



EPICS

Congress Coverage: ASCO GI 2022 Highlights

January 26, 2022

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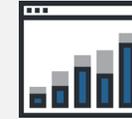
VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
January 26, 2022



**DISEASE STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



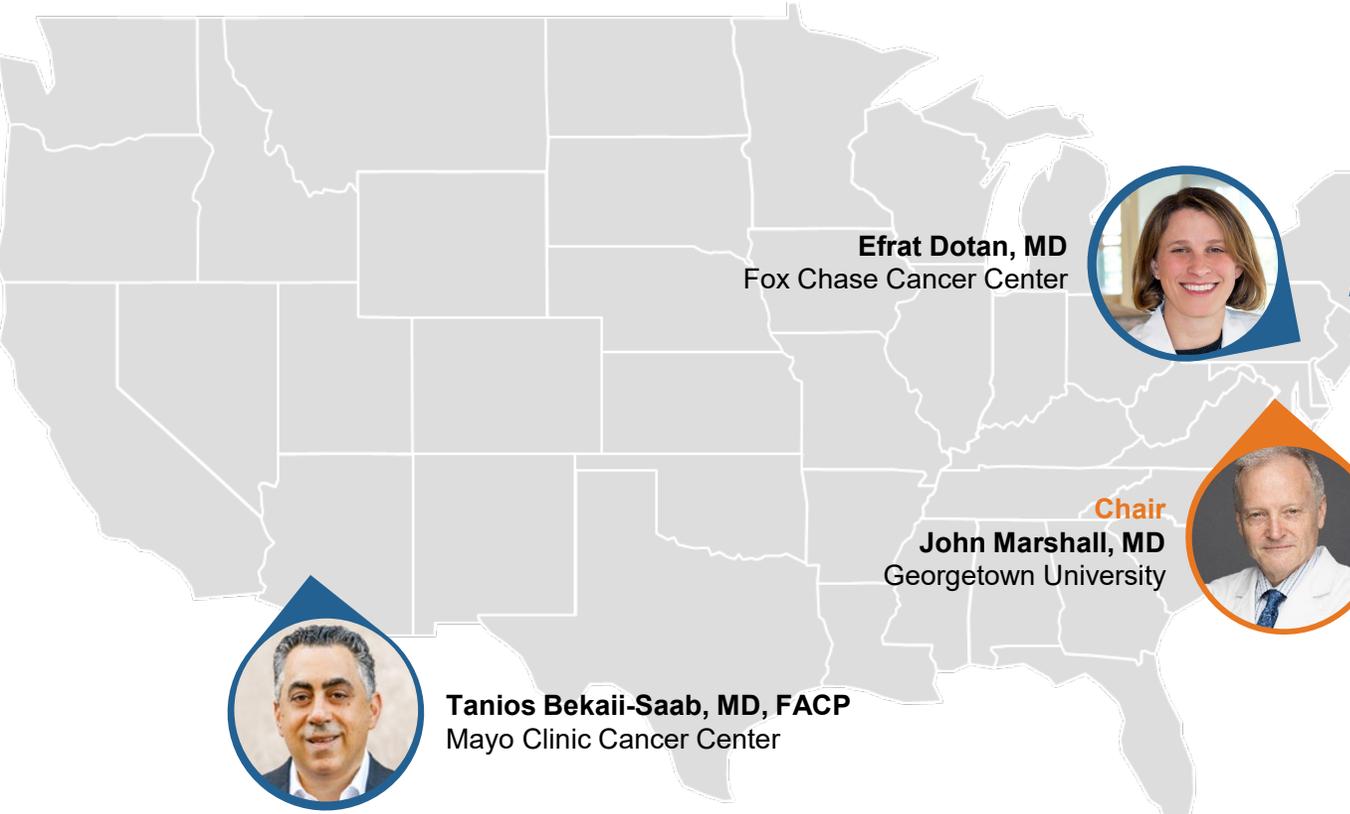
PANEL: Key experts in
GI malignancies

- > 4 from US
- > 4 from Europe



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

Panel Consisting of 4 US and 4 European GI Cancer Experts



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



Efrat Dotan, MD
Fox Chase Cancer Center



Chair
John Marshall, MD
Georgetown University



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



Dirk Arnold, MD, PhD
University of Hamburg



Gerald Prager, MD, PhD
University of Vienna



Julien Taieb, MD, PhD
University of Paris



Daniele Santini, MD, PhD
University of Rome



Meeting Agenda

| Time (EST) | Topic | Speaker/Moderator |
|---------------|--|---|
| 10.00 – 10.05 | Welcome and Introductions | John L. Marshall, MD |
| 10.05 – 10.10 | Metastatic Colorectal Cancer – Targeted Therapy | Efrat Dotan, MD |
| 10.10 – 10.30 | Discussion: Metastatic Colorectal Cancer – Targeted Therapy | Moderator: John L. Marshall, MD |
| 10.30 – 10.35 | Metastatic Colorectal Cancer – Targeted Therapy: Key Takeaways | Efrat Dotan, MD |
| 10.35 – 10.40 | Metastatic Colorectal Cancer – Immunotherapy | Daniele Santini, MD, PhD |
| 10.40 – 11.00 | Discussion: Colorectal Cancer – Immunotherapy | Moderator: John L. Marshall, MD |
| 11.00 – 11.05 | Metastatic Colorectal Cancer – Immunotherapy: Key Takeaways | Daniele Santini, MD, PhD |
| 11.05 – 11.15 | Hepatocellular Carcinoma | Tanios S. Bekaii-Saab, MD, FACP |
| 11.15 – 11.35 | Discussion: Hepatocellular Carcinoma | Moderator: John L. Marshall, MD |
| 11.35 – 11.40 | Hepatocellular Carcinoma – Key Takeaways | Tanios S. Bekaii-Saab, MD, FACP |
| 11.40 – 11.45 | Break | |
| 11.45 – 11.55 | Gastric and Gastroesophageal Junction (GEJ) Cancers | Julien Taieb, MD, PhD (Neoadjuvant and HER2+); David Ilson, MD, PhD (Immunotherapy) |
| 11.55 – 12.15 | Discussion: Gastric and Gastroesophageal Junction Cancers | Moderator: John L. Marshall, MD |
| 12.15 – 12.20 | Gastric and Gastroesophageal Junction Cancers – Key Takeaways | Julien Taieb, MD, PhD, and David Ilson, MD, PhD |
| 12.20 – 12.30 | Pancreatic Cancer and Biliary Tract Cancer | Dirk Arnold, MD, PhD (Pancreatic cancer) Gerald Prager, MD, PhD (Biliary tract cancer) |
| 12.30 – 12.50 | Discussion: Pancreatic Cancer and Biliary Tract Cancer | Moderator: John L. Marshall, MD |
| 12.50 – 12.55 | Pancreatic Cancer and Biliary Tract Cancer – Key Takeaways | Dirk Arnold, MD, PhD, and Gerald Prager, MD, PhD |
| 12.55 – 1.00 | Summary and Closing Remarks | John L. Marshall, MD |



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Congress Highlights

Metastatic Colorectal Cancer – Targeted Therapy

Phase I/II trial of encorafenib, cetuximab, and nivolumab in patients with microsatellite stable, BRAFV600E metastatic colorectal cancer

Morris et al. 2022, ASCO GI 12

STUDY POPULATION

100 patients with BRAFV600E metastatic colorectal cancer, microsatellite stable, who were not previously treated with systemic therapy for metastatic disease. The study population was divided into two groups: 50 patients in the control group and 50 patients in the treatment group. The control group received best supportive care, and the treatment group received encorafenib, cetuximab, and nivolumab. The primary endpoint was overall survival, and the secondary endpoints were progression-free survival and quality of life.

RESULTS

Median overall survival was significantly longer in the treatment group compared to the control group. The median overall survival in the treatment group was 12.1 months, compared to 8.5 months in the control group. The median progression-free survival in the treatment group was 6.2 months, compared to 4.5 months in the control group.

KEY CONCLUSIONS

Combining encorafenib, cetuximab, and nivolumab significantly improved overall survival and progression-free survival in patients with BRAFV600E metastatic colorectal cancer, microsatellite stable.

TOXICITY PROFILE



RESPONSE RATES



Trastuzumab deruxtecan in patients with HER2-expressing mCRC: Final results of the DESTINY-CRC01 phase 2 trial

Yoshino et al. 2022, ASCO GI 119

STUDY POPULATION

1. 100 patients with HER2-expressing mCRC, who were previously treated with 1-3 lines of systemic therapy, were enrolled in the study. The patients were randomized to receive either trastuzumab deruxtecan (n=50) or placebo (n=50). The primary endpoint was overall survival (OS) at 12 weeks. The secondary endpoints were progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL). The study was conducted in a multicenter, randomized, controlled, phase 2 trial.

RESULTS

1. The median OS was significantly longer in the trastuzumab deruxtecan group compared to the placebo group (12.1 weeks vs 8.5 weeks, p=0.001). The median PFS was also significantly longer in the trastuzumab deruxtecan group (4.2 weeks vs 3.1 weeks, p=0.001).

KEY CONCLUSIONS

Trastuzumab deruxtecan significantly improved OS and PFS in patients with HER2-expressing mCRC compared to placebo.

OS AND PFS FROM START OF TREATMENT TO 12 WEEKS



RESPONSE RATE AND TOXICITY PROFILE



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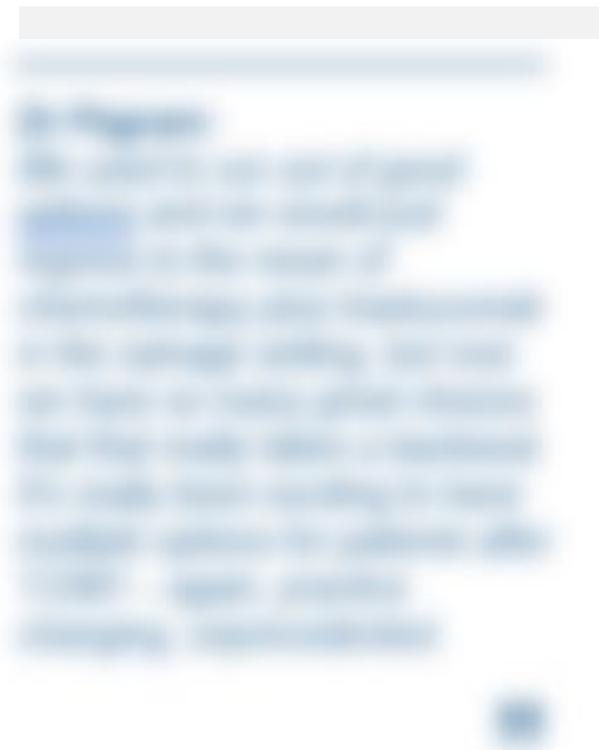
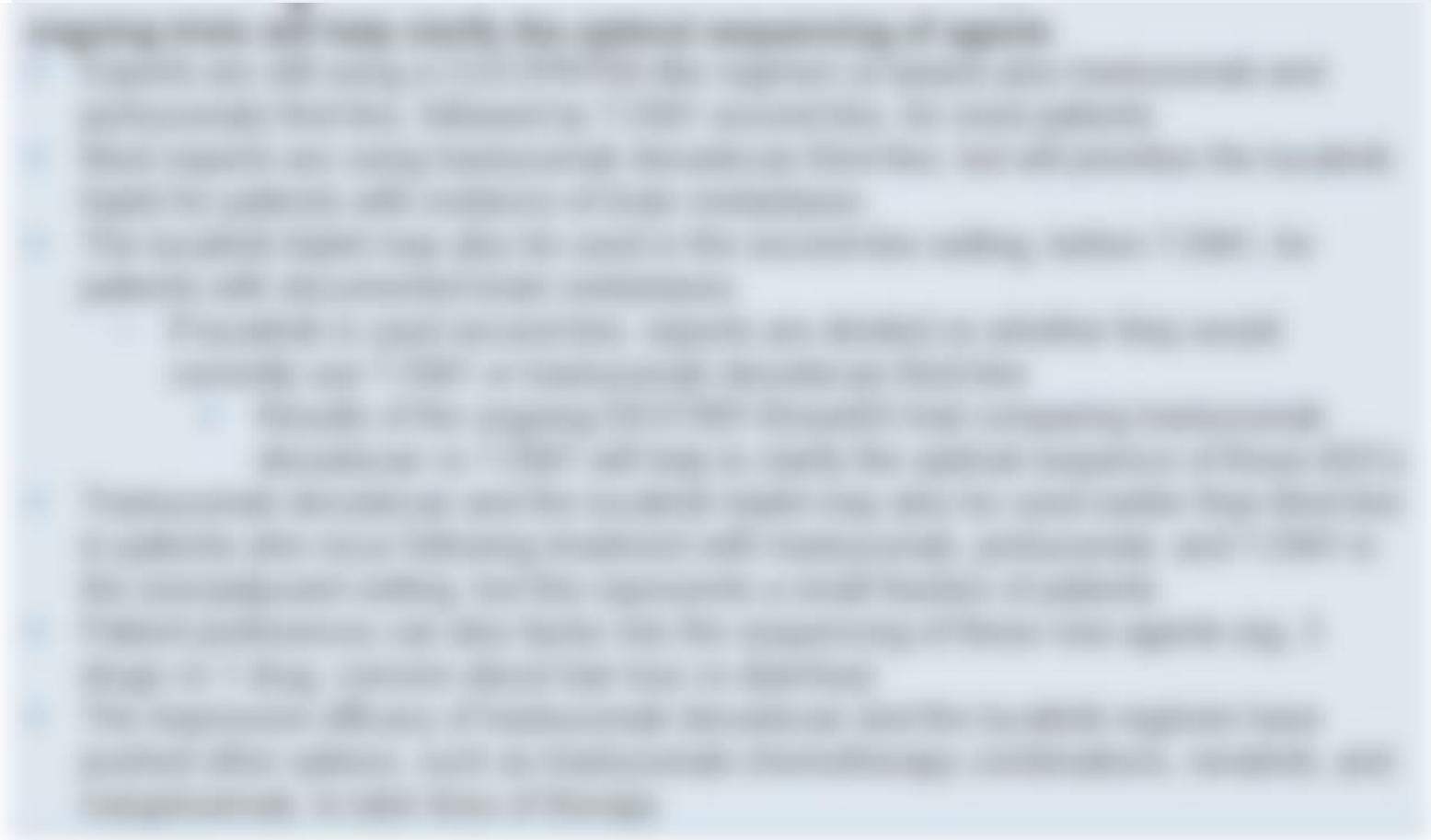
Key Insights

Metastatic Colorectal Cancer – Targeted Therapy

Experts Discussed Investigational Approaches for *BRAF* V600E-Mutated mCRC

ENCORAFENIB + CETUXIMAB + NIVOLUMAB

Most experts were cautiously enthusiastic about the results from the phase I/II trial of the



Experts Discussed Evolving Treatment Paradigms for HER2-Expressing mCRC

DESTINY-CRC01

BIOMARKER TESTING

The data from DESTINY-CRC01 investigating T-DXd in HER2-expressing mCRC are

Upfront NGS testing is considered SOC for all

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Congress Highlights

Metastatic Colorectal Cancer – Immunotherapy

Nivolumab + mFOLFOX6/BEV versus mFOLFOX6/BEV for 1L treatment of mCRC: Phase 2 results from CheckMate 9X8

Lenz et al. 2022, ASCO GI 8

STUDY POPULATION

Study Population

The population of the primary endpoint (OS) in the CheckMate 9X8 trial was patients who were randomized to a treatment for the primary effect of nivolumab compared with placebo in the first-line setting (1L).

- Patients who received nivolumab or placebo and mFOLFOX6/BEV in the first-line setting were included in the primary endpoint analysis. Patients who received nivolumab or placebo and mFOLFOX6/BEV in the second-line setting were excluded from the primary endpoint analysis.
- The OS in the nivolumab + mFOLFOX6/BEV group was significantly better than the OS in the placebo + mFOLFOX6/BEV group.

SAFETY

Safety

There were no safety issues with the use of "top up" nivolumab, which was used to increase nivolumab exposure to address nivolumab levels that were below the target.

- The addition of an anti-PD-1 drug (nivolumab) may increase the severity of immune-related adverse events (irAEs) compared with placebo. The addition of nivolumab to mFOLFOX6/BEV was associated with increased irAEs compared with placebo.
- The use of nivolumab may increase the risk of irAEs, including immune-related colitis, hepatitis, and pneumonitis. Patients who received nivolumab + mFOLFOX6/BEV had a higher rate of irAEs compared with placebo + mFOLFOX6/BEV.

Phase I/II study of regorafenib and pembrolizumab in refractory microsatellite stable colorectal cancer (MSSCRC)

Barzi et al. 2022, ASCO GI 15

STUDY POPULATION

> Pts with MSS mCRC refractory to or intolerant of chemotherapy

CONCLUSIONS

> The trial did not meet the primary endpoint

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Phase II trial of cabozantinib plus durvalumab in chemotherapy refractory advanced pMMR/MSS CRC: CAMILLA CRC cohort results

Saeed et al. 2022, ASCO GI 135

STUDY POPULATION

> Pts with pMMR/MSS CRC that had progressed on 2 or more lines

SAFETY

> The most frequent G1–2 AEs were fatigue (53%), nausea (42%),

[Blurred content area containing detailed study population and safety data]

One-year duration of nivolumab plus ipilimumab in patients with MSI/dMMR mCRC: Long-term follow-up of GERCOR NIPICOL

Cohen et al. 2022, ASCO GI 13

STUDY POPULATION

> Pts with MSI/dMMR mCRC previously treated with

OUTCOME

> Median follow-up was 34.5 months

Background

The addition of an anti-PD-1 agent (nivolumab) to the immunotherapy regimen (ipilimumab) is a promising approach for the treatment of patients with MSI/dMMR mCRC. However, the long-term efficacy of this combination is still unclear.

- Patients who received nivolumab plus ipilimumab and who were still alive at the end of the study had a median overall survival of 34.5 months (95% CI, 28.5-40.5 months).
- The addition of nivolumab to ipilimumab did not result in a statistically significant improvement in overall survival compared with ipilimumab alone.

Conclusion

These data suggest that the use of "front-line" immunotherapy (nivolumab plus ipilimumab) is a promising approach for the treatment of patients with MSI/dMMR mCRC. However, the long-term efficacy of this combination is still unclear.

- The addition of an anti-PD-1 agent (nivolumab) to the immunotherapy regimen (ipilimumab) did not result in a statistically significant improvement in overall survival compared with ipilimumab alone.
- The use of nivolumab plus ipilimumab as a "front-line" immunotherapy regimen is still unclear.

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Key Insights

Metastatic Colorectal Cancer – Immunotherapy

Experts Debated the Prospects for Immunotherapy in Microsatellite Stable mCRC

ICI + CHEMOTHERAPY OR REGORAFENIB

Overall, results with IO combinations in MSS/pMMR mCRC have been disappointing

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Experts Discussed Data With IO-IO Combinations in MSI-H/dMMR CRC

IPILIMUMAB + NIVOLUMAB IN MSI/dMMR CRC

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Hepatocellular Carcinoma

Lenvatinib combined with transarterial chemoembolization as first-line treatment of advanced HCC: Phase 3 LAUNCH trial results

Peng et al. 2022, ASCO GI 380

STUDY POPULATION

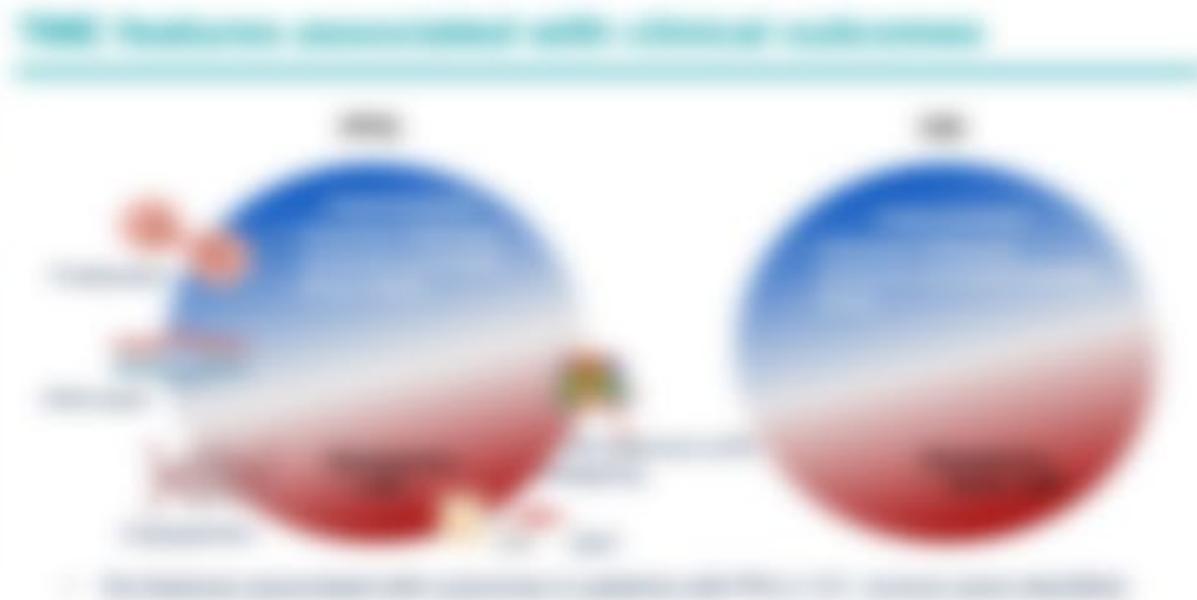
Study Population

Patients with advanced HCC, ECOG performance grade 0-1, and no prior systemic anticancer therapy. The study population was stratified by the presence or absence of macrovascular comorbidities (MVC).

Primary Endpoint

Overall survival (OS) was the primary endpoint, defined as the time from random assignment to death attributable to any cause. OS was assessed using Kaplan-Meier plots. The primary endpoint was analyzed in the overall population and in the MVC and non-MVC subgroups.

PRIMARY ENDPOINT: OS



Phase 3 HIMALAYA trial: Tremelimumab and durvalumab as first-line therapy in unresectable HCC

Abou-Alfa et al. 2022, ASCO GI 379

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STUDY POPULATION

Study Population

The study population consisted of patients with unresectable HCC who had not received prior systemic anticancer therapy. The primary endpoint was overall survival (OS).

Study Design

The study was a phase 3, randomized, controlled trial comparing the combination of tremelimumab and durvalumab to the combination of atezolizumab and durvalumab in patients with unresectable HCC. The primary endpoint was overall survival (OS).

PRIMARY ENDPOINT: OS



Safety and efficacy of durvalumab plus bevacizumab in unresectable HCC: Results from the phase 2 study 22

Lim et al. 2022, ASCO GI 436

STUDY POPULATION

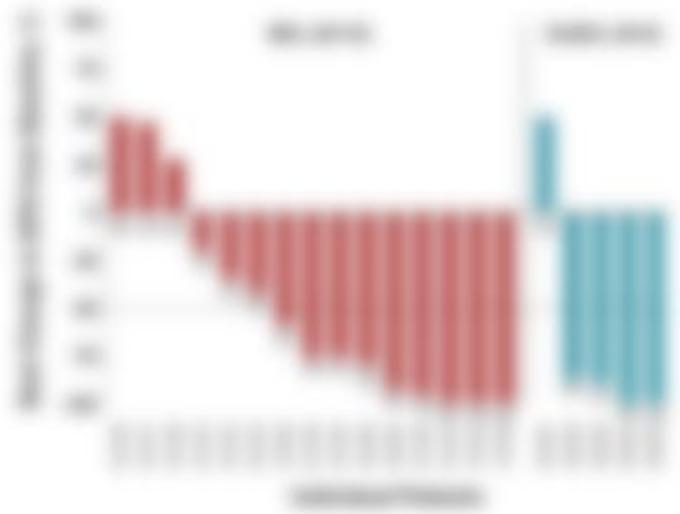
Background

- Phase 2 dose-toxicity study of D10.101, a PD-L1-inhibiting mAb, in patients with locally advanced HCC and CHC.
- Primary objective was to define maximum tolerated dose and recommended starting regimen.

Results

- 21 patients were enrolled, including 15 patients with HCC.
- DLTs were 1st neutropenia and 1st diarrhea.
- DL neutropenia occurred in 20% of patients, 100% successfully resolved.
- DL diarrhea occurred in 100% of patients, 100% successfully resolved.
- DL grade 3 neutropenia occurred in 20% of patients, no DL neutropenia observed.
- DL grade 3 diarrhea occurred in 20% of patients, 100% successfully resolved.
- CRP was 47% (2/3), 47% (3/6) for HCC cohort and 50% (2/4), 25% (1/4) for CHC cohort.
- 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks.

EXPERT CONCLUSIONS



Key takeaway: D10.101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced HCC and CHC. Experts mentioned neutropenia as a potential concern and the need to identify the best strategies in which to use this agent.

IMbrave150: Exploratory analysis of patients with unresectable HCC treated with atezolizumab beyond radiological progression

Toh et al. 2022, ASCO GI 470

STUDY POPULATION AND BACKGROUND

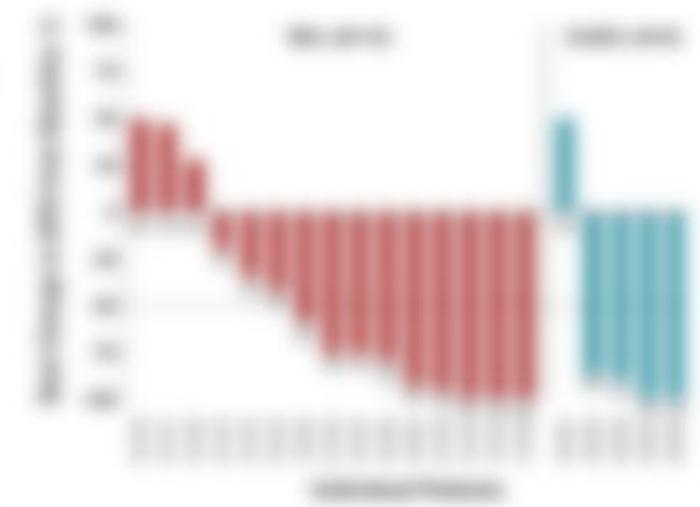
Background

- Phase 3, open-label, randomized study of IMbrave150, a PD-L1-inhibiting HCC, in patients with unresectable HCC and SBCLC.
- Primary objective was to assess outcomes of IMbrave150 and second-line therapy regimen.

Results

- 21 patients were enrolled, including 10 patients with HCC.
- 20.5% were 1st reoperations and 10.2% deaths.
- 10.2% reoperations occurred in 20% of patients, 10.2% reoperations occurred in 20% of patients.
- 10.2% reoperations occurred in 20% of patients, 10.2% reoperations occurred in 20% of patients.
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OS BY POST-PROGRESSION TREATMENT



Key takeaway: IMbrave150 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced HCC and SBCLC. Experts mentioned reoperation as a potential concern and the need to identify the best strategies in which to use this agent.

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Key Insights

Hepatocellular Carcinoma

Experts Discussed Approaches Combining Systemic and Locoregional Therapies for Unresectable HCC

LAUNCH TRIAL – LENVATINIB ± TACE

KEYNOTE MESSAGE – LENVATINIB ± TACE

The combination of lenvatinib and TACE is a promising approach for unresectable HCC. This combination may improve overall survival compared to lenvatinib monotherapy. The combination of lenvatinib and TACE is a promising approach for unresectable HCC. This combination may improve overall survival compared to lenvatinib monotherapy.

KEYNOTE MESSAGE – LENVATINIB ± TACE

Although the combination of lenvatinib and TACE is a promising approach for unresectable HCC, this combination may improve overall survival compared to lenvatinib monotherapy. The combination of lenvatinib and TACE is a promising approach for unresectable HCC. This combination may improve overall survival compared to lenvatinib monotherapy.



KEYNOTE MESSAGE – LENVATINIB ± TACE

The combination of lenvatinib and TACE is a promising approach for unresectable HCC. This combination may improve overall survival compared to lenvatinib monotherapy.

Experts Discussed First-Line Trials Incorporating Immunotherapies for Unresectable HCC

HIMALAYA

KEY TAKEAWAYS

The HIMALAYA trial is a phase 3, randomized, controlled trial comparing the combination of atezolizumab and bevacizumab to sorafenib in patients with unresectable hepatocellular carcinoma (HCC). The trial is currently ongoing and is expected to complete enrollment in late 2020. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to progression (TTP), and quality of life (QoL). The combination of atezolizumab and bevacizumab is expected to show superior OS compared to sorafenib.

KEY TAKEAWAYS

The HIMALAYA trial is a phase 3, randomized, controlled trial comparing the combination of atezolizumab and bevacizumab to sorafenib in patients with unresectable hepatocellular carcinoma (HCC). The trial is currently ongoing and is expected to complete enrollment in late 2020. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to progression (TTP), and quality of life (QoL). The combination of atezolizumab and bevacizumab is expected to show superior OS compared to sorafenib.



KEY TAKEAWAYS

The HIMALAYA trial is a phase 3, randomized, controlled trial comparing the combination of atezolizumab and bevacizumab to sorafenib in patients with unresectable hepatocellular carcinoma (HCC). The trial is currently ongoing and is expected to complete enrollment in late 2020. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to progression (TTP), and quality of life (QoL). The combination of atezolizumab and bevacizumab is expected to show superior OS compared to sorafenib.

Experts Reviewed the Current Algorithm and Practice Patterns in Advanced HCC

CURRENT PRACTICE PATTERNS FOR UNRESECTABLE HCC

KEY TAKEAWAYS

The current practice patterns for unresectable HCC are largely driven by the availability of systemic therapies and the patient's performance and comorbidities. The most common practice patterns include best supportive care, palliative care, and systemic therapy. The use of systemic therapy is increasing, but there is still a need for more research to optimize the use of these therapies in this population.

KEY TAKEAWAYS

Although the current practice patterns for unresectable HCC are largely driven by the availability of systemic therapies and the patient's performance and comorbidities, there is still a need for more research to optimize the use of these therapies in this population. The most common practice patterns include best supportive care, palliative care, and systemic therapy. The use of systemic therapy is increasing, but there is still a need for more research to optimize the use of these therapies in this population.



KEY TAKEAWAYS

The current practice patterns for unresectable HCC are largely driven by the availability of systemic therapies and the patient's performance and comorbidities. The most common practice patterns include best supportive care, palliative care, and systemic therapy. The use of systemic therapy is increasing, but there is still a need for more research to optimize the use of these therapies in this population.

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Congress Highlights

Gastric and Gastroesophageal Junction (GEJ)
Cancers

Neoadjuvant nivolumab/ipilimumab and adjuvant nivolumab in localized MSI-H/dMMR oeso-gastric adenocarcinoma: GERCOR NEONIPIGA

Andre et al. 2022, ASCO GI 244

STUDY POPULATION

Study Design

Phase III, randomized, controlled trial comparing neoadjuvant nivolumab/ipilimumab followed by adjuvant nivolumab (N+I) to neoadjuvant chemotherapy followed by adjuvant nivolumab (C+I).

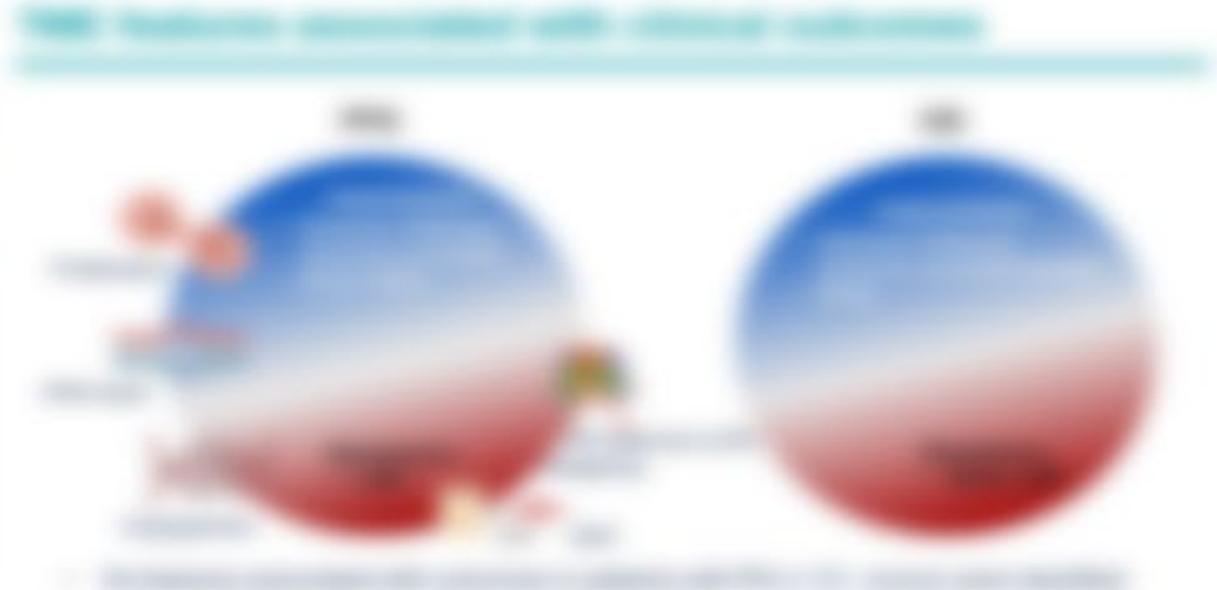
Population

Patients with localized MSI-H/dMMR oeso-gastric adenocarcinoma, ECOG performance grade 0-1, and no prior systemic anticancer therapy.

Primary Endpoints

Event-free survival (EFS) and overall survival (OS).

EVENT-FREE SURVIVAL



Trastuzumab deruxtecan in HER2+ advanced gastric or GEJ adenocarcinoma: Final OS results from phase 2 DESTINY-Gastric01

Yamaguchi et al. 2022, ASCO GI 242

STUDY POPULATION

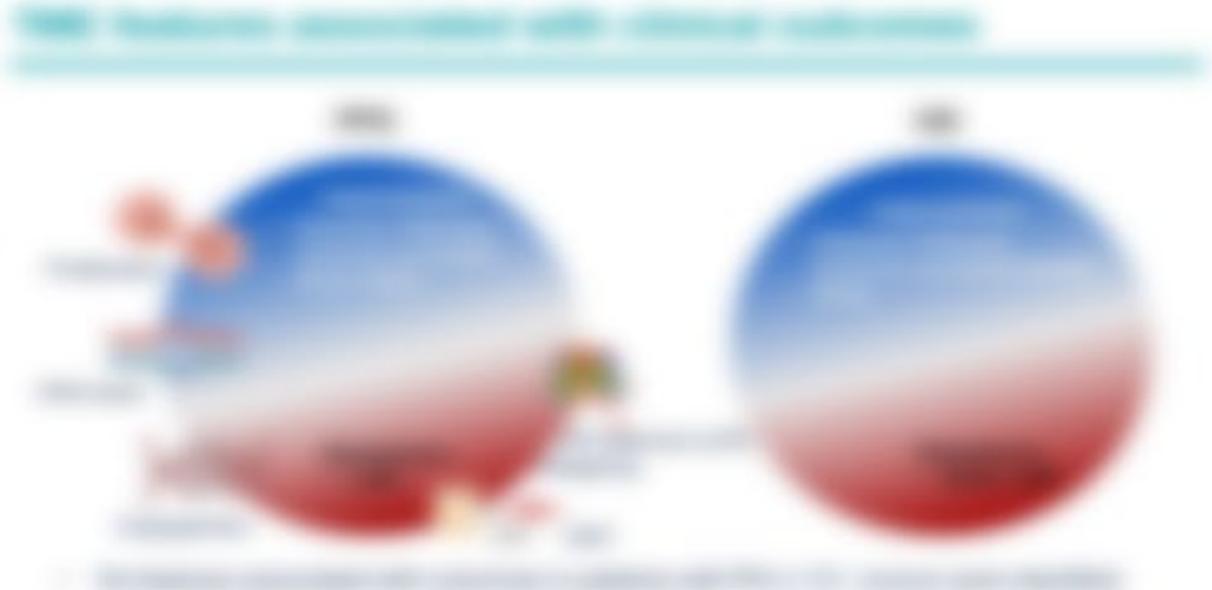
Study Population

HER2+ advanced gastric or GEJ adenocarcinoma

Final OS results from phase 2 DESTINY-Gastric01

Yamaguchi et al. 2022, ASCO GI 242

RESPONSE



Chemotherapy +/- nivolumab as 1L treatment for advanced GC/GEJC/EAC: Expanded analyses from CheckMate 649

Shitara et al. 2022, ASCO GI 240

STUDY POPULATION

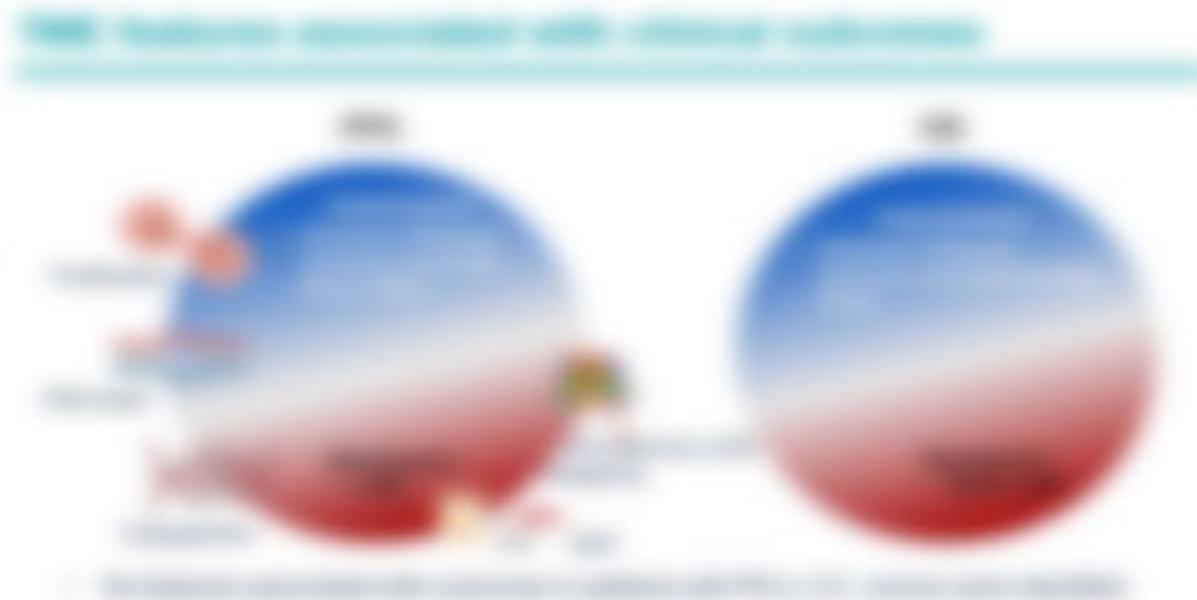
Study Population

Patients with advanced gastric cancer, gastroesophageal junction cancer, or esophageal adenocarcinoma who had not received prior systemic anticancer therapy.

Key Characteristics:

- Median age: 65 years
- Median time from diagnosis to randomization: 12.5 months
- Median time from randomization to first treatment: 1.5 months
- Median time from randomization to death: 11.5 months

PROGRESSION-FREE SURVIVAL 2



Pembrolizumab +/- chemotherapy vs chemotherapy alone for PD-L1+ advanced gastric or GEJ adenocarcinoma: KEYNOTE-062 update

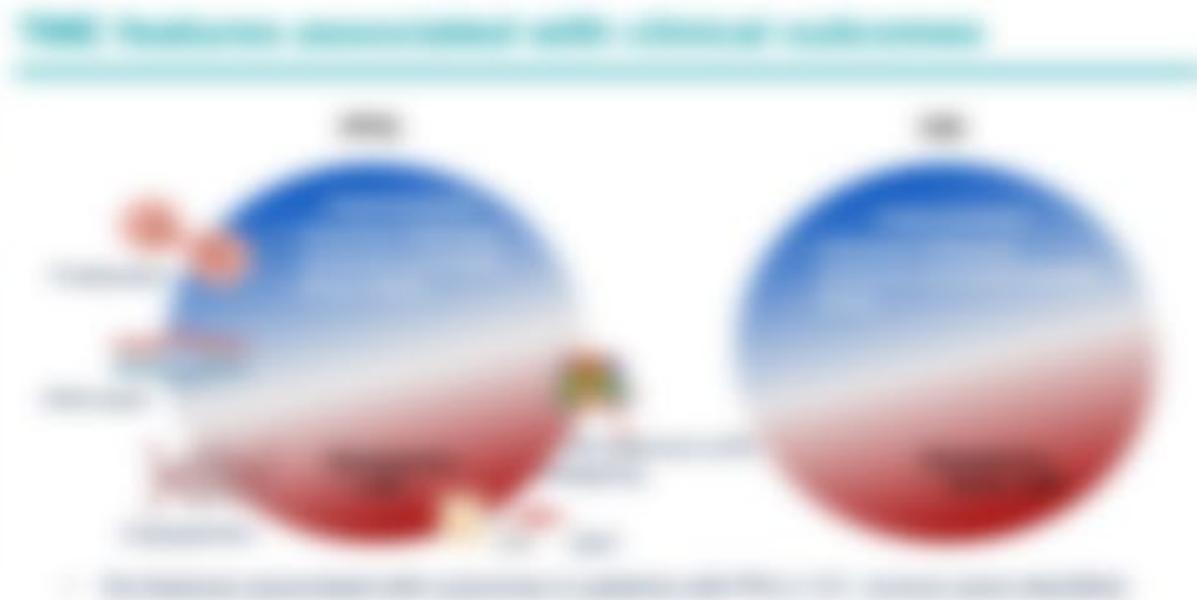
Wainberg et al. 2022, ASCO GI 243

STUDY POPULATION

Study Population

Patients with advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma, PD-L1 positive (Tumor Proportion Score ≥ 1%), and Eastern Cooperative Oncology Group performance grade 0-2 were eligible for the study. The study population was divided into two groups: pembrolizumab plus chemotherapy (n=200) and chemotherapy alone (n=200). The primary endpoint was overall survival (OS), defined as the time from random assignment to death from any cause. Secondary endpoints included progression-free survival (PFS), quality of life, and safety.

OVERALL SURVIVAL – PEMBROLIZUMAB + CHEMO



A phase Ib/II study of AK104, a PD-1/CTLA-4 bispecific antibody, combined with chemotherapy as 1L therapy for advanced G/GEJ cancer

Ji et al. 2022, ASCO GI 308

STUDY POPULATION

Study Design

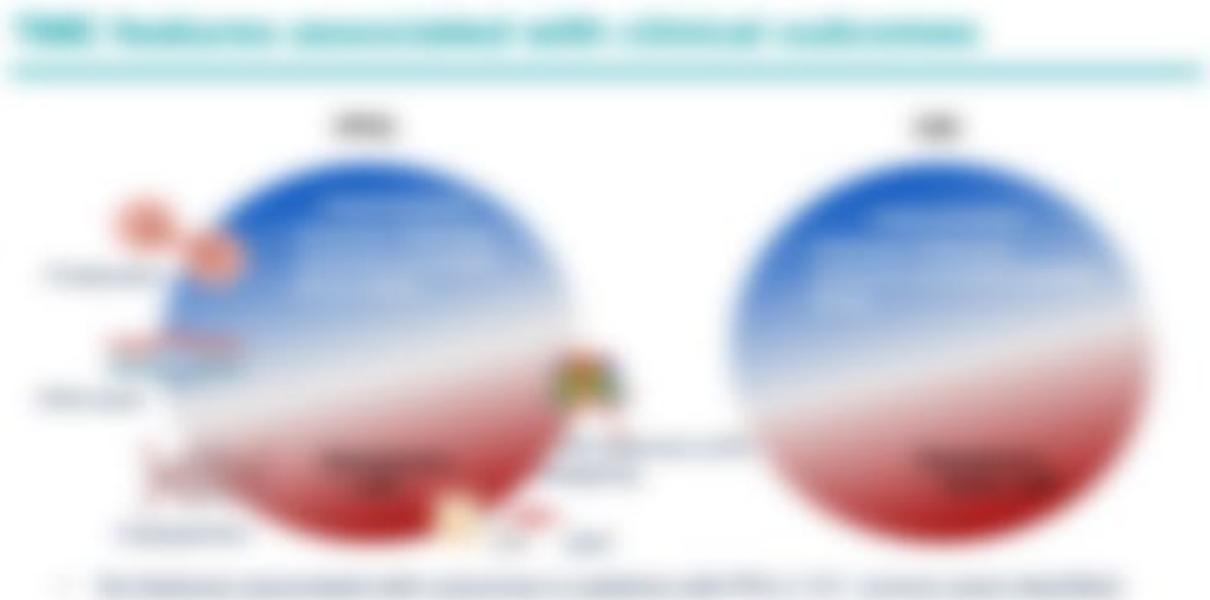
Study Population

Primary Endpoints

Secondary Endpoints

Statistical Methods

RESPONSE



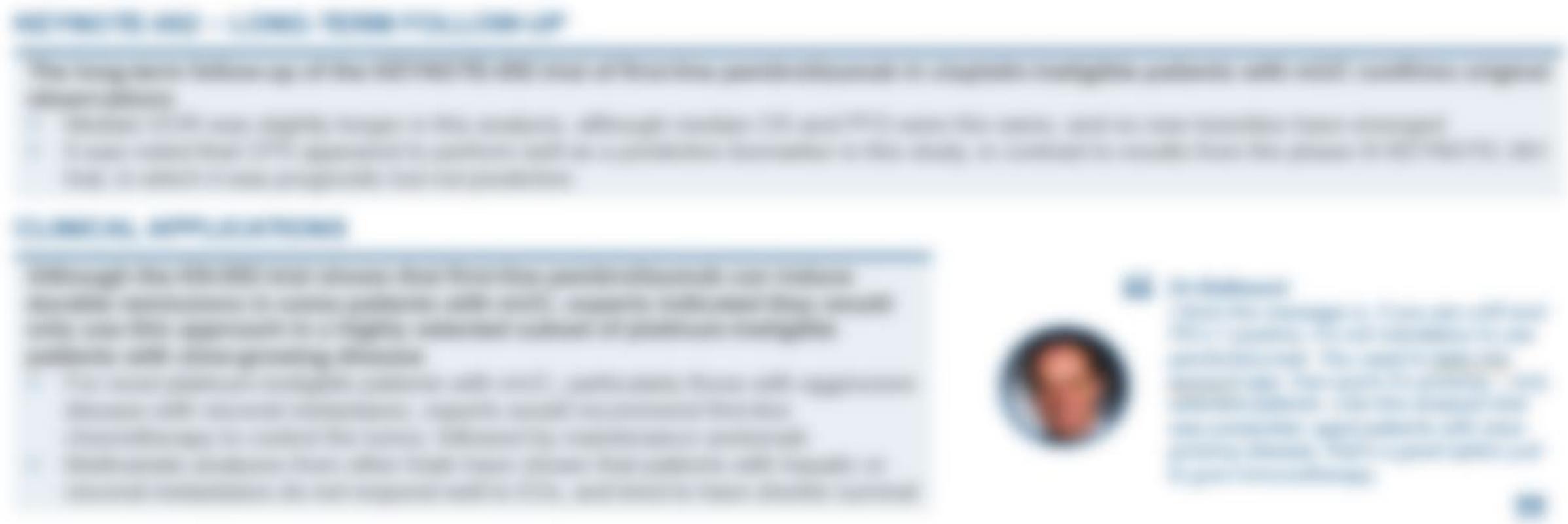
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Key Insights

Gastric and Gastroesophageal Junction (GEJ)
Cancers

Experts Debated the Role of Neoadjuvant Therapy for Resectable MSI-H Gastric or Gastroesophageal Cancers

NEONIPIGA



Experts Discussed Results of Immunotherapy Trials in Unresectable Gastric/GEJ Cancers

CHECKMATE 649

KEY TAKEAWAYS

The results of the phase 3 CheckMate 649 trial, which compared nivolumab plus chemotherapy to chemotherapy alone in patients with unresectable gastric or gastroesophageal junction (GEJ) cancer, were presented at the 2020 ASCO Annual Meeting. The trial met its primary endpoint, showing that the combination of nivolumab and chemotherapy significantly improved overall survival compared to chemotherapy alone. The most common side effects were fatigue, diarrhea, and decreased appetite.

CLINICAL SIGNIFICANCE

Although the overall survival benefit was modest, the combination of nivolumab and chemotherapy is now considered a standard of care for patients with unresectable gastric or GEJ cancer. The trial also showed that the combination was well-tolerated, with a manageable side effect profile. The results of this trial are expected to lead to a change in clinical practice, with more patients receiving the combination of nivolumab and chemotherapy as their first-line treatment.



CONCLUSION

The results of the CheckMate 649 trial demonstrate that the combination of nivolumab and chemotherapy is a more effective and well-tolerated treatment option for patients with unresectable gastric or GEJ cancer compared to chemotherapy alone. This combination is now considered a standard of care for these patients.

Experts Reviewed Results From Trials of Targeted Therapies for Advanced G/GEJ Cancers

HER2-TARGETED THERAPY

KEY TAKEAWAYS

The results of the HER2-targeted therapy trials for advanced G/GEJ cancers were reviewed by experts. The trials showed that HER2-targeted therapy can improve outcomes for patients with advanced G/GEJ cancers. The results were positive and suggest that HER2-targeted therapy is a promising treatment option for these patients.

KEY TAKEAWAYS

HER2-targeted therapy is a promising treatment option for patients with advanced G/GEJ cancers. The results of the trials were positive and suggest that HER2-targeted therapy can improve outcomes for these patients. The results were reviewed by experts and found to be significant.



KEY TAKEAWAYS

The results of the trials were positive and suggest that HER2-targeted therapy is a promising treatment option for patients with advanced G/GEJ cancers. The results were reviewed by experts and found to be significant.

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Congress Highlights

Pancreatic Cancer and Biliary Tract Cancer

KRYSTAL-1: Adagrasib (MRTX849) in unresectable/metastatic pancreatic cancer (PDAC) and other GI tumors harboring a KRASG12C mutation

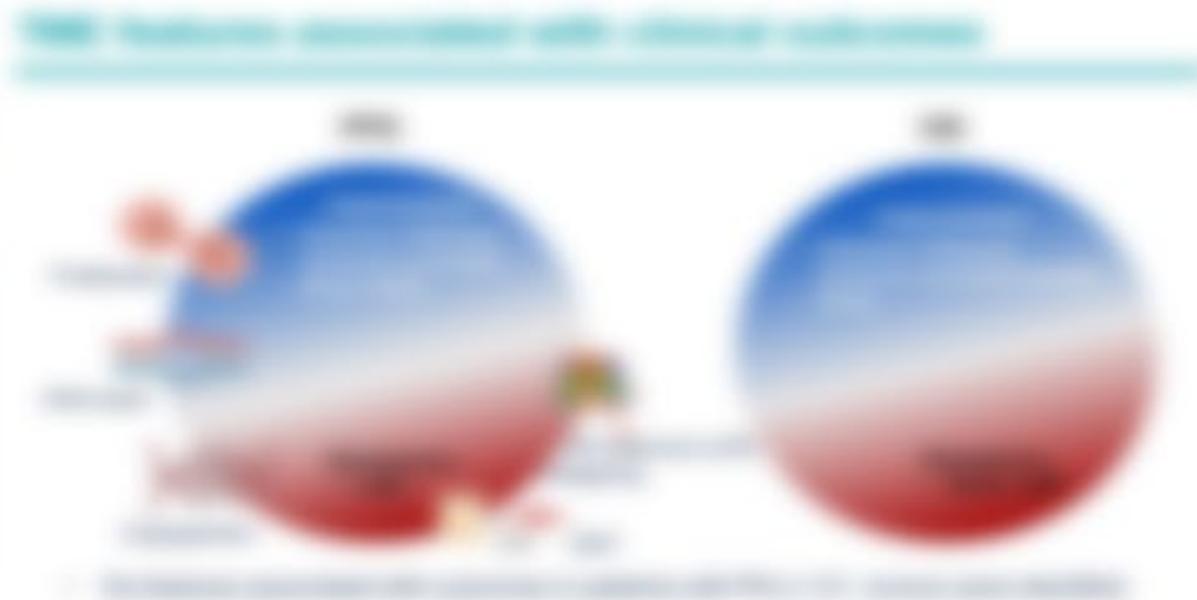
Bekaii-Saab et al. 2022, ASCO GI 519

STUDY POPULATION

Study Population

Patients with unresectable/metastatic PDAC harboring a KRASG12C mutation who had not received prior systemic therapy for unresectable/metastatic PDAC were eligible for the study. The study population included patients who were either KRASG12C mutation positive or KRASG12C mutation negative.

RESPONSE IN UNRESECTABLE/METASTATIC PDAC



Phase III study of modified folfirinox +/- sintilimab in metastatic and recurrent pancreatic cancer in China: The CISPD3 trial.

Fu et al. 2022, ASCO GI 560

STUDY POPULATION

Study Design: Phase III, randomized, controlled trial.

Primary Endpoint: Overall Survival (OS).

Secondary Endpoints: Progression-Free Survival (PFS), Objective Response Rate (ORR), Quality of Life (QoL).

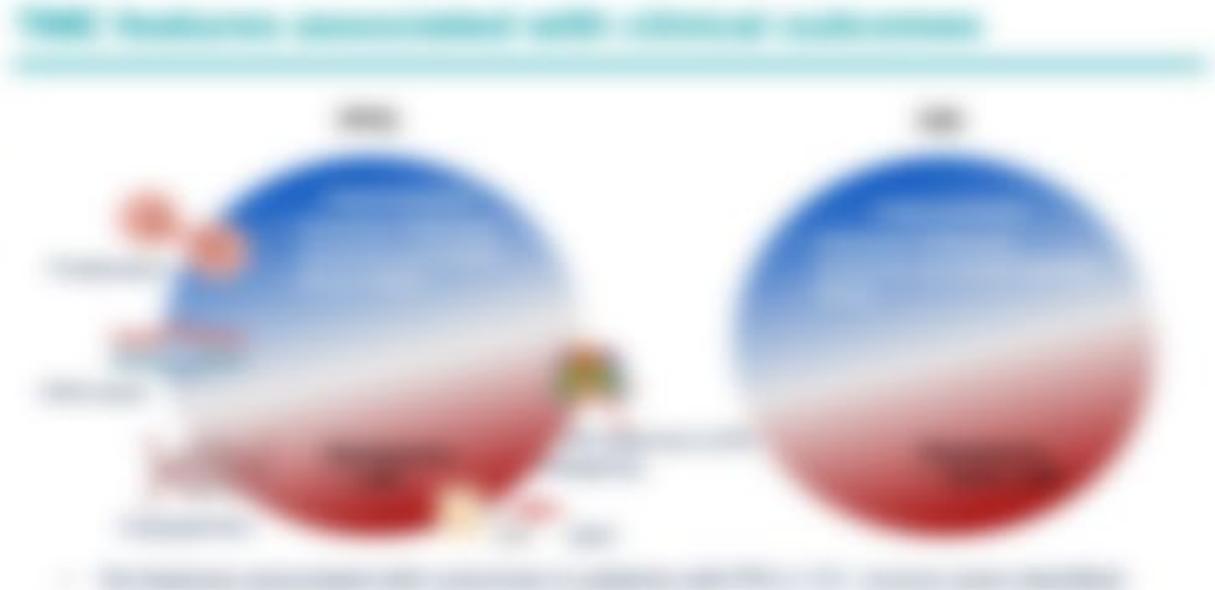
Study Population: Patients with metastatic and recurrent pancreatic cancer who had not received prior systemic chemotherapy for advanced disease.

Randomization: Patients were randomized to receive either modified folfirinox (mFOLFIRINOX) or mFOLFIRINOX plus sintilimab.

Interventions: The control group received mFOLFIRINOX, and the experimental group received mFOLFIRINOX plus sintilimab.

Results: The study demonstrated that the combination of mFOLFIRINOX and sintilimab significantly improved OS compared to mFOLFIRINOX alone in patients with metastatic and recurrent pancreatic cancer.

PRIMARY ENDPOINT: OS



Trybeca-1: Phase 3 study of chemotherapy +/- eryaspase as 2L treatment in patients with advanced pancreatic adenocarcinoma

Hammel et al. 2022, ASCO GI 518

STUDY POPULATION

Study Population

Patients with advanced pancreatic adenocarcinoma who had received at least one prior systemic therapy for their disease and were ineligible for or had completed a standard of care regimen.

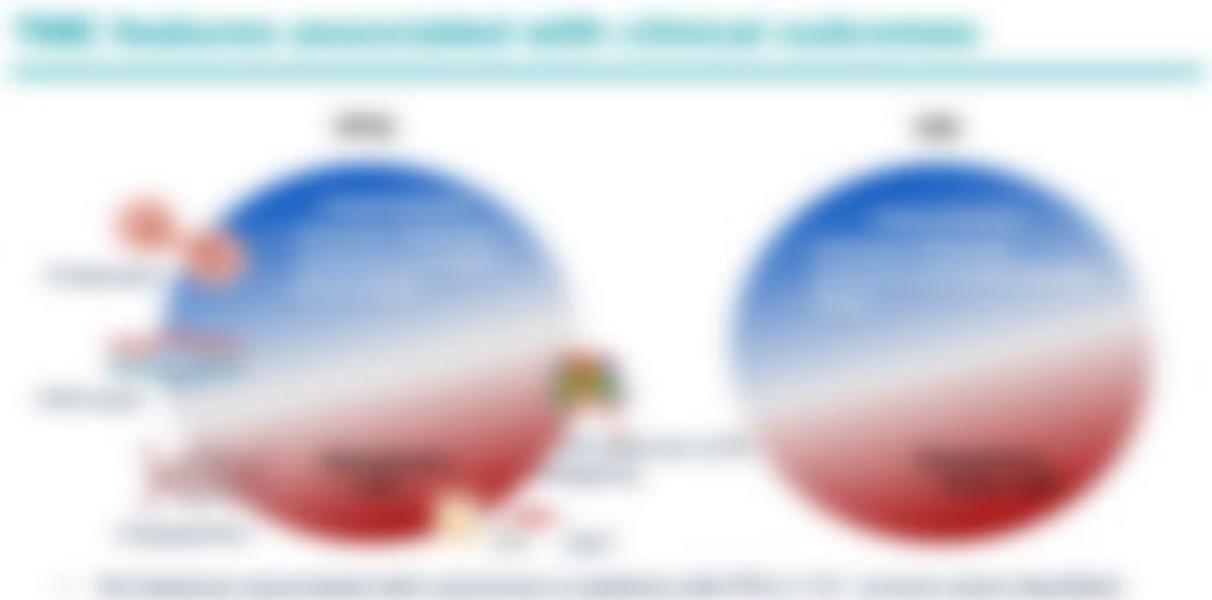
Primary Endpoint

Overall survival (OS) at 12 months.

Secondary Endpoints

Quality of life, progression-free survival (PFS), and adverse events.

PRIMARY ENDPOINT: OS



TOPAZ-1: A phase 3 study of durvalumab in combination with GemCis in patients with advanced biliary tract cancer

Oh et al. 2022, ASCO GI 378

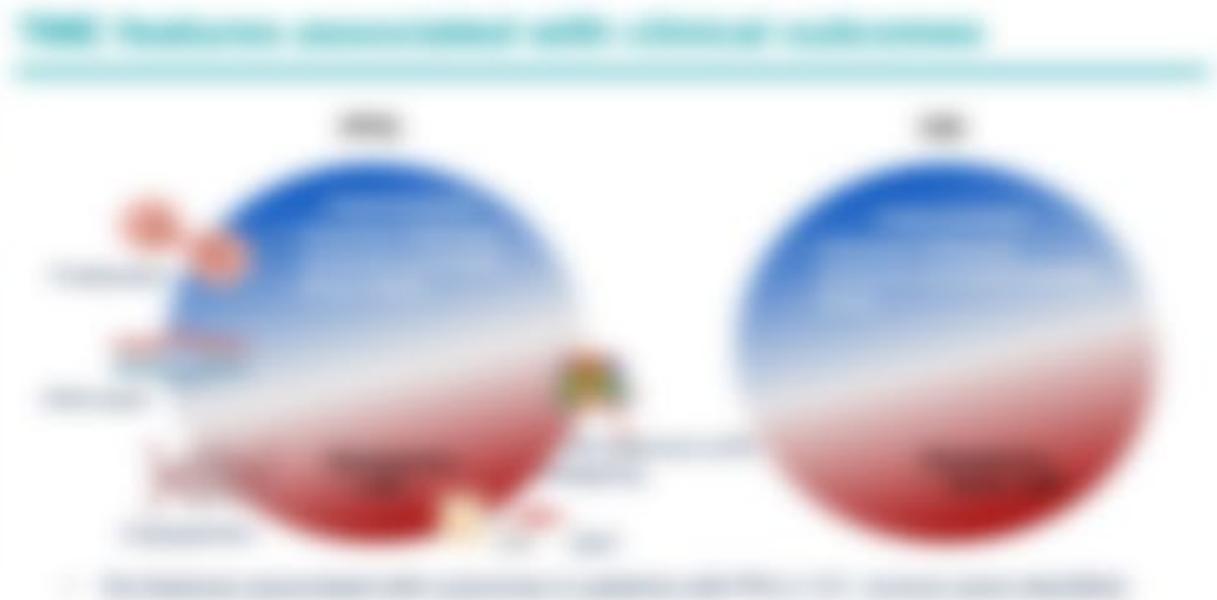
STUDY POPULATION

Study Population

Patients with advanced biliary tract cancer (BTC) who were previously untreated and had no prior systemic anticancer therapy. The study population included patients with cholangiocarcinoma and gallbladder cancer. Key characteristics of the study population are summarized in the table below.

| Characteristic | Number of Patients (n) |
|----------------------------|------------------------|
| Total Study Population | 400 |
| Cholangiocarcinoma | 200 |
| Gallbladder Cancer | 200 |
| Median Age (years) | 65 |
| Male/Female | 200/200 |
| ECOG Performance Grade 0-1 | 380 |
| ECOG Performance Grade 2 | 20 |

PRIMARY ENDPOINT: OS



Phase II study of pembrolizumab plus olaparib in patients with advanced cholangiocarcinoma: Interim results

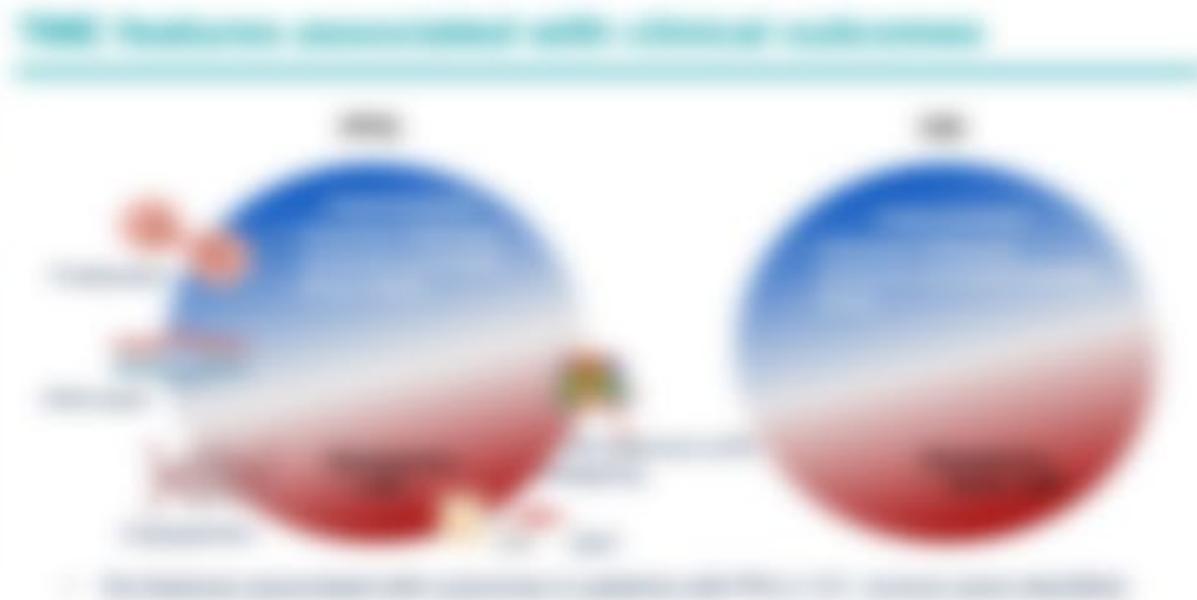
Yin et al. 2022, ASCO GI 452

STUDY POPULATION

Study Population

Patients with advanced cholangiocarcinoma who had not received prior systemic therapy for their disease. The study population included patients who were either PD-L1 positive or PD-L1 negative. The study population was stratified by PD-L1 status and by the presence of a germline BRCA1/2 mutation.

PRIMARY ENDPOINT: iDFS



EPICS

Key Insights

Pancreatic Cancer and Biliary Tract Cancer

Experts Discussed Current Results and the Future of Research for Pancreatic Adenocarcinoma

KRYSTAL-1 (KRAS G12C-MUTATED GI CANCERS)

KEYNOTE 187: KRAS G12C-MUTATED GI CANCERS

The KRAS G12C mutation is a driver mutation in pancreatic adenocarcinoma and other gastrointestinal (GI) cancers. The KRAS G12C mutation is a targetable mutation, and the KRAS G12C inhibitor, KRYSTAL-1, is being evaluated in a phase 1b study in patients with KRAS G12C-mutated GI cancers. The study is currently recruiting patients and is expected to complete enrollment in late 2023.

KEYNOTE 187: KRAS G12C-MUTATED GI CANCERS

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Experts Debated the Impact of New Data for Biliary Tract Cancers

TOPAZ-1

KEY TAKEAWAYS

The TOPAZ-1 trial, which compared the combination of pembrolizumab and gemtuzumab with gemtuzumab alone in patients with unresectable biliary tract cancer, showed a statistically significant improvement in overall survival for the combination group. This finding suggests that the combination of immunotherapy and targeted therapy may be a promising approach for the treatment of biliary tract cancer.

CLINICAL SIGNIFICANCE

Although the TOPAZ-1 trial showed a statistically significant improvement in overall survival for the combination group, the absolute benefit was modest. This highlights the need for further research to optimize the combination of immunotherapy and targeted therapy for biliary tract cancer. Additionally, the trial included a subgroup of patients with gallbladder cancer, which showed a similar trend of improved survival for the combination group.



CONCLUSION

The TOPAZ-1 trial provides evidence that the combination of pembrolizumab and gemtuzumab may be a promising treatment approach for unresectable biliary tract cancer. However, the absolute benefit was modest, and further research is needed to optimize this combination and explore other potential treatment strategies.

