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Conference Coverage: ESMO 2023 – Focus on Gastrointestinal (GI) Malignancies

Thursday, 2 November 2023

Full Report

Report Contents

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Meeting Snapshot

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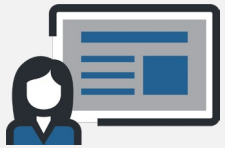
LIVE ROUNDTABLE

DATE:
2 November 2023



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in GI cancers
> 3 from the US
> 5 from Europe

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

Panel Consisting of 3 US and 5 European GI Experts

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Joleen Hubbard, MD
Allina Health Cancer Institute

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

CHAIR
Tanios S. Bekaii-Saab, MD, FACP
Mayo Clinic, Phoenix

Elizabeth Smyth, MD
Oxford University Hospitals National Health Service Foundation Trust

Dirk Arnold, MD, PhD
University of Hamburg

Julien Taieb, MD, PhD
Georges Pompidou European Hospital

Gerald Prager, MD
Medical University of Vienna

Chiara Cremolini, MD, PhD
University of Pisa

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Meeting Agenda (1/2)

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Time (MST/CET)	Topic	Speaker/Moderator
8.00 AM – 8.05 AM 15.00 – 15.05	Welcome and Introductions	Tanios S. Bekaii-Saab, MD, FACP
8.05 AM – 8.15 AM 15.05 – 15.15	**CRC – Including Targeted Therapy**	Chiara Cremolini, MD, PhD
8.15 AM – 8.30 AM 15.15 – 15.30	Key Questions and Topics for Discussion	Tanios S. Bekaii-Saab, MD, FACP
8.30 AM – 8.40 AM 15.30 – 15.40	**MSS and MSI-H CRC**	Joleen Hubbard, MD
8.40 AM – 8.55 AM 15.40 – 15.55	Key Questions and Topics for Discussion	Tanios S. Bekaii-Saab, MD, FACP
8.55 AM – 9.00 AM 15.55 – 16.00	Key Takeaways: CRC Including Targeted Therapy + MSS and MSI-H CRC	Joleen Hubbard, MD, and Chiara Cremolini, MD, PhD
9.00 AM – 9.10 AM 16.00 – 16.10	**Gastric and GEJ Cancers** *Early disease*	Elizabeth Smyth, MD
9.10 AM – 9.25 AM 16.10 – 16.25	Key Questions and Topics for Discussion	Tanios S. Bekaii-Saab, MD, FACP
9.25 AM – 9.30 AM 16.25 – 16.30	*Break*	

Meeting Agenda (2/2)

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Time (MST/CET)	Topic	Speaker/Moderator
9.30 AM – 9.40 AM 16.30 – 16.40	**Gastric and GEJ Cancers** *Metastatic disease*	Julien Taieb, MD, PhD
9.40 AM – 9.50 AM 16.40 – 16.50	**Gastric and GEJ Cancers** *Metastatic disease*	Dirk Arnold, MD, PhD
9.50 AM – 10.15 AM 16.50 – 17.15	Key Questions and Topics for Discussion	Tanios S. Bekaii-Saab, MD, FACP
10.15 AM – 10.20 AM 17.15 – 17.20	Key Takeaways: Gastric and GEJ Cancers	Elizabeth Smyth, MD; Julien Taieb, MD, PhD; Dirk Arnold, MD, PhD
10.20 AM – 10.30 AM 17.20 – 17.30	**Pancreatic Cancer**	Philip A. Philip, MD, PhD
10.30 AM – 10.35 AM 17.30 – 17.35	**Biliary Tract Cancer**	Gerald Prager, MD
10.35 AM – 10.55 AM 17.35 – 17.55	Key Questions and Topics for Discussion	Tanios S. Bekaii-Saab, MD, FACP
10.55 AM – 11.00 AM 17.55 – 18.00	Key Takeaways: Pancreatic Cancer and Biliary Tract Cancer	Philip A. Philip, MD, PhD, and Gerald Prager, MD
11.00 AM 18.00	Summary and Closing Remarks	Tanios S. Bekaii-Saab, MD, FACP

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Congress Highlights

CRC – Including Targeted Therapy

The PEGASUS trial: post-surgical liquid biopsy-guided treatment of stage III and high-risk stage II colon cancer patients

Lonardi S, et al. LBA28

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BACKGROUND

- Retrospective studies demonstrated an impressive prognostic impact of circulating tumor DNA (ctDNA, LB) positivity on colon cancer relapse after radical resection as proxy of minimal

10 Recurrences in ctDNA-Negative Patients

Sotorasib plus panitumumab versus standard-of-care for chemorefractory KRAS G12C-mutated metastatic colorectal cancer (mCRC): CodeBreak 300 phase 3 study

Pietrantonio F, et al. LBA10

EPICS

BACKGROUND

- The first phase III primary results for sotorasib (soto), a *KRAS* G12C inhibitor, +

	Sotorasib 960 mg + Panitumumab	Sotorasib 240 mg + Panitumumab	Investigator's Choice

Panitumumab (P) + FOLFIRINOX or mFOLFOX6 in unresectable metastatic colorectal cancer (mCRC) patients (pts) with RAS/BRAF wild-type (WT) tumor status from circulating DNA (cirDNA). First results of the randomized phase II PANIRINOX-UCGI28 study

Mazard T, et al. LBA30

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BACKGROUND

> For shrinkage of *RAS/BRAF* WT tumors, anti-EGFR antibodies + triplet chemo have

	Arm A FOLFIRINOX+p	Arm B mFOLFOX6+p

First-line systemic treatment in patients with initially unresectable colorectal cancer liver metastases (CRLM): overall survival of the phase III CAIRO5 study of the Dutch Colorectal Cancer Group

Punt CJ, et al. LBA27

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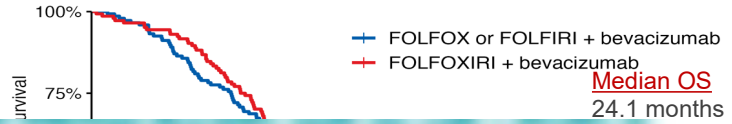
BACKGROUND

> CAIRO5 aimed to find the optimal systemic induction regimen to convert initially

Right-sided and/or *RAS/BRAF* mut



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Key Insights

CRC – Including Targeted Therapy

CRC – Including Targeted Therapy (1/3)

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ctDNA in CRC

> Following the presentation from the PEGASUS trial (LBA28), experts from the US and EU agreed that ctDNA is very interesting to examine

CRC – Including Targeted Therapy (2/3)

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First-line treatment of mCRC

CAIRO5 (LBA27)

> *"I think there is a problem with CAIRO. I don't know if it is the* [study] *population, the way patients were managed in the Netherlands, maybe*

CRC – Including Targeted Therapy (3/3)

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KRAS G12C-mutated mCRC

CodeBreaK 300 (LBA10)

> The data are considered practice changing for this small group of patients: "*I would like to think the results are practice changing; I mean, the*

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Congress Highlights

MSS and MSI-H CRC

Neoadjuvant nivolumab plus relatlimab (anti-LAG3) in locally advanced MMR-deficient colon cancers: the NICHE-3 study

Verschoor YL, et al. LBA31

EPICS

BACKGROUND

> Neoadjuvant immunotherapy has shown promising responses in various tumor types. In the

Patient Characteristics (n = 19)		
T stage	T2	5%
	T3	58%

Pembrolizumab versus chemotherapy in microsatellite instability-high (MSI-H)/mismatch repair-deficient (dMMR) metastatic colorectal cancer (mCRC): 5-year follow-up of the randomized phase 3 KEYNOTE-177 study

Shiu KK, et al. LBA32

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BACKGROUND

> In the phase III KEYNOTE-177 (NCT02563002) study, pembro vs chemo improved PFS

OS Results After 73.3 Months

A phase II clinical trial of sintilimab plus chidamide combined with or without bevacizumab in patients with MSS/pMMR metastatic colorectal cancer

Wang F, et al. 556MO

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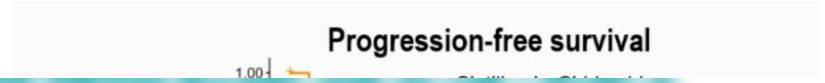
BACKGROUND

> Immune checkpoint inhibitors (ICI) have shown significant clinical benefit for pts with MSI-



A Phase II, multicenter, open-label study of PolyPEPI1018 in combination with atezolizumab in participants with relapsed or refractory microsatellite-stable metastatic colorectal cancer (MSS mCRC) (Oberto-301): initial results

Hubbard J, et al. 640P

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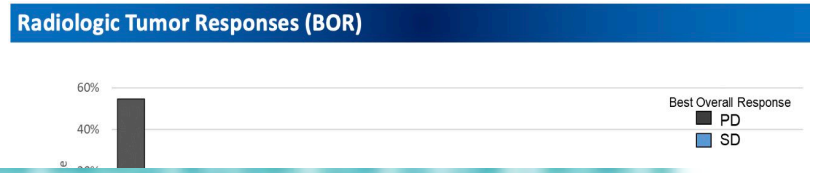
BACKGROUND

> Additional interventions are needed to convert immunologically “cold” MSS CRC tumors



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Key Insights

MSS and MSI-H CRC

MSS and MSI-H Colorectal Cancer (1/2)

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MSS CRC – exploring new avenues

> *"Research in this field will continue to be incremental, rather than transformational." "We cannot neglect that we make small-steps progress"*

[redacted]

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MSS and MSI-H Colorectal Cancer (2/2)

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MSI-H CRC

NICHE-3 (LBA31)

> Data from NICHE-3 are viewed positively; however, it is yet to be determined if an anti-LAG3 is better than an anti–CTLA-4 antibody, and

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Congress Highlights

Gastric and GEJ Cancers

Early disease

Pembrolizumab plus chemotherapy vs chemotherapy as neoadjuvant and adjuvant therapy in locally-advanced gastric and gastroesophageal junction cancer: The Phase 3 KEYNOTE-585 study

Shitara K, et al. LBA74

BACKGROUND

> The phase III KEYNOTE-585 study (NCT03221426) evaluated

Pathological complete response (pCR) to durvalumab plus FLOT in resectable gastric and gastroesophageal junction cancer (GC/GEJC): interim results of the global, phase 3 MATTERHORN study

Janjigian YY, et al. LBA73

EPICS

BACKGROUND

> The global, phase III, randomized, double-blind, placebo-controlled

Overall Survival of Perioperative or Postoperative Adjuvant Oxaliplatin with S-1 versus Adjuvant Oxaliplatin with Capecitabine in Locally Advanced Gastric or Gastro-Oesophageal Junction Adenocarcinoma Undergoing D2 Gastrectomy: An Updated Analysis of RESOLVE Trial

Zhang X, et al. LBA78

EPICS

BACKGROUND

> The RESOLVE study demonstrated a disease-free survival (DFS) benefit from

A: Adj- | **B**: Adj- | **C**: Peri- | **B** vs **A** (non- | **C** vs **A**

Neoadjuvant chemoradiotherapy followed by surgery versus active surveillance for oesophageal cancer (SANO-trial): a phase-III stepped-wedge cluster randomised trial

Van der Wilk BJ, et al. LBA75

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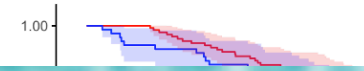
BACKGROUND

> One-third of pts with esophageal cancer have a pCR after neoadjuvant chemoradiotherapy



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Key Insights

Gastric and GEJ Cancers

Early disease

Gastric and GEJ Cancers

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Perioperative treatment in early disease

MATTERHORN and KEYNOTE-585 trials

Immunotherapy regimens

> It was noted that a number of patients from both MATTERHORN (LBA73) and KEYNOTE-585 (LBA74) likely had metastatic disease

[redacted]

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Congress Highlights

Gastric and GEJ Cancers

Metastatic disease

Updated efficacy and safety results from phase 3 SPOTLIGHT study evaluating zolbetuximab + mFOLFOX6 as first-line (1L) treatment for patients with claudin-18 isoform 2-positive (CLDN18.2+), HER2−, locally advanced (LA) unresectable or metastatic gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma

Ajani JA, et al. LBA82

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BACKGROUND

> The phase III SPOTLIGHT study showed statistically significant improvement with first-line

PO: PFS (centrally reviewed)	Zolbetuximab + mFOLFOX6	Placebo + mFOLFOX6
No. events/no. patients	157/283	184/282
Median PFS, months (95% CI)	**11.04** (9.69–12.52)	**8.94** (8.21–10.41)

Updated efficacy and safety results from phase 3 GLOW study evaluating zolbetuximab + CAPOX as first-line (1L) treatment for patients with claudin-18 isoform 2-positive (CLDN18.2+), HER2−, locally advanced (LA) unresectable or metastatic gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma

Lordick F, et al. LBA81

EPICS

BACKGROUND

> The phase III GLOW study showed statistically significant improvement with first-line

PFS	Zolbetuximab + CAPOX	Placebo + CAPOX
Events/patients, n/N	146/254	178/253
Median PFS, months (95% CI)	8.28 (7.46–9.00)	6.80 (6.14–8.11)
HR (95% CI)	0.682 (0.545–0.854)	
P value	0.0004	

Tislelizumab (TIS) Plus Chemotherapy (Chemo) vs Placebo (PBO) Plus Chemo as First-Line (1L) Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (GC/GEJC): Final Analysis Results of the RATIONALE-305 Study

Xu RH, et al. LBA80

EPICS

BACKGROUND

- TIS (anti–PD-1 antibody) + chemo demonstrated significant OS benefit vs PBO + chemo as

Endpoint	TIS + Chemo (n = 501)	PBO + Chemo (n = 496)
OS		

GEMSTONE-303: prespecified progression-free survival (PFS) and overall survival (OS) final analyses of a phase 3 study of sugemalimab plus chemotherapy vs placebo plus chemotherapy in treatment-naïve advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma

Zhang X, et al. LBA79

EPICS

BACKGROUND

> GEMSTONE-303 is a randomized, double-blinded, multicenter phase III trial evaluating

Sugemalimab : fully human anti-PD-L1 mAb

5-fluorouracil and oxaliplatin with or without docetaxel in the first-line treatment of HER2 negative locally advanced (LA) unresectable or metastatic gastric or gastro-esophageal junction (GEJ) adenocarcinoma (GASTFOX-PRODIGE 51): a randomized phase 3 trial sponsored by the FFCD

Zaanan A, et al. LBA77

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BACKGROUND

> The perioperative FLOT triplet chemotherapy regimen is the standard of care for localized

The primary results of an intergroup phase III randomized controlled trial comparing ramucirumab plus irinotecan with irinotecan in the third or later line treatment beyond progression after ramucirumab for advanced gastric cancer (RINDBeRG Trial)

Kadowaki S, et al. LBA76

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BACKGROUND

> Ramucirumab is an mAb that targets VEGFR2 and has been shown to improve

Primary endpoint: OS (FAS population[a])

Pembrolizumab plus Trastuzumab and Chemotherapy for HER2+ Metastatic Gastric or Gastroesophageal Junction (mG/GEJ) Adenocarcinoma: Survival results from the Phase 3, Randomized, Double-blind, Placebo-controlled. KEYNOTE-811 Study

Janjigian Y, et al. 1511O

EPICS

BACKGROUND

- In a previous analysis of the phase III KEYNOTE-811 study, pembro-trastuzumab and chemo vs placebo-trastuzumab and chemo provided an ORR of 74% vs 52% in the first 264

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Key Insights

Gastric and GEJ Cancers

Metastatic disease

Gastric and GEJ Cancers (1/3)

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Metastatic gastric and GEJ cancers

Claudin 18.2-positive tumors

> The benefit shown in the SPOTLIGHT (LBA82) and GLOW (LBA 81) studies is considered clinically relevant and the experts believe these

Gastric and GEJ Cancers (2/3)

EPICS

Metastatic gastric and GEJ cancers

HER2-positive and PD-L1–positive tumors

> Updated results from KEYNOTE-811 (1511O) were not deemed as interesting as expected, and adding pembrolizumab to trastuzumab was

Gastric and GEJ Cancers (3/3)

EPICS

Metastatic gastric and GEJ cancers

HER2-positive and PD-L1–positive tumors (cont.)

> There are differences between Europe and the US on how the KEYNOTE-811 regimen may be administered to patients. Full access to the

[redacted]

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Congress Highlights

Pancreatic cancer

Neoadjuvant chemotherapy with FOLFIRINOX versus neoadjuvant gemcitabine-based chemoradiotherapy for borderline resectable and resectable pancreatic cancer (PREOPANC-2): a multicenter randomized controlled trial

Koerkamp BG, et al. LBA83

EPICS

BACKGROUND

> The PREOPANC trial demonstrated an OS benefit of neoadjuvant gemcitabine-based

OVERALL SURVIVAL

Nab-paclitaxel plus gemcitabine versus modified FOLFIRINOX or S-IROX in metastatic or recurrent pancreatic cancer (JCOG1611, GENERATE): A multicentre, randomized, open-label, three-arm, phase 2/3 trial

Ohba A, et al. 1616O

EPICS

BACKGROUND

- Both *nab*-paclitaxel + gemcitabine and modified FOLFIRINOX are equivalently recommended as

Overall Survival (Updated: May 2023)

Pelareorep (pela) + atezolizumab (atezo) and chemotherapy in first-line (1L) advanced or metastatic pancreatic ductal adenocarcinoma (PDAC) patients – Results from the GOBLET study

Arnold D, et al. 1623P

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BACKGROUND

> Pela is an intravenously delivered, unmodified oncolytic reovirus that selectively replicates

Efficacy

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Key Insights

Pancreatic cancer

Pancreatic Cancer

EPICS

Neoadjuvant treatment for borderline-resectable and resectable pancreatic cancer

PREOPANC-2 trial (LAB83)

> The experts expected that FOLFIRINOX would be

Metastatic pancreatic cancer

GENERATE trial (1616O)

> Data from the GENERATE trial came as a surprise to the experts; one US expert

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Congress Highlights

Biliary tract cancer

Tinengotinib in patients with advanced, fibroblast growth factor receptor (FGFR) inhibitor refractory/relapsed cholangiocarcinoma

Pelster S, et al. 95MO

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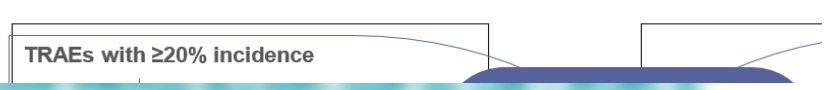
BACKGROUND

> FGFR inhibitors (FGFRi) have a proven role for the management of *FGFR*-altered



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

Delaunay B, et al. 121P

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BACKGROUND

> *FGFR2* fusions or rearrangements occur in up to 14% of pts with intrahepatic

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

Figure 1 : PFS and OS

Efficacy and safety of durvalumab plus gemcitabine and cisplatin in Chinese participants with advanced biliary tract cancer: extension cohort of the Phase 3, randomised, double-blind, placebo-controlled, global TOPAZ-1 study

Qin S, et al. 98P

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BACKGROUND

> At the TOPAZ-1 (NCT03875235) primary analysis, first-line treatment with durva (D) +

Figure 2. Kaplan-Meier analysis of overall survival in the China Mainland cohort

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Key Insights

Biliary tract cancer

Biliary Tract Cancer

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Metastatic cholangiocarcinoma with *FGFR2* fusion/rearrangement or mutation

> The data from the combined phase I, Ib/II, and II trials (95MO) of

Immune checkpoint inhibition in metastatic cholangiocarcinoma

> Data from the Chinese patients in the TOPAZ-1 trial (98P)

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