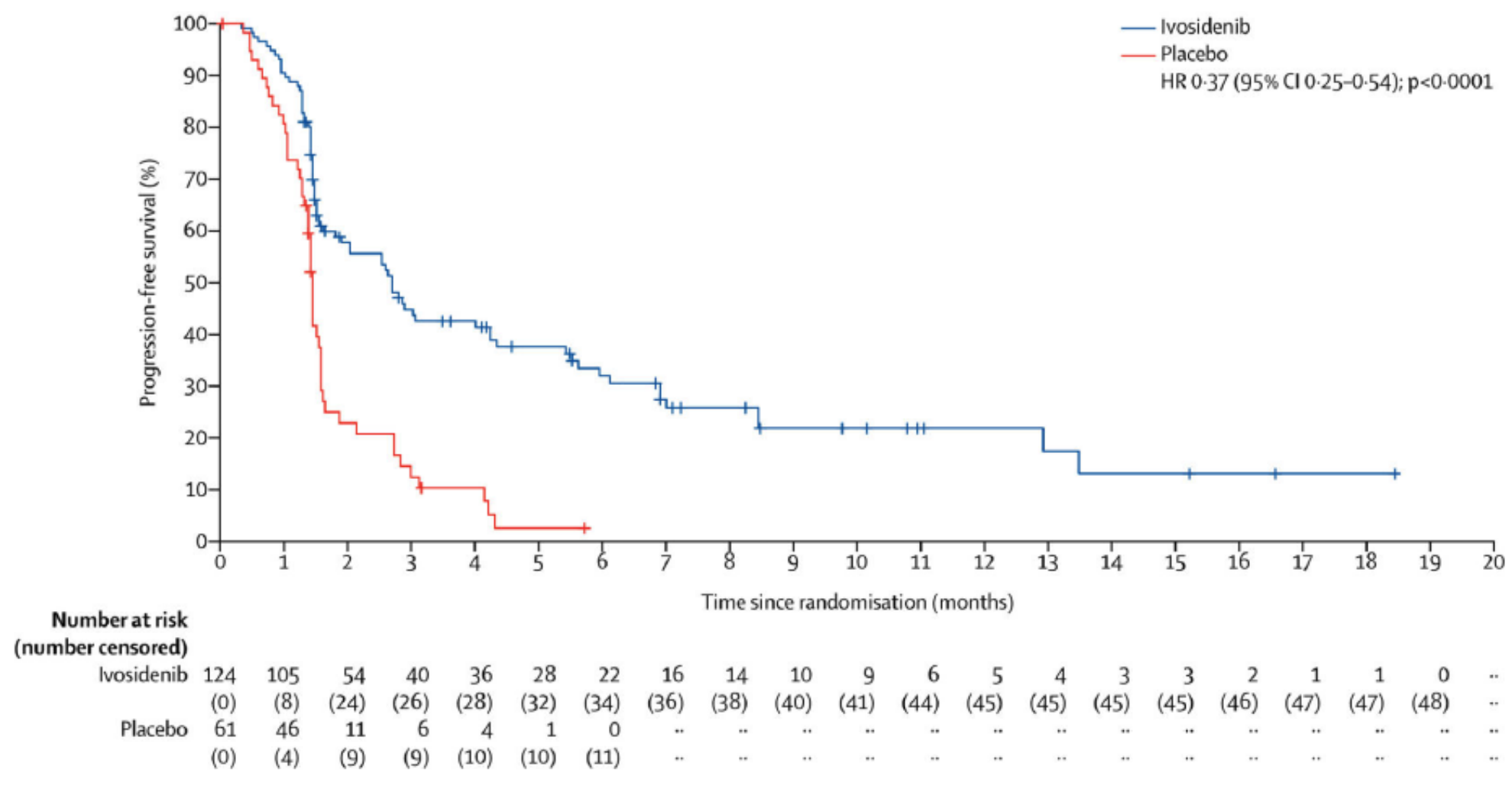
Ivosidenib	126	113	97	85	72	62	53	48	42	32	25	18	14	10	7	6	5	2
Placebo	61	50	43	35	29	27	21	18	17	12	8	4	4	2	1	1	1	
Placebo (RPSFT adjusted)	61	49	37	29	21	14	6	4	2	1	1							

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)

RPSFT = rank-preserving structural failure time

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

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Case Presentation: 55-year-old man is diagnosed with Stage IV BTC with no actionable mutations

Dr Sean Warsch (Asheville, North Carolina)

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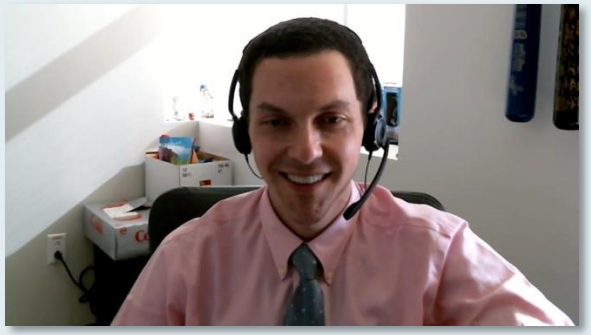

Dr Jeremy Lorber
(Beverly Hills, California)

Case Presentation: 74-year-old woman is newly diagnosed with HER2-positive carcinoma of the gallbladder of biliary tract origin with peritoneal metastases

Dr Brian Mulherin
(Indianapolis, Indiana)

Case Presentation: 67-year-old man with metastatic HER2-low (IHC 2+) gallbladder cancer receives 1L pembrolizumab/cisplatin/gemcitabine

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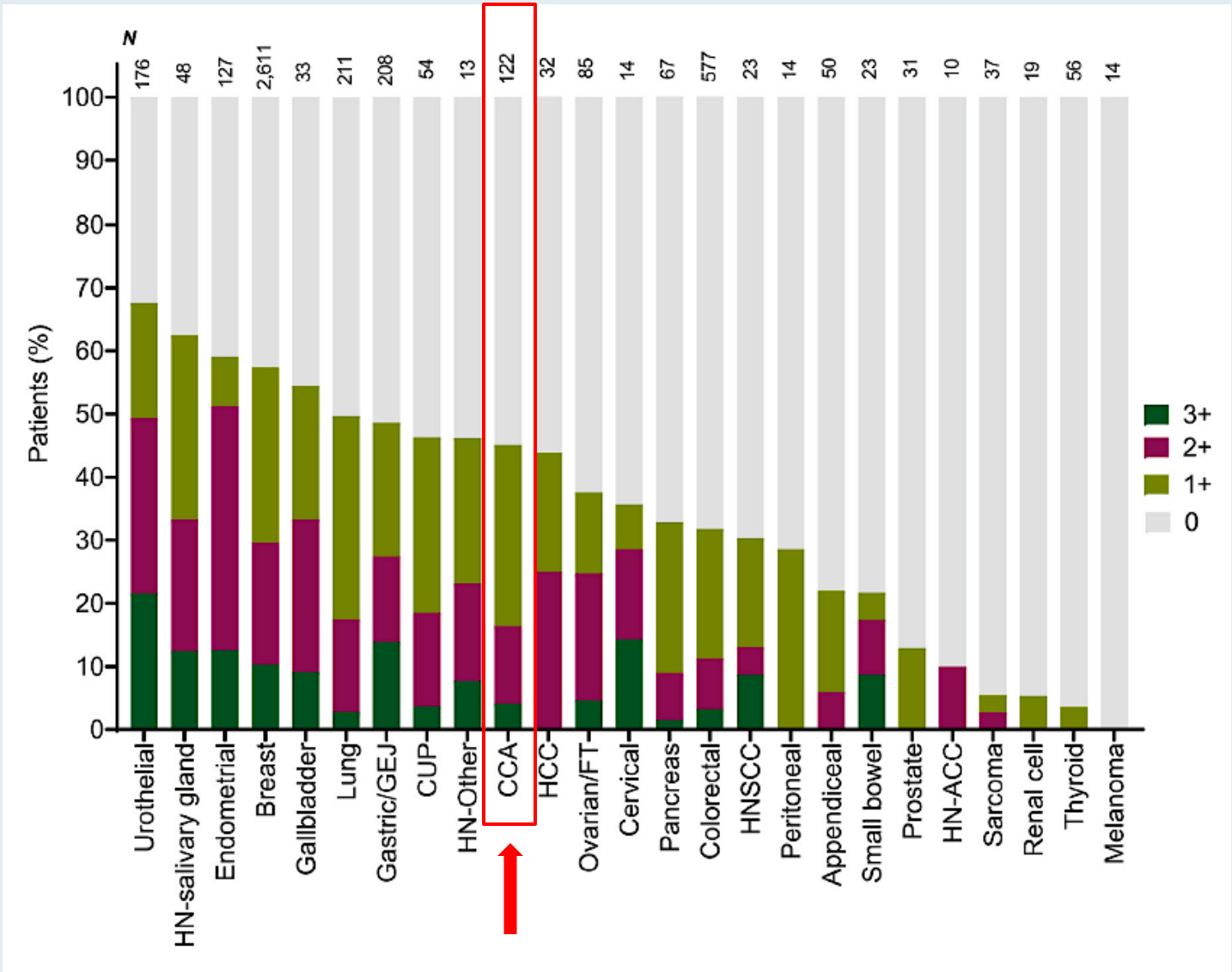
Distribution of HER2 IHC Expression Levels Across Cancers



Uzunparmak B et al. *Ann Oncol* 2023 November;34(11):1035-46.

FDA Grants Accelerated Approval to Zanidatamab for Previously Treated Unresectable or Metastatic HER2-Positive Biliary Tract Cancer

Press Release – November 20, 2024

"The Food and Drug Administration granted accelerated approval to zanidatamab-hrii, a bispecific HER2-directed antibody, for previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test.

Efficacy was evaluated in HERIZON-BTC-01 (NCT04466891), an open-label multicenter, single-arm trial in 62 patients with unresectable or metastatic HER2-positive (IHC3+) BTC. Patients were required to have received at least one prior gemcitabine-containing regimen in the advanced disease setting. The major efficacy outcome measures were objective response rate (ORR) and duration of response (DOR) as determined by an independent central review according to RECIST v1.1. ORR was 52% and median DOR was 14.9 months.

The prescribing information contains a boxed warning for embryo-fetal toxicity. The most common adverse reactions reported in at least 20% of patients who received zanidatamab-hrii were diarrhea, infusion-related reactions, abdominal pain, and fatigue.The recommended zanidatamab-hrii dose is 20 mg/kg administered as an intravenous infusion once every 2 weeks until progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-zanidatamab-hrii-previously-treated-unresectable-or-metastatic-her2

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2024 ASCO ANNUAL MEETING

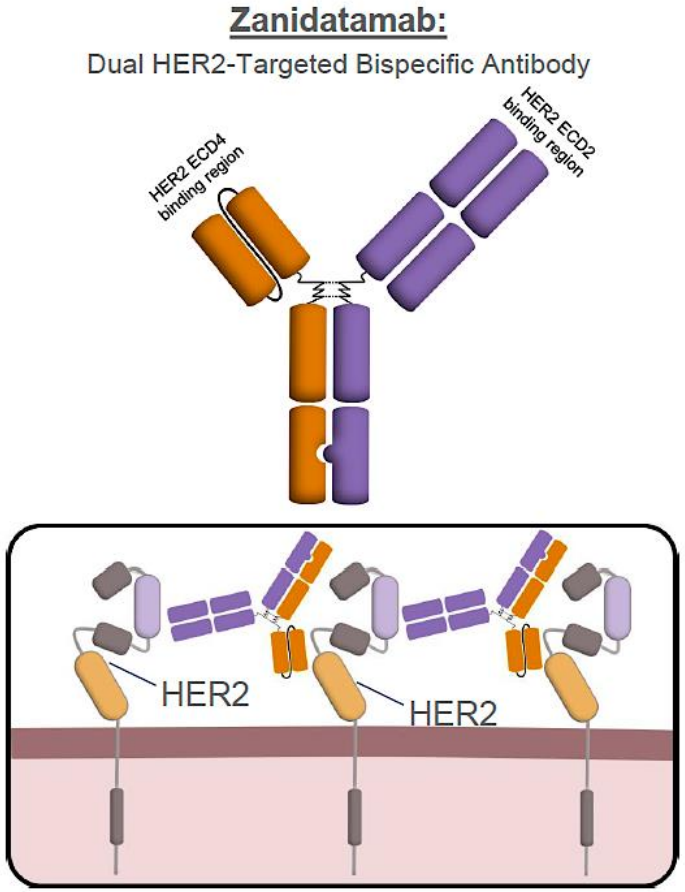
Abstract 4091

Zanidatamab in Previously Treated HER2-Positive Biliary Tract Cancer: Overall Survival and Longer Follow-Up From the Phase 2b HERIZON-BTC-01 Study

Shubham Pant,[1,*] Jia Fan,[2] Do-Youn Oh,[3] Hye Jin Choi,[4] Jin Won Kim,[5] Heung-Moon Chang,[6] Lequn Bao,[7] Hui-Chuan Sun,[2] Teresa Macarulla,[8] Feng Xie,[9] Jean-Philippe Metges,[10] Jie-Er Ying,[11] John A Bridgewater,[12] Mohamedtaki A Tejani,[13] Emerson Y Chen,[14] Harpreet Wasan,[15] Michel Ducreux,[16] Yi Zhao,[17] Phillip M Garfin,[18] James J Harding[19]

RTP RESEARCH TO PRACTICE

HERIZON-BTC-01: Zanidatamab Mechanism of Action and Study Background



- BTC accounts for less than 1% of adult cancers and is associated with a poor prognosis[1,2]
- After failure of first-line treatment, subsequent chemotherapy is associated with a median OS of approximately 6-9 months and poor tolerability[3,4]
- Zanidatamab is a humanized, IgG1-like, HER2-targeted bispecific antibody that binds to 2 distinct domains on HER2[5]
- After a median follow-up of 12.4 months (data cutoff: October 10, 2022), zanidatamab showed encouraging antitumor activity (41.3% cORR) with rapid and durable responses and a manageable safety profile in patients with previously treated HER2-positive BTC[6]

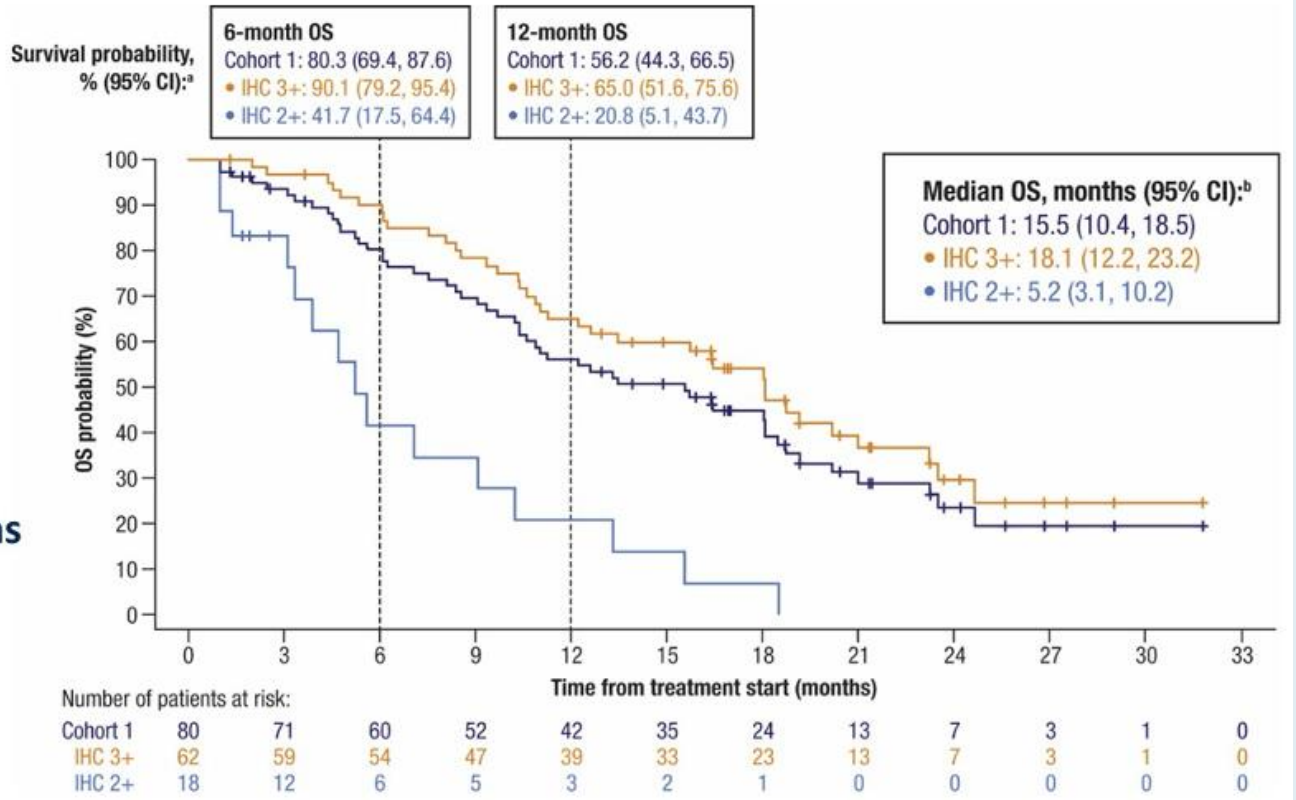
Here, we report the efficacy, including OS, and safety of zanidatamab in patients with HER2-positive BTC enrolled in HERIZON-BTC-01 with additional follow-up

cORR = confirmed objective response rate; OS = overall survival

Pant S et al. ASCO 2024;Abstract 4091; Rha SY et al. ESMO 2024;Abstract 516MO.

HERIZON-BTC-01: Long-Term Efficacy Outcomes

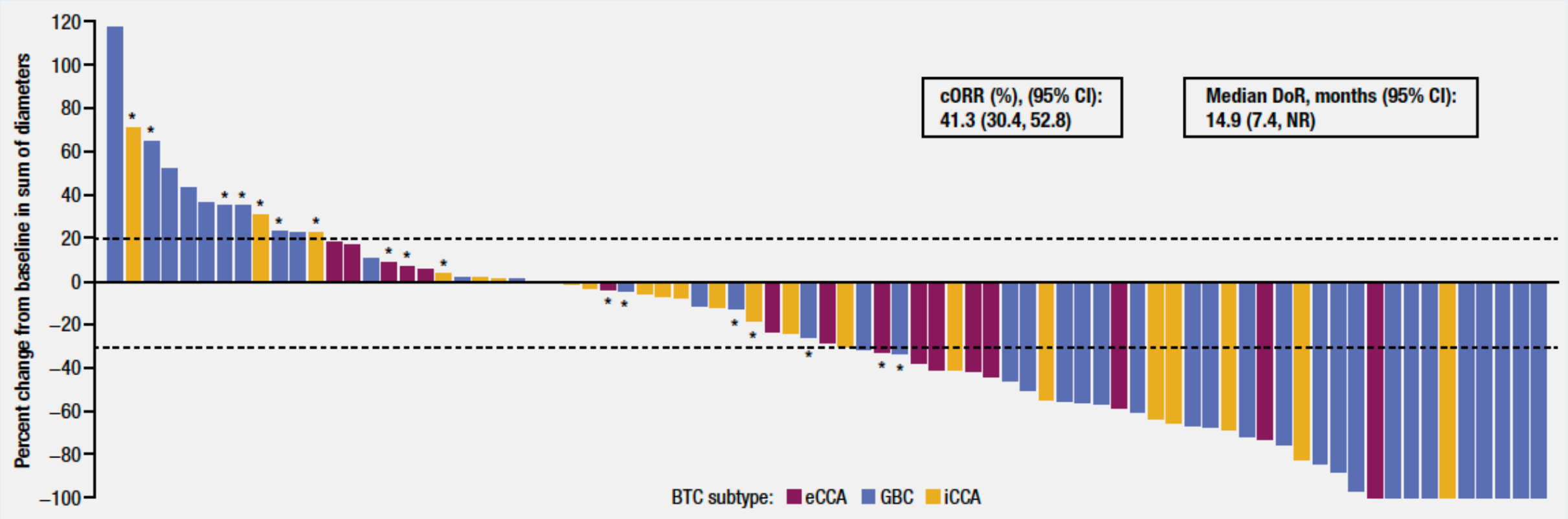
- The median (range) duration of follow-up was 22 (16-34) months (data cutoff: July 28, 2023)
- **cORR (41.3%) and DCR (68.8%) were maintained from the primary analysis;[1] 1 additional patient achieved a CR**
  - In a pre-planned subgroup analysis of cORR by HER2 expression, responses were observed in both IHC 3+ (cORR: 51.6%) and IHC 2+ (cORR: 5.6%)
- **The median DOR (95% CI) increased to 14.9 (7.4, NR) months from the primary analysis[1]**
- **The median OS (95% CI) was 15.5 (10.4, 18.5) months**



CR = complete response; NR = not reached

Pant S et al. ASCO 2024;Abstract 4091.

HERIZON-BTC-01: Target Lesion Reduction in Patients Treated with Zanidatamab



eCCA = extrahepatic cholangiocarcinoma; GBC = gallbladder cancer; iCCA = intrahepatic cholangiocarcinoma

Mercade TM et al. ESMO 2024;Abstract 62TiP.

HERIZON-BTC-01: Long-Term Safety Outcomes

- **The safety profile of zanidatamab was largely unchanged with additional follow-up**
- **There were no deaths related to zanidatamab treatment**
- **TRAEs leading to dose reductions remained infrequent**
  - Grade 3 diarrhea (n=1), grade 1 diarrhea and grade 1 nausea (n=1), and grade 2 weight decreased (n=1)
- **One patient experienced serious TRAEs since the prior analysis** (alanine aminotransferase increased and aspartate aminotransferase increased)
- **No patients discontinued treatment due to TRAEs since the prior analysis**

All Patients (Cohort 1 and Cohort 2)	N=87	
Any TEAE, n (%)	84 (96.6)	
Any TRAE, n (%)	63 (72.4)	
Grade 1-2	45 (51.7)	
Grade 3-4[a]	18 (20.7)	
Grade 5	0 (0)	
Serious TRAEs[b]	8 (9.2)	
TRAEs leading to treatment discontinuation, n (%)	2 (2.3)[c]	
Most common TRAEs,[d] n (%)	**All grades**	**Grades 3-4**
Diarrhea	32 (36.8)	4 (4.6)
Infusion-related reaction	29 (33.3)	1 (1.1)
Ejection fraction decreased	9 (10.3)	3 (3.4)
Nausea	8 (9.2)	1 (1.1)
Alanine aminotransferase increased	6 (6.9)	1 (1.1)
Aspartate aminotransferase increased	6 (6.9)	2 (2.3)
Vomiting	6 (6.9)	0 (0)
Fatigue	5 (5.7)	0 (0)
Anemia	4 (4.6)	3 (3.4)
AESI, n (%)		
Infusion-related reaction	29 (33.3)	1 (1.1)
Confirmed cardiac events	5 (5.7)	3 (3.4)
Non-infectious pulmonary toxicities	1 (1.1)	1 (1.1)

TRAE = treatment-related adverse event; TEAE = treatment-emergent adverse event

Pant S et al. ASCO 2024;Abstract 4091.

HERIZON-BTC-01: Author Conclusions

- In this long-term analysis, zanidatamab monotherapy demonstrated durable and sustained antitumor activity in previously treated patients with HER2-positive unresectable, locally advanced, or metastatic BTC; these results support the clinically meaningful benefit of continued treatment with zanidatamab
  - The cORR was maintained (41.3%) and there are now 2 complete responses
  - The median DOR increased to 14.9 months from the prior analysis
  - Zanidatamab led to a median OS of 15.5 months (18.1 months in patients with IHC 3+ tumors)
- The safety profile remained manageable with favorable tolerability and infrequent discontinuations
- The efficacy (including OS) and manageable safety profile of zanidatamab is notable in this patient population who historically have had poor outcomes and high unmet needs
- The clinical development of zanidatamab in the treatment of HER2-positive BTC continues with the ongoing, global, randomized phase 3 study (HERIZON-BTC-02; NCT06282575) that is investigating zanidatamab in combination with standard-of-care therapy in the first-line setting for patients with HER2-positive BTC

Pant S et al. ASCO 2024;Abstract 4091.

Zanidatamab Dose Optimization in Patients with HER2-Positive Biliary Tract Cancer

Trueman S et al.

Gastrointestinal Cancers Symposium 2025;Abstract 546.

Ongoing Phase III Trials Evaluating HER2-Targeted Strategies for Treatment-Naïve HER2-Positive Advanced BTC

Study	N	Eligibility	Randomization arms	Estimated primary completion
HERIZON-BTC-302	286	• Locally advanced unresectable or metastatic BTC • No more than 2 cycles of systemic therapy with gemcitabine + platinum agent +/- PD-1/L1 inhibitor (durvalumab or pembrolizumab) • No prior HER2-targeted agent	• Zanidatamab + SoC • SoC	July 2028
DESTINY-BTC01	620	• Unresectable, previously untreated, locally advanced or metastatic BTC • Histologically confirmed HER2-expressing (IHC 3+ or IHC 2+) BTC • No prior HER2-targeted agent	• T-DXd + rilvegostomig • T-DXd • Gemcitabine + platinum + durvalumab	June 2028

SoC = standard of care; T-DXd = trastuzumab deruxtecan

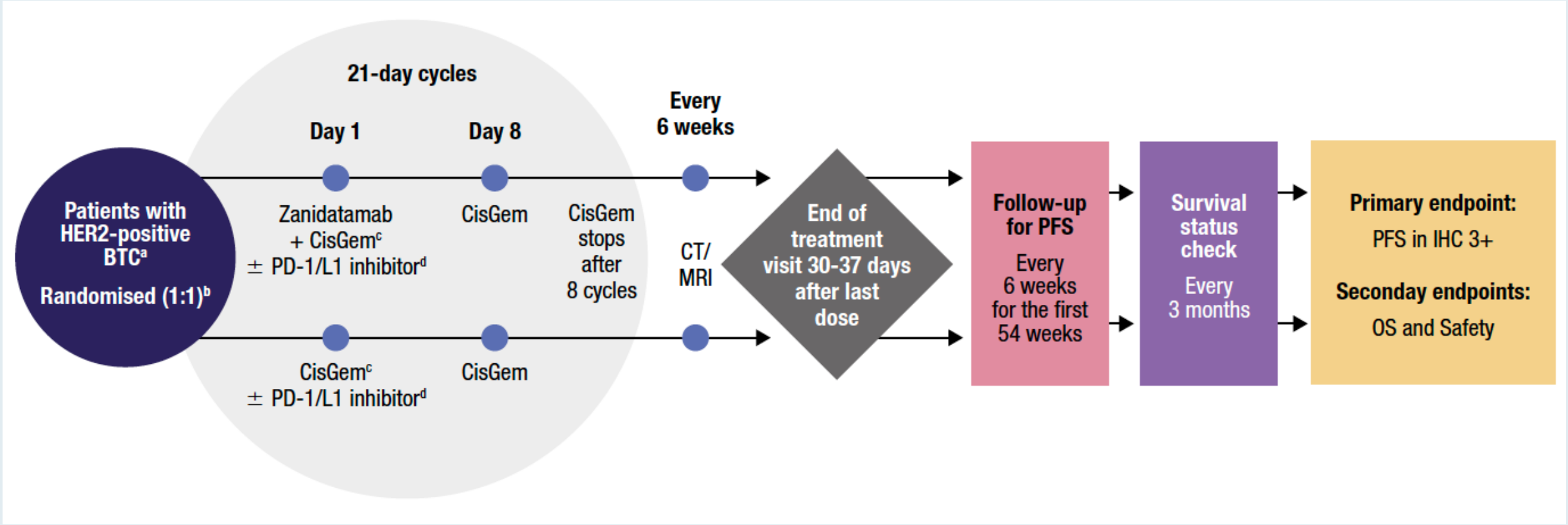
www.clinicaltrials.gov. Accessed January 2025.

HERIZON-BTC-302: A Phase 3 Study of Zanidatamab with Standard-of-Care (SOC) Therapy vs SOC Alone for First-Line Treatment of Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Advanced/ Metastatic Biliary Tract Cancer (BTC)

Harding J et al.

Gastrointestinal Cancers Symposium 2025;Abstract TPS648.

HERIZON-BTC-302: Ongoing Pivotal Phase III Trial Design

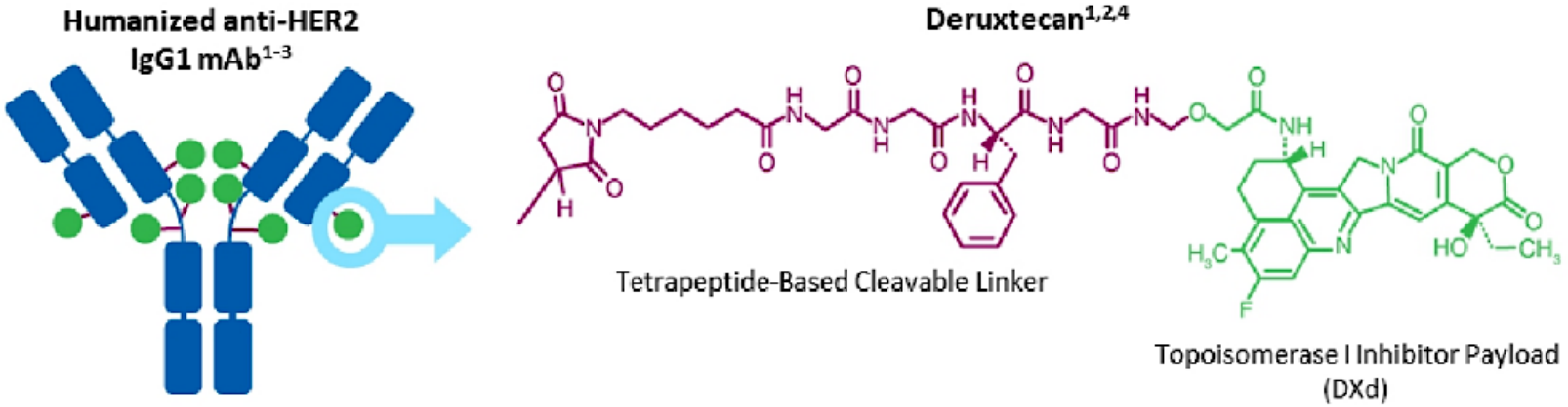


Harding J et al. Gastrointestinal Cancers Symposium 2025;Abstract TPS648.

Antibody-Drug Conjugate Trastuzumab Deruxtecan (T-DXd)

T-DXd is an ADC with 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug to antibody ratio ≈ 8
Payload with short systemic half-life
Stable linker-payload
Tumor-selective cleavable linker
Membrane-permeable payload

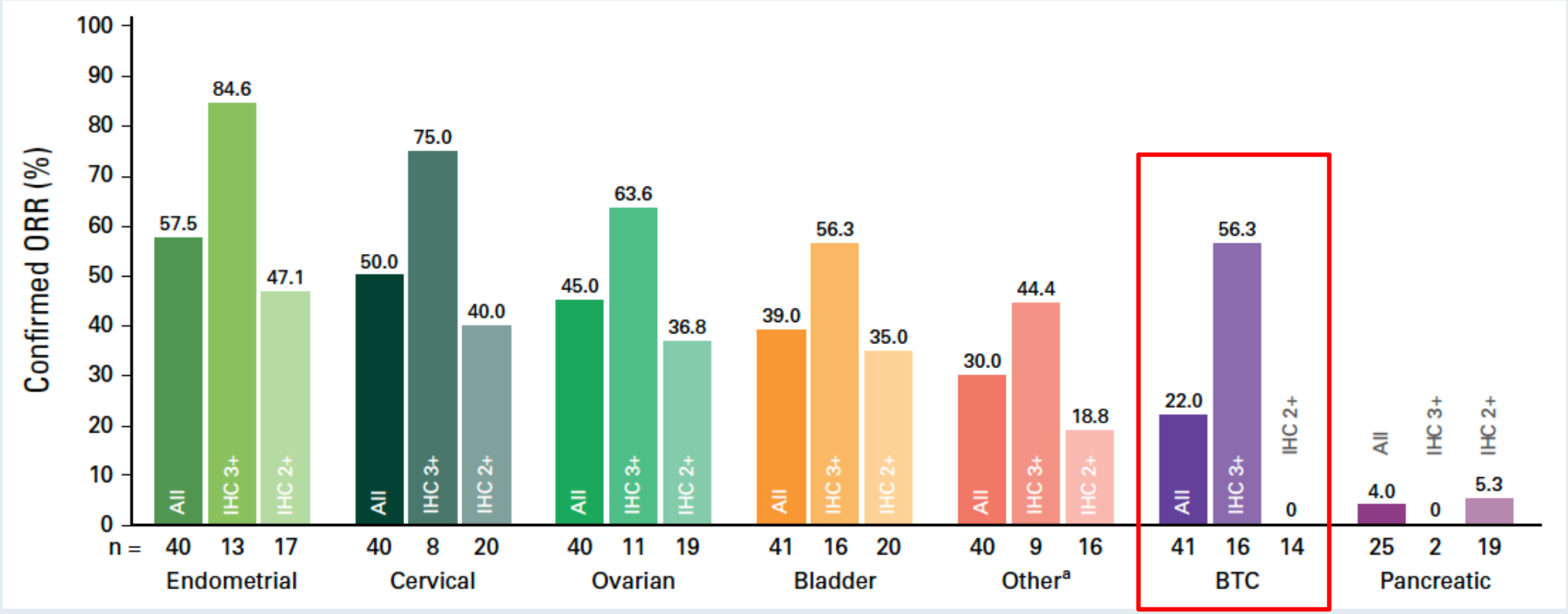
Smit EF et al. ASCO 2020;Abstract 9504.

Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

Funda Meric-Bernstam, MD[1]; Vicky Makker, MD[2,3]; Ana Oaknin, MD[4]; Do-Youn Oh, MD[5]; Susana Banerjee, PhD[6]; Antonio González-Martín, MD[7]; Kyung Hae Jung, MD[8]; Iwona Ługowska, MD[9]; Luis Manso, MD[10]; Aránzazu Manzano, MD[11]; Bohuslav Melichar, MD[12]; Salvatore Siena, MD[13]; Daniil Stroyakovskiy, MD[14]; Anitra Fielding, MBChB[15]; Yan Ma, MSc[16]; Soham Puvvada, MD[15]; Norah Shire, PhD[15]; and Jung-Yun Lee, MD[17]

J Clin Oncol 2024 January 1;42(1):47-58

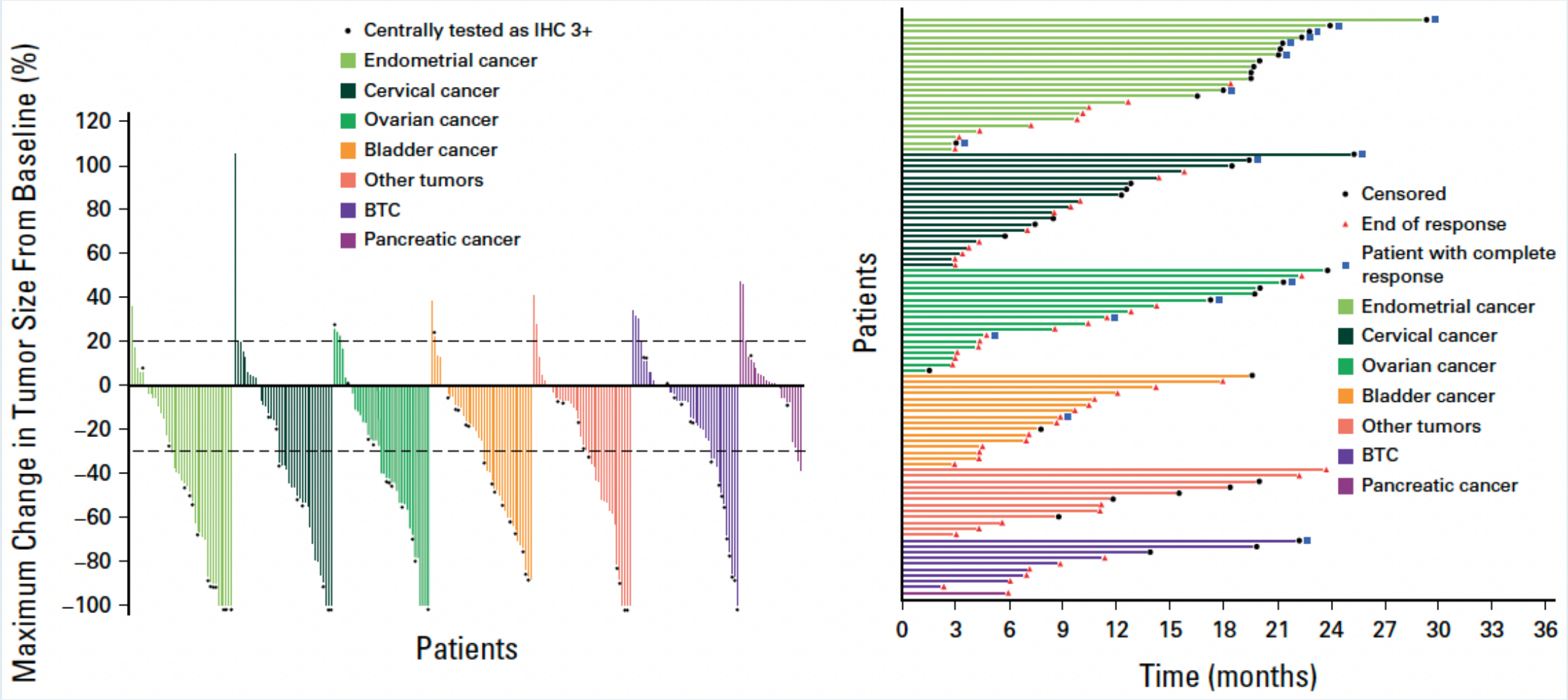
DESTINY-PanTumor02: Response with T-DXd for Patients with HER2-Expressing Solid Tumors



[a] Extramammary Paget disease, oropharyngeal neoplasm, head and neck cancer, and salivary gland cancer

Meric-Bernstam F et al. *J Clin Oncol* 2024 January 1;42(1):47-58.

DESTINY-PanTumor02: Maximum Change in Tumor Size with T-DXd for Patients with HER2-Expressing Solid Tumors



Meric-Bernstam F et al. *J Clin Oncol* 2024 January 1;42(1):47-58.

Poster 4090

Trastuzumab deruxtecan in patients with HER2-expressing biliary tract cancer and pancreatic cancer: outcomes from DESTINY-PanTumor02

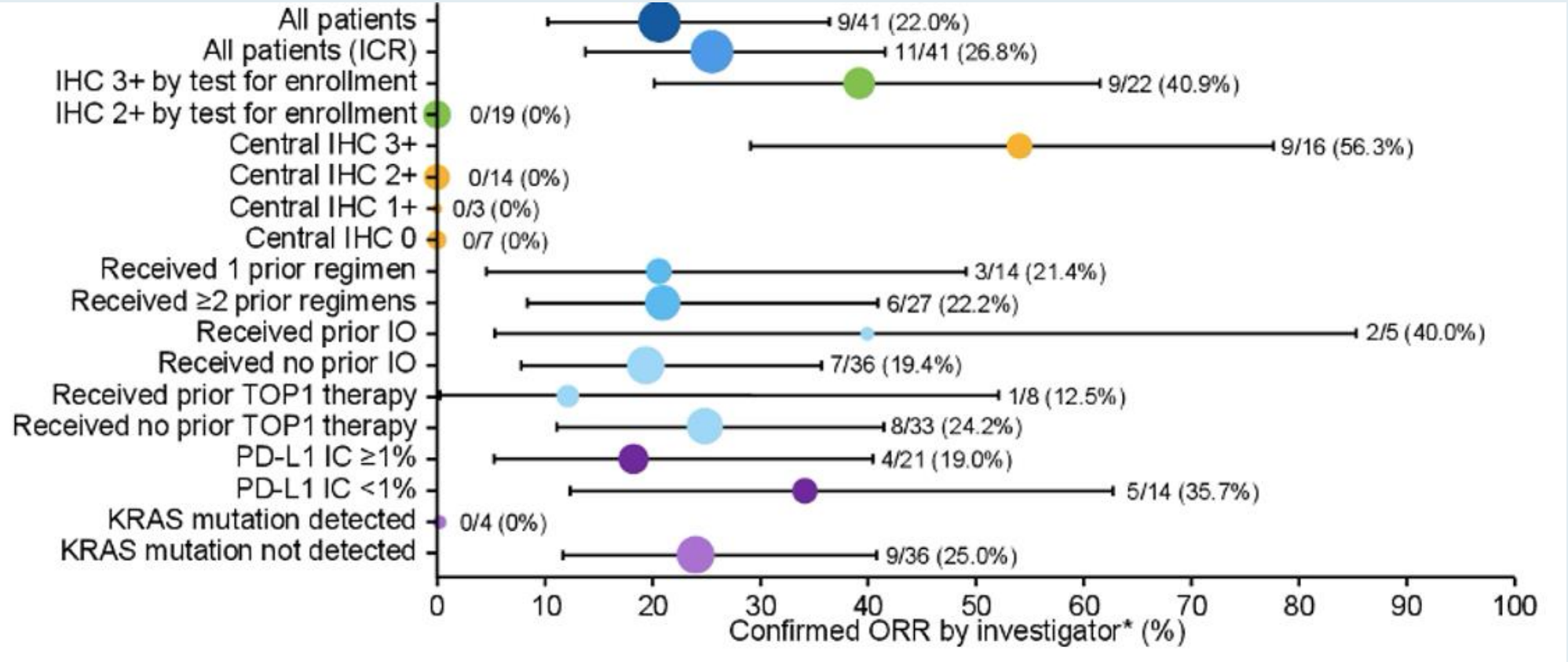
Do-Youn Oh,[1] Iwona Ługowska,[2] Daniil Stroyakovskiy,[3] Kyung Hae Jung,[4] Olivier Dumas,[5] Konstantin Penkov,[6] Arunee Dechaphunkul,[7] Ana Oaknin,[8] Seung Tae Kim,[9] Naureen Starling,[10] Busyamas Chewaskulyong,[11] Chanchai Charonpongsuntorn,[12] Deborah Doroshow,[13] Sheng-Yen Hsiao,[14] Yi-Ping Hung,[15] Lindsey Jung,[16] Nataliya Kuptsova-Clarkson,[17] Flavia Michelini,[18] Soham Puvvada,[17] Funda Meric-Bernstam[19]

[1]Department of Internal Medicine, Seoul National University Hospital, Republic of Korea; [2]Early Phase Clinical Trials Unit, Maria Skłodowska-Curie National Research Institute and Oncology Centre, Warsaw, Poland; [3]Healthcare Department, Moscow City Oncology Hospital No. 62, Russia; [4]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [5]Hôtel-Dieu de Québec, Canada; [6]Clinical Hospital "RZHD-Medicine", Saint Petersburg, Russia; [7]Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [8]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology, University Hospital Vall d'Hebron, Barcelona, Spain; [9]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Republic of Korea; [10]Gastrointestinal Unit, The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [11]Medical Oncology Unit, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Thailand; [12]Medical Oncology Unit, Department of Internal Medicine, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, Thailand; [13]Icahn School of Medicine at Mount Sinai, New York, NY, US; [14]Division of Hematology-Oncology, Department of Internal Medicine, Chi Mei Medical Center, Liouying, Tainan, Taiwan; [15]Taipei Veterans General Hospital, Taiwan; [16]AstraZeneca, Gaithersburg, MD, US; [17]Oncology R&D, AstraZeneca, Gaithersburg, MD, US; [18]Translational Medicine, Oncology R&D, AstraZeneca, Waltham, MA, US; [19]Department of Investigational Cancer Therapeutics, University of Texas MD Anderson Cancer Center, Houston, TX, US

ASCO 2024

RTP RESEARCH TO PRACTICE

DESTINY-PanTumor02 Trial of T-DXd for Patients with HER2-Expressing BTC and Pancreatic Cancer: ORR in the BTC Cohort

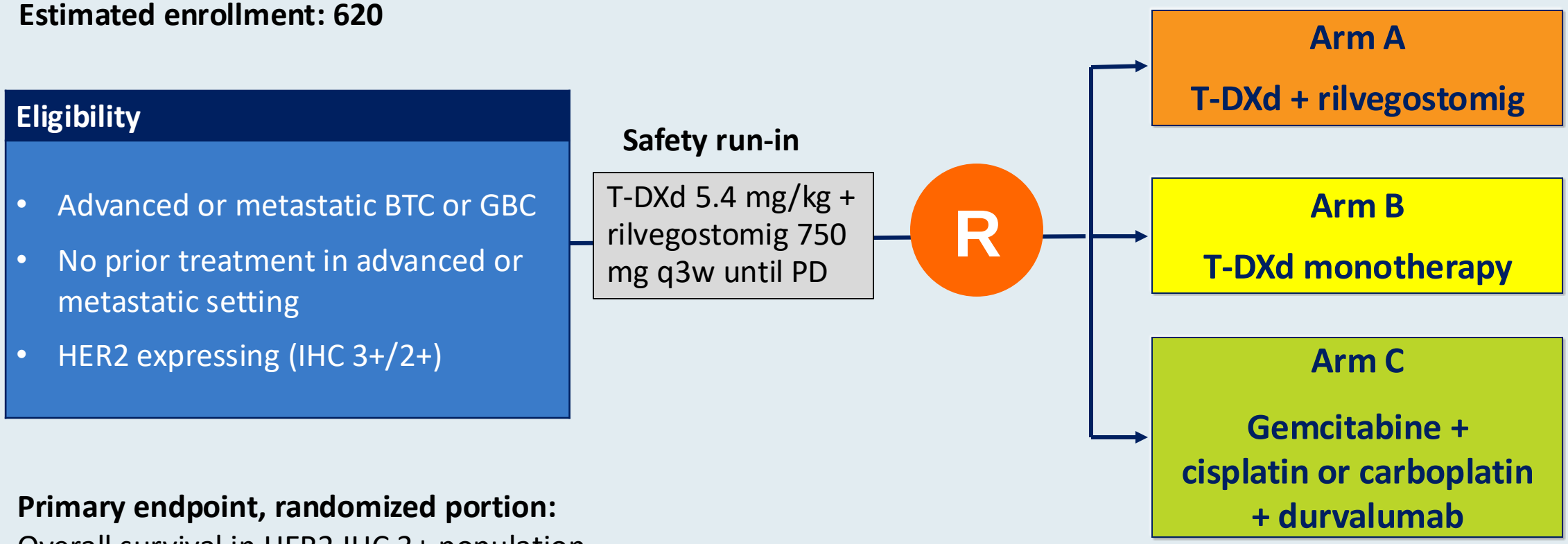


ORR = objective response rate; IHC = immunohistochemistry; IO = immuno-oncology; IC = immune cells

Oh D-Y et al. ASCO 2024;Abstract 4090.

DESTINY-BTC01: Ongoing Phase III Trial of T-DXd and Rilvegostomig versus Standard of Care for First-Line, Advanced HER2-Expressing BTC

Trial identifier: NCT06467357 (Open)
Estimated enrollment: 620



Primary endpoint, randomized portion:
Overall survival in HER2 IHC 3+ population

GBC = gallbladder cancer; PD = disease progression

Ikeda M et al. ESMO Asia Congress 2024;Abstract 261TiP; www.clinicaltrials.gov. Accessed January 2025.

BARCELONA 2024 ESMO congress

516MO – Zanidatamab + Chemotherapy in First-Line Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Advanced/Metastatic Colorectal Cancer (CRC)

Part 1 of a Phase 2 Study

Sun Young Rha,[1] Keun-Wook Lee,[2] Soohyeon Lee,[3] Yoon-Koo Kang,[4] Sreenivasa Chandana,[5] Anrried Escalante,[6] Chengzhi Xie,[7] Phillip Garfin,[8] Syma Iqbal[9]

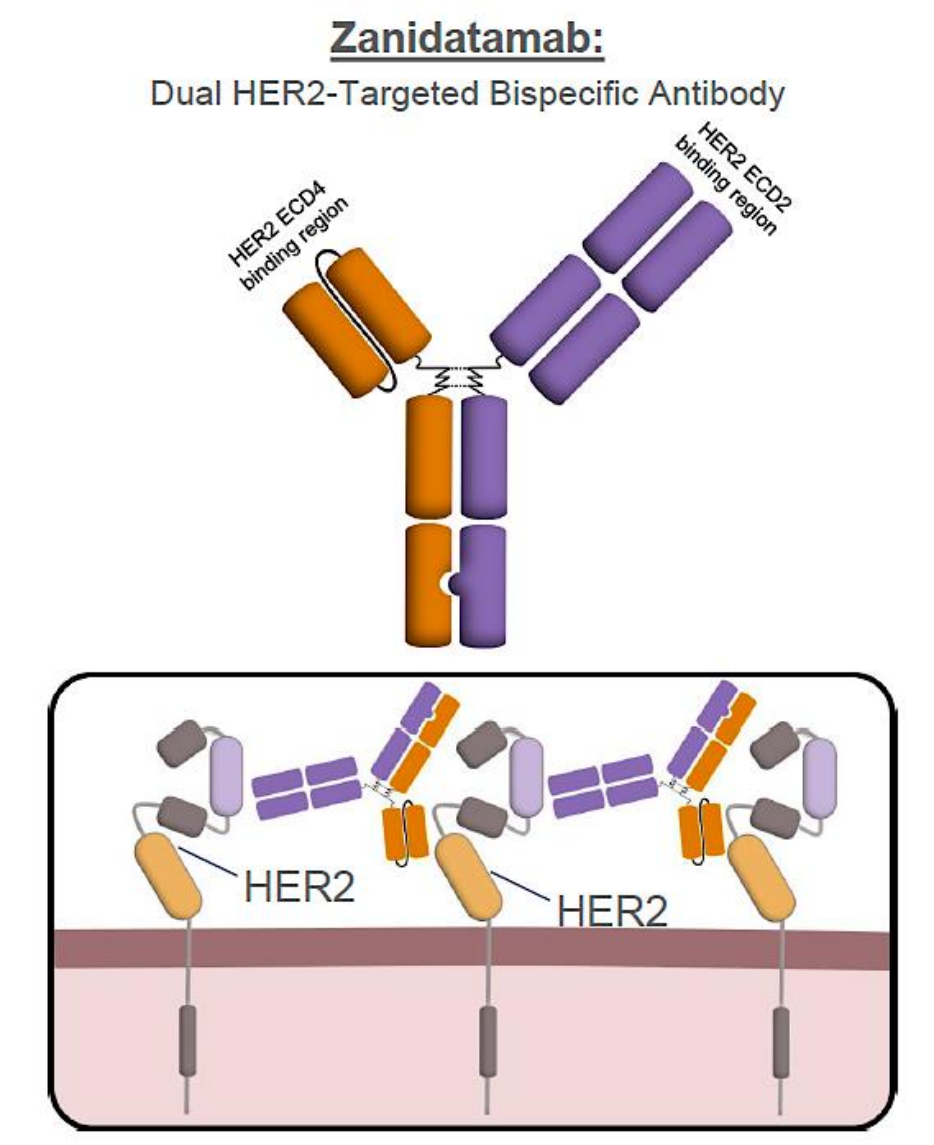
[1]Yonsei Cancer Center, Yonsei University College of Medicine, Yonsei University Health System, Seoul, South Korea; [2]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; [3]Korea University Anam Hospital, Korea University College of Medicine, Seoul, South Korea; [4]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [5]The Cancer & Hematology Centers, Grand Rapids, MI, USA; [6]ICEGCLINIC, Santiago, Chile; [7]Jazz Pharmaceuticals, Philadelphia, PA, USA; [8]Jazz Pharmaceuticals, Palo Alto, CA, USA; [9]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA

Presenter: Professor Sun Young Rha

14 September 2024

RTP RESEARCH TO PRACTICE

Zanidatamab: Mechanism of Action

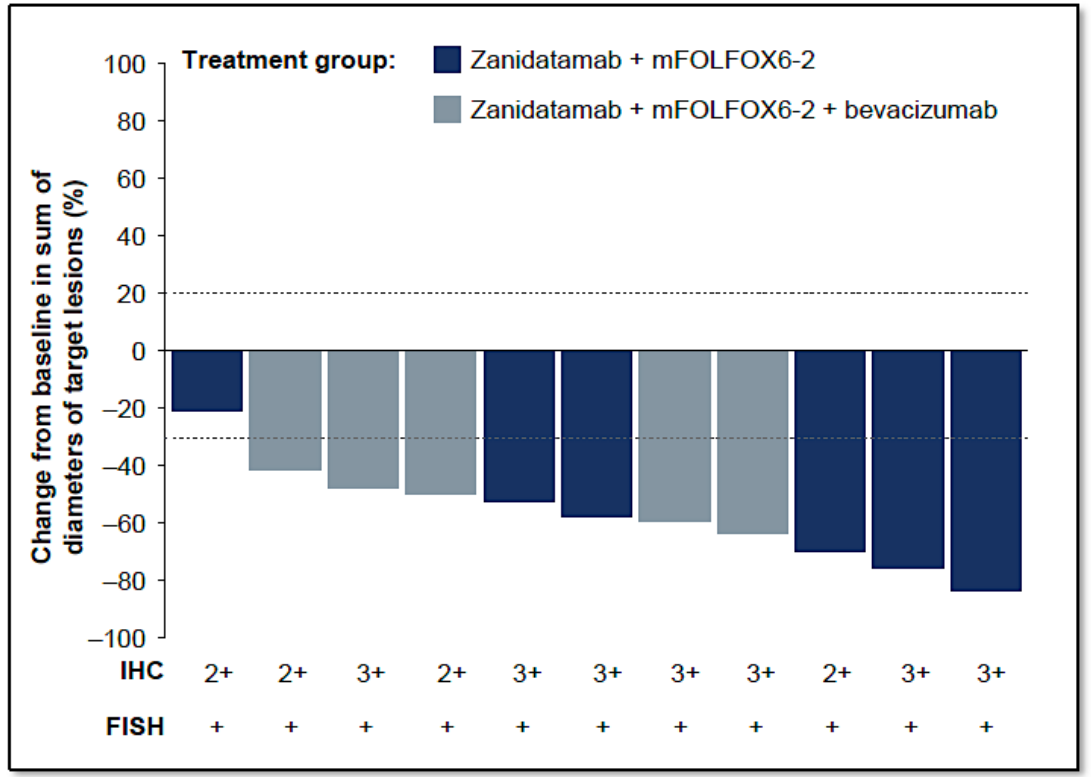


Rha SY et al. ESMO 2024;Abstract 516MO.

Response to First-Line Zanidatamab in Combination with Chemotherapy for Patients with HER2-Positive Metastatic Colorectal Cancer (mCRC)

	Zanidatamab + mFOLFOX6-2 (n=6)	Zanidatamab + mFOLFOX6-2 + bevacizumab (n=5)	Total (N=11)
cORR			
n (%)	5 (83.3)	5 (100)	10 (90.9)
95% CI	35.9, 99.6	47.8, 100	58.7, 99.8
cBOR, n (%)			
CR	0 (0)	0 (0)	0 (0)
PR	5 (83.3)	5 (100)	10 (90.9)
SD	1 (16.7)	0 (0)	1 (9.1)
PD	0 (0)	0 (0)	0 (0)
DCR[b]			
n (%)	6 (100)	5 (100)	11 (100)
95% CI	54.1, 100	47.8, 100	71.5, 100

Median (range) duration of response:
Not reached (2.9+-16.7+) months



Dotted lines indicate 20% increase or 30% decrease in sum of diameters of target tumours.

Rha SY et al. ESMO 2024;Abstract 516MO.

Adverse Events with First-Line Zanidatamab in Combination with Chemotherapy for Patients with HER2-Positive mCRC

	Zanidatamab + mFOLFOX6-2 (n=6)		Zanidatamab + mFOLFOX6-2 + bevacizumab (n=7)[a]		Total (N=13)	
Any TEAE, n (%)	6 (100)		7 (100)		13 (100)	
Any TRAE,[b] n (%) Grade 1-2 Grade 3-4 Grade 5	6 (100) 4 (66.7) 2 (33.3) 0 (0)		7 (100) 4 (57.1) 3 (42.9) 0 (0)		13 (100) 8 (61.5) 5 (38.5) 0 (0)	
Serious TRAE,[b] n (%)	1 (16.7)		1 (14.3)		2 (15.4)	
TRAEs leading to zanidatamab discontinuation, n (%)	0 (0)		0 (0)		0 (0)	
Most common TRAEs,[b,c] n (%)	**Any grade**	**Grade 3-4**	**Any grade**	**Grade 3-4**	**Any grade**	**Grade 3-4**
Diarrhoea	4 (66.7)	1 (16.7)	7 (100)	2 (28.6)	11 (84.6)	3 (23.1)
Nausea	4 (66.7)	0 (0)	5 (71.4)	1 (14.3)	9 (69.2)	1 (7.7)
Peripheral sensory neuropathy	4 (66.7)	0 (0)	3 (42.9)	1 (14.3)	7 (53.8)	1 (7.7)
Fatigue	1 (16.7)	0 (0)	3 (42.9)	1 (14.3)	4 (30.8)	1 (7.7)
Infusion-related reaction	2 (33.3)	0 (0)	2 (28.6)	0 (0)	4 (30.8)	0 (0)
Stomatitis	3 (50.0)	0 (0)	1 (14.3)	0 (0)	4 (30.8)	0 (0)
Ejection fraction decreased	2 (33.3)	0 (0)	1 (14.3)	1 (14.3)	3 (23.1)	1 (7.7)
Vomiting	1 (16.7)	0 (0)	2 (28.6)	1 (14.3)	3 (23.1)	1 (7.7)

- Two of 12 DLT-evaluable patients had DLTs (diarrhoea) – 1 in each regimen
  - ✓ Diarrhoea resolved with concomitant medication
- Three serious TRAEs in 2 patients
  - ✓ One patient experienced dehydration[d]
  - ✓ One patient experienced colitis and acute kidney injury
- No discontinuations of zanidatamab due to TRAEs and no treatment-related deaths

Rha SY et al. ESMO 2024;Abstract 516MO.

Agenda

Introduction: Biology and Epidemiology; Classification

Module 1: Localized Biliary Tract Cancers (BTCs)

Module 2: First-Line Treatment of Metastatic BTC

Module 3: HER2-Positive Advanced BTC

Module 4: Management of Mixed Hepatocellular Carcinoma (HCC)/BTC Tumors

Module 5: Advanced Cholangiocarcinoma with an FGFR2 Fusion

Module 6: Other Important Issues in BTC

Teaching Cases from Investigators: The Application of Available Research to the Clinical Care of Patients with Hepatocellular Carcinoma

A CME Symposium Held in Conjunction with the 2025 ASCO® Gastrointestinal Cancers Symposium

Thursday, January 23, 2025

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

Faculty

Anthony El-Khoueiry, MD

Aiwu Ruth He, MD, PhD

Richard S Finn, MD

Stacey Stein, MD

Moderator

Stephen “Fred” Divers, MD

RTP RESEARCH TO PRACTICE

Management of mixed HCC/BTC tumors

Research To Practice at 2025 ASCO® Gastrointestinal Cancers Symposium

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Biology and Epidemiology; Classification

Module 1: Localized Biliary Tract Cancers (BTCs)

Module 2: First-Line Treatment of Metastatic BTC

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Module 5: Advanced Cholangiocarcinoma with an FGFR2 Fusion

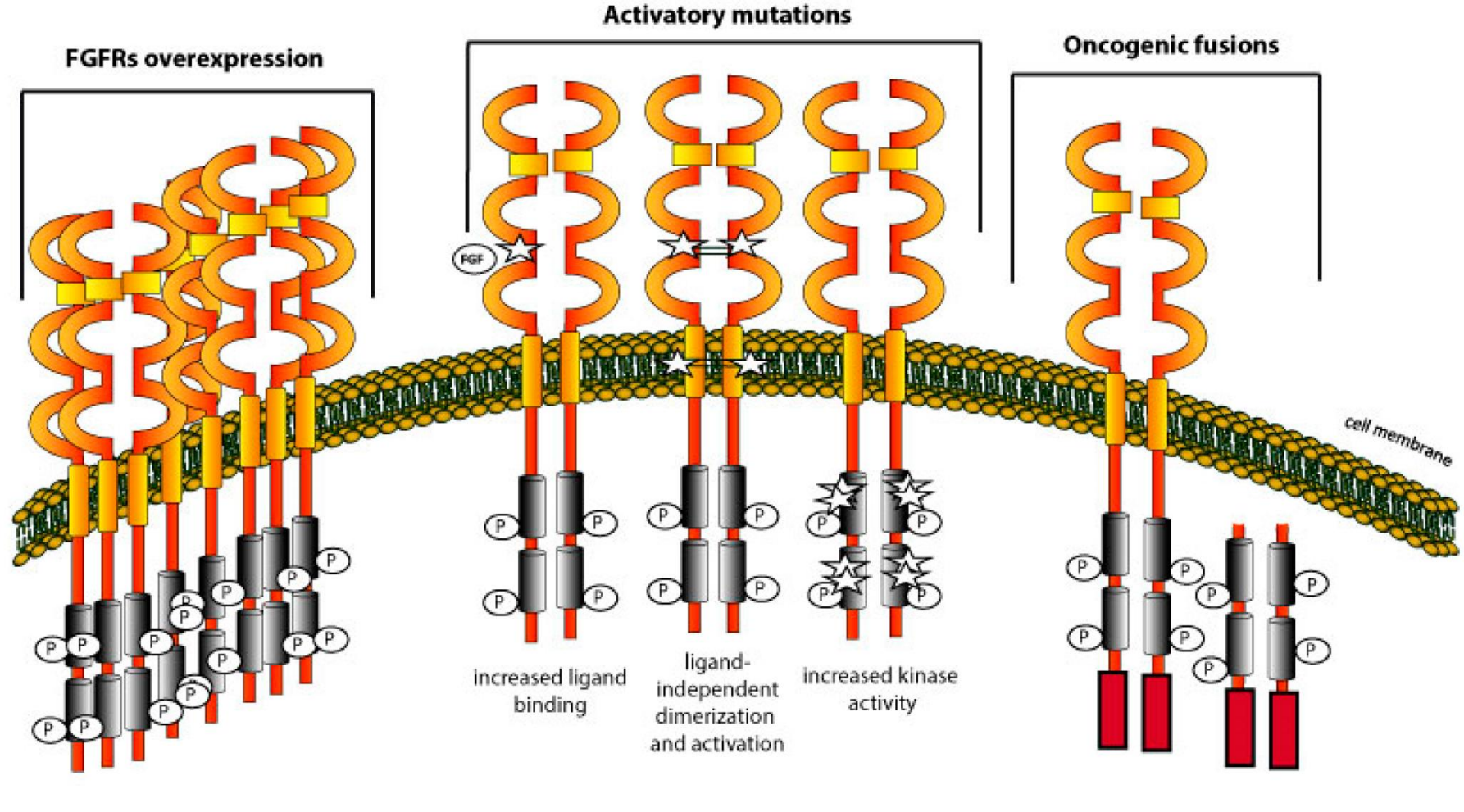
Module 6: Other Important Issues in BTC

Case Presentation: 78-year-old man presents with BTC with an FGFR2-WRN fusion

Dr Sean Warsch (Asheville, North Carolina)

RTP RESEARCH TO PRACTICE

Targeting Cellular Trafficking of FGFR as a Therapeutic Target for Intrahepatic Cholangiocarcinoma



Porębska N et al. *J Clin Med* 2019 December 20;8(1):7.

Efficacy of FDA-Approved FGFR Inhibitors for FGFR2 Fusion-Positive Cholangiocarcinoma

	Pemigatinib (N = 108)	Futibatinib (N = 67)
Objective response rate	37.0%	42.0%
Disease control rate	82.4%	83.0%
Median progression-free survival	7.0 mo	9.0 mo
Median overall survival	17.5 mo	21.7 mo
Toxicities	Hyperphosphatemia, alopecia, diarrhea	Hyperphosphatemia, diarrhea, dry mouth

Vogel A et al. *ESMO Open* 2024;9(6):103488; Goyal L et al. *N Engl J Med* 2023;388:228-39.

RTP RESEARCH TO PRACTICE

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

ORIGINAL RESEARCH

An open-label study of pemigatinib in cholangiocarcinoma: final results from FIGHT-202☆

A. Vogel[1,2,3*], V. Sahai[4], A. Hollebecque[5], G. M. Vaccaro[6], D. Melisi[7], R. M. Al Rajabi[8], A. S. Paulson[9], M. J. Borad[10], D. Gallinson[11], A. G. Murphy[12], D.-Y. Oh[13], E. Dotan[14], D. V. Catenacci[15], E. Van Cutsem[16], C. F. Lihou[17], H. Zhen[17], M. L. Veronese[18] & G. K. Abou-Alfa[19,20,21]

[1]Hannover Medical School, Hannover, Germany; [2]Toronto General Hospital, Toronto; [3]Princess Margaret Cancer Centre, Toronto, Canada; [4]University of Michigan, Ann Arbor, USA; [5]Gustave Roussy Cancer Center, Paris, France; [6]Providence Cancer Center, Portland, USA; [7]Università degli studi di Verona, Verona, Italy; [8]University of Kansas Medical Center, Kansas City; [9]Baylor University Medical Center, Dallas; [10]Mayo Clinic Cancer Center, Phoenix; [11]Morristown Memorial Hospital, Morristown; [12]Johns Hopkins University School of Medicine, Baltimore, USA; [13]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Integrated Major in Innovative Medical Science, Seoul National University Graduate School, Seoul, Republic of Korea; [14]Fox Chase Cancer Center, Philadelphia; [15]University of Chicago Medicine, Chicago, USA; [16]University Hospitals Gasthuisberg, Leuven & University of Leuven, Leuven, Belgium; [17]Incyte Corporation, Wilmington, USA; [18]Incyte International Biosciences Sàrl, Morges, Switzerland; [19]Memorial Sloan Kettering Cancer Center, New York; [20]Weill Medical College at Cornell University, New York, USA; [21]Trinity College Dublin School of Medicine, Dublin, Ireland

2024;9(6):103488.

FIGHT-202 Final Results: Response to Pemigatinib

Parameter	*FGFR2* fusions or rearrangements (n = 108)	Other *FGF/FGFR* alterations (n = 20)	No *FGF/FGFR* alterations (n = 17)
Duration of follow-up, median (range), months	42.9 (19.9-52.2)	47.5 (43.7-51.1)	51.9 (49.5-53.7)
ORR, *n* (%)	40 (37.0)	0	0
95% CI	27.9-46.9	0-16.8	0-19.5
Best overall response, *n* (%)			
CR	3 (2.8)	0	0
PR	37 (34.3)	0	0
SD	49 (45.4)	8 (40.0)	3 (17.6)
Progressive disease	16 (14.8)	7 (35.0)	11 (64.7)
Not evaluable	3 (2.8)	5 (25.0)	3 (17.6)
Time to response, median (range), months	2.7 (0.7-16.6)	—	—
DOR			
Events, *n* (%)	30 (75.0)	0	0
Censored, *n* (%)	10 (25.0)	0	0
Median (95% CI), months	9.1 (6.0-14.5)	—	—
≥12 months, *n* (%)[a]	12 (30.0)	—	—
Kaplan—Meier estimate (95% CI)			
6 months	67.8 (50.4-80.3)	—	—
12 months	41.2 (24.8-56.8)	—	—
DCR, *n* (%)	89 (82.4)	8 (40.0)	3 (17.6)
95% CI	73.9-89.1	19.1-63.9	3.8-43.4

PR = partial response; SD = stable disease

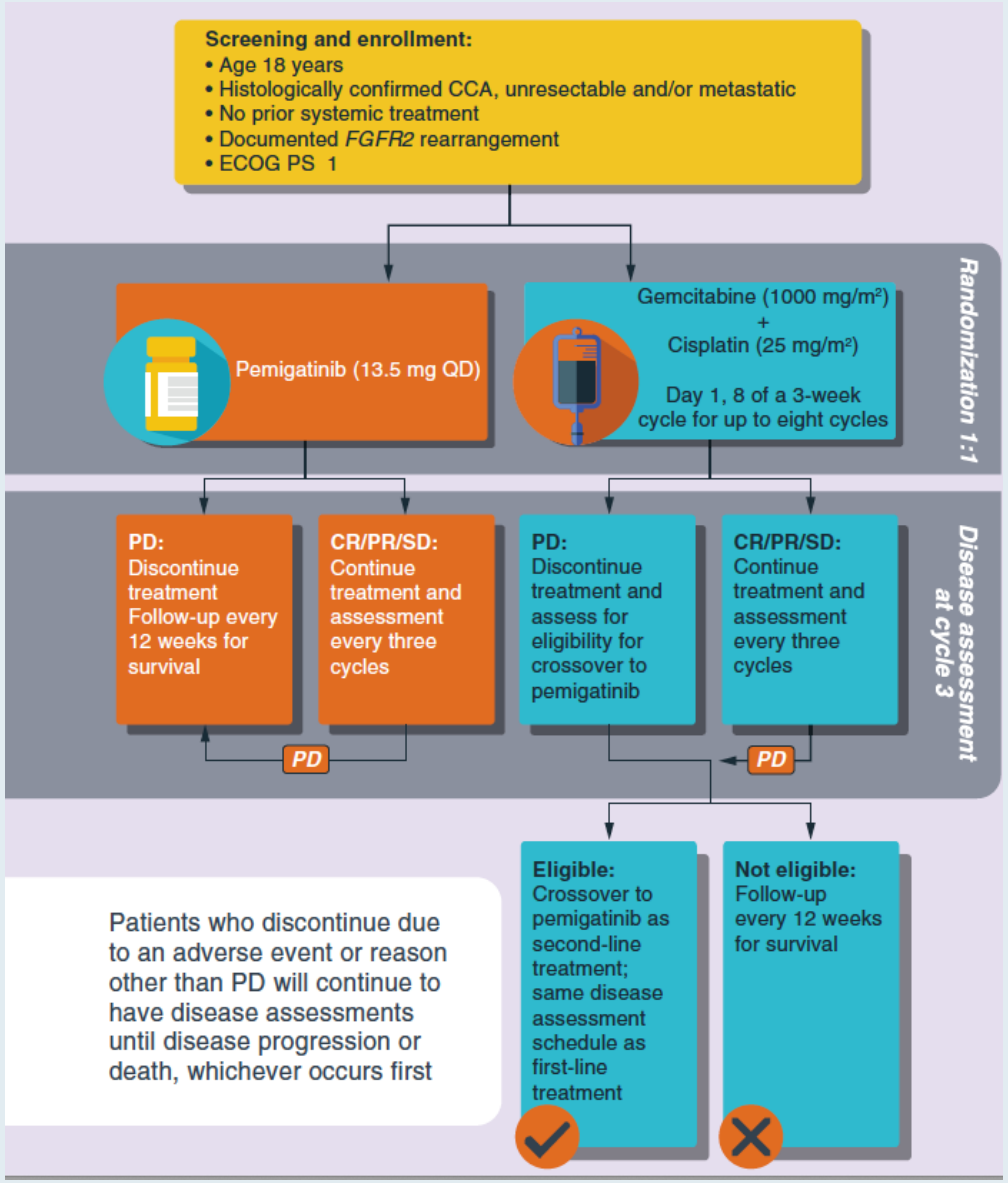
Vogel A et al. *ESMO Open* 2024;9(6):103488.

RTP RESEARCH TO PRACTICE

FIGHT-302: Ongoing Phase III Trial of First-Line Pemigatinib versus Gemcitabine and Cisplatin for Advanced Cholangiocarcinoma with FGFR2 Rearrangements

Trial identifier: NCT03656536 (Closed)
Actual enrollment: 167

Primary endpoint: Progression-free survival



Bekaii-Saab T et al. *Future Oncol* 2020;16(30):2385-99; www.cllinicaltrials.gov. Accessed January 2025.

The NEW ENGLAND JOURNAL of MEDICINE

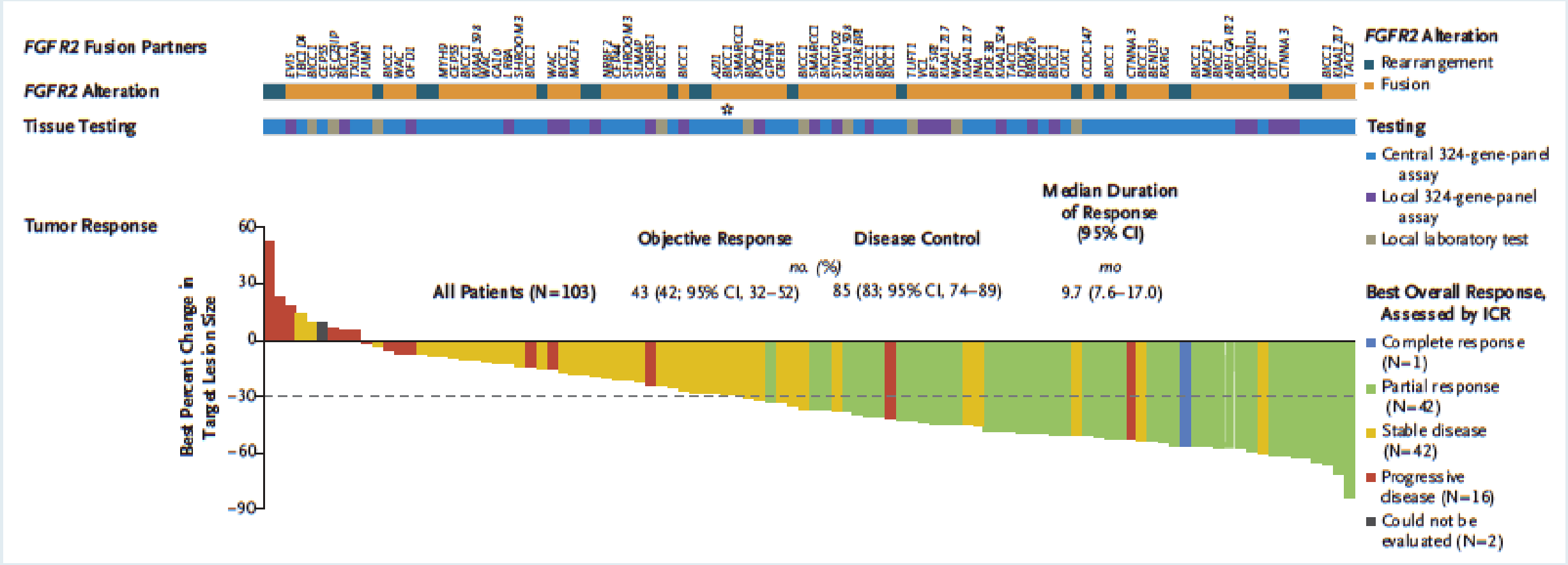
ORIGINAL ARTICLE

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



Median PFS: 9.0 mos
Median OS: 21.7 mos

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

Agenda

Introduction: Biology and Epidemiology; Classification

Module 1: Localized Biliary Tract Cancers (BTCs)

Module 2: First-Line Treatment of Metastatic BTC

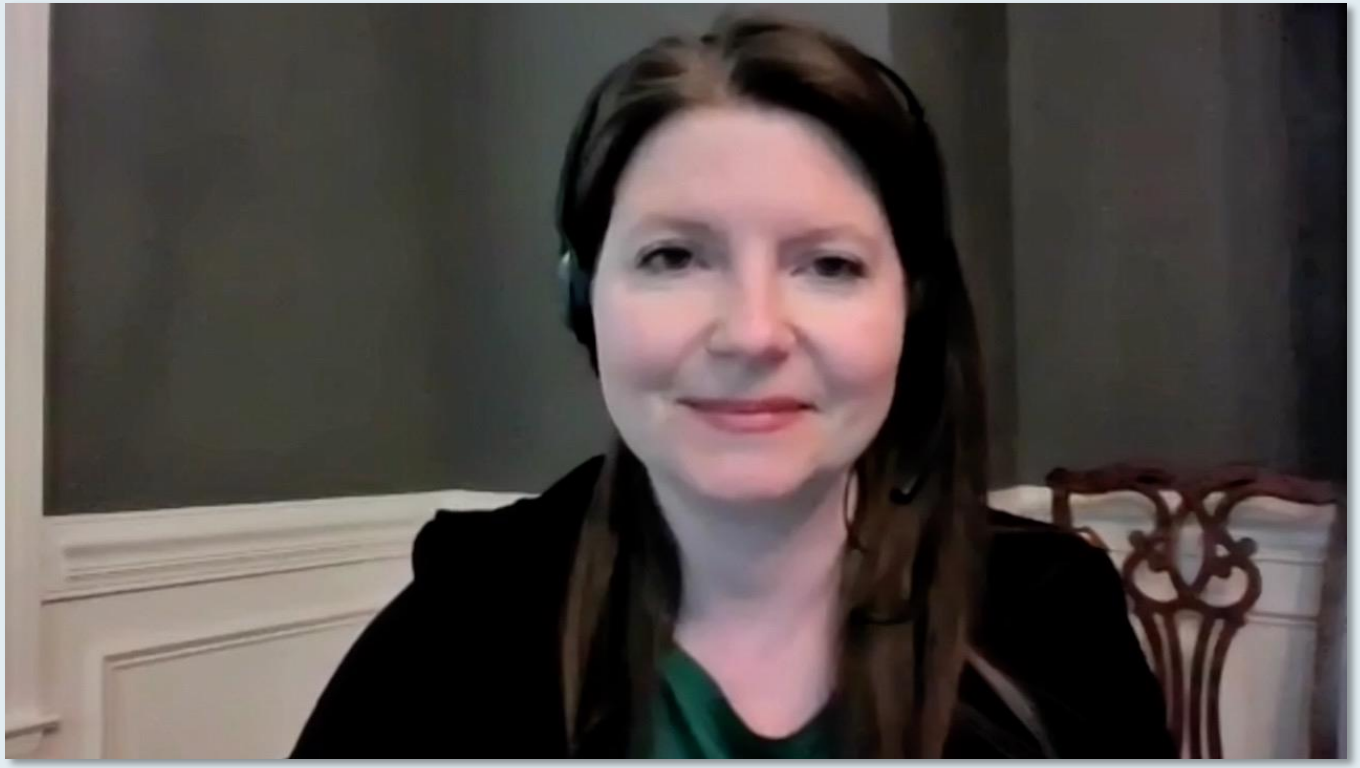
Module 3: HER2-Positive Advanced BTC

Module 4: Management of Mixed Hepatocellular Carcinoma (HCC)/BTC Tumors

Module 5: Advanced Cholangiocarcinoma with an FGFR2 Fusion

Module 6: Other Important Issues in BTC

Case Presentation: 66-year-old man with metastatic cholangiocarcinoma and very poor PS receives gemcitabine (TMB low, KRAS G12A, PIK3CA, and ARID1A mutations)



Dr Jennifer Dallas (Charlotte, North Carolina)

RTP
RESEARCH TO PRACTICE

Case Presentation: 63-year-old woman with cholangiocarcinoma receives gemcitabine/cisplatin

Dr Henna Malik (Houston, Texas)

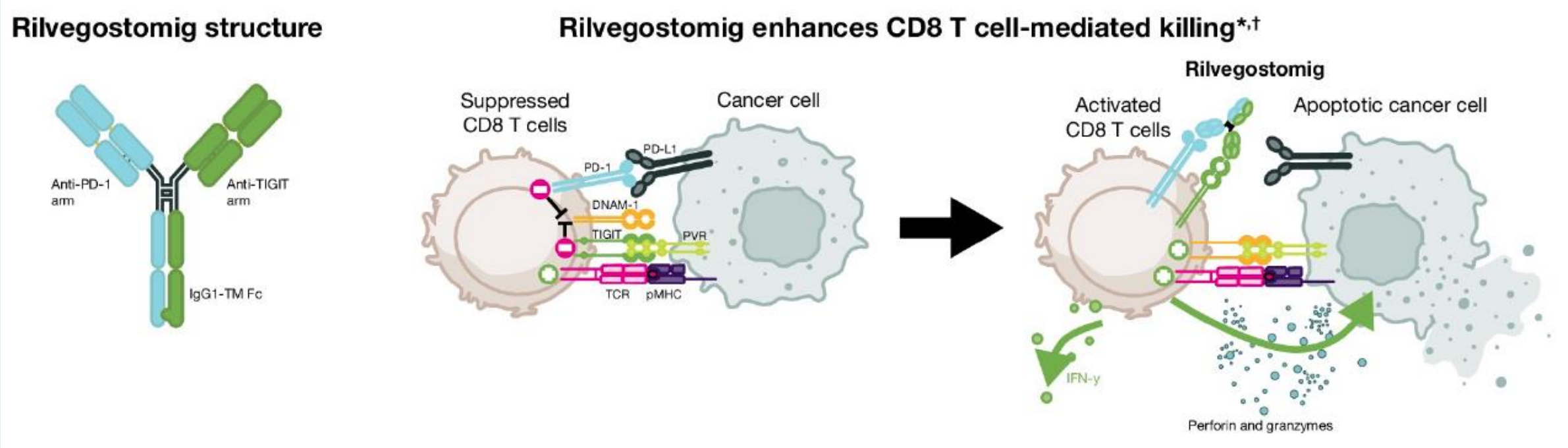
RTP
RESEARCH
TO PRACTICE

A Phase 3, Randomized Study of Adjuvant Rilvegostomig plus Chemotherapy in Resected Biliary Tract Cancer: ARTEMIDE-Biliary01

Fan J et al.

ASCO 2024;Abstract TPS4199.

Rilvegostomig: A Bispecific Antibody Targeting PD-1 and TIGIT



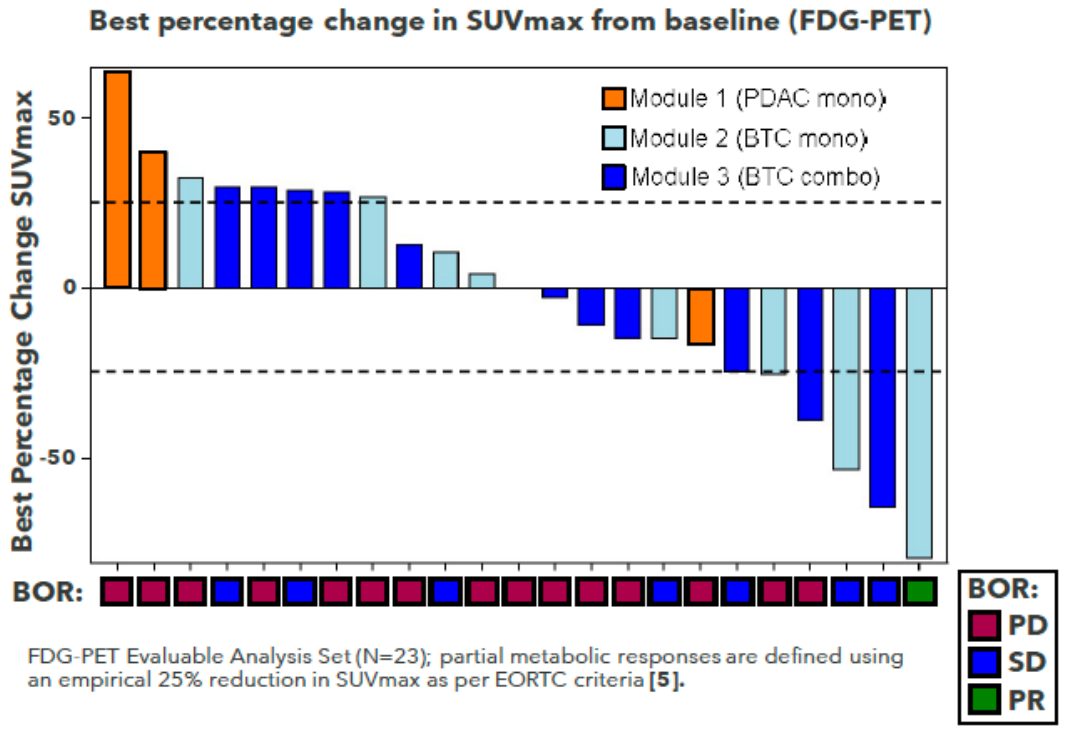
Fan J et al. ASCO 2024;Abstract TPS4199.

Phase II Results of the Porcupine (PORCN) Inhibitor Zamaporvint (RXC004) in Patients with Pancreatic and Biliary Tract Cancer

Bridgewater JA et al.

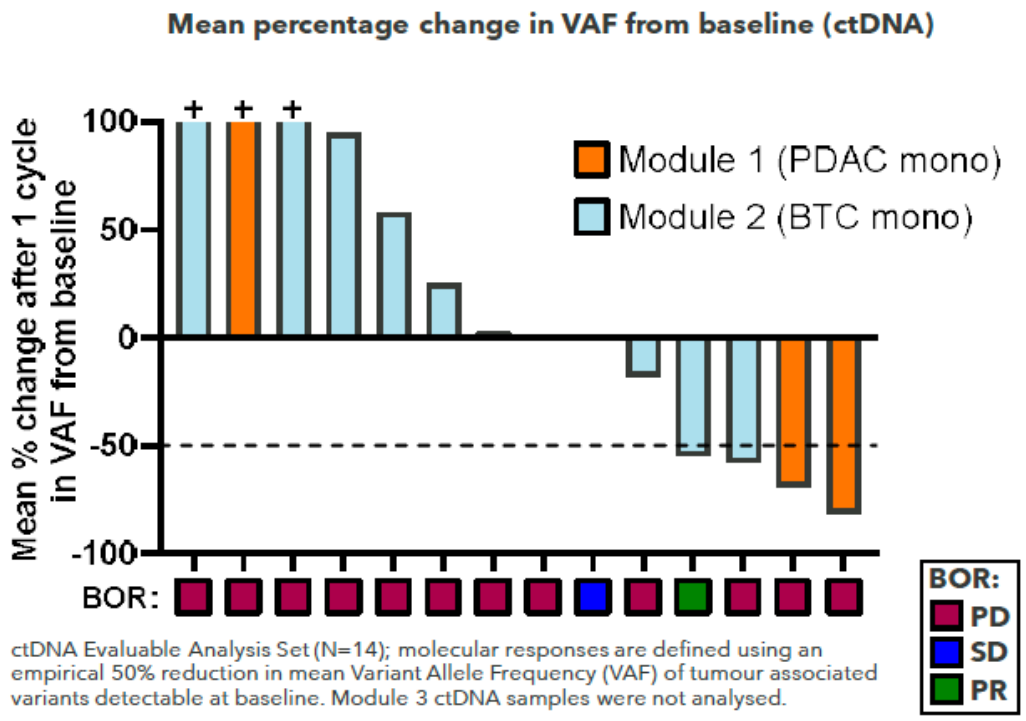
ESMO GI 2024;Abstract 391P.

Response to Zamaporvint in Patients with Pancreatic and Biliary Tract Cancer



FDG-PET Evaluable Analysis Set (N=23); partial metabolic responses are defined using an empirical 25% reduction in SUVmax as per EORTC criteria [5].

- In M1 (PDAC monotherapy); no metabolic responses (0/3 patients)
- In M2 (BTC monotherapy); 3/8 patients (38%) with partial metabolic response
- In M3 (BTC combination); 2/12 patients (17%) with partial metabolic response



ctDNA Evaluable Analysis Set (N=14); molecular responses are defined using an empirical 50% reduction in mean Variant Allele Frequency (VAF) of tumour associated variants detectable at baseline. Module 3 ctDNA samples were not analysed.

- In M1 (PDAC monotherapy); 2/3 patients (67%) with molecular response
- In M2 (BTC monotherapy); 2/11 patients (18%) with molecular response

FDG-PET = fluorodeoxyglucose positron emission tomography; ctDNA = circulating tumor DNA; PDAC = pancreatic ductal adenocarcinoma; BOR = best overall response; PD = progressive disease; SD = stable disease; PR = partial response

Bridgewater JA et al. ESMO GI 2024;Abstract 391P.

ORIGINAL ARTICLE

OPEN

Phase 2 trial of bintrafusp alfa as second-line therapy for patients with locally advanced/metastatic biliary tract cancers

Changhoon Yoo[1] | Milind M. Javle[2] | Helena Verdaguer Mata[3] | Filippo de Braud[4] | Jörg Trojan[5] | Jean-Luc Raoul[6] | Jin Won Kim[7] | Makoto Ueno[8] | Choong-kun Lee[9] | Susumu Hijioka[10] | Antonio Cubillo[11,12] | Junji Furuse[8] | Nilofer Azad[13] | Masashi Sato[14] | Yulia Vugmeyster[15] | Andreas Machl[15] | Marcis Bajars[16] | John Bridgewater[17] | Do-Youn Oh[18] | Mitesh J. Borad[19]

Hepatology 2023 September 1;78(3):758-70

A Phase IIa Clinical Trial of First-Line Cyclical Therapy Alternating Gemcitabine, Cisplatin, and Durvalumab with Pemigatinib for Advanced Biliary Tract Cancers with FGFR2-Alterations

Li C et al.

Gastrointestinal Cancers Symposium 2025;Abstract TPS645.

Niraparib in Patients with BRCA-Mutated Unresectable or Recurrent Biliary Tract, Pancreatic and Other Gastrointestinal Cancers: An Investigator-Initiated Phase 2 Trial (NIR-B trial)

Kawamoto Y et al.

Gastrointestinal Cancers Symposium 2025;Abstract 589.

Molecular and Clinical Determinants of Targeted Therapy (TT) Outcomes in Biliary Tract Cancer (BTC): Analysis of a Prospectively Maintained Next Generation Sequencing (NGS) Biorepository

Cowzer D et al.

Gastrointestinal Cancers Symposium 2025;Abstract 555.

Outcomes for BTC Treated with Matched Targeted Therapy

Target	Median PFS, months (95% CI)
IDH1/2 (N = 72)	4.2 (2.9-6.8)
FGFR2 (N=37)	7.4 (6.5-9.4)
ERBB2 (N =22)	8.2 (2.95-16.7)
MSI $_{high}$ (N = 14)	NR (10.15-NR)
TMB_{high} (N=12)	2.69 (1.64-NR)
BRAF V600E (N=7)	16.6 (3.7-NR)

Cowzer D et al. Gastrointestinal Cancers Symposium 2025;Abstract 555.

ABC-12: Exploring the Microbiome in Patients (pts) with Advanced Biliary Tract Cancer (BTC) in a First-Line Study of Durvalumab in Combination with Cisplatin/Gemcitabine (Cis/Gem)

McNamara MG et al.

ASCO 2023;Abstract TPS4183.

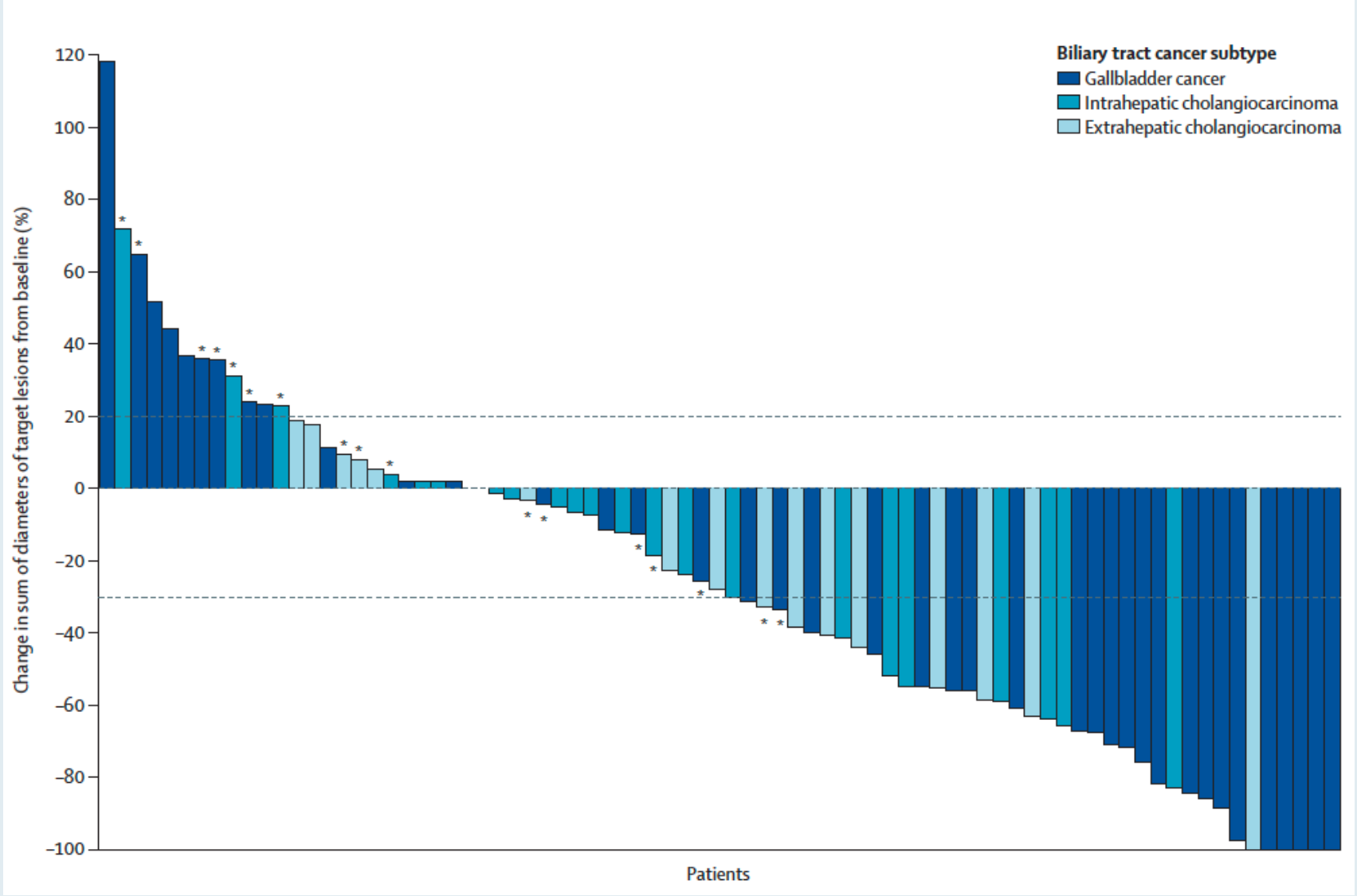
Appendix

Zanidatamab for *HER2*-amplified, unresectable, locally advanced or metastatic biliary tract cancer (HERIZON-BTC-01): a multicentre, single-arm, phase 2b study

James J Harding, Jia Fan*, Do-Youn Oh, Hye Jin Choi, Jin Won Kim, Heung-Moon Chang, Lequn Bao, Hui-Chuan Sun, Teresa Macarulla, Feng Xie, Jean-Phillippe Metges, Jie'er Ying, John Bridgewater, Myung-Ah Lee, Mohamedtaki A Tejani, Emerson Y Chen, Dong Uk Kim, Harpreet Wasan, Michel Ducreux, Yuanyuan Bao, Lisa Boyken, Jiafang Ma, Phillip Garfin, Shubham Pant, on behalf of the HERIZON-BTC-01 study group†*

***Lancet Oncol* 2023 July;24(7):772-82**

HERIZON-BTC-01: Target Lesion Reduction



Harding JJ et al. *Lancet Oncol* 2023 July;24(7):772-82.

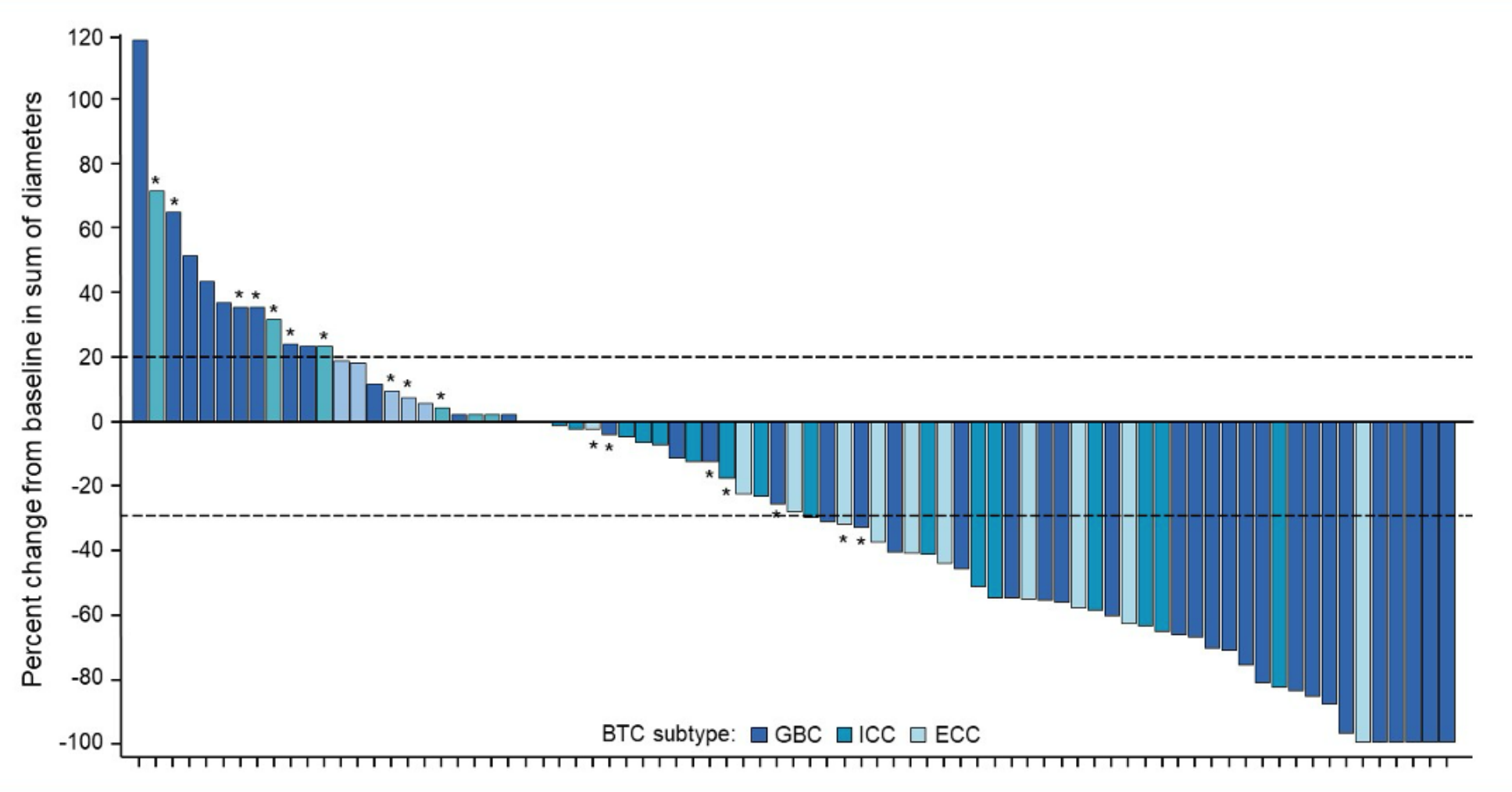
2023 ASCO ANNUAL MEETING

Abstract 4008

Results from the Pivotal Phase 2b HERIZON-BTC-01 Study: Zanidatamab in Previously-treated HER2-amplified Biliary Tract Cancer (BTC)

Shubham Pant, MD[1]; Jia Fan, MD, PhD[2]; Do-Youn Oh, MD, PhD[3]; Hye Jin Choi, MD, PhD[4]; Jin Won Kim, MD, PhD[5]; Heung-Moon Chang, MD, PhD[6]; Lequn Bao, MD[7]; Sun Huichuan, MD, PhD[2]; Teresa Macarulla, MD, PhD[8]; Feng Xie, MD[9]; Jean-Philippe Metges, MD[10]; Jie'er Ying, MD[11]; John A Bridgewater, MD, PhD[12]; Myung-Ah Lee, MD, PhD[13]; Mohamedtaki A Tejani, MD[14]; Emerson Y Chen, MD, MCR[15]; Dong Uk Kim, MD[16]; Harpreet Wasan, MD, FRCP[17]; Michel Ducreux, MD, PhD[18]; Yuanyuan Bao, MS[19]; Lin Yang, PhD[20]; JiaFang Ma, MD[19]; Phillip M Garfin, MD[20]; James J Harding, MD[21]

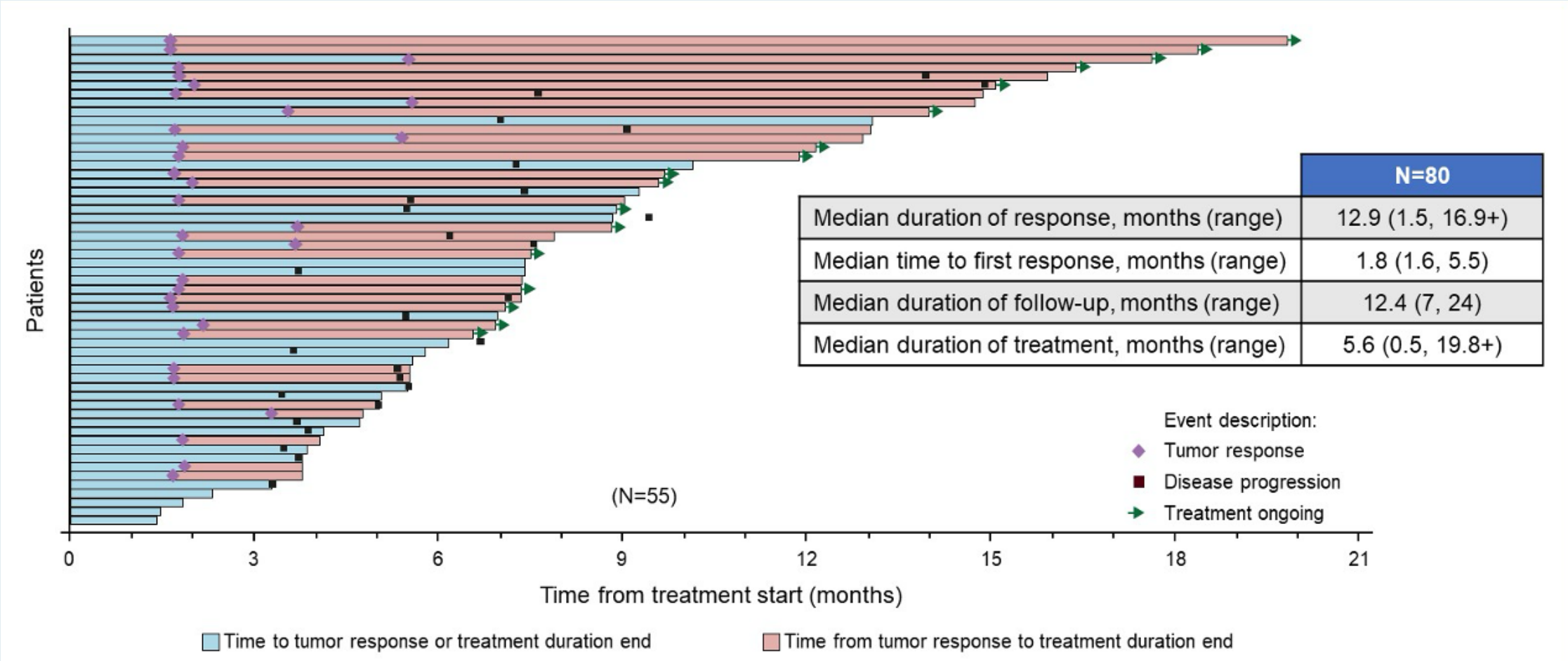
HERIZON-BTC-01: Target Lesion Reduction (Cohort 1)



GBC = gallbladder cancer; ICC = intrahepaticintrahepatic cholangiocarcinoma; ECC = extrahepatic cholangiocarcinoma

Pant S et al. ASCO 2023;Abstract 4008.

HERIZON-BTC-01: Treatment Duration for Patients with Response or Stable Disease per RECIST v1.1 (Cohort 1)



	N=80
Median duration of response, months (range)	12.9 (1.5, 16.9+)
Median time to first response, months (range)	1.8 (1.6, 5.5)
Median duration of follow-up, months (range)	12.4 (7, 24)
Median duration of treatment, months (range)	5.6 (0.5, 19.8+)

Pant S et al. ASCO 2023;Abstract 4008.

HERIZON-BTC-01: Adverse Events

	Cohort 1 (N = 80)		Total (N = 87)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any TEAE, n (%)	78 (97.5)	46 (57.5)	84 (96.6)	52 (59.8)
Any TRAE, n (%)	61 (76.3)	15 (18.8)	63 (72.4)	16 (18.4)
Serious TRAE, n (%)	7 (8.8)	7 (8.8)	7 (8.0)	7 (8.0)
TRAEs leading to treatment discontinuation, n (%)	2 (2.5)	1 (1.3)	2 (2.3)	1 (1.1)
TRAEs leading to death, n (%)	0	0	0	0
TRAEs, any Grade occurring in ≥ 10% of patients or Grade ≥ 3 in ≥ 2 patients, n (%)				
Diarrhea	32 (40.0)	4 (5.0)	32 (36.8)	4 (4.6)
IRR	28 (35.0)	1 (1.3)	29 (33.3)	1 (1.1)
Ejection fraction decreased	8 (10.0)	3 (3.8)	8 (9.2)	3 (3.4)
Nausea	8 (10.0)	1 (1.3)	8 (9.2)	1 (1.1)
Anemia	4 (5.0)	2 (2.5)	4 (4.6)	2 (2.3)

TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event.

- 2 TRAEs led to zanidatamab discontinuation:
  - 1 Grade 2 ejection fraction decreased
  - 1 Grade 3 pneumonitis
- 3 patients had TRAES that led to dose reductions:
  - 1 Grade 3 diarrhea
  - 1 Grade 3 diarrhea and Grade 3 nausea
  - 1 Grade 2 weight decreased
- No serious TRAEs occurred in more than 1 patient
- No Grade 4 TRAES; no treatment-related deaths

IRR = infusion-related reaction

Pant S et al. ASCO 2023;Abstract 4008.

HERIZON-BTC-01: Adverse Events of Special Interest (AESIs)

		Cohort 1 (N = 80)		Total (N = 87)	
		Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
AESI, n (%)	IRR	28 (35.0)	1 (1.3)	29 (33.3)	1 (1.1)
	Confirmed cardiac events	5 (6.3)	3 (3.8)	5 (5.7)	3 (3.4)
	Non-infectious pulmonary toxicities	1 (1.3)	1 (1.3)	1 (1.1)	1 (1.1)
Select AE, n (%)[1]	Diarrhea	38 (47.5)	6 (7.5)	38 (43.7)	6 (6.9)

[1] AESIs that occurred in at least 1 patient

- IRR events: all events resolved, generally within 1 day; most occurred with the first cycle of treatment (26/29); most had no recurrence (26/29)
- Confirmed cardiac events: decreased LVEF in 5 patients (5.7%). Patients were clinically asymptomatic, and the events were confounded by pre-existing or concurrent conditions.
- Diarrhea: all but 2 events (both Grade 3) were managed in the outpatient setting, typically with loperamide; most events (87/99) were resolved at the time of data cutoff; median time to resolution of 2.0 days (range, 1 – 267)

Pant S et al. ASCO 2023;Abstract 4008.

Safety and Efficacy of Anti-HER2 Agents in the Treatment of Biliary Tract Cancers: A Systematic Review

Naleid N et al.

Gastrointestinal Cancers Symposium 2025;Abstract 639.

Poster 4090

Trastuzumab deruxtecan in patients with HER2-expressing biliary tract cancer and pancreatic cancer: outcomes from DESTINY-PanTumor02

Do-Youn Oh,[1] Iwona Ługowska,[2] Daniil Stroyakovskiy,[3] Kyung Hae Jung,[4] Olivier Dumas,[5] Konstantin Penkov,[6] Arunee Dechaphunkul,[7] Ana Oaknin,[8] Seung Tae Kim,[9] Naureen Starling,[10] Busyamas Chewaskulyong,[11] Chanchai Charonpongsuntorn,[12] Deborah Doroshow,[13] Sheng-Yen Hsiao,[14] Yi-Ping Hung,[15] Lindsey Jung,[16] Nataliya Kuptsova-Clarkson,[17] Flavia Michelini,[18] Soham Puvvada,[17] Funda Meric-Bernstam[19]

[1]Department of Internal Medicine, Seoul National University Hospital, Republic of Korea; [2]Early Phase Clinical Trials Unit, Maria Skłodowska-Curie National Research Institute and Oncology Centre, Warsaw, Poland; [3]Healthcare Department, Moscow City Oncology Hospital No. 62, Russia; [4]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [5]Hôtel-Dieu de Québec, Canada; [6]Clinical Hospital "RZHD-Medicine", Saint Petersburg, Russia; [7]Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [8]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology, University Hospital Vall d'Hebron, Barcelona, Spain; [9]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Republic of Korea; [10]Gastrointestinal Unit, The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [11]Medical Oncology Unit, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Thailand; [12]Medical Oncology Unit, Department of Internal Medicine, Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, Thailand; [13]Icahn School of Medicine at Mount Sinai, New York, NY, US; [14]Division of Hematology-Oncology, Department of Internal Medicine, Chi Mei Medical Center, Liouying, Tainan, Taiwan; [15]Taipei Veterans General Hospital, Taiwan; [16]AstraZeneca, Gaithersburg, MD, US; [17]Oncology R&D, AstraZeneca, Gaithersburg, MD, US; [18]Translational Medicine, Oncology R&D, AstraZeneca, Waltham, MA, US; [19]Department of Investigational Cancer Therapeutics, University of Texas MD Anderson Cancer Center, Houston, TX, US

ASCO 2024

RTP RESEARCH TO PRACTICE

DESTINY-PanTumor02 Trial of T-DXd for Patients with HER2-Expressing BTC and Pancreatic Cancer: Secondary Efficacy Outcomes in the BTC Cohort

Characteristic	All patients	All patients (ICR)	HER2 IHC 3+	HER2 IHC 2+	HER2 IHC 1+	HER2 IHC 0
n	41	41	16	14	3	7
Confirmed ORR, n (%) 95% CI	9 (22.0) 10.6, 37.6	11 (26.8) 14.2, 42.9	9 (56.3) 29.9, 80.2	0	0	0
Median DOR, months 95% CI	8.6 2.1, NE	10.9 5.5, NE	8.6 2.1, NE	–	–	–
Median PFS, months 95% CI	4.6 3.1, 6.0	4.1 2.8, 5.3	7.4 2.8, 12.5	4.2 2.8, 6.0	5.1 1.2, NE	3.1 1.2, 5.6
Median OS, months 95% CI	7.0 4.6, 10.2	7.0 4.6, 10.2	12.4 2.8, NE	6.0 3.7, 11.7	5.1 1.6, NE	7.6 3.0, 10.2
DCR at 12 weeks, % 95% CI	65.9 49.4, 79.9	51.2 35.1, 67.1	68.8 41.3, 89.0	71.4 41.9, 91.6	66.7 9.4, 99.2	57.1 18.4, 90.1

DOR = duration of response; PFS = progression-free survival; OS = overall survival; DCR = disease control rate

Oh D-Y et al. ASCO 2024;Abstract 4090.

DESTINY-PanTumor02 Trial of T-DXd for Patients with HER2-Expressing BTC and Pancreatic Cancer: Safety Summary

n (%)	Biliary tract cancer (n=41)	Pancreatic cancer (n=25)
Any drug-related TEAEs	33 (80.5)	15 (60.0)
Drug-related TEAEs Grade ≥3	19 (39.0)	7 (28.0)
Serious drug-related TEAEs	5 (12.2)	3 (12.0)
Drug-related TEAEs associated with dose discontinuations	5 (12.2)	1 (4.0)
Drug-related TEAEs associated with dose interruptions	7 (17.1)	0
Drug-related TEAEs associated with dose reductions	9 (22.0)	0
Drug-related TEAEs associated with deaths	0	0

Analyses (by investigator) include patients with biliary tract cancer and pancreatic cancer who received ≥1 dose of T-DXd (n=41 and n=25, respectively); median total treatment duration was 3.45 (range 0.7–23.7) months and 2.07 (range 0.7–12.4) months, respectively
TEAE, treatment-emergent adverse event

Oh D-Y et al. ASCO 2024;Abstract 4090.

What Clinicians Want to Know: Addressing Current Questions Related to Novel Treatment Approaches for Urothelial Bladder Cancer and Prostate Cancer

A CME Symposium Held in Conjunction with the 2025 ASCO® Genitourinary Cancers Symposium

Thursday, February 13, 2025
7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty (Bladder Cancer)

Terence Friedlander, MD
Matthew D Galsky, MD

Faculty (Prostate Cancer)

Neeraj Agarwal, MD, FASCO
Andrew J Armstrong, MD, ScM

Moderator

Elisabeth I Heath, 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 for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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