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EPICS

Global Perspectives in Gastrointestinal Malignancies in 2022 and Beyond

Full Report

17 and 23 September 2022

Report Contents

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Meeting Snapshot

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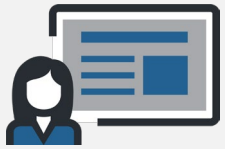
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
17 and 23 September 2022



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in gastrointestinal (GI) malignancies

> 8 from the US and 3 from the EU

GI CANCER-SPECIFIC DISCUSSIONS on therapeutic advances and their application in clinical decision-making

Day 1: Panel Consisting of 5 US and 3 European GI Cancer Experts

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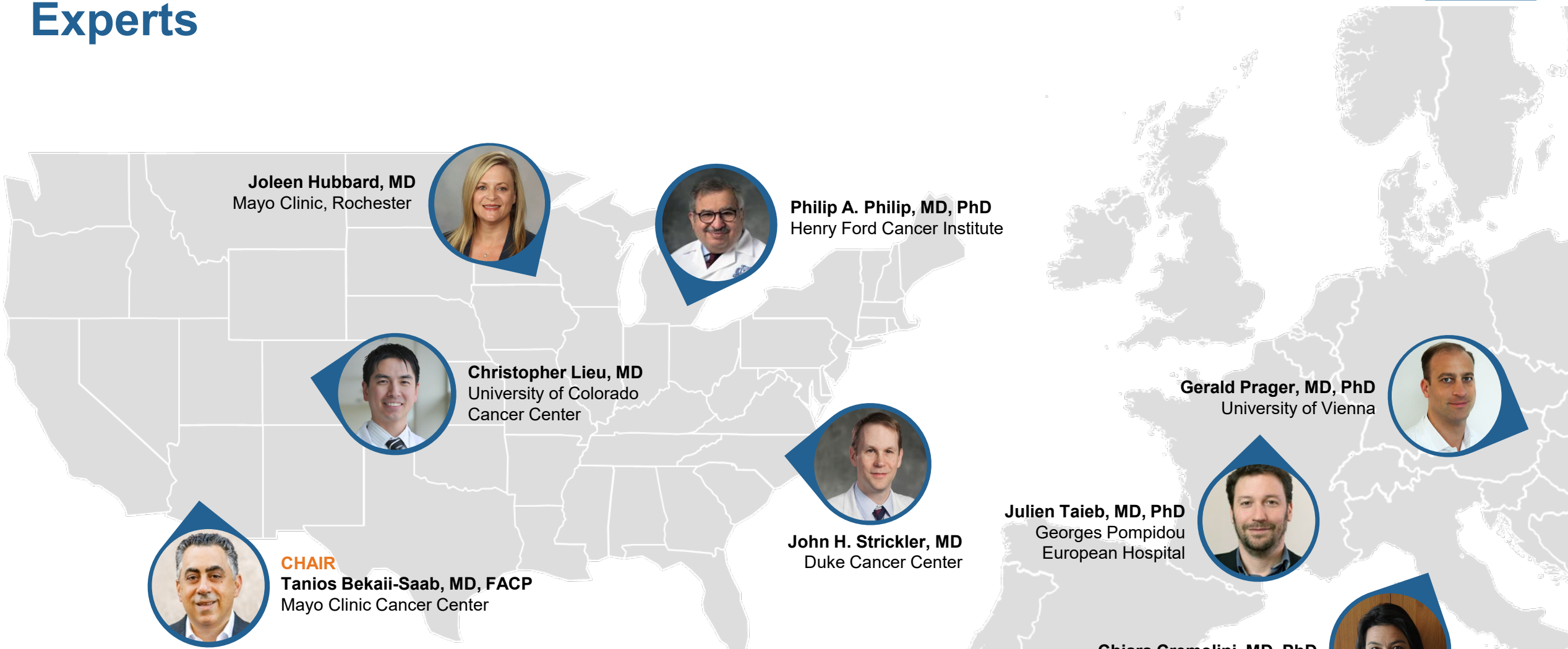

Joleen Hubbard, MD
Mayo Clinic, Rochester

Philip A. Philip, MD, PhD
Henry Ford Cancer Institute

Christopher Lieu, MD
University of Colorado
Cancer Center

John H. Strickler, MD
Duke Cancer Center

CHAIR
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Mayo Clinic Cancer Center

Gerald Prager, MD, PhD
University of Vienna

Julien Taieb, MD, PhD
Georges Pompidou
European Hospital

Chiara Cremolini, MD, PhD
University of Pisa

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Meeting Agenda Day 1

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Time (EST)	Topic	Speaker/Moderator
9.00 AM – 9.05 AM	Welcome and Introductions	Tanios Bekaii-Saab, MD, FACP
9.05 AM – 9.15 AM	Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments	Joleen Hubbard, MD
9.15 AM – 9.50 AM	Discussion: Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments	All
9.50 AM – 9.55 AM	Summary of Key Takeaways	Joleen Hubbard, MD
9.55 AM – 10.05 AM	Colorectal Cancer – Immunotherapy	Gerald Prager, MD, PhD
10.05 AM – 10.40 AM	Discussion: Colorectal Cancer – Immunotherapy	All
10.40 AM – 10.45 AM	Summary of Key Takeaways	Gerald Prager, MD, PhD
10.45 AM – 10.55 AM	Break	
10.55 AM – 11.05 AM	Hepatocellular Carcinoma	Philip A. Philip, MD, PhD
11.05 AM – 11.50 AM	Discussion: Hepatocellular Carcinoma	All
11.50 AM – 11.55 AM	Summary of Key Takeaways	Philip A. Philip, MD, PhD
11.55 AM – 12.00 PM	Meeting Close	Tanios Bekaii-Saab, MD, FACP

Day 2: Panel Consisting of 6 US and 2 European GI Cancer Experts

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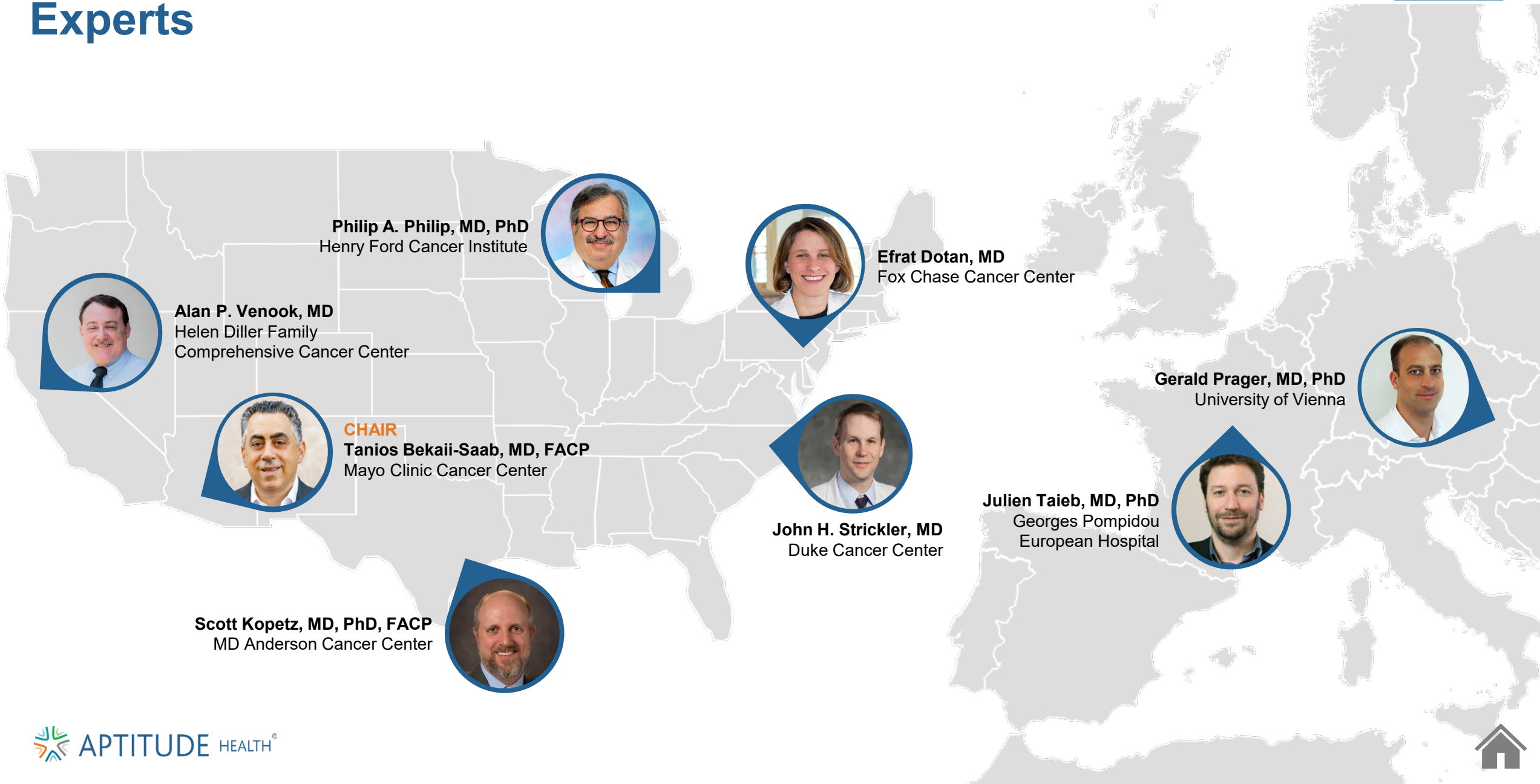

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Efrat Dotan, MD
Fox Chase Cancer Center

Alan P. Venook, MD
Helen Diller Family
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Scott Kopetz, MD, PhD, FACP
MD Anderson Cancer Center

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Meeting Agenda Day 2

EPICS

Time (EST)	Topic	Speaker/Moderator
9.00 AM – 9.05 AM	Welcome and Introductions	Tanios Bekaii-Saab, MD, FACP
9.05 AM – 9.15 AM	Gastroesophageal Junction (GEJ) and Gastric Cancer	Julien Taieb, MD, PhD
9.15 AM – 10.05 AM	Discussion: Gastroesophageal Junction (GEJ) and Gastric Cancer	All
10.05 AM – 10.10 AM	Summary of Key Takeaways	Julien Taieb, MD, PhD
10.10 AM – 10.20 AM	Rectal Cancer	Alan P. Venook, MD
10.20 AM – 11.05 AM	Discussion: Rectal Cancer	All
11.05 AM – 11.10 AM	Summary of Key Takeaways	Alan P. Venook, MD
11.10 AM – 11.20 AM	Break	
11.20 AM – 11.30 AM	Pancreatic Cancer and Biliary Tract Cancer	Efrat Dotan, MD
11.30 AM – 12.20 PM	Discussion: Pancreatic Cancer and Biliary Tract Cancer	All
12.20 PM – 12.25 PM	Summary of Key Takeaways	Efrat Dotan, MD
12.25 PM – 12.30 PM	Meeting Close	Tanios Bekaii-Saab, MD, FACP

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Metastatic Colorectal Cancer – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments

Metastatic CRC – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (1/4)

Presented by Joleen Hubbard, MD

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KRAS G12C mutation

> *KRAS* G12C mutations occur in 3%–5% of mCRC patients

KRAS G12C

> Data from the phase Ib CodeBreak 101 study, of sotorasib in

Metastatic CRC – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (2/4)

Presented by Joleen Hubbard, MD

EPICS

***HER2* amplification**

> *HER2* amplification/overexpression occurs in ~3%–5% of all patients with mCRC

Metastatic CRC – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (3/4)

Presented by Joleen Hubbard, MD

EPICS

VEGF inhibitors

> Fruquintinib is a tyrosine kinase inhibitor of VEGFR-1, -2, and -3

Metastatic CRC – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (4/4)

Presented by Joleen Hubbard, MD

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Presenter's conclusions

Metastatic Colorectal Cancer (CRC) – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (1/4)

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First-line chemotherapy backbone

> Overall, in the US and EU, FOLFOX is the preferred backbone option with anti-EGFR therapy and, depending on the toxicity profile,

[redacted]

Metastatic Colorectal Cancer (CRC) – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (2/4)

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***RAS* wild-type**

> Data from the FRESCO-2 study (LBA 25) are regarded as impactful and experts agreed fruquintinib will become another treatment choice in later lines post-

[redacted]

Metastatic Colorectal Cancer (CRC) – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (3/4)

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***HER2* amplification**

> The data from the MOUNTAINEER study of tucatinib and trastuzumab (LBA27) are convincing, and OS for these

Metastatic Colorectal Cancer (CRC) – Chemotherapy, Targeted Therapies, and Biomarker-Driven Treatments (4/4)

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NGS

> In the US, community centers often send out their samples to third-party testing facilities, which may be more robust than

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Colorectal Cancer – Immunotherapy

Colorectal Cancer – Immunotherapy (1/2)

Presented by Gerald Prager, MD, PhD

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dMMR/MSI-H CRC

> In the NICHE-2 study in locally advanced MMR-deficient colon cancer (LBA7), patients were treated with neoadjuvant ipi plus nivo, and

Colorectal Cancer – Immunotherapy (2/2)

Presented by Gerald Prager, MD, PhD

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ICI plus targeted therapy

Data were summarized from

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Colorectal Cancer – Immunotherapy (1/2)

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Neoadjuvant use of immune checkpoint inhibitors (ICIs) in dMMR/MSI-H CRC

> *"The early data that we have seen in the neoadjuvant setting really does suggest that when you are not dealing with stage 4, the impact of immunotherapy*

Colorectal Cancer – Immunotherapy (2/2)

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ICI in MSI-high metastatic disease

> Overall, experts use single-agent pembrolizumab in the first line, unless there is a need for a quick response in a patient who has extensive

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Hepatocellular Carcinoma

Hepatocellular Cancer (1/2)

Presented by Philip A. Philip, MD, PhD

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Second-line treatment

> Updated data from the KEYNOTE-240 study of pembro vs placebo in sorafenib-treated, advanced hepatocellular carcinoma were presented

Hepatocellular Cancer (2/2)

Presented by Philip A. Philip, MD, PhD

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Sequencing

> *"This is what I think of the sequencing. The first question will be, is atezo plus bev a possibility?"*

Hepatocellular Carcinoma (HCC) (1/2)

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Frontline treatment

> Atezo plus bevacizumab remains the treatment of choice for patients eligible for this regimen: "*Nothing has succeeded to beat the atezo plus bev, sometimes*

[redacted]

Hepatocellular Carcinoma (HCC) (2/2)

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Clinical trials

> The challenge with many of the trials showing positive data remains the selection of Child-Pugh A patients, and Child-Pugh B 7 and 8

[redacted]

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Gastroesophageal Junction and Gastric Cancer

GEJ and Gastric Cancer (1/4)

Presented by Julien Taieb, MD, PhD

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HER2-positive GEJ and gastric cancer

> Updated analysis of the phase II DESTINY-Gastric02 in Western patients was presented (1205MO): "*Trastuzumab deruxtecan conjugate*

GEJ and Gastric Cancer (2/4)

Presented by Julien Taieb, MD, PhD

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HER2-negative GEJ and gastric cancer
ICI in first-line trials

GEJ and Gastric Cancer (3/4)

Presented by Julien Taieb, MD, PhD

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HER2-negative GEJ and gastric cancer
ICI in second-line trials

GEJ and Gastric Cancer (4/4)

Presented by Julien Taieb, MD, PhD

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Biomarkers

> The role of DKN-01 and tislelizumab plus chemotherapy as first line in the phase IIa DisTinGuish trial (1213P) showed that "*it will take a bit*

Gastroesophageal Junction (GEJ) and Gastric Cancer (1/4)

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> Overall, no practice-changing data were presented at ESMO

ICI in first line

> Candidates for ICI are those who have no contraindication for immunotherapy and CPS ≥5, patients with MSI-H, as well as those who are EBV

Gastroesophageal Junction (GEJ) and Gastric Cancer (2/4)

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ICI in the neoadjuvant setting

> There is excitement as to the role of ICI in the neoadjuvant setting, and it will be interesting to see how the field of ICI in the adjuvant or

Gastroesophageal Junction (GEJ) and Gastric Cancer (3/4)

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HER2-positive GEJ and gastric cancer

> A proposed treatment sequence for the US is

randomized phase 2 study – (ICML) Zhang 408

- Experts believe the resolution of molecular phenotype is possible in real time, and these vulnerabilities can potentially be targeted

Promising tolerability and efficacy results from dose-escalation in an ongoing phase I/II study of trastuzumab with pralatuzumab vedotin for relapsed/refractory B-cell NHL – (ENA) Ghosh #6222

- The regimen is seen as effective, exciting, safe, and broadly applicable to many patients

Bevacizumab (bevacu) monotherapy for elderly/unfit patients with first-line DLBCL continues to show promising safety and efficacy with durable complete responses – (ENA) Chyzewski #EP161

- This approach is seen as a great solution for a patient population in whom giving immunochemotherapy is difficult. It is viewed as effective and safe

FIRST-MIND: a phase 3b, open-label, randomized study to assess safety of tafasitamab or tafasitamab + lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL – (ENA) Beriada #EP166

- Experts believe the combination of tafasitamab + lenalidomide with R-CHOP is safe. However, they would like to see phase III data to confirm its activity in this setting

Long-term analyses from L-MIND, a phase II study of tafasitamab plus lenalidomide (len) in patients with R/R DLBCL – (ICML) Duell #28

- The L-MIND regimen is seen as useful in the specific patient population with refractory disease. It was noted to be effective, very safe, and well tolerated. Some of the responses seen were clearly very durable

Gastroesophageal Junction (GEJ) and Gastric Cancer (4/4)

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Novel targets

> CLDN18.2 is considered an interesting target and preliminary data from the Claudin18.2-specific CAR T cells, as well as from zolbetuximab

[redacted]

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Rectal Cancer

Rectal Cancer (1/3)

Presented by Alan P. Venook, MD

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Total neoadjuvant therapy (TNT)

> *"Virtually every study in the US that's been done in the past decade in rectal cancer has used a total neoadjuvant approach as the platform,*

Rectal Cancer (2/3)

Presented by Alan P. Venook, MD

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dMMR rectal cancer

> The phase II study of dostarlimab in patients with stage II or III MSI-H or dMM rectal cancer was presented (Cercek A, et al. *N Engl J Med*

Rectal Cancer (3/3)

Presented by Alan P. Venook, MD

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RAPIDO study

> The trial examines the role of short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) vs preoperative

Rectal Cancer (1/2)

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Different modalities of neoadjuvant chemotherapy remain a standard of care

> The TNT regimen is widely used. However, it was noted that "*there is a population that we're overtreating here . . . so, while it's very easy to*

Rectal Cancer (2/2)

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Non-operative management of rectal cancer

> Organ preservation is a goal for many patients, particularly elderly patients with comorbidities who are not fit surgery, and young patients if they have a complete response to neoadjuvant therapy: "*This has to be a very good discussion with the patients, because they really need a tight follow-up*

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Pancreatic Cancer and Biliary Tract Cancer

Pancreatic Cancer and Biliary Tract Cancer (1/3)

Presented by Efrat Dotan, MD

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Locally advanced pancreatic cancer

> The phase III randomized trial PRODIGE 29-UCGI 26(NEOPAN) comparing chemotherapy with FOLFIRINOX or gemcitabine in locally

Pancreatic Cancer and Biliary Tract Cancer (2/3)

Presented by Efrat Dotan, MD

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Metastatic pancreatic cancer

> Extended OS results from the POLO study of active maintenance olaparib in patients with metastatic pancreatic cancer and a germline

Pancreatic Cancer and Biliary Tract Cancer (3/3)

Presented by Efrat Dotan, MD

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Metastatic biliary tract cancer

> Updated OS from the phase III TOPAZ-1 study of durva or placebo plus gemcitabine and cisplatin in patients with advanced biliary tract

Pancreatic Cancer and Biliary Tract Cancer (1/4)

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Pancreatic cancer
Locally advanced disease

Pancreatic Cancer and Biliary Tract Cancer (2/4)

EPICS

Pancreatic cancer
Biomarkers

Pancreatic Cancer and Biliary Tract Cancer (3/4)

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Biliary tract cancer

> The challenge with this disease is the associated comorbidities and complications that may arise

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Pancreatic Cancer and Biliary Tract Cancer (4/4)

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Biliary tract cancer

Biomarkers

> Patients with biliary tract cancer need to be molecularly profiled up front, and it is a very exciting time now with the ongoing identification of