Inside the Issue: Targeted and Immunotherapeutic Approaches for Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, November 29, 2023
5:00 PM – 6:00 PM ET

Faculty

Lipika Goyal, MD, MPhil
Milind Javle, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Faculty

Lipika Goyal, MD, MPhil
Director of Gastrointestinal Oncology
Stanford Cancer Center
Associate Professor
Stanford University School of Medicine
Palo Alto, California

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Milind Javle, MD
Professor
Department of Gastrointestinal Medical Oncology
Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center
Houston, Texas

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Seagen Inc, and Taiho Oncology Inc.

RTP
RESEARCH
TO PRACTICE

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: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

RTP
RESEARCH
TO PRACTICE

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.

Faculty
Dr Goyal — Disclosures

Advisory Board and Consulting Agreements	AbbVie Inc, Alentis Therapeutics AG, AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Cogent Biosciences, Eisai Inc, Exelixis Inc, Genentech, a member of the Roche Group, H3 Biomedicine, Incyte Corporation, Kinnate Biopharma, Merck, Servier Pharmaceuticals LLC, Sirtex Medical Ltd, Surface Oncology, Taiho Oncology Inc, TransThera Biosciences, Tyra Biosciences
Data and Safety Monitoring Board/Committee	AstraZeneca Pharmaceuticals LP

Faculty
Dr Javle — Disclosures

Advisory Committee	AbbVie Inc, Agios Pharmaceuticals Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Biocartis, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Daiichi Sankyo Inc, EMD Serono Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Lilly, Meclon Pharmaceuticals, MSD, Novartis, OncoSil Medical Ltd, QED Therapeutics, Servier Pharmaceuticals LLC, Taiho Oncology Inc, TransThera Sciences
Contracted Research	Agios Pharmaceuticals Inc, Bristol Myers Squibb, Boehringer Ingelheim Pharmaceuticals Inc, Celgene Corporation, Daiichi Sankyo Inc, EMD Serono Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Lilly, Meclon Pharmaceuticals, MSD, Novartis, OncoSil Medical Ltd, QED Therapeutics, Servier Pharmaceuticals LLC, Taiho Oncology Inc, TransThera Sciences

Survey Participant
Dr Abou-Alfa — Disclosures

Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Autem Therapeutics, Berry Genomics, BioNTech SE, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Eisai Inc, Exelixis Inc, FibroGen Inc, Genentech, a member of the Roche Group, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Merck, Merus BV, Neogene Therapeutics, Novartis, Servier Pharmaceuticals LLC, Tempus, Thetis Pharmaceuticals, Vector Pharma, Yiviva
Contracted Research	Agenus Inc, Arcus Biosciences, AstraZeneca Pharmaceuticals LP, BioNTech SE, Bristol Myers Squibb, Digestive Care Inc, Elicio Therapeutics, Genentech, a member of the Roche Group, Helsinn Healthcare SA, Puma Biotechnology Inc, QED Therapeutics, Yiviva
Nonrelevant Financial Relationship	Parker Institute for Cancer Immunotherapy

Survey Participant
Dr Borad — Disclosures

Advisory Committee	Cadila Pharmaceuticals, Compass Therapeutics, Diffusion Pharmaceuticals, Eisai Inc, Elevar Therapeutics, Exelixis Inc, Imugene, Imvax Inc, Jazz Pharmaceuticals Inc, KaliVir Immunotherapeutics, Kriya Therapeutics, Merck, OncoMyx Therapeutics, Revolution Medicines, Tempus, Zymeworks Inc
Contracted Research	AstraZeneca Pharmaceuticals LP, Biond Biologics, Compass Therapeutics, Dragonfly Therapeutics, HiFiBiO Therapeutics, JSI Bio, Quaint Pharmaceuticals, Servier Pharmaceuticals LLC, Turnstone Biologics, ZielBio
Stock Options/Ownership — Public Company	Abeona Therapeutics, ADC Therapeutics, Assertio, bluebird bio, Homology Medicines Inc, Intercept Pharmaceuticals Inc
Nonrelevant Financial Relationship	George Clinical

RTP
RESEARCH
TO PRACTICE

Survey Participant
Prof Bridgewater — Disclosures

Conflicts of interest to be declared

RTP
RESEARCH
TO PRACTICE

Survey Participant
Dr Kelley — Disclosures

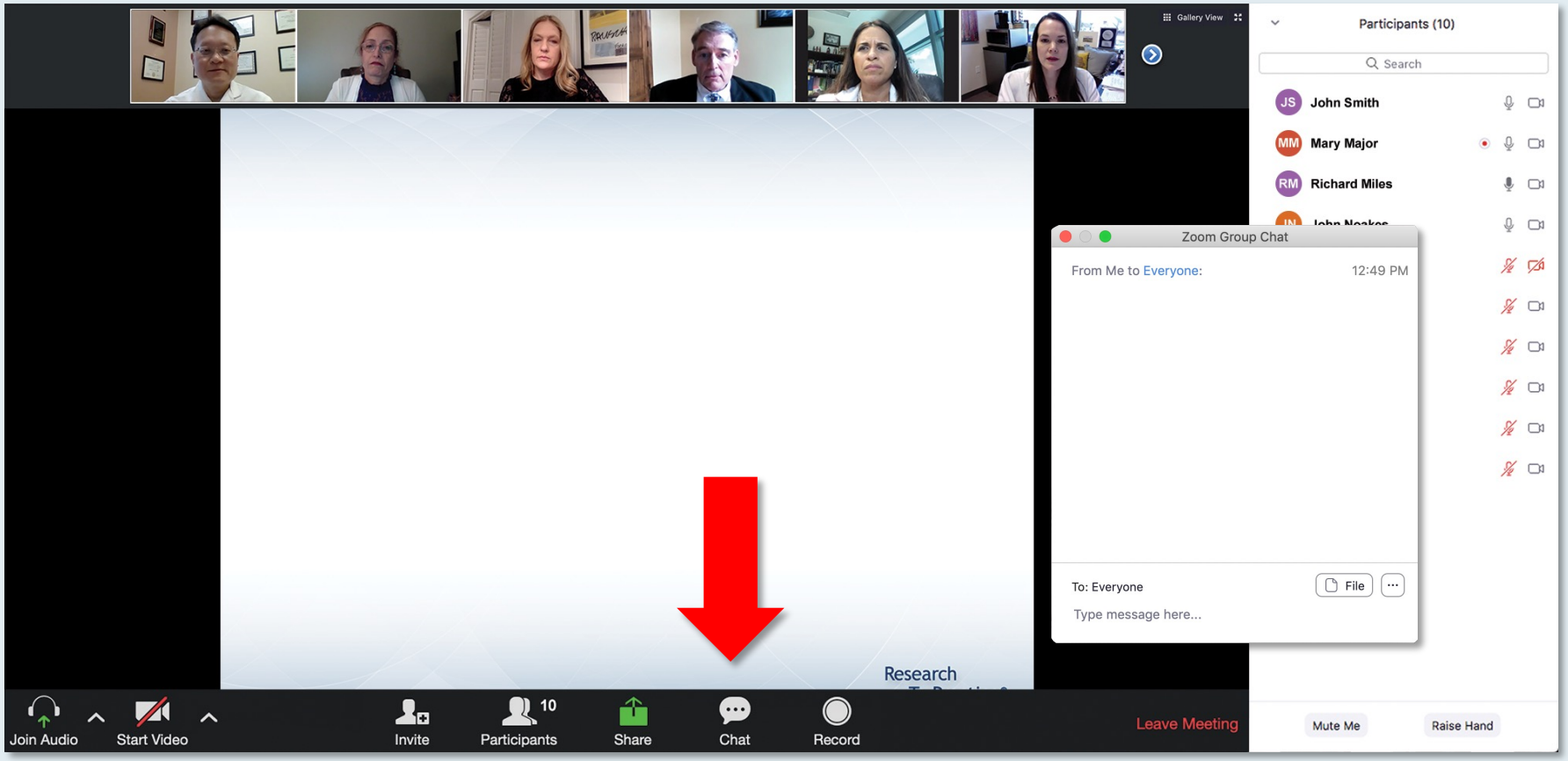
Advisory Committee (Payments to Insitution)	Agios Pharmaceuticals Inc, AstraZeneca Pharmaceuticals LP, Exelixis Inc, Ipsen Biopharmaceuticals Inc, Merck
Consulting Agreements (Payments to Self)	Compass Therapeutics, Exact Sciences Corporation, J-Pharma Co Ltd, Kinnate Biopharma, Regeneron Pharmaceuticals Inc, Tyra Biosciences
Contracted Research (Payment to Institution for Trial Conduct)	Agios Pharmaceuticals Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Compass Therapeutics, EMD Serono Inc, Exelixis Inc, Genentech, a member of the Roche Group, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Partner Therapeutics, QED Therapeutics, Servier Pharmaceuticals LLC, Surface Oncology, Taiho Oncology Inc, Tyra Biosciences
Independent Data Monitoring Committee (Unpaid Service)	Genentech, a member of the Roche Group, Merck

RTP
RESEARCH
TO PRACTICE

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

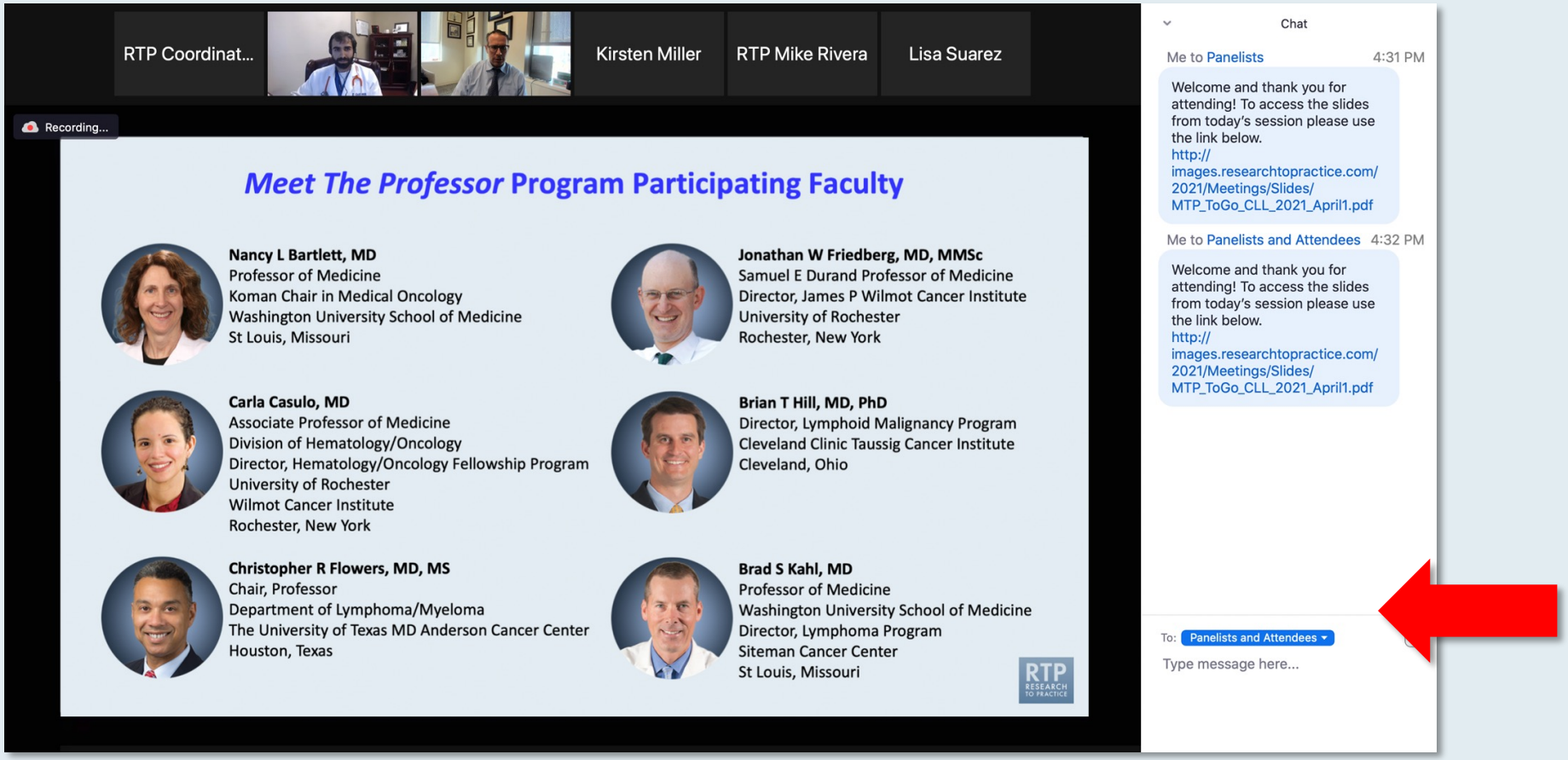


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

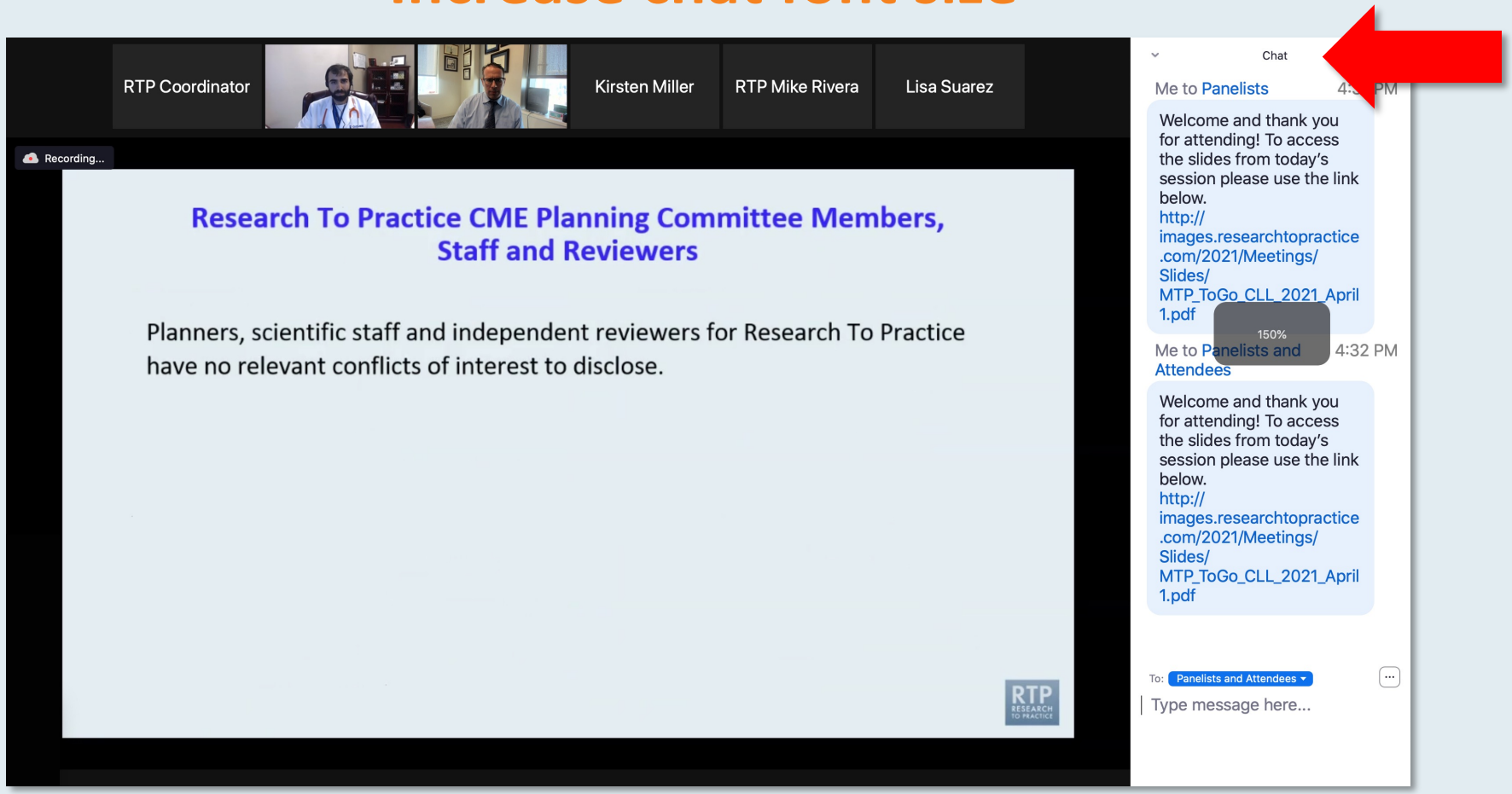


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

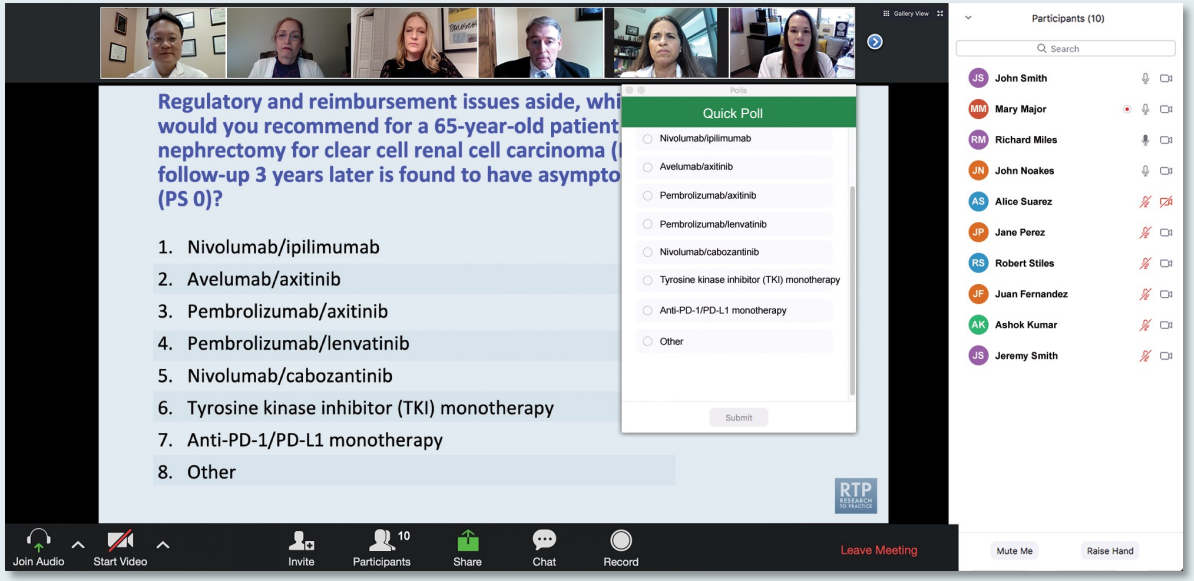
Increase chat font size



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

RTP RESEARCH TO PRACTICE

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



ONCOLOGY TODAY

WITH DR NEIL LOVE

Special Edition — Management of Hepatobiliary Cancers

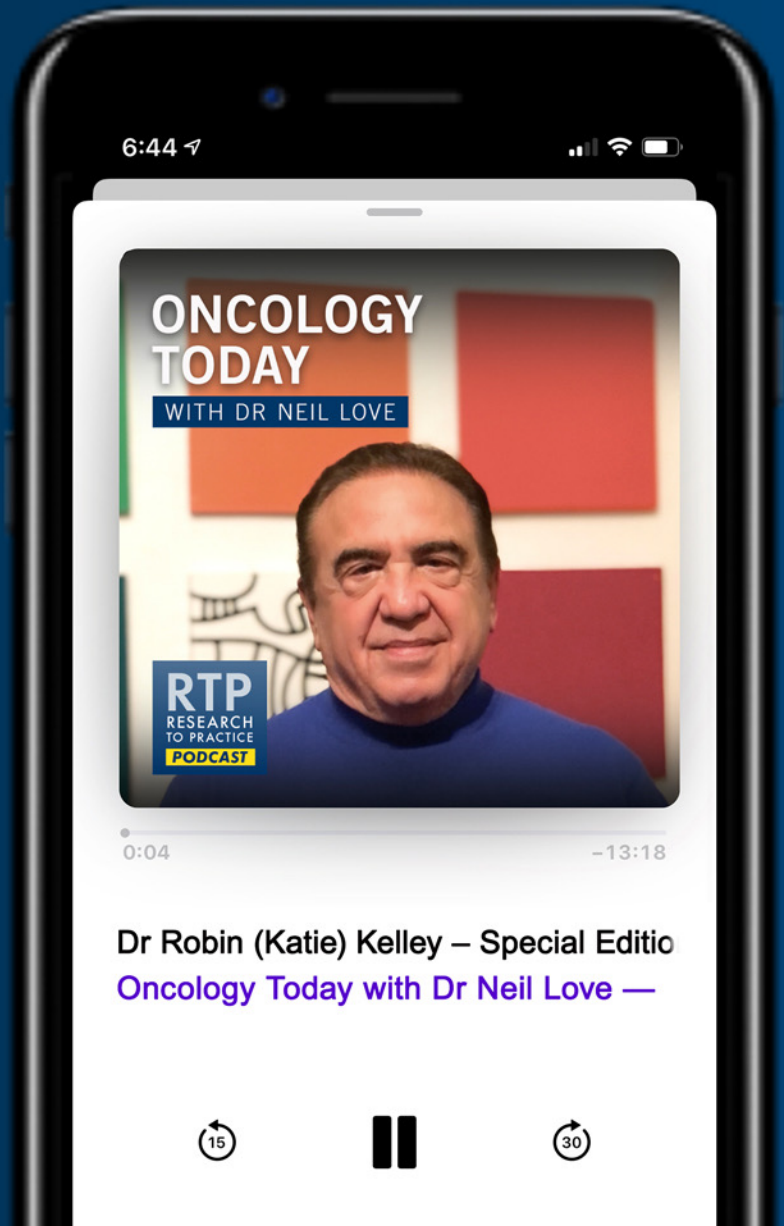
DR ROBIN (KATIE) KELLEY

UCSF HELEN DILLER FAMILY COMPREHENSIVE CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Breast Cancer

A 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

ER-Positive Metastatic Breast Cancer

Tuesday, December 5, 2023

7:15 PM – 9:15 PM CT

Localized HER2-Negative Breast Cancer

Wednesday, December 6, 2023

7:15 PM – 9:15 PM CT

HER2-Low Breast Cancer

Thursday, December 7, 2023

7:15 PM – 8:45 PM CT

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of ER-Positive Metastatic Breast Cancer

Part 1 of a 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

Tuesday, December 5, 2023

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Francois-Clement Bidard, MD, PhD
Erika Hamilton, MD
Komal Jhaveri, MD
Virginia Kaklamani, MD, DSc
Hope S Rugo, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Localized HER2-Negative Breast Cancer

Part 2 of a 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

Wednesday, December 6, 2023

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Harold J Burstein, MD, PhD
Matthew P Goetz, MD
Sara A Hurvitz, MD, FACP
Joyce O'Shaughnessy, MD
Lajos Pusztai, MD, DPhil, FASCO

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Low Breast Cancer

Part 3 of a 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

Thursday, December 7, 2023

7:15 PM – 8:45 PM CT (8:15 PM – 9:45 PM ET)

Faculty

Aditya Bardia, MD, MPH

Lisa A Carey, MD, ScM, FASCO

Shanu Modi, MD

Professor Peter Schmid, FRCP, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hematologic Cancers

A 4-Part CME Friday Satellite Symposium Series Preceding the 65th ASH Annual Meeting and Exposition

Friday, December 8, 2023

Follicular, Mantle Cell and Hodgkin Lymphoma
7:30 AM – 10:00 AM PT

Diffuse Large B-Cell Lymphoma
11:30 AM – 1:30 PM PT

Chronic Lymphocytic Leukemia
3:15 PM – 5:15 PM PT

Multiple Myeloma
7:00 PM – 9:00 PM PT

Moderator
Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Follicular, Mantle Cell and Hodgkin Lymphoma (Part 1 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

7:30 AM – 10:00 AM PT (10:30 AM – 1:00 PM ET)

Faculty

Jeremy S Abramson, MD, MMSc
Stephen M Ansell, MD, PhD
Nancy L Bartlett, MD
Jonathon B Cohen, MD
Jonathan W Friedberg, MD, MMSc
Brad S Kahl, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Diffuse Large B-Cell Lymphoma (Part 2 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

11:30 AM – 1:30 PM PT (2:30 PM – 4:30 PM ET)

Faculty

Michael Dickinson, MD
Grzegorz S Nowakowski, MD
Gilles Salles, MD, PhD
Laurie H Sehn, MD, MPH
Jason Westin, MD, MS

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Chronic Lymphocytic Leukemia (Part 3 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

3:15 PM – 5:15 PM PT (6:15 PM – 8:15 PM ET)

Faculty

Farrukh T Awan, MD
Matthew S Davids, MD, MMSc
Stephen J Schuster, MD
William G Wierda, MD, PhD
Jennifer Woyach, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Multiple Myeloma (Part 4 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Amrita Krishnan, MD
Sagar Lonial, MD
Robert Z Orlowski, MD, PhD
Noopur Raje, MD
Paul G Richardson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

JOIN US IN 2024 FOR THE RETURN OF

The Annual
National General Medical Oncology Summit

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

MARCH 22-24, 2024

JW Marriott Miami Turnberry

To Learn More or to Register, Visit
www.ResearchToPractice.com/Meetings/GMO2024

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE

Inside the Issue: Targeted and Immunotherapeutic Approaches for Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, November 29, 2023
5:00 PM – 6:00 PM ET

Faculty

Lipika Goyal, MD, MPhil
Milind Javle, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Faculty

Lipika Goyal, MD, MPhil
Director of Gastrointestinal Oncology
Stanford Cancer Center
Associate Professor
Stanford University School of Medicine
Palo Alto, California

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Milind Javle, MD
Professor
Department of Gastrointestinal Medical Oncology
Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center
Houston, Texas

RTP
RESEARCH
TO PRACTICE

Survey Participants

Ghassan Abou-Alfa, MD, MBA
Attending
Memorial Sloan Kettering Cancer Center
Professor
Weill Cornell Medical College at Cornell University
Adjunct Professor
Trinity College Dublin (Ireland)
New York, New York

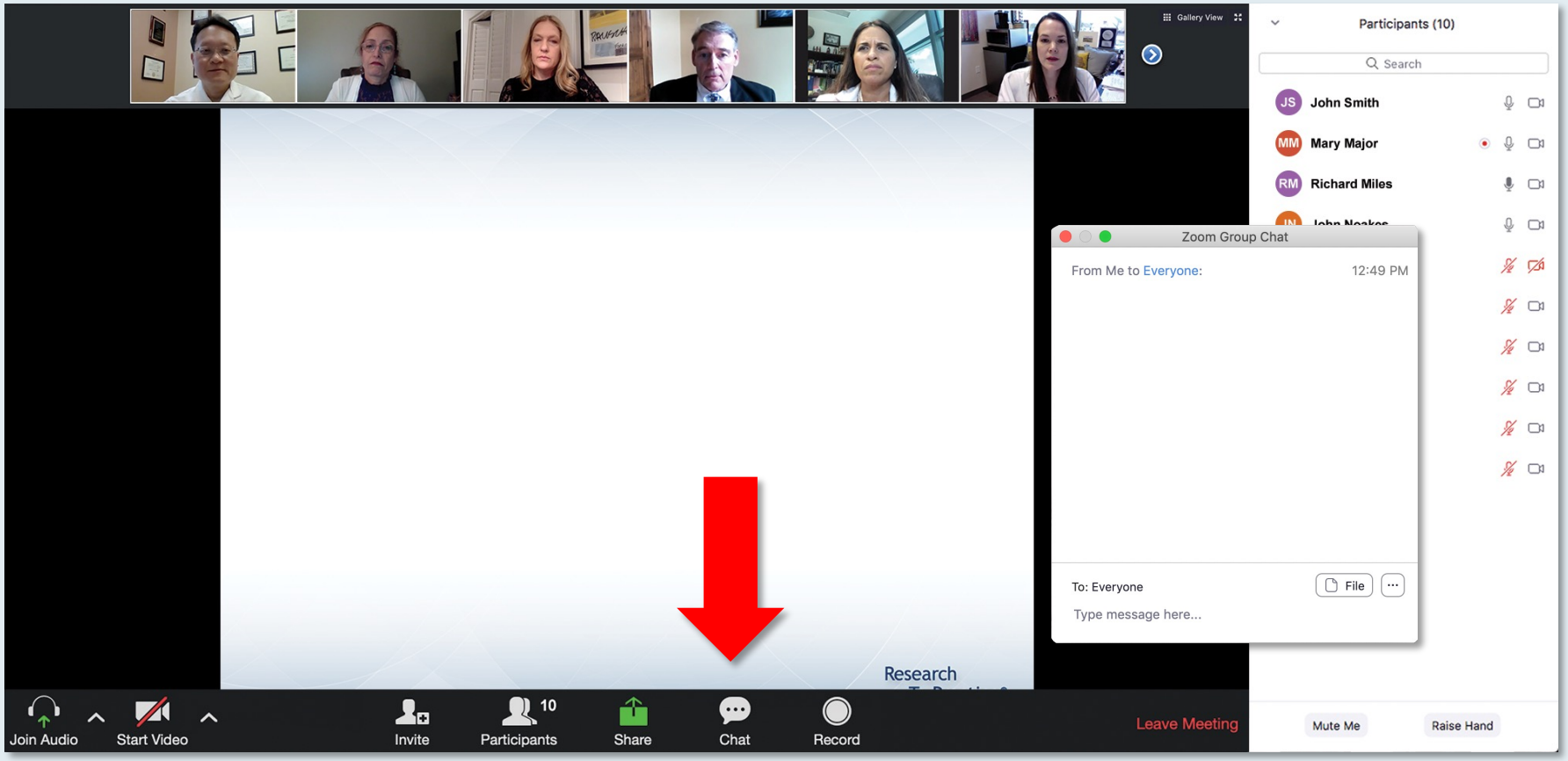
John Bridgewater, MBBS, PhD
University College London Hospitals NHS Foundation Trust
London, United Kingdom

Mitesh J Borad, MD
Professor of Medicine
Mayo Clinic College of Medicine and Science
Program Leader, Gene and Virus Therapy Program
Mayo Clinic Comprehensive Cancer Center
Director, Precision Cancer Therapeutics Cancer Program
Mayo Clinic Center for Individualized Medicine
Scottsdale, Arizona

Robin (Katie) Kelley, MD
Professor of Clinical Medicine
Division of Hematology/Oncology
Helen Diller Family Comprehensive Cancer Center
University of California, San Francisco (UCSF)
San Francisco, California

RTP
RESEARCH TO PRACTICE

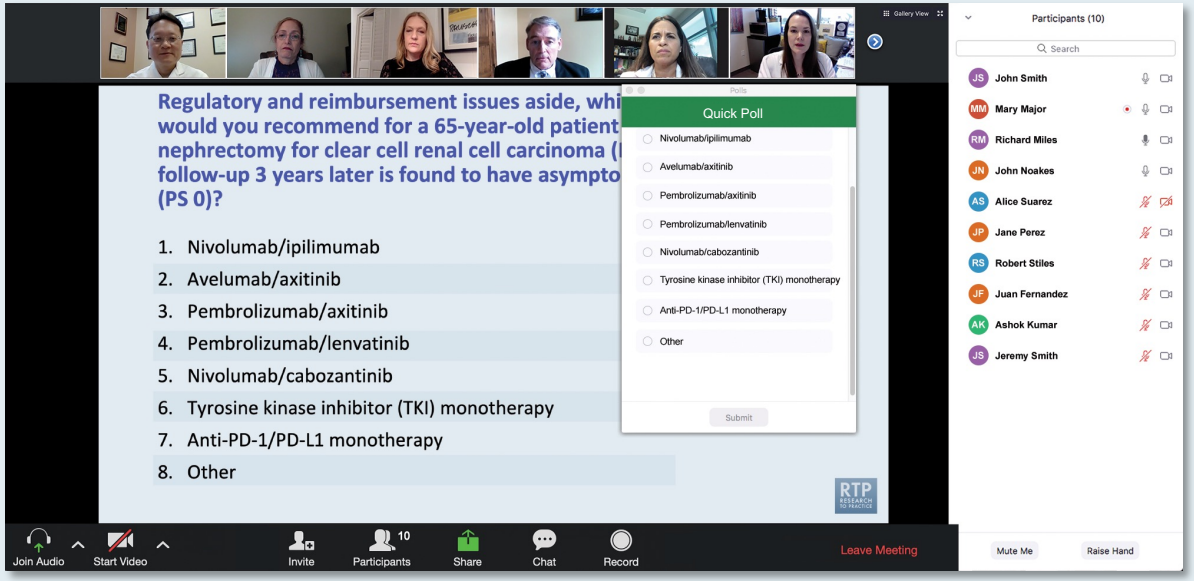
We Encourage Clinicians in Practice to Submit Questions



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

RTP RESEARCH TO PRACTICE

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



Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Breast Cancer

A 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

ER-Positive Metastatic Breast Cancer

Tuesday, December 5, 2023

7:15 PM – 9:15 PM CT

Localized HER2-Negative Breast Cancer

Wednesday, December 6, 2023

7:15 PM – 9:15 PM CT

HER2-Low Breast Cancer

Thursday, December 7, 2023

7:15 PM – 8:45 PM CT

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of ER-Positive Metastatic Breast Cancer

Part 1 of a 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

Tuesday, December 5, 2023

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Francois-Clement Bidard, MD, PhD
Erika Hamilton, MD
Komal Jhaveri, MD
Virginia Kaklamani, MD, DSc
Hope S Rugo, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Localized HER2-Negative Breast Cancer

Part 2 of a 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

Wednesday, December 6, 2023

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Harold J Burstein, MD, PhD
Matthew P Goetz, MD
Sara A Hurvitz, MD, FACP
Joyce O'Shaughnessy, MD
Lajos Pusztai, MD, DPhil, FASCO

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Low Breast Cancer

Part 3 of a 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

Thursday, December 7, 2023

7:15 PM – 8:45 PM CT (8:15 PM – 9:45 PM ET)

Faculty

Aditya Bardia, MD, MPH

Lisa A Carey, MD, ScM, FASCO

Shanu Modi, MD

Professor Peter Schmid, FRCP, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hematologic Cancers

A 4-Part CME Friday Satellite Symposium Series Preceding the 65th ASH Annual Meeting and Exposition

Friday, December 8, 2023

Follicular, Mantle Cell and Hodgkin Lymphoma
7:30 AM – 10:00 AM PT

Diffuse Large B-Cell Lymphoma
11:30 AM – 1:30 PM PT

Chronic Lymphocytic Leukemia
3:15 PM – 5:15 PM PT

Multiple Myeloma
7:00 PM – 9:00 PM PT

Moderator
Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Follicular, Mantle Cell and Hodgkin Lymphoma (Part 1 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

7:30 AM – 10:00 AM PT (10:30 AM – 1:00 PM ET)

Faculty

Jeremy S Abramson, MD, MMSc
Stephen M Ansell, MD, PhD
Nancy L Bartlett, MD
Jonathon B Cohen, MD
Jonathan W Friedberg, MD, MMSc
Brad S Kahl, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Diffuse Large B-Cell Lymphoma (Part 2 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

11:30 AM – 1:30 PM PT (2:30 PM – 4:30 PM ET)

Faculty

Michael Dickinson, MD
Grzegorz S Nowakowski, MD
Gilles Salles, MD, PhD
Laurie H Sehn, MD, MPH
Jason Westin, MD, MS

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Chronic Lymphocytic Leukemia (Part 3 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

3:15 PM – 5:15 PM PT (6:15 PM – 8:15 PM ET)

Faculty

Farrukh T Awan, MD
Matthew S Davids, MD, MMSc
Stephen J Schuster, MD
William G Wierda, MD, PhD
Jennifer Woyach, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Multiple Myeloma (Part 4 of a 4-Part Series)

A CME Friday Satellite Symposium and Virtual Event Preceding the 65th ASH Annual Meeting

Friday, December 8, 2023

7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Amrita Krishnan, MD
Sagar Lonial, MD
Robert Z Orlowski, MD, PhD
Noopur Raje, MD
Paul G Richardson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

JOIN US IN 2024 FOR THE RETURN OF

The Annual
National General Medical Oncology Summit

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

MARCH 22-24, 2024

JW Marriott Miami Turnberry

To Learn More or to Register, Visit
www.ResearchToPractice.com/Meetings/GMO2024

ONCOLOGY TODAY

WITH DR NEIL LOVE

Special Edition — Management of Hepatobiliary Cancers

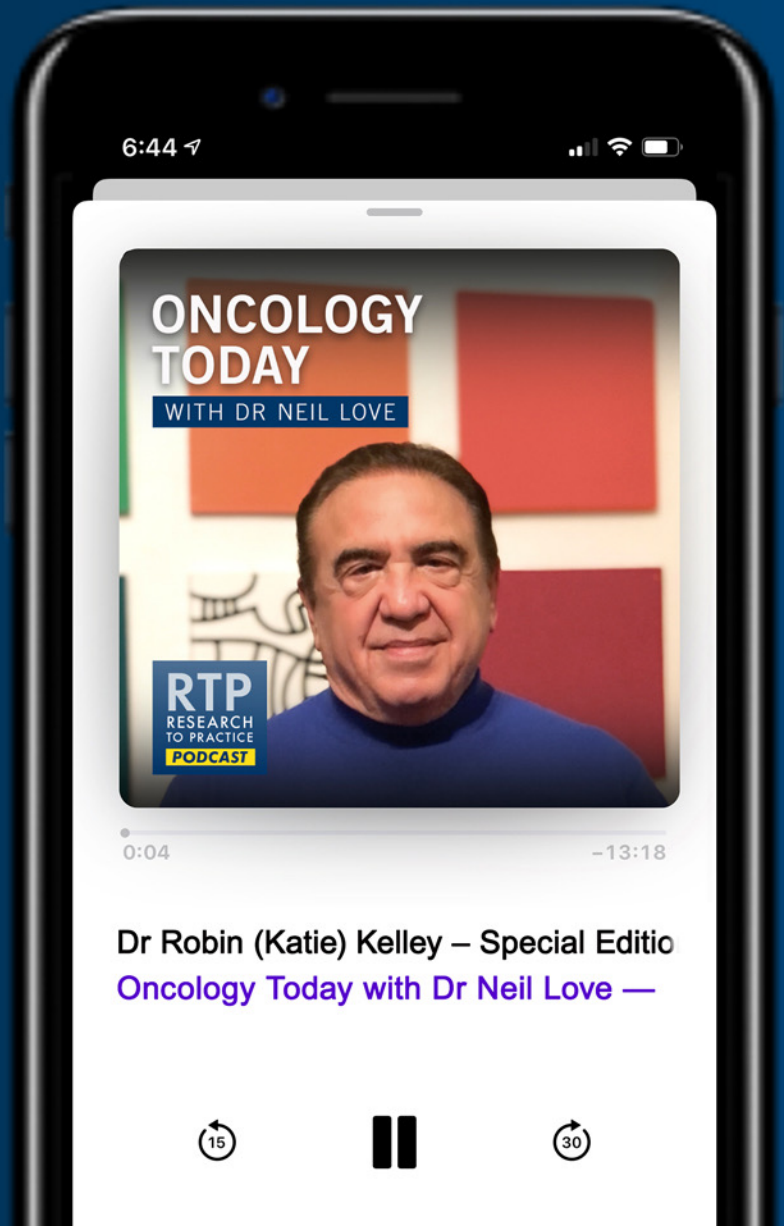
DR ROBIN (KATIE) KELLEY

UCSF HELEN DILLER FAMILY COMPREHENSIVE CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Inside the Issue: Targeted and Immunotherapeutic Approaches for Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, November 29, 2023
5:00 PM – 6:00 PM ET

Faculty

Lipika Goyal, MD, MPhil
Milind Javle, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Seagen Inc, and Taiho Oncology Inc.

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.

Faculty
Dr Goyal — Disclosures

Advisory Board and Consulting Agreements	AbbVie Inc, Alentis Therapeutics AG, AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Cogent Biosciences, Eisai Inc, Exelixis Inc, Genentech, a member of the Roche Group, H3 Biomedicine, Incyte Corporation, Kinnate Biopharma, Merck, Servier Pharmaceuticals LLC, Sirtex Medical Ltd, Surface Oncology, Taiho Oncology Inc, TransThera Biosciences, Tyra Biosciences
Data and Safety Monitoring Board/Committee	AstraZeneca Pharmaceuticals LP

Faculty
Dr Javle — Disclosures

Advisory Committee	AbbVie Inc, Agios Pharmaceuticals Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Biocartis, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Daiichi Sankyo Inc, EMD Serono Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Lilly, Meclon Pharmaceuticals, MSD, Novartis, OncoSil Medical Ltd, QED Therapeutics, Servier Pharmaceuticals LLC, Taiho Oncology Inc, TransThera Sciences
Contracted Research	Agios Pharmaceuticals Inc, Bristol Myers Squibb, Boehringer Ingelheim Pharmaceuticals Inc, Celgene Corporation, Daiichi Sankyo Inc, EMD Serono Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Lilly, Meclon Pharmaceuticals, MSD, Novartis, OncoSil Medical Ltd, QED Therapeutics, Servier Pharmaceuticals LLC, Taiho Oncology Inc, TransThera Sciences

Survey Participant
Dr Abou-Alfa — Disclosures

Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Autem Therapeutics, Berry Genomics, BioNTech SE, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Eisai Inc, Exelixis Inc, FibroGen Inc, Genentech, a member of the Roche Group, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Merck, Merus BV, Neogene Therapeutics, Novartis, Servier Pharmaceuticals LLC, Tempus, Thetis Pharmaceuticals, Vector Pharma, Yiviva
Contracted Research	Agenus Inc, Arcus Biosciences, AstraZeneca Pharmaceuticals LP, BioNTech SE, Bristol Myers Squibb, Digestive Care Inc, Elicio Therapeutics, Genentech, a member of the Roche Group, Helsinn Healthcare SA, Puma Biotechnology Inc, QED Therapeutics, Yiviva
Nonrelevant Financial Relationship	Parker Institute for Cancer Immunotherapy

Survey Participant
Dr Borad — Disclosures

Advisory Committee	Cadila Pharmaceuticals, Compass Therapeutics, Diffusion Pharmaceuticals, Eisai Inc, Elevar Therapeutics, Exelixis Inc, Imugene, Imvax Inc, Jazz Pharmaceuticals Inc, KaliVir Immunotherapeutics, Kriya Therapeutics, Merck, OncoMyx Therapeutics, Revolution Medicines, Tempus, Zymeworks Inc
Contracted Research	AstraZeneca Pharmaceuticals LP, Biond Biologics, Compass Therapeutics, Dragonfly Therapeutics, HiFiBiO Therapeutics, JSI Bio, Quaint Pharmaceuticals, Servier Pharmaceuticals LLC, Turnstone Biologics, ZielBio
Stock Options/Ownership — Public Company	Abeona Therapeutics, ADC Therapeutics, Assertio, bluebird bio, Homology Medicines Inc, Intercept Pharmaceuticals Inc
Nonrelevant Financial Relationship	George Clinical

RTP
RESEARCH
TO PRACTICE

Survey Participant
Prof Bridgewater — Disclosures

Conflicts of interest to be declared

RTP
RESEARCH
TO PRACTICE

Survey Participant
Dr Kelley — Disclosures

Advisory Committee (Payments to Insitution)	Agios Pharmaceuticals Inc, AstraZeneca Pharmaceuticals LP, Exelixis Inc, Ipsen Biopharmaceuticals Inc, Merck
Consulting Agreements (Payments to Self)	Compass Therapeutics, Exact Sciences Corporation, J-Pharma Co Ltd, Kinnate Biopharma, Regeneron Pharmaceuticals Inc, Tyra Biosciences
Contracted Research (Payment to Institution for Trial Conduct)	Agios Pharmaceuticals Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Compass Therapeutics, EMD Serono Inc, Exelixis Inc, Genentech, a member of the Roche Group, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Partner Therapeutics, QED Therapeutics, Servier Pharmaceuticals LLC, Surface Oncology, Taiho Oncology Inc, Tyra Biosciences
Independent Data Monitoring Committee (Unpaid Service)	Genentech, a member of the Roche Group, Merck

RTP
RESEARCH
TO PRACTICE

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

RTP
RESEARCH
TO PRACTICE

Current Management Approaches for Patients with Advanced Biliary Tract Cancers (BTCs)

Lipika Goyal, MD, MPhil

Director, Gastrointestinal Oncology Program

Associate Professor, Stanford School of Medicine

Stanford MEDICINE
School of Medicine

New Frontiers in Advanced Biliary Tract Cancers

Milind Javle, MD

Hubert L. and Olive Stringer Professor

Chair, NCI Task Force, Hepatobiliary Cancers

GI Medical Oncology

UT MD Anderson Cancer Center

Houston, TX 77030

Email: mjavle@mdanderson.org

Twitter @JavleMilind

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

RTP
RESEARCH
TO PRACTICE

Key Data Sets

Lipika Goyal, MD, MPhil

- Goyal L et al. Futibatinib for FGFR2-rearranged intrahepatic cholangiocarcinoma. *N Engl J Med* 2023 January 19;388(3):228-39.
- Valle J et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *N Engl J Med* 2010 April 8;362(14):1273-81.
- Oh D-Y et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer. *NEJM Evid* 2022;1(8).
- Kelley RK et al. Pembrolizumab in combination with gemcitabine and cisplatin compared with gemcitabine and cisplatin alone for patients with advanced biliary tract cancer (KEYNOTE-966): A randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2023 June 3;401(10391):1853-65.
- Goyal L et al. Case 8-2021: A 34-year-old woman with cholangiocarcinoma. *N Engl J Med* 2021 March 18;384(11):1054-64.
- Lamarca A et al. Molecular targeted therapies: Ready for "prime time" in biliary tract cancer. *J Hepatol* 2020 July;73(1):170-85.

Key Data Sets

Lipika Goyal, MD, MPhil (continued)

- Kendre G et al. Charting co-mutation patterns associated with actionable drivers in intrahepatic cholangiocarcinoma. *J Hepatol* 2023 March;78(3):614-26.
- Javle M et al. Phase II study of BGJ398 in patients with FGFR-altered advanced cholangiocarcinoma. *J Clin Oncol* 2018 January 20;36(3):276-82.
- Abou-Alfa GK et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: A multicentre, open-label, phase 2 study. *Lancet Oncol* 2020 May;21(5):671-84.
- Vogel A et al. Pemigatinib for previously treated locally advanced or metastatic cholangiocarcinoma: Final results from FIGHT-202. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract LBAO-2.
- Goyal L et al. Targeting FGFR inhibition in cholangiocarcinoma. *Cancer Treat Rev* 2021 April;95:102170.
- Hollebecque A et al. LBA12 Efficacy of RLY-4008, a highly selective FGFR2 inhibitor in patients (pts) with an FGFR2-fusion or rearrangement (f/r), FGFR inhibitor (FGFRi)-naïve cholangiocarcinoma (CCA): ReFocus trial. *Ann Onc* 2022;33(Suppl 7):1381.

Key Data Sets

Lipika Goyal, MD, MPhil (continued)

- Javle MM et al. A phase II study of FGFR1-3 inhibitor tinengotinib as monotherapy in patients with advanced or metastatic cholangiocarcinoma: Interim analysis. Gastrointestinal Cancers Symposium 2023;Abstract 539.
- Liu A et al. Genetics and epigenetics of glioblastoma: Applications and overall incidence of IDH1 mutation. *Front Oncol* 2016 January 29;6:16.
- Abou-Alfa GK et al. Ivosidenib in IDH1-mutant, chemotherapy-refractory cholangiocarcinoma (ClarIDHy): A multicentre, randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Oncol* 2020 June;21(6):796-807.
- Berchuck JE et al. The clinical landscape of cell-free DNA alterations in 1671 patients with advanced biliary tract cancer. *Ann Oncol* 2022 December;33(12):1269-83.
- Zhu AX et al. Final overall survival efficacy results of ivosidenib for patients with advanced cholangiocarcinoma with IDH1 mutation: The Phase 3 randomized clinical ClarIDHy trial. *JAMA Oncol* 2021;7(11):1669-77.

Key Data Sets

Milind Javle, MD

- Javle M et al. Temporal changes in cholangiocarcinoma incidence and mortality in the United States from 2001 to 2017. *Oncologist* 2022 October 1;27(10):874-83.
- Hatia RI et al. Independent of primary sclerosing cholangitis and cirrhosis, early adulthood obesity is associated with cholangiocarcinoma. *Cancer Epidemiol Biomarkers Prev* 2023 October 2;32(10):1338-47.
- Valderrama A et al. Treatment patterns and clinical outcomes among patients with biliary tract cancers in a large commercially insured US population. Gastrointestinal Cancers Symposium 2022;Abstract 398.
- Javle M et al. Biliary cancer: Utility of next-generation sequencing for clinical management. *Cancer* 2016 December 15;122(24):3838-47.
- Subbiah V et al. Dabrafenib plus trametinib in patients with BRAFV600E-mutated biliary tract cancer (ROAR): A phase 2, open-label, single-arm, multicentre basket trial. *Lancet Oncol* 2020 September;21(9):1234-43.

Key Data Sets

Milind Javle, MD (continued)

- Javle M et al. Pertuzumab and trastuzumab for HER2-positive, metastatic biliary tract cancer (MyPathway): A multicentre, open-label, phase 2a, multiple basket study. *Lancet Oncol* 2021 September;22(9):1290-300.
- Meric-Bernstam F et al. Zanidatamab (ZW25) in HER2-positive biliary tract cancers (BTCs): Results from a phase I study. Gastrointestinal Cancers Symposium 2021;Abstract 299.
- Harding JJ et al. Zanidatamab for HER2-amplified, unresectable, locally advanced or metastatic biliary tract cancer (HERIZON-BTC-01): A multicentre, single-arm, phase 2b study. *Lancet Oncol* 2023 July;24(7):772-82.
- Nakamura Y et al. Tucatinib and trastuzumab for previously treated HER2-positive metastatic biliary tract cancer (SGNTUC-019): A phase 2 basket study. ASCO 2023;Abstract 4007.
- Nakamura Y et al. Tucatinib and trastuzumab for previously treated human epidermal growth factor receptor 2-positive metastatic biliary tract cancer (SGNTUC-019): A phase II basket study. *J Clin Oncol* 2023 September 26;[Online ahead of print].

Key Data Sets

Milind Javle, MD (continued)

- Meric-Bernstam F et al. Efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) interim results. ASCO 2023;Abstract LBA3000.
- Engstrom LD et al. MRTX1719 is an MTA-cooperative PRMT5 inhibitor that exhibits synthetic lethality in preclinical models and patients with MTAP-deleted cancer. *Cancer Discov* 2023 November 1;13(11):2412-31.
- Oh D-Y et al. CTX-009 (ABL001), a bispecific antibody targeting DLL4 and VEGF A, in combination with paclitaxel in patients with advanced biliary tract cancer (BTC): A phase 2 study. Gastrointestinal Cancers Symposium 2023;Abstract 540.
- Meric-Bernstam F et al. Fam-trastuzumab deruxtecan-nxki (T-DXd) for pretreated patients (pts) with HER2-expressing solid tumors: Primary analysis from the DESTINY-PanTumor02 (DP-02) study. ESMO 2023;Abstract LBA34.
- Ohba A et al. Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing unresectable or recurrent biliary tract cancer (BTC): An investigator-initiated multicenter phase 2 study (HERB trial). ASCO 2022;Abstract 4006.

Agenda
Management of Advanced Biliary Tract Cancers

INTRODUCTION

MODULE 1: First-Line Systemic Treatment

MODULE 2: Targeted Treatment

- HER2
- FGFR
- BRAF
- IDH

RTP
RESEARCH
TO PRACTICE

Agenda
Management of Advanced Biliary Tract Cancers

INTRODUCTION

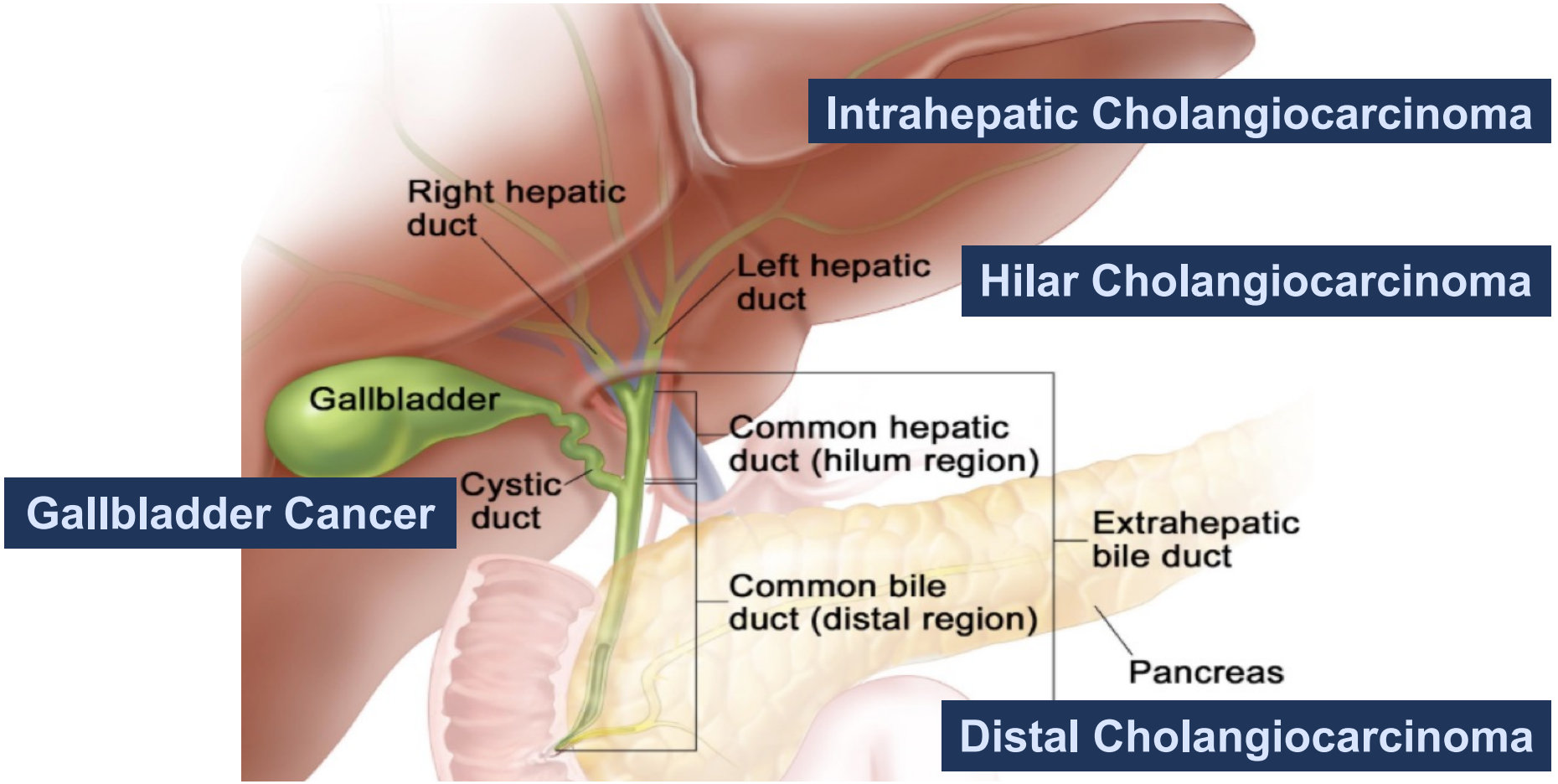
MODULE 1: First-Line Systemic Treatment

MODULE 2: Targeted Treatment

- HER2
- FGFR
- BRAF
- IDH

RTP
RESEARCH
TO PRACTICE

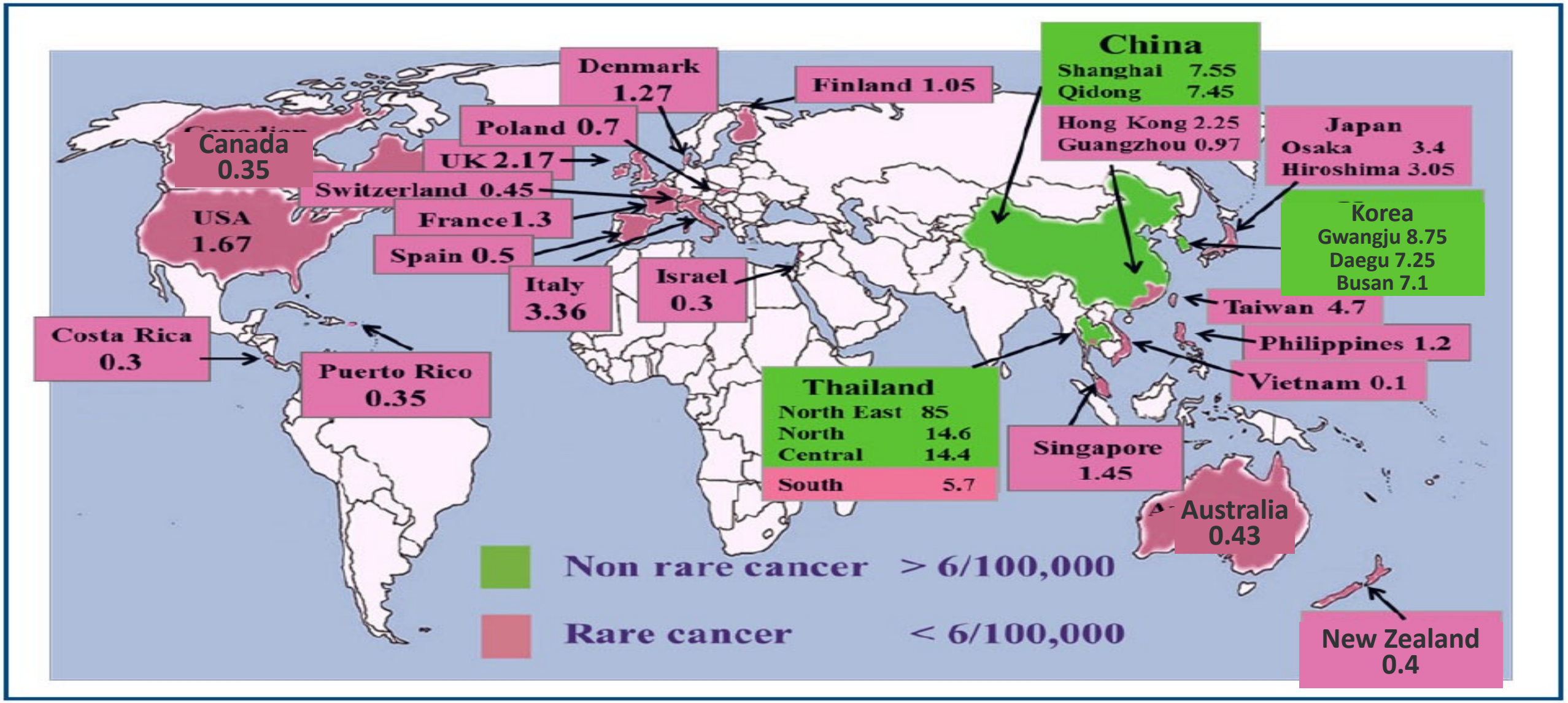
Biliary Tract Cancers (BTCs)



NCI Bile Duct Cancer PDQ 2017

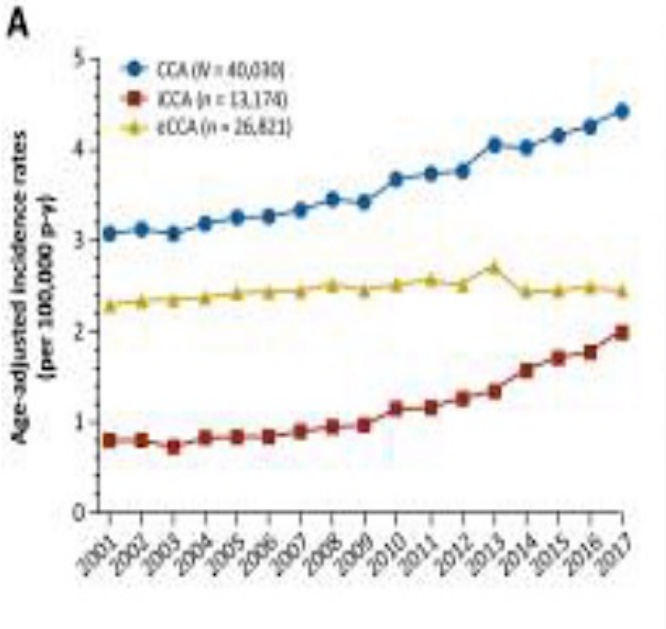
Courtesy of Milind Javle, MD

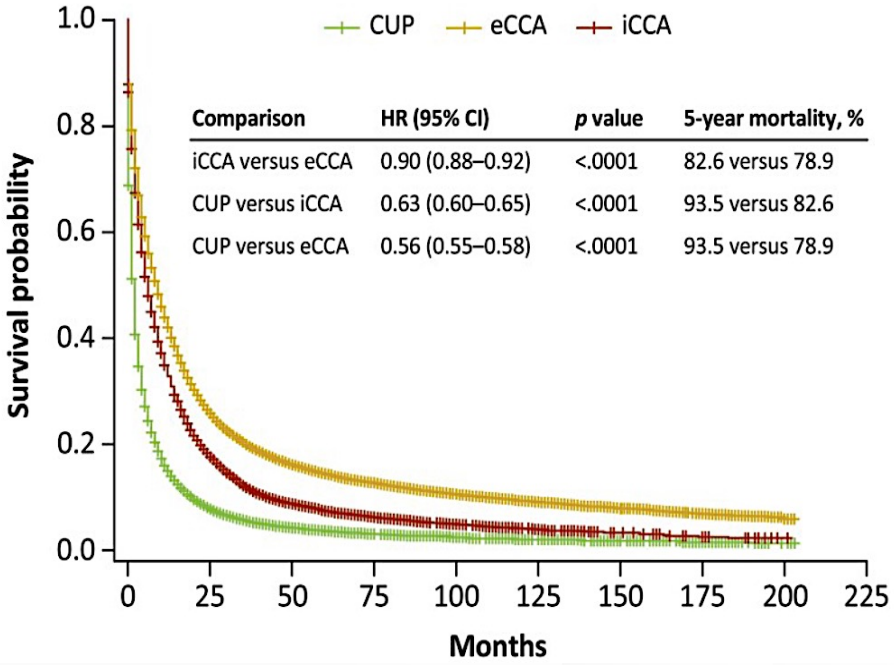
Cholangiocarcinoma Worldwide



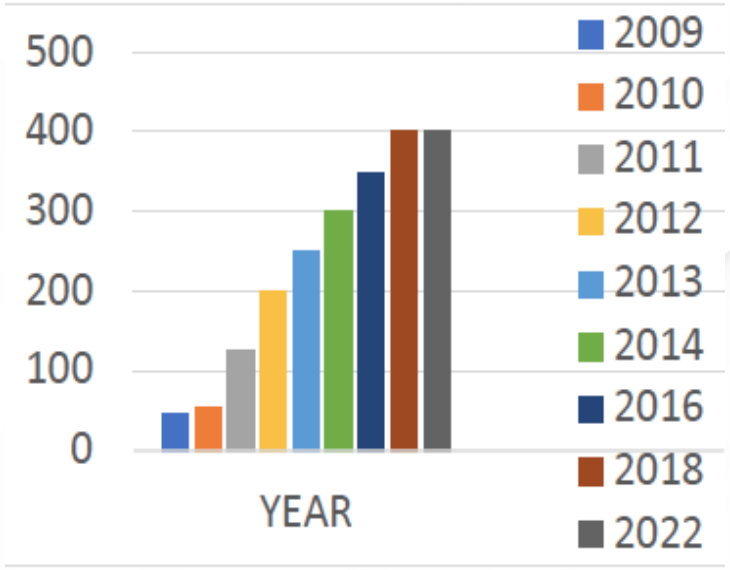
Courtesy of Milind Javle, MD

Rising Incidence of Cholangiocarcinoma





Comparison	HR (95% CI)	*p* value	5-year mortality, %
iCCA versus eCCA	0.90 (0.88–0.92)	<.0001	82.6 versus 78.9
CUP versus iCCA	0.63 (0.60–0.65)	<.0001	93.5 versus 82.6
CUP versus eCCA	0.56 (0.55–0.58)	<.0001	93.5 versus 78.9



Obesity's link to cancer: Texas has nation's highest liver cancer mortality rate^

In the city of Houston, the observed number of intrahepatic bile duct cancers was significantly greater than expected in Texas

Javle M, et al. *Oncologist.* 2022.

^https://www.tmc.edu/news/2019/03/obesitys-link-to-cancer/#single-article-body

Courtesy of Milind Javle, MD

CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION | RESEARCH ARTICLE

Independent of Primary Sclerosing Cholangitis and Cirrhosis, Early Adulthood Obesity Is Associated with Cholangiocarcinoma

Rikita I. Hatia[1], Madhulika Eluri[2], Ernest T. Hawk[3], Akram Shalaby[4], Elif Karatas[5], Ahmed Shalaby[6], Ahmed Abdelhakeem[7], Reham Abdel-Wahab[8,9], Ping Chang[2], Asif Rashid[10], Prasun K. Jalal[11], Christopher I. Amos[12], Younghun Han[12], Tannaz Armaghany[13], Rachna T. Shroff[14], Donghui Li[2], Milind Javle[2], and Manal M. Hassan[1]

ABSTRACT

Background: It is estimated that 6% to 20% of all cholangiocarcinoma (CCA) diagnoses are explained by primary sclerosing cholangitis (PSC), but the underlying risk factors in the absence of PSC are unclear. We examined associations of different risk factors with intrahepatic cholangiocarcinoma (ICC) and extrahepatic cholangiocarcinoma (ECC) in the United States.

Methods: We conducted a case–control study of 121 patients with ECC and 308 patients with ICC treated at MD Anderson Cancer Center between May 2014 and March 2020, compared with 1,061 healthy controls. Multivariable logistic regression analysis was applied to estimate the adjusted OR (AOR) and 95% confidence interval (CI) for each risk factor.

Results: Being Asian, diabetes mellitus, family history of cancer, and gallbladder stones were associated with higher odds of developing ICC and ECC. Each 1-unit increase in body mass index in early adulthood (ages 20–40 years) was associated with a decrease in age at diagnosis of CCA (6.7 months, $P < 0.001$; 6.1 months for ICC, $P = 0.001$; 8.2 months for ECC, $P = 0.007$). A family history of cancer was significantly associated with the risk of ICC and ECC development; the AORs (95% CI) were 1.11 (1.06–1.48) and 1.32 (1.01–2.00) for ICC and ECC, respectively.

Conclusions: In this study, early adulthood onset of obesity was significantly associated with CCA and may predict early diagnosis at younger age than normal weight individuals.

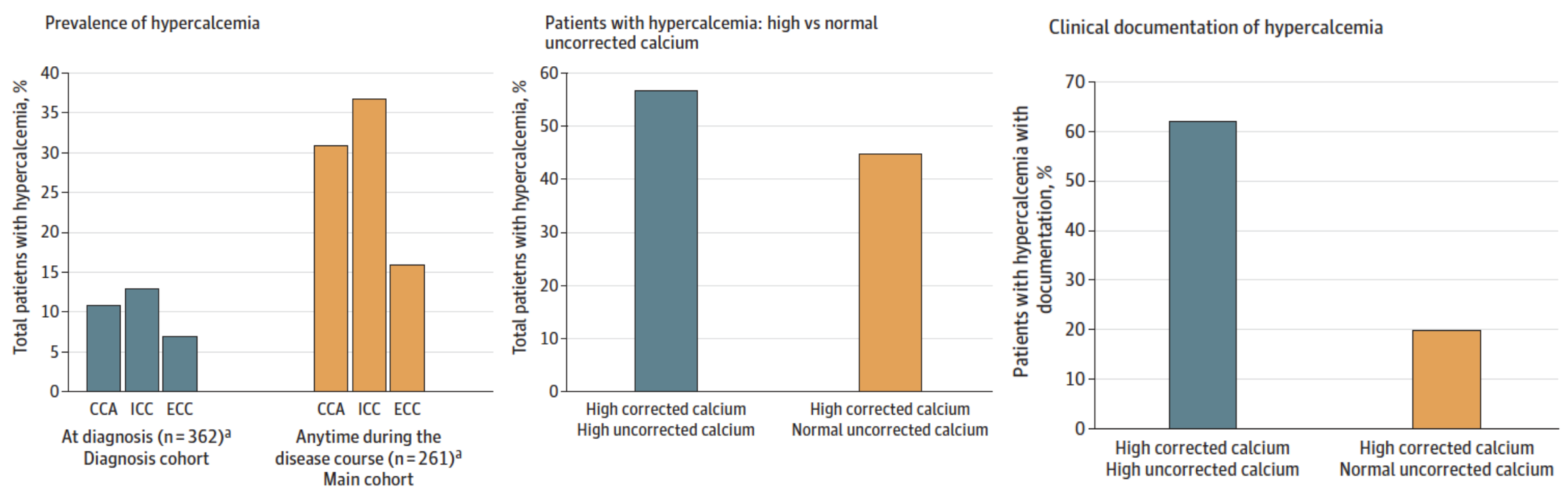
Impact: The study highlights the association between obesity and CCA, independent of PSC. There is a need to consider the mechanistic pathways of obesity in the absence of fatty liver and cirrhosis.

Introduction

tumor) and distal CCA. Altogether, CCAs are the second most common primary liver tumor, representing 10% to 15% of all primary

Courtesy of Milind Javle, MD

Prevalence and Clinicopathologic Characteristics of Hypercalcemia in Patients with Cholangiocarcinoma

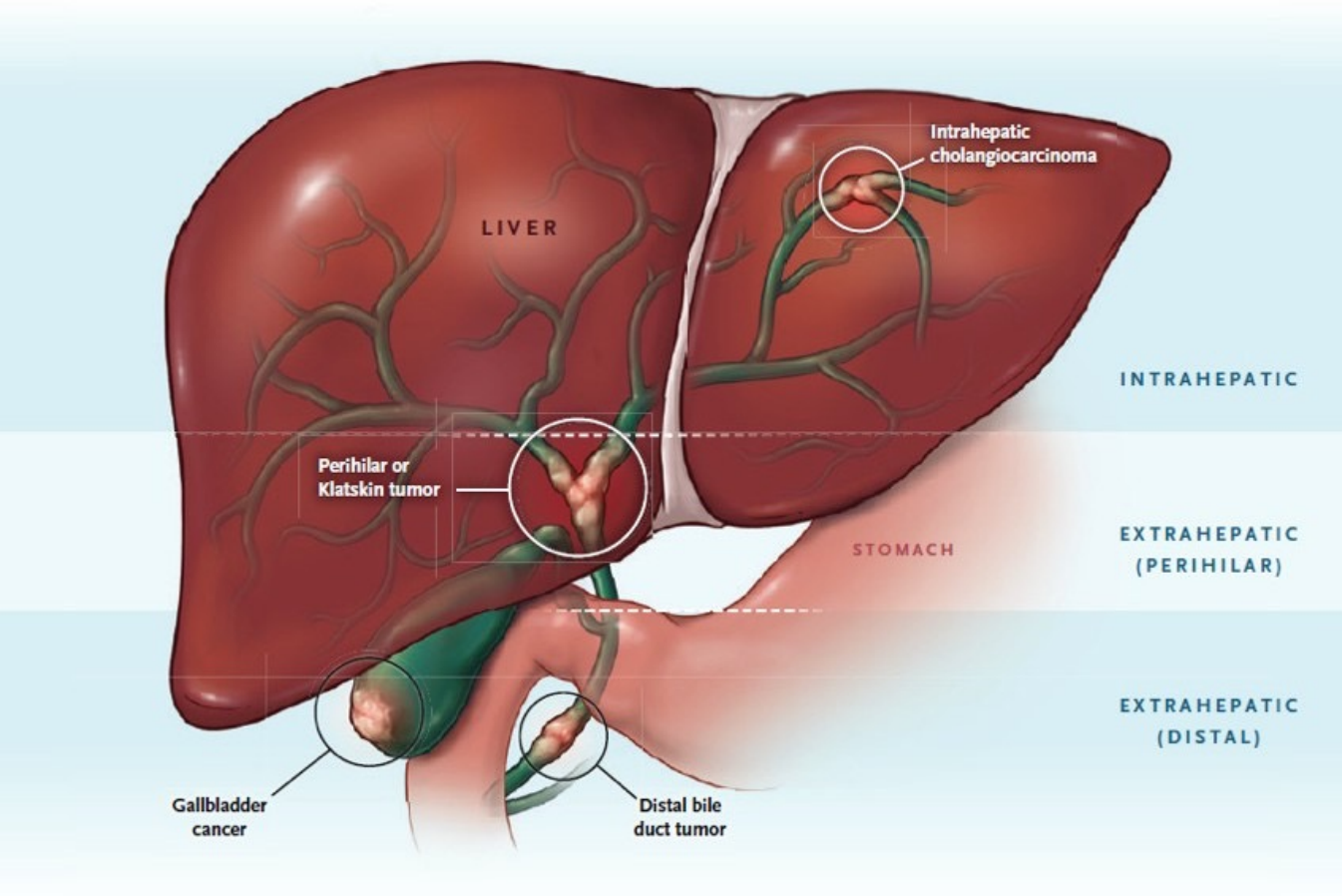


CCA = cholangiocarcinoma; ICC = intrahepatic cholangiocarcinoma; ECC = extrahepatic cholangiocarcinoma

[a] A total of 138 patients fulfilled criteria for the diagnosis cohort and the main cohort and were included in both.

Konstantinidou E et al. *JAMA Oncol* 2023 May 1;9(5):714-7.

Biliary Tract Cancers

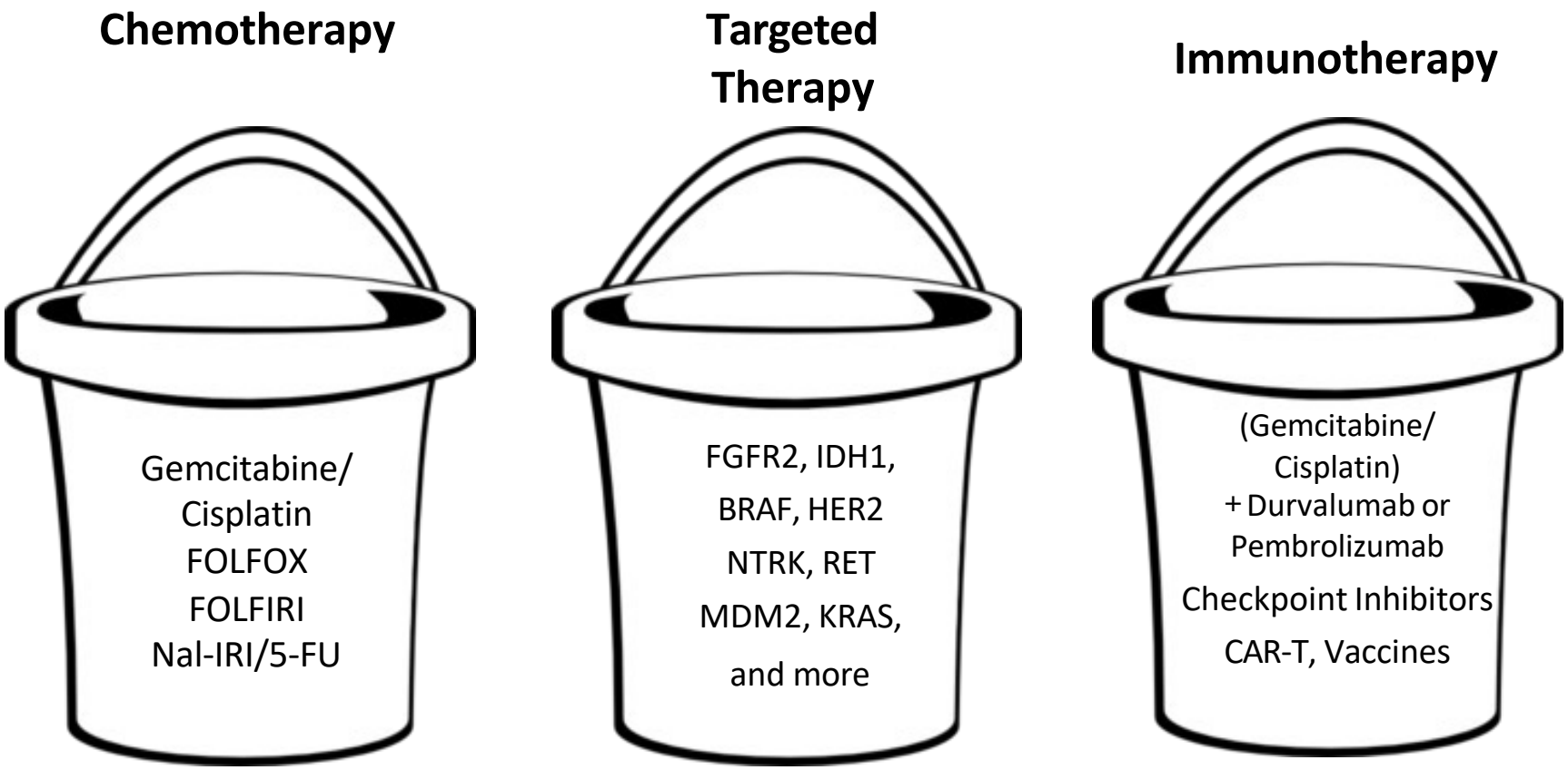


- Biliary Tract Cancer is uncommon (<1% all adult cancers)
- Aggressive malignancies with poor survival outcomes[1]
  - With first-line gemcitabine/cisplatin/durvalumab or gemcitabine/cisplatin/pembrolizumab: median OS, ≈12-13 months[2]
  - With second-line FOLFOX: median OS, 6.2 months; ORR, 5%[3]
- A molecularly heterogeneous disease
  - 40–50% of ICC harbor actionable alterations
  - 10-20% of ECC harbor actionable alterations
  - 20-30% of GBCAs harbor actionable alterations

Goyal L, et al. *N Engl J Med,* 2022

Courtesy of Lipika Goyal, MD, MPhil

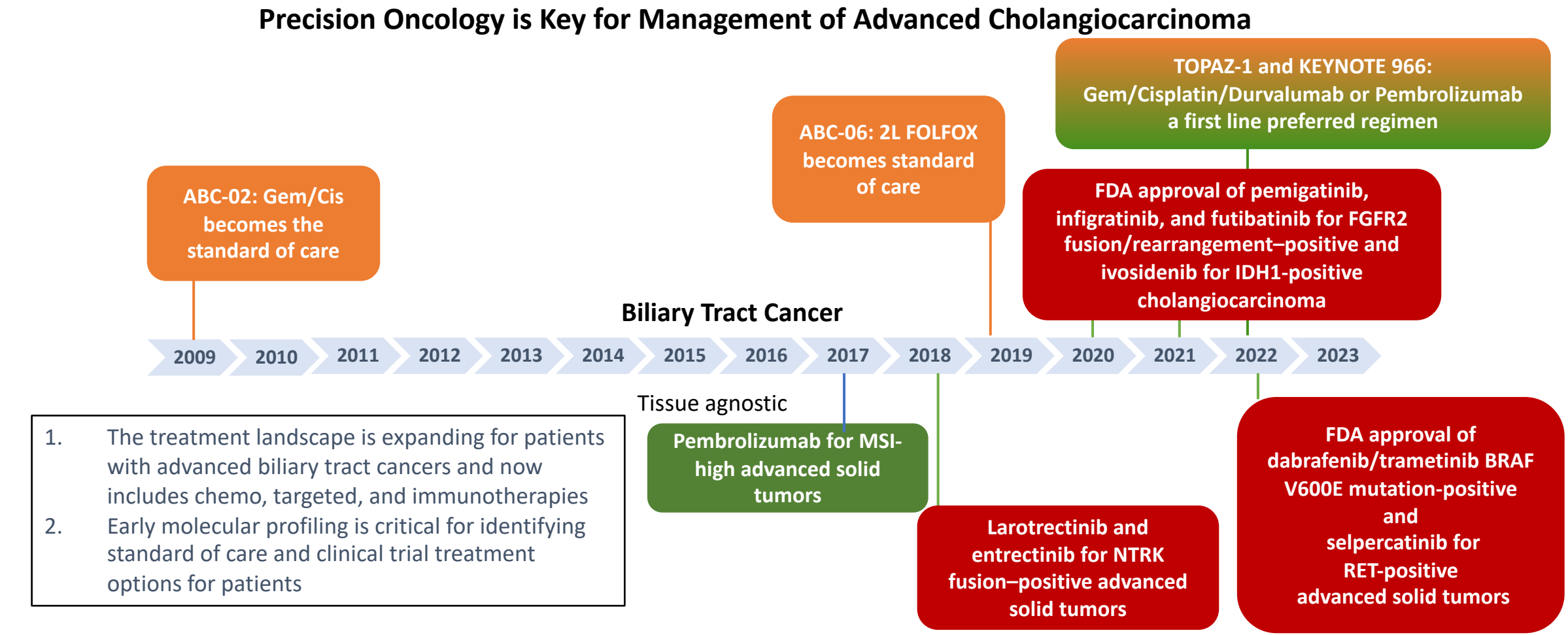
Systemic Therapy for Unresectable and Metastatic Biliary Tract Cancer



BRAF, v-raf murine sarcoma viral oncogene homolog B; CAR, chimeric antigen receptor; FGFR2, fibroblast growth factor receptor 2; FOLFOX, folinic acid, fluorouracil and oxaliplatin; HER2, human epidermal growth factor receptor; IDH, isocitrate dehydrogenase; MAPK, mitogen-activated protein kinase; NTRK, neurotrophic tyrosine kinase; PI3K, phosphatidylinositol-3-kinase; RET, rearranged during transfection.
Image credit: Clipart Panda.

Courtesy of Lipika Goyal, MD, MPhil

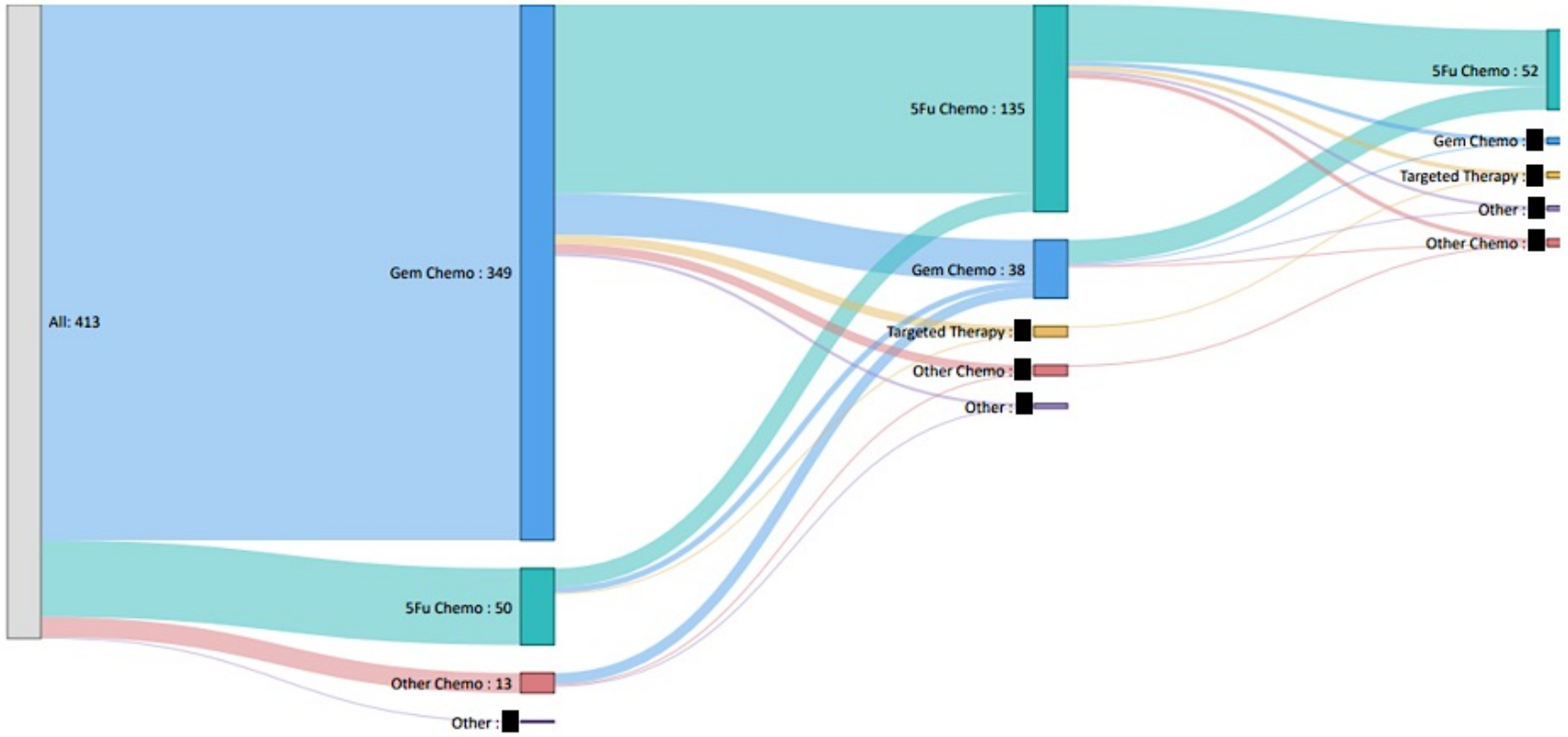
Conclusions



2L, second line; BRAF, v-raf murine sarcoma viral oncogene homolog B; FDA, US Food and Drug Administration; FGFR, fibroblast growth factor receptor; FOLFOX, folinic acid, fluorouracil and oxaliplatin; Gem/Cis, gemcitabine/ cisplatin; IDH, isocitrate dehydrogenase; MEK, mitogen-activated protein kinase kinase; MSI, microsatellite instability; NTRK, neurotrophic tyrosine kinase.
Valle JW, et al. Cancer Discov 2017;7(9):943–962; Goyal L, et al. Cancer Treat Rev 2021;95:102170; National Comprehensive Cancer Network (2021). Hepatobiliary cancers: NCCN evidence blocks. Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary_blocks.pdf. Abou-Alfa GK, et al (2019). Ann Oncol (ESMO Congress Abstracts), 30(suppl_5). Abstract 1867; Subbiah V, et al. Lancet 2020;21(9):1234–1243.

Courtesy of Lipika Goyal, MD, MPhil

Treatment Patterns



- 85% of patients initiated gemcitabine-based chemotherapy as their first line treatment
- About 46% patients initiated second line treatments, which were predominantly 5FU-based chemotherapies
- Few patients (17%) moved to third line of treatment
- Median time on treatment was 3.2 (1st line) and 2.7 (both 2nd and 3rd line) months

Gem Chemo: gemcitabine monotherapy and combination therapy
5Fu Chemo: 5-fluorouracil (or capecitabine) monotherapy and combination therapy (includes 5FU+Gem combination)
Other chemo: any other chemotherapy regimen
Targeted therapy: pemigatinib or ivosidenib monotherapy and combination therapy
Other: any other regimen

Valderrama, Elluri, et al. ASCO GI 2022

Courtesy of Milind Javle, MD

Agenda
Management of Advanced Biliary Tract Cancers

INTRODUCTION

MODULE 1: First-Line Systemic Treatment

MODULE 2: Targeted Treatment

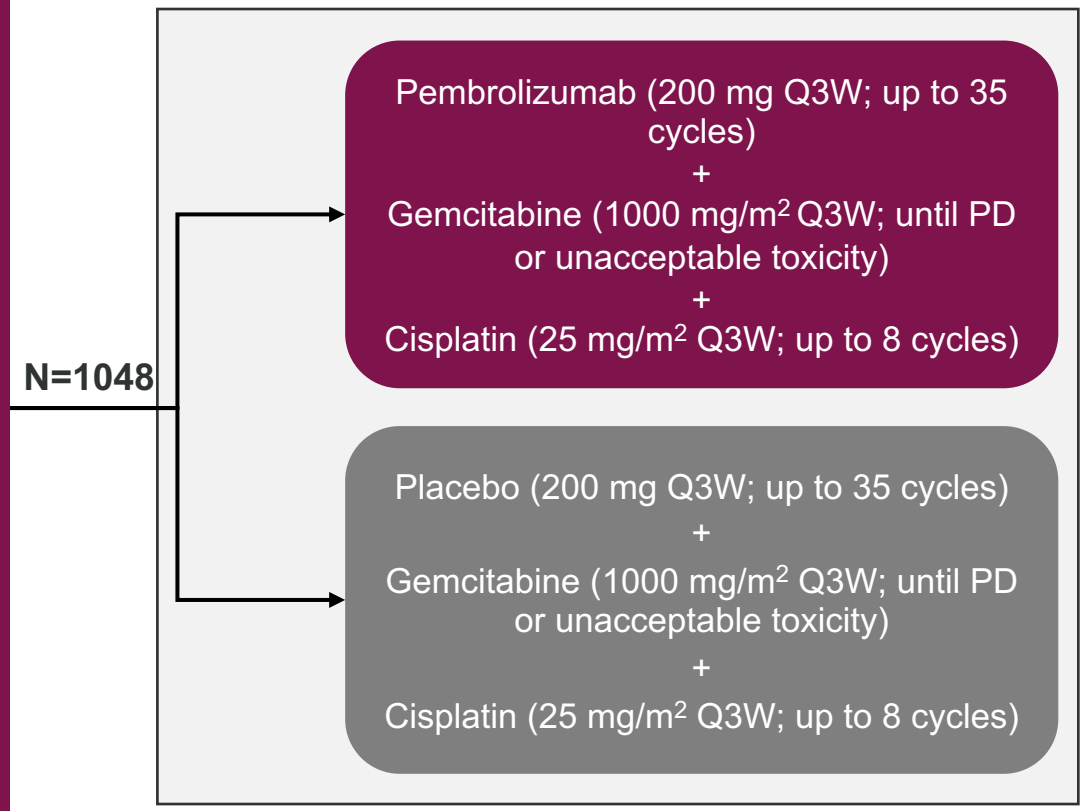
- HER2
- FGFR
- BRAF
- IDH

RTP
RESEARCH
TO PRACTICE

KEYNOTE-966: pembrolizumab plus GemCis versus GemCis alone in first-line advanced and/or unresectable BTC

Screening/baseline:

- Histologically confirmed diagnosis of advanced (metastatic) and/or unresectable (locally advanced) BTC (ampullary cancer excluded)
- Measurable disease based on RECIST v1.1, as determined by the site investigator
- No prior systemic therapies
- No CNS metastases and/or carcinomatous meningitis
- Participants with a history of hepatitis B/C can be enrolled if they meet study criteria
- Availability of archival tumor tissue sample or newly obtained core or excisional biopsy of a tumor lesion
- Life expectancy >3 months
- Adequate organ function



Status	Active, not recruiting
Estimated completion date	August 31, 2023

Primary objective:

- OS

Secondary objectives:

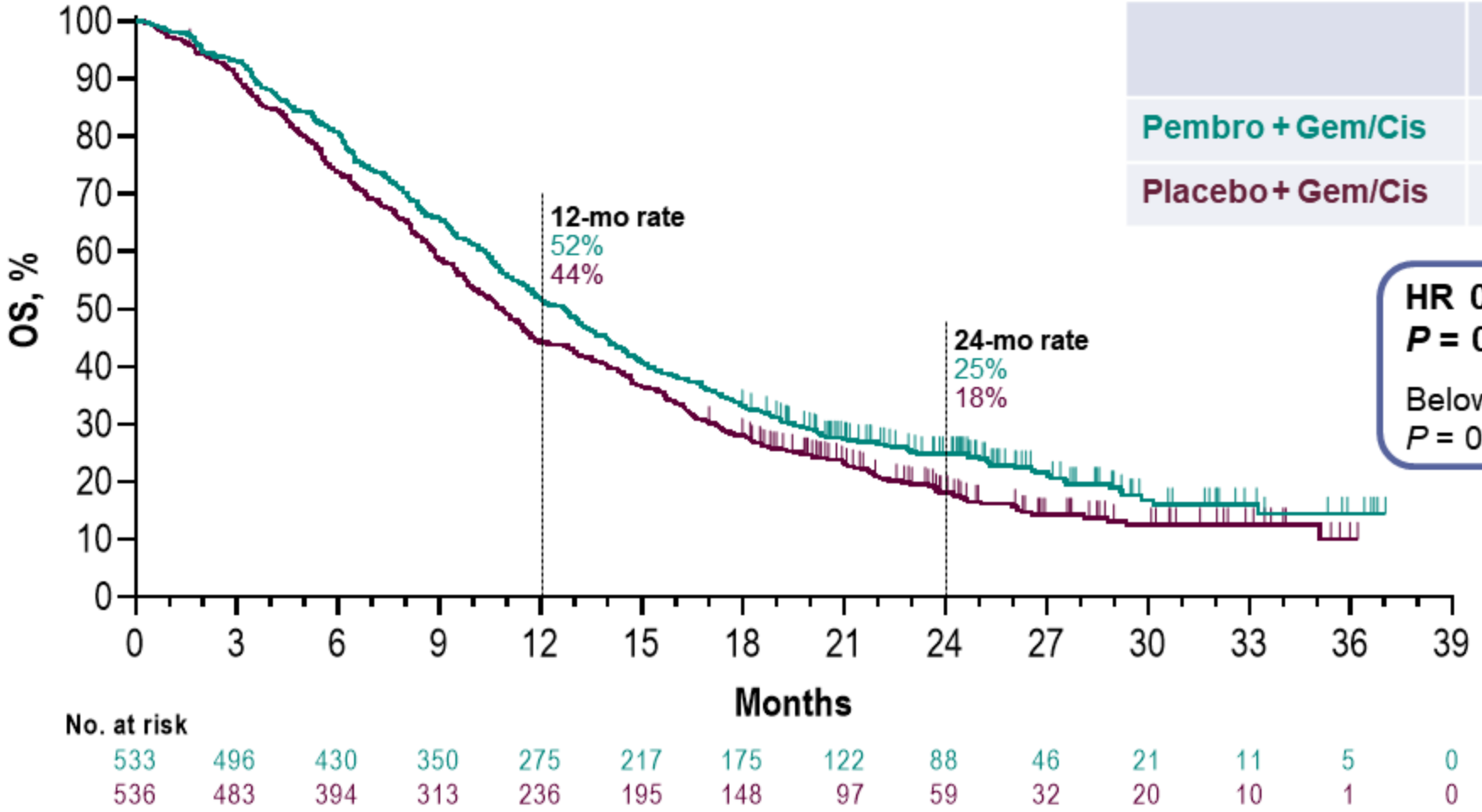
- ORR (RECIST v1.1; BICR)
- DOR (RECIST v1.1; BICR)
- PFS (RECIST v1.1; BICR)

Safety outcomes:

- Number of patients experiencing more than one adverse event
- Discontinuations due to adverse events

Courtesy of Milind Javle, MD

Overall Survival at Final Analysis



	Pts w/ Event	Median (95% CI), mo
Pembro + Gem/Cis	78%	12.7 (11.5-13.6)
Placebo + Gem/Cis	83%	10.9 (9.9-11.6)

HR 0.83 (95% CI, 0.72-0.95)
***P* = 0.0034**

Below the signficance boundary of *P* = 0.0200

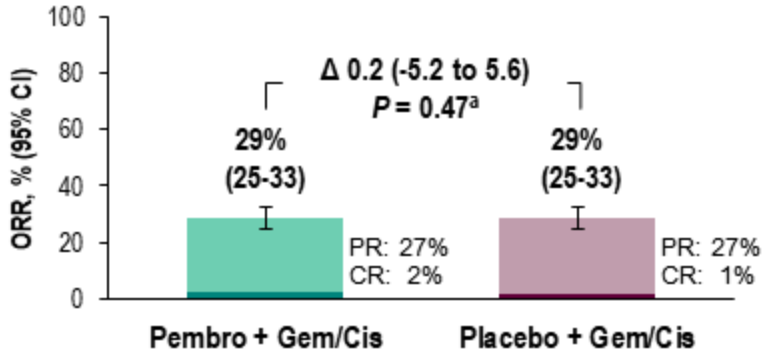
Data cutoff date: December 15, 2022.

Courtesy of Milind Javle, MD

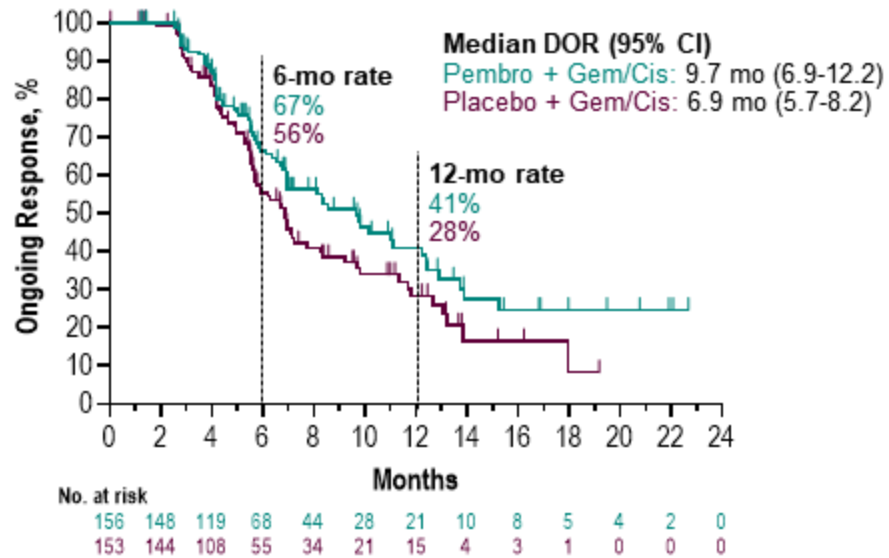
Objective Response Rate and Duration of Response

Interim Analysis 1

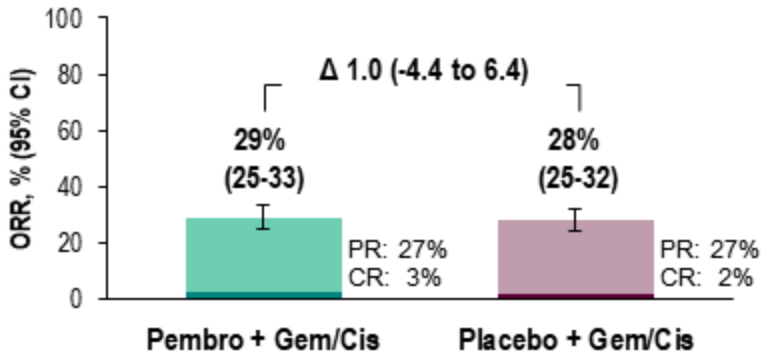
ORR

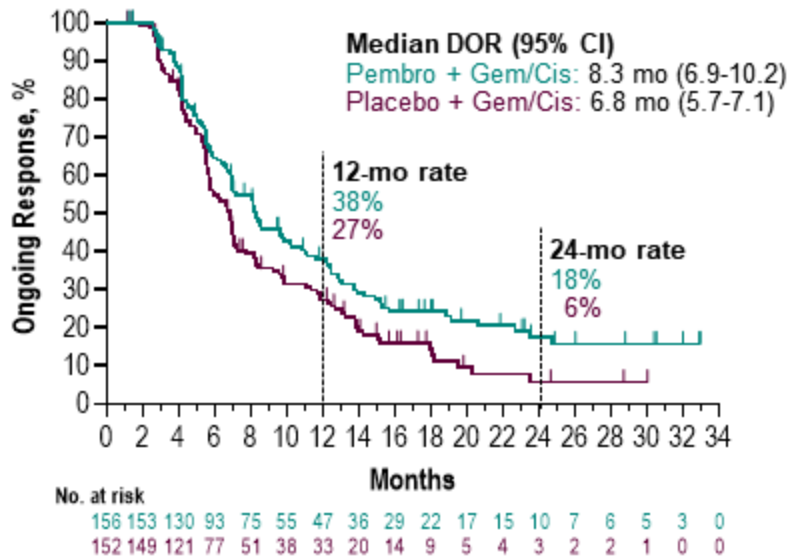


DOR



Final Analysis





ORR was assessed per RECIST v1.1 by BICR. [a]Above the significance boundary of $P = 0.0125$.
Data cutoff date: December 15, 2021 (IA1) and December 15, 2022 (FA). IA1 was the prespecified final analysis of ORR. ORR analysis at FA was exploratory.

Courtesy of Milind Javle, MD

TOPAZ-1 study design: GemCis/Durvalumab vs GemCis/Placebo[1,*]

Randomised, double-blind, multicentre, global, Phase 3 study

Key eligibility
- Locally advanced or metastatic BTC (ICC, ECC, or GBC)
- Previously untreated if unresectable or metastatic at initial diagnosis
- Recurrent disease >6 months after curative surgery or adjuvant therapy
- ECOG PS 0 or 1

Stratification factors
- Disease status
  - Initially unresectable versus recurrent
- Primary tumour location
  - ICC versus ECC versus GBC

R (1:1)
(N=685)

Durvalumab 1500 mg Q3W + GemCis* (up to 8 cycles) → **Durvalumab 1500 mg Q4W until PD**

Placebo Q3W + GemCis* (up to 8 cycles) → **Placebo Q4W until PD**

Primary endpoint
- OS

Key secondary endpoints
- PFS
- ORR
- DoR
- Safety

Exploratory endpoint
- Efficacy and safety by primary tumour location
  - ICC versus ECC versus GBC

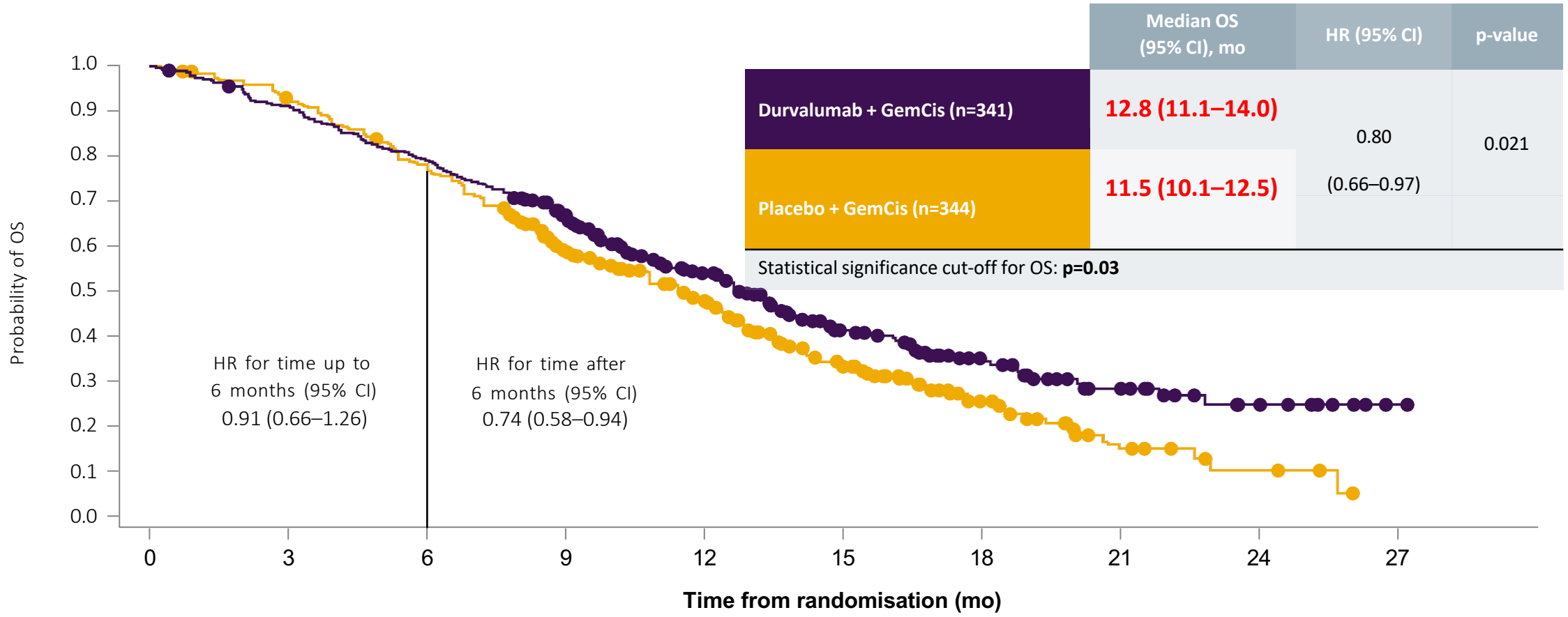
*On Days 1 and 8 Q3W up to 8 cycles

BTC, biliary tract cancer; DoR, duration of response; ECC, extrahepatic cholangiocarcinoma; ECOG, Eastern Cooperative Oncology Group; GBC, gallbladder cancer; GemCis, gemcitabine (1000 mg/m^2) and cisplatin (25 mg/m^2); ICC, intrahepatic cholangiocarcinoma; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PS, performance status; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomised

1. Oh D-Y, et al. *NEJM Evid* Published online 1 June 2022. doi:10.1056/EVIDoa2200015

Courtesy of Lipika Goyal, MD, MPhil

TOPAZ-1: Overall Survival – GemCis/Durvalumab vs GemCis/Placebo[1,*]



Number of patients at risk

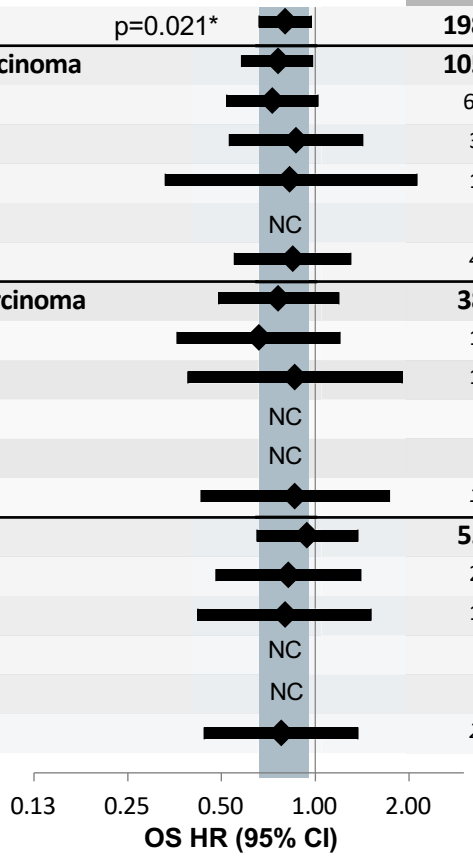
Durvalumab + GemCis	341	309	268	208	135	79	49	24	9	1
Placebo + GemCis	344	317	261	183	125	65	29	10	4	0

*Median duration of follow-up (95% CI) was 16.8 (14.8–17.7) months with durvalumab + GemCis and 15.9 (14.9–16.9) months with placebo + GemCis
CI, confidence interval; GemCis, gemcitabine and cisplatin; HR, hazard ratio; mo, months; OS, overall survival
1. Oh D-Y, et al. *NEJM Evid* Published online 1 June 2022. doi:10.1056/EVIDoa2200015

Courtesy of Lipika Goyal, MD, MPhil

TOPAZ-1: Overall Survival – ICC vs ECC vs GBCA

- OS benefit with durvalumab was consistent in patients with ICC and ECC, and in patients with GBC in Asia, Europe, and North America



	Durvalumab + GemCis (N=341)		Placebo + GemCis (N=344)		OS HR† (95% CI)
	Events, n/N (%)	Median OS (95% CI), mo	Events, n/N (%)	Median OS (95% CI), mo	
Full analysis set[1]	**198/341 (58.1)**	**12.8 (11.1–14.0)**	**226/344 (65.7)**	**11.5 (10.1–12.5)**	**0.80 (0.66–0.97)‡**
Intrahepatic cholangiocarcinoma	**105/190 (55.3)**	**13.5 (11.9–15.1)**	**126/193 (65.3)**	**11.5 (9.8–12.8)**	**0.76 (0.58–0.98)§**
Asia	60/100 (60.0)	13.0 (9.8–14.6)	81/111 (73.0)	11.4 (9.2–12.5)	0.72 (0.52–1.02)§
Europe	31/61 (50.8)	13.5 (9.5–18.8)	35/61 (57.4)	14.0 (8.0–18.3)	0.87 (0.53–1.42)§
North America	11/21 (52.4)	15.1 (6.8–NC)	9/18 (50.0)	13.3 (5.3–NC)	0.83 (0.33–2.12)§
South America	3/8 (37.5)	NR (2.3–NC)	1/3 (33.3)	NR (8.0–NC)	NC‖
Europe + North America	*42/82 (51.2)*	*13.7 (10.9–18.1)*	*44/79 (55.7)*	*13.6 (8.5–17.7)*	*0.85 (0.55–1.30)§*
Extrahepatic cholangiocarcinoma	**38/66 (57.6)**	**12.7 (9.8–16.6)**	**42/65 (64.6)**	**12.1 (7.8–14.4)**	**0.76 (0.49–1.19)§**
Asia	18/35 (51.4)	16.6 (12.6–NC)	27/42 (65.3)	12.8 (7.7–17.3)	0.66 (0.36–1.20)§
Europe	14/23 (60.9)	9.1 (8.7–NC)	12/19 (63.2)	14.4 (7.0–NC)	0.86 (0.39–1.90)§
North America	5/6 (83.3)	11.0 (0.9–NC)	3/4 (75.0)	9.6 (3.4–NC)	NC‖
South America	1/2 (50.0)	NR (10.0–NC)	0	NC	NC‖
Europe + North America	*19/29 (65.5)*	*9.8 (8.7–16.2)*	*15/23 (65.2)*	*12.1 (7.0–14.4)*	*0.86 (0.43–1.73)§*
Gallbladder cancer	**55/85 (64.7)**	**10.7 (8.9–13.2)**	**58/86 (67.4)**	**11.0 (8.7–12.8)**	**0.94 (0.65–1.37)§**
Asia	25/43 (58.1)	13.3 (9.0–20.1)	29/43 (67.4)	12.6 (8.4-17.7)	0.82 (0.48–1.40)§
Europe	18/24 (75.0)	9.6 (5.2–11.1)	22/27 (81.5)	8.1 (4.9–11.0)	0.80 (0.42–1.51)§
North America	5/10 (50.0)	12.2 (2.6–NC)	4/6 (66.7)	10.2 (5.7–NC)	NC‖
South America	7/8 (87.5)	8.1 (0.9–NC)	3/10 (30.0)¶	NR (2.0–NC)	NC‖
Europe + North America	*23/34 (67.6)*	*10.3 (6.6–12.2)*	*26/33 (78.8)*	*8.7 (6.0–11.0)*	*0.78 (0.44–1.37)§*

*Two-sided p-value. Threshold of significance for the interim analysis was 0.03. †Durvalumab plus GemCis versus placebo plus GemCis. ‡Calculated from a stratified Cox proportional hazards model. §Calculated from an unstratified Cox proportional hazards model. ‖Not calculated due to an insufficient number of events. ¶The small cohort of patients with GBC in South America who received placebo outperformed expectations compared with other regions. Investigations continue to understand this outcome

CI, confidence interval; ECC, extrahepatic cholangiocarcinoma; GBC, gallbladder cancer; GemCis, gemcitabine and cisplatin; HR, hazard ratio; ICC, intrahepatic cholangiocarcinoma; mo, months; NC, non-calculable; NR, not reached; OS, overall survival

1. Oh D-Y, et al. *NEJM Evid* Published online 1 June 2022. doi:10.1056/EVIDoa2200015

Courtesy of Lipika Goyal, MD, MPhil

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic cholangiocarcinoma, no targetable mutations on next-generation sequencing (NGS) and PS 0?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Liposomal irinotecan + fluorouracil + leucovorin
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Durvalumab + liposomal irinotecan/fluorouracil
 Dr Borad	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFIRI

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for an 80-year-old patient with controlled hypertension and diabetes with metastatic cholangiocarcinoma and no targetable mutations on NGS?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	5-FU or FOLFOX
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Capecitabine
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Durvalumab + liposomal irinotecan/fluorouracil
 Dr Borad	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Regorafenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFOX or FOLFIRI

Agenda
Management of Advanced Biliary Tract Cancers

INTRODUCTION

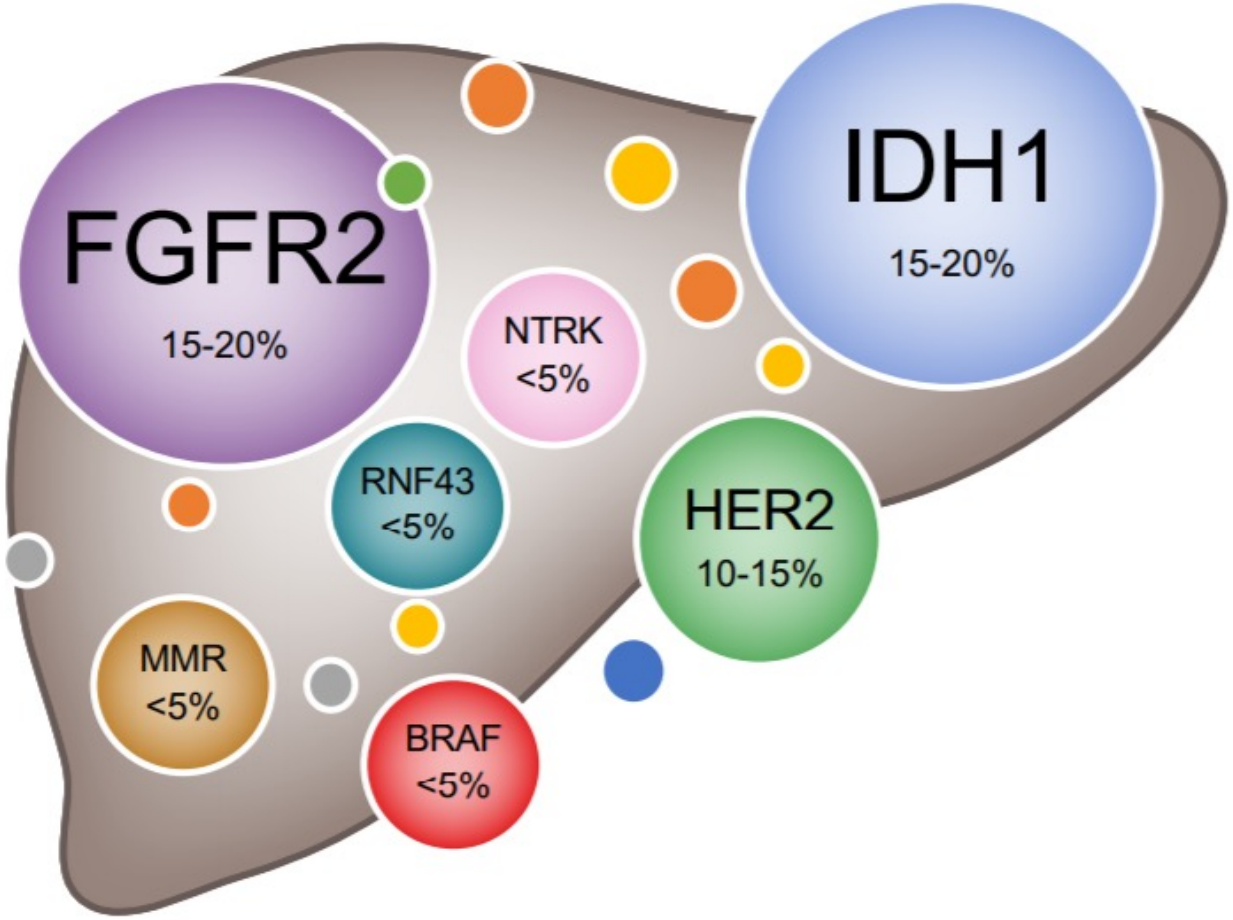
MODULE 1: First-Line Systemic Treatment

MODULE 2: Targeted Treatment

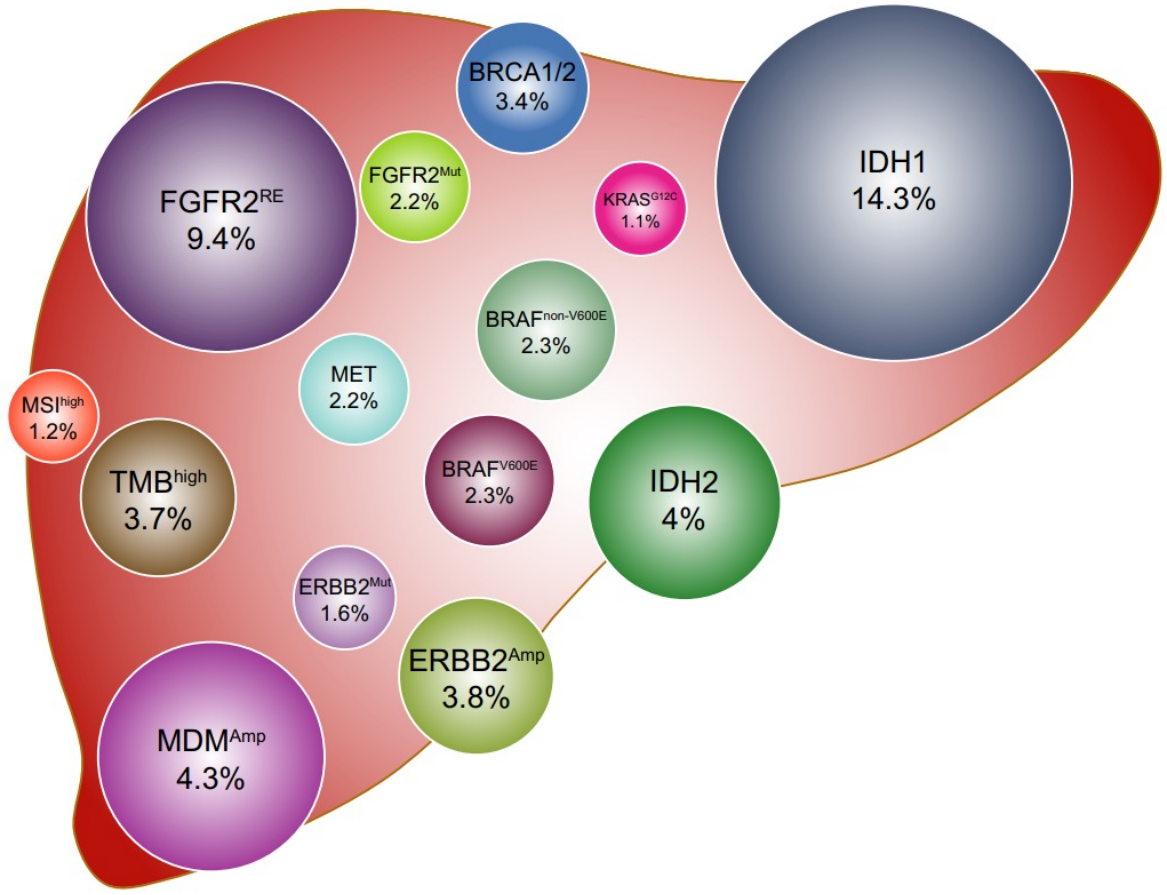
- HER2
- FGFR
- BRAF
- IDH

RTP
RESEARCH
TO PRACTICE

Targets in Biliary Tract Cancer



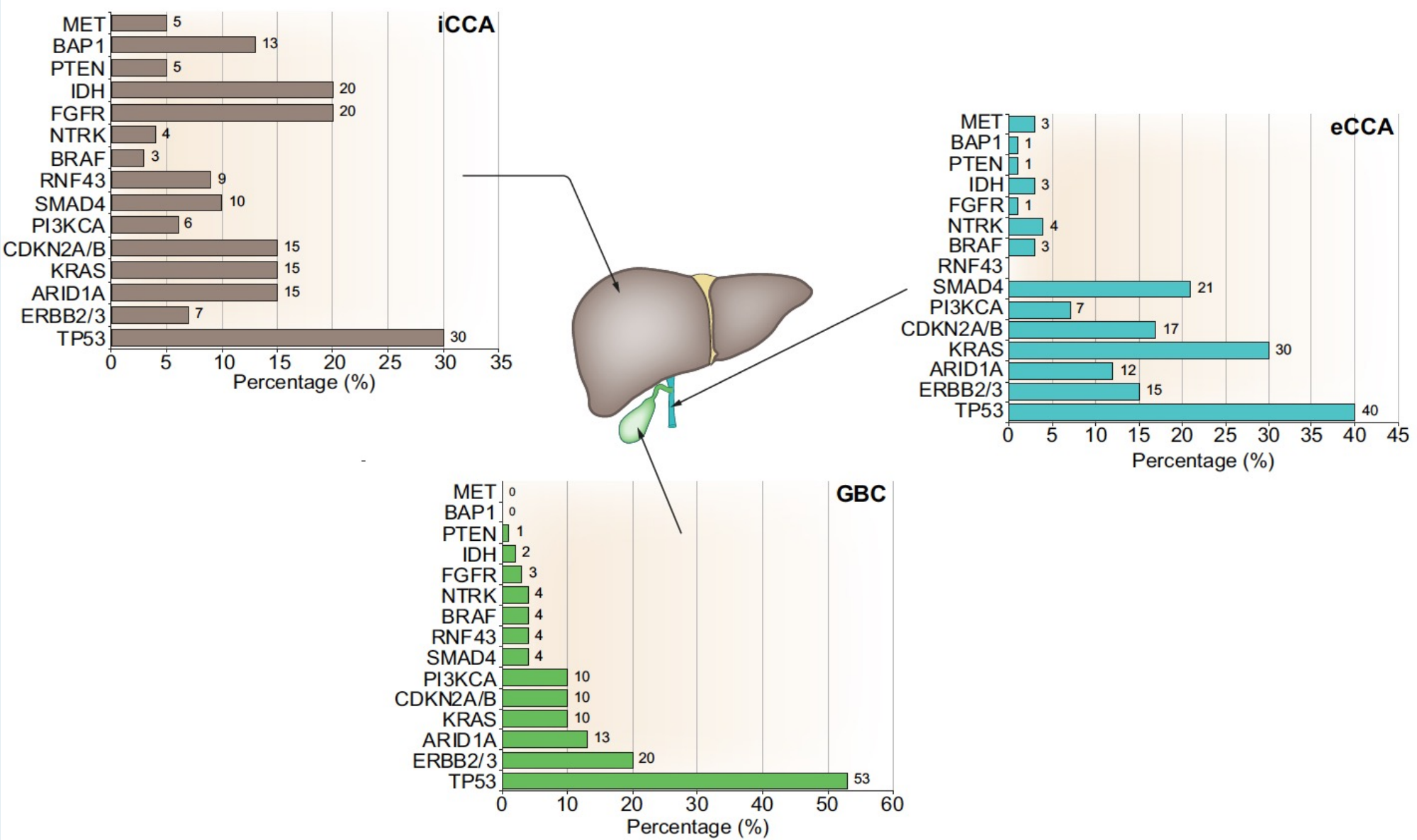
Lamarca et al. *J Hepatol.* 2020



Kendre et al. *J Hepatol.* 2023

Courtesy of Lipika Goyal, MD, MPhil

Molecular Profiling of Biliary Tract Cancers



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

Lamarca A et al. *J Hepatol* 2020 July;73(1):170-85.

RTP RESEARCH TO PRACTICE

Incidence of mutations in targetable pathways in biliary cancers

CGP findings	ICCA	ECCA	GBC
Total GA/patient	3.6	4.4	4.0
CRGA/patient	2.0	2.1	2.0
ERBB2 amplifications	4%	**11%**	**16%**
BRAF substitutions	**5%**	**3%**	1%
KRAS substitutions	22%	42%	11%
PI3KCA substitutions	5%	**7%**	14%
FGFR1–3 fusions and amplifications	**11%**	0	3%
CDKN2A/B loss	27%	17%	19%
IDH1/2 substitutions	**20%**	0	0
ARID1A alterations	18%	12%	13%
MET amplifications	2%	0	1%

Javle M, et al. *Cancer* 2016;122:3838–3847

Courtesy of Milind Javle, MD

Which specific assay or assays do you generally use to test for targetable mutations in your patients with advanced biliary tract cancers?

 Dr Goyal	Tissue-based (Foundation Medicine, Caris, institutional assay) and liquid biopsy (Guardant360®)
 Dr Javle	Tissue-based (Oncomine, Foundation Medicine, Caris) and liquid biopsy (Guardant360®)
 Dr Abou-Alfa	Tissue-based (IMPACT)
 Dr Borad	Tissue-based (Caris) and liquid biopsy (Guardant360®)
 Prof Bridgewater	Tissue-based (North Thames Genomic Laboratory Hub DNA and RNA panels)
 Dr Kelley	Tissue-based (UCSF500, Caris, Tempus) and liquid biopsy (Guardant360®)

Agenda
Management of Advanced Biliary Tract Cancers

INTRODUCTION

MODULE 1: First-Line Systemic Treatment

MODULE 2: Targeted Treatment

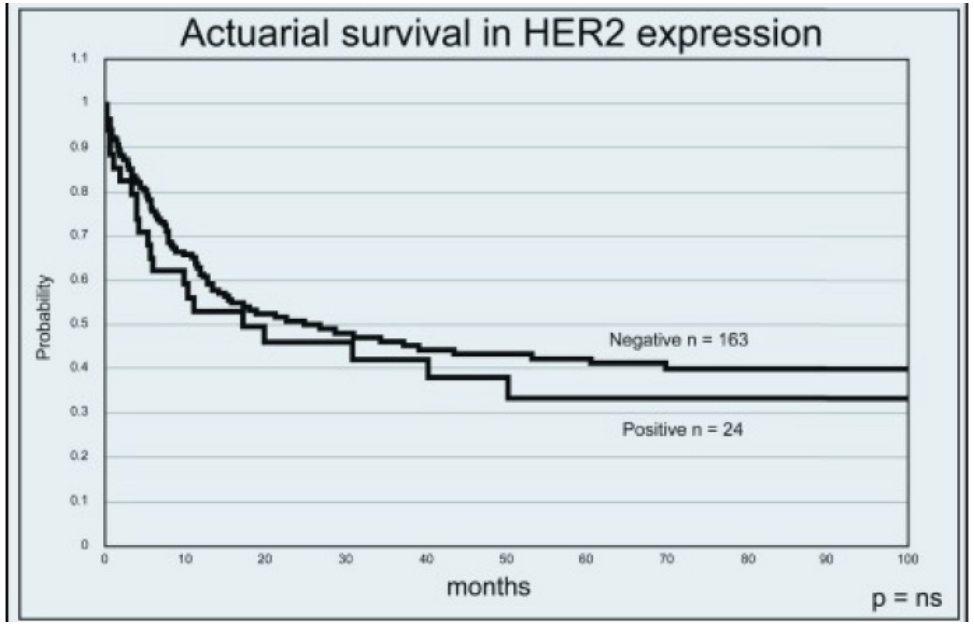
- HER2
- FGFR
- BRAF
- IDH

RTP
RESEARCH
TO PRACTICE

HER 2/neu expression GB Cancer

Demographics

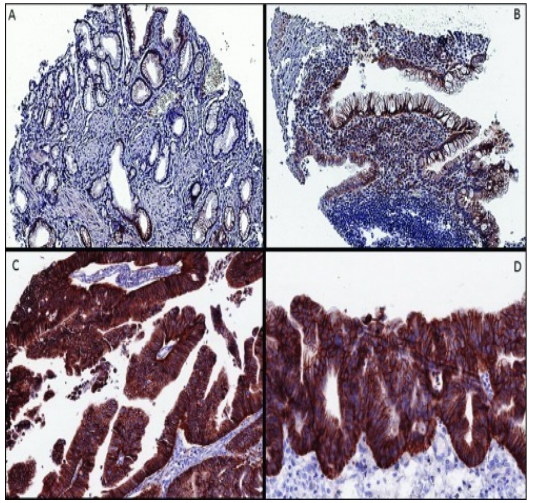
Gender	*n* (total)	Mean age	SD
Female	165	61.6	13.5
Male	22	69.0	14.3
Total	187	62.5	14.4



Gallbladder cancer (N=187)

HER2/ neu expression

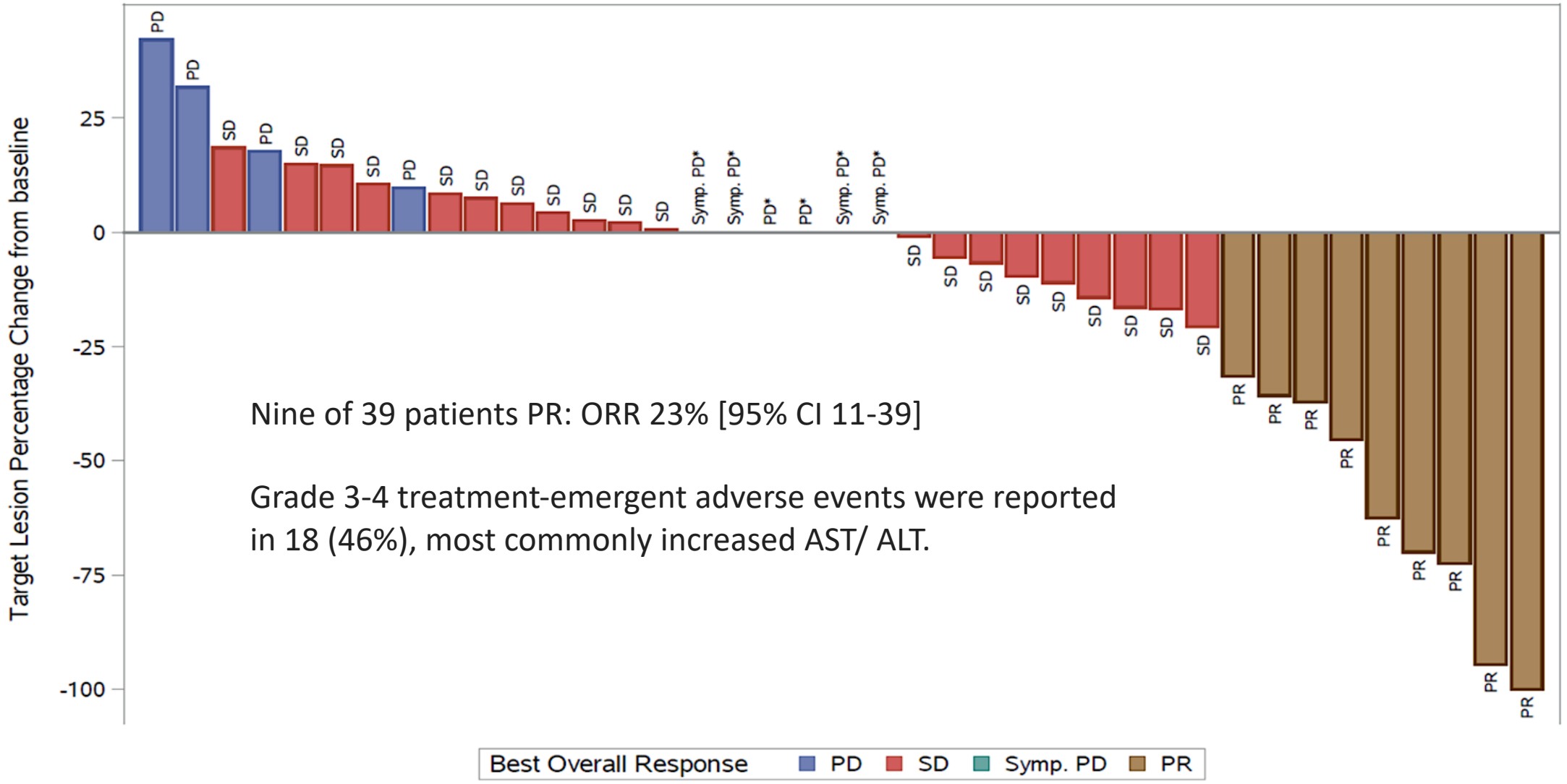
- 90 (48.1%) stained negative,
- 35 (18.7%) were 1+, 38 (20.3%) were 2+,
- 24 (12.8%) were considered positive (3+)



Gastrointest Cancer Res. 2014 Mar-Apr; 7(2): 42–48

Courtesy of Milind Javle, MD

MyPathway: Trastuzumab plus pertuzumab for HER2/neu-amplified BTC



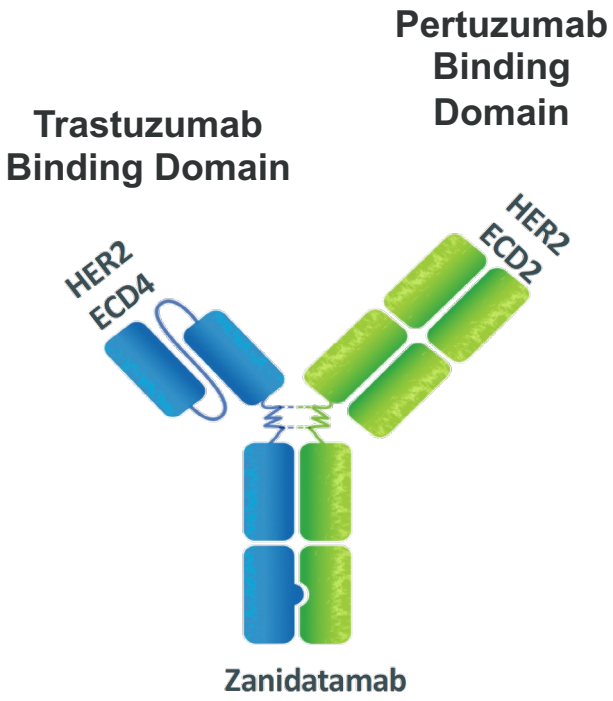
Nine of 39 patients PR: ORR 23% [95% CI 11-39]

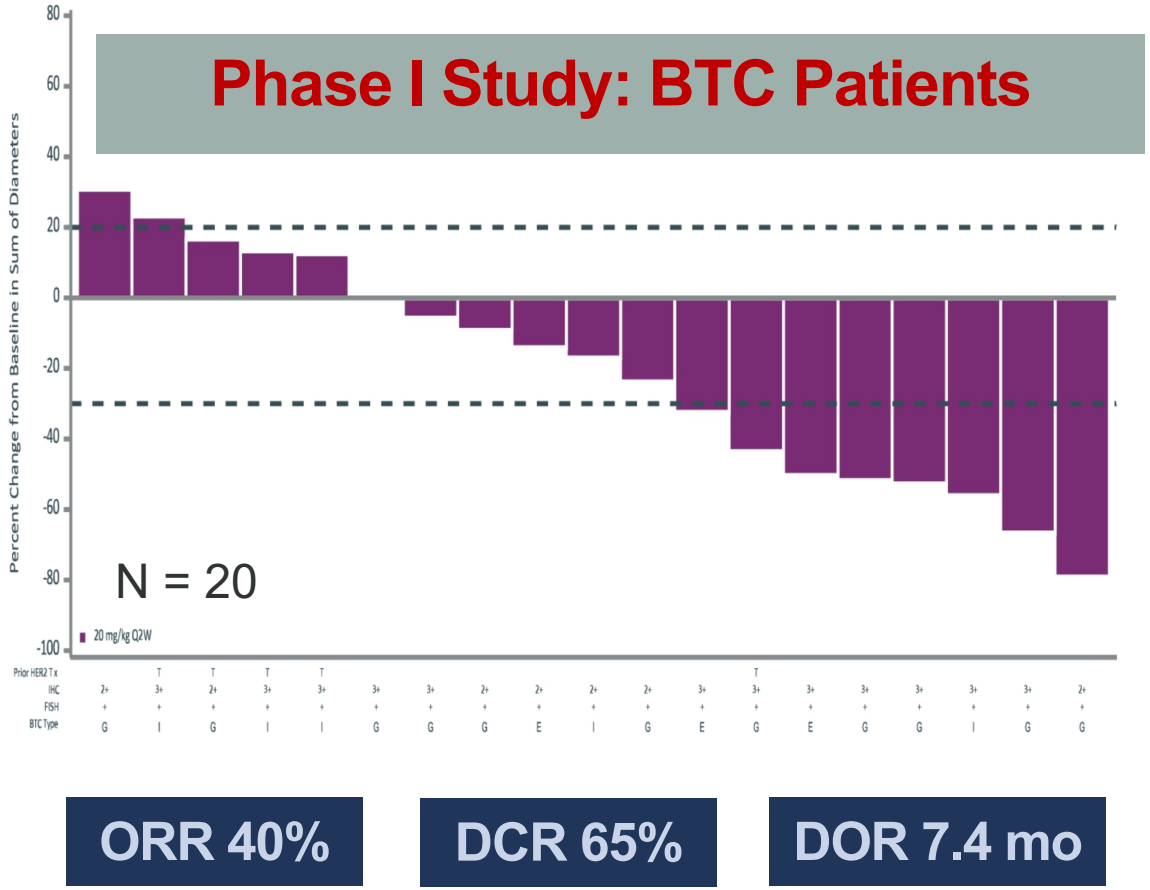
Grade 3-4 treatment-emergent adverse events were reported in 18 (46%), most commonly increased AST/ ALT.

Javle M, et al. Lancet Oncol 2021 Sep;22(9):1290-1300.

Courtesy of Milind Javle, MD

Zanidatamab: Bispecific HER2-Targeted Antibody





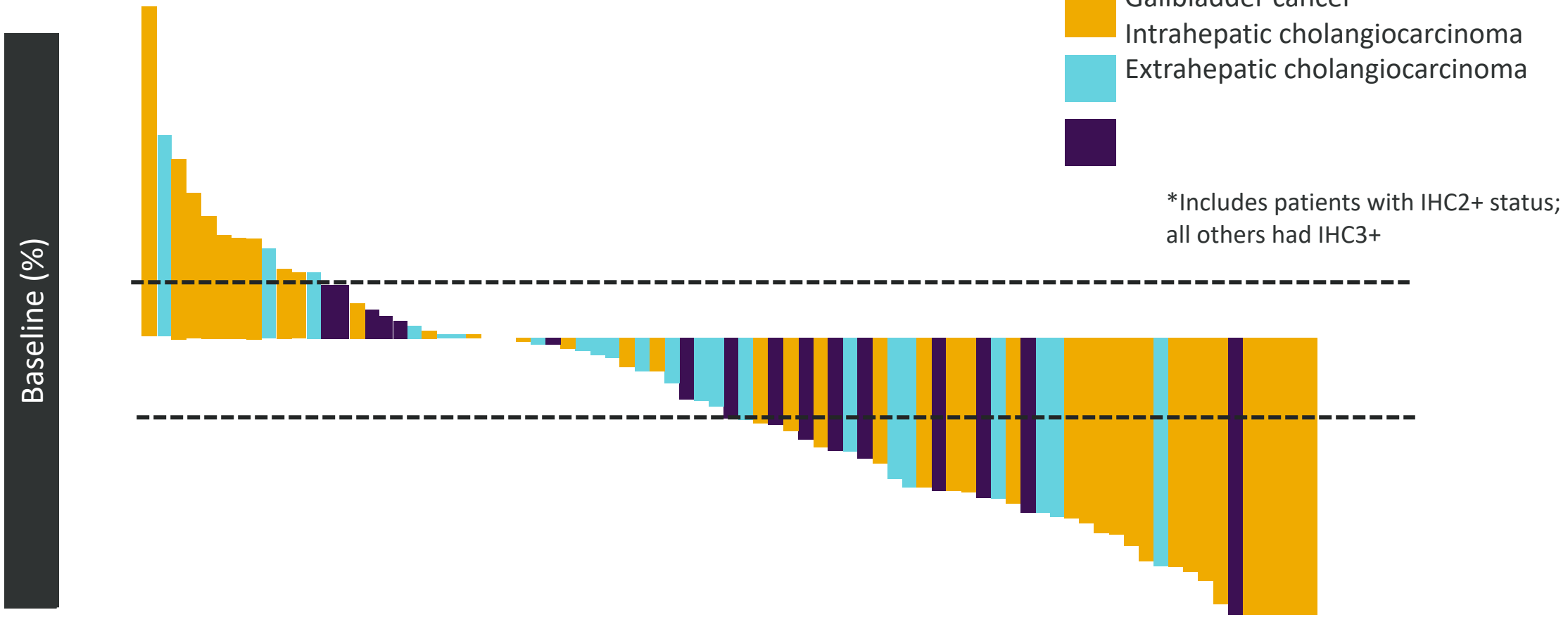
ORR 40% **DCR 65%** **DOR 7.4 mo**

Meric-Bernstam et al, *J Clin Oncol* 2021

Courtesy of Milind Javle, MD

HERIZON-BTC-01: Change in Target Lesion Size From Baseline (Cohort 1)

- Target lesions decreased in 68.4% of patients



Pant. ASCO 2023. Abstr 4008. Harding. Lancet Oncol. 2023;[Epub].

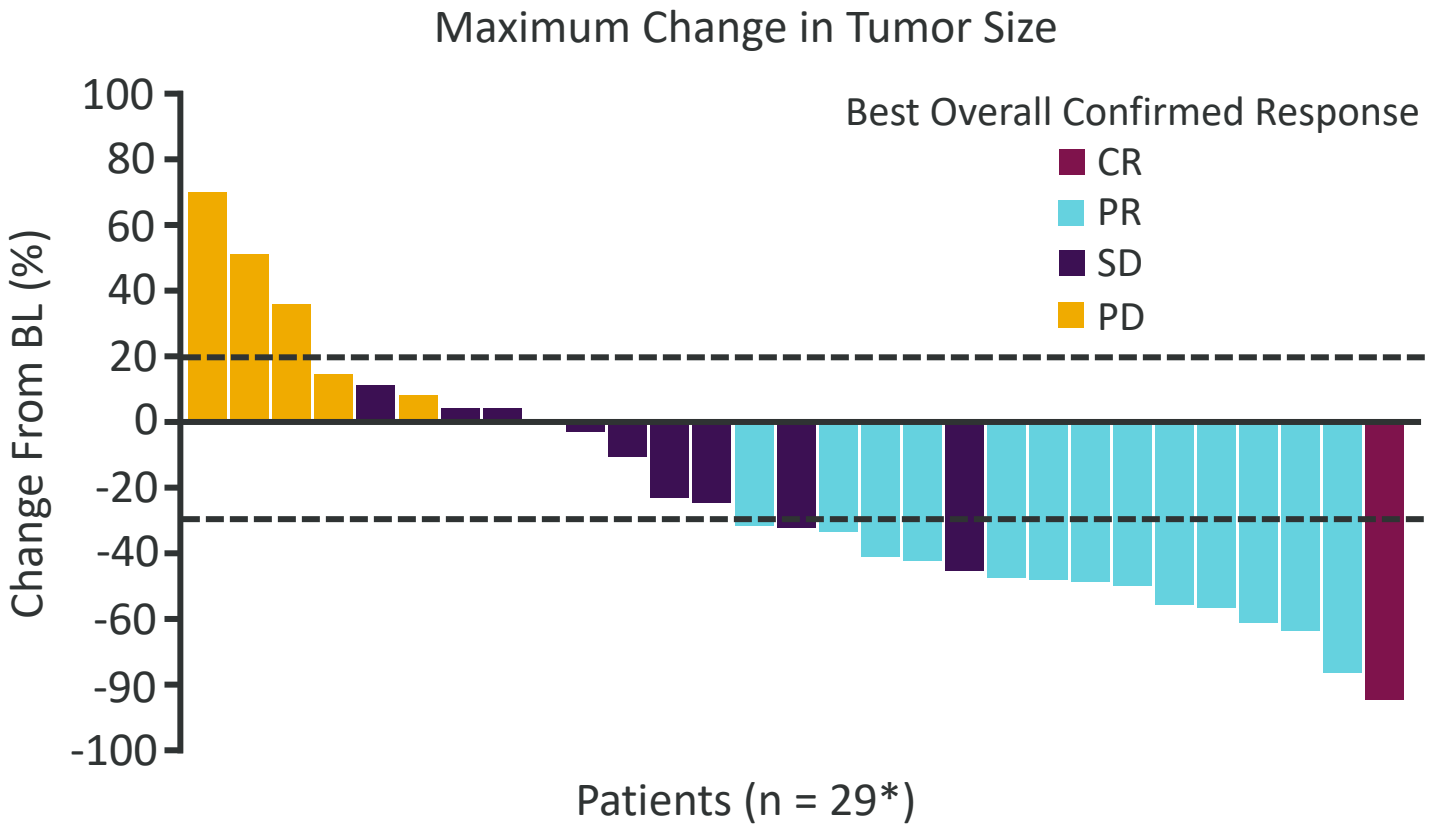
Courtesy of Milind Javle, MD

Tucatinib and Trastuzumab for Previously Treated Human Epidermal Growth Factor Receptor 2–Positive Metastatic Biliary Tract Cancer (SGNTUC-019): A Phase II Basket Study

Yoshiaki Nakamura, MD, PhD[1]; Nobumasa Mizuno, MD, PhD[2]; Yu Sunakawa, MD, PhD[3]; Jean-Luc Canon, MD[4]; Matthew D. Galsky, MD[5]; Erika Hamilton, MD[6]; Hidetoshi Hayashi, MD, PhD[7]; Guy Jerusalem, MD, PhD[8]; Seung Tae Kim, MD[9]; Keun-Wook Lee, MD, PhD[10]; Lionel Aurelien Kankeu Fonkoua, MD[11]; Bradley J. Monk, MD[12]; Danny Nguyen, MD[13]; Do-Youn Oh, MD, PhD[14]; Alicia Okines, MD, MBChB[15]; David M. O'Malley, MD[16]; Paula Pohlmann, MD[17]; Martin Reck, MD, PhD[18]; Sang Joon Shin, MD[19]; Kazuki Sudo, MD, PhD[20]; Shunji Takahashi, MD, PhD[21]; Cedric Van Marcke, MD, PhD[22]; Evan Y. Yu, MD[23]; Roman Groisberg, MD[24]; Jorge Ramos, DO[25]; Sherry Tan, PhD[25]; Thomas E. Stinchcombe, MD[26]; and Tanios Bekaii-Saab, MD[27]

J Clin Oncol 2023 September 26;[Online ahead of print]

Tucatinib + Trastuzumab for HER2+ BTC: Response



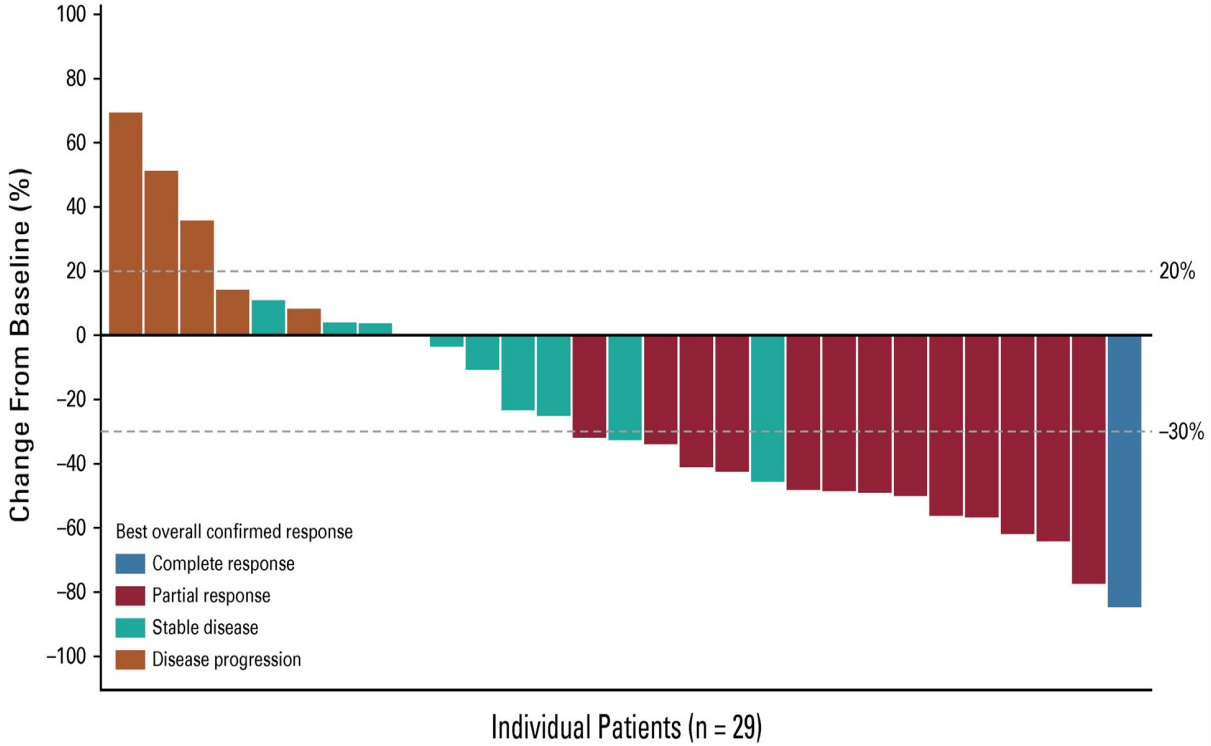
Outcome	Patients (N = 30)
Best overall response, n (%)	
▪ CR	1 (3.3)
▪ PR	13 (43.3)
▪ SD	9 (30.0)
▪ PD	6 (20.0)
▪ Not available	1 (3.3)*
Confirmed ORR, % (90% CI) (primary endpoint)	**46.7 (30.8-63.0)**
Median DoR, mo (90% CI)	6.0 (5.5-6.9)
DCR, n (%)	23 (76.7)
Median time to first response, mo (range)	2.1 (1.2-4.3)

- Reduction in tumor size observed in 70.0% of patients

Nakamura Y et al. ASCO 2023. Abstr 4007; *J Clin Oncol* 2023 Sep 26: Online ahead of print.

Courtesy of Milind Javle, MD

TUCATINIB/TRASTUZUMAB IN BTC



IHC[a]	NA	NA	2+	3+	2+	NA	NA	2+	NA	3+	2+	3+	NA	NA	NA	3+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	3+	3+	NA
FISH/CISH[b]	+	NA	+	NA	+	+	NA	+	NA	NA	+	+	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
NGS[b]	NA	+ (T)	NA	NA	+ (T)	+ (T)	+ (B)	NA	+ (T)	NA	+ (T)	NA	+ (T)	+ (T)	+ (T)	NA	+ (B)	+ (T)	+ (B)	+ (T)	+ (T)	+ (T)	+ (T)	+ (B)	+ (T)	+ (B)	+ (T)	+ (T)	+ (T)

HER2 NGS amplified, HER2 IHC3+, HER2 ISH+

RESPONSE RATE = 46.7% (IHC3+/IHC2+)

TIME TO RESPONSE = 2.1 mth

PFS = 5.5 mth

DURATION OF RESPONSE = 6 mth

1 YEAR SURVIVAL = 53.6%, MEDIAN OS = 15.5 mth

DISEASE CONTROL RATE = 76.7%

TOXICITIES = Pyrexia, diarrhea

N = 30 Patients (80 IHC3+/IHC2+)

Nakamura Y et al. *J Clin Oncol* 2023 Sep 26: Online ahead of print.

Courtesy of Mitesh Borad, MD

Tucatinib with Trastuzumab for HER2-Positive Biliary Tract Cancers: Most Common Treatment-Emergent Adverse Events (TEAEs)

	Total (N = 30), No. (%)	
TEAE	Any Grade	Grade ≥3[a]
Any TEAE	30 (100)	18 (60.0)
Pyrexia	13 (43.3)	0
Diarrhea	12 (40.0)	2 (6.7)
Infusion-related reaction	8 (26.7)	0
Blood creatinine increased	8 (26.7)	1 (3.3)
ALT increased	8 (26.7)	2 (6.7)
Nausea	7 (23.3)	3 (10.0)
Chills	7 (23.3)	0
Decreased appetite	7 (23.3)	3 (10.0)
Aspartate aminotransferase increased	6 (20.0)	2 (6.7)
Malaise	5 (16.7)	0
Vomiting	4 (13.3)	0
Fatigue	4 (13.3)	1 (3.3)

TEAE (cont)	Any Grade	Grade ≥3
Anemia	4 (13.3)	2 (6.7)
Stomatitis	4 (13.3)	0
Hyponatremia	4 (13.3)	1 (3.3)
Abdominal pain upper	4 (13.3)	0
Abdominal pain	4 (13.3)	0
Hepatic function abnormal	4 (13.3)	1 (3.3)
Cholangitis	4 (13.3)	3 (10.0)
COVID-19	4 (13.3)	1 (3.3)
Dry skin	3 (10.0)	0
Dizziness	3 (10.0)	0
Back pain	3 (10.0)	0

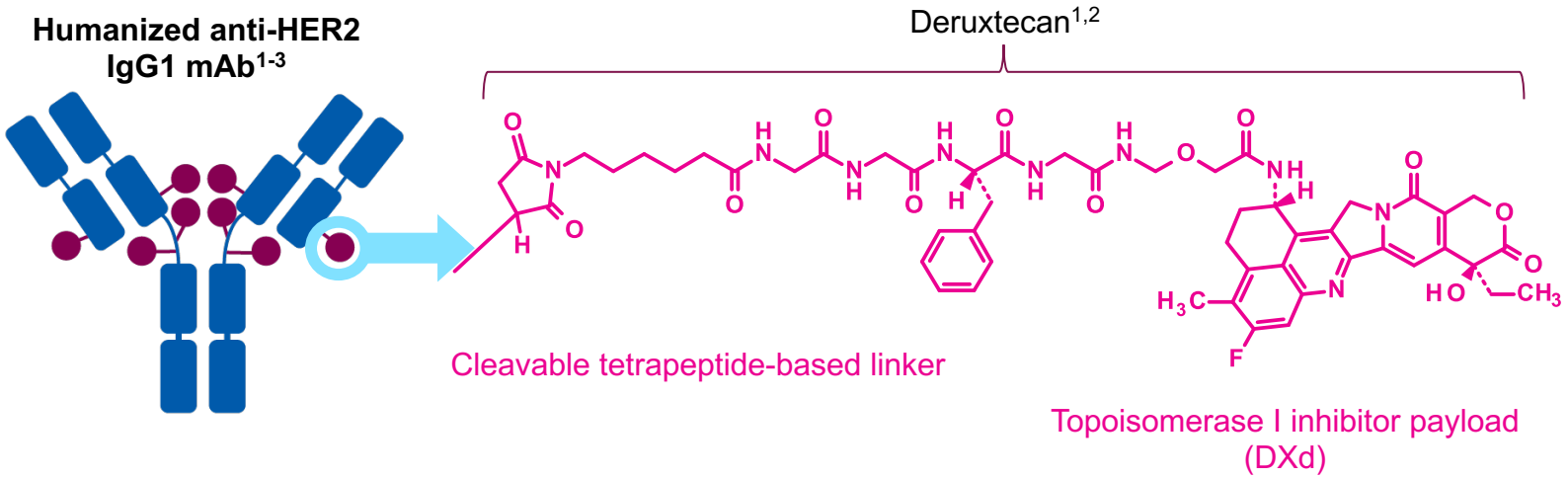
Nakamura Y et al. *J Clin Oncol* 2023 September 26;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Trastuzumab Deruxtecan (T-DXd) was Designed with 7 Key Attributes

T-DXd is an ADC composed of 3 parts[1,2]:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload (an exatecan derivative, DXd)
- A tetrapeptide-based cleavable linker that covalently bonds the other 2 components



- Payload mechanism of action: topoisomerase I inhibitor[1,2,a]
- High potency of payload[1,2,a]
- High drug to antibody ratio ≈8[1,2,a]
- Payload with short systemic half-life[1,2,a]
- Stable linker-payload[1,2,a]
- Tumor-selective cleavable linker[1,2,a]
- Bystander antitumor effect[1,4,a]

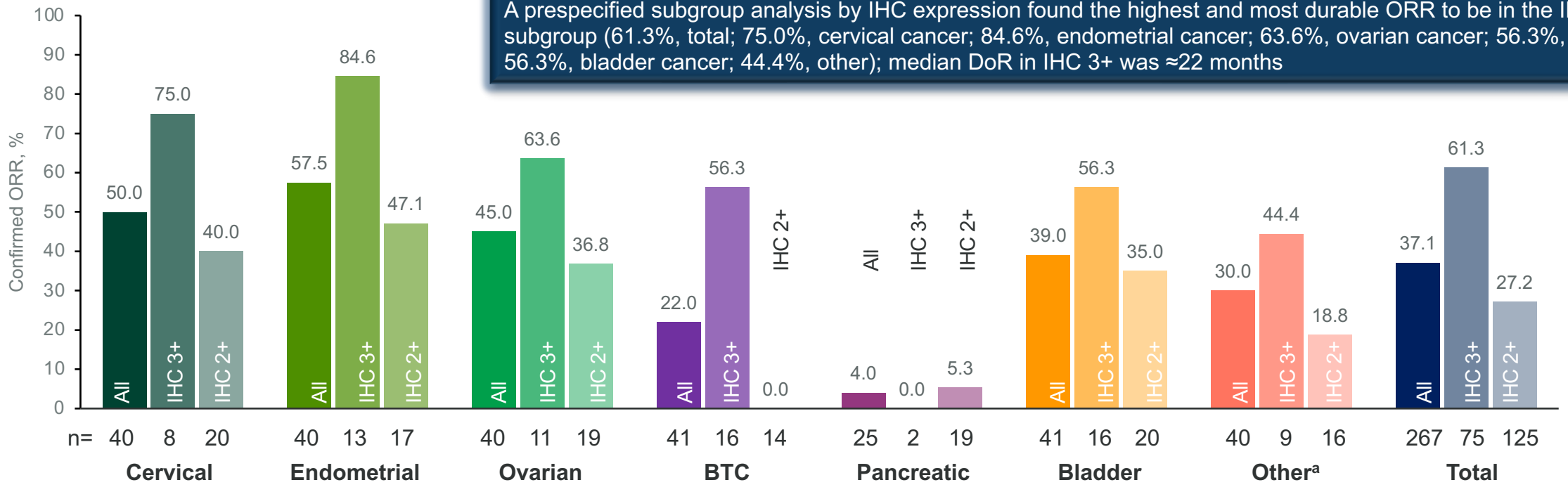
Courtesy of Milind Javle, MD

[a] The clinical relevance of these features is under investigation.

1. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. 2. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097-5108. 3. Trail PA, et al. *Pharmacol Ther.* 2018;181:126-142. 4. Ogitani Y, et al. *Cancer Sci.* 2016;107(7):1039-1046.

Objective Response Rate by HER2 status

A prespecified subgroup analysis by IHC expression found the highest and most durable ORR to be in the IHC 3+ subgroup (61.3%, total; 75.0%, cervical cancer; 84.6%, endometrial cancer; 63.6%, ovarian cancer; 56.3%, BTC; 56.3%, bladder cancer; 44.4%, other); median DoR in IHC 3+ was ≈22 months



	All patients (n=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DoR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

Courtesy of Milind Javle, MD

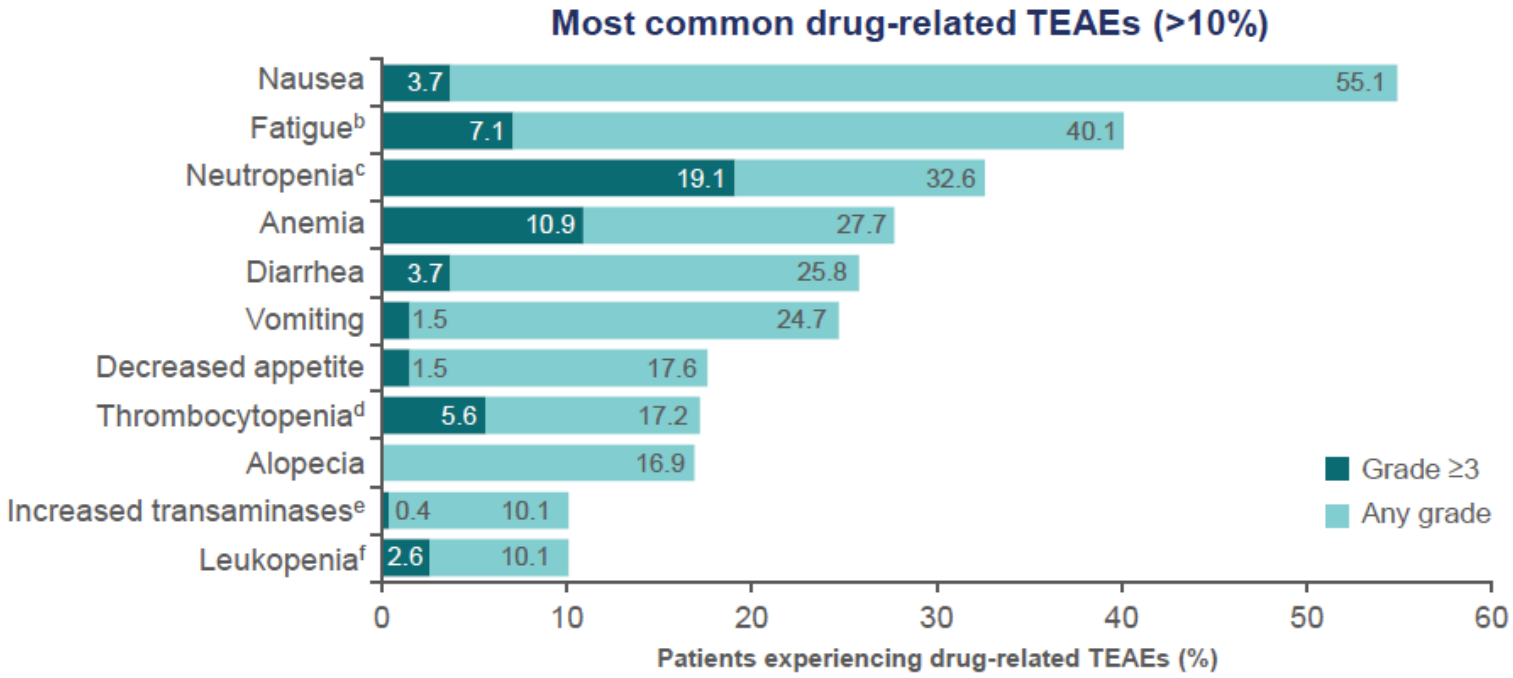
Analysis of ORR was performed in patients who received ≥1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25], IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75) or IHC 2+ (n=125) status. Analysis of DoR was performed in patients with objective response who received ≥1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status.

[a]Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer.

Meric-Bernstam F et al. Presented at: ASCO Annual Meeting; June 4-6, 2023; Chicago, IL.

DESTINY-PanTumor02: Safety Summary

n (%)	All patients (N=267)
Any drug-related TEAEs	226 (84.6)
Drug-related TEAEs Grade ≥3	109 (40.8)
Serious drug-related TEAEs	36 (13.5)
Drug-related TEAEs associated with dose discontinuations	23 (8.6)
Drug-related TEAEs associated with dose interruptions	54 (20.2)
Drug-related TEAEs associated with dose reductions	54 (20.2)
Drug-related TEAEs associated with deaths	4 (1.5)[a]



ILD/pneumonitis adjudicated as T-DXd related, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
All patients (N=267)	7 (2.6)	17 (6.4)	1 (0.4)	0	3 (1.1)	28 (10.5)

Analyses were performed in patients who received ≥1 dose of T-DXd (N=267); median total treatment duration 5.6 months (range 0.4–31.1)
[a]Included pneumonia (n=1), organizing pneumonia (n=1), pneumonitis (n=1), and neutropenic sepsis (n=1); [b]category includes the preferred terms fatigue, asthenia, and malaise; [c]category includes the preferred terms neutrophil count decreased and neutropenia; [d]category includes the preferred terms platelet count decreased and thrombocytopenia; [e]category includes the preferred terms aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased, hypertransaminasemia; [f]category includes the preferred terms white blood cell count decreased and leukopenia
ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event

Meric-Bernstam F et al. ESMO 2023;Abstract LBA34.

RTP RESEARCH TO PRACTICE

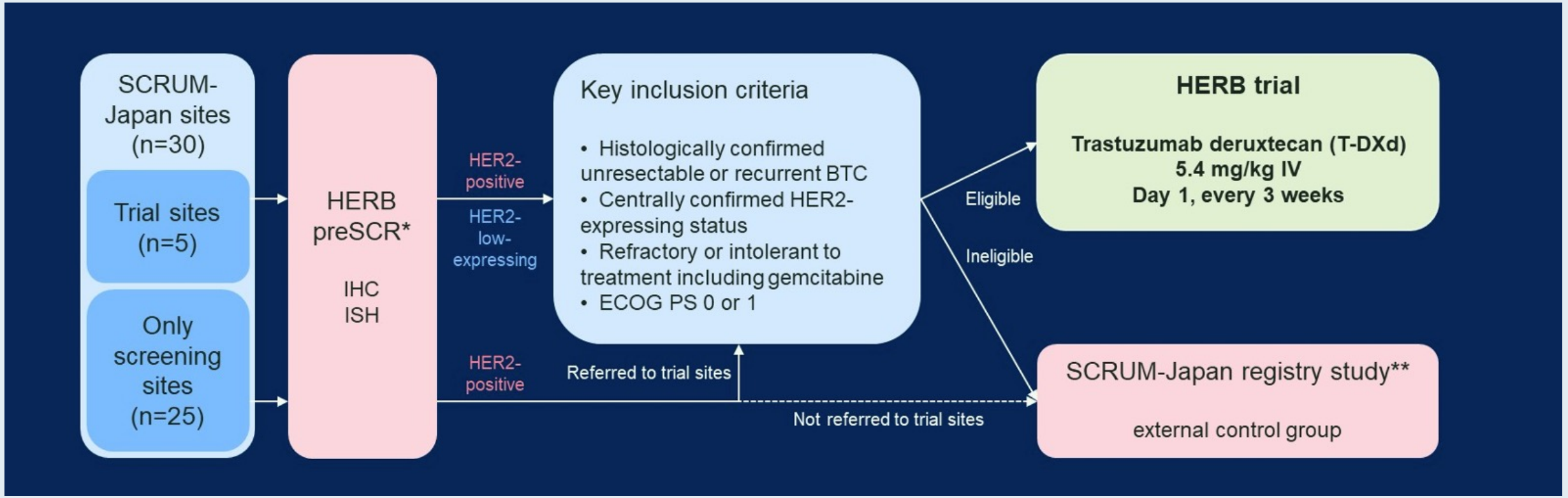
2022 ASCO® ANNUAL MEETING

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

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

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

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



Ohba A et al. ASCO 2022;Abstract 4006.

HERB Primary Endpoint: Confirmed ORR by Blinded Independent Central Review with T-DXd for Biliary Tract Cancer

- Tumor response

*: P =0.01

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

- Best percentage change

Ohba A et al. ASCO 2022;Abstract 4006.

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

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

Ohba A et al. ASCO 2022;Abstract 4006.

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

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

Ohba A et al. ASCO 2022;Abstract 4006.

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

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

Ohba A et al. ASCO 2022;Abstract 4006.

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with HER2-overexpressing (IHC 3+) advanced biliary tract cancer (PS = 0)?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Zanidatamab
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Trastuzumab/pertuzumab
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Zanidatamab
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Zanidatamab

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for an 80-year-old patient with controlled hypertension and diabetes with HER2-overexpressing (IHC 3+) advanced biliary tract cancer?

	First line	Second line
 Dr Goyal	Zanidatamab	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Trastuzumab/pertuzumab
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Zanidatamab
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Zanidatamab

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with HER2-low (IHC 1+ or 2+/FISH-negative) advanced biliary tract cancer (PS = 0)?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Liposomal irinotecan + fluorouracil + leucovorin
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Durvalumab + liposomal irinotecan/fluorouracil
 Dr Borad	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Trastuzumab deruxtecan

Based on your knowledge of available data, would you attempt to access zanidatamab for a patient with HER2-overexpressing (IHC 3+) advanced biliary tract cancer outside of a clinical trial setting if it were available?

 Dr Goyal	Yes
 Dr Javle	Yes
 Dr Abou-Alfa	Yes
 Dr Borad	No
 Prof Bridgewater	Yes
 Dr Kelley	No

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, based on your knowledge of currently available data, would you attempt to access tucatinib/trastuzumab for a patient with HER2-overexpressing (IHC 3+) advanced biliary tract cancer outside of a clinical trial setting?

 Dr Goyal	No
 Dr Javle	Yes
 Dr Abou-Alfa	Yes
 Dr Borad	No
 Prof Bridgewater	No
 Dr Kelley	No

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, what would you estimate is the percent chance that a patient will experience toxicity during treatment with trastuzumab deruxtecan that will require withholding dosing or discontinuation? What is the primary toxicity leading to withholding dosing or discontinuation?

	Chance of holding or discontinuation	Primary toxicity
 Dr Goyal	30%	Neutropenia
 Dr Javle	5%	Cardiac
 Dr Abou-Alfa	Need additional experience with AE management	Need additional experience with AE management
 Dr Borad	5%	Myelosuppression
 Prof Bridgewater	50%	Neutropenia
 Dr Kelley	~25%	Pulmonary

AE = adverse event

Based on your personal clinical experience and knowledge of available data, what would you estimate is the percent chance that a patient will experience toxicity during treatment with tucatinib/trastuzumab that will require withholding dosing or discontinuation? What is the primary toxicity leading to withholding dosing or discontinuation?

	Chance of holding or discontinuation	Primary toxicity
 Dr Goyal	30%	Diarrhea
 Dr Javle	10%	Diarrhea
 Dr Abou-Alfa	Need additional experience with AE management	Need additional experience with AE management
 Dr Borad	5%	Diarrhea
 Prof Bridgewater	50%	Diarrhea
 Dr Kelley	Not sure	NA

AE = adverse event

Agenda
Management of Advanced Biliary Tract Cancers

INTRODUCTION

MODULE 1: First-Line Systemic Treatment

MODULE 2: Targeted Treatment

- HER2
- FGFR
- BRAF
- IDH

Selective FGFR Inhibitors for FGFR2 Fusions or Rearrangement Positive Cholangiocarcinoma[1–5]

Pemigatinib
ATP-competitive FGFR1–3 inhibitor

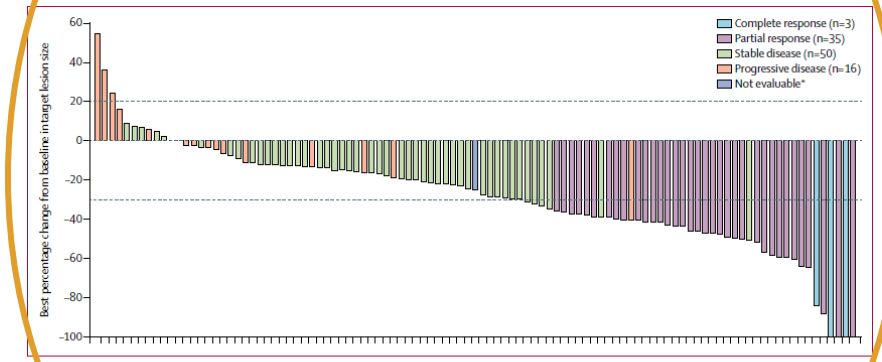
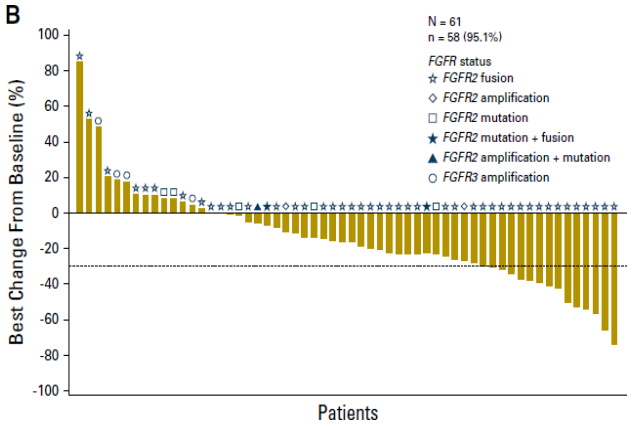


Figure 2: **Best percentage change from baseline in target lesion size for individual patients with *FGFR2* fusions or rearrangements**
Coloured bars indicate confirmed responses assessed by RECIST 1·1. FGFR=fibroblast growth factor receptor. RECIST 1.1=Response Evaluation Criteria in Solid Tumours version 1.1. *Patient had a decrease in target lesion size but was not evaluable for response using RECIST.

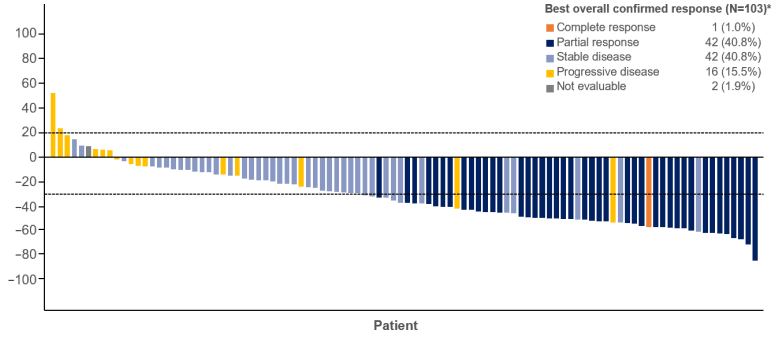
ORR: 37.0%
DCR: 82.4%
PFS: 7.0 months

Infigratinib
ATP-competitive FGFR1–3 inhibitor



ORR: 18.8% (updated: 23.1%)
DCR: 83.3% (updated: 84.3%)
PFS (updated): 7.3 months)

Futibatinib
covalently binding FGFR1–4 inhibitor



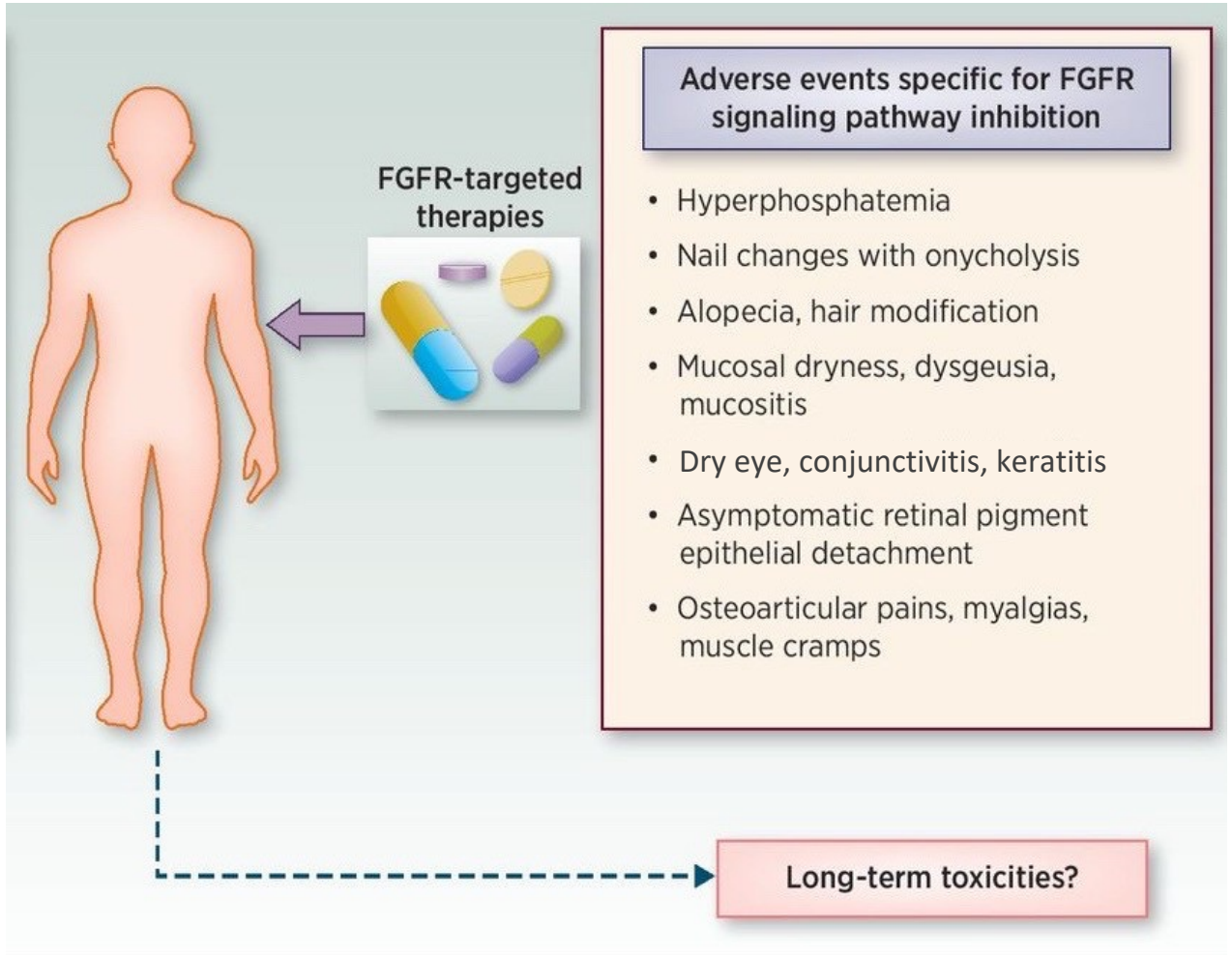
ORR: 41.7%
DCR: 82.5%
PFS: 9.0 months

ATP, adenosine triphosphate; DCR, disease control rate; FGFR, fibroblast growth factor receptor; ORR, overall response rate; PFS, progression-free survival.

1. Javle M, et al. J Clin Oncol 2018;36(3):276–282; 2. Javle M, et al. ASCO Gastrointestinal (GI) Cancers Symposium, 2021;
3. Abou-Alfa GK, et al. Lancet Oncol 2020;21(5):671–684; 4, Vogel A et al. ESMO 2022; Abstract O-27. 5. Goyal L, et al. New Eng J Med, 2023

Courtesy of Lipika Goyal, MD, MPhil

FGFR Inhibitors: Unique Class-Specific Side Effects

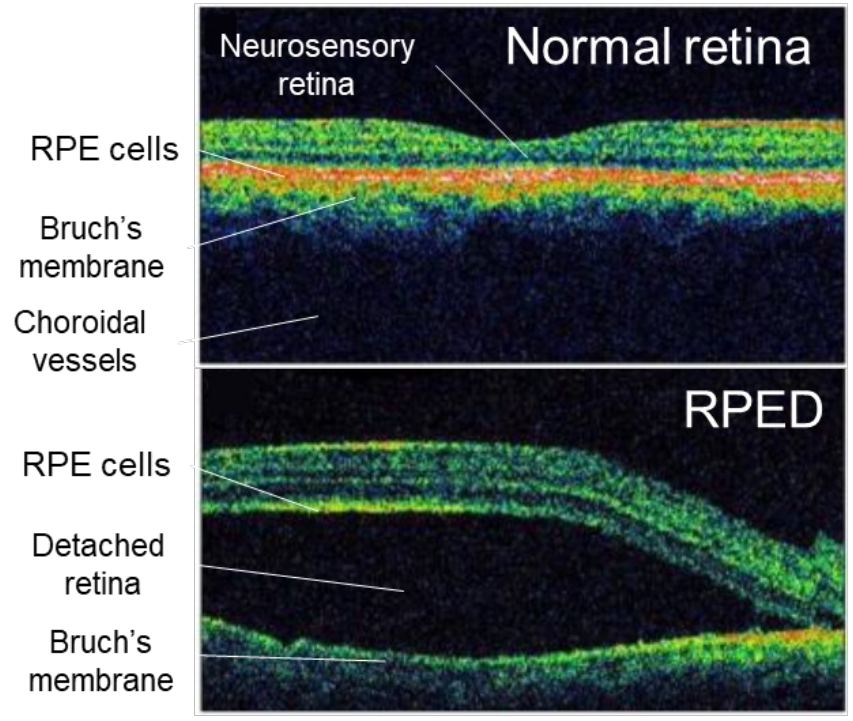


- Take-home messages:
  - Hyperphosphatemia is the most common side effect of FGFR inhibitors
  - All patients should have a baseline eye exam prior to starting FGFR inhibitors

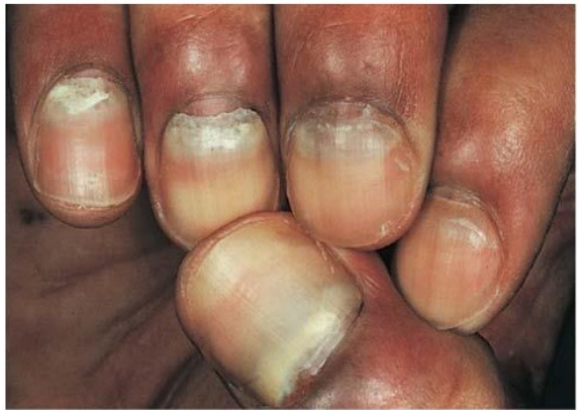
FGFR, fibroblast growth factor receptor.
Touat M, et al. Clin Cancer Res 2015;21(12):2684–94; Goyal L, et al. Cancer Treat Rev 2021;95:102170.

Notable FGFRi-Related AEs

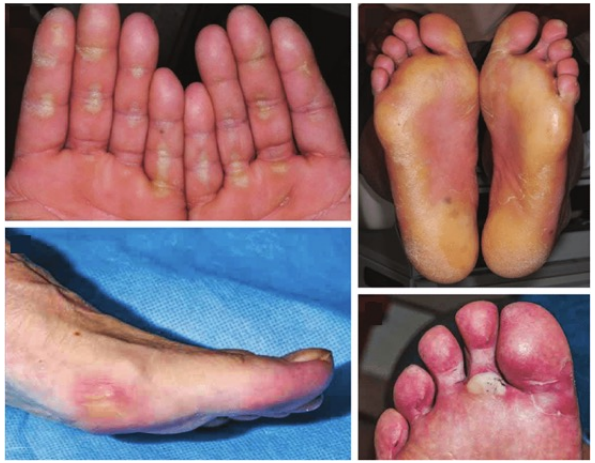
RPED Presentation[1]



Onychomadesis Presentation[2]



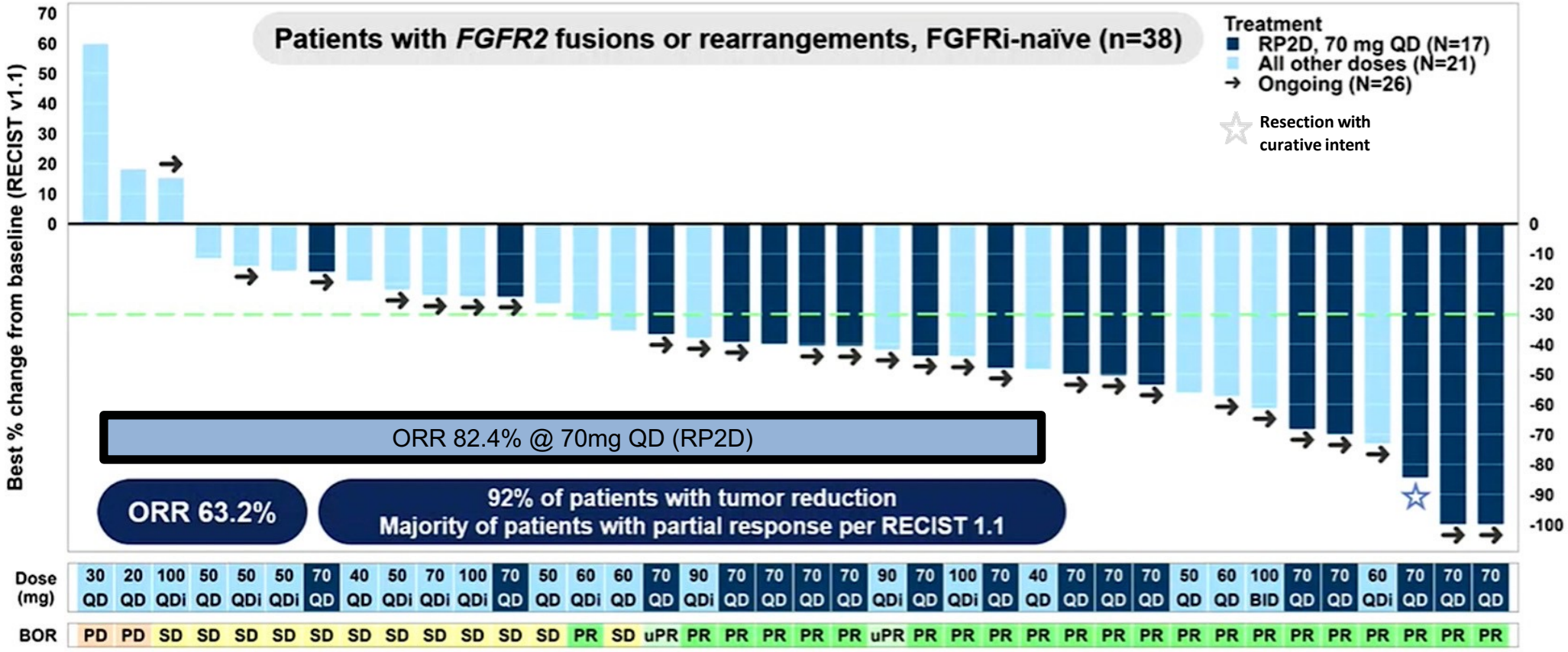
PPE Presentation[3]



Courtesy of Milind Javle, MD

RLY-4008, FGFR2-specific inhibitor, in FGFR2-fusion or Rearrangement+ Cholangiocarcinoma

Radiographic tumor regression and response per RECIST 1.1 across all doses



BID, twice daily; BOR, best overall response; CCA, cholangiocarcinoma; DoR, duration of response; FGFR, fibroblast growth factor receptors; FGFRi, fibroblast growth factor receptor inhibitor; ORR, objective response rate; PD, progressive disease; PR, partial response; QD, once daily; QDi once daily on an intermittent schedule; RP2D, recommended phase 2 dose; SD, stable disease; uPR, unconfirmed partial response.

Hollebecque A, et al. Ann Onc 2022;33(suppl_7):S808-S869.

Courtesy of Lipika Goyal, MD, MPhil

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic cholangiocarcinoma with an FGFR alteration (PS = 0)?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Futibatinib
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Futibatinib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Futibatinib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Futibatinib

Regulatory and reimbursement issues aside, would you consider a second FGFR inhibitor for a patient with metastatic cholangiocarcinoma who previously experienced disease progression while receiving a different FGFR inhibitor?

 Dr Goyal	Yes, futibatinib or next-generation FGFR inhibitor
 Dr Javle	Yes, futibatinib
 Dr Abou-Alfa	Yes, pemigatinib or futibatinib
 Dr Borad	Yes, futibatinib
 Prof Bridgewater	Yes, depends on resistance mechanism
 Dr Kelley	Yes, futibatinib after prior pemigatinib

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for an 80-year-old patient with controlled hypertension and diabetes with metastatic cholangiocarcinoma and an FGFR alteration?

	First line	Second line
 Dr Goyal	Futibatinib	Clinical trial
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Pemigatinib
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Futibatinib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Futibatinib
 Dr Kelley	Futibatinib	Dose-reduced FOLFOX

Based on your personal clinical experience and knowledge of available data, what would you estimate is the percent chance that a patient will experience toxicity during treatment with pemigatinib that will require withholding dosing or discontinuation? What is the primary toxicity leading to withholding dosing or discontinuation?

	Chance of holding or discontinuation	Primary toxicity
 Dr Goyal	40%	Mucositis, nail toxicity, ocular
 Dr Javle	10%	Diarrhea, mucositis, ocular
 Dr Abou-Alfa	Need additional experience with AE management	Need additional experience with AE management
 Dr Borad	20%	Skin/ocular
 Prof Bridgewater	100%	Mucositis
 Dr Kelley	~25%	Nail, mouth, hand/foot syndrome, ocular

AE = adverse event

Based on your personal clinical experience and knowledge of available data, what would you estimate is the percent chance that a patient will experience toxicity during treatment with futibatinib that will require withholding dosing or discontinuation? What is the primary toxicity leading to withholding dosing or discontinuation?

	Chance of holding or discontinuation	Primary toxicity
 Dr Goyal	40%	Mucositis, nail toxicity, PPE
 Dr Javle	10%	Diarrhea, mucositis, ocular
 Dr Abou-Alfa	Need additional experience with AE management	Need additional experience with AE management
 Dr Borad	30%	Skin/ocular
 Prof Bridgewater	100%	Mucositis
 Dr Kelley	~20%	Nail, mouth, hand/foot syndrome, ocular

AE = adverse event, PPE = palmar-plantar erythrodysesthesia

Agenda
Management of Advanced Biliary Tract Cancers

INTRODUCTION

MODULE 1: First-Line Systemic Treatment

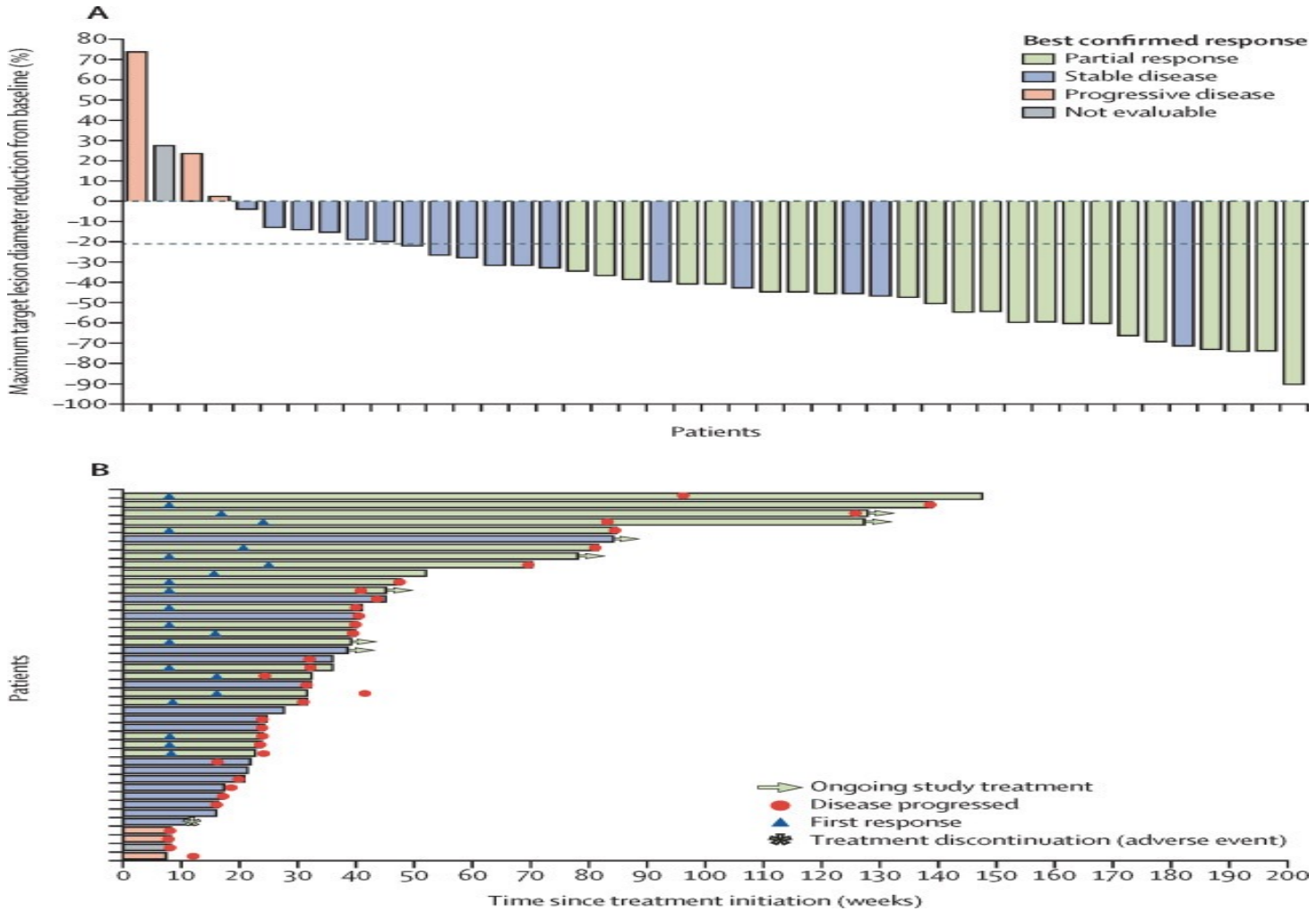
MODULE 2: Targeted Treatment

- HER2
- FGFR
- BRAF
- IDH

RTP
RESEARCH
TO PRACTICE

BRAF V600E mutated cholangiocarcinoma

Efficacy of Dabrafenib + Trametinib



Subbiah V, et al. *Lancet Oncol* 2020;21:1234–1243

Courtesy of Milind Javle, MD

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic cholangiocarcinoma and a BRAF V600E mutation (PS = 0)?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Dabrafenib/trametinib
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Dabrafenib/trametinib
 Dr Abou-Alfa	Dabrafenib/trametinib	Durvalumab + cisplatin/gemcitabine
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Dabrafenib/trametinib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Cetuximab/encorafenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Dabrafenib/trametinib

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for an 80-year-old patient with controlled hypertension and diabetes with metastatic cholangiocarcinoma and a BRAF V600E mutation?

	First line	Second line
 Dr Goyal	Dabrafenib/trametinib	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Dabrafenib/trametinib
 Dr Abou-Alfa	Dabrafenib/trametinib	Durvalumab + cisplatin/gemcitabine
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Dabrafenib/trametinib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Cetuximab/encorafenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Dabrafenib/trametinib

Agenda
Management of Advanced Biliary Tract Cancers

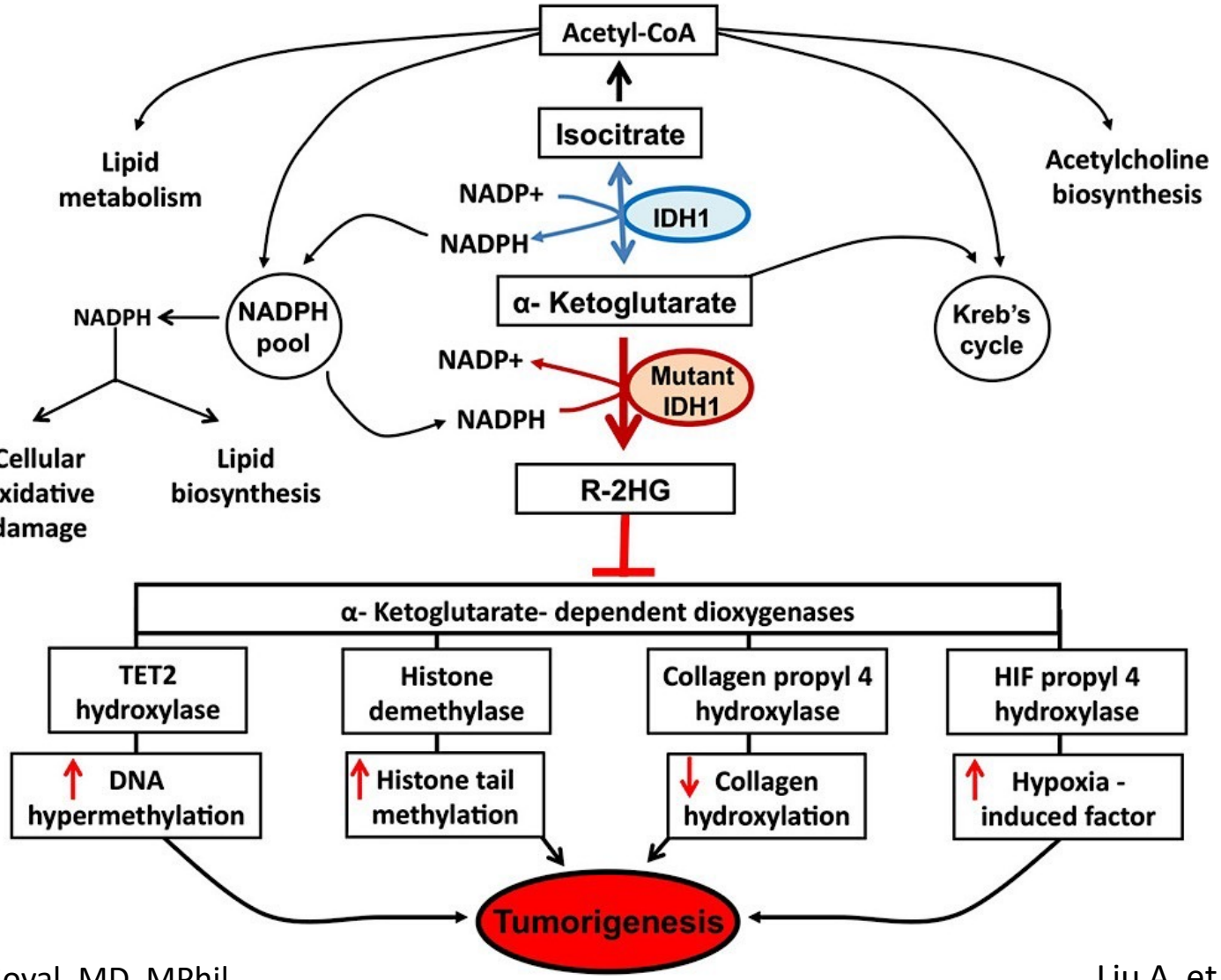
INTRODUCTION

MODULE 1: First-Line Systemic Treatment

MODULE 2: Targeted Treatment

- HER2
- FGFR
- BRAF
- IDH

IDH1 mutations

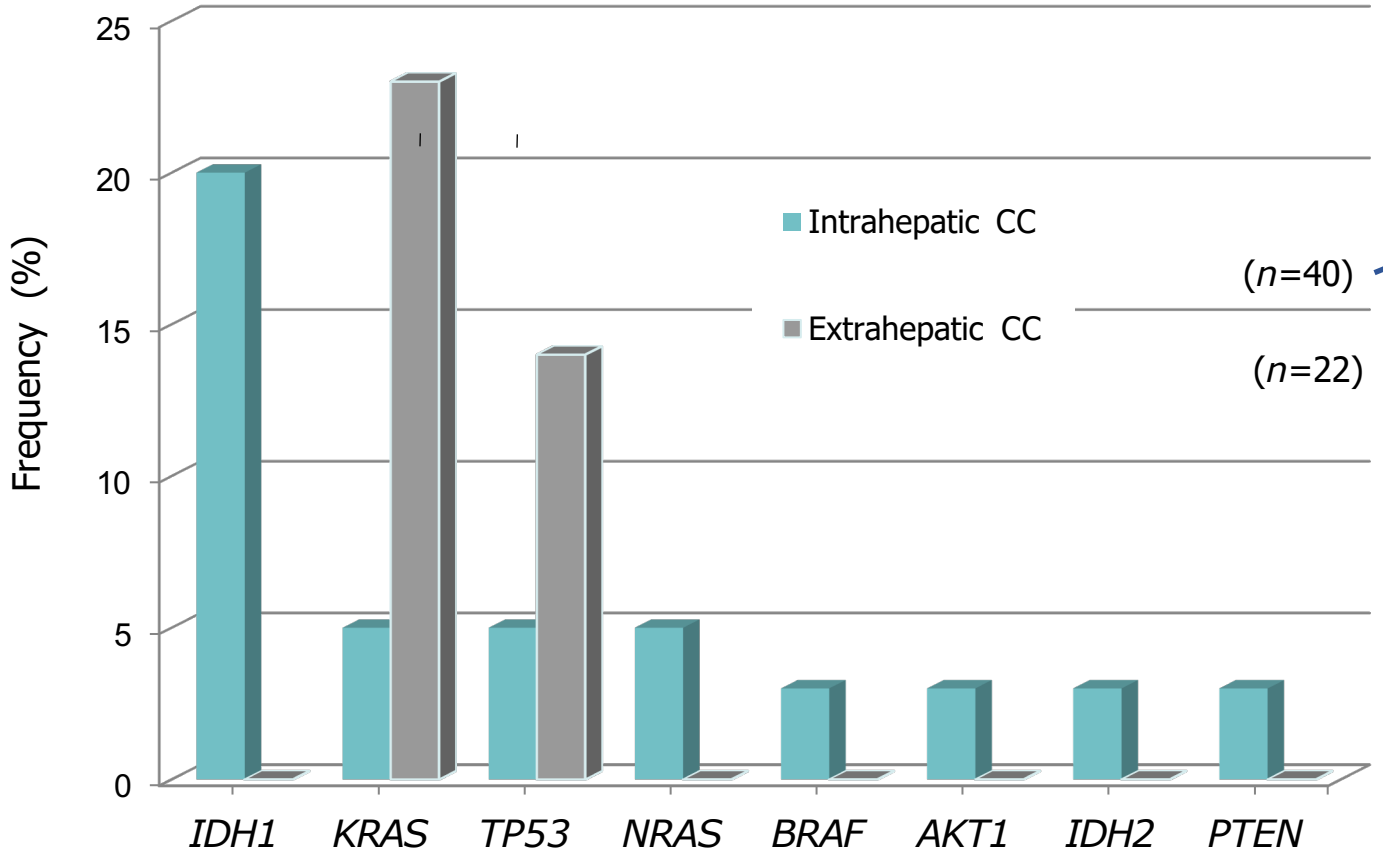


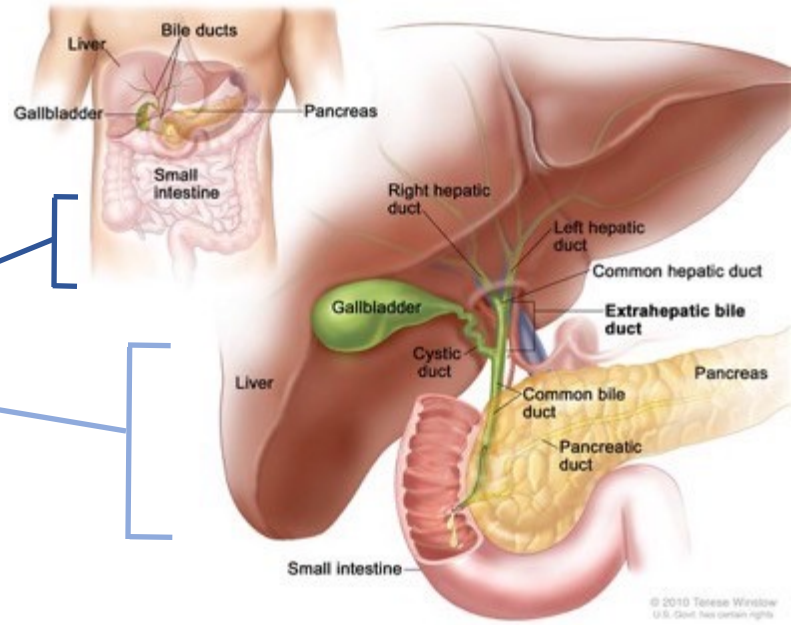
- IDH 1 / 2 mutation: **20 % ICC**

Courtesy of Lipika Goyal, MD, MPhil

Liu A et al. Front. Oncol 2016; 6:1-9

IDH1 Mutations are seen in ICC and rarely in ECC





CC = cholangiocarcinoma; KRAS = Kirsten rat sarcoma viral oncogene homolog; NRAS = neuroblastoma RAS viral oncogene homolog.
Image courtesy of the National Cancer Institute.
Borger et al, 2011.

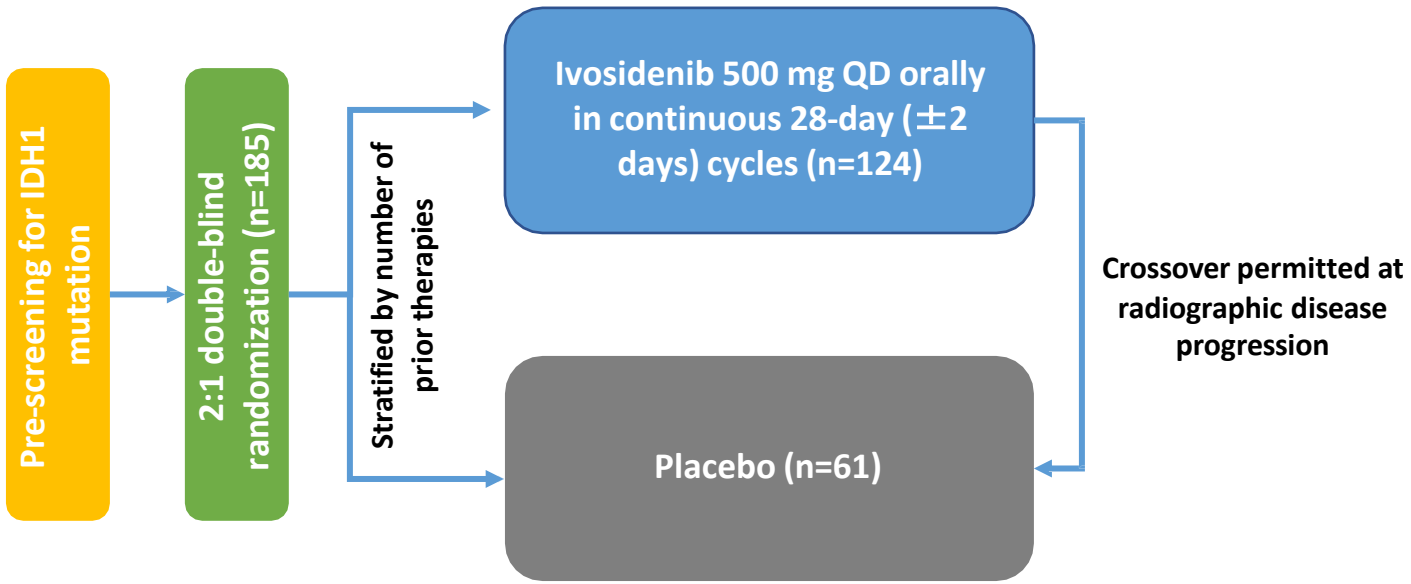
Courtesy of Lipika Goyal, MD, MPhil

Ivosidenib in *IDH1*-Mutant Cholangiocarcinoma

Randomized, double-blind, placebo-controlled, multicenter phase 3 trial

Key eligibility criteria

- ≥18 years of age
- Histologically confirmed diagnosis of cholangiocarcinoma
- Centrally confirmed IDH1 mutation status by next-generation sequencing
- ECOG performance status score 0 or 1
- 1–2 prior therapies (at least 1 gemcitabine- or 5-fluorouracil-containing regimen)
- Measurable lesion as defined by RECIST v1.1
- Adequate hematologic, hepatic and renal function



An independent data monitoring committee monitored the safety data throughout the study

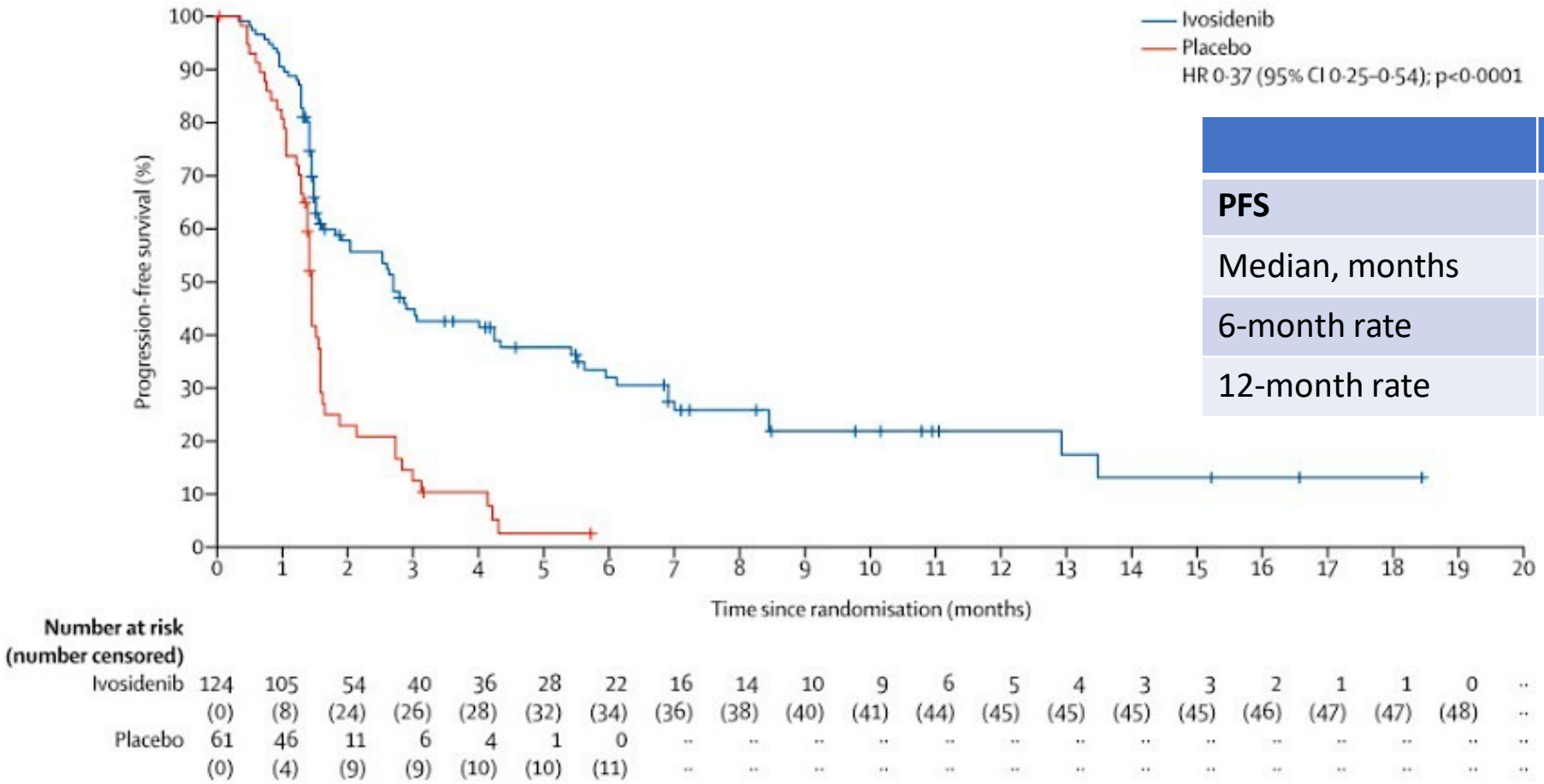
Primary end point: PFS
Secondary end points: OS, ORR, safety, QOL

ECOG, Eastern Cooperative Oncology Group; IDH, isocitrate dehydrogenase; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily; QOL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors.
Abou-Alfa GK, et al. Lancet Oncol 2020;21:796–807; NCT02989857.

Courtesy of Lipika Goyal, MD, MPhil

IDH1-Mutant Cholangiocarcinoma: Phase III Study of Ivosidenib

A



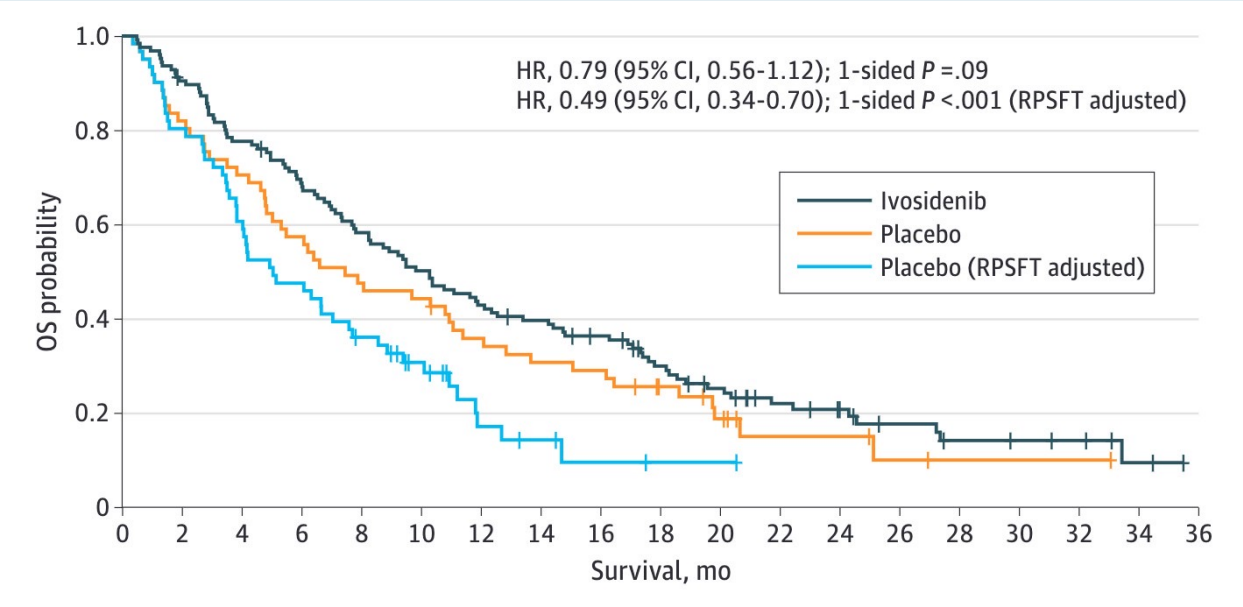
	Ivosidenib	Placebo
PFS		
Median, months	2.7	1.4
6-month rate	32%	NE
12-month rate	22%	NE

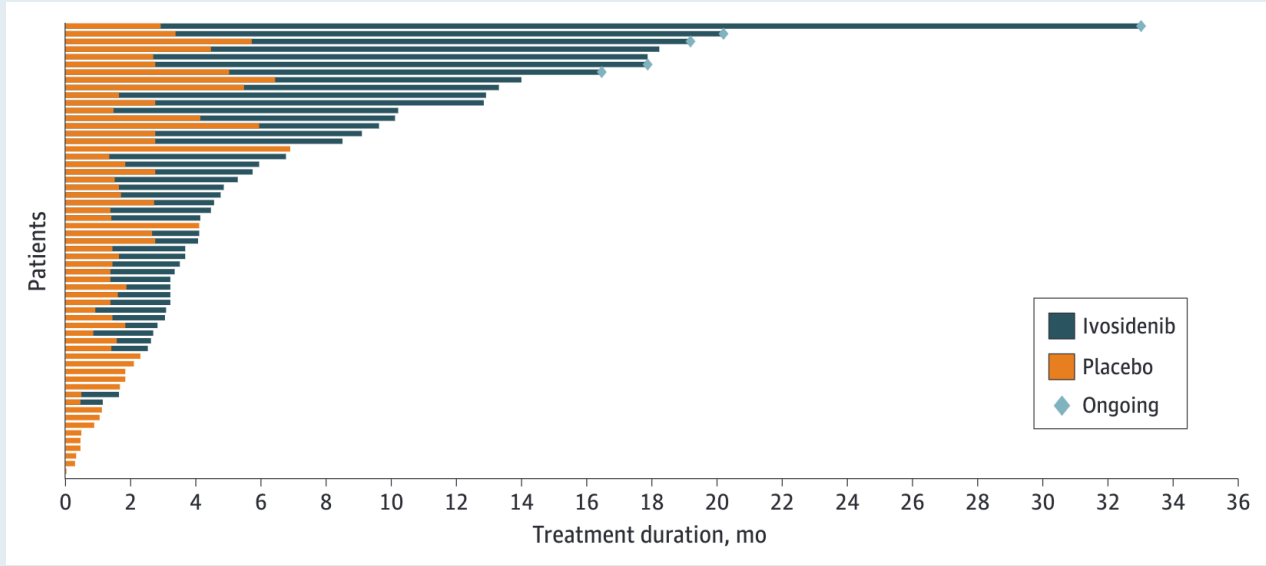
Primary end point: PFS
Secondary end points: OS, ORR, safety, QOL

CI, confidence interval; HR, hazard ratio; IDH1, isocitrate dehydrogenase 1; PFS, progression-free survival.
Abou-Alfa GK, et al. Lancet Oncol 2020;21:796–807.

Courtesy of Lipika Goyal, MD, MPhil

ClarIDHy: Overall Survival (OS) and Treatment Duration in the Intent-to-Treat Population





RPSFT = rank-preserving structural failure time

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

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic cholangiocarcinoma with an IDH1 mutation (PS = 0)?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Ivosidenib

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for an 80-year-old patient with controlled hypertension and diabetes with metastatic cholangiocarcinoma and an IDH1 mutation?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Ivosidenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	Ivosidenib

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for a 65-year-old patient with metastatic cholangiocarcinoma and an IDH2 mutation (PS = 0)?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Liposomal irinotecan + fluorouracil + leucovorin
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Enasidenib or durvalumab + liposomal irinotecan/fluorouracil
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Enasidenib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Enasidenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFOX or FOLFIRI

Regulatory and reimbursement issues aside, what would be your preferred first- and second-line systemic treatments for an 80-year-old patient with controlled hypertension and diabetes with metastatic cholangiocarcinoma and an IDH2 mutation?

	First line	Second line
 Dr Goyal	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFOX
 Dr Javle	Durvalumab + cisplatin/gemcitabine	Liposomal irinotecan + fluorouracil + leucovorin
 Dr Abou-Alfa	Durvalumab + cisplatin/gemcitabine	Enasidenib or durvalumab + liposomal irinotecan/fluorouracil
 Dr Borad	Durvalumab + cisplatin/gemcitabine	Enasidenib
 Prof Bridgewater	Durvalumab + cisplatin/gemcitabine	Enasidenib
 Dr Kelley	Pembrolizumab + cisplatin/gemcitabine or durvalumab + cisplatin/gemcitabine	FOLFOX or FOLFIRI

Based on your personal clinical experience and knowledge of available data, what would you estimate is the percent chance that a patient will experience toxicity during treatment with ivosidenib that will require withholding dosing or discontinuation? What is the primary toxicity leading to withholding dosing or discontinuation?

	Chance of holding or discontinuation	Primary toxicity
 Dr Goyal	10%	Nausea, QTc prolongation
 Dr Javle	5%	QTc
 Dr Abou-Alfa	Need additional experience with AE management	Need additional experience with AE management
 Dr Borad	5%	Anemia
 Prof Bridgewater	10%	Diarrhea
 Dr Kelley	<5%	None/minimal

AE = adverse event

How Far We Have Come…

- No drug approved <2020; 6 FDA approvals in 3 years, several NCCN designations
- Immunotherapy for these cancers is a promising area, Gem/cis and Durvalumab/Pembrolizumab is current standard of care 1L
- The advent of molecular profiling, targeted therapies, multiagent chemotherapy has led to a ‘sea change’ in management of BTC
- IDH1, FGFR, Her2/neu, BRAFV600E, DDR, MTAP loss, Angiogenesis promising areas
- Model for ‘Precision Medicine’ in GI cancers

Courtesy of Milind Javle, MD

Novel Agents in Trials

Compound	Action	Trial Phase
Surufatinib	Angiogenesis	Phase 2/3 (China)
Milademetan	Mdm2	Phase 2
BI 907828	Mdm2	Phase 2
Pamiparib Olaparib	PARP	Phase 2
CTX-009 + Paclitaxel	VEGFR/ DLL	Phase 2
Spartalizumab Dostarlimab PRMT5, MTA inhibitors	PD1 MTAP loss	Phase 2 Phase 2

Courtesy of Milind Javle, MD

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Breast Cancer

A 3-Part CME Satellite Symposium Series in Partnership with the 2023 San Antonio Breast Cancer Symposium®

ER-Positive Metastatic Breast Cancer

Tuesday, December 5, 2023

7:15 PM – 9:15 PM CT

Localized HER2-Negative Breast Cancer

Wednesday, December 6, 2023

7:15 PM – 9:15 PM CT

HER2-Low Breast Cancer

Thursday, December 7, 2023

7:15 PM – 8:45 PM CT

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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

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

RTP
RESEARCH
TO PRACTICE