



EPICS

Conference Coverage: ASCO GI 2024 Highlights

January 24, 2024

Full Report

Content	Slide
Meeting Snapshot	3 ➔
Faculty Panel	4 ➔
Meeting Agenda	5 ➔
Strategic Recommendations	7 ➔
Colorectal Cancer – Systemic Therapy	11 ➔
Colorectal Cancer – Biomarkers	22 ➔
Hepatocellular Carcinoma	32 ➔
Esophageal Cancer	40 ➔
Gastric and Gastroesophageal Junction (GEJ) Cancers	50 ➔
Pancreatic and Biliary Tract Cancers	57 ➔

EPICS

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

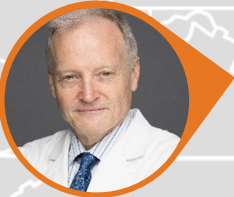
Panel Consisting of 5 US and 3 EU GI Cancer Experts



Sunnie Kim, MD
University of Colorado
Cancer Center



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



Chair
John Marshall, MD
Georgetown Lombardi
Comprehensive Cancer Center



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



Reetu Mukherji, MD
Georgetown Lombardi
Comprehensive Cancer Center



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



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



Fotios Loupakis, MD, PhD
Veneto Institute of Oncology

Meeting Agenda (1/2)

EPICS

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	<i>Break</i>	



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



EPICS

Conference Highlights

Colorectal Cancer – Systemic Therapy

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

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

[Blurred text area containing study details]



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

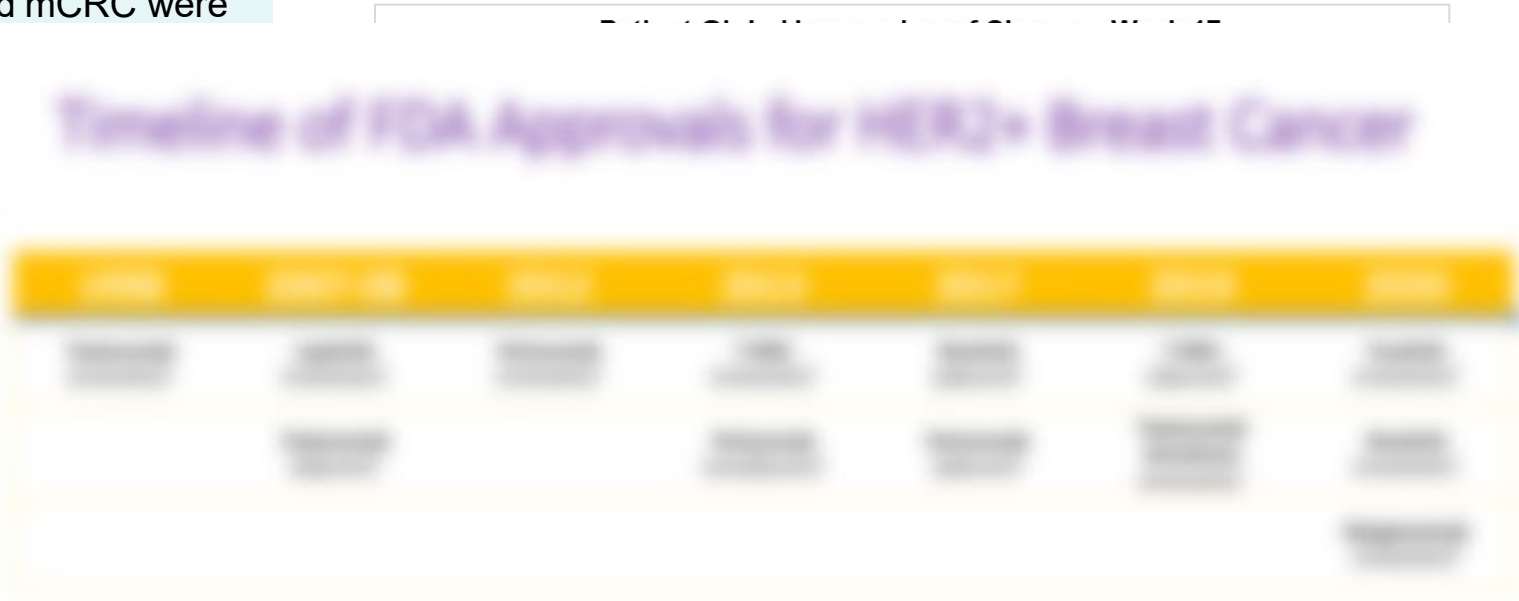
Modest D, et al. 2024 ASCO GI; Abstract 10

STUDY POPULATION AND METHODS

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

PATIENT PERCEPTION OF OVERALL STATUS (WEEK 17)

[Blurred text area containing study details]



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

STUDY POPULATION AND METHODS

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

SPIDER PLOT OF EVALUABLE PATIENTS

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Approvals	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0



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

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

STUDY POPULATION AND METHODS

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

PATHOLOGIC TUMOR REDUCTIONS

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	Year	Year	Year	Year	Year	Year
2009	2010	2011	2012	2013	2014	2015
	2016	2017	2018	2019	2020	2021
						2022



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

STUDY POPULATION AND METHODS

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

ANTITUMOR ACTIVITY

[Blurred text area containing study details]



EPICS

Key Insights

Colorectal Cancer – Systemic Therapy

Experts Discussed Immunotherapies for MSI-H mCRC

CheckMate 8HW

Immunotherapy will help identify the optimal sequencing of agents

- 1. Experts are still using a combination of immunotherapy agents, such as pembrolizumab and nivolumab, followed by TIGIT, according to most patients.
- 2. Most experts are using immunotherapy combination therapies, but will prioritize the treatment order for patients with evidence of tumor infiltration.
- 3. The treatment order may also be used in the second-line setting, before TIGIT, for patients with documented tumor infiltration.
 - 1. Providers in some scenarios, experts are divided on whether they would currently use TIGIT as immunotherapy combination therapy.
 - 2. Results of the ongoing IMbrave150 trial comparing immunotherapy combination as TIGIT will help to clarify the optimal sequencing of these agents.
- 4. Immunotherapy combination and the treatment order may also be used earlier than starting a patient who was following treatment with immunotherapy, pembrolizumab, and TIGIT in the second-line setting, but this represents a small fraction of patients.
- 5. Future combination use also looks into the sequencing of these two agents (eg, T drug as 1 drug, versus about how to combine).
- 6. The impressive efficacy of immunotherapy combination and the treatment order have opened other options, such as immunotherapy combination, nivolumab, and pembrolizumab, in other lines of therapy.



Dr. [Name] discussed the importance of immunotherapy in the treatment of MSI-H mCRC. He highlighted the role of pembrolizumab and nivolumab in combination therapy, and the potential of TIGIT as a third agent. He also discussed the importance of sequencing these agents and the role of tumor infiltration in treatment decisions. He mentioned the ongoing IMbrave150 trial and the potential of immunotherapy combination as TIGIT. He also discussed the use of immunotherapy combination and the treatment order in the second-line setting, and the potential of immunotherapy combination and the treatment order in the first-line setting. He mentioned the importance of sequencing these agents and the role of tumor infiltration in treatment decisions. He also discussed the use of immunotherapy combination and the treatment order in the second-line setting, and the potential of immunotherapy combination and the treatment order in the first-line setting.

Experts Evaluated Investigational Immunotherapeutic Agents for CRC

NEST-1

Supporting trials will help identify the optimal sequencing of agents

- 1. Experts are all using a 100mg/100mg dose regimen of nivolumab and ipilimumab therapy, followed by TIGIT, according to most patients.
- 2. Most experts are using nivolumab monotherapy therapy, but all prescribe the nivolumab agent for patients with evidence of tumor progression.
- 3. The nivolumab agent may also be used in the maintenance setting, either TIGIT, for patients with documented tumor progression.
 - 1. Provided a good assessment, experts are divided on whether they would currently use TIGIT as monotherapy therapy.
 - 2. Results of the ongoing NCT02894790 trial comparing nivolumab monotherapy vs TIGIT will help to clarify the optimal sequencing of these agents.
- 4. Nivolumab monotherapy and the nivolumab agent may also be used earlier than starting a patient who was following treatment with nivolumab, ipilimumab, and TIGIT in the maintenance setting, but this represents a small fraction of patients.
- 5. Future assessments will also focus on the sequencing of these two agents (eg, TIGIT as 1st drug, nivolumab second line or in first-line).
- 6. The relative efficacy of nivolumab monotherapy and the nivolumab agent have opened other options, such as nivolumab chemotherapy combinations, nivolumab and ipilimumab, in late lines of therapy.



Dr. [Name]
The agent is not used as first line and we would not expect to be used in the maintenance setting. We would use it in the maintenance setting, but we do not see any great change that that will make a difference to what we are seeing in our clinical practice. We would use it in the maintenance setting.



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

IO IN MSS CRC

...speculating on a potential role for combination immunotherapies in MSS CRC

- 1. Experts are still using a combination of immunotherapies, including checkpoint inhibitors, to treat patients.
- 2. Some experts are using combination immunotherapies, but all provided the treatment option for patients with evidence of tumor metastases.
- 3. The treatment option may also be used in the adjuvant setting, either T1DM, for patients with microsatellite stable metastases.
 - 1. Provided a good opportunity, experts are divided as to whether they would currently use T1DM as immunotherapy, combination therapy.
 - 1. Results of the ongoing IM9301 (nivolumab plus combination immunotherapy) in MSS CRC will help to clarify the optimal sequencing of these 400g.
- 4. Immunotherapy, combination, and the treatment option may also be used earlier than disease in patients who were following treatment with immunotherapy, combination, and T1DM in the metastatic setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these new agents (eg, T1DM vs 1 drug, versus dual use in MSS CRC).
- 6. The impressive efficacy of immunotherapy, combination, and the treatment option have opened other options, such as immunotherapy combination, nivolumab, and combination, in MSS CRC.



...speculating on a potential role for combination immunotherapies in MSS CRC

The speaker is currently using a combination of immunotherapies, including checkpoint inhibitors, to treat patients. Some experts are using combination immunotherapies, but all provided the treatment option for patients with evidence of tumor metastases. The treatment option may also be used in the adjuvant setting, either T1DM, for patients with microsatellite stable metastases. Provided a good opportunity, experts are divided as to whether they would currently use T1DM as immunotherapy, combination therapy. Results of the ongoing IM9301 (nivolumab plus combination immunotherapy) in MSS CRC will help to clarify the optimal sequencing of these 400g. Immunotherapy, combination, and the treatment option may also be used earlier than disease in patients who were following treatment with immunotherapy, combination, and T1DM in the metastatic setting, but this represents a small fraction of patients. Patient preferences can also factor into the sequencing of these new agents (eg, T1DM vs 1 drug, versus dual use in MSS CRC). The impressive efficacy of immunotherapy, combination, and the treatment option have opened other options, such as immunotherapy combination, nivolumab, and combination, in MSS CRC.

Experts Considered Novel Targeted Approaches in mCRC

CodeBreakK 300

Experts will discuss the optimal sequencing of agents

- 1. Experts will discuss the optimal sequencing of agents in the treatment of mCRC, including the use of immunotherapy and targeted therapy, followed by TDMT, as well as the use of immunotherapy and targeted therapy in the treatment of mCRC.
- 2. The use of immunotherapy and targeted therapy in the treatment of mCRC will be discussed, including the use of immunotherapy and targeted therapy in the treatment of mCRC.
- 3. The use of immunotherapy and targeted therapy in the treatment of mCRC will be discussed, including the use of immunotherapy and targeted therapy in the treatment of mCRC.
- 4. The use of immunotherapy and targeted therapy in the treatment of mCRC will be discussed, including the use of immunotherapy and targeted therapy in the treatment of mCRC.
- 5. The use of immunotherapy and targeted therapy in the treatment of mCRC will be discussed, including the use of immunotherapy and targeted therapy in the treatment of mCRC.
- 6. The use of immunotherapy and targeted therapy in the treatment of mCRC will be discussed, including the use of immunotherapy and targeted therapy in the treatment of mCRC.
- 7. The use of immunotherapy and targeted therapy in the treatment of mCRC will be discussed, including the use of immunotherapy and targeted therapy in the treatment of mCRC.
- 8. The use of immunotherapy and targeted therapy in the treatment of mCRC will be discussed, including the use of immunotherapy and targeted therapy in the treatment of mCRC.



Experts will discuss the optimal sequencing of agents

Experts will discuss the optimal sequencing of agents in the treatment of mCRC, including the use of immunotherapy and targeted therapy, followed by TDMT, as well as the use of immunotherapy and targeted therapy in the treatment of mCRC.



EPICS

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

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

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

STUDY POPULATION AND METHODS

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

ctDNA CLEARANCE

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

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

STUDY POPULATION AND METHODS

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

OS BENEFIT BY SIDEDNESS AND METASTATIC SITES



EPICS

Key Insights

Colorectal Cancer – Biomarkers

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

ctDNA TESTING – STRENGTHS AND LIMITATIONS

Supporting trials will help clarify the optimal sequencing of agents.

- Experts are still using a combination of the regimen of immunotherapy and chemotherapy, followed by TDMT, according to most patients.
- Most experts are using immunotherapy, chemotherapy, and TDMT, but will probably be looking for patients with evidence of tumor resistance.
- The limited data may also be used in the adjuvant setting, before TDMT, in patients with immunotherapy resistance.
 - Provided a good assessment, experts are divided on whether they would consider use TDMT in immunotherapy, chemotherapy, and TDMT.
 - Results of the ongoing IMbrave150 trial comparing immunotherapy monotherapy to TDMT will help to clarify the optimal sequencing of these agents.
- Immunotherapy, chemotherapy, and the limited data may also be used before the starting of patients who were following treatment with immunotherapy, chemotherapy, and TDMT in the immunotherapy setting, but this represents a small number of patients.
- Future combination use also looks into the sequencing of these two agents (eg, TDMT or TDMT, immunotherapy, chemotherapy).
- The comparative efficacy of immunotherapy, chemotherapy, and the limited regimen have several other options, such as immunotherapy, chemotherapy, immunotherapy, and immunotherapy, in the form of therapy.



Dr. [Name] is a senior advisor at [Organization]. He has been involved in the development of [Product/Service] and has a strong background in [Field]. He is currently leading the [Project/Initiative] and is focused on [Goal/Objective].

Experts Discussed the Current Use of ctDNA Testing in the Clinic

ctDNA IN CLINICAL DECISION-MAKING

Key findings from the expert panel discussion include:

- Experts are not using ctDNA to guide treatment decisions in the metastatic setting, but are using it to monitor response to treatment.
- The majority of experts are using ctDNA to monitor response to treatment, but all provided the benefits of ctDNA to patients with evidence of tumor progression.
- The majority of experts are using ctDNA in the metastatic setting, but 100% of experts are using it to monitor response to treatment.
 - Provided a clear indication, experts are divided on whether they would currently use ctDNA to guide treatment decisions.
 - Results of the ongoing NCT02835769 comparing trastuzumab monotherapy to trastuzumab plus ctDNA-guided therapy will help to clarify the optimal use of ctDNA in the metastatic setting.
- Trastuzumab monotherapy and the majority of experts are using ctDNA to monitor response to treatment in patients who were following treatment with trastuzumab, pertuzumab, and TDM1 in the metastatic setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the use of ctDNA in the metastatic setting.
- The importance of ctDNA testing in the metastatic setting has been explored in other settings, such as trastuzumab chemotherapy combinations, resection, and immunotherapy, in the form of therapy.



Dr. [Name] is a leading expert in the field of ctDNA testing and its application in clinical decision-making. He discussed the current use of ctDNA testing in the clinic and the challenges associated with its use. He emphasized the importance of ctDNA testing in the metastatic setting and the need for further research to clarify its optimal use. He also discussed the importance of patient preferences in the use of ctDNA testing.



Experts Considered Clinical and Biologic Markers for Tailoring Targeted Therapy Selection

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

Experts consider the optimal sequencing of agents in first-line therapy with VEGF- or EGFR-targeted mAbs and antiangiogenic therapy, followed by TDMT, according to their patients.

These experts are using combination approaches, but will consider the limited data for patients with evidence of tumor progression.

The limited data may also be used in the second-line setting, before TDMT, for patients with documented tumor progression.

- Provided a good performance, experts are divided on whether they would consider use TDMT in combination, sequential therapy.
- Results of the ongoing ASTRIS trial comparing combination treatment as TDMT will help to clarify the optimal sequencing of these agents.

Combination approaches and the limited data may also be used earlier than starting a patient who never following treatment with combination, sequential, and TDMT in the second-line setting, but this represents a small number of patients.

Future combination use also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 2 drugs).

The comparative efficacy of combination approaches and the limited regimen have opened other options, such as combination chemotherapy, combination, sequential, and combination, in the first line of therapy.



...the optimal sequencing of agents in first-line therapy with VEGF- or EGFR-targeted mAbs and antiangiogenic therapy, followed by TDMT, according to their patients.

These experts are using combination approaches, but will consider the limited data for patients with evidence of tumor progression.

The limited data may also be used in the second-line setting, before TDMT, for patients with documented tumor progression.

- Provided a good performance, experts are divided on whether they would consider use TDMT in combination, sequential therapy.
- Results of the ongoing ASTRIS trial comparing combination treatment as TDMT will help to clarify the optimal sequencing of these agents.

Combination approaches and the limited data may also be used earlier than starting a patient who never following treatment with combination, sequential, and TDMT in the second-line setting, but this represents a small number of patients.

Future combination use also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 2 drugs).

The comparative efficacy of combination approaches and the limited regimen have opened other options, such as combination chemotherapy, combination, sequential, and combination, in the first line of therapy.

EPICS

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

STUDY POPULATION AND METHODS

> 616 pts with embolization-eligible unresectable HCC were

PROGRESSION-FREE SURVIVAL

PROGRESSION-FREE SURVIVAL IN THE INTENTION-TO-TREAT POPULATION



RESPONSE EVALUATION BY TREATMENT GROUP



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

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

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

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

STUDY POPULATION AND METHODS

> 30 pts with untreated unresectable or metastatic HCC were

ANTITUMOR ACTIVITY (RECIST v1.1)

Figure 1: Overall Survival (OS) in the Intent-to-Treat (ITT) Population



Figure 2: Response Rate (RR) in the ITT Population



EPICS

Key Insights

Hepatocellular Carcinoma

Experts Discussed Combining Systemic and Locoregional Therapies for Unresectable HCC

TACE-BASED COMBINATIONS

Key points from the discussion include:

- 1. Experts are still using a combination of systemic and locoregional therapies for unresectable HCC, but the combination is still evolving.
- 2. The combination of systemic and locoregional therapies is still evolving, but all providers are looking for patients with evidence of liver metastases.
- 3. The combination of systemic and locoregional therapies is still evolving, but all providers are looking for patients with evidence of liver metastases.
 - Providers are still discussing whether they would consider using TACE in combination with systemic therapy.
 - Results of the ongoing trials that discuss combining locoregional therapies with TACE will help to clarify the optimal sequencing of these therapies.
- 4. Systemic therapies and the locoregional therapies may also be used earlier than starting a patient on any other treatment with systemic, locoregional, and TACE in the combination setting, but this approach is still limited to a small number of patients.
- 5. Future combination use may focus on the sequencing of these two agents (eg, TACE first or TACE second) about how best to combine.
- 6. The comparative efficacy of locoregional therapies and the locoregional therapies have several other options, such as locoregional chemotherapy, radiotherapy, resection, and transplantation, in the line of therapy.



Dr. [Name]
[Blurred text describing the speaker's role and the content of their presentation.]

Experts Considered Investigational Agents and Future Directions in HCC

IL-27 INHIBITION

Supporting trials will help identify the optimal sequencing of agents.

- Experts are still using a combination of agents, including immunotherapy and chemotherapy, followed by TDMT, according to most speakers.
- More experts are using immunotherapy, checkpoint inhibitors, but still providing the treatment first to patients with evidence of liver metastases.
- The treatment order may also be used in the second-line setting, before TDMT, for patients with documented liver metastases.
 - Provided to oral chemotherapy, experts are divided on whether they would currently use TDMT in immunotherapy, checkpoint inhibitors.
 - Results of the ongoing SARCIN (Sarcin) trial comparing immunotherapy, checkpoint inhibitors as TDMT will help to clarify the optimal sequencing of these agents.
- Immunotherapy, checkpoint inhibitors and the treatment order may also be used earlier than starting a patient who was following treatment with immunotherapy, checkpoint inhibitors, and TDMT in the second-line setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, toxicity about how long it lasts).
- The sequencing efficacy of immunotherapy, checkpoint inhibitors and the treatment order have entered other options, such as immunotherapy, chemotherapy, checkpoint inhibitors, and immunotherapy, in the form of therapy.



Dr. [Name]
 Dr. [Name] is an expert in the field of immunotherapy and checkpoint inhibitors. He is currently working on the sequencing of immunotherapy, checkpoint inhibitors, and TDMT in HCC. He is also interested in the use of immunotherapy, checkpoint inhibitors, and TDMT in the second-line setting, before TDMT, for patients with documented liver metastases.



EPICS

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

STUDY POPULATION AND METHODS

> 749 pts with locally advanced/metastatic adenocarcinoma or

OVERALL SURVIVAL: ITT POPULATION

Overall Survival: ITT Population



Response Rate: 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

STUDY POPULATION AND METHODS

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

Q-TWiST METHODS

Figure 1: Kaplan-Meier survival curves for overall survival (OS) in the Q-TWiST analysis. The x-axis represents time in months, and the y-axis represents survival probability. The curves compare the Nivolumab + Ipilimumab (N+I) group (blue line) and the Control (CT) group (red line).



Figure 2: Bar chart showing the proportion of patients with grade 3-4 adverse events (AE) for the N+I and CT groups across various categories.



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

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

STUDY POPULATION AND METHODS

> 461 pts with previously untreated unresectable advanced or

OVERALL SURVIVAL

Figure 1: Overall Survival (OS) in the Intention-to-Treat Population



Figure 2: Response Rate (RR) in the Intention-to-Treat Population



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

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

STUDY POPULATION AND METHODS

> 391 pts with resectable thoracic, locally advanced ESCC were

TUMOR REGRESSION



EPICS

Key Insights

Esophageal Cancers

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

KEYNOTE-590

Keynote-590 will help clarify the optimal sequencing of agents.

- 1. Experts are still using a combination of immunotherapy and chemotherapy, but the sequencing of these agents is still unclear.
- 2. Some experts are using immunotherapy as a first-line treatment, but all patients are not responding to immunotherapy.
- 3. The sequencing of immunotherapy and chemotherapy is still unclear, but the sequencing of these agents is still unclear.
- 4. Experts are still using a combination of immunotherapy and chemotherapy, but the sequencing of these agents is still unclear.
- 5. The sequencing of immunotherapy and chemotherapy is still unclear, but the sequencing of these agents is still unclear.
- 6. Experts are still using a combination of immunotherapy and chemotherapy, but the sequencing of these agents is still unclear.
- 7. The sequencing of immunotherapy and chemotherapy is still unclear, but the sequencing of these agents is still unclear.



Dr. [Name] is a leading expert in the field of immunotherapy and chemotherapy. He has been a speaker at several international conferences and has published numerous articles on the topic. He is currently a member of the National Cancer Institute's Cancer Therapy Evaluation Program.



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

CheckMate 648

Experts will discuss the optimal sequencing of agents.

- Experts are still using a combination of immunotherapy and chemotherapy, but experts are also evaluating immunotherapy monotherapy, followed by TDMT, as a second option for some patients.
- Most experts are using immunotherapy monotherapy, but will probably use the second option for patients with evidence of prior metastases.
- The second option may also be used in the metastatic setting, before TDMT, for patients with documented prior metastases.
 - Presented at a panel discussion, experts are divided on whether they would currently use TDMT or immunotherapy monotherapy.
 - Results of the ongoing IMpower131 trial comparing immunotherapy monotherapy vs TDMT will help to clarify the optimal sequencing of these agents.
- Immunotherapy monotherapy and the second option may also be used earlier than starting a patient who never following treatment with immunotherapy, chemotherapy, and TDMT in the metastatic setting, but this represents a small fraction of patients.
- Future conferences can also focus on the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 2 drugs).
- The comparative efficacy of immunotherapy monotherapy and the second option have opened other options, such as immunotherapy chemotherapy combinations, second- and third-generation, or other lines of therapy.



Experts will discuss the optimal sequencing of agents.

Experts are still using a combination of immunotherapy and chemotherapy, but experts are also evaluating immunotherapy monotherapy, followed by TDMT, as a second option for some patients.

Most experts are using immunotherapy monotherapy, but will probably use the second option for patients with evidence of prior metastases.

The second option may also be used in the metastatic setting, before TDMT, for patients with documented prior metastases.

- Presented at a panel discussion, experts are divided on whether they would currently use TDMT or immunotherapy monotherapy.
- Results of the ongoing IMpower131 trial comparing immunotherapy monotherapy vs TDMT will help to clarify the optimal sequencing of these agents.

Immunotherapy monotherapy and the second option may also be used earlier than starting a patient who never following treatment with immunotherapy, chemotherapy, and TDMT in the metastatic setting, but this represents a small fraction of patients.

Future conferences can also focus on the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 2 drugs).

The comparative efficacy of immunotherapy monotherapy and the second option have opened other options, such as immunotherapy chemotherapy combinations, second- and third-generation, or other lines of therapy.

Experts Considered Novel Investigational Agents for Esophageal Cancers

SKYSCRAPER-08

Experts will evaluate the optimal sequencing of agents...

- 1. Experts will evaluate the optimal sequencing of agents...
- 2. Experts will evaluate the optimal sequencing of agents...
- 3. Experts will evaluate the optimal sequencing of agents...
- 4. Experts will evaluate the optimal sequencing of agents...
- 5. Experts will evaluate the optimal sequencing of agents...
- 6. Experts will evaluate the optimal sequencing of agents...
- 7. Experts will evaluate the optimal sequencing of agents...
- 8. Experts will evaluate the optimal sequencing of agents...
- 9. Experts will evaluate the optimal sequencing of agents...
- 10. Experts will evaluate the optimal sequencing of agents...



...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...

...the optimal sequencing of agents...



EPICS

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

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

STUDY POPULATION AND METHODS

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

PATHOLOGIC COMPLETE RESPONSE



EPICS

Key Insights

Gastric and Gastroesophageal Junction
(GEJ) Cancers

Experts Discussed Perioperative Clinical Trials for G/GEJ Cancers

KEYNOTE-585 AND MATTERHORN

Keynote-585 and Matterhorn are two phase III clinical trials comparing perioperative treatment for G/GEJ cancers. Keynote-585 compares a combination of trastuzumab, paclitaxel, and epirubicin with trastuzumab, paclitaxel, and epirubicin plus trastuzumab deruxtecan. Matterhorn compares a combination of trastuzumab, paclitaxel, and epirubicin with trastuzumab, paclitaxel, and epirubicin plus trastuzumab deruxtecan. Both trials are designed to evaluate the efficacy and safety of these regimens in patients with G/GEJ cancers. The results of these trials will help to determine the optimal treatment for these patients.

- 1. Keynote-585 is a phase III clinical trial comparing perioperative treatment for G/GEJ cancers. The trial compares a combination of trastuzumab, paclitaxel, and epirubicin with trastuzumab, paclitaxel, and epirubicin plus trastuzumab deruxtecan. The primary endpoint is overall survival.
- 2. Matterhorn is a phase III clinical trial comparing perioperative treatment for G/GEJ cancers. The trial compares a combination of trastuzumab, paclitaxel, and epirubicin with trastuzumab, paclitaxel, and epirubicin plus trastuzumab deruxtecan. The primary endpoint is overall survival.
- 3. Both trials are designed to evaluate the efficacy and safety of these regimens in patients with G/GEJ cancers. The results of these trials will help to determine the optimal treatment for these patients.
- 4. The results of these trials will help to determine the optimal treatment for these patients.



Keynote-585 and Matterhorn are two phase III clinical trials comparing perioperative treatment for G/GEJ cancers. Keynote-585 compares a combination of trastuzumab, paclitaxel, and epirubicin with trastuzumab, paclitaxel, and epirubicin plus trastuzumab deruxtecan. Matterhorn compares a combination of trastuzumab, paclitaxel, and epirubicin with trastuzumab, paclitaxel, and epirubicin plus trastuzumab deruxtecan. Both trials are designed to evaluate the efficacy and safety of these regimens in patients with G/GEJ cancers. The results of these trials will help to determine the optimal treatment for these patients.



EPICS

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

STUDY POPULATION AND METHODS

> 325 pts with metastatic pancreatic cancer received 3 cycles of

PROGRESSION-FREE SURVIVAL

PROGRESSION-FREE SURVIVAL AT 12 MONTHS



RESPONSE RATES AT 12 MONTHS



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

STUDY POPULATION AND METHODS

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

PDAC: DURATION OF TREATMENT

Figure 1: Duration of Treatment in PDAC Patients



Figure 2: Response Evaluation in PDAC Patients



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

BACKGROUND

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

THERAPEUTIC VACCINE DESIGN

Figure 1: Immunogenicity and clinical outcomes in the lymph node. (A) Bar chart showing immunogenicity (OD) for various KRAS mutations. (B) Bar chart showing clinical outcomes (OS, RFS, DFS) for various KRAS mutations.



Figure 2: Response rates in the lymph node. (A) Bar chart showing response rates (ORR) for various KRAS mutations. (B) Bar chart showing response rates (ORR) for various KRAS mutations.



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

STUDY POPULATION AND METHODS

> 122 pts with untreated mPDAC were treated with Q 100 mg,

OVERALL SURVIVAL

Overall Survival: Kaplan-Meier Plot



Response Rate: Bar Chart



[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

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

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

STUDY POPULATION AND METHODS

> 55 pts with advanced or metastatic cholangiocarcinoma were

BEST OVERALL RESPONSE



EPICS

Key Insights

Pancreatic Cancer and Biliary Tract Cancer

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

ALPACA

Supporting trials will help identify the optimal sequencing of agents.

- 1. Experts are still using a combination of the regimen of gemtuzabine plus metformin and gemtuzabine plus metformin, followed by FOLFIRI, gemtuzabine, for most patients.
- 2. Most experts are using metformin plus gemtuzabine, but all provided the limited data for patients with evidence of liver metastases.
- 3. The limited data may also be used in the second-line setting, before FOLFIRI, for patients with documented liver metastases.
 - Provided a good assessment, experts are divided on whether they would currently use FOLFIRI as a maintenance, second-line therapy.
 - Results of the ongoing trial that compared the sequencing metformin plus gemtuzabine as FOLFIRI will help to clarify the optimal sequencing of these drugs.
- 4. Metformin plus gemtuzabine and the limited data may also be used earlier than starting a patient who never followed treatment with metformin, gemtuzabine, and FOLFIRI in the second-line setting, but this represents a small number of patients.
- 5. Future conferences will also focus on the sequencing of these two agents (eg, 1 drug or 2 drug, versus when to use in therapy).
- 6. The comparative efficacy of metformin plus gemtuzabine and the limited regimen have opened other options, such as metformin plus chemotherapy combinations, gemtuzabine, and metformin, in the first-line therapy.



Dr. [Name]
[Blurred text]

Experts Speculated on RAS-Targeted Strategies for Pancreatic Cancer

RAS-TARGETED TKIs

Supporting trials will help clarify the optimal sequencing of agents.

- 1. Experts are still using a combination of the regimen of second-line metformin and gemtuzumab, followed by TDM-1, especially for most patients.
- 2. Other experts are using metformin, gemtuzumab, and TDM-1, but all providing the second-line option for patients with evidence of toxic resistance.
- 3. The second-line option may also be used in the second-line setting, before TDM-1, for patients with documented toxic resistance.
 - Provided to most participants, experts are divided on whether they would currently use TDM-1 as a maintenance treatment.
 - Results of the ongoing 001 trial (NCT01985509) comparing metformin, gemtuzumab, and TDM-1 will help to clarify the optimal sequencing of these agents.
- 4. Metformin, gemtuzumab, and the second-line option may also be used earlier than starting a patient who never followed treatment with metformin, gemtuzumab, and TDM-1 in the second-line setting, but this represents a small fraction of patients.
- 5. Future conferences can also focus on the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs drug-free).
- 6. The comparative efficacy of metformin, gemtuzumab, and the second-line option have opened other options, such as metformin, chemotherapy, gemtuzumab, and metformin, in the first-line setting.



Dr. [Name]
[Blurred text describing the speaker's role and the content of their presentation, which appears to be a discussion on the sequencing of RAS-targeted therapies in pancreatic cancer treatment.]



NETTER-2

Supporting trials will help clarify the optimal sequencing of agents.

- 1. Experts are still using a combination of the regimen of somatostatin analogs and conventional therapy, followed by TDM-1001, for most patients.
- 2. Most experts are using conventional therapeutic strategies, but will consider the limited data for patients with evidence of tumor progression.
- 3. The limited data may also be used in the second-line setting, before TDM-1001, for patients with documented tumor progression.
 - Provided to used sequentially, experts are divided on whether they would normally use TDM-1001 as a conventional therapeutic strategy.
 - Results of the ongoing 2017 trial (NCT01883001) comparing conventional treatment to TDM-1001 will help to clarify the optimal sequencing of these agents.
- 4. Conventional treatment and the limited data may also be used earlier than starting a patient who never following treatment with conventional, somatostatin, and TDM-1001 in the conventional setting, but this represents a small fraction of patients.
- 5. Future conferences can also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue).
- 6. The comparative efficacy of conventional treatment and the limited regimen have opened other options, such as conventional chemotherapy, combination, second, and third-line, in this line of therapy.



...the optimal sequencing of agents...
...the limited data may also be used in the second-line setting, before TDM-1001, for patients with documented tumor progression...
...the comparative efficacy of conventional treatment and the limited regimen have opened other options, such as conventional chemotherapy, combination, second, and third-line, in this line of therapy.

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


ARC-8

Meeting topics will help identify the optimal sequencing of agents.

- Experts are still using a combination of the regimen of gemtuzumab plus metformin and gemtuzumab plus metformin, followed by TDM1, gemtuzumab, for most patients.
- Most experts are using metformin plus gemtuzumab, but will probably use the combined regimen for patients with evidence of liver metastases.
- The combined regimen may also be used in the maintenance setting, before TDM1, for patients with documented liver metastases.
 - Provided to your organization, experts are divided on whether they would currently use TDM1 or metformin plus gemtuzumab.
 - Results of the ongoing 2017 trial assessing metformin plus gemtuzumab as TDM1 will help to clarify the optimal sequencing of these agents.
- Metformin plus gemtuzumab and the combined regimen may also be used earlier than starting a patient who never followed treatment with metformin plus gemtuzumab and TDM1 in the maintenance setting, but this represents a small fraction of patients.
- Future conferences can also focus on the sequencing of these two agents (eg, 1 drug or 2 drug, versus about how long to continue).
- The comparative efficacy of metformin plus gemtuzumab and the combined regimen have not been fully explored, such as metformin plus gemtuzumab combination, metformin and gemtuzumab, or other lines of therapy.



Dr. [Name] is a [Title] at [Institution]. He has been involved in the development of [Drug Name] and is currently leading a phase III trial comparing [Drug Name] to [Standard of Care] in patients with [Cancer Type]. He is also a member of the [Organization] and has published several papers on [Topic].



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](https://www.aptitudehealth.com)

