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Conference Coverage: ASCO GI 2024 Highlights

January 24, 2024

Full Report

Report Contents

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Meeting Snapshot

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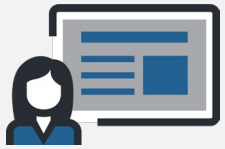
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
January 24, 2024



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in GI malignancies

- > 5 from US
- > 3 from Europe

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

Panel Consisting of 5 US and 3 EU GI Cancer Experts

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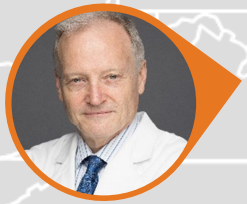
Sunnie Kim, MD
University of Colorado
Cancer Center

David H. Ilson, MD, PhD
Memorial Sloan Kettering
Cancer Center

Dirk Arnold, MD, PhD
Asklepios Tumor Center,
University of Hamburg



Chair
John Marshall, MD
Georgetown Lombardi
Comprehensive Cancer Center

Reetu Mukherji, MD
Georgetown Lombardi
Comprehensive Cancer Center

Eric Van Cutsem, MD, PhD
University Hospitals
Gasthuisberg, University of
Leuven

Tanios Bekaii-Saab, MD, FACP
Mayo Clinic Cancer Center

Fotios Loupakis, MD, PhD
Veneto Institute of Oncology

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Meeting Agenda (1/2)

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Time (ET/CET)	Topic	Speaker/Moderator
8.30 AM – 8.35 AM/14.30 – 14.35	**Welcome, Introductions, and Meeting Objectives**	John Marshall, MD
8.35 AM – 8.40 AM/14.35 – 14.40	**Colorectal Cancer – Systemic Therapy**	Dirk Arnold, MD, PhD
8.40 AM – 8.55 AM/14.40 – 14.55	Discussion	John Marshall, MD
8.55 AM – 9.00 AM/14.55 – 15.00	Key Takeaways	Dirk Arnold, MD, PhD
9.00 AM – 9.10 AM/15.00 – 15.10	**Colorectal Cancer – Biomarkers**	Reetu Mukherji, MD
9.10 AM – 9.25 AM/15.10 – 15.25	Discussion	John Marshall, MD
9.25 AM – 9.30 AM/15.25 – 15.30	Key Takeaways	Reetu Mukherji, MD
9.30 AM – 9.35 AM/15.30 – 15.35	**Hepatocellular Carcinoma**	Tanios Bekaii-Saab, MD, FACP
9.35 AM – 9.50 AM/15.35 – 15.50	Discussion	John Marshall, MD
9.50 AM – 9.55 AM/15.50 – 15.55	Key Takeaways	Tanios Bekaii-Saab, MD, FACP
9.55 AM – 10.00 AM/15.55 – 16.00	*Break*	

Meeting Agenda (2/2)

EPICS

Time (ET/CET)	Topic	Speaker/Moderator
10.00 AM – 10.10 AM/16.00 – 16.10	**Esophageal Cancers**	Sunnie Kim, MD
10.10 AM – 10.25 AM/16.10 – 16.25	Discussion	John Marshall, MD
10.25 AM – 10.30 AM/16.25 – 16.30	Key Takeaways	Sunnie Kim, MD
10.30 AM – 10.35 AM/16.30 – 16.35	**Gastric and Gastroesophageal Junction (GEJ) Cancers**	David Ilson, MD, PhD
10.35 AM – 10.50 AM/16.35 – 16.50	Discussion	John Marshall, MD
10.50 AM – 10.55 AM/16.50 – 16.55	Key Takeaways	David Ilson, MD, PhD
10.55 AM – 11.05 AM/16.55 – 17.05	**Pancreatic Cancer and Biliary Tract Cancer**	Eric Van Cutsem, MD, PhD
11.05 AM – 11.25 AM/17.05 – 17.25	Discussion	John Marshall, MD
11.25 AM – 11.30 AM/17.25 – 17.30	Key Takeaways	Eric Van Cutsem, MD, PhD
11.30 AM/17.30	**Summary and Closing Remarks**	John Marshall, MD

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Conference Highlights

Colorectal Cancer – Systemic Therapy

Nivolumab + ipilimumab vs chemotherapy as first-line treatment for MSI-H/dMMR mCRC: First results of CheckMate 8HW

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André T, et al. 2024 ASCO GI; Abstract LBA768

STUDY POPULATION AND METHODS

- 303 pts with MSI-H/dMMR mCRC were randomized 2:1 to first-

PROGRESSION-FREE SURVIVAL

HRQOL in patients with mCRC treated with sotorasib + panitumumab vs trifluridine/tipiracil or regorafenib in CodeBreaK 300

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Modest D, et al. 2024 ASCO GI; Abstract 10

STUDY POPULATION AND METHODS

- 160 pts with chemo-refractory *KRAS* G12C-mutated mCRC were

PATIENT PERCEPTION OF OVERALL STATUS (WEEK 17)

Phase Ib/II study of ADG126 (a masked anti–CTLA-4 SAFEbody) + pembrolizumab in patients with MSS CRC

Li D, et al. 2024 ASCO GI; Abstract 127

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STUDY POPULATION AND METHODS

- 24 pts with chemo-refractory MSS mCRC (free of liver mets) were

SPIDER PLOT OF EVALUABLE PATIENTS

Neoadjuvant botensilimab + balstilimab in resectable mismatch repair-proficient and -deficient CRC: NEST-1 clinical trial

Kasi PM, et al. 2024 ASCO GI; Abstract 117

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STUDY POPULATION AND METHODS

- 12 pts with colon or rectal cancers eligible for resection were

PATHOLOGIC TUMOR REDUCTIONS

Amivantamab monotherapy in R/R metastatic CRC: OrigAMI-1, an open-label, phase Ib/II study

Oberstein PE, et al. 2024 ASCO GI; Abstract 135

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STUDY POPULATION AND METHODS

- Pts with R/R mCRC (*RAS/RAF* WT) received treatment with

ANTITUMOR ACTIVITY

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Key Insights

Colorectal Cancer – Systemic Therapy

Experts Discussed Immunotherapies for MSI-H mCRC

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CheckMate 8HW

ongoing trials will help clarify the optimal sequencing of agents.

- Experts are still using a [redacted] doublet regimen (a taxane plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients.
- Most experts are using trastuzumab deruxtecan third-line, but will prioritize the tucatinib triplet for patients with evidence of brain metastases.
- The tucatinib triplet may also be used in the second-line setting, before T-DM1, for patients with documented brain metastases.
  - If tucatinib is used second-line, experts are divided on whether they would currently use T-DM1 or trastuzumab deruxtecan third-line.
    - Results of the ongoing DESTINY-Breast03 trial comparing trastuzumab deruxtecan vs T-DM1 will help to clarify the optimal sequence of these ADCs.
- Trastuzumab deruxtecan and the tucatinib triplet may also be used earlier than third-line in patients who recur following treatment with trastuzumab, pertuzumab, and T-DM1 in the (neo)adjuvant setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the sequencing of these new agents (eg, 3 drugs vs 1 drug, concern about hair loss vs diarrhea).
- The impressive efficacy of trastuzumab deruxtecan and the tucatinib regimen have pushed other options, such as trastuzumab-chemotherapy combinations, neratinib, and margetuximab, to later lines of therapy.

Dr Pegram:
We used to run out of good options and we would just regress to the mean of chemotherapy plus trastuzumab in the salvage setting, but now we have so many great choices that that really takes a backseat. It's really been exciting to have multiple options for patients after T-DM1 — again, practice changing, unprecedented.

Experts Evaluated Investigational Immunotherapeutic Agents for CRC

EPICS

NEST-1

ongoing trials will help clarify the optimal sequencing of agents

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Experts Speculated on a Potential Role for Combination Immunotherapies in MSS CRC

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IO IN MSS CRC

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Experts Considered Novel Targeted Approaches in mCRC

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CodeBreaK 300

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Conference Highlights

Colorectal Cancer – Biomarkers

ctDNA for informing adjuvant chemotherapy in stage II/III CRC: Interim analysis of BESPOKE CRC study

Kasi PM, et al. 2024 ASCO GI; Abstract 9

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STUDY POPULATION AND METHODS

- 689 pts with stage II/III CRC underwent ctDNA testing using the

DFS BY ctDNA STATUS DURING MRD WINDOW

ctDNA dynamics in patients with CRC with molecular residual disease: Updated analysis from GALAXY study in CIRCULATE-JAPAN

Yukami H, et al. 2024 ASCO GI; Abstract 6

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STUDY POPULATION AND METHODS

> 2998 pts with radically resected, stage I-IV CRC underwent serial

ADJUVANT COHORT CLEARANCE ANALYSIS

Phase II results of ctDNA as a predictive biomarker in adjuvant chemotherapy in stage II colon cancer: NRG-GI005 (COBRA)

Morris V, et al. 2024 ASCO GI; Abstract 5

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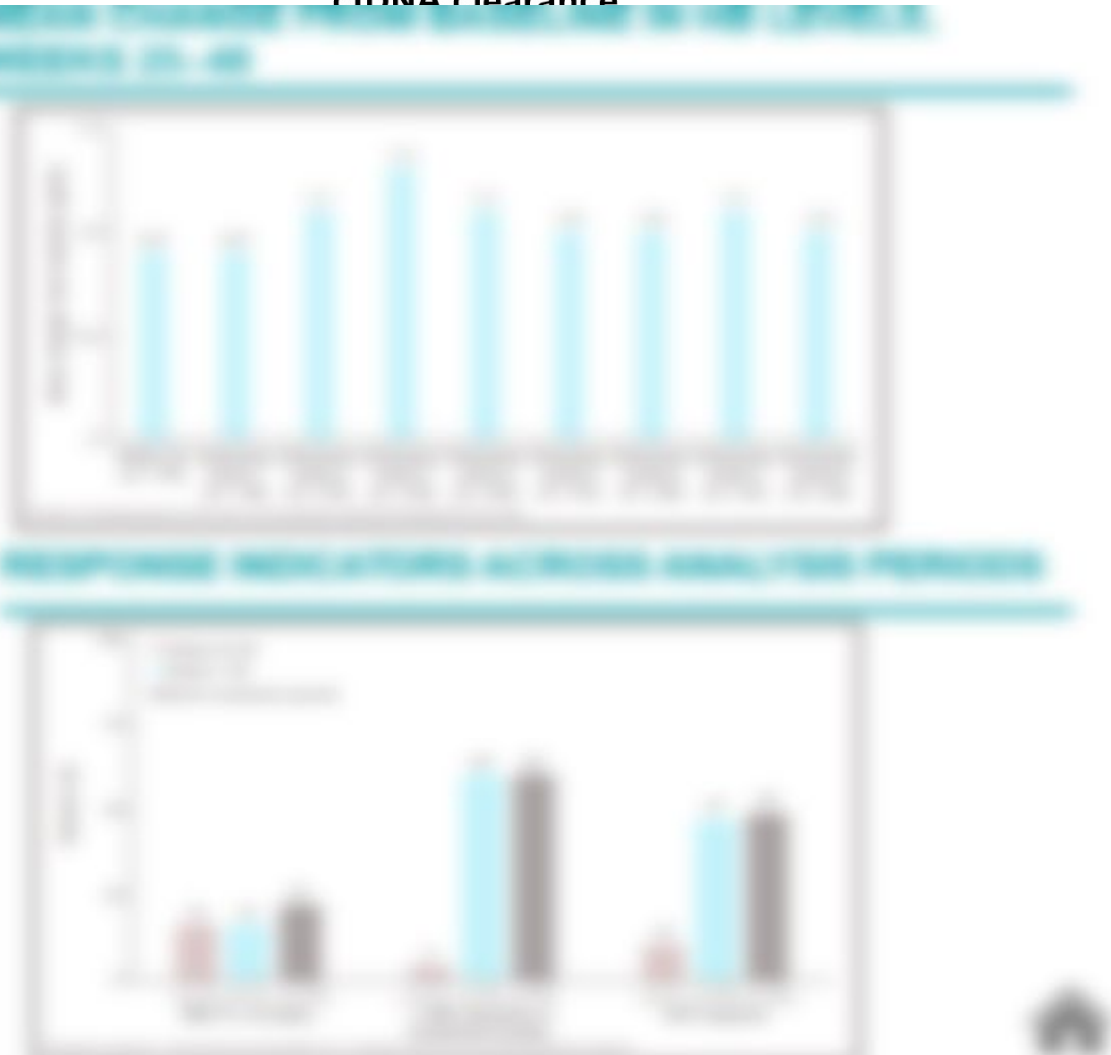
STUDY POPULATION AND METHODS

- 635 pts with resected stage II CRC deemed suitable for active

ctDNA CLEARANCE



ctDNA analysis informing adjuvant chemotherapy in locally advanced rectal cancer: The randomized AGITG DYNAMIC-Rectal study

Tie J, et al. 2024 ASCO GI; Abstract 12

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STUDY POPULATION AND METHODS

- 230 pts with locally advanced rectal cancer received neoadjuvant

RECURRENCE-FREE SURVIVAL BY ctDNA STATUS

Refining first-line treatment decision in *RAS* WT mCRC by combining clinical biomarkers: Results of phase III FIRE-3 trial (AIO KRK0306)

Holch JW, et al. 2024 ASCO GI; Abstract 13

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STUDY POPULATION AND METHODS

> 400 pts with *RAS* WT mCRC from the first-line FIRE-3 trial

OS BENEFIT BY SIDEDNESS AND METASTATIC SITES

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Key Insights

Colorectal Cancer – Biomarkers

Experts Discussed Current Data and Ongoing Investigational Directions With ctDNA Testing in CRC

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ctDNA TESTING – STRENGTHS AND LIMITATIONS

Experts Discussed the Current Use of ctDNA Testing in the Clinic

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ctDNA IN CLINICAL DECISION-MAKING

Experts Considered Clinical and Biologic Markers for Tailoring Targeted Therapy Selection

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FIRST-LINE THERAPY WITH VEGF- OR EGFR-TARGETED mAbs

ongoing trials will help clarify the optimal sequencing of agents

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Conference Highlights

Hepatocellular Carcinoma

EMERALD-1: Phase III study of TACE + durvalumab ± bevacizumab in unresectable HCC eligible for embolization

Lencioni R, et al. 2024 ASCO GI; Abstract LBA432

EPICS

STUDY POPULATION AND METHODS

- 616 pts with embolization-eligible unresectable HCC were

PROGRESSION-FREE SURVIVAL

TACE combined with cadonilimab and lenvatinib for unresectable HCC: A phase II clinical trial

Liang G, et al. 2024 ASCO GI; Abstract 478

EPICS

STUDY POPULATION AND METHODS

- 60 pts with unresectable intermediate HCC were treated with

BEST RESPONSE

Adjuvant radiotherapy after curative resection of HCC with narrow margin (≤1 cm): The phase II randomized RAISE trial

Ming K, et al. 2024 ASCO GI; Abstract 722

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STUDY POPULATION AND METHODS

- 148 pts with HCC who had undergone an R0 resection with close

RECURRENCE-FREE SURVIVAL

Phase II study of triplet blockade of the IL-27, PD-(L)1, and VEGF pathways with casdozokitug (casdozo, SRF388) + atezo + bev in uHCC

Li J, et al. 2024 ASCO GI; Abstract 470

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STUDY POPULATION AND METHODS

- 30 pts with untreated unresectable or metastatic HCC were

ANTITUMOR ACTIVITY (RECIST v1.1)

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Key Insights

Hepatocellular Carcinoma

Experts Discussed Combining Systemic and Locoregional Therapies for Unresectable HCC

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TACE-BASED COMBINATIONS

ongoing trials will help clarify the optimal sequencing of agents

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Experts Considered Investigational Agents and Future Directions in HCC

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IL-27 INHIBITION

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Conference Highlights

Esophageal Cancers

First-line pembrolizumab + chemotherapy for advanced esophageal cancer: 5-year outcomes from KEYNOTE-590

Shah MA, et al. 2024 ASCO GI; Abstract 250

EPICS

STUDY POPULATION AND METHODS

> 749 pts with locally advanced/metastatic adenocarcinoma or

OVERALL SURVIVAL: ITT POPULATION

Q-TWiST analysis comparing nivolumab + ipilimumab or nivolumab + CT vs CT in advanced ESCC: CheckMate 648

Chau I, et al. 2024 ASCO GI; Abstract 251

EPICS

STUDY POPULATION AND METHODS

- 970 pts with previously untreated ESCC were randomized to N + I

Q-TWiST METHODS

Nivolumab + chemo or ipilimumab vs chemo as first-line treatment for advanced ESCC: Biomarker analyses from CheckMate 648

Lei M, et al. 2024 ASCO GI; Abstract 252

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STUDY POPULATION AND METHODS

> Tumor samples from pts enrolled in CM 648 were analyzed for

OVERALL SURVIVAL BY TMB STATUS

SKYSCRAPER-08: Phase III study of first-line tiragolumab + atezolizumab and chemotherapy in ESCC

Hsu CH, et al. 2024 ASCO GI; Abstract 245

EPICS

STUDY POPULATION AND METHODS

- 461 pts with previously untreated unresectable advanced or

OVERALL SURVIVAL

Chemotherapy + camrelizumab vs chemotherapy alone as neoadjuvant treatment for resectable ESCC: Phase III ESCORT-NEO

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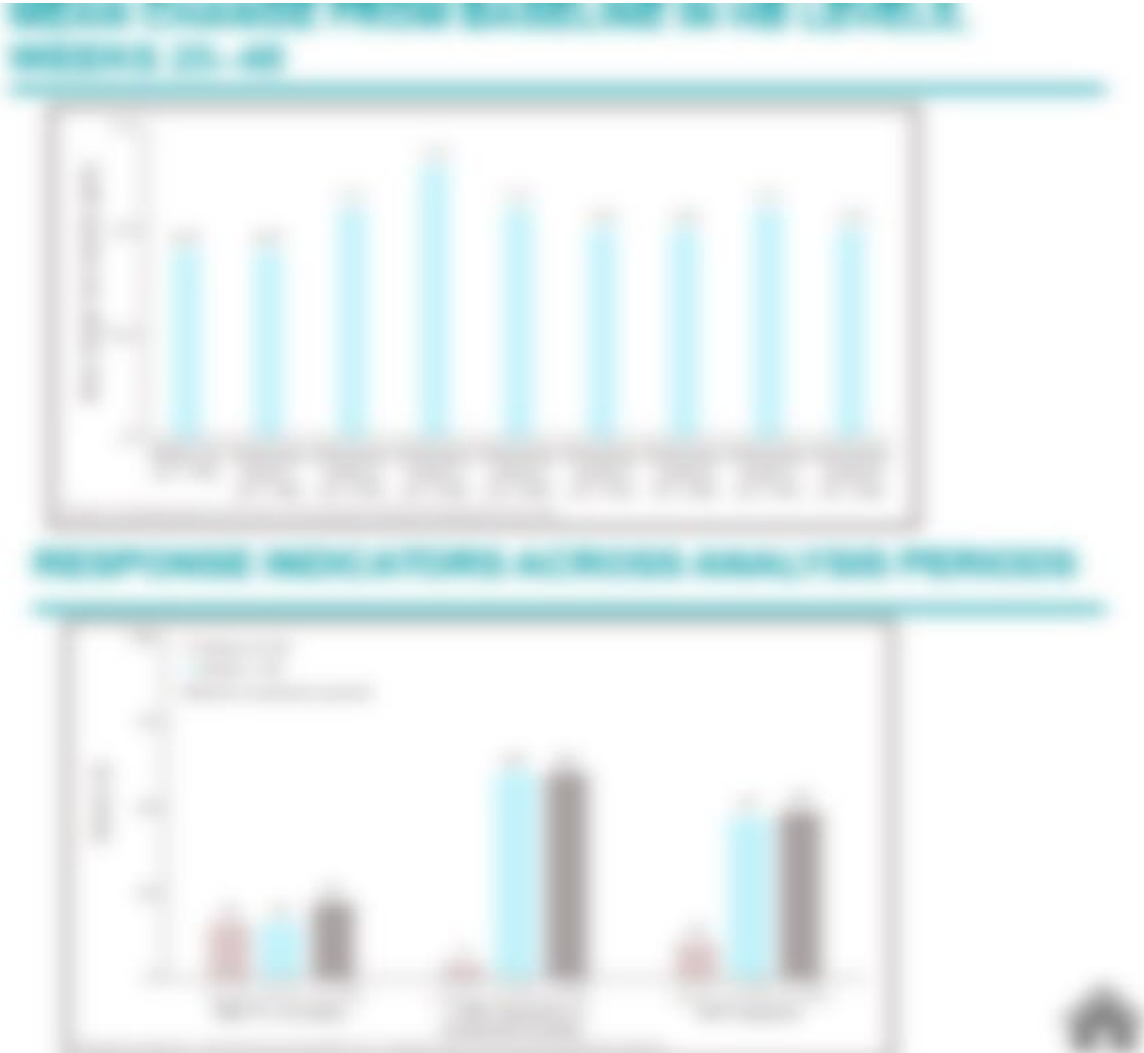
Li Y, et al. 2024 ASCO GI; Abstract LBA244

STUDY POPULATION AND METHODS

> 391 pts with resectable thoracic, locally advanced ESCC were

TUMOR REGRESSION



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Key Insights

Esophageal Cancers

Experts Discussed Results From Trials Evaluating IO Combinations for Advanced Esophageal Cancers (1/2)

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KEYNOTE-590

ongoing trials will help clarify the optimal sequencing of agents

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Experts Discussed Results From Trials Evaluating IO Combinations for Advanced Esophageal Cancers (2/2)

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CheckMate 648

ongoing trials will help clarify the optimal sequencing of agents

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Experts Considered Novel Investigational Agents for Esophageal Cancers

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SKYSCRAPER-08

ongoing trials will help clarify the optimal sequencing of agents

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Conference Highlights

Gastric and Gastroesophageal Junction (GEJ) Cancers

Pembrolizumab + FLOT vs FLOT as neoadjuvant and adjuvant therapy in locally advanced G/GEJ cancer: Interim analysis of KEYNOTE-585

Al-Batran E, et al. 2024 ASCO GI; Abstract 247

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STUDY POPULATION AND METHODS

- 804 pts with locally advanced G/GEJ cancer were randomized to

EVENT-FREE SURVIVAL: FLOT COHORT

pCR to FLOT ± durvalumab in resectable G/GEJ cancer: Subgroup analysis by region from the phase III MATTERHORN study

Janjigian YY, et al. 2024 ASCO GI; Abstract LBA246

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STUDY POPULATION AND METHODS

- 948 pts with resectable stage II, III, or IVA G/GEJ cancer were

PATHOLOGIC COMPLETE RESPONSE

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Key Insights

Gastric and Gastroesophageal Junction (GEJ) Cancers

Experts Discussed Perioperative Clinical Trials for G/GEJ Cancers

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KEYNOTE-585 AND MATTERHORN

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a CLEOPATRA-like regimen (a taxane plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients.
- Most experts are using trastuzumab deruxtecan third-line, but will prioritize the tucatinib triplet for patients with evidence of brain metastases.
- The tucatinib triplet may also be used in the second-line setting, before T-DM1, for patients with documented brain metastases.
  - If tucatinib is used second-line, experts are divided on whether they would currently use T-DM1 or trastuzumab deruxtecan third-line.
    - Results of the ongoing DESTINY-Breast03 trial comparing trastuzumab deruxtecan vs T-DM1 will help to clarify the optimal sequence of these ADCs.
- Trastuzumab deruxtecan and the tucatinib triplet may also be used earlier than third-line in patients who recur following treatment with trastuzumab, pertuzumab, and T-DM1 in the (neo)adjuvant setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the sequencing of these new agents (eg, 3 drugs vs 1 drug, concern about hair loss vs diarrhea).
- The impressive efficacy of trastuzumab deruxtecan and the tucatinib regimen have pushed other options, such as trastuzumab-chemotherapy combinations, neratinib, and margetuximab, to later lines of therapy.

Dr Pegram:
We used to run out of good options and we would just regress to the mean of chemotherapy plus trastuzumab in the salvage setting, but now we have so many great choices that that really takes a backseat. It's really been exciting to have multiple options for patients after T-DM1 — again, practice changing, unprecedented

Experts Considered Implications of MSI Status in G/GEJ Cancers

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PERIOPERATIVE ICIs IN NON–MSI-H CANCERS

Experts Discussed Current Standards in Perioperative Therapy for Resectable G/GEJ Cancers

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FLOT

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a CLOSE/FLOT4-like regimen (a taxane plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients.
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Conference Highlights

Pancreatic Cancer and Biliary Tract Cancer

Alternating gem–*nab*-pac and gem monotherapy or continuous gem–*nab*-pac after induction for first-line mPC: Phase II ALPACA study

Dorman K, et al. 2024 ASCO GI; Abstract 605

EPICS

STUDY POPULATION AND METHODS

- 325 pts with metastatic pancreatic cancer received 3 cycles of

PROGRESSION-FREE SURVIVAL

Preliminary activity and safety results of *KRAS* G12C inhibitor glecirasib (JAB-21822) in patients with pancreatic cancer and other solid tumors

Li J, et al. 2024 ASCO GI; Abstract 604

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STUDY POPULATION AND METHODS

- 50 pts with previously treated G12C cancers (31 PDAC and 19

PDAC: DURATION OF TREATMENT

AMPLIFY-7P: Phase I/II study of adjuvant amphiphile immunotherapy ELI-002 7P for G12D, G12R, G12V, G12C, G12A, G12S, G13D *KRAS*-mut PDAC

Wainberg ZA, et al. 2024 ASCO GI; Abstract TPS720

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BACKGROUND

> ELI-002 7P is a lymph node-targeted immunotherapy composed

THERAPEUTIC VACCINE DESIGN

ARC-8: Phase I/Ib randomized study of quemliclustat + gem–*nab*-pac ± zimberelimab in patients with treatment-naive metastatic PDAC

Wainberg ZA, et al. 2024 ASCO GI; Abstract 665

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STUDY POPULATION AND METHODS

- 122 pts with untreated mPDAC were treated with Q 100 mg

OVERALL SURVIVAL

[177Lu]Lu-DOTATATE in newly diagnosed advanced grade 2 or 3 well-differentiated gastroenteropancreatic NETs: Phase III NETTER-2 study

Singh S, et al. 2024 ASCO GI; Abstract LBA588

EPICS

STUDY POPULATION AND METHODS

- 226 pts with well-differentiated high-grade G2 or G3 (Ki-67 ≥10%

PROGRESSION-FREE SURVIVAL

Atezolizumab + chemotherapy ± bevacizumab in advanced biliary tract cancer: Results from a randomized phase II trial (IMbrave151)

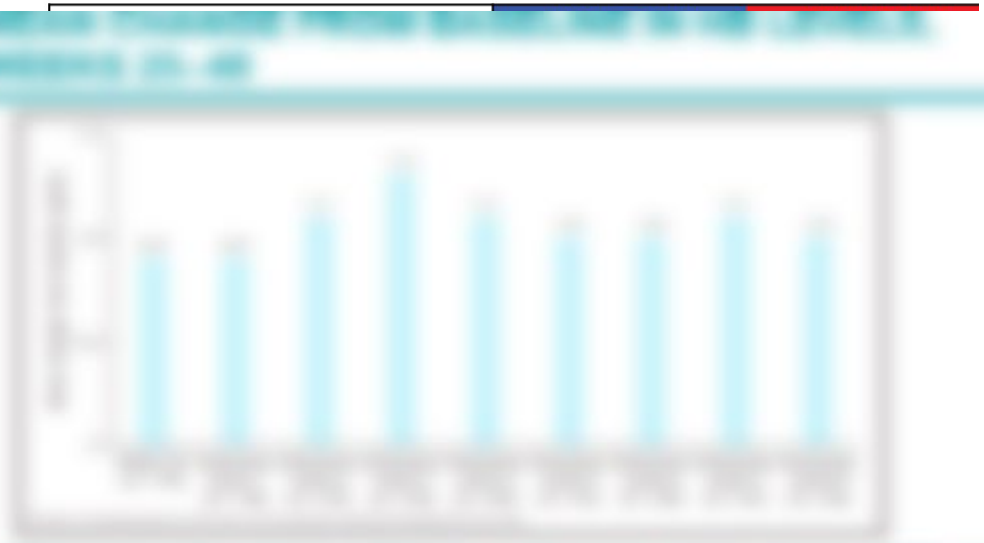
El-Khoueiry AB, et al. 2024 ASCO GI; Abstract 435

EPICS

STUDY POPULATION AND METHODS

- 162 pts with previously untreated advanced biliary tract cancer

PROGRESSION-FREE SURVIVAL



Phase II results of FGFR1-3 inhibitor tinengotinib as monotherapy in patients with advanced/metastatic cholangiocarcinoma

Javle MM, et al. 2024 ASCO GI; Abstract 434

EPICS

STUDY POPULATION AND METHODS

- 55 pts with advanced or metastatic cholangiocarcinoma were

BEST OVERALL RESPONSE

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Key Insights

Pancreatic Cancer and Biliary Tract Cancer

Experts Discussed Practical Strategies to Improve Current Regimens for Metastatic Pancreatic Cancer

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ALPACA

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Experts Speculated on RAS-Targeted Strategies for Pancreatic Cancer

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RAS-TARGETED TKIs

Experts Debated Radioligand Approaches for NETs

EPICS

NETTER-2

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Experts Considered Novel Agents for the Treatment of Pancreatic and Biliary Tract Cancers

EPICS

ARC-8

ongoing trials will help clarify the optimal sequencing of agents

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[redacted]

Progress

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APTITUDE HEALTH®

US 5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Wilhelmina van Pruisenweg 104
2595 AN The Hague, the Netherlands

UK 6th Floor, 2 Kingdom Street
London, W2 6BD, United Kingdom

aptitudehealth.com