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Congress Coverage: ASCO GI 2022 Highlights

January 26, 2022

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Meeting Snapshot

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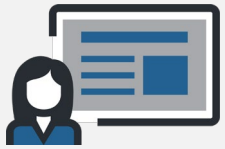
VIRTUAL CLOSED-DOOR ROUNDTABLE

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

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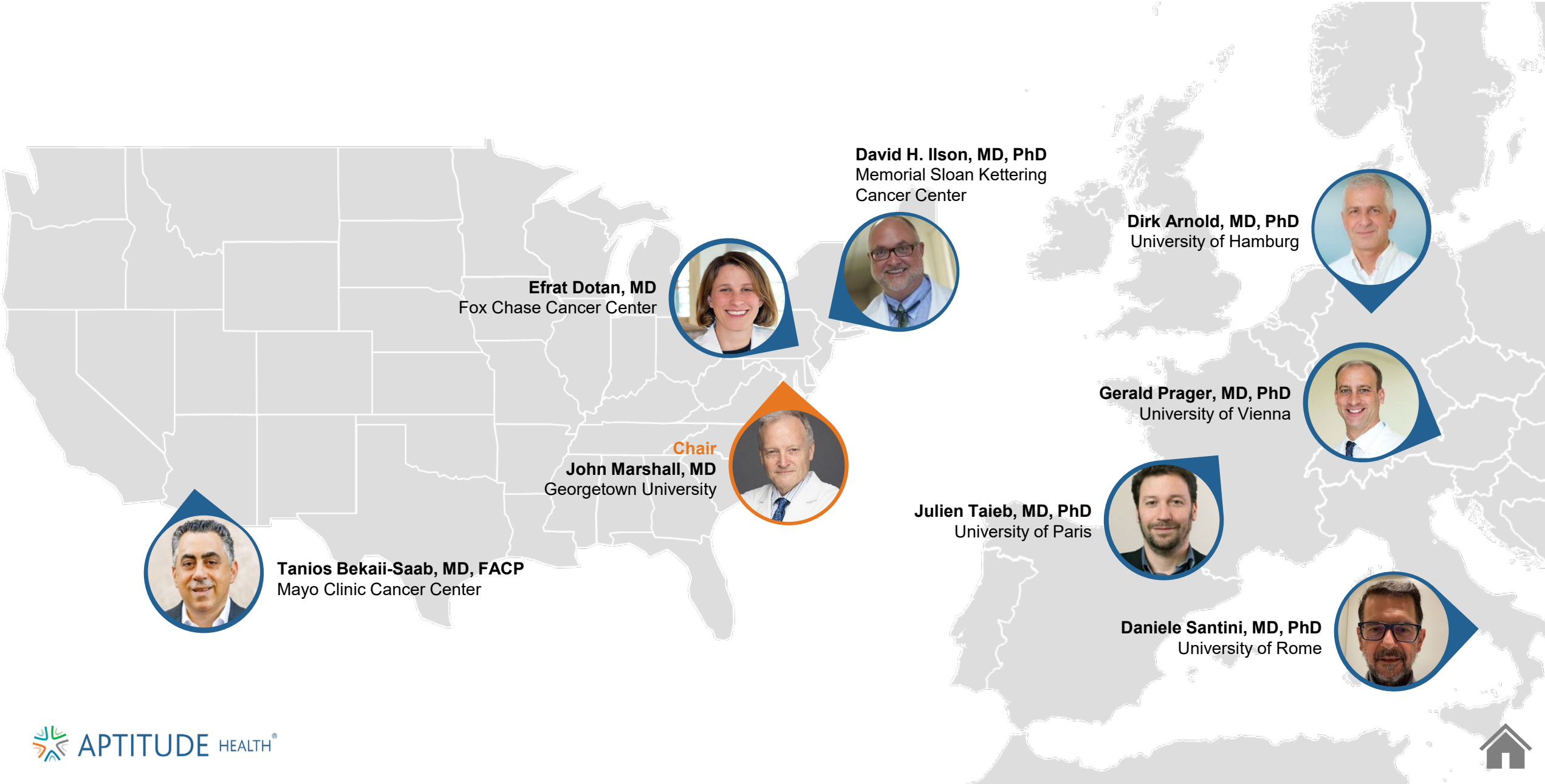

David H. Ilson, MD, PhD
Memorial Sloan Kettering Cancer Center

Efrat Dotan, MD
Fox Chase Cancer Center

Chair
John Marshall, MD
Georgetown University

Tanios Bekaii-Saab, MD, FACP
Mayo Clinic 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

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Meeting Agenda

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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

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

Yoshino et al. 2022, ASCO GI 119

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Key Insights

Metastatic Colorectal Cancer – Targeted Therapy

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

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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

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DESTINY-CRC01

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

BIOMARKER TESTING

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

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STUDY POPULATION

[redacted]

SAFETY

[redacted]

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

Barzi et al. 2022, ASCO GI 15

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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

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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%),

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

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STUDY POPULATION

> Pts with MSI/dMMR mCRC previously treated with

OUTCOME

> Median follow-up was 34.5 months

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Key Insights

Metastatic Colorectal Cancer – Immunotherapy

Experts Debated the Prospects for Immunotherapy in Microsatellite Stable mCRC

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ICI + CHEMOTHERAPY OR REGORAFENIB

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

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

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IPILIMUMAB + NIVOLUMAB IN MSI/dMMR CRC

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Congress Highlights

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

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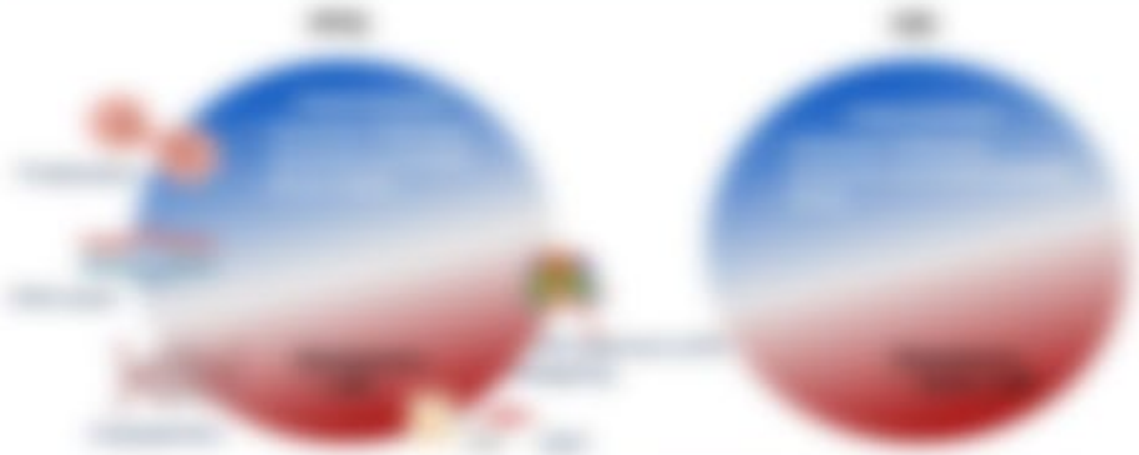
STUDY POPULATION

[illegible]

PRIMARY ENDPOINT: OS

[illegible]



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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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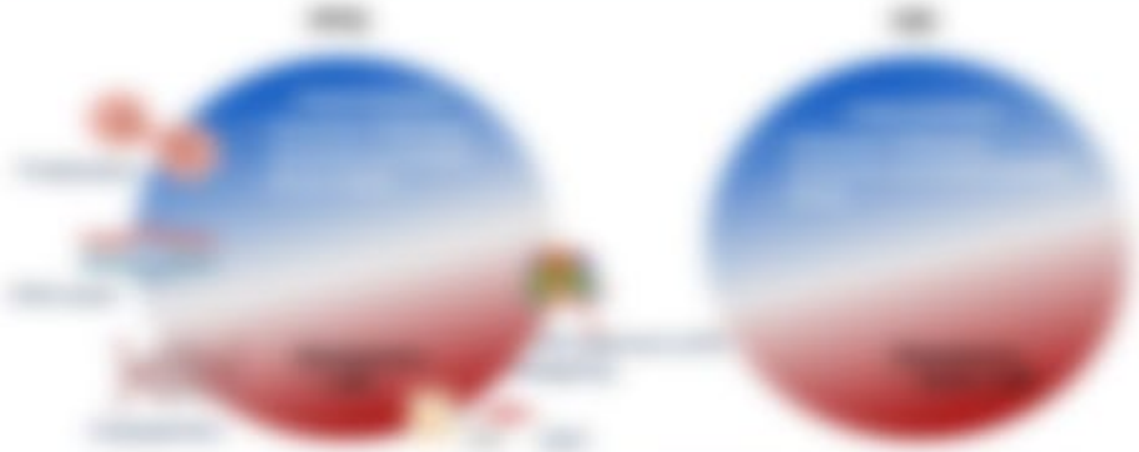
STUDY POPULATION

PRIMARY ENDPOINT: OS



Phase 1b/2 study (Deductive): Tivozanib plus durvalumab in advanced HCC: Efficacy in previously untreated patients

Iyer et al. 2022, ASCO GI 462

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STUDY POPULATION

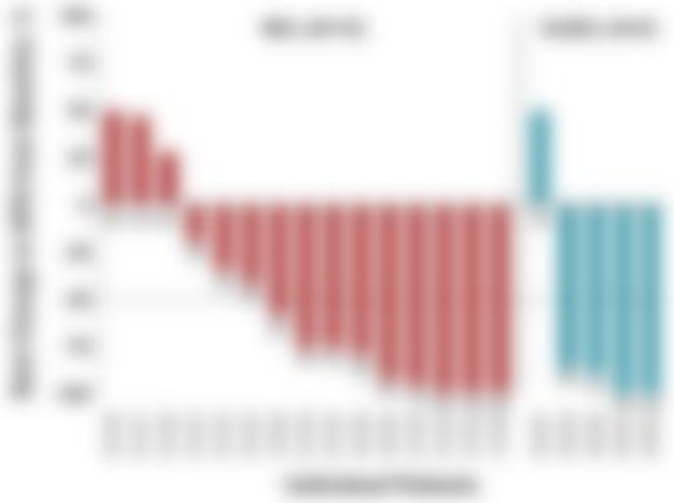
Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
- DLTs were G4 neutropenia and G3 diarrhea
- G4 neutropenia occurred in 28% of patients; G-CSF successfully ameliorated neutropenia
- On-study reversible G3 neuropathy occurred in 9% of patients; no G4 neuropathy occurred
- ORR was 47% (3 CR, 4 PR) for MCL cohort and 80% (2 CR, 2 PR) for DLBCL cohort
- 8 responding patients have ongoing responses ranging from 27 weeks to 58 weeks

EXPERT CONCLUSIONS



Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

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

Lim et al. 2022, ASCO GI 436

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STUDY POPULATION

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
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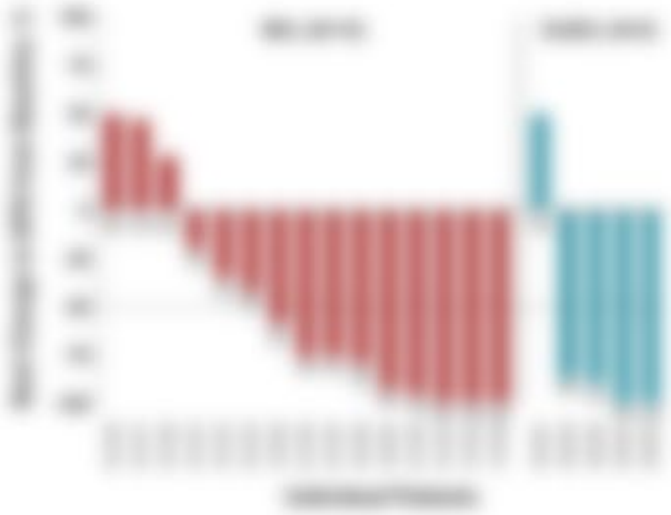
- On-study reversible G3 neuropathy occurred in 9% of patients; no G4 neuropathy occurred
- ORR was 47% (3 CR, 4 PR) for MCL cohort and 80% (2 CR, 2 PR) for DLBCL cohort
- 8 responding patients have ongoing responses ranging from 23 weeks to 58 weeks

EXPERT CONCLUSIONS



Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

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

Toh et al. 2022, ASCO GI 470

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STUDY POPULATION AND BACKGROUND

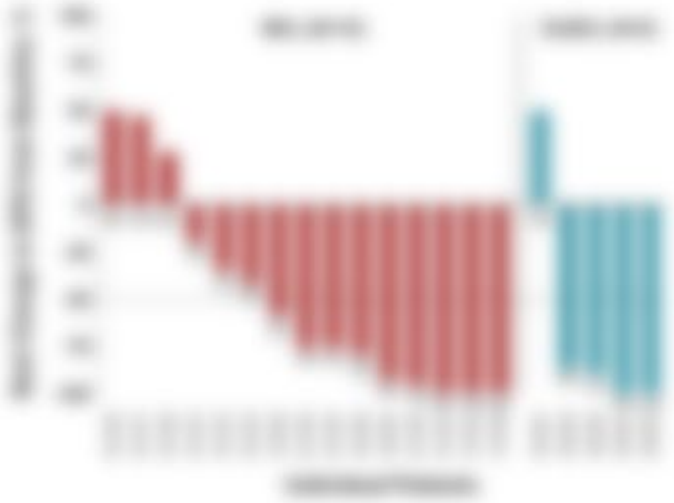
Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated NSCLC and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with NSCLC
- DLTs were G4 neutropenia and G3 diarrhea
- G4 neutropenia occurred in 28% of patients; G-CSF successfully ameliorated neutropenia
- On-study reversible G3 neuropathy occurred in 9% of patients; no G4 neuropathy occurred
- ORR was 47% (3 CR, 4 PR) for NSCLC cohort and 80% (2 CR, 2 PR) for DLBCL cohort
- 8 responding patients have ongoing responses ranging from 27 weeks to 58 weeks

OS BY POST-PROGRESSION TREATMENT



Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced NSCLC and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

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Key Insights

Hepatocellular Carcinoma

Experts Discussed Approaches Combining Systemic and Locoregional Therapies for Unresectable HCC

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LAUNCH TRIAL – LENVATINIB ± TACE

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Experts Discussed First-Line Trials Incorporating Immunotherapies for Unresectable HCC

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HIMALAYA

Experts Reviewed the Current Algorithm and Practice Patterns in Advanced HCC

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CURRENT PRACTICE PATTERNS FOR UNRESECTABLE HCC

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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

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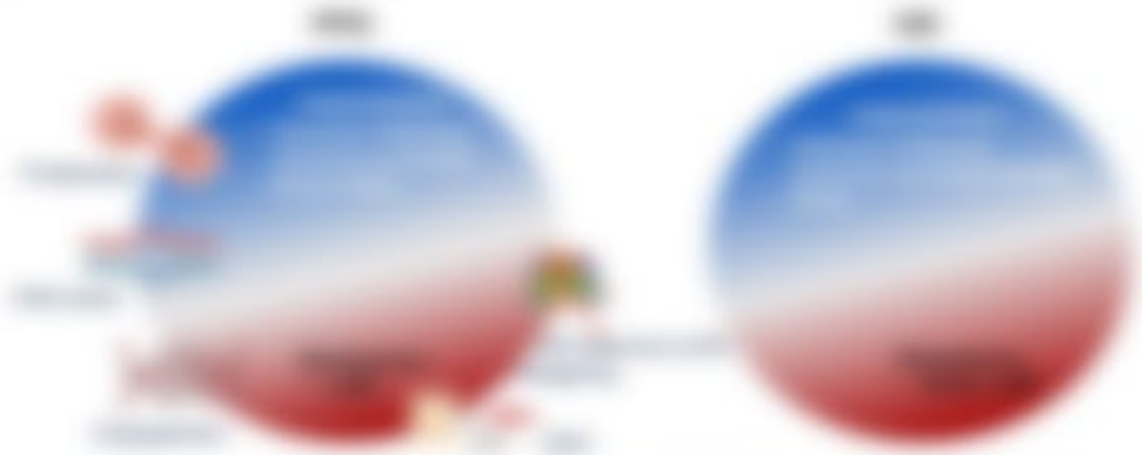
STUDY POPULATION

EVENT-FREE SURVIVAL



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

Yamaguchi et al. 2022, ASCO GI 242

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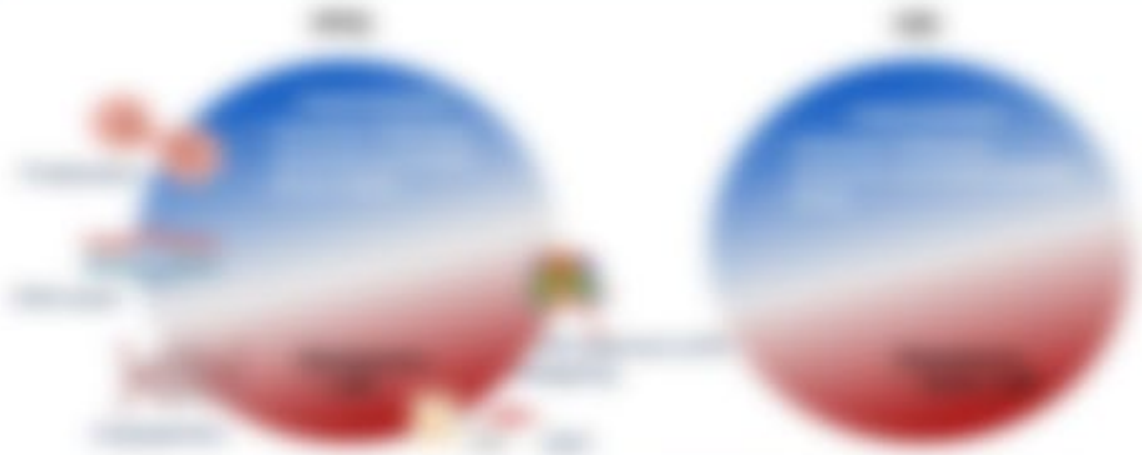
STUDY POPULATION

RESPONSE



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

Shitara et al. 2022, ASCO GI 240

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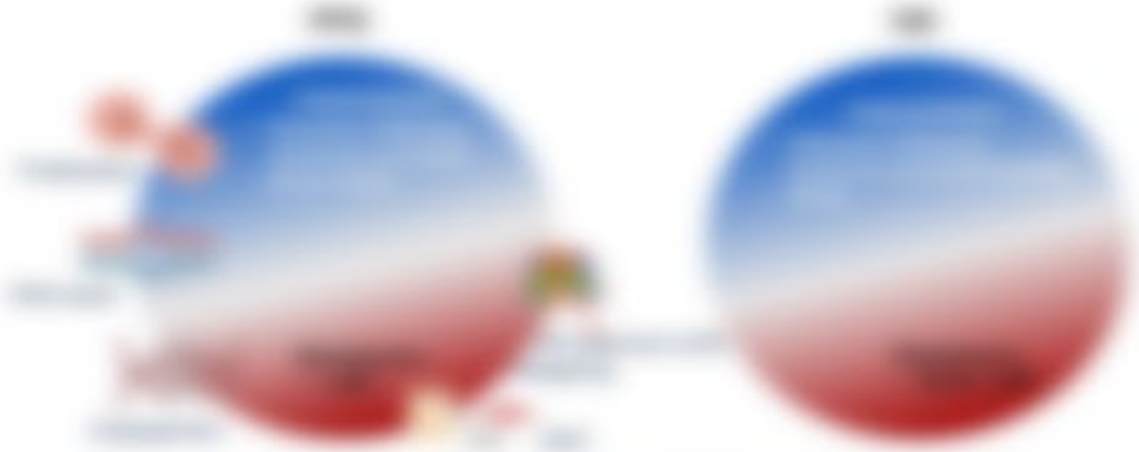
STUDY POPULATION

[redacted]

PROGRESSION-FREE SURVIVAL 2

[redacted]



[redacted]

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

Wainberg et al. 2022, ASCO GI 243

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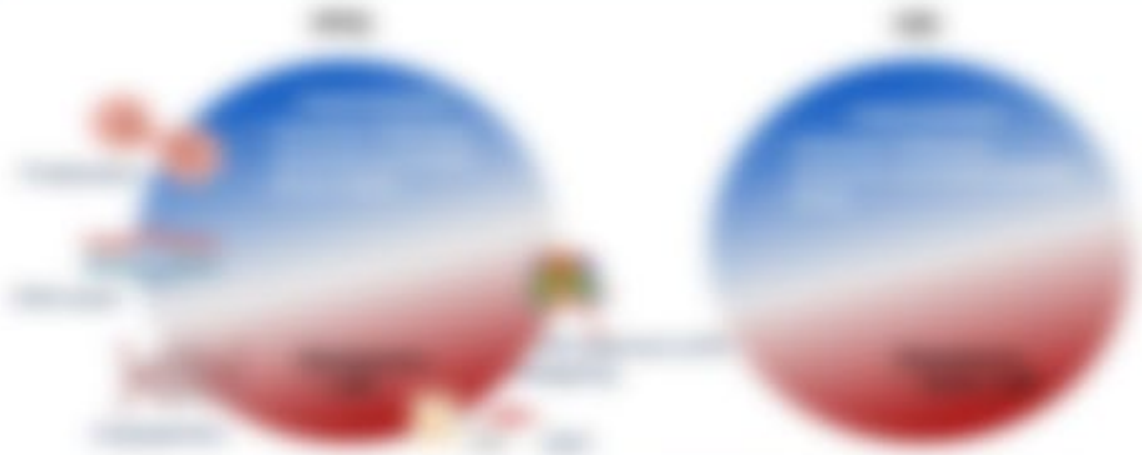
STUDY POPULATION

OVERALL SURVIVAL – PEMBROLIZUMAB + CHEMO



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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

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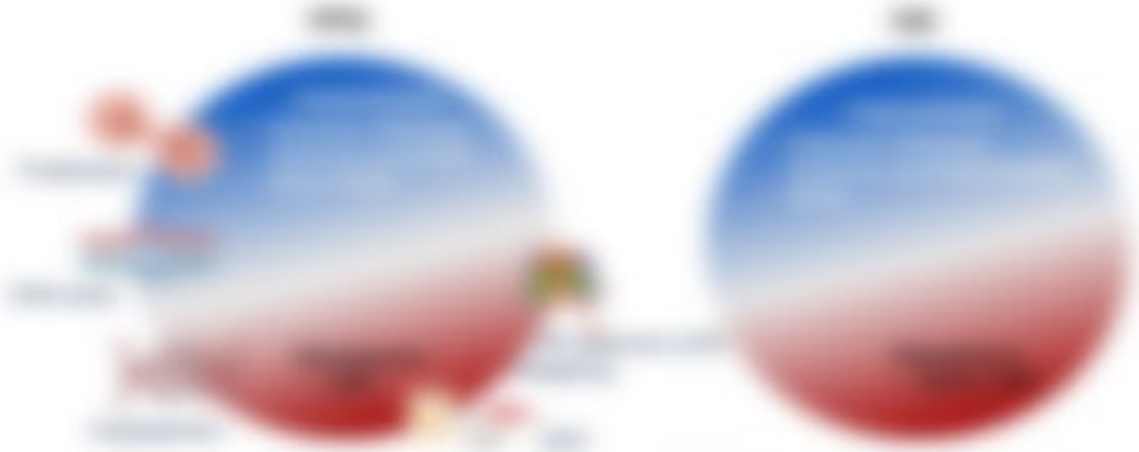
STUDY POPULATION

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

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NEONIPIGA

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

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CHECKMATE 649

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

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HER2-TARGETED THERAPY

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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

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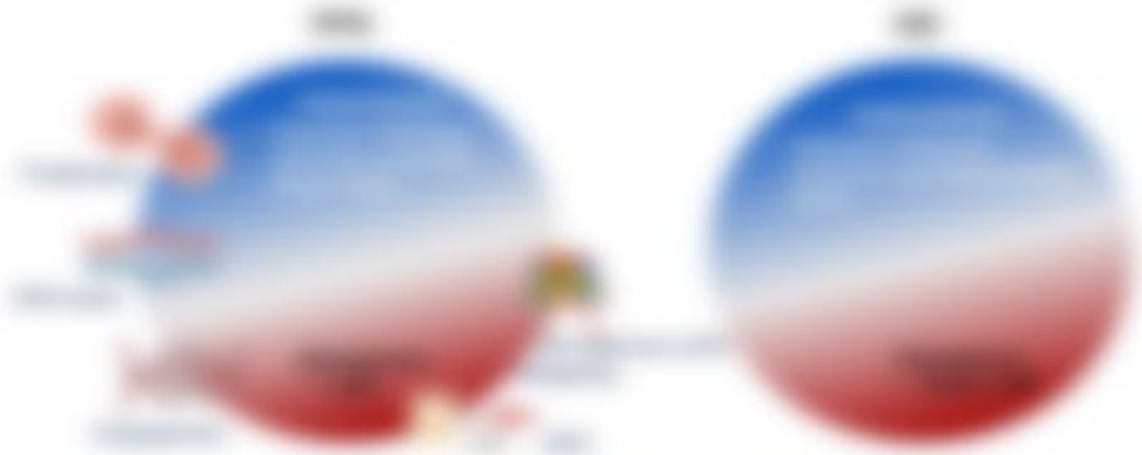
STUDY POPULATION

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

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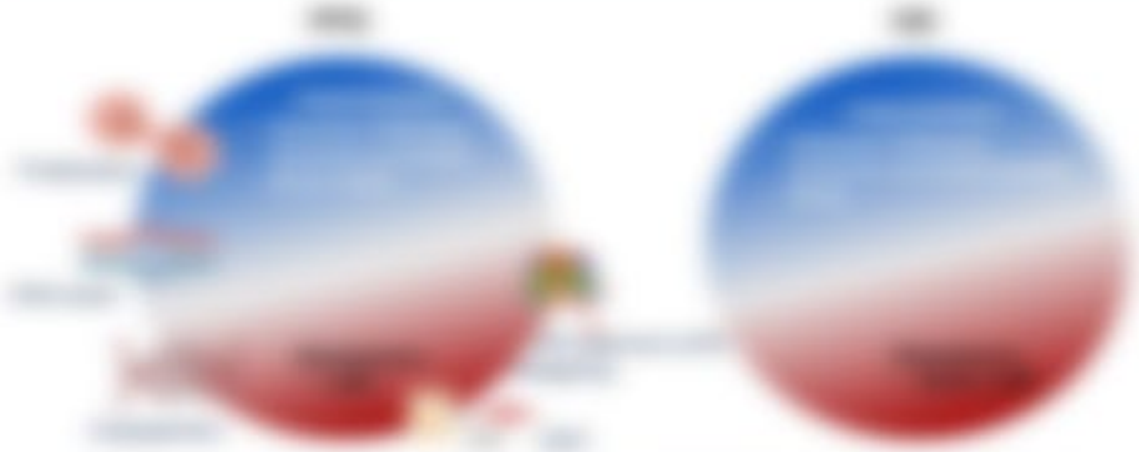
STUDY POPULATION

PRIMARY ENDPOINT: OS



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

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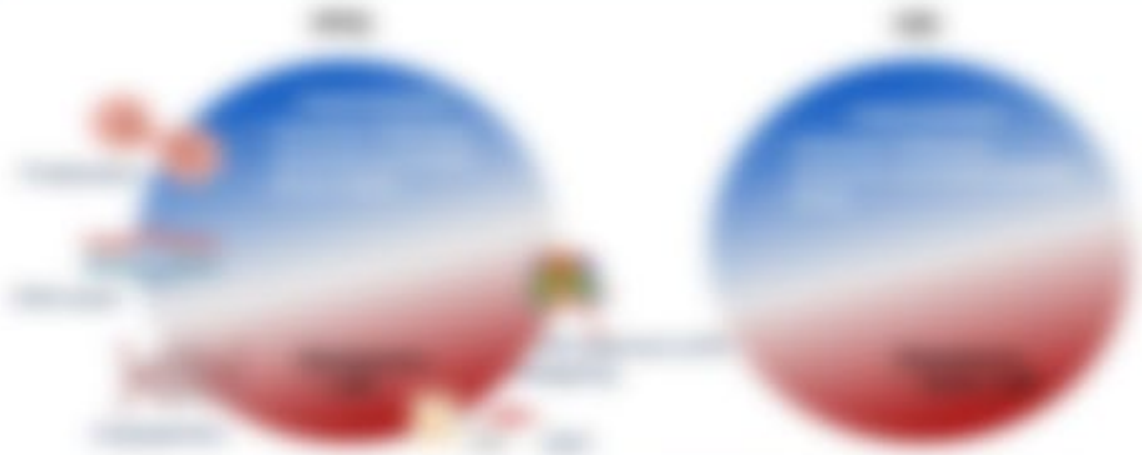
Hammel et al. 2022, ASCO GI 518

STUDY POPULATION

PRIMARY ENDPOINT: OS



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

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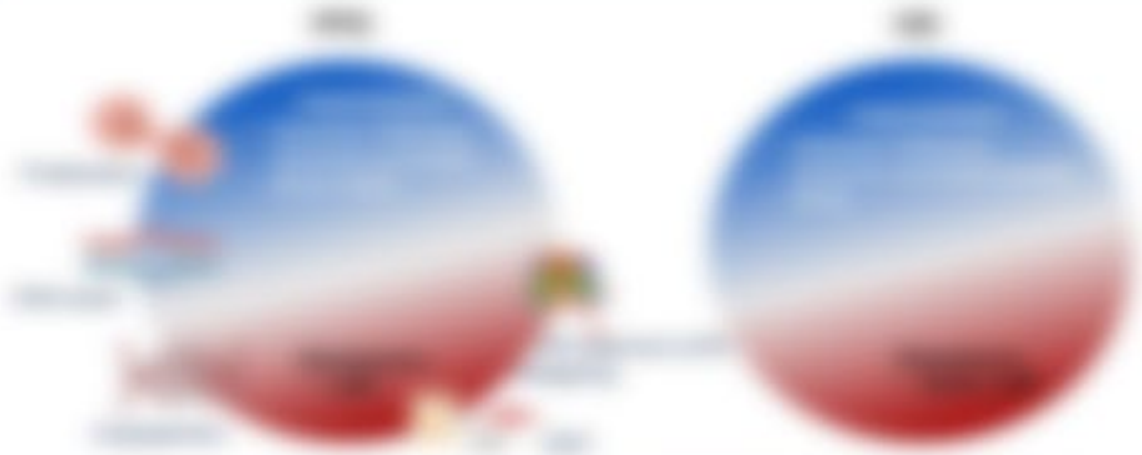
Oh et al. 2022, ASCO GI 378

STUDY POPULATION

PRIMARY ENDPOINT: OS



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

Yin et al. 2022, ASCO GI 452

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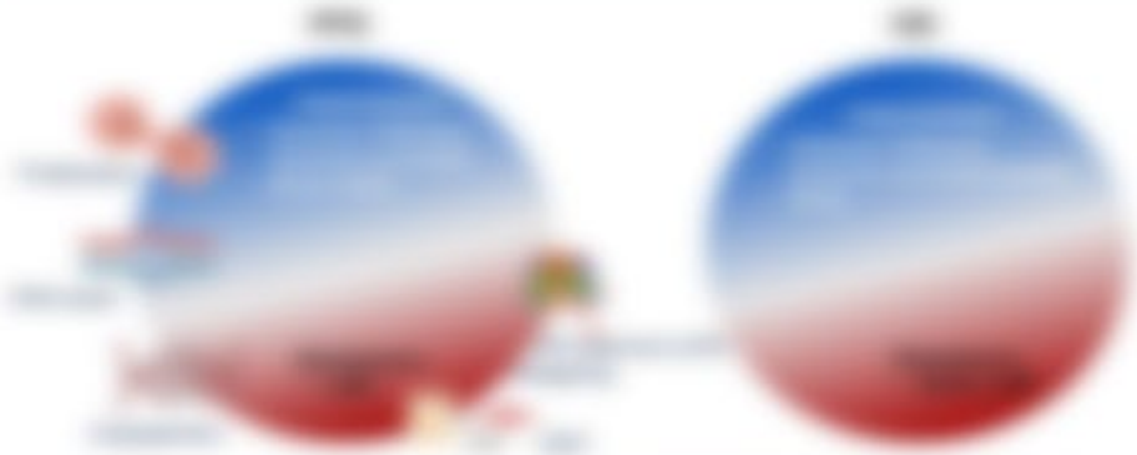
STUDY POPULATION

PRIMARY ENDPOINT: iDFS



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Key Insights

Pancreatic Cancer and Biliary Tract Cancer

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

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KRYSTAL-1 (*KRAS* G12C-MUTATED GI CANCERS)

Experts Debated the Impact of New Data for Biliary Tract Cancers

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TOPAZ-1