



EPICS

**EPICS CONGRESS
COVERAGE: ASCO 2021 –
FOCUS ON GI**

Thursday, January 21, 2021

FULL REPORT

FACULTY EXPERTS

EPICS

Chair
Axel Grothey, MD



Dirk Arnold, MD, PhD



Cathy Eng, MD, FACP



David H. Ilson, MD, PhD



Scott Kopetz, MD, PhD



Fotios Loupakis, MD, PhD



Eric Van Cutsem, MD, PhD



Tanios Bekaii-Saab, MD, FACP

Time EST	Topic	Speaker/ Moderator
10.00 – 10.05	Welcome and Introductions	Axel Grothey, MD
10.05 – 10.20	Colorectal Cancer – Chemotherapy and Targeted Therapy	Eric Van Cutsem, MD, PhD
10.20 – 10.40	Discussion	Moderator: Axel Grothey, MD
10.40 – 10.45	Colorectal Cancer – Chemotherapy and Targeted Therapy: Key Takeaways	Eric Van Cutsem, MD, PhD
10.45 – 11.00	Colorectal Cancer – Immunotherapy	Scott Kopetz, MD, PhD
11.00 – 11.20	Discussion	Moderator: Axel Grothey, MD
11.20 – 11.25	Colorectal Cancer – Immunotherapy: Key Takeaways	Scott Kopetz, MD, PhD
11.25 – 11.40	Hepatocellular Carcinoma	Tanios S. Bekaii-Saab, MD, FACP
11.40 – 12.00	Discussion	Moderator: Axel Grothey, MD
12.00 – 12.05	Hepatocellular Carcinoma – Key Takeaways	Tanios S. Bekaii-Saab, MD, FACP
12.05 – 12.10	<i>Break</i>	
12.10 – 12.25	Gastroesophageal Cancers	David Ilson, MD, PhD
12.25 – 12.45	Discussion	Moderator: Axel Grothey, MD
12.45 – 12.50	Gastroesophageal Cancers – Key Takeaways	David Ilson, MD, PhD
12.50 – 1.00	Pancreatic Cancer	Dirk Arnold, MD, PhD
1.00 – 1.20	Discussion	Moderator: Axel Grothey, MD
1.20 – 1.25	Pancreatic Cancer – Key Takeaways	Dirk Arnold, MD, PhD
1.25 – 1.30	Summary and Closing Remarks	Axel Grothey, MD

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Colorectal Cancer – Chemotherapy and Targeted Therapy

ERIC VAN CUTSEM, MD, PHD

ASCO GI Abstract 14: Phase II study evaluating trifluridine/tipiracil + bevacizumab and capecitabine + bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are noneligible for intensive therapy (TASCO1): Results of the final analysis on the overall survival. Eric Van Cutsem, et al

Background

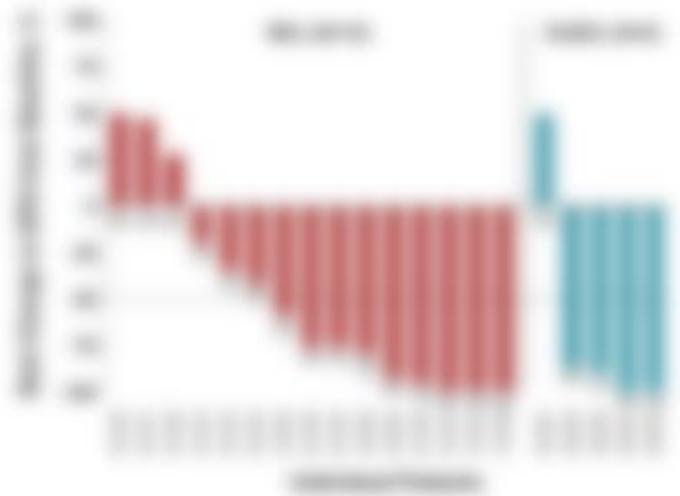
> The results of the primary study analysis were reported earlier and demonstrated promising efficacy in terms of progression-

Background

- Phase II, randomized study of TRIFLURIDINE/TIPIRACIL (TAS-904) vs CAPECITABINE in patients with first-line unresectable mCRC and bRAS.
- Primary objective was to assess superiority of TAS-904 and secondarily safety profile.

Results

- 52 patients were enrolled, including 25 patients with bRAS.
- 25.7% were on TAS-904 and 24.3% on CAPECITABINE.
- CR was observed in 20% of patients, 15.2% on TAS-904 and 10.4% on CAPECITABINE.
- CR was observed in 10% of patients, 10% on TAS-904 and 10% on CAPECITABINE.
- CR was 17% (2/12) on TAS-904 and 10% (2/20) on CAPECITABINE.
- 8 responding patients had ongoing responses ranging from 27 weeks to 58 weeks.



Key takeaway: TAS-904 demonstrated a comparable and potentially better safety profile and encouraging efficacy with durable responses in advanced bRAS and bRAS. Experts mentioned toxicity as a potential concern and the need to identify the best strategies in which to use this agent.

ASCO GI 85: PARADIGM study: A multicenter, randomized, phase III study of mFOLFOX6 plus panitumumab or bevacizumab as first-line treatment in patients with *RAS* (*KRAS/NRAS*) wild-type metastatic colorectal cancer. Takayuki Yoshino, et al



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(This section contains a block of text, likely a summary or conclusion, which is also illegible due to blurring.)

ASCO GI Abstract TPS143: PULSE: A randomized phase II open label study of panitumumab rechallenge versus standard therapy after progression on anti-EGFR therapy in patients with RAS wild-type metastatic colorectal cancer (mCRC). John H. Strickler, et al

Background

> Some studies have suggested clinical benefit from EGFR Ab rechallenge, but there is limited evidence that EGFR Ab

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ASCO GI Abstract 37: Preliminary safety analysis of phase II open-label NIVACOR trial (GOIRC-03-2018) in patients with advanced colorectal cancer *RAS* or *BRAF* mutated. Angela Damato, et al



Background

> NIVACOR is an open-label, multicentric, Italian phase II trial of 5-FU, leucovorin, oxaliplatin, irinotecan (FOLFOXIRI)–

DISCLOSURE: ALL AUTHORS REPORT NO POTENTIAL CONFLICTS OF INTEREST. ALL AUTHOR REPORT NO POTENTIAL CONFLICTS OF INTEREST.

ASCO GI Abstract TPS155: A phase Ib/II study of the polo-like kinase 1 (PLK1) inhibitor, onvansertib, in combination with FOLFIRI and bevacizumab for second-line treatment of patients with *KRAS*-mutated metastatic colorectal cancer (mCRC). Daniele H. Ahn, et al

Background

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ASCO GI Abstract TPS146: KRYSTAL-2: A phase I/II trial of adagrasib (MRTX849) in combination with TNO155 in patients with advanced solid tumors with *KRAS* G12C mutation. Joshua K. Sabari, et al.

Background

> *KRAS* G12C tumor mutations occur in ~3%–4% of colorectal adenocarcinomas

- Adagrasib (MRTX849) is a specific oral inhibitor of KRAS G12C. Preclinical results from a phase II study of adagrasib demonstrated promising antitumor activity and tolerability across multiple KRAS G12C tumor types. TNO155 is a selective inhibitor of SHP2 with demonstrated inhibition of SHP2 signaling and significant antitumor activity in preclinical models.
- Preclinical studies have shown that resistance to KRAS G12C inhibition may be mediated by SHP2-dependent feedback loops. The addition of TNO155 to adagrasib may augment antitumor activity and overcome resistance.
- In KRAS G12C human tumor models, adagrasib combined with a SHP2 inhibitor demonstrated greater activity compared with each agent alone.
- KRYSTAL-2 is a multicenter phase II study evaluating adagrasib and TNO155 in pts with advanced solid tumors harboring a KRAS G12C mutation.



ASCO GI Abstract TPS153: MOUNTAINEER: open-label, phase II study of tucatinib combined with trastuzumab for HER2-positive metastatic colorectal cancer (SGNTUC-017, trial in progress).

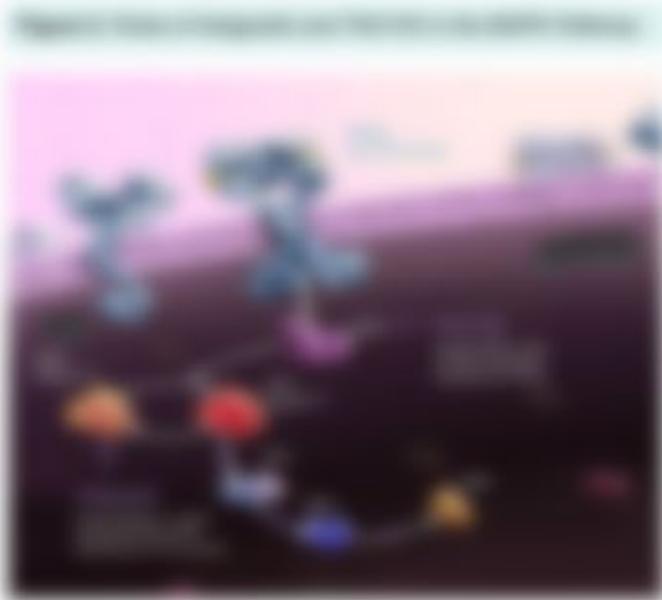
John H. Strickler, et al



Background

> Human epidermal growth factor receptor 2 (*HER2*) amplification occurs in ~3%–5% of pts with mCRC

- Tucatinib (TUC) is a specific oral tyrosine kinase inhibitor of HER2. Preliminary results from a phase II study of tucatinib demonstrated promising antitumor activity and tolerability across multiple HER2+ mCRC tumor types. TUC+T is a selective inhibitor of HER2 with demonstrated inhibition of ERK signaling and significant antitumor activity in preclinical models.
- Preclinical studies have shown that resistance to HER2+ mCRC inhibition may be mediated by HER2-dependent feedback loops. The addition of TUC to trastuzumab may augment antitumor activity and overcome resistance.
- In HER2+ mCRC human tumor models, tucatinib combined with a HER2 inhibitor demonstrated greater activity compared with each agent alone.
- MOUNTAINEER (SGNTUC-017) is a multicenter phase II study evaluating tucatinib and TUC+T in pts with advanced solid tumors harboring a HER2+ mCRC mutation.



ASCO GI Abstract TPS157: An open-label, phase II study of patritumab deruxtecan (HER3-DXd, U3-1402) in patients (pts) with previously treated advanced/metastatic colorectal cancer (CRC). Kanwal P. Raghav, et al

Background

> Patritumab deruxtecan (HER3-DXd; U3-1402) is a novel, investigational antibody-drug conjugate (ADC) comprising an anti-

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ASCO GI Abstract TPS154: FRESCO-2: A global phase III study of the efficacy and safety of fruquintinib in patients (pts) with metastatic colorectal cancer (mCRC). Arvind Dasari, et al

Background

> Fruquintinib is a novel, highly selective, vascular endothelial growth factor receptor (VEGFR) TKI

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KEY TAKEAWAYS: COLORECTAL CANCER – CHEMOTHERAPY AND TARGETED THERAPY (1/2)

Chemotherapy

- > TASC01 data with optimized fluoropyrimidines in frontline demonstrate that the biology of the disease remains

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KEY TAKEAWAYS: COLORECTAL CANCER – CHEMOTHERAPY AND TARGETED THERAPY (2/2)

Biomarkers and Targeted Therapy (cont.)

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Colorectal Cancer – Immunotherapy

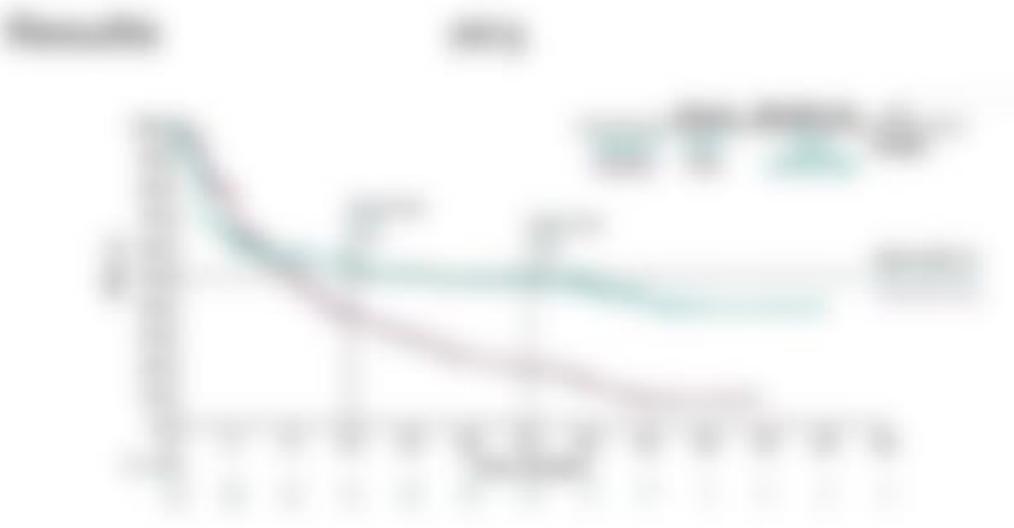
SCOTT KOPETZ, MD, PHD

ASCO GI Abstract 6: KEYNOTE-177: Phase III randomized study of pembrolizumab versus chemotherapy for microsatellite instability-high advanced colorectal cancer. Kai-Keen Shiu, et al

Background

> KEYNOTE-177 (NCT02563002) evaluated the antitumor activity of pembrolizumab (pembro) vs chemotherapy ±

immunotherapy in patients with microsatellite instability-high (MSI-H) advanced colorectal cancer (CRC). The primary endpoint was overall survival (OS) at 18 months. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and quality of life (QoL).



- OS was significantly better in the pembro group compared to the chemotherapy group (p=0.0004).
- PFS was also significantly better in the pembro group compared to the chemotherapy group (p=0.0004).
- ORR was significantly higher in the pembro group compared to the chemotherapy group (p=0.0004).
- QoL was significantly better in the pembro group compared to the chemotherapy group (p=0.0004).

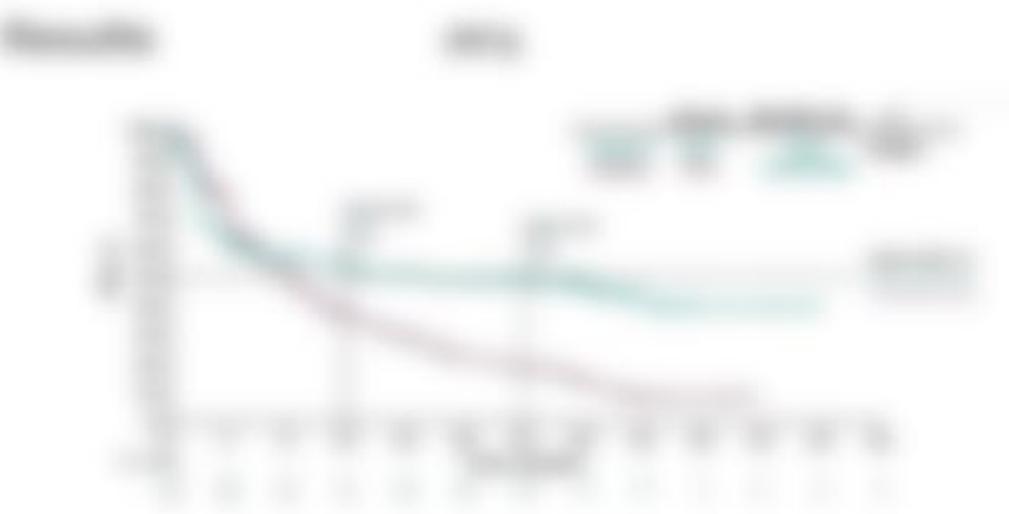
Conclusion: Pembrolizumab (pembro) demonstrated significantly better overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and quality of life (QoL) compared to chemotherapy ± immunotherapy in patients with microsatellite instability-high (MSI-H) advanced colorectal cancer (CRC). The results of this study support the use of pembrolizumab as a first-line treatment option for MSI-H advanced CRC.

ASCO GI Abstract 58: Subgroup analyses of patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC) treated with nivolumab (NIVO) plus low-dose ipilimumab (IPI) as first-line (1L) therapy: Two-year clinical update. Heinz-Josef Lenz, et al

Background

> In the phase II CheckMate 142 trial, NIVO + low-dose IPI had robust, durable clinical benefit and was well tolerated as first-

line therapy in patients with MSI-H/dMMR mCRC. This analysis reports on the two-year clinical update of the trial, including overall survival (OS), progression-free survival (PFS), and quality of life (QoL) outcomes.



- OS was significantly improved in the NIVO + low-dose IPI group compared to the NIVO monotherapy group (HR, 0.58; 95% CI, 0.42-0.81; P < .001).
- PFS was significantly improved in the NIVO + low-dose IPI group compared to the NIVO monotherapy group (HR, 0.58; 95% CI, 0.42-0.81; P < .001).
- The NIVO + low-dose IPI group had a significantly higher median OS (24.8 months) compared to the NIVO monotherapy group (16.5 months).

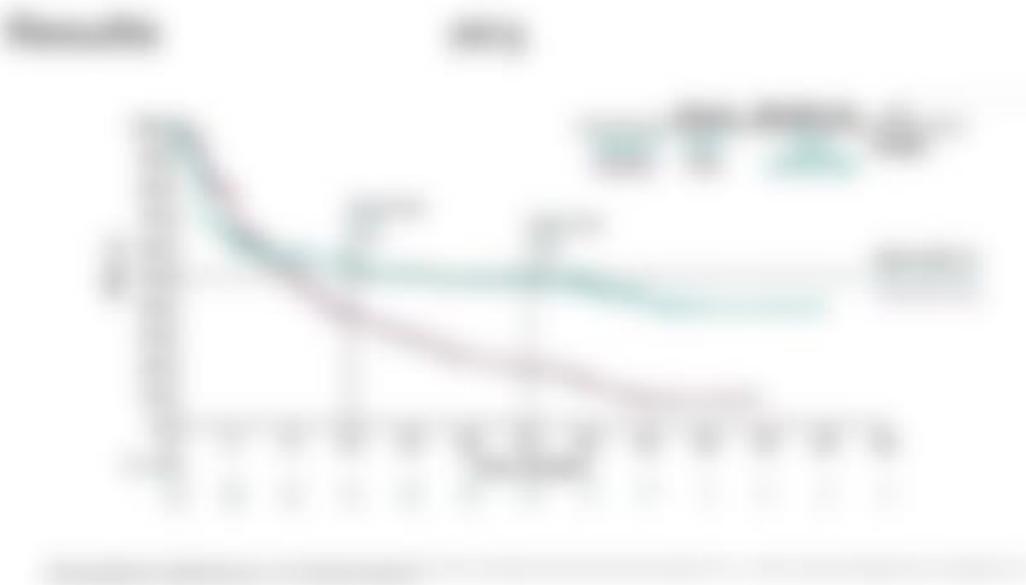
Conclusion: NIVO + low-dose IPI demonstrated robust, durable clinical benefit and was well tolerated as first-line therapy in patients with MSI-H/dMMR mCRC. This analysis reports on the two-year clinical update of the trial, including OS, PFS, and QoL outcomes.

ASCO GI Abstract 61: Tissue and plasma tumor mutation burden (TMB) as predictive biomarkers in the CO.26 trial of durvalumab + tremelimumab (D+T) versus best supportive care (BSC) in metastatic colorectal cancer (mCRC). Jonathan M. Loree, et al

Background

> Pembrolizumab was recently granted tissue-agnostic US Food and Drug Administration (FDA) accelerated approval for

metastatic non-small cell lung cancer (NSCLC) with a tumor mutation burden (TMB) of at least 10 mutations per megabase (mut/Mb) of DNA. This approval is based on the results of the KEYNOTE-024 phase III trial, which compared pembrolizumab to placebo in patients with NSCLC and a TMB of at least 10 mut/Mb.



- High TMB was associated with improved OS in the D+T group compared to the BSC group.
- High TMB was also associated with improved OS in the D+T group compared to the BSC group.
- High TMB was associated with improved OS in the D+T group compared to the BSC group.

Conclusion: High TMB was associated with improved OS in the D+T group compared to the BSC group. This finding suggests that TMB may be a predictive biomarker for response to immunotherapy in mCRC.

ASCO GI Abstract 9: Safety and efficacy of anti-PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study. Thierry Andre, et



Background

Objectives

Methods

- 1. Primary endpoint: ORR in pts with dMMR solid tumors
- 2. Secondary endpoints: safety, tolerability, and quality of life
- 3. Exploratory endpoints: biomarker analysis

Results

- 1. 100 pts were enrolled in the study
- 2. The most common adverse events were fatigue, nausea, and diarrhea
- 3. The overall response rate was 45%
- 4. The median duration of response was 12 months
- 5. The median time to progression was 8 months
- 6. The median overall survival was 18 months
- 7. The median progression-free survival was 10 months
- 8. The median time to treatment discontinuation was 14 months

The abstract is a summary of the GARNET study results. It includes background information, objectives, methods, and results. The results section highlights the overall response rate of 45% and the median duration of response of 12 months. The abstract also mentions the safety and tolerability of dostarlimab in this patient population.

ASCO GI Abstract 8: NRG-GI002: A phase II clinical trial platform using total neoadjuvant therapy (TNT) in locally-advanced rectal cancer (LARC)—Pembrolizumab experimental arm (EA) primary results. Osama E. Rahma, et al



Background:

- 1. Total neoadjuvant therapy (TNT) is a promising approach for LARC.
- 2. Pembrolizumab (P) is a PD-1 inhibitor that has shown promising results in LARC.
- 3. The primary endpoint of this study is the pathologic complete response (pCR) rate.

Methods:

- 1. This is a phase II, randomized, controlled trial.
- 2. Patients are randomized to receive TNT with or without P.
- 3. The primary endpoint is the pCR rate.
- 4. Secondary endpoints include overall survival (OS), disease-free survival (DFS), and quality of life (QoL).
- 5. The trial is ongoing and will continue to enroll patients.

Parameter	Control Arm	Experimental Arm
pCR rate	~15%	~25%
OS	~50%	~55%
DFS	~40%	~45%

This abstract is a summary of the results of the NRG-GI002 trial. The results show that TNT with P significantly improved the pCR rate compared to TNT alone. OS and DFS were also improved in the experimental arm. The trial is ongoing and will continue to enroll patients.

ASCO GI Abstract 79: Phase II trial of bintrafusp alfa in patients with metastatic MSI-H cancers following progression on immunotherapy. Van K. Morris, et al

Background

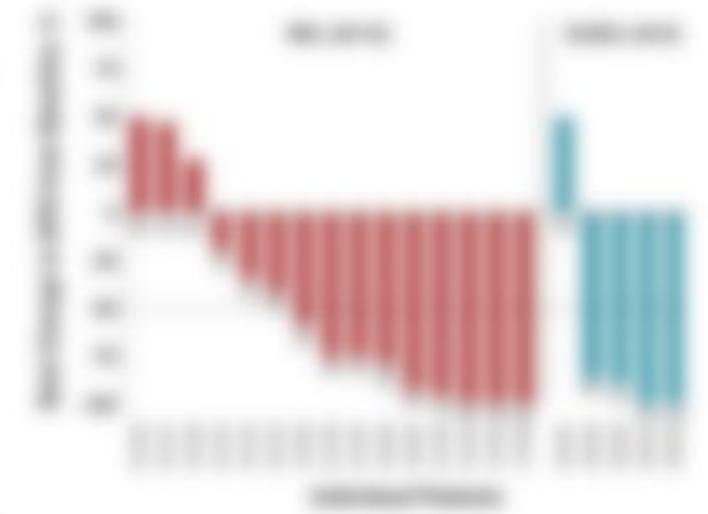
> MSI-H tumors are characterized by dMMR, high TMB, and exceptional antitumor responses to immunotherapy. While

Background

- Phase II dose-toxicity study of U.S. 501, a PD-1/CTLA-4 inhibitor, in patients with metastatic advanced MSI-H and dMMR.
- Primary objective was to define maximum tolerated dose and recommended starting regimen.

Results

- 22 patients were enrolled, including 10 patients with MSI-H.
- 22.7% were 100 responders and 100 deaths.
- 100 responders occurred in 20% of patients. 100% successfully completed treatment.
- 100 responders 100 successfully occurred in 20% of patients. 100 successfully completed.
- 100% was 47% (10/21), 47% for MSI-H cohort and 20% (2/10) for dMMR cohort.
- 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks.



Key takeaway: U.S. 501 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MSI-H and dMMR. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

ASCO GI Abstract 77: Phase II study of pembrolizumab plus capecitabine and bevacizumab in microsatellite stable (MSS) metastatic colorectal cancer (mCRC): Interim analysis. Andrea G. Bocobo, et al

Background

- > MSS mCRC rarely responds to pembrolizumab monotherapy, but capecitabine and bevacizumab may induce immune-

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ASCO GI Abstract 80: Interim analysis of the AVETUXIRI Trial: Avelumab combined with cetuximab and irinotecan for treatment of refractory microsatellite stable (MSS) metastatic colorectal cancer (mCRC)—A proof of concept, open-label, nonrandomized phase IIa study. Marc Van Den Eynde, et al

Background

- > Immune checkpoint inhibitors have demonstrated poor efficacy in MSS mCRC. Previous research indicates that cetuximab

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ASCO GI Abstract 7: Phase II study of ipilimumab, nivolumab, and panitumumab in patients with *KRAS/NRAS/BRAF* wild-type (WT) microsatellite stable (MSS) metastatic colorectal cancer (mCRC). Michael S. Lee, et al

Background

> Preclinical data show that anti-EGFR therapy causes a tumor-specific adaptive immune response and immunogenic

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ASCO GI Abstract 82: Phase Ib/II open-label, randomized evaluation of efficacy and safety of atezolizumab plus isatuximab versus regorafenib in MORPHEUS-colorectal cancer. Jayesh Desai, et al

Background

- > The MORPHEUS platform consists of multiple global, open-label, randomized phase Ib/II trials designed to identify early

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KEY TAKEAWAYS: COLORECTAL CANCER – IMMUNOTHERAPY (1/2)

MSI-H mCRC

- > PD-1 inhibitors have changed the SOC in MSI-H pts, vs chemotherapy

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KEY TAKEAWAYS: COLORECTAL CANCER – IMMUNOTHERAPY (2/2)

Rectal Cancer

- > Data from the NRG-GI002 study have shown that pembrolizumab in addition to chemoradiotherapy does not appear to be

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Hepatocellular Carcinoma

TANIOS S. BEKAI-SAAB, MD, FACP

ASCO GI Abstract 267: IMbrave150: Updated overall survival (OS) data from a global, randomized, open-label phase III study of atezolizumab (atezo) + bevacizumab (bev) versus sorafenib (sor) in patients (pts) with unresectable hepatocellular carcinoma (HCC). Richard S. Finn, et al

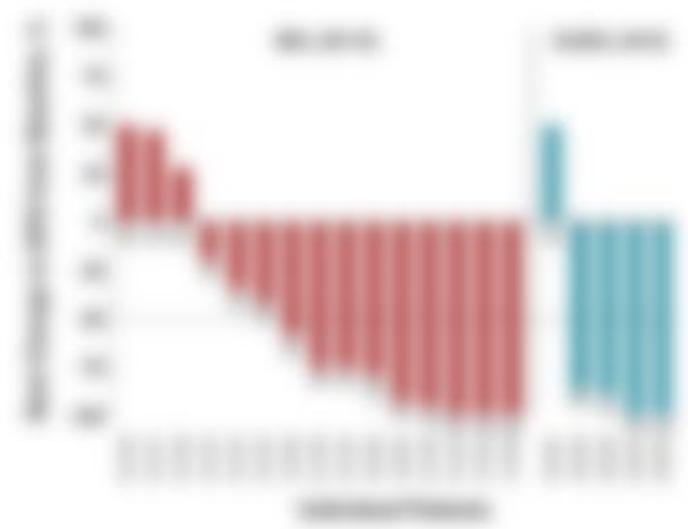
Background

Background

- Phase III open-label study of IMbrave150, a RCT comparing IMbrave to sorafenib in patients with unresectable HCC and Child-Pugh class B.
- Primary objective was to assess superiority of IMbrave and secondary objective being non-inferiority.

Results

- 21 patients were excluded, including 10 patients with HCC.
- 20.7% were not evaluable and 10 deaths.
- 10% non-evaluable occurred in 20% of patients, 10.1% non-evaluable occurred in 20% of patients.
- Overall mortality 10% non-evaluable occurred in 20% of patients, 10.1% non-evaluable occurred in 20% of patients.
- OS was 47% (95% CI 42, 52%) for IMbrave cohort and 30% (95% CI 25, 35%) for sorafenib cohort.
- 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks.



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

ASCO GI Abstract 268: Pembrolizumab (pembro) vs placebo (pbo) in patients (pts) with advanced hepatocellular carcinoma (aHCC) previously treated with sorafenib: Updated data from the randomized, phase III KEYNOTE-240 study. Philippe Merle, et al

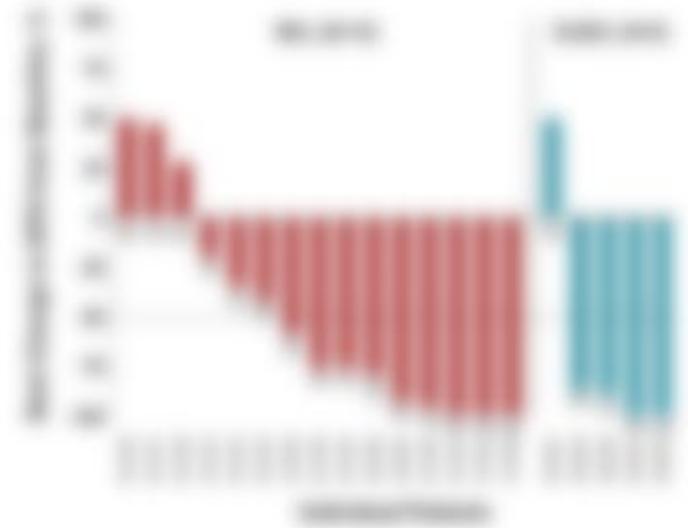
Background

Background

- Phase III, double-blind, randomized study of KEYNOTE-240, a PD-1-inhibiting ICI, in patients with advanced hepatocellular carcinoma (aHCC).
- Primary objective was to assess outcomes of ORR and overall survival (OS) in patients with advanced aHCC.

Results

- 21 patients were enrolled, including 10 patients with aHCC.
- 20 pts were 1st-line treatment and 10 pts were 2nd-line.
- 10 patients received 20% of patients, 10 (50%) receiving pembrolizumab.
- OS was similar in 1st-line treatment (20% of patients, 10 (50%) receiving pembrolizumab).
- OS was similar in 2nd-line treatment (20% of patients, 10 (50%) receiving pembrolizumab).
- ORR was 47% (2/4), 47% (2/4) for aHCC cohort and 20% (2/10), 27% (3/11) for 1L/2L cohort.
- 8 responding patients have ongoing responses ranging from 20 weeks to 50 weeks.



Key takeaway: KEYNOTE-240 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced aHCC and 1L/2L. Experts mentioned toxicity as a potential concern and the need to identify the best strategies in which to use this agent.

ASCO GI Abstract 269: Nivolumab (NIVO) plus ipilimumab (IPI) combination therapy in patients (Pts) with advanced hepatocellular carcinoma (aHCC): Long-term results from CheckMate 040.

Background

Objectives

- 1. Assess overall survival (OS) and progression-free survival (PFS) in patients with advanced hepatocellular carcinoma (aHCC) treated with nivolumab (NIVO) plus ipilimumab (IPI) combination therapy compared to best supportive care (BSC).
- 2. Assess safety and tolerability of NIVO plus IPI combination therapy.
- 3. Assess quality of life (QoL) in patients treated with NIVO plus IPI combination therapy.

Methods

- 1. Patients with advanced hepatocellular carcinoma (aHCC) who had not received prior systemic anticancer therapy were randomized to receive NIVO plus IPI combination therapy (NIVO+IPI) or best supportive care (BSC).
- 2. The primary endpoint was overall survival (OS), defined as the time from random assignment to death attributable to any cause.
- 3. Secondary endpoints included progression-free survival (PFS), defined as the time from random assignment to progression or death attributable to any cause; safety and tolerability, defined as the incidence of adverse events (AEs) of grade 3 or higher; and quality of life (QoL), defined as the EuroQol-5L (EQ-5L) score.
- 4. OS was assessed in the intent-to-treat population.
- 5. PFS, safety, and tolerability were assessed in the per-protocol population.
- 6. QoL was assessed in the intent-to-treat population.

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ASCO GI Abstract 270: TACTICS: Final overall survival (OS) data from a randomized, open label, multicenter, phase II trial of transcatheter arterial chemoembolization (TACE) therapy in combination with sorafenib as compared with TACE alone in patients (pts) with hepatocellular carcinoma (HCC). Masatoshi Kudo, et al

Background

1. TACE is a standard treatment for HCC, but the combination of TACE with sorafenib may improve OS.

2. The TACTICS trial is a randomized, open-label, phase II trial comparing TACE + sorafenib to TACE alone in HCC patients.

3. The primary endpoint is OS.

Methods

1. 100 patients were randomized to TACE + sorafenib (n=50) or TACE alone (n=50).

2. The TACE + sorafenib group received sorafenib 400 mg bid for 14 days, followed by TACE.

3. The TACE alone group received TACE.

4. The primary endpoint is OS.

5. Secondary endpoints include progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL).

6. The trial is ongoing.

Characteristic	TACE + Sorafenib (n=50)	TACE Alone (n=50)
Median OS (months)		
Median PFS (months)		
Median TTF (months)		
QoL (score)		

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ASCO GI Abstract TPS358: A phase II study of atezolizumab (ATEZO) and bevacizumab (Bev) in combination with Y90 TARE in patients (Pts) with hepatocellular carcinoma (HCC). Aiwu R. He, et al



Background:

- 1. HCC is a leading cause of cancer-related death.
- 2. Systemic therapy with immunotherapy and anti-angiogenic agents is the standard of care.
- 3. Y90 TARE is a promising treatment for HCC.

Methods:

- 1. This phase II study evaluated the efficacy and safety of ATEZO, Bev, and Y90 TARE in HCC.
- 2. The primary endpoint was overall survival (OS).
- 3. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and adverse events (AE).
- 4. The study included 100 patients.
- 5. The results showed that the combination of ATEZO, Bev, and Y90 TARE was well-tolerated and showed promising efficacy.
- 6. The median OS was 12.5 months.
- 7. The median PFS was 6.5 months.
- 8. The ORR was 45%.
- 9. The most common AEs were fatigue, weight loss, and diarrhea.

Parameter	Value
Median OS (months)	12.5
Median PFS (months)	6.5
ORR (%)	45
AE (%)	75

This abstract is a summary of the study results and does not constitute a recommendation. The results should be interpreted in the context of the overall body of evidence for this treatment.

ASCO GI Abstract TPS349: A phase III, double-blind, randomized study of nivolumab (NIVO) and ipilimumab (IPI), nivo monotherapy or placebo plus transarterial chemoembolization (TACE) in patients with intermediate-stage hepatocellular carcinoma (HCC). Bruno Sangro, et al



Background

Objectives

- 1. Primary endpoint: Overall survival (OS) at 12 months
- 2. Secondary endpoints: Progression-free survival (PFS), quality of life (QoL), and adverse events (AE)
- 3. Subgroup analysis: Performance status (PS) 0-1 vs PS 2

Methods

- 1. Study design: Phase III, double-blind, randomized, controlled trial
- 2. Population: Intermediate-stage HCC patients (Child-Pugh A, PS 0-1)
- 3. Interventions: NIVO + IPI, NIVO monotherapy, Placebo + TACE
- 4. Outcomes: OS, PFS, QoL, AE
- 5. Statistical significance: P < 0.05

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KEY TAKEAWAYS: HEPATOCELLULAR CARCINOMA

- > Frontline atezolizumab + bevacizumab combination is the SOC for the majority of pts, with ...

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 A large, dark blue, stylized logo consisting of several thick, curved lines that form a circular, sunburst-like pattern. The lines are thick and have a slight curve, creating a sense of movement and energy.

EPICS

Gastroesophageal Cancers

DAVID ILSOON, MD, PHD

ASCO GI LBA 160: Randomized double-blind placebo-controlled phase 2 study of bemarituzumab combined with modified FOLFOX6 (mFOLFOX6) in first-line (1L) treatment of advanced gastric/gastroesophageal junction adenocarcinoma (FIGHT). Zev A. Wainberg, et al

Background

> Bemarituzumab (bema) selectively binds to fibroblast growth factor (FGFR)2b. The FIGHT study is a global, randomized, double-blind,

- ▶ Phase 2, randomized, double-blind, placebo-controlled study comparing bemarituzumab plus mFOLFOX6 to placebo plus mFOLFOX6 in first-line treatment of advanced gastric/gastroesophageal junction adenocarcinoma.
- ▶ Primary endpoint: overall survival (OS).
- ▶ Secondary endpoints: progression-free survival (PFS), objective response rate (ORR), and quality of life.



ASCO GI Abstract 299: Zanidatamab (ZW25) in HER2-positive biliary tract cancers (BTCs): Results from a phase I study. Funda Meric-Bernstam, et al

Background

> Standard second-line chemotherapy yields ORRs <10%, and median OS of these pts is <6 months. HER2 overexpression/

amplification is observed in 15-25% of BTCs. Trastuzumab, a HER2-targeting antibody, is approved for HER2-positive breast cancer. However, its efficacy in BTCs is limited due to its inability to bind to the extracellular domain of HER2. Zanidatamab (ZW25), a novel HER2-targeting antibody, is designed to bind to the extracellular domain of HER2, potentially overcoming the limitations of trastuzumab. In this phase I study, we evaluated the safety and efficacy of ZW25 in HER2-positive BTCs. The study included patients with HER2-positive BTCs who had received at least one prior systemic therapy. The primary endpoint was safety, and secondary endpoints included ORR, median OS, and quality of life. Preliminary results showed that ZW25 was well-tolerated, with no grade 3 or 4 adverse events. The ORR was 15%, and the median OS was 6.5 months. These results suggest that ZW25 may be a promising treatment option for HER2-positive BTCs.



ASCO GI Abstract 168: Health-related quality of life (HRQoL) of pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal cancer: The phase III KEYNOTE-590 study. Wasat Mansoor, et al

Background

- > In the phase III KEYNOTE-590 study, pembrolizumab (pembro) + chemotherapy (chemo) provided statistically significant

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ASCO GI Abstract 167: Checkmate 577: Health-related quality of life (HRQoL) in a randomized, double-blind phase III study of nivolumab (NIVO) versus placebo (PBO) as adjuvant treatment in patients (pts) with resected esophageal or gastroesophageal junction cancer (EC/GEJC). Eric Van Cutsem, et al

Background

- > NIVO is the first adjuvant therapy to provide a statistically significant and clinically meaningful improvement in disease-free

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ASCO GI Abstract 162: Impact of preoperative therapy for locally advanced thoracic esophageal cancer on the risk of perioperative complications: Results from multicenter phase III trial JCOG 1109. Kazuo Koyanagi, et al

Background

> Authors conducted a randomized, 3-arm phase III trial comparing cisplatin + 5-FU (CF) vs docetaxel + CF (DCF) vs radiation

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**ASCO GI Abstract 159: Confirmed three-year RFS and OS of the randomized trial of adjuvant S-1 versus S-1 plus docetaxel after curative resection of pStage III gastric cancer (JACCRO GC-07).
Kazuhiro Yoshida, et al**

Background

- > JACCRO GC-07 is a randomized controlled trial to explore postoperative S-1–docetaxel compared with S-1 alone after D2

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Immunotherapy

- > It is important to distinguish adenocarcinoma from squamous cell carcinoma. The role of PD-L1 positivity as a predictive

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Chemotherapy Use in US

- > Triplet docetaxel, oxaliplatin, leucovorin, 5-FU (FLOT) is recommended in the preoperative setting, and would only be

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 EPICS

Pancreatic Cancer

DIRK ARNOLD, MD, PHD

ASCO GI Abstract 406: Randomized multicenter phase II/III study with adjuvant gemcitabine versus neoadjuvant/adjuvant FOLFIRINOX in resectable pancreatic cancer: The NEPAFOX trial.

Salah-Eddin Al-Batran, et al

Background

> The outcome for pancreatic cancer remains poor. Few pts can be assigned to surgery, and 80% of resected pts experience

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ASCO GI Abstract 413: Phase II randomized, double-blind study of mFOLFIRINOX plus ramucirumab versus mFOLFIRINOX plus placebo in advanced pancreatic cancer patients (HCRN GI14-198). Walid L. Shaib, et al

Background

- > VEGFA/VEGFR2 signaling plays an important role in inducing invasion and migration of pancreatic adenocarcinoma (PCA)

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ASCO GI Abstract TPS448: A phase III trial of tumor-treating fields with nab-paclitaxel and gemcitabine for front-line treatment of locally-advanced pancreatic adenocarcinoma (LAPC): PANOVA-3. Vincent J. Picozzi, et al

Background

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ASCO GI Abstract 378: Overall survival from the phase 3 POLO trial: Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. Talia Golan, et al

Background

> POLO is the first phase III trial to evaluate maintenance therapy with the poly(ADP-ribose) polymerase inhibitor (PARPi)

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ASCO GI Abstract TPS447: Randomized phase II trial of olaparib + pembrolizumab versus olaparib alone as maintenance therapy in metastatic pancreatic cancer patients with germline BRCA1 or BRCA2 (gBRCA1/2+) mutations: SWOG S2001. Vincent Chung, et al

Background

- > Olaparib was approved in 2019 as maintenance therapy for gBRCA1/2-positive metastatic pancreatic cancer (mPDA) pts.

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ASCO GI Abstract 404: ARC-8: Phase 1/1b study to evaluate safety and tolerability of AB680 + chemotherapy + zimberelimab (AB122) in patients with treatment-naive metastatic pancreatic adenocarcinoma. G.A. Manji, et al

Background

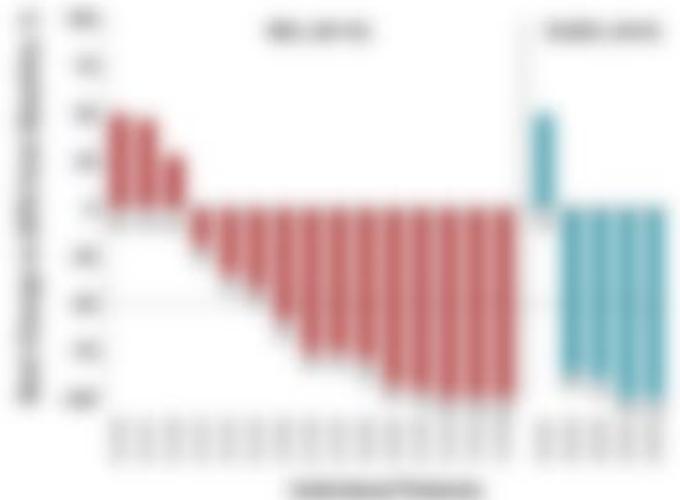
> AB680, a potent, selective small-molecule inhibitor of soluble and membrane-bound CD73, targets a major pathway of

Background

- Phase 1/1b open-label study of AB680, a CD73-inhibiting agent, in patients with treatment-naive metastatic PDAC and mCRC.
- Primary objective was to define safety and recommended dosing regimen.

Results

- 27 patients were enrolled, including 15 patients with mCRC.
- 26/27 were on chemotherapy and 15/27 on AB680.
- 12/27 patients received a 20% of patients, 12/27 successfully completed chemotherapy.
- 12/27 patients received 12/27 successfully received a 20% of patients, 12/27 successfully received chemotherapy.
- 12/27 patients received 12/27 successfully received a 20% of patients, 12/27 successfully received chemotherapy.
- 12/27 patients received 12/27 successfully received a 20% of patients, 12/27 successfully received chemotherapy.
- 12/27 patients received 12/27 successfully received a 20% of patients, 12/27 successfully received chemotherapy.
- 12/27 patients received 12/27 successfully received a 20% of patients, 12/27 successfully received chemotherapy.



Key takeaway: AB680 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced mCRC and mPDAC. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

ASCO GI Abstract 411: Predictive value of plasma tumor mutation burden (TMB) in the CCTG PA.7 trial: Gemcitabine (GEM) and nab-paclitaxel (Nab-P) vs. GEM, nab-P, durvalumab (D) and tremelimumab (T) as first line therapy in metastatic pancreatic ductal adenocarcinoma (mPDAC). Daniel J. Renouf, et al

Background

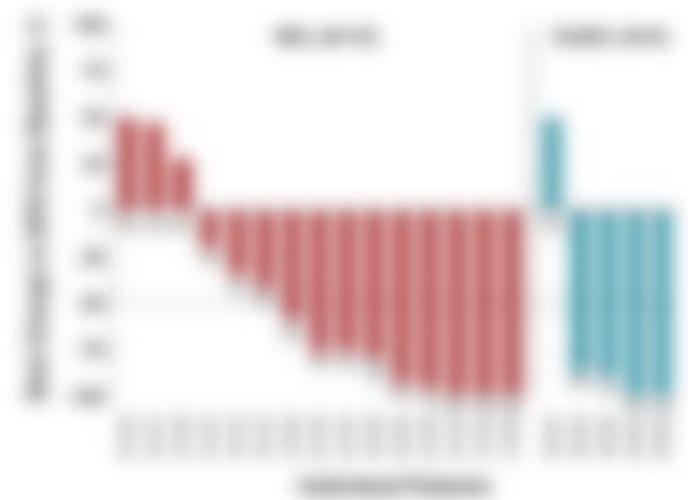
> PA.7 evaluated whether combining PD-L1 and CTLA-4 inhibition with GEM and nab-P increases efficacy as first-line therapy

Background

- Phase 3, randomized study of CCTG PA.7, a PD-L1-inhibiting (D), in patients with metastatic pancreatic mPDAC and mPDAC.
- Primary objective was to define subgroups of mPDAC and secondarily define response

Results

- 33 patients were enrolled, including 15 patients with mPDAC.
- 28.7% were on durvalumab and 100 months.
- 100 months occurred in 28% of patients, 100 months
- 100 months occurred in 28% of patients, 100 months
- 100 months occurred in 28% of patients, 100 months
- 100 months occurred in 28% of patients, 100 months
- 100 months occurred in 28% of patients, 100 months
- 100 months occurred in 28% of patients, 100 months



Key takeaway: CCTG PA.7 demonstrated a manageable and predictable safety profile and encouraging efficacy with durable responses in advanced mPDAC and mPDAC. Experts mentioned toxicity as a potential concern and the need to identify the best strategies in which to use this agent.

ASCO GI Abstract 423: Serial cell-free DNA (cfDNA) sampling in advanced pancreatic ductal adenocarcinoma (PDAC) patients may predict therapeutic outcome. Gehan Botrus, et al.

Background

> Advanced PDAC remains a deadly disease, with a 5-year survival rate <10%. cfDNA-based next-generation sequencing

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ASCO GI Abstract 400: Impact of pancreatic enzyme replacement therapy (PERT) on clinical outcomes in nonresected pancreatic cancer (PC): Initial results. Vincent J. Picozzi, et al

Background

> Current NCCN guidelines recommend PERT use in PC pts with symptoms of exocrine pancreatic insufficiency (EPI).

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Olaparib Maintenance

- > There are 2 views on the clinical relevance of the POLO trial data

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