

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

*A CME/MOC-Accredited Live Webinar*

**Wednesday, August 6, 2025**

**5:00 PM – 6:00 PM ET**

## **Faculty**

**Haley Ellis, MD**

**James J Harding, MD**

## **Moderator**

**Neil Love, MD**

# Faculty



**Haley Ellis, MD**  
Medical Oncologist  
Massachusetts General Hospital  
Instructor of Medicine  
Harvard Medical School  
Boston, Massachusetts



**MODERATOR**  
**Neil Love, MD**  
Research To Practice  
Miami, Florida



**James J Harding, MD**  
Associate Attending  
Memorial Sloan Kettering Cancer Center  
Assistant Professor of Medicine  
Weill Cornell Medical College  
New York, New York

## Commercial Support

This activity is supported by educational grants from Incyte Corporation and Jazz Pharmaceuticals Inc.

## Dr Love — Disclosures

**Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeOne, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Clovis Oncology, Coherus BioSciences, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Hologic Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.



# 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.

## Dr Ellis — Disclosures

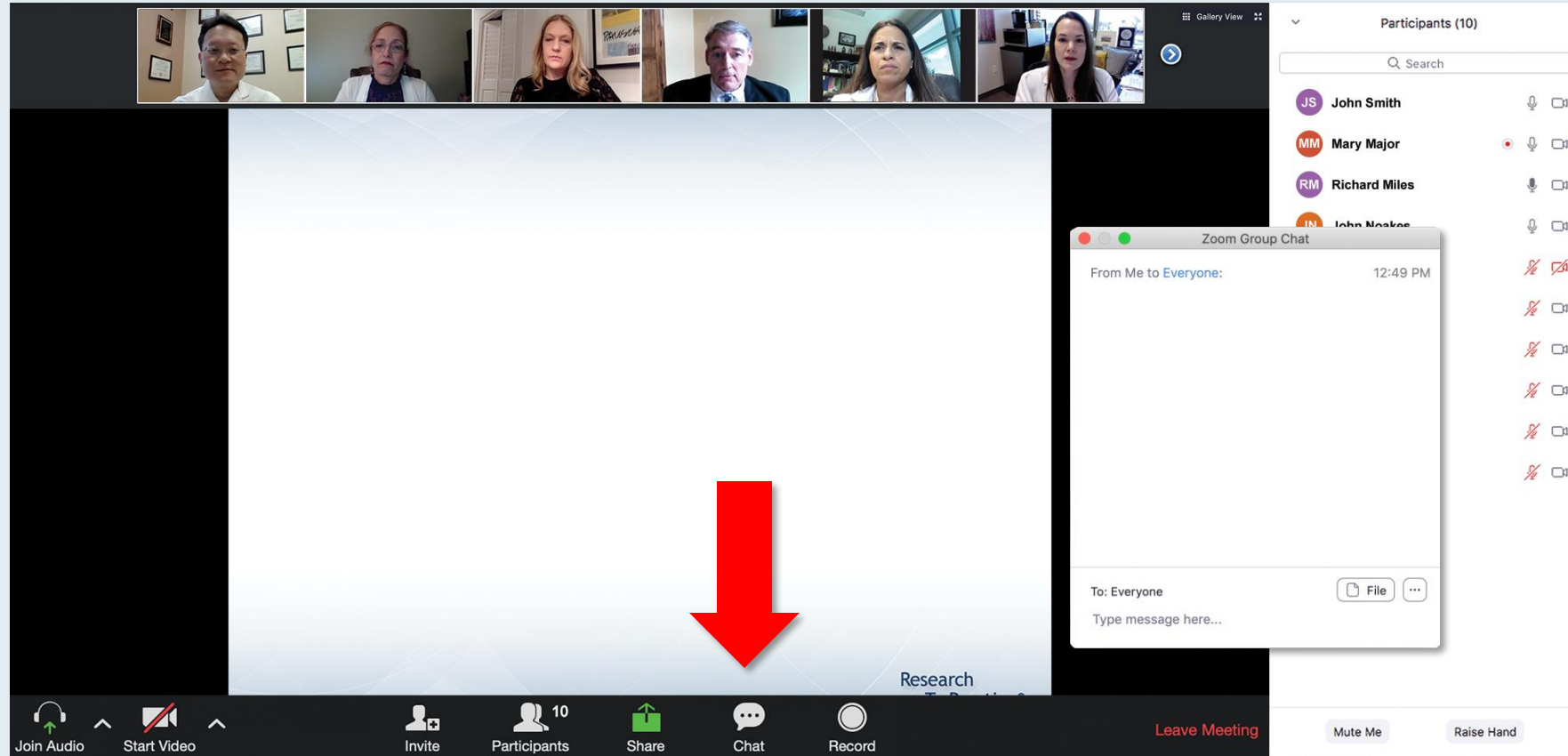
<b>Advisory Committees</b>	AstraZeneca Pharmaceuticals LP, Cogent Biosciences, Jazz Pharmaceuticals Inc
<b>Honoraria</b>	Incyte Corporation, Jazz Pharmaceuticals Inc
<b>Nonrelevant Financial Relationships</b>	Medscape, OncLive, The Jackson Laboratory

# Dr Harding — Disclosures

<b>Consulting Agreements</b>	Amgen Inc, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Cogent Biosciences, Elevar Therapeutics, Exelixis Inc, Jazz Pharmaceuticals Inc, Merck, RayzeBio Inc, Servier Pharmaceuticals LLC
<b>Data and Safety Monitoring Boards/Committees</b>	Merck

**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.**

# We Encourage Clinicians in Practice to Submit Questions









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

# Familiarizing Yourself with the Zoom Interface

## Expand chat submission box

The screenshot shows a Zoom meeting interface. At the top, there's a header bar with participant names: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below this, a slide titled "Meet The Professor Program Participating Faculty" is displayed. The slide lists six faculty members with their photos and titles. To the right of the slide, a chat window is open, showing messages from "Me to Panelists" and "Me to Panelists and Attendees". A red arrow points to the white line above the chat submission box, indicating where to drag to expand the box.

**Meet The Professor Program Participating Faculty**

 <p><b>Nancy L Bartlett, MD</b> Professor of Medicine Koman Chair in Medical Oncology Washington University School of Medicine St Louis, Missouri</p>	 <p><b>Jonathan W Friedberg, MD, MMSc</b> Samuel E Durand Professor of Medicine Director, James P Wilmot Cancer Institute University of Rochester Rochester, New York</p>
 <p><b>Carla Casulo, MD</b> Associate Professor of Medicine Division of Hematology/Oncology Director, Hematology/Oncology Fellowship Program University of Rochester Wilmot Cancer Institute Rochester, New York</p>	 <p><b>Brian T Hill, MD, PhD</b> Director, Lymphoid Malignancy Program Cleveland Clinic Taussig Cancer Institute Cleveland, Ohio</p>
 <p><b>Christopher R Flowers, MD, MS</b> Chair, Professor Department of Lymphoma/Myeloma The University of Texas MD Anderson Cancer Center Houston, Texas</p>	 <p><b>Brad S Kahl, MD</b> Professor of Medicine Washington University School of Medicine Director, Lymphoma Program Siteman Cancer Center St Louis, Missouri</p>

**Chat**

Me to Panelists 4:31 PM

Welcome and thank you for attending! To access the slides from today's session please use the link below.  
[http://images.researchtopractice.com/2021/Meetings/Slides/MTP\\_ToGo\\_CLL\\_2021\\_April1.pdf](http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April1.pdf)

Me to Panelists and Attendees 4:32 PM

Welcome and thank you for attending! To access the slides from today's session please use the link below.  
[http://images.researchtopractice.com/2021/Meetings/Slides/MTP\\_ToGo\\_CLL\\_2021\\_April1.pdf](http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April1.pdf)

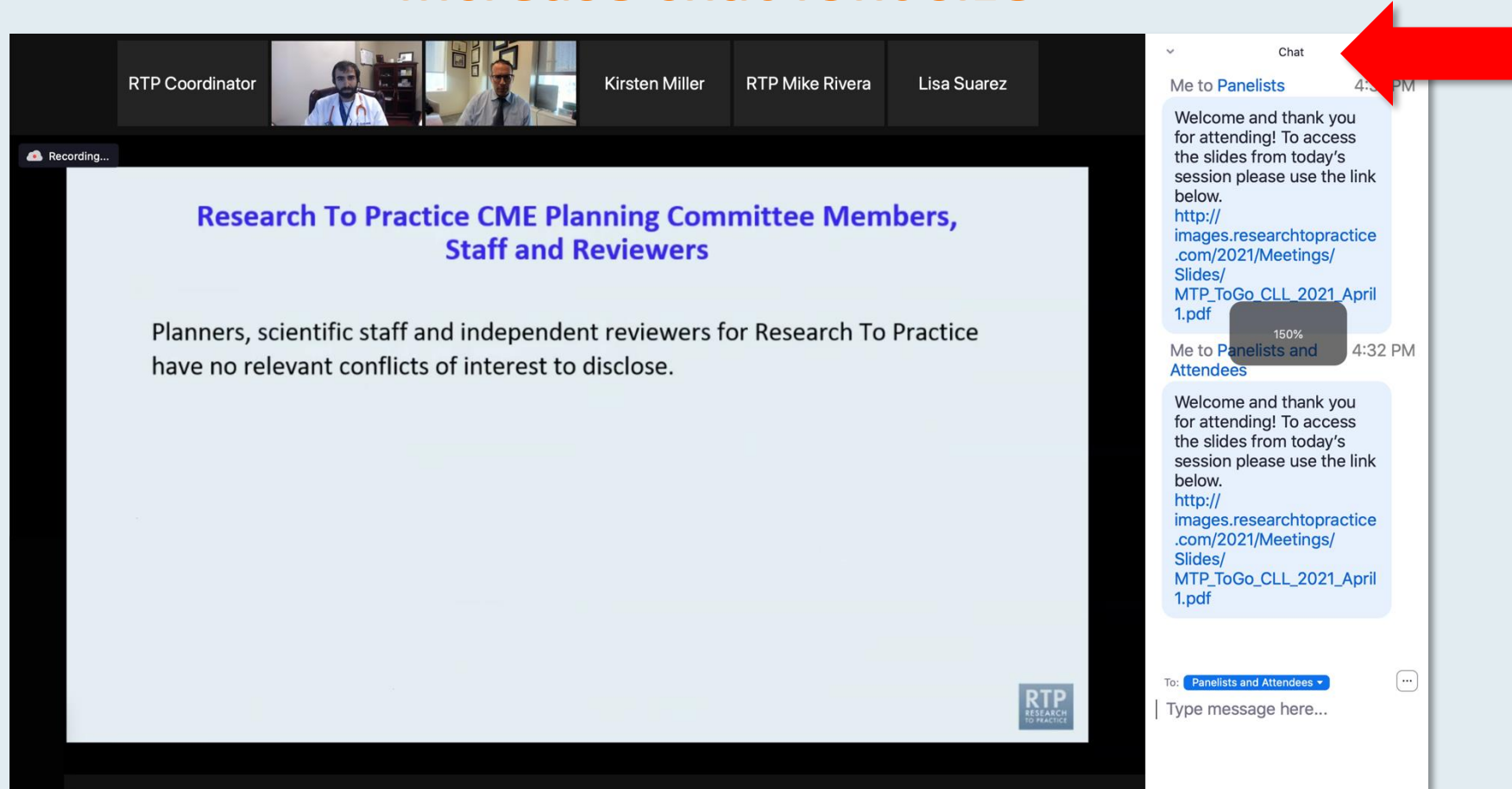
To: Panelists and Attendees

Type message here...

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

# Familiarizing Yourself with the Zoom Interface

## Increase chat font size



The screenshot displays a Zoom meeting interface. At the top, a video bar shows participants: RTP Coordinator, Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. The main area shows a presentation slide titled "Research To Practice CME Planning Committee Members, Staff and Reviewers" with the text: "Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose." The bottom right corner of the slide features the RTP Research To Practice logo. On the right side, the chat window is open, showing two messages from "Me to Panelists" and "Me to Panelists and Attendees". A red arrow points to the font size icon (a square with "150%") in the chat window's header area.

**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

The screenshot shows a Zoom meeting interface. At the top, a gallery view of participants is visible. The main content area displays a presentation slide with the following text:

**Meet The Professor**  
**Optimizing the Selection and Sequencing of Therapy for Patients with Metastatic Gastrointestinal Cancer**  
**Wednesday, August 25, 2022**  
**5:00 PM – 6:00 PM EST**  
**Faculty**  
**Wells A Messersmith, MD**  
**Moderator**  
**Neil Love, MD**

A "Quick Survey" pop-up is overlaid on the slide, listing treatment options:

- ☐ Ceritinib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
- ☐ Ceritinib + pomalidomide +/- dexamethasone
- ☐ Elotuzumab + lenalidomide +/- dexamethasone
- ☐ Elotuzumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Isaxozim + Rd
- ☐ Other

The "Participants (10)" list on the right includes: John Smith, Mary Major, Richard Miles, John Noakes, Alice Suarez, Jane Perez, Robert Stiles, Juan Fernandez, Ashok Kumar, and Jeremy Smith.

The screenshot shows a Zoom meeting interface. At the top, a gallery view of participants is visible. The main content area displays a presentation slide with the following text:

**Regulatory and reimbursement issues aside, what would you recommend for a 65-year-old patient with clear cell renal cell carcinoma (ccRCC) who has a follow-up 3 years later is found to have asymptomatic (PS 0)?**

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- ☐ Nivolumab/ipilimumab
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- ☐ Pembrolizumab/axitinib
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- ☐ Nivolumab/cabozantinib
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# Biliary Tract Cancers — Reviewing Patient Cases with Prof John Bridgewater



PROF JOHN BRIDGEWATER  
UCL CANCER INSTITUTE



# Cancer Q&A: Addressing Common Questions Posed by Patients with Relapsed/Refractory Multiple Myeloma

*A CME/MOC-Accredited Webinar Developed in Partnership with CancerCare®*

**Thursday, August 7, 2025**

**5:00 PM – 6:00 PM ET**

## **Faculty**

**Natalie S Callander, MD**

**Sagar Lonial, MD, FACP**

## **Moderator**

**Neil Love, MD**

# The Implications of Recent Datasets for the Current and Future Management of Breast Cancer — An ASCO 2025 Review

*A CME/MOC-Accredited Live Webinar*

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**Sara A Hurvitz, MD, FACP**

**Sara M Tolaney, MD, MPH**

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# **Selection and Sequencing of Therapy for Metastatic Triple-Negative Breast Cancer**

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**Professor Peter Schmid, FRCP, MD, PhD**

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# Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Care of Patients with Relapsed/Refractory Multiple Myeloma

*Part 1 of a 2-Part CME/MOC-, NCPD- and ACPE-Accredited Satellite Symposium Series During the Society of Hematologic Oncology 2025 Annual Meeting*

**Thursday, September 4, 2025**

**6:42 PM – 7:42 PM CT**

## **Faculty**

**Meletios-Athanasios (Thanos) C Dimopoulos, MD**

**Hans Lee, MD**

**Noopur Raje, MD**

## **Moderator**

**Joseph Mikhael, MD, MEd**

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**Friday, September 5, 2025  
11:47 AM – 12:47 PM CT**

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**Jennifer Crombie, MD  
Laurie H Sehn, MD, MPH**

## **Moderator**

**Jeremy S Abramson, MD, MMSc**

# **Addressing Current Knowledge and Practice Gaps in the Community — Optimizing the Use of Oral Selective Estrogen Receptor Degraders for Metastatic Breast Cancer, Part 2**

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**Joyce O'Shaughnessy, MD**

## **Moderator**

**Neil Love, MD**

*Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to 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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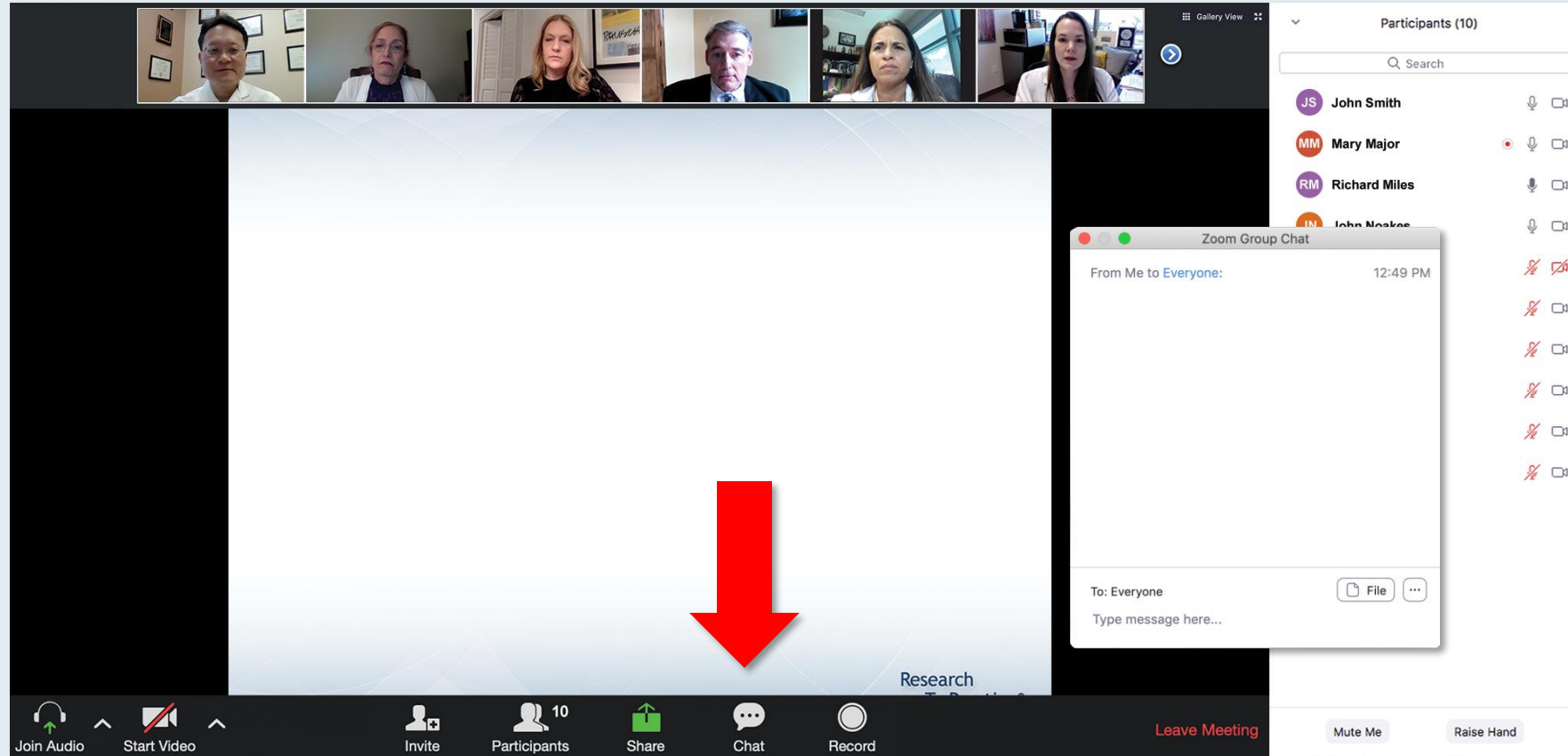


**MODERATOR**  
**Neil Love, MD**  
Research To Practice  
Miami, Florida



**James J Harding, MD**  
Associate Attending  
Memorial Sloan Kettering Cancer Center  
Assistant Professor of Medicine  
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# Contributing Medical Oncologists



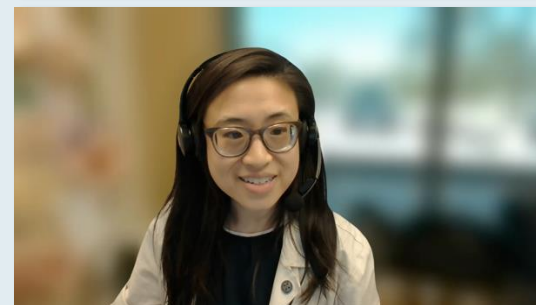
**Warren S Brenner, MD**  
Lynn Cancer Institute  
Boca Raton, Florida



**Shaachi Gupta, MD, MPH**  
Florida Cancer Specialists  
Lake Worth, Florida



**Philip L Brooks, MD**  
Northern Light Eastern Maine Medical  
Center and Lafayette Family Cancer  
Institute  
Brewer, Maine



**Kimberly Ku, MD**  
Illinois Cancer Care  
Bloomington, Illinois



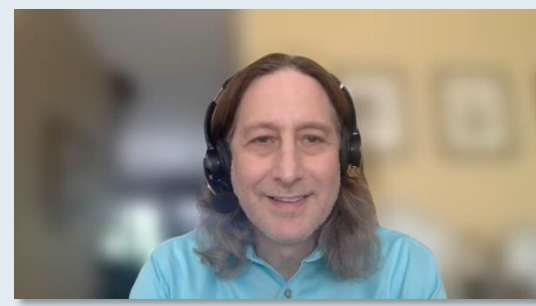
**Farshid Dayyani, MD, PhD**  
Stern Center for Cancer Clinical  
Trials and Research  
Orange, California



**Joseph Martins, MD**  
UT Health Science Center  
Tyler, Texas



**Justin Peter Favaro, MD, PhD**  
Oncology Specialists of Charlotte  
Charlotte, North Carolina



**Neil Morganstein, MD**  
Atlantic Health System  
Summit, New Jersey

# Agenda

**Introduction:** Is Biliary Tract Cancer (BTC) the New Non-Small Cell Lung Cancer? ... Why?

**Case 1:** Do BTC Subtypes Respond Differently to Checkpoint Inhibitors?

**Case 2:** Anti-HER2-Directed Therapy for HER2-Low BTC?

**Case 3:** FGFR Inhibitors in the Front-Line Setting?

**Case 4:** Bone and Muscle Pain with an FGFR Inhibitor

**Case 5:** Improved Targeted Clinical Benefit for Specific FGFR Mutations?

**Case 6:** Sequencing of Available HER2-Targeted Agents

**Case 7:** IDH Inhibitors in Combination with Chemotherapy as Initial Therapy?

**Case 8:** BRAF and IDH Mutations — Which Targeted Treatment First?

**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?

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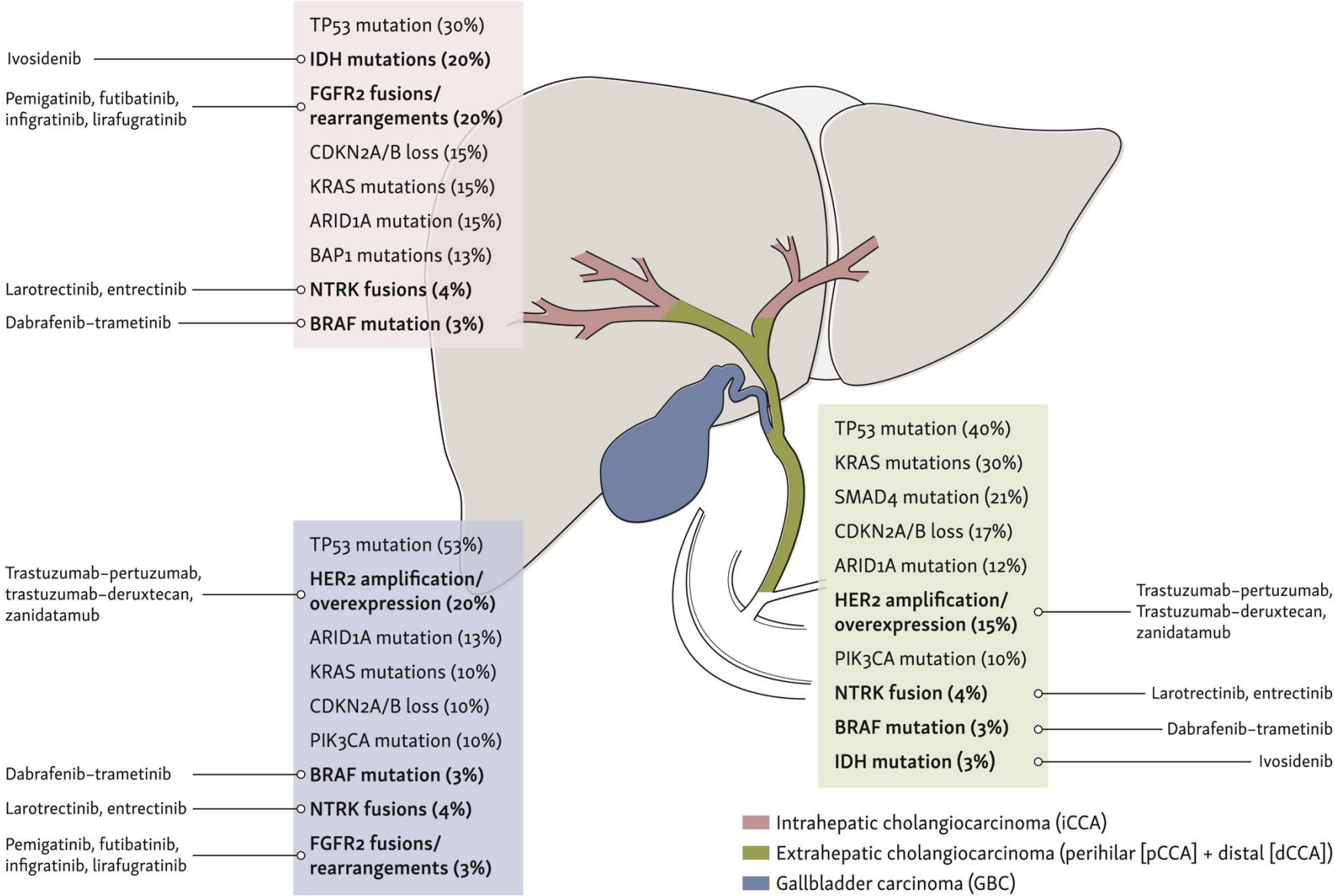
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# BTC harbor targetable genomic alterations



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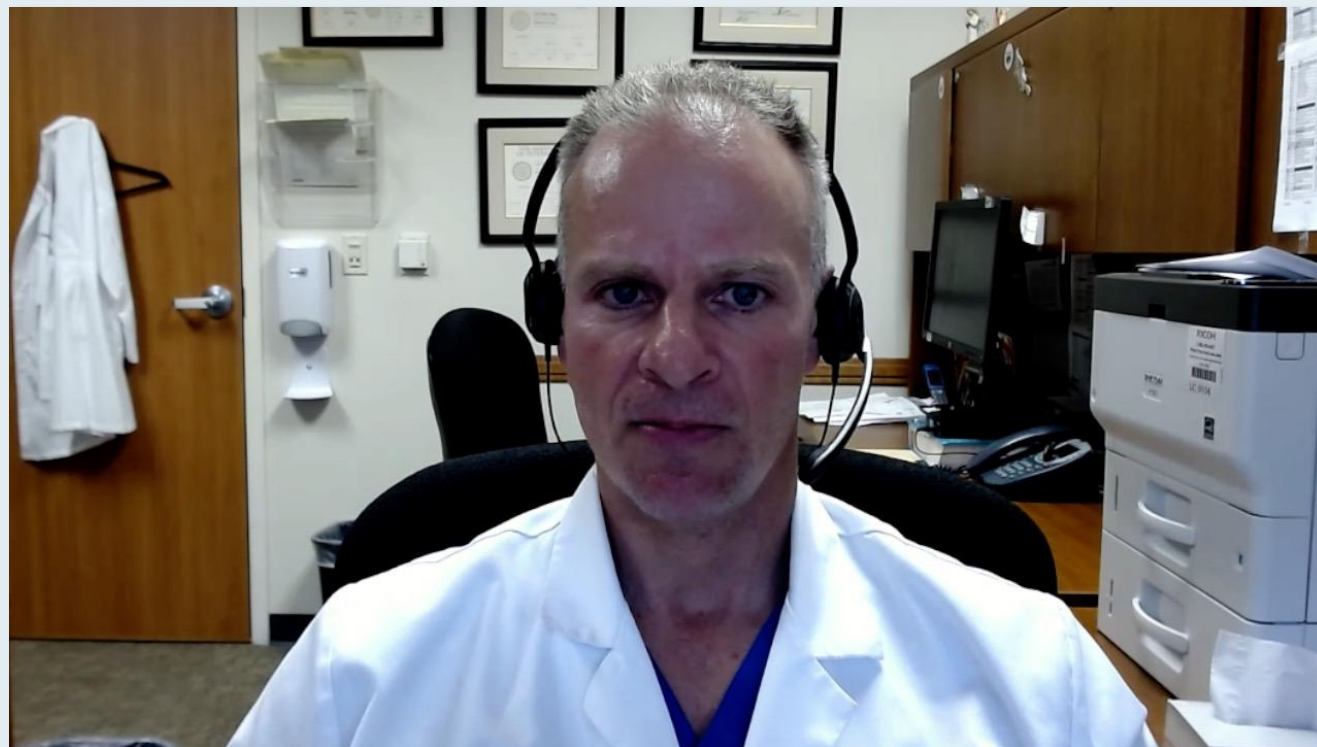
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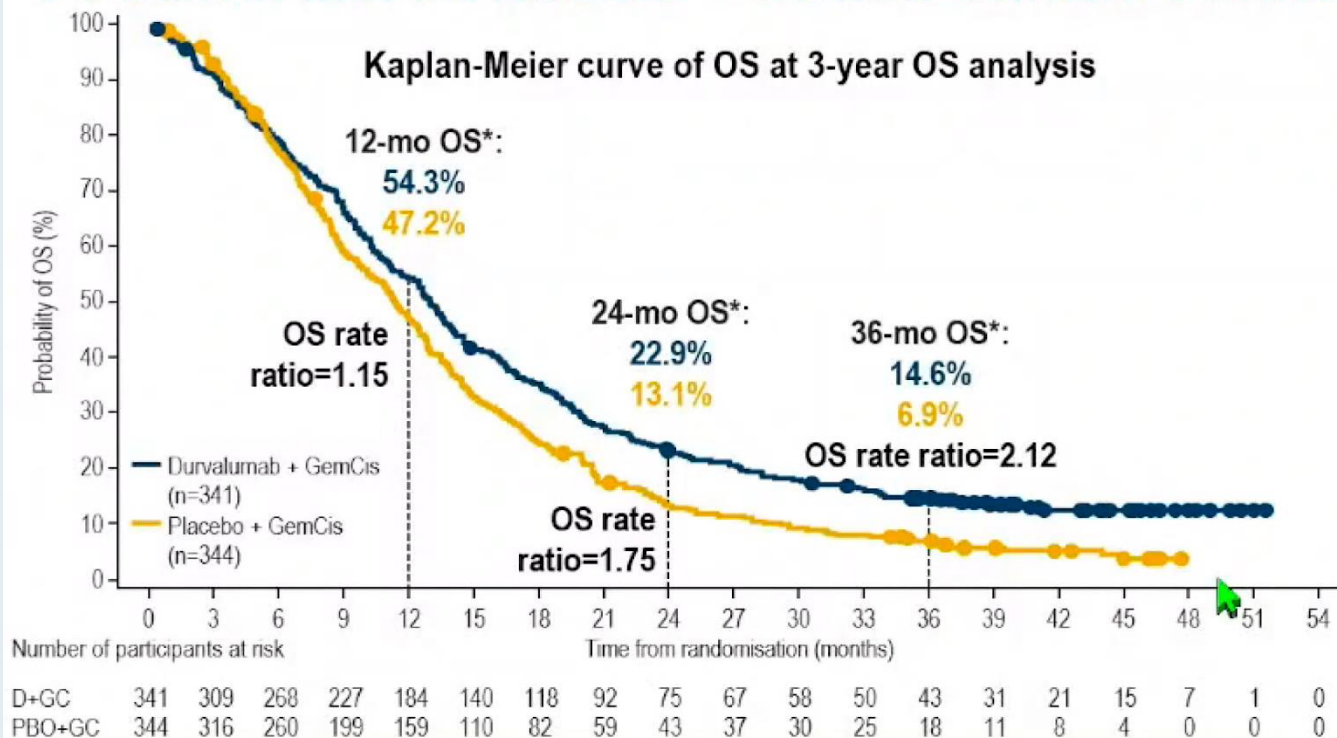
## Case Presentation: 75-year-old woman with metastatic cholangiocarcinoma who received first-line gemcitabine/cisplatin with durvalumab



**Dr Warren Brenner (Boca Raton, Florida)**

# TOPAZ-1 Trial: 3-Year Overall Survival (OS) Update

## OS benefit with durvalumab + GemCis continued at the updated DCO



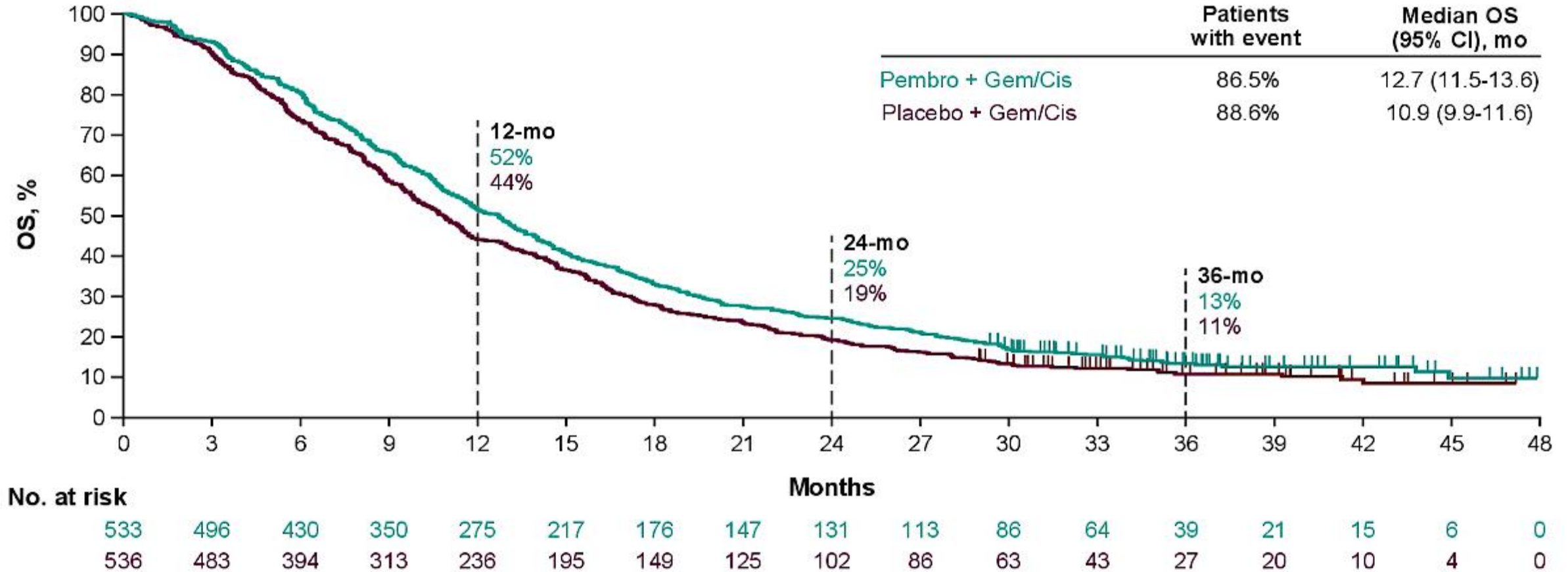
	Primary analysis <sup>1,†</sup> DCO: 11 Aug 2021		3-year OS analysis <sup>†</sup> DCO: 23 Oct 2023	
	D+GC (n=341)	PBO+GC (n=344)	D+GC (n=341)	PBO+GC (n=344)
Median OS* (95% CI), months	12.8 (11.1–14.0)	11.5 (10.1–12.5)	12.9 (11.6–14.1)	11.3 (10.1–12.5)
OS HR <sup>§</sup> (95% CI)	0.80 (0.66–0.97)		0.74 (0.63–0.87)	

At 36-months, the survival rate in the durvalumab + GemCis arm was more than double the survival rate in the placebo + GemCis arm

GemCis = gemcitabine/cisplatin; DCO = data cutoff

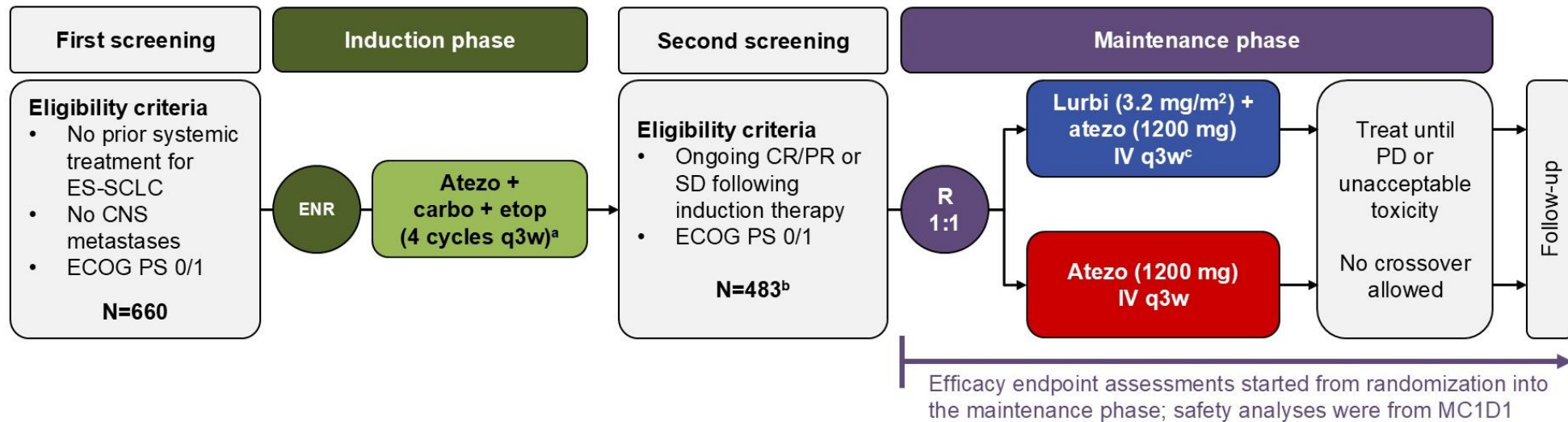


# KEYNOTE-966 Trial: 3-Year OS Update



– Median OS of 12.7 months (95% CI 11.5-13.6) in the pembrolizumab arm vs 10.9 months (95% CI 9.9-11.6) in the placebo arm (HR 0.86, 95% CI 0.75-0.98; nominal  $P = 0.0099$ )

# IMforte Study Design



## Stratification factors for randomization

- ECOG PS (0/1)
- LDH ( $\leq$ ULN/ $>$ ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

## Primary endpoints

IRF-PFS and OS

## Secondary endpoints included

INV-PFS, ORR, DOR, and safety

Last patient randomized: April 30, 2024

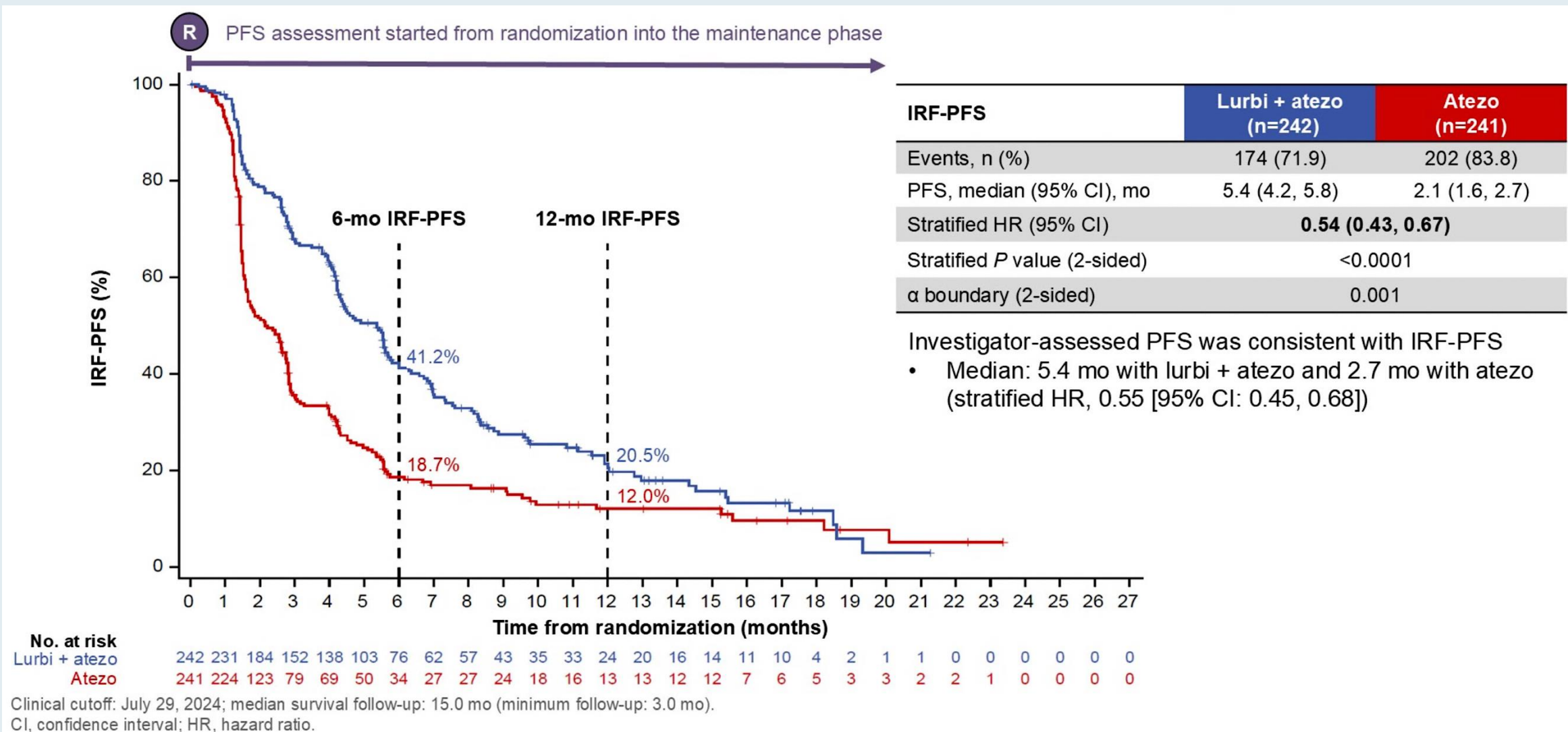
Clinical cutoff: July 29, 2024

ClinicalTrials.gov ID: NCT05091567.

<sup>a</sup> Administered per standard dose. <sup>b</sup> 73% of patients continued from induction to maintenance. <sup>c</sup> With prophylactic granulocyte colony-stimulating factor and anti-emetics. atezo, atezolizumab; BL, baseline; carbo, carboplatin; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; ENR, enrollment; etop, etoposide; INV-PFS, investigator-assessed PFS; IRF-PFS, independent review facility-assessed PFS; IV, intravenously; LDH, lactate dehydrogenase; lurbi, lurbinectedin; MC1D1, maintenance Cycle 1 Day 1; PCI, prophylactic cranial irradiation; q3w, every 3 weeks; R, randomization; ULN, upper limit of normal; Y/N, yes/no.

CR = complete response; PR = partial response; SD = stable disease; PD = disease progression

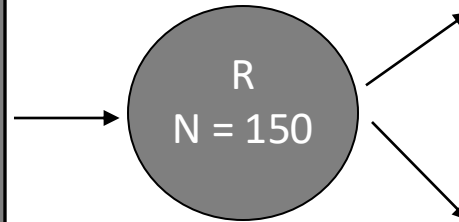
# IMforte: PFS from Randomization into Maintenance Phase



# NEODISCO Trial: Neoadjuvant Gemcitabine and Cisplatin in Combination with Perioperative Pembrolizumab versus Up-Front Surgery for Patients with Primary Resectable and Borderline-Resectable Perihilar and Distal Cholangiocarcinoma

## Key Eligibility Criteria

- Age  $\geq 18$  years
- ECOG PS 0-1
- Confirmed resectable or borderline resectable pCCA and dCCA
- No prior therapy with anti-PD-1 or anti-PD-L1 antibodies or other agents directed to another stimulatory or co-inhibitory T-cell receptor



Neoadjuvant gemcitabine + cisplatin +  
perioperative pembrolizumab (IV)

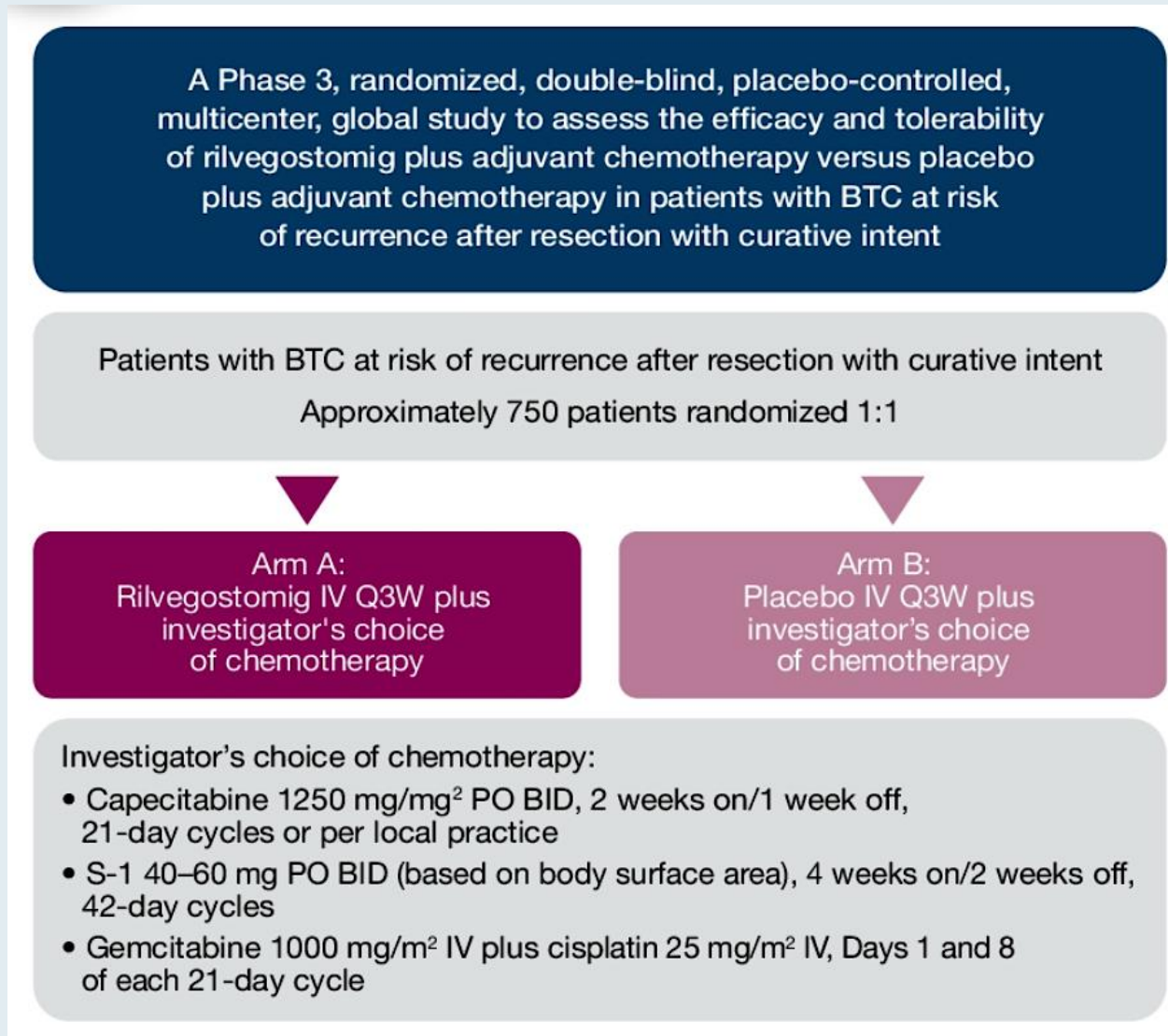
Surgery

## **Primary Outcome Measure: Event-free survival**

pCCA = perihilar cholangiocarcinoma; dCCA = distal cholangiocarcinoma; IV = intravenous



# ARTEMIDE-Biliary01 Trial: Rilvegostomig and Chemotherapy as Adjuvant Therapy for Biliary Tract Cancer After Resection



# Agenda

**Introduction:** Is Biliary Tract Cancer (BTC) the New Non-Small Cell Lung Cancer? ... Why?

**Case 1:** Do BTC Subtypes Respond Differently to Checkpoint Inhibitors?

**Case 2:** Anti-HER2-Directed Therapy for HER2-Low BTC?

**Case 3:** FGFR Inhibitors in the Front-Line Setting?

**Case 4:** Bone and Muscle Pain with an FGFR Inhibitor

**Case 5:** Improved Targeted Clinical Benefit for Specific FGFR Mutations?

**Case 6:** Sequencing of Available HER2-Targeted Agents

**Case 7:** IDH Inhibitors in Combination with Chemotherapy as Initial Therapy?

**Case 8:** BRAF and IDH Mutations — Which Targeted Treatment First?

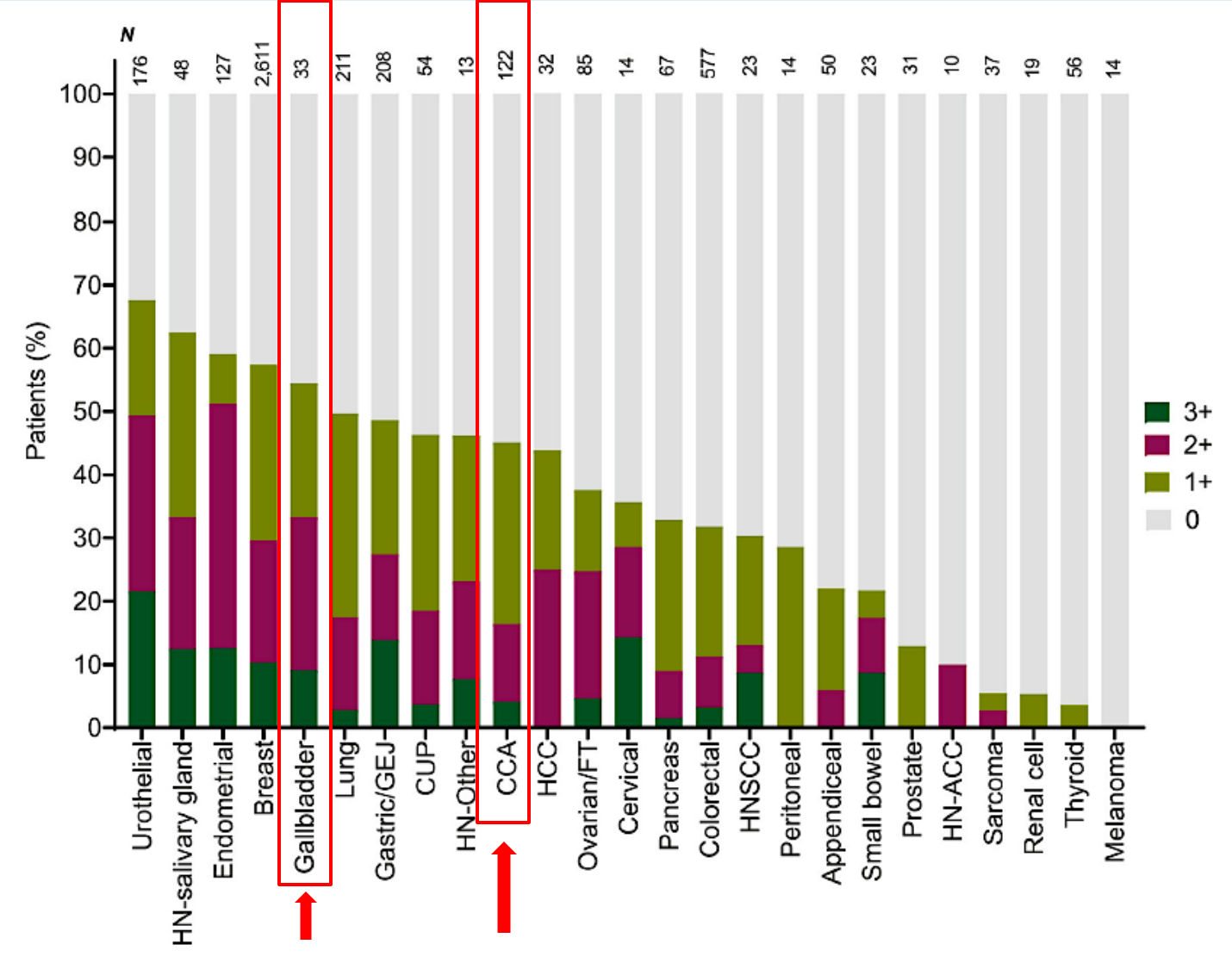
**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?

**Case Presentation: 79-year-old man with history of Crohn's disease and metastatic biliary cancer (HER2 IHC 2+) discontinues first-line chemotherapy/IO due to exacerbation of Crohn's**



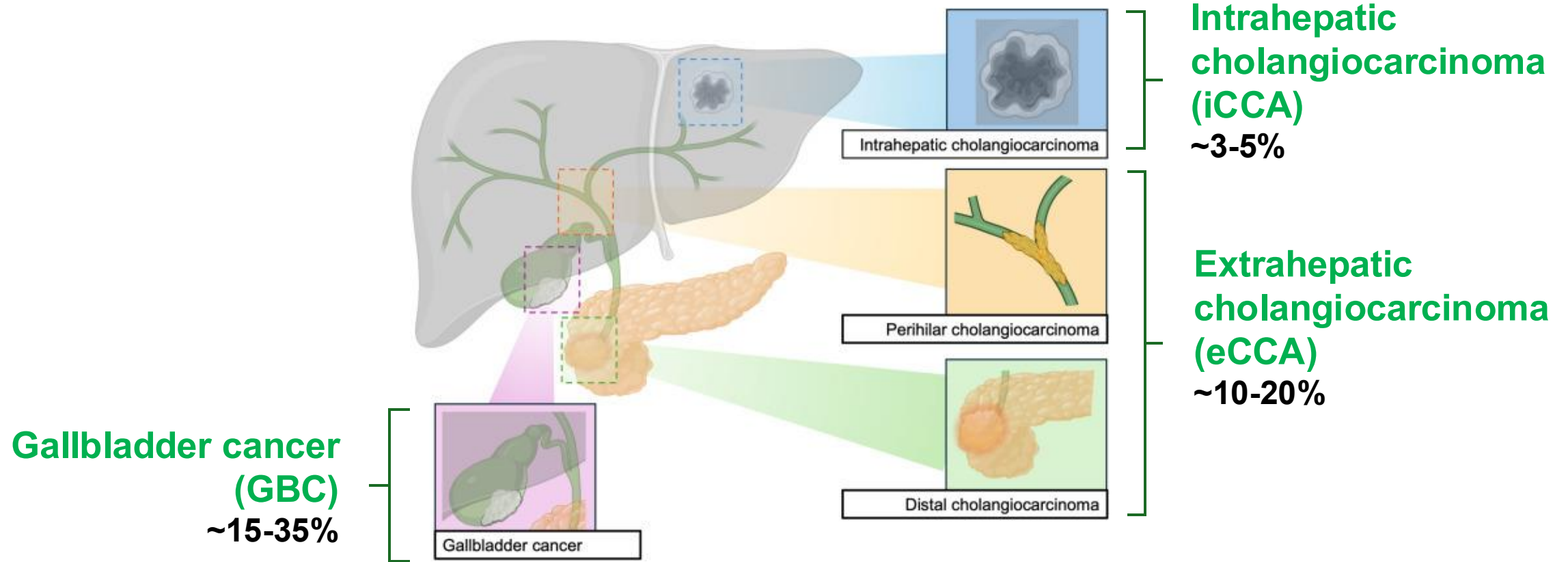
**Dr Neil Morganstein (Summit, New Jersey)**

# Distribution of HER2 IHC Expression Levels Across Cancer Types



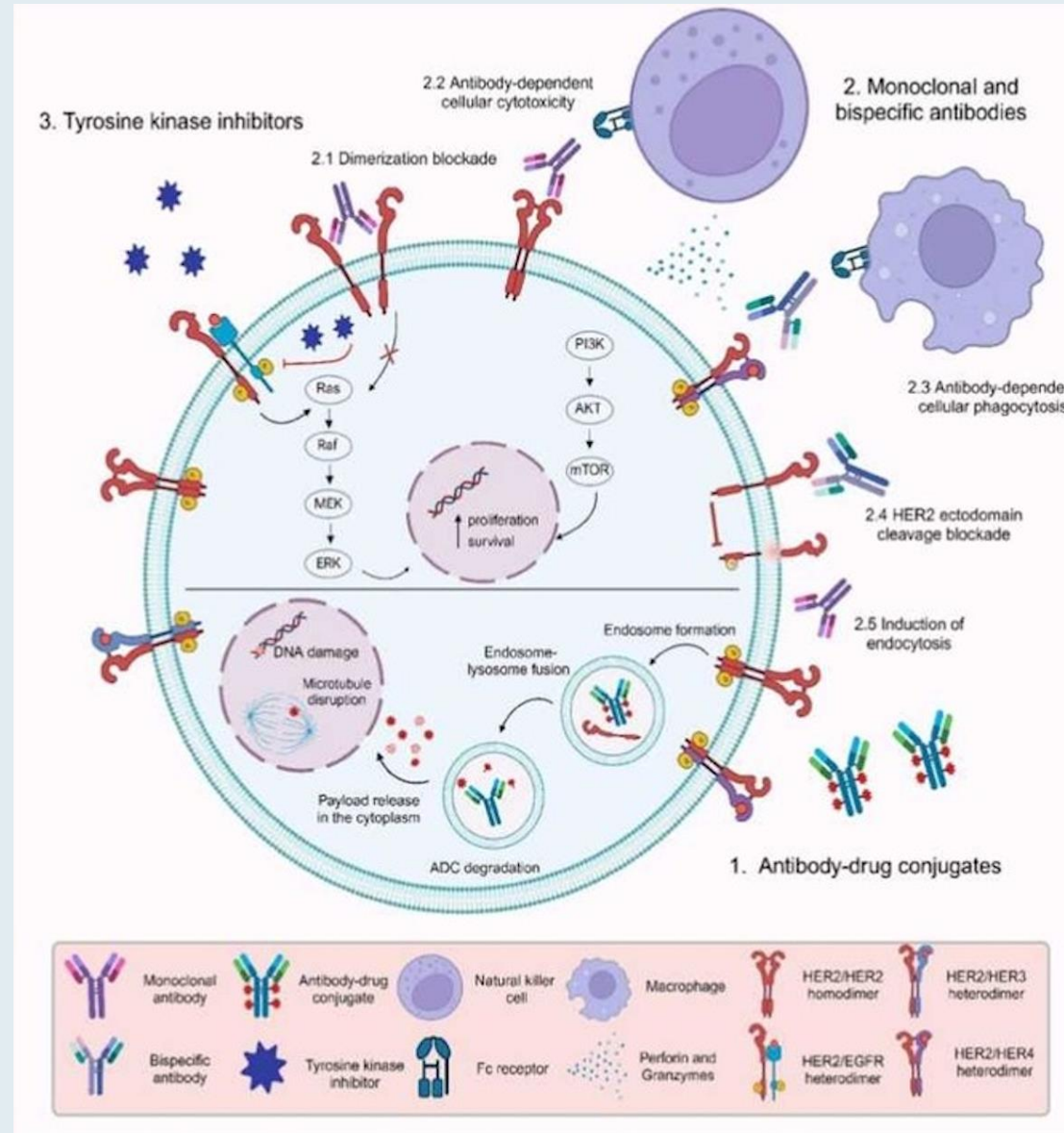


# HER2 amplification/overexpression spans all BTC subtypes



HER2 positivity is associated with a **worse prognosis** in advanced BTC

# HER2-Targeted Modalities in Biliary Tract Cancers









# HER2 testing in BTC: who, when, and how

✓ **WHO:** All patients with locally advanced or metastatic BTC (GBC, eCCA, iCCA)

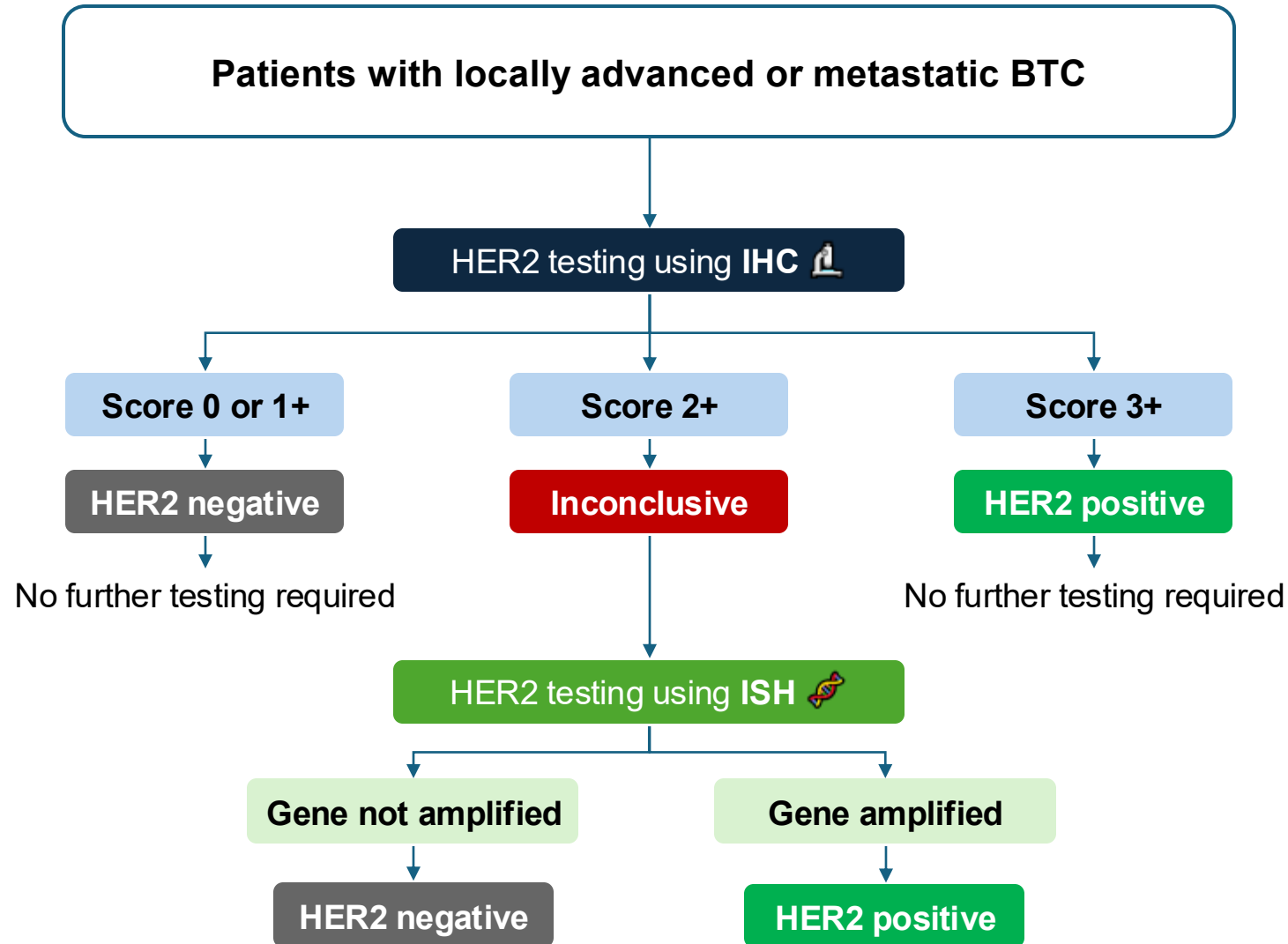
✓ **WHEN:** At diagnosis

- 1<sup>st</sup> line trials!
- Future direction: consider earlier testing for neoadjuvant/perioperative strategies

✓ **HOW:**

	Immunohistochemistry (IHC) 	<i>In situ</i> hybridization (ISH) 	Next-generation sequencing (NGS) 
What it detects	HER2 protein	<i>ERBB2</i> DNA	<i>ERBB2</i> DNA
What it indicates	HER2 overexpression	<i>ERBB2</i> amplification	<i>ERBB2</i> amplification
Tissue and/or blood-based			

# HER2 testing in BTC follows gastroesophageal cancer guidelines



# Comprehensive HER2 testing with NGS *and* IHC is important

Correlation of HER2 grading using NGS and IHC		
	NGS result	
	HER2 not amplified* (n=182)	HER2 amplified* (n=19)
<b>IHC score</b>		
0	30%	0%
1+	25%	11%
2+	40%	58%
3+	5%	32%
<b>HER2 IHC classification</b>		
HER2 negative	85%	16%
HER2 positive	15%	68%
N/A (2+, ISH not done)	0%	21%



**~15% discordance** between HER2 assessment by NGS vs IHC in BTC

# Evolving treatment landscape in HER2+ BTC in second-line setting and beyond

	Treatment	Trial	# BTC pts	Prior HER2 Tx	HER2 Status	ORR	DCR	mDOR (mo)	mPFS (mo)	mOS (mo)
ABC-06 <sup>1</sup> 2021	FOLFOX	Phase 3	162	--	--	5%	33%	--	4.0	6.2
MyPathway <sup>2</sup> 2021	Trastuzumab + Pertuzumab	Phase 2a	39	No	IHC 3+, ISH+, or NGS Amp	23%	51%	10.8	4.0	10.9
KCSG-HB19-14 <sup>3</sup> 2023	Trastuzumab + FOLFOX	Phase 2	34	No	IHC 3+, IHC 2+/ISH+, or NGS Amp	29%	79%	4.9	5.1	10.7
HERIZON-BTC-01 <sup>4</sup> 2023	Zanidatamab	Phase 2b	62 80	No	IHC 3+ IHC 3+ or IHC 2+/Amp	52% 41%	79% 69%	14.9 12.9	7.2 5.5	18.1 15.5
SGNTUC-019 <sup>5</sup> 2023	Trastuzumab + Tucatinib	Phase 2	30	No	IHC 3+, ISH+, or NGS Amp	47%	77%	6.0	5.5	15.5
DESTINY-PanTumor02 <sup>6</sup> 2023	Trastuzumab Deruxtecan	Phase 2	16 41 14	Yes (17%)	IHC 3+ IHC 3+ or 2+ IHC 2+	56% 22% 0%	78% -- --	22.1 8.6 --	7.4 4.6 4.2	12.4 7.0 6.0
HERB <sup>7</sup> 2024	Trastuzumab Deruxtecan	Phase 2	22 8	Yes (n=0)	IHC 3+ or IHC 2+/ISH+ IHC 2+/ISH-, IHC 1+, or IHC 0/ISH+	36% 13%	82% 75%	7.4 --	5.1 3.5	7.1 8.9

<sup>1</sup>Lamarca et al. Lancet Oncol 2021 | <sup>2</sup>Javle et al. Lancet Oncol 2021 | <sup>3</sup>Lee et al. Lancet Gastroenterol Hepatol 2023 | <sup>4</sup>Harding, Fan, et al. Lancet Oncol 2023 | <sup>5</sup>Nakamura et al. J Clin Oncol 2023 | <sup>6</sup>Meric-Bernstam et al. J Clin Oncol 2023 | <sup>7</sup>Ohba et al. J Clin Oncol 2024  
Courtesy of Haley Ellis, MD

# Agenda

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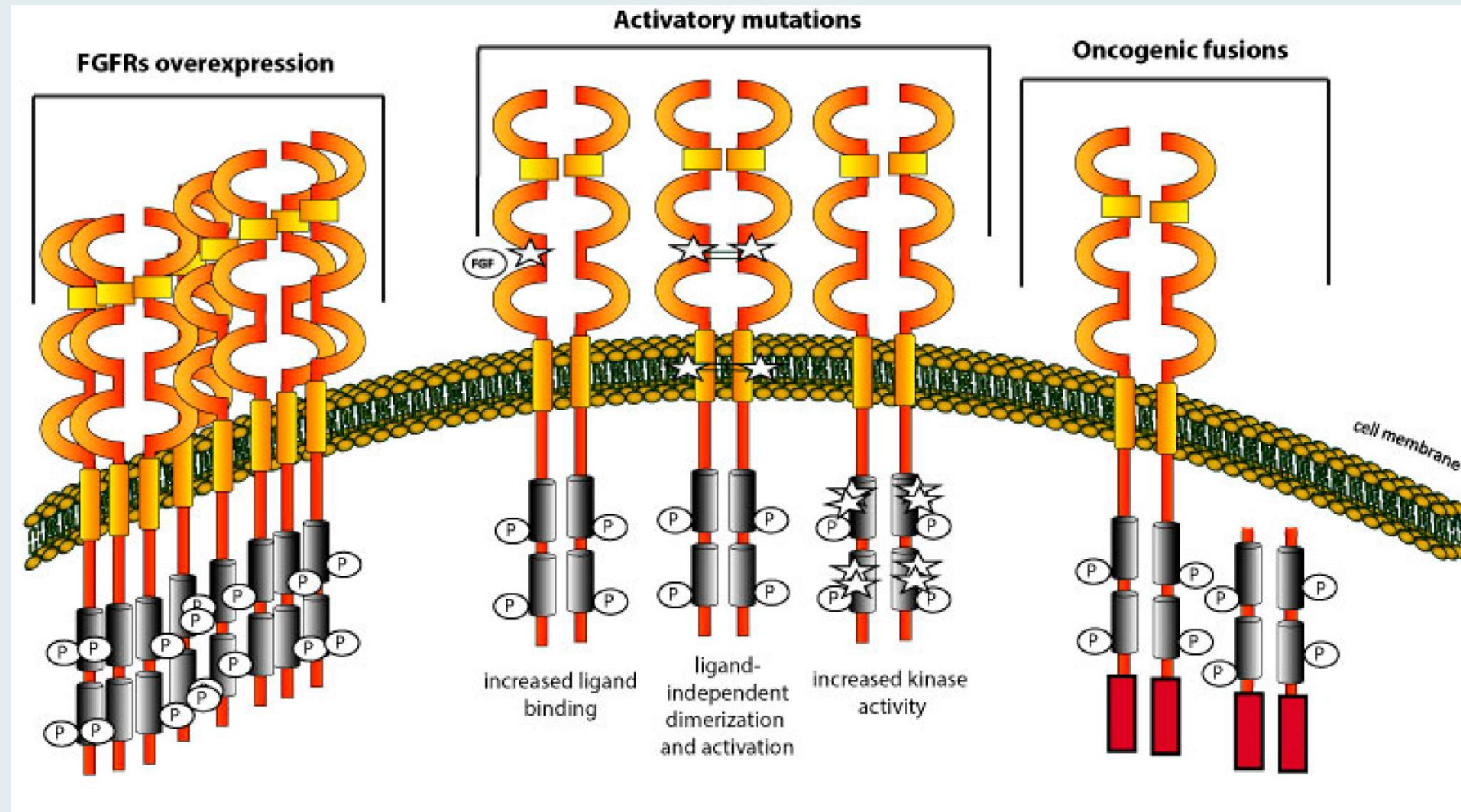
**Case Presentation: 72-year-old man with metastatic cholangiocarcinoma (FGFR2 rearrangement) receives gemcitabine/oxaliplatin with durvalumab and experiences a rapid clinical decline**



**Dr Kimberly Ku (Bloomington, Illinois)**



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



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

	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

ORIGINAL RESEARCH

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

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

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

2024;9(6):103488.

# FIGHT-202 Final Results: Response to Pemigatinib

Parameter	<i>FGFR2</i> fusions or rearrangements ( <i>n</i> = 108)	Other <i>FGF/FGFR</i> alterations ( <i>n</i> = 20)	No <i>FGF/FGFR</i> alterations ( <i>n</i> = 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, <i>n</i> (%)	40 (37.0)	0	0
95% CI	27.9-46.9	0-16.8	0-19.5
Best overall response, <i>n</i> (%)			
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, <i>n</i> (%)	30 (75.0)	0	0
Censored, <i>n</i> (%)	10 (25.0)	0	0
Median (95% CI), months	9.1 (6.0-14.5)	—	—
≥12 months, <i>n</i> (%) <sup>a</sup>	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, <i>n</i> (%)	89 (82.4)	8 (40.0)	3 (17.6)
95% CI	73.9-89.1	19.1-63.9	3.8-43.4

ORR = objective response rate

## 121P- PemiBil : efficacy and safety of PEMIGATINIB in advanced cholangiocarcinoma with FGFR2 fusions/rearrangements in real-world, results of multicentric French cohort from ACABI consortium

B. Delaunay<sup>1</sup>, A. Hollebecque<sup>2</sup>, M. Bouattour<sup>3</sup>, J.F. Blanc<sup>4</sup>, E. Assenat<sup>5</sup>, A. Turpin<sup>6</sup>, M. Sarabi<sup>7</sup>, G. Roth<sup>8</sup>, D. Tougeron<sup>9</sup>, J. Edeline<sup>10</sup>, M. Ben Abdelghani<sup>11</sup>, A. Vienne<sup>12</sup>, S. Hiret<sup>13</sup>, P. Artru<sup>14</sup>, M. Stacoffe<sup>15</sup>, D. Malka<sup>16</sup>, C. Neuzillet<sup>17</sup>, A. Lievre<sup>18</sup>, R. Guimbaud<sup>1</sup>, N. Fares<sup>1</sup>



# Real-World Efficacy with Pemigatinib

The objective response rate was 45,3% with 3 (5,7%) complete responses and 21 (39,6%) partial responses (n = 24).  
The disease control rate was 88,7% in the whole cohort.

The median progression free survival (PFS) was 9 months (IIQ 6-14) and the median overall survival (OS) was 18 months (IIQ 12-NA) (*Figure 1*) .

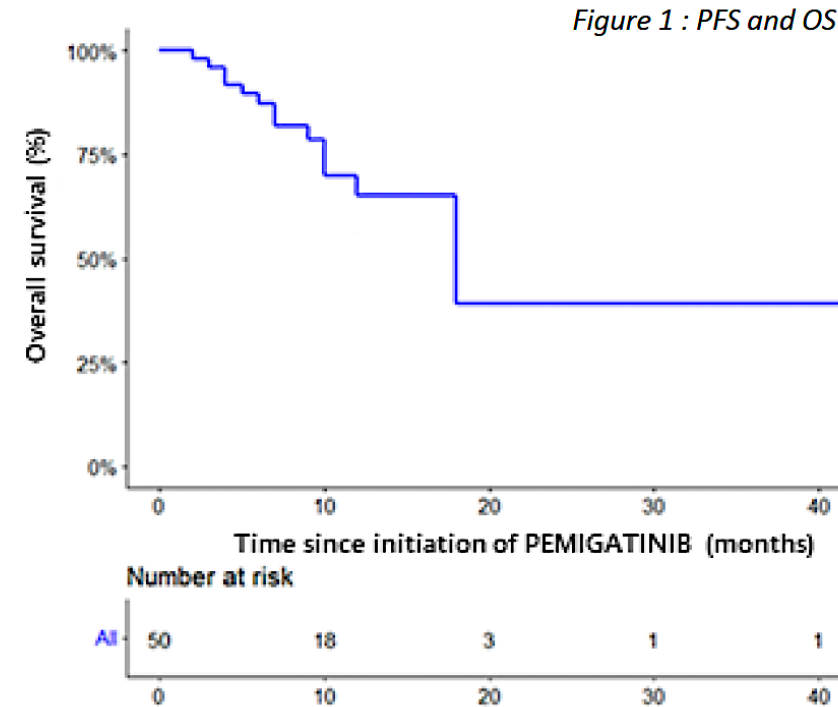
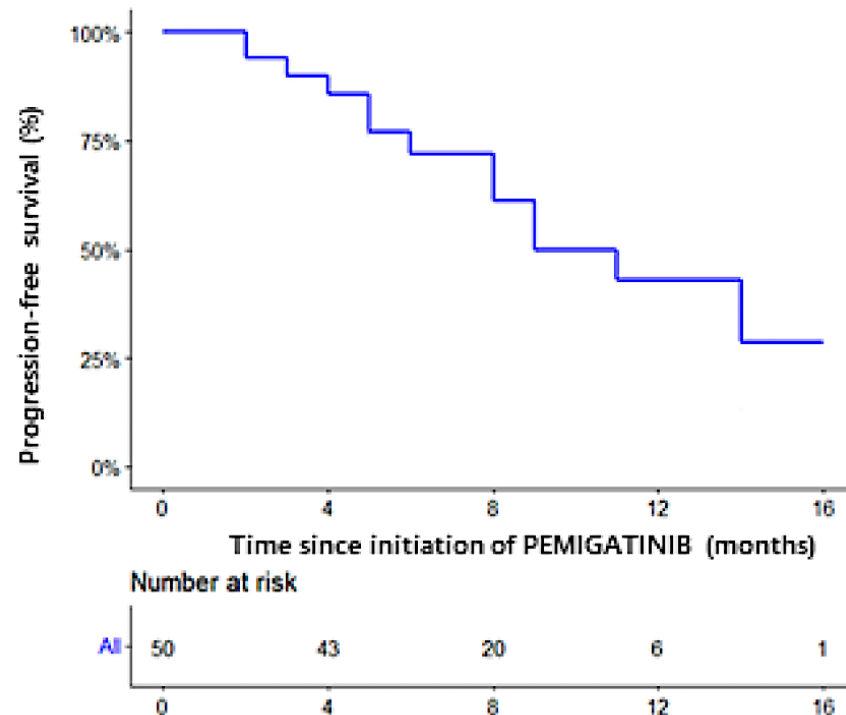


Figure 1 : PFS and OS

# Real-World Safety with Pemigatinib

Adverse event at 13,5 mg dose (n = 48)	All grade n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)
Hyperphosphatemia	28 (58)	13 (27)	15 (31)	-
Nail toxicities	28 (58)	15 (31)	10 (21)	3 (6)
Dry eye	20 (42)	14 (29)	6 (12)	-
Keratitis	5 (10)	4 (8)	1 (2)	1 (2)
Retinal detachment	4 (8)	3 (6)	1 (2)	-
Asthenia	28 (58)	18 (37)	6 (12)	4 (8)
Weight decreased	16 (33)	15 (31)	1 (2)	-
Erythema	7 (15)	5 (10)	2 (4)	-
Palmo-plantar erythrodysesthesia	14 (29)	6 (12)	6 (12)	2 (4)
Myalgia	15 (31)	12 (25)	1 (2)	2 (4)
Dysgeusia	6 (12)	5 (10)	1 (2)	-
Stomatitis	23 (48)	12 (25)	9 (18)	2 (4)
Diarrhea	14 (29)	10 (21)	4 (8)	-
Nausea / vomiting	8 (17)	7 (15)	1 (2)	-
Alopecia	12 (25)	2 (4)	10 (21)	-
Arthralgia	5 (10)	3 (6)	1 (2)	1 (2)
Anemia	13 (27)	6 (12)	6 (12)	1 (2)
Hepatic cytolysis	9 (19)	6 (12)	2 (4)	1 (2)
Hypophosphatemia	6 (12)	4 (8)	2 (4)	-

Table 2: toxicities at 13,5 mg dose

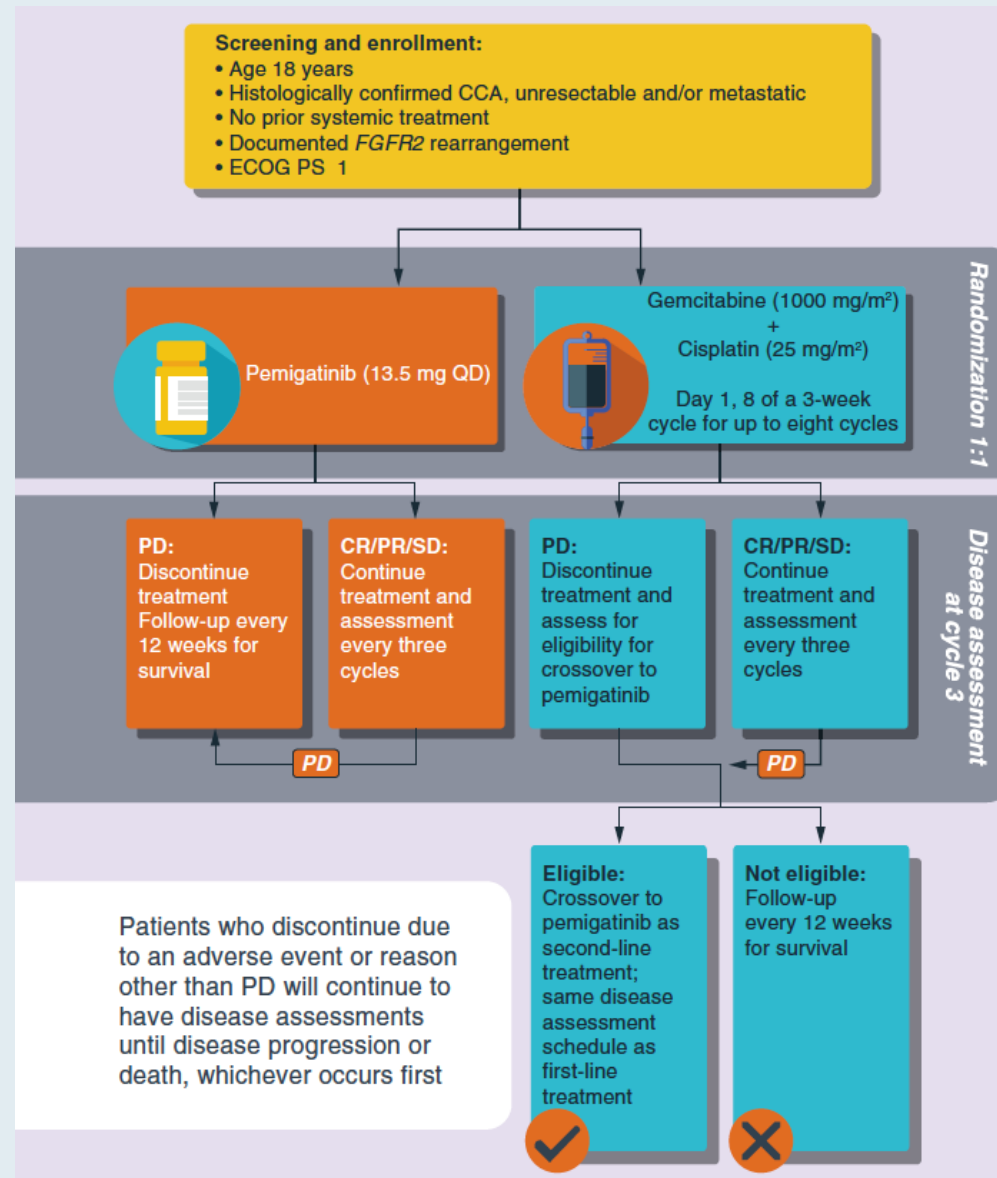
# FIGHT-302: An Ongoing Phase III Trial of First-Line Pemigatinib versus Gemcitabine/Cisplatin for Advanced Cholangiocarcinoma with FGFR2 Rearrangements

Trial identifier: NCT03656536 (Closed)  
Actual enrollment: 167

Primary endpoint: Progression-free survival

CCA = cholangiocarcinoma; PD = disease progression

Bekaii-Saab T et al. *Future Oncol* 2020;16(30):2385-99;  
[www.clinicaltrials.gov](http://www.clinicaltrials.gov). Accessed August 2025.





# Phase IIa Study of First-Line Cyclical Therapy Alternating Durvalumab/Gemcitabine/Cisplatin with Pemigatinib

- In this monocenter, single-arm, and 3-year phase 2 clinical trial, treatment-naïve patients with FGFR2-altered advanced BTCs, PS  $\leq 1$ , are eligible (**Figure 2**).
- Cyclical therapy is alternated between two therapy-blocks, starting from C-IO block (2 cycles of gemcitabine, cisplatin and durvalumab, 28-day/cycle), then FGFRi block (3 cycles of pemigatinib on day 1-14 of 21-day/cycle). Block-switch continues until progressive disease (PD), and then we will continue alternated block until the next PD (more details in **Figure 3**).
- A sample size of 30 is calculated based on an expected 12-month OS rate of  $\geq 55\%$ .

## Eligibility criteria:

- Biliary tract cancers:
  - 1) *Cholangiocarcinoma*
  - 2) *Gallbladder cancer*
  - 3) *Ampullary cancer*
- Advanced or metastatic disease;
- *FGFR2* fusions, rearrangements, or other GOF mutations;
- Treatment-naïve;
- ECOG PS 0 or 1;
- Life expectancy:  $\geq 4$  months.

## Monocenter, single arm, phase II trial.

Receive cyclical therapy alternating with:

A. Chemoimmunotherapy (CIO) block:

- 1) Gemcitabine
- 2) Cisplatin
- 3) Durvalumab

B. FGFR inhibitor (FGFRi) block

- 1) Pemigatinib

## Assessment:

Restaging scans  
after each block;  
Adverse events;  
Follow up survivals.

## Objectives:

- Primary objectives:
  - ❖ *12-month OS.*
- Secondary objectives:
  - ❖ *Overall response rate*
  - ❖ *Disease control rate*
  - ❖ *Duration of therapies*
  - ❖ *Progression-free survival*
  - ❖ *Overall survival*
  - ❖ *Adverse events*
- Exploratory objectives:
  - ❖ *ctDNA dynamics*

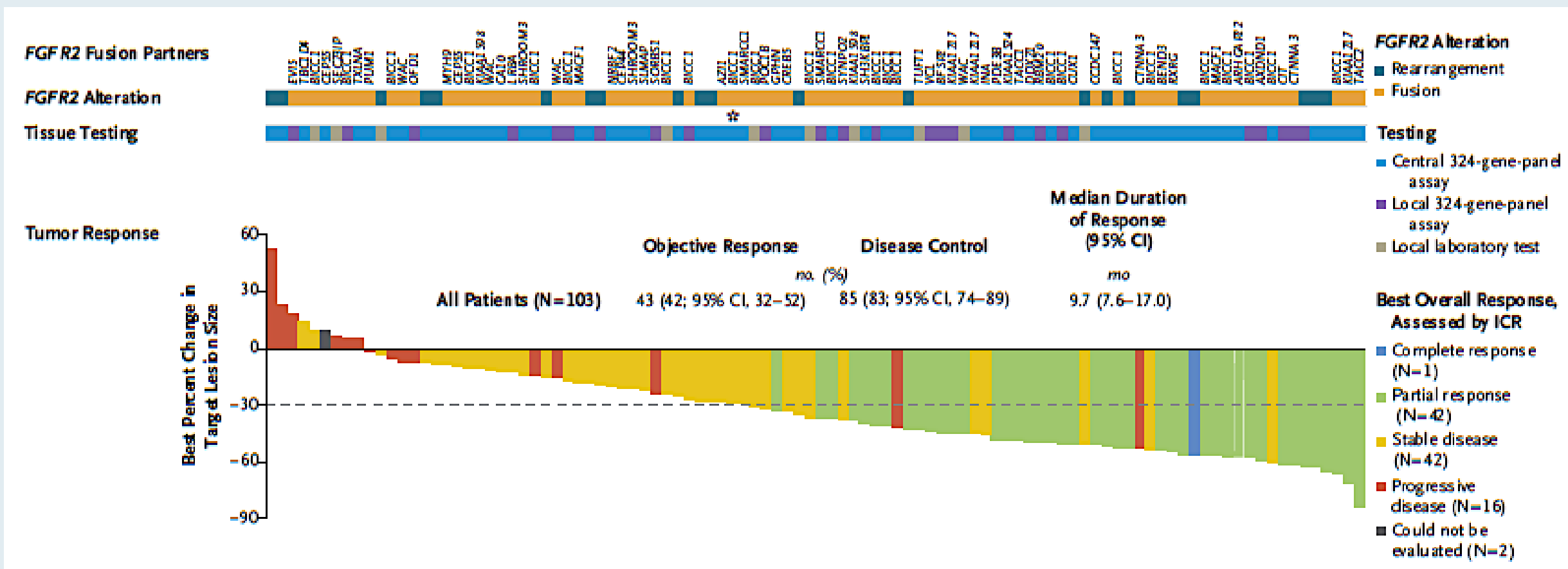
ORIGINAL ARTICLE

# 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. Klümper, 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: A Phase II Study of Futibatinib for Intrahepatic Cholangiocarcinoma with FGFR2 Fusions or Rearrangements



Median PFS: 9.0 mo  
Median OS: 21.7 mo

# Agenda

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**Case 7:** IDH Inhibitors in Combination with Chemotherapy as Initial Therapy?

**Case 8:** BRAF and IDH Mutations — Which Targeted Treatment First?

**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?

**Case Presentation: 60-year-old man with metastatic cholangiocarcinoma (FGFR2 rearrangement) experiences severe muscle pain while receiving infigratinib**



**Dr Joseph Martins (Tyler, Texas)**

# Agenda

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**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?



## Case Presentation: 49-year-old woman with Stage IV recurrent cholangiocarcinoma (FGFR2 rearrangement) receives pemigatinib



**Dr Justin Favaro (Charlotte, North Carolina)**



# Phase I/II Trial of Pemigatinib in Combination with Atezolizumab and Bevacizumab for Advanced Cholangiocarcinoma with FGFR2 Fusion

## Key Eligibility Criteria

- Age  $\geq 18$  years
- Metastatic or advanced unresectable cholangiocarcinoma
- FGFR2 fusion or rearrangement
- Refractory, intolerant, received or refused access to first-line gemcitabine-based therapy +/- durvalumab or pembrolizumab
- ECOG PS of 0 or 1

Non-  
randomized  
N = 25

Pemigatinib (PO)  
Atezolizumab (IV)  
Bevacizumab (IV)

**Primary Outcome Measures:** Safety and adverse events

PO = By mouth; IV = Intravenous

# Phase II Study of Pemigatinib and Durvalumab for Previously Treated Advanced Intrahepatic Cholangiocarcinoma with FGFR2 Fusion or Rearrangement

## Key Eligibility Criteria

- Age  $\geq 18$  years
- Locally advanced unresectable or metastatic intrahepatic cholangiocarcinoma with FGFR2 fusion or rearrangement
- ECOG PS of 0 or 1
- FGFR inhibitor-naïve
- Received gemcitabine, cisplatin and durvalumab or another anti-PD-1 Ab with either disease progression, intolerance to cytotoxic chemotherapy or at least 6 months of therapy with stable disease or partial response.
- Neo(adjuvant) therapy permitted if no disease recurrence  $\leq 6$  mo after completion

Non-  
randomized  
N=38

Pemigatinib 13.5 mg (PO)  
Durvalumab 1,500 mg (IV)

**Primary Outcome Measure:** Confirmed objective response rate

Ab = antibody

# Pemigatinib with Afatinib for Advanced Refractory Solid Tumors

## Key Eligibility Criteria

- Age  $\geq 18$  years
- Advanced solid tumor where standard curative or palliative measures are no longer effective, appropriate or safe
- FGFR1-2 fusion, rearrangement, activating mutation or FGFR2 extracellular domain in-frame deletion
- ECOG PS 0-1

Non-  
randomized  
N=70

## Phase Ia Dose Escalation

Afatinib q21d (PO)

Pemigatinib q21d (PO)

## Phase Ib Cohort 1 (FGFRi-naïve)

Afatinib q21d (PO)

Pemigatinib q21d (PO)

## Phase Ib Cohort 2 (FGFRi-pretreated)

Afatinib q21d (PO)

Pemigatinib q21d (PO)

**Primary Outcome Measures:** maximum tolerated dose, objective response rate

FGFRi = FGFR inhibitor

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**Case 4:** Bone and Muscle Pain with an FGFR Inhibitor

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**Case 6: Sequencing of Available HER2-Targeted Agents**

**Case 7:** IDH Inhibitors in Combination with Chemotherapy as Initial Therapy?

**Case 8:** BRAF and IDH Mutations — Which Targeted Treatment First?

**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?

## Case Presentation: 63-year-old woman with HER2-positive cholangiocarcinoma develops metastatic disease during adjuvant capecitabine therapy



**Dr Neil Morganstein (Summit, New Jersey)**

# 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.”

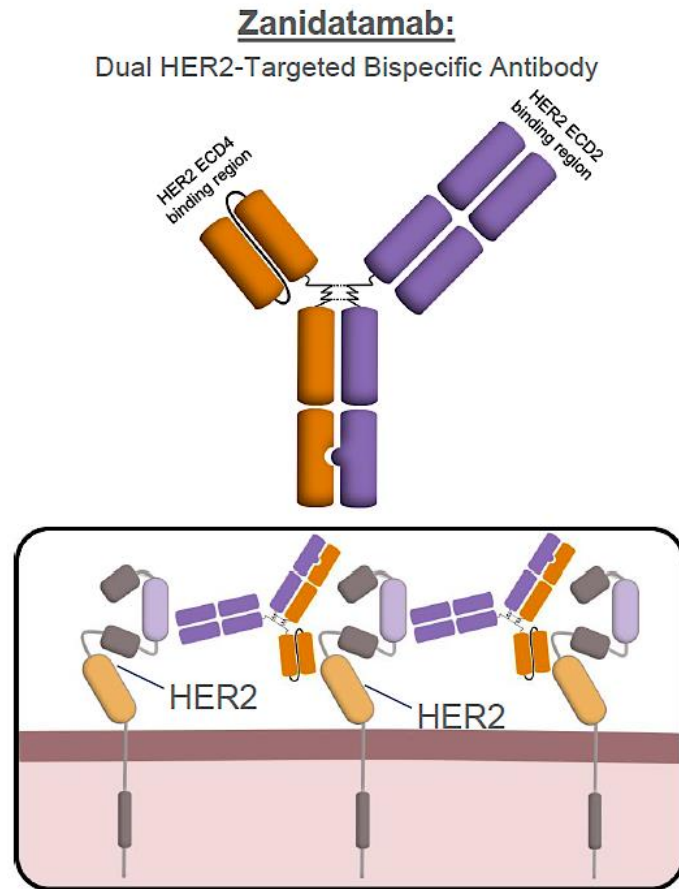
<https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-zanidatamab-hrii-previously-treated-unresectable-or-metastatic-her2>

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



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



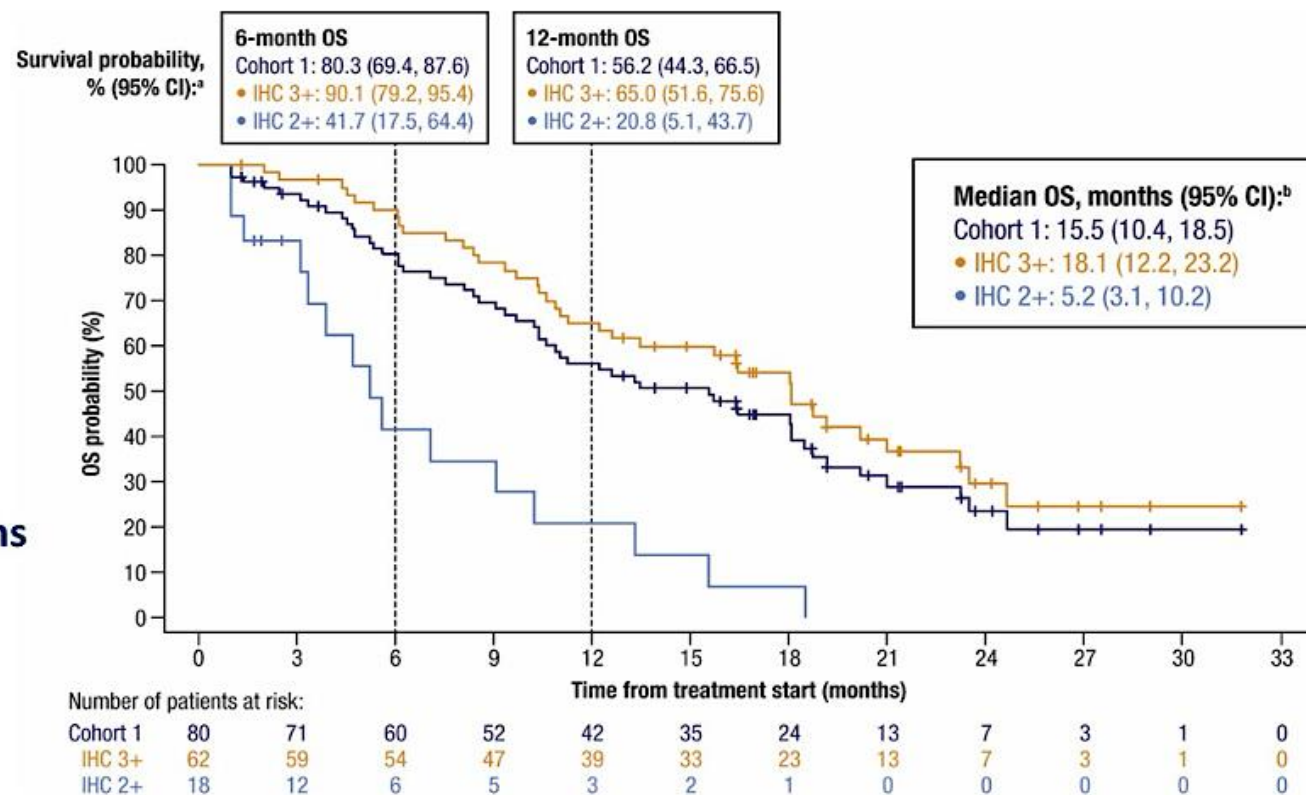
- BTC accounts for less than 1% of adult cancers and is associated with a poor prognosis<sup>1,2</sup>
- After failure of first-line treatment, subsequent chemotherapy is associated with a median OS of approximately 6-9 months and poor tolerability<sup>3,4</sup>
- Zanidatamab is a humanized, IgG1-like, HER2-targeted bispecific antibody that binds to 2 distinct domains on HER2<sup>5</sup>
- 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<sup>6</sup>

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

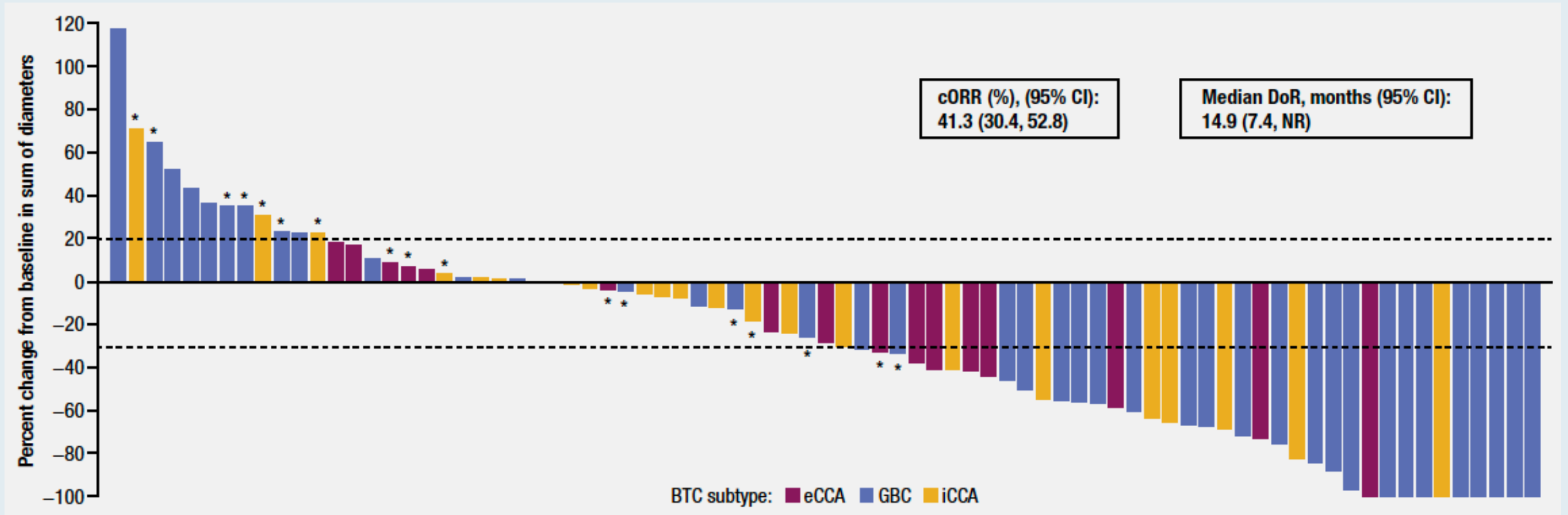
# HERIZON-BTC-01: Long-Term Efficacy Outcomes

- 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;<sup>1</sup> 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<sup>1</sup>**
- The median OS (95% CI) was 15.5 (10.4, 18.5) months**



DCR = disease control rate; CR = complete response; DOR = duration of response; NR = not reached

# HERIZON-BTC-01: Target Lesion Reduction with Zanidatamab



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



# 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 <sup>a</sup>	18 (20.7)	
Grade 5	0 (0)	
Serious TRAEs <sup>b</sup>	8 (9.2)	
TRAEs leading to treatment discontinuation, n (%)	2 (2.3) <sup>c</sup>	
Most common TRAEs, <sup>d</sup> 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; AESI = adverse event of special interest

# 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

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

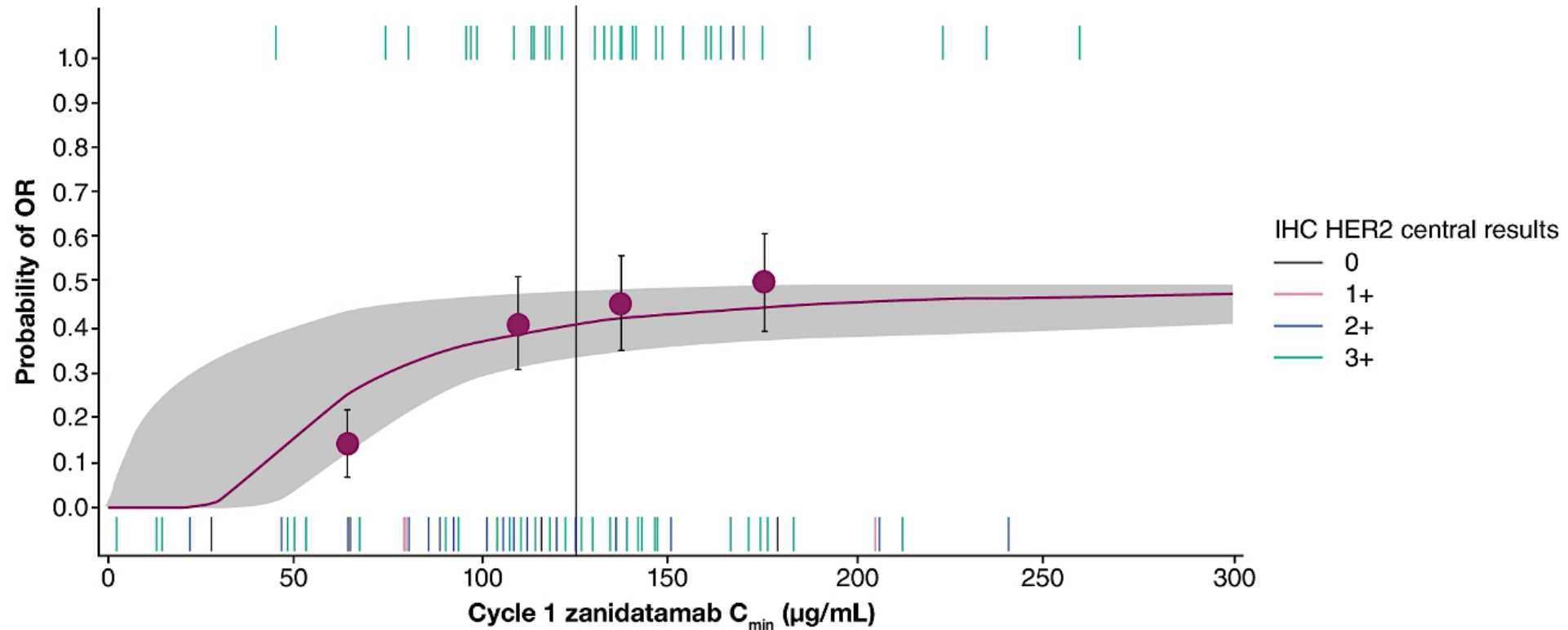
Trueman S et al.

Gastrointestinal Cancers Symposium 2025;Abstract 546.



# Zanidatamab Pharmacokinetics

Figure 3. Zanidatamab Exposure-Efficacy Relationship in Patients With BTC



## Conclusions

- This analysis supports the approved dose of zanidatamab (20 mg/kg Q2W) for patients with HER2-positive BTC based on:
  - Reaching the desired target exposure (IC90 for LDGI)
  - Saturating target-mediated elimination pathway
  - The exposure-response analysis showing that exposures following this dose support the efficacy (exposures for the majority of patients on the plateau) and safety (no correlation with grade  $\geq 3$  diarrhea) balance in the BTC population



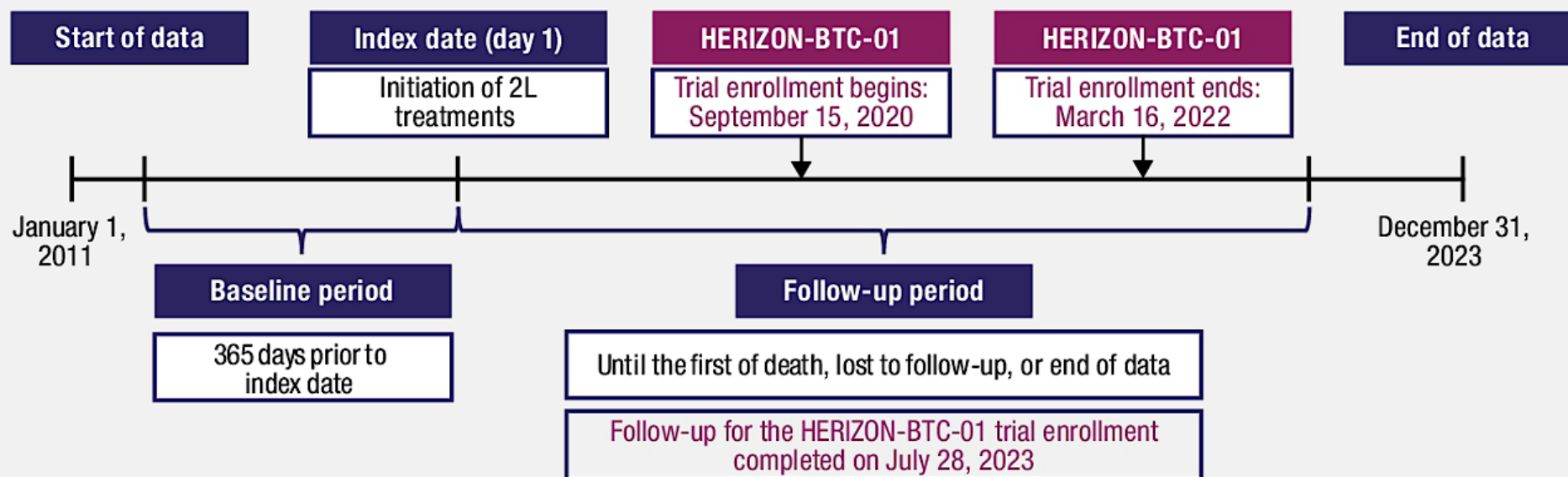
# Survival Outcomes for Zanidatamab-hrii Compared to Chemotherapy in Previously Treated HER2-Positive (IHC3+) Biliary Tract Cancer (BTC): HERIZON-BTC-01 vs a Real-World (RW) External Control Arm (ECA)

Kim RD et al.

ASCO 2025;Abstract 4101.

# HERIZON-BTC-01 versus a Real-World External Control Arm (ECA)

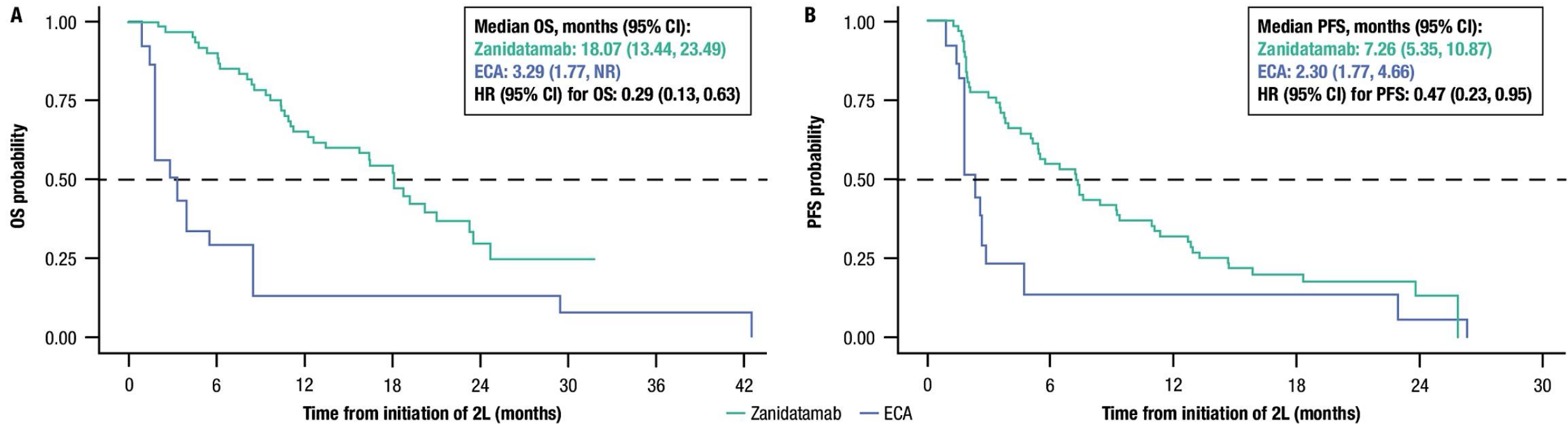
- This study compared 2 cohorts:
  - **Zanidatamab** - patients from the HERIZON-BTC-01 trial (NCT04466891) with HER2+ (IHC 3+), unresectable, locally advanced, or metastatic BTC (iCCA, eCCA, GBC) who had received prior gemcitabine-containing therapy
    - Patients had received zanidatamab 20 mg/kg intravenously every 2 weeks
  - **ECA** - constructed using data from the Flatiron Health Research Analytic Database (longitudinal, deidentified, patient-level database derived from electronic health records [EHRs] at community and academic cancer clinics in the USA)
    - Patients had received 2L chemotherapy, as defined in the database



Note: A total of 29,000 patients were initially assessed, with 290 patients meeting the criteria listed.  
2L, second-line

# HERIZON-BTC-01 versus a Real-World ECA: Survival

Figure 3. SMR-Weighted (A) OS and (B) PFS



SMR = standardized mortality ratio; OS = overall survival; PFS = progression-free survival

# HERIZON-BTC-01 versus a Real-World ECA: 6-Month and 12-Month Outcomes

	6 Months		12 Months	
	Survival	Difference in Survival	Survival	Difference in Survival
<b>OS, % (95% CI)</b>				
Zanidatamab	90 (83, 98)	61 (32, 90)	65 (54, 78)	52 (29, 74)
ECA	29 (11, 75)		13 (3, 55)	
<b>PFS, % (95% CI)</b>				
Zanidatamab	55 (44, 69)	41 (20, 62)	32 (22, 46)	18 (-2, 39)
ECA	14 (4, 47)		14 (4, 47)	

CI, confidence interval; ECA, external control arm; OS, overall survival; PFS, progression-free survival.

# **Antitumour Activity and Safety of First-Line Zanidatamab + Cisplatin-Gemcitabine in Patients with HER2-Expressing Biliary Tract Cancer (BTC)**

Oh D-Y et al.

ESMO GI 2025;Abstract 319P.

# Phase II Study of First-Line Zanidatamab with Cisplatin/Gemcitabine

- This is a global, open-label, 2-part, phase 2 trial (NCT03929666) evaluating zanidatamab plus standard combination chemotherapy for HER2-expressing advanced gastrointestinal cancers, including gastro-oesophageal adenocarcinoma,<sup>13</sup> colorectal cancer,<sup>14</sup> and BTC

**Figure 2. Study Design**

## Eligibility criteria

- Aged  $\geq 18$  years at the time of signing informed consent
- Unresectable, locally advanced, recurrent, or metastatic HER2-expressing BTC (including GBC, ICCA, and eCCA)
- HER2: IHC 3+; or IHC 0, 1+, or 2+ with gene amplification (FISH+) per central assessment
- Baseline ECOG PS of 0 or 1
- No prior HER2-targeted treatment
- No more than 1 cycle of any standard gemcitabine-based chemotherapy regimen

## Zanidatamab

1800 mg (patients  $< 70$  kg) or  
2400 mg (patients  $\geq 70$  kg) IV Q3W

Patients received mandatory prophylaxis for potential infusion-related reactions<sup>a</sup> before every zanidatamab infusion and mandatory antidiarrhoeal prophylaxis<sup>b</sup> for at least the first 7 days during the first treatment cycle.

+

## CisGem

Cisplatin 25 mg/m<sup>2</sup> IV  
Gemcitabine 1000 mg/m<sup>2</sup> IV  
on days 1 and 8 of each 21-day cycle

Continuation of chemotherapy was at the discretion of the investigator and patient after cycle 6.<sup>c</sup> Patients who stopped CisGem without disease progression and for reasons not related to zanidatamab toxicity could continue on zanidatamab monotherapy.

CT/MRI scans  
Q6W per  
RECIST v1.1

## Primary endpoint<sup>d</sup>

- Investigator-assessed confirmed objective response rate

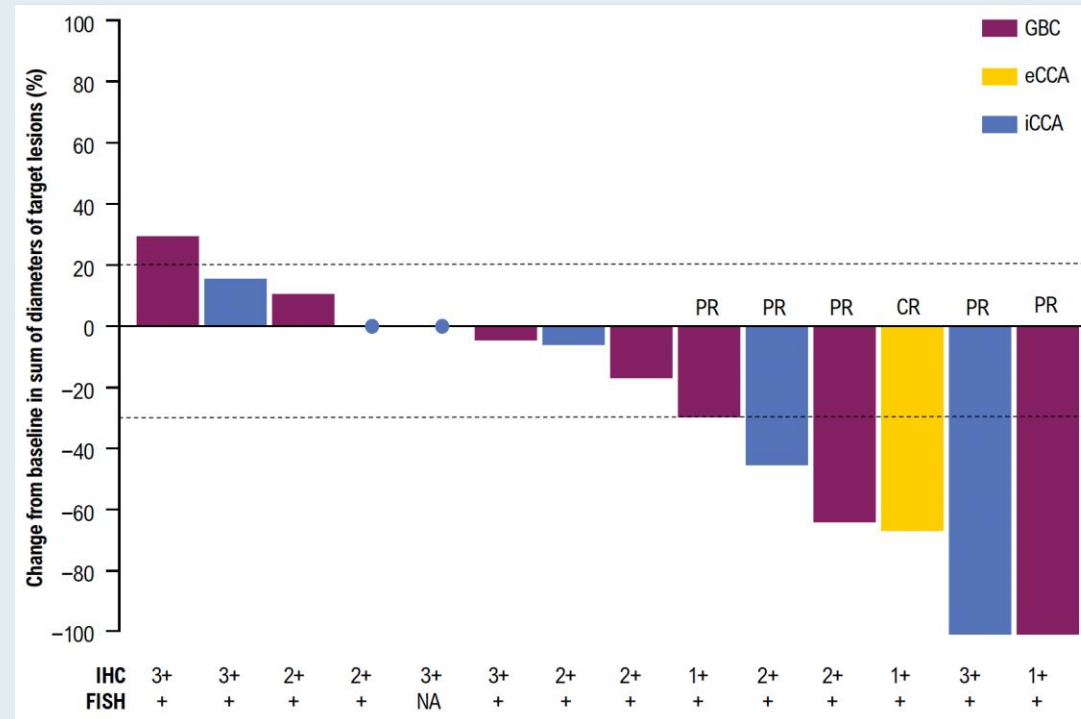
## Select secondary endpoints<sup>d</sup>

- Disease control rate
- Duration of response
- Progression-free survival
- Overall survival
- Rate and severity of adverse events



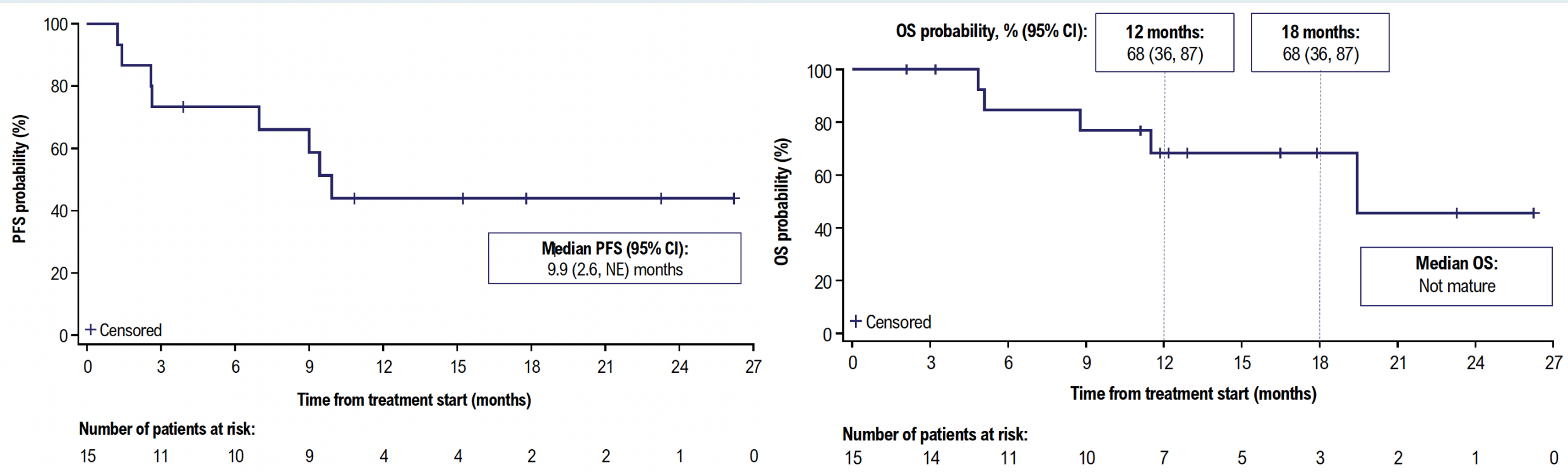
# Phase II Study of First-Line Zanidatamab with Chemotherapy: Response

	Response-Evaluable Patients <sup>a</sup> (n = 14)
<b>Confirmed objective response rate, n (% [95% CI])</b>	6 (43 [18, 71])
<b>Best confirmed response, n (%)</b>	
Complete response	1 (7)
Partial response	5 (36)
Stable disease	6 (43)
Progressive disease	2 (14)
<b>Disease control rate<sup>b</sup>, n (% [95% CI])</b>	12 (86 [57, 98])

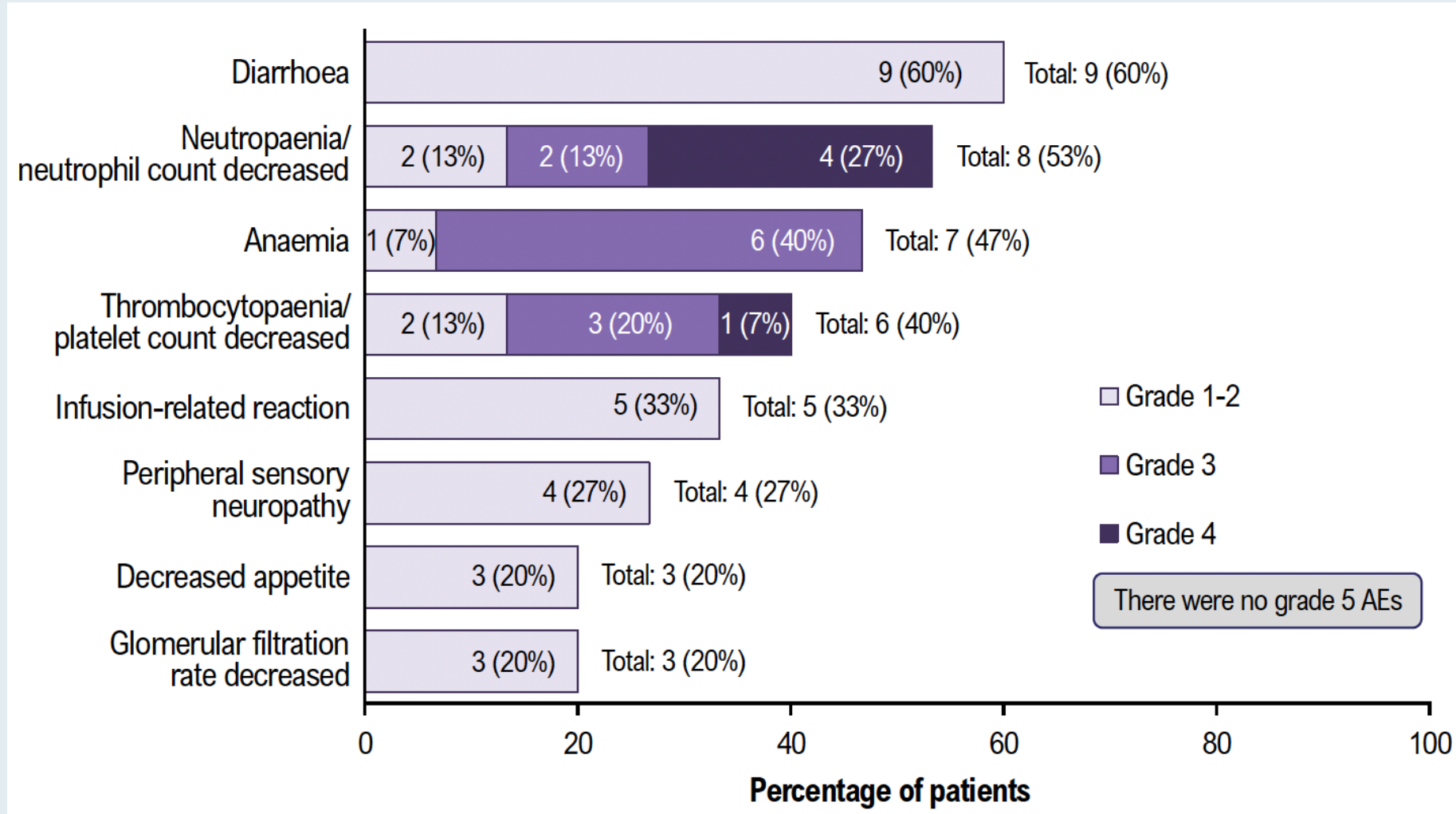




# Phase II Study of First-Line Zanidatamab with Chemotherapy: PFS and OS



# Phase II Study of First-Line Zanidatamab with Chemotherapy: Safety



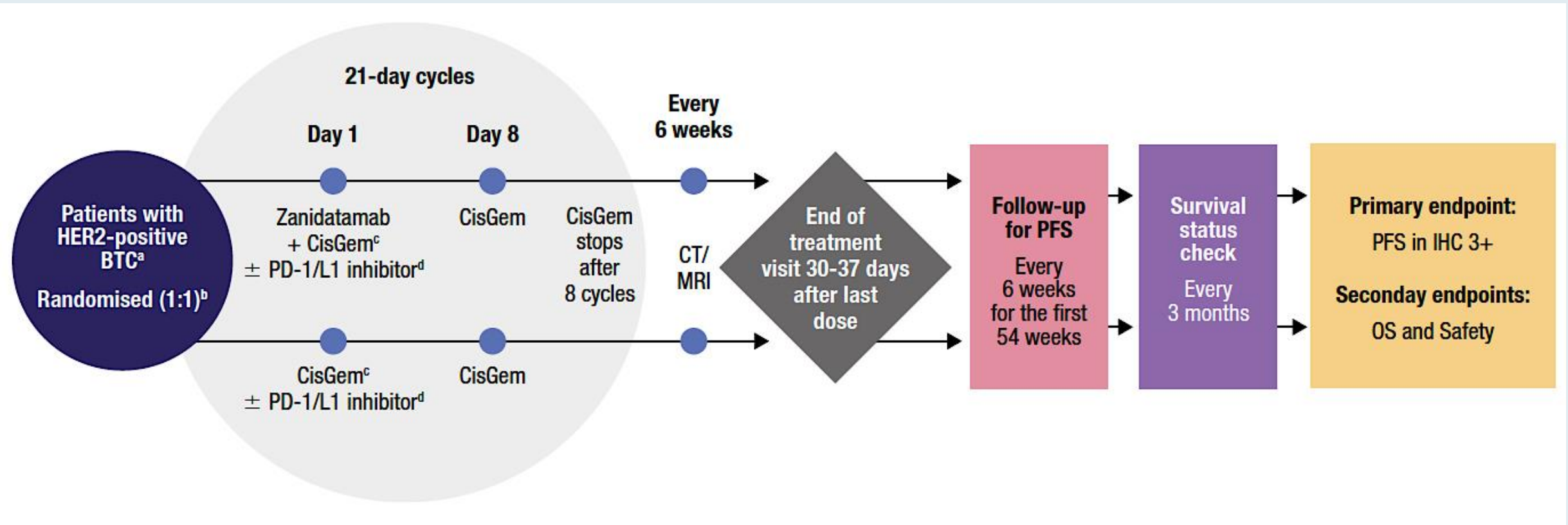
AEs = adverse events

# **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 JJ et al.

Gastrointestinal Cancers Symposium 2025;Abstract TPS648.

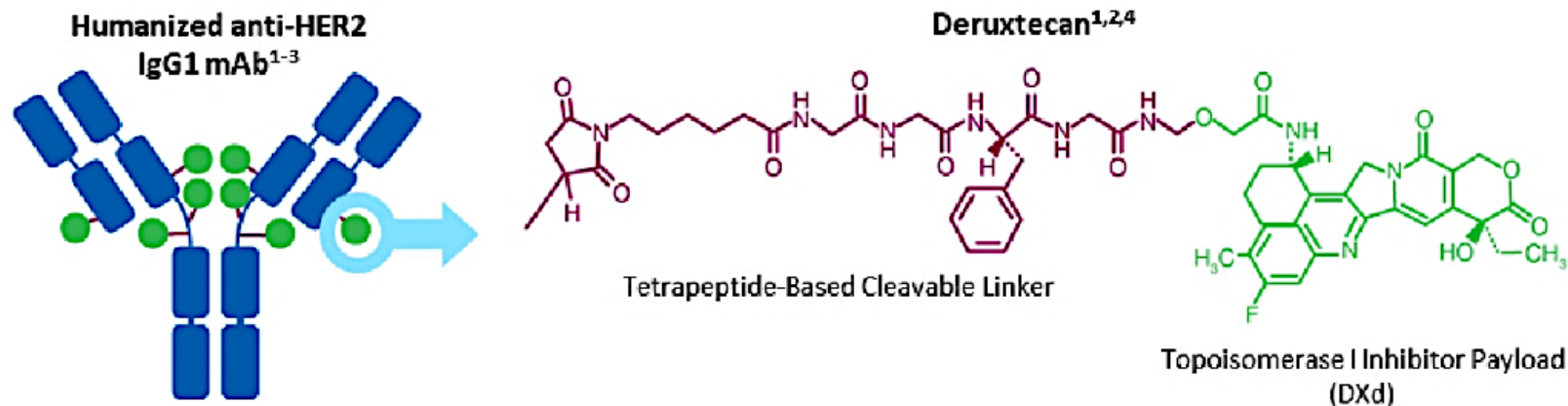
# HERIZON-BTC-302: Ongoing Pivotal Phase III Trial Design



# 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  $\approx 8$












Payload with short systemic half-life

Stable linker-payload

Tumor-selective cleavable linker

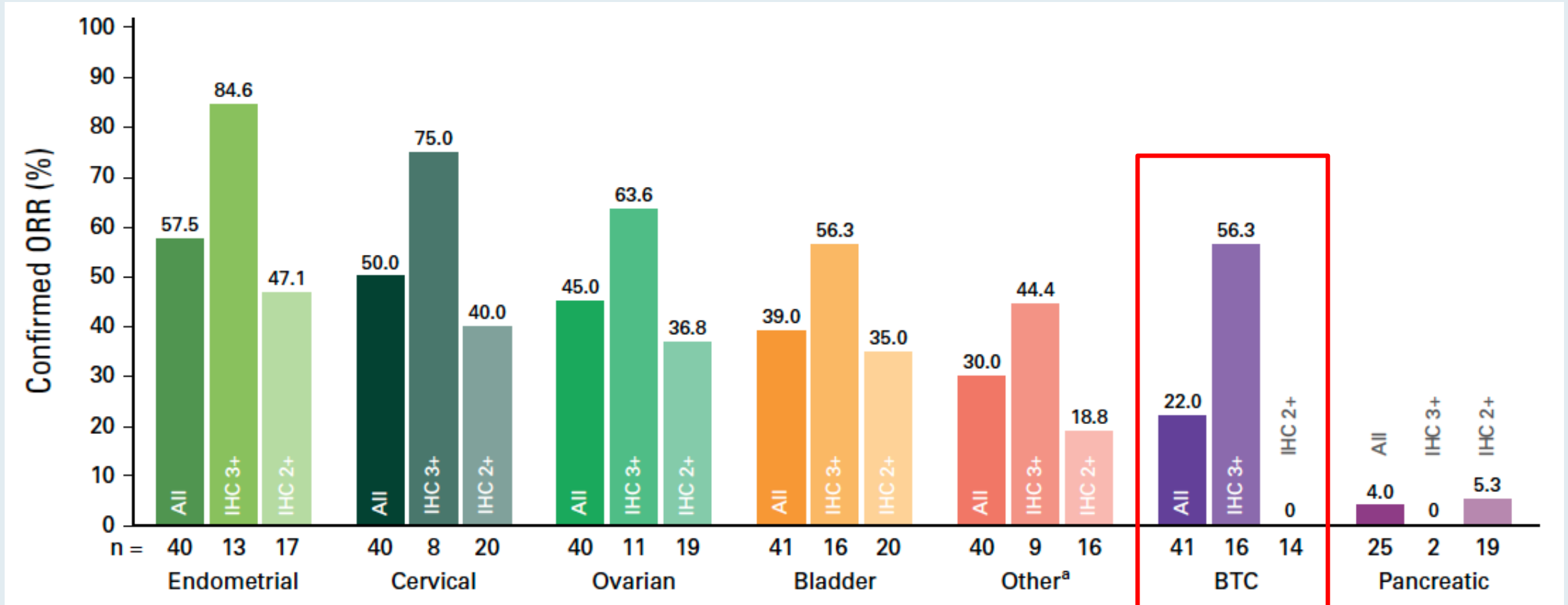
Membrane-permeable payload

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

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

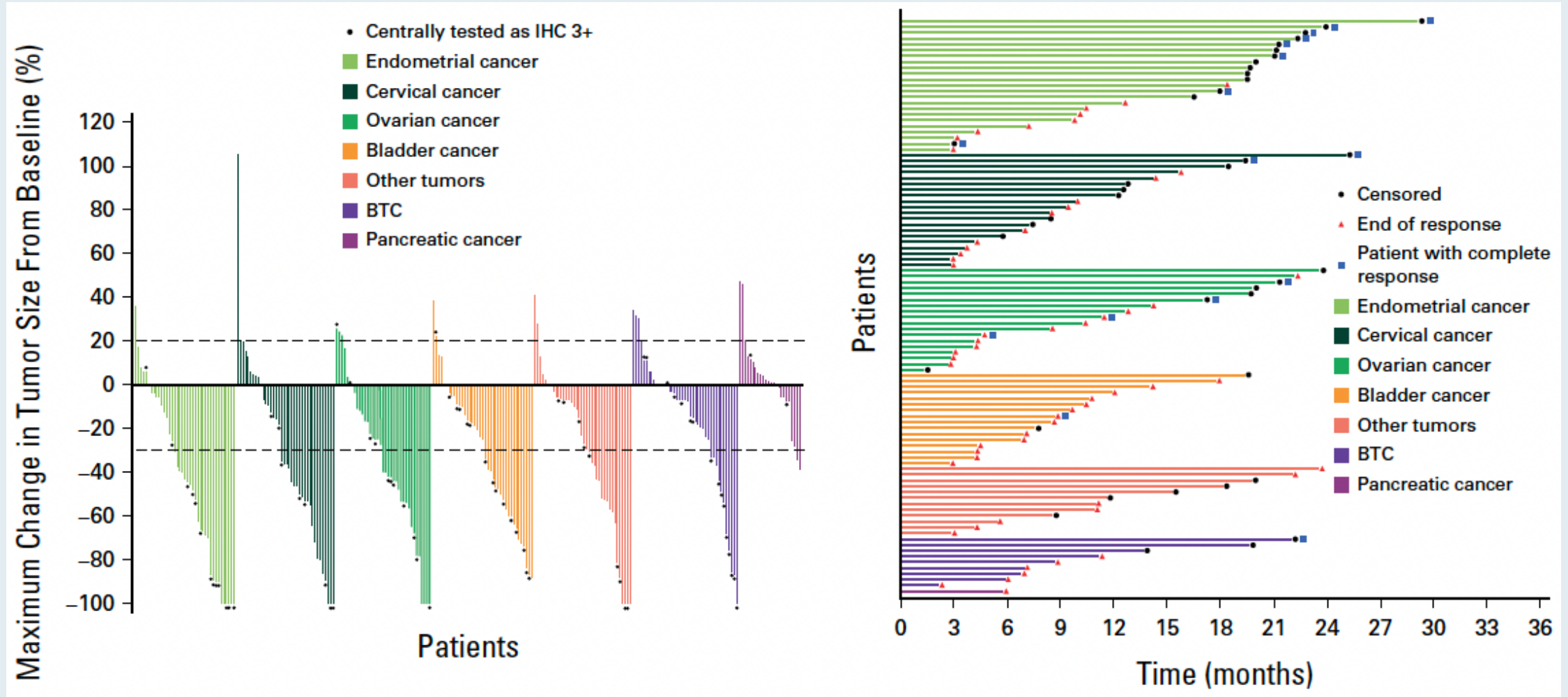
# DESTINY-PanTumor02: Response with T-DXd for Patients with HER2-Expressing Solid Tumors



<sup>a</sup> Extramammary Paget disease, oropharyngeal neoplasm, head and neck cancer, and salivary gland cancer



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

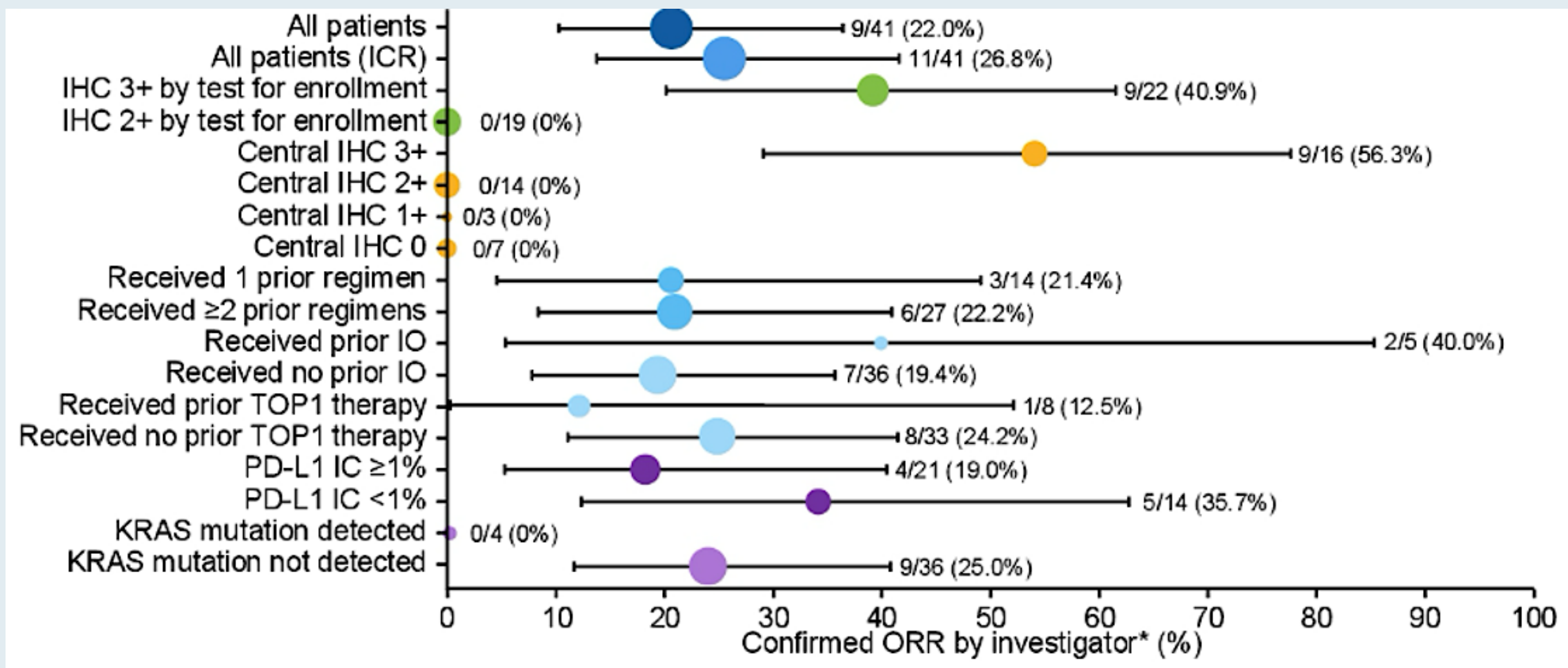


## Trastuzumab deruxtecan in patients with HER2-expressing biliary tract cancer and pancreatic cancer: outcomes from DESTINY-PanTumor02

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

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

# 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



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

Trial identifier: NCT06467357 (Open)  
Estimated enrollment: 620

## Eligibility

- Advanced or metastatic BTC or GBC
- No prior treatment in advanced or metastatic setting
- HER2 expressing (IHC 3+/2+)

## Safety run-in

T-DXd 5.4 mg/kg +  
rilvegostomig 750 mg  
q3w until PD

R

## Arm A

T-DXd + rilvegostomig

## Arm B

T-DXd monotherapy

## Arm C

Gemcitabine +  
cisplatin or carboplatin  
+ durvalumab

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

GBC = gallbladder cancer; PD = disease progression

# 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	<ul style="list-style-type: none"> <li>Locally advanced unresectable or metastatic BTC</li> <li>No more than 2 cycles of systemic therapy with gemcitabine + platinum agent +/- PD-1/L1 inhibitor (durvalumab or pembrolizumab)</li> <li>No prior HER2-targeted agent</li> </ul>	<ul style="list-style-type: none"> <li>Zanidatamab + standard therapy</li> <li>Standard therapy</li> </ul>	December 2028
DESTINY-BTC01	620	<ul style="list-style-type: none"> <li>Unresectable, previously untreated, locally advanced or metastatic BTC</li> <li>Histologically confirmed HER2-expressing (IHC 3+ or IHC 2+) BTC</li> <li>No prior HER2-targeted agent</li> </ul>	<ul style="list-style-type: none"> <li>T-DXd + rilvegostomig</li> <li>T-DXd</li> <li>Gemcitabine + platinum + durvalumab</li> </ul>	June 2028

# Phase III TAB-2 Trial: First-Line Trastuzumab with Chemotherapy versus Chemotherapy Alone for HER2-Positive Advanced BTC

## Key Eligibility Criteria

- Age  $\geq 18$  years
- Gallbladder cancer, intrahepatic cholangiocarcinoma or perihilar cholangiocarcinoma
- HER2-positive by IHC or FISH
- ECOG PS 0-2
- Adjuvant chemotherapy permitted if completed  $\geq 12$  months prior to enrollment

R  
N=70

Trastuzumab 8 mg/kg q1d1 (IV)  
6 mg/kg subsequent dosing q21d  
with chemotherapy

+

Gemcitabine + cisplatin OR  
gemcitabine + cisplatin +  
*nab* paclitaxel

Gemcitabine + cisplatin OR  
gemcitabine + cisplatin +  
*nab* paclitaxel

**Primary Outcome Measure:** Progression-free survival

IV = Intravenous; PS = performance status; PFS = progression-free survival

# Agenda

**Introduction:** Is Biliary Tract Cancer (BTC) the New Non-Small Cell Lung Cancer? ... Why?

**Case 1:** Do BTC Subtypes Respond Differently to Checkpoint Inhibitors?

**Case 2:** Anti-HER2-Directed Therapy for HER2-Low BTC?

**Case 3:** FGFR Inhibitors in the Front-Line Setting?

**Case 4:** Bone and Muscle Pain with an FGFR Inhibitor

**Case 5:** Improved Targeted Clinical Benefit for Specific FGFR Mutations?

**Case 6:** Sequencing of Available HER2-Targeted Agents

**Case 7: IDH Inhibitors in Combination with Chemotherapy as Initial Therapy?**

**Case 8:** BRAF and IDH Mutations — Which Targeted Treatment First?

**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?



## Case Presentation: 52-year-old man with hilar cholangiocarcinoma and PD s/p gemcitabine/capecitabine is found to have IDH1-mutant disease



**Dr Shaachi Gupta (Lake Worth, Florida)**

# Agenda

**Introduction:** Is Biliary Tract Cancer (BTC) the New Non-Small Cell Lung Cancer? ... Why?

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**Case 8:** BRAF and IDH Mutations — Which Targeted Treatment First?

**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?

## Case Presentation: 77-year-old man with IDH1- and BRAF-mutant metastatic cholangiocarcinoma



**Dr Philip Brooks (Brewer, Maine)**

# Agenda

**Introduction:** Is Biliary Tract Cancer (BTC) the New Non-Small Cell Lung Cancer? ... Why?

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**Case 7:** IDH Inhibitors in Combination with Chemotherapy as Initial Therapy?

**Case 8:** BRAF and IDH Mutations — Which Targeted Treatment First?

**Case 9:** Measurable Residual Disease (MRD) as a Biomarker?

## Case Presentation: 53-year-old man with recurrent metastatic cholangiocarcinoma with a BRAF V600E mutation receives dabrafenib/trametinib



**Dr Farshid Dayyani (Orange, California)**



# Contributing Medical Oncologists



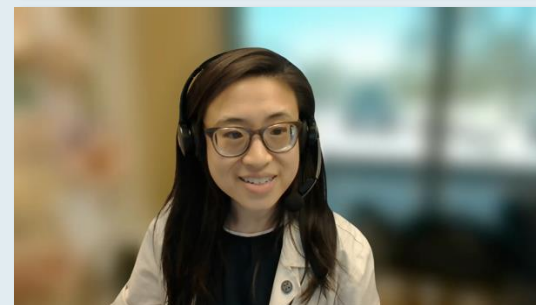
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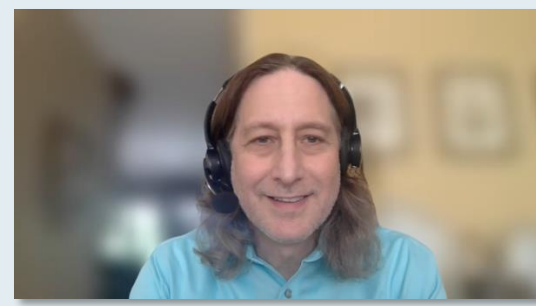
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Summit, New Jersey



# Cancer Q&A: Addressing Common Questions Posed by Patients with Relapsed/Refractory Multiple Myeloma

*A CME/MOC-Accredited Webinar Developed in Partnership with CancerCare®*

**Thursday, August 7, 2025**

**5:00 PM – 6:00 PM ET**

## **Faculty**

**Natalie S Callander, MD**

**Sagar Lonial, MD, FACP**

## **Moderator**

**Neil Love, MD**

*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.*