



EPICS

Conference Coverage: ESMO 2024 – Focus on Gastrointestinal (GI) Malignancies

19 September 2024

8.00 AM – 11.00 AM MST/17.00 – 20.00 CEST

Content	Slide
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Metastatic Colorectal Cancer (mCRC) – Including Targeted Therapy	➔
Microsatellite Stable (MSS) and Microsatellite Instability-High (MSI-H) CRC	➔
Rectal Cancer	➔
Gastric and Gastroesophageal Junction (GEJ) Cancers	➔
Pancreatic Cancer and Biliary Tract Cancer	➔
Hepatocellular Carcinoma (HCC)	➔

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LIVE
ROUNDTABLE



DATE:
19 September 2024



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

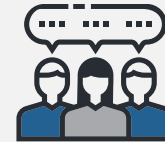


INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts
in GI malignancies

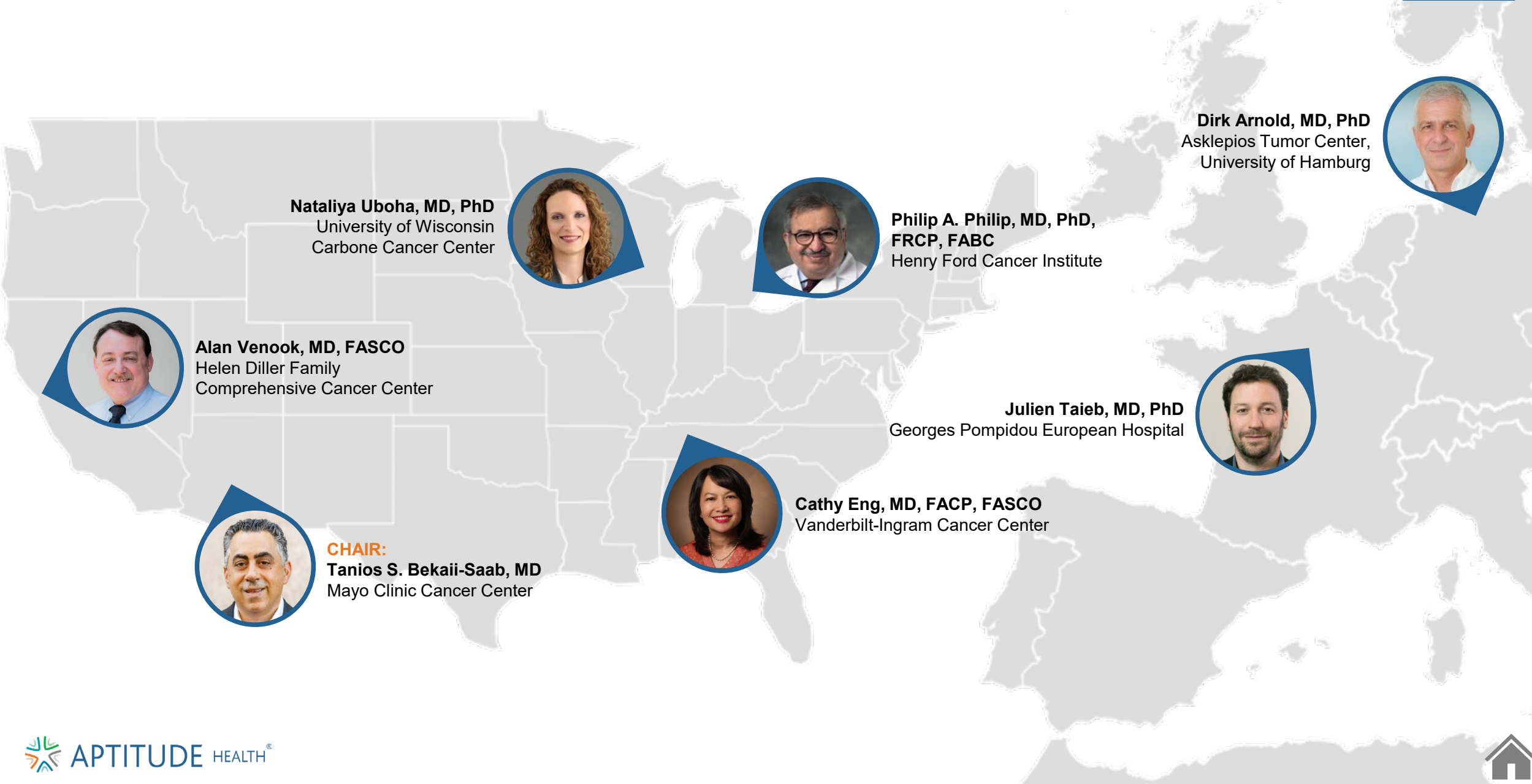
- > 5 from the US
- > 2 from Europe



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

Panel Consisting of 5 US and 2 European GI Cancer Experts

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Nataliya Uboha, MD, PhD
University of Wisconsin
Carbone Cancer Center



**Philip A. Philip, MD, PhD,
FRCP, FABC**
Henry Ford Cancer Institute



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



Alan Venook, MD, FASCO
Helen Diller Family
Comprehensive Cancer Center



Julien Taieb, MD, PhD
Georges Pompidou European Hospital



CHAIR:
Tanios S. Bekaii-Saab, MD
Mayo Clinic Cancer Center



Cathy Eng, MD, FACP, FASCO
Vanderbilt-Ingram Cancer Center



Meeting Agenda (1/2)

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Time (MST/CEST)	Topic	Speaker/Moderator
8.00 AM – 8.05 AM/17.00 – 17.05	Welcome and Introductions	Tanios S. Bekaii-Saab, MD
8.05 AM – 8.15 AM/17.05 – 17.15	Metastatic Colorectal Cancer (mCRC) – Including Targeted Therapy	Julien Taieb, MD, PhD
8.15 AM – 8.25 AM/17.15 – 17.25	Discussion	All
8.25 AM – 8.35 AM/17.25 – 17.35	Microsatellite Stable (MSS) and High Microsatellite Instability (MSI-H) CRC	Dirk Arnold, MD, PhD
8.35 AM – 8.50 AM/17.35 – 17.50	Discussion	All
8.50 AM – 8.55 AM/17.50 – 17.55	Key Takeaways	Julien Taieb, MD, PhD, and Dirk Arnold, MD, PhD
8.55 AM – 9.05 AM/17.55 – 18.05	Rectal Cancer	Cathy Eng, MD, FACP, FASCO
9.05 AM – 9.15 AM/18.05 – 18.15	Discussion	All
9.15 AM – 9.20 AM/18.15 – 18.20	Key Takeaways	Cathy Eng, MD, FACP, FASCO
9.20 AM – 9.25 AM/18.20 – 18.25	BREAK	



Meeting Agenda (2/2)

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Time (MST/CEST)	Topic	Speaker/Moderator
9.25 AM – 9.35 AM/18.25 – 18.35	Gastric and Gastroesophageal Junction (GEJ) Cancers	Nataliya Uboha, MD, PhD
9.35 AM – 9.50 AM/18.35 – 18.50	Discussion	All
9.50 AM – 9.55 AM/18.50 – 18.55	Key Takeaways	Nataliya Uboha, MD, PhD
9.55 AM – 10.05 AM/18.55 – 19.05	Pancreatic Cancer and Biliary Tract Cancer	Philip A. Philip, MD, PhD, FRCP, FABC
10.05 AM – 10.20 AM/19.05 – 19.20	Discussion	All
10.20 AM – 10.25 AM/19.20 – 19.25	Key Takeaways	Philip A. Philip, MD, PhD, FRCP, FABC
10.25 AM – 10.40 AM/19.25 – 19.40	Hepatocellular Carcinoma (HCC)	Alan Venook, MD, FASCO
10.40 AM – 10.55 AM/19.40 – 19.55	Discussion	All
10.55 AM – 11.00 AM/19.55 – 20.00	Key Takeaways	Alan Venook, MD, FASCO
11.00 AM/20.00	Summary and Closing Remarks	Tanios S. Bekaii-Saab, MD



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Congress Highlights

mCRC – Including Targeted Therapy

Sotorasib (soto), panitumumab (pani) and FOLFIRI in the first-line (1L) setting for KRAS G12C-mutated metastatic colorectal cancer (mCRC): Safety and efficacy analysis from the phase 1b CodeBreakK 101 study

Siena S, et al. Abstract 5050

STUDY POPULATION

100 patients with KRAS G12C-mutated mCRC, who were previously treated with 1-3 lines of systemic therapy, were enrolled in the study. The patients were randomized to receive either soto (n=50) or placebo (n=50) in combination with panitumumab and FOLFIRI. The primary endpoint was overall survival (OS) at 12 weeks. The secondary endpoints were progression-free survival (PFS) and quality of life (QoL). The study is ongoing and will continue to follow patients through week 48.

RESULTS

At 12 weeks, 100 patients were evaluable for OS. The median OS was 12.5 weeks in the soto group and 11.5 weeks in the placebo group. The difference was not statistically significant.

KEY CONCLUSIONS

Combining sotorasib with panitumumab and FOLFIRI in the first-line setting for KRAS G12C-mutated mCRC is safe and shows promising efficacy.

OS AT 12 WEEKS



RESPONSE RATE AT 12 WEEKS



Encorafenib + Cetuximab (EC) + FOLFIRI for BRAF V600E-Mutant Metastatic Colorectal Cancer (mCRC): Updated Results From the BREAKWATER Safety Lead-In (SLI)

Tabernero J, et al. Abstract 515MO

BACKGROUND

STUDY POPULATION

1. 1000 patients with mCRC, BRAF V600E mutant, ECOG performance grade 0-1, no prior systemic therapy, and no prior BRAF inhibitor treatment. Patients were randomized to receive either EC + FOLFIRI (n=500) or FOLFIRI (n=500). The primary endpoint was overall survival (OS) at 12 weeks. Secondary endpoints included progression-free survival (PFS), time to treatment failure (TTF), and quality of life. The study is ongoing, and patients are being followed up through week 48.

RESULTS

2. At 12 weeks, 100% of patients received EC, 100% of patients received FOLFIRI, 100% of patients received cetuximab, and 100% of patients received irinotecan. The OS at 12 weeks was significantly higher in the EC + FOLFIRI group compared to the FOLFIRI group.

KEY CONCLUSIONS

Combining cetuximab with EC + FOLFIRI significantly improved OS at 12 weeks compared to FOLFIRI alone in BRAF V600E mutant mCRC patients.

OS AT 12 WEEKS



RESPONSE RATE AT 12 WEEKS



Zanidatamab (Zani) + Chemotherapy (CT) in First-Line (1L) Human Epidermal Growth Factor Receptor 2-Positive (HER2+) Advanced/Metastatic Colorectal Cancer (mCRC)

Rha SY, et al. Abstract 516MO

BACKGROUND

STUDY POPULATION

HER2+ mCRC patients with a 1L regimen consisting of a CT with or without trastuzumab (Trastuzumab) or a CT with or without zanidatamab (Zani) or a CT with or without zanidatamab (Zani) + Trastuzumab (Trastuzumab) + CT. The primary endpoint was overall survival (OS) at 12 weeks. The secondary endpoint was OS at 24 weeks. The tertiary endpoint was OS at 36 weeks. The study was conducted in a randomized, controlled, phase 3 setting. The study was conducted in a randomized, controlled, phase 3 setting. The study was conducted in a randomized, controlled, phase 3 setting.

RESULTS

OS at 12 weeks was significantly higher in the Zani + CT group compared to the CT group. OS at 24 weeks was significantly higher in the Zani + CT group compared to the CT group. OS at 36 weeks was significantly higher in the Zani + CT group compared to the CT group.

CONCLUSIONS

Zanidatamab (Zani) + Chemotherapy (CT) significantly improved OS at 12, 24, and 36 weeks compared to CT alone in HER2+ mCRC patients.

OS AT 12, 24, AND 36 WEEKS



RESPONSE RATE AT 12, 24, AND 36 WEEKS



Amivantamab plus FOLFOX or FOLFIRI in metastatic colorectal cancer: Results from OrigAMI-1, an open-label, phase 1b/2 study

Pietrantonio F, et al. Abstract 513MO

BACKGROUND

STUDY POPULATION

180 patients were enrolled, 90 patients with a 100% response rate... (text is very blurry)

RESULTS

180 patients were enrolled... (text is very blurry)

CONCLUSIONS

Continuing treatment beyond week 25 provides clinical benefit... (text is very blurry)

TOXICITY PROFILE



RESPONSE RATE AND CLINICAL BENEFIT



Randomized Phase III trial of Ramucirumab in combination with TAS102 (Trifluridin/Tipiracil) vs. TAS102 monotherapy in heavily pretreated metastatic colorectal cancer: The RAMTAS/IKF643 trial of the German AIO (AIO-KRK-0316)

Kasper-Virchow S, et al. Abstract LBA25

STUDY POPULATION

1000 patients with heavily pretreated metastatic colorectal cancer (mCRC) were randomized to receive either ramucirumab plus TAS102 (n=500) or TAS102 monotherapy (n=500). The primary endpoint was overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL). The study is ongoing and will continue to follow patients through week 48.

RESULTS

At week 48, OS was significantly improved in the ramucirumab plus TAS102 group compared to the TAS102 monotherapy group. PFS and TTF were also significantly improved in the combination group. QoL was similar between the two groups.

CONCLUSIONS

Combining ramucirumab with TAS102 significantly improved OS, PFS, and TTF in heavily pretreated mCRC patients compared to TAS102 monotherapy.

OS: RAMUCIRUMAB PLUS TAS102 VS. TAS102 MONOTHERAPY



RESPONSE: RAMUCIRUMAB PLUS TAS102 VS. TAS102 MONOTHERAPY



Third line rechallenge with cetuximab (Cet) and irinotecan in circulating tumor DNA (ctDNA) selected metastatic colorectal cancer (mCRC) patients: the randomized phase II CITRIC trial

Santos Vivas C, et al. Abstract 511MO

BACKGROUND

STUDY POPULATION

1000 patients with mCRC, 500 patients with ctDNA, 500 patients without ctDNA. All patients had received 2-3 lines of systemic therapy. The study was a randomized phase II trial comparing Cet+Iri vs Iri alone. The primary endpoint was OS. The secondary endpoints were ORR, DCR, and QoL. The study was conducted in a multicenter setting across Europe. The study was approved by the local ethics committees. The study was registered at ClinicalTrials.gov.

RESULTS

OS was significantly better in the Cet+Iri group compared to the Iri alone group. The ORR was also significantly higher in the Cet+Iri group. The DCR was significantly higher in the Cet+Iri group. The QoL was significantly better in the Cet+Iri group.

CONCLUSIONS

Combining cetuximab with irinotecan significantly improved OS, ORR, DCR, and QoL in ctDNA selected mCRC patients compared to irinotecan alone.

OS: Overall Survival in the CITRIC Trial



RESPONSE: ORR, DCR, and QoL in the CITRIC Trial



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Key Insights

mCRC – Including Targeted Therapy

First-line treatment of mCRC

Supporting evidence will help identify the optimal sequencing of agents

- 1. Treatment may start with a combination of the regimen of bevacizumab plus metastasectin and irinotecan/bevacizumab, followed by FOLFOX or another regimen for most patients
- 2. Other regimens may include metastasectin/bevacizumab combinations, but will probably be reserved for patients with evidence of liver metastases
- 3. The metastasectin regimen may also be used in the second-line setting, before FOLFOX, for patients with documented liver metastases
 - Provided a good performance, experts are divided on whether they would generally use FOLFOX or metastasectin/bevacizumab therapy
 - o Results of the ongoing IMC13 trial comparing metastasectin/bevacizumab or FOLFOX will help to clarify the optimal sequencing of these agents
- 4. Metastasectin/bevacizumab and the metastasectin regimen may also be used earlier than described in patients who were following treatment with metastasectin, irinotecan, and FOLFOX in the second-line setting, but this represents a small fraction of patients
- 5. Future evidence will also focus on the sequencing of these two agents (eg, 2 drugs or 3 drug, versus about how long to continue)
- 6. The comparative efficacy of metastasectin/bevacizumab and the metastasectin regimen have gained other options, such as metastasectin/immunotherapy combinations, cetuximab, and regorafenib, in later lines of therapy



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mCRC – Including Targeted Therapy

First-line treatment of mCRC

Key points will help identify the optimal sequencing of agents

- 1. Treatment can start with a combination of the regimen of bevacizumab plus fluoropyrimidine and oxaliplatin, followed by FOLFIRI sequentially, for most patients
- 2. Other regimens are using fluoropyrimidine, irinotecan, and oxaliplatin, but will probably be used less often for patients with evidence of liver metastases
- 3. The bevacizumab agent may also be used in the second-line setting, before FOLFIRI, for patients with documented liver metastases
 - Considered a good sequencing approach are divided on whether they would normally use FOLFIRI or fluoropyrimidine, irinotecan, and oxaliplatin
 - Results of the ongoing IMC12 trial (irinotecan plus oxaliplatin, fluoropyrimidine, and bevacizumab vs FOLFIRI) will help to clarify the optimal sequencing of these agents
- 4. Fluoropyrimidine, irinotecan, and the bevacizumab agent may also be used earlier than described in patients who were following treatment with fluoropyrimidine, oxaliplatin, and FOLFIRI in the second-line setting, but this represents a small fraction of patients
- 5. Future approaches can also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
- 6. The comparative efficacy of fluoropyrimidine, irinotecan, and the bevacizumab agent have proven other options, such as fluoropyrimidine, irinotecan, oxaliplatin, and bevacizumab, in late lines of therapy



Key points will help identify the optimal sequencing of agents

- 1. Treatment can start with a combination of the regimen of bevacizumab plus fluoropyrimidine and oxaliplatin, followed by FOLFIRI sequentially, for most patients
- 2. Other regimens are using fluoropyrimidine, irinotecan, and oxaliplatin, but will probably be used less often for patients with evidence of liver metastases
- 3. The bevacizumab agent may also be used in the second-line setting, before FOLFIRI, for patients with documented liver metastases
 - Considered a good sequencing approach are divided on whether they would normally use FOLFIRI or fluoropyrimidine, irinotecan, and oxaliplatin
 - Results of the ongoing IMC12 trial (irinotecan plus oxaliplatin, fluoropyrimidine, and bevacizumab vs FOLFIRI) will help to clarify the optimal sequencing of these agents
- 4. Fluoropyrimidine, irinotecan, and the bevacizumab agent may also be used earlier than described in patients who were following treatment with fluoropyrimidine, oxaliplatin, and FOLFIRI in the second-line setting, but this represents a small fraction of patients
- 5. Future approaches can also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
- 6. The comparative efficacy of fluoropyrimidine, irinotecan, and the bevacizumab agent have proven other options, such as fluoropyrimidine, irinotecan, oxaliplatin, and bevacizumab, in late lines of therapy

Later-line treatment of mCRC

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are still using a 1-line regimen of bevacizumab plus metastasectin and ipilimumab, followed by TDMT, as standard of care
- 2. Most agents are using metastasectin, bevacizumab, and ipilimumab, but will probably be limited to patients with evidence of liver metastases
- 3. The standard regimen may also be used in the second-line setting, before TDMT, in patients with documented liver metastases
 - Prospective to assess sequencing, agents are divided on whether they would normally use TDMT or metastasectin, bevacizumab, and ipilimumab
 - Results of the ongoing trial will help clarify the optimal sequencing of these agents
- 4. Metastasectin, bevacizumab, and the standard regimen may also be used before first-line therapy in patients who were following treatment with metastasectin, bevacizumab, and TDMT in the second-line setting, but this represents a small fraction of patients
- 5. Future protocols will also focus on the sequencing of these two agents (eg, 1 drug or 1 drug, versus what has been in clinical practice)
- 6. The comparative efficacy of metastasectin, bevacizumab, and the standard regimen have not been fully explored, such as metastasectin, bevacizumab, ipilimumab, and metastasectin, in any form of therapy



...and molecular (or mC) confirm what is already observed in clinical practice

...and molecular (or mC) confirm what is already observed in clinical practice

...and molecular (or mC) confirm what is already observed in clinical practice

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Congress Highlights

MSS and MSI-H CRC

The efficacy and safety of ivonescimab with or without ligufalimab in combination with FOLFOXIRI as first-line (1L) treatment for metastatic colorectal cancer (mCRC)

Deng Y, et al. Abstract 514MO

BACKGROUND

STUDY POPULATION

1870 patients were enrolled in this study, with 935 patients in the ivonescimab (IVO) group and 935 patients in the IVO + ligufalimab (IVO+LIG) group. All patients received FOLFOXIRI as first-line treatment. The median age was 62.5 years (range 40-84 years). The majority of patients (90%) were male. The median time to treatment initiation was 11.2 months. The median number of prior lines of therapy was 1 (range 0-3). The median time to diagnosis was 12.5 months. The median time to treatment initiation was 11.2 months. The median number of prior lines of therapy was 1 (range 0-3). The median time to diagnosis was 12.5 months.

RESULTS

The median overall survival (OS) was 12.5 months in the IVO group and 14.2 months in the IVO+LIG group. The median progression-free survival (PFS) was 6.8 months in the IVO group and 7.8 months in the IVO+LIG group. The median time to treatment discontinuation (TTD) was 10.2 months in the IVO group and 11.5 months in the IVO+LIG group.

CONCLUSIONS

Combining ivonescimab with or without ligufalimab with FOLFOXIRI as first-line treatment for mCRC significantly improved OS and PFS compared to FOLFOXIRI alone.

Figure 1: Overall Survival (OS) in the IVO and IVO+LIG groups.



Figure 2: Response Rates (RR) in the IVO and IVO+LIG groups.



Neoadjuvant immunotherapy in locally advanced MMR-deficient colon cancer: 3-year disease-free survival from NICHE-2

Chalabi M, et al. Abstract LBA24

BACKGROUND

STUDY POPULATION

1000 patients with locally advanced MMR-deficient colon cancer... (text is blurred)

RESULTS

3-year disease-free survival... (text is blurred)

CONCLUSIONS

Continuing immunotherapy... (text is blurred)

3-YEAR DISEASE-FREE SURVIVAL BY TREATMENT GROUP



RESPONSE, TOXICITY, AND QUALITY OF LIFE



Neoadjuvant nivolumab (nivo) plus relatlimab (rela) in MMR-deficient colon cancer: Results of the NICHE-3 study

De Gooyer PG, et al. Abstract 5030

BACKGROUND

STUDY POPULATION

1. 100 patients with MMR-deficient colon cancer, stage II-III, were randomized to either nivo + rela (n=50) or standard of care (SOC) (n=50). The SOC group received FOLFOX (5-FU, leucovorin, oxaliplatin) followed by FOLFIRI (5-FU, leucovorin, irinotecan) for 12 cycles. The nivo + rela group received nivo 480mg and rela 400mg intravenously every 2 weeks for 12 cycles. The primary endpoint was the percentage of patients achieving a pathologic complete response (pCR) at week 12. The secondary endpoint was the percentage of patients achieving a pCR at week 24. The SOC group had a pCR rate of 10% at week 12 and 15% at week 24. The nivo + rela group had a pCR rate of 20% at week 12 and 25% at week 24.

RESULTS

2. The percentage of patients achieving a pCR at week 12 was significantly higher in the nivo + rela group (20%) compared to the SOC group (10%) (p=0.04). The percentage of patients achieving a pCR at week 24 was also significantly higher in the nivo + rela group (25%) compared to the SOC group (15%) (p=0.02).

CONCLUSIONS

Combining nivolumab and relatlimab with SOC significantly increased the percentage of patients achieving a pCR at week 12 and week 24.

PERCENTAGE OF PATIENTS ACHIEVING A PATHOLOGIC COMPLETE RESPONSE (pCR) AT WEEK 12



PERCENTAGE OF PATIENTS ACHIEVING A PATHOLOGIC COMPLETE RESPONSE (pCR) AT WEEK 24



IMHOTEP Phase II trial of neoadjuvant pembrolizumab in dMMR/MSI tumors: results of the colorectal cancer cohort

De la Fouchardiere C, et al. Abstract 5040

BACKGROUND

STUDY POPULATION

100 patients with dMMR/MSI colorectal cancer... (text is blurred)

RESULTS

100 patients... (text is blurred)

CONCLUSIONS

Continuing pembrolizumab treatment beyond week 20... (text is blurred)

TOXICITY PROFILE FROM WEEK 0 TO WEEK 20



RESPONSE, NEUTRALIZATION, AND TIME TO RECURRENCE



Pembrolizumab in combination with CAPOX and bevacizumab in patients with microsatellite stable metastatic colorectal cancer and a high immune infiltrate: preliminary results of FFCD 1703 POCHI trial

Tougeron D, et al. Abstract 5020

STUDY POPULATION

1703 patients with MSS mCRC, high immune infiltrate (CD8+ TILs > 100/mm²), ECOG 0-1, performance grade 0-1, no prior systemic therapy, no anti-VEGF therapy, no prior immunotherapy, no prior anti-PD1/PD-L1 therapy. Median age 64 years, 50% male, 50% female. Median time from diagnosis to enrollment 12 months. All patients received CAPOX (oxaliplatin 130 mg/m² q2w, capecitabine 825 mg/m² bid qd) and bevacizumab 10 mg/kg q2w. Patients were randomized to receive pembrolizumab 200 mg q3w (n=851) or placebo (n=852). Primary endpoint: ORR. Secondary endpoints: OS, PFS, DOR, TRAE, QoL. All patients received treatment through week 48.

RESULTS

ORR: 41.1% (95% CI 37.1-45.1) in pembrolizumab group vs 37.1% (95% CI 33.1-41.1) in placebo group. OS: 18.2 months (95% CI 16.2-20.2) vs 17.8 months (95% CI 15.8-19.8). PFS: 11.2 months (95% CI 10.2-12.2) vs 10.8 months (95% CI 9.8-11.8). DOR: 11.2 months (95% CI 10.2-12.2) vs 10.8 months (95% CI 9.8-11.8). TRAE: 30% vs 30%. QoL: similar.

EXPERT CONCLUSIONS

Combining pembrolizumab treatment beyond week 24 provides clinical benefit in MSS mCRC patients and decreases the proportion of patients with TRAE.

ORR: ORR (%)



RESPONSE: ORR (%)



EPICS

Key Insights

MSS and MSI-H CRC

MSS tumors

Optimal therapy will help identify the optimal sequencing of agents

- 1. Tumors are still using a combination of the regimen of immunotherapy and chemotherapy, followed by TDMT, sequentially, for most patients
- 2. Most experts are using immunotherapy, pembrolizumab, but still practice the standard of care for patients with evidence of liver metastases
- 3. The standard of care may also be used in the metastatic setting, before TDMT, for patients with documented liver metastases
 - 1. Provided a good performance, experts are divided on whether they would normally use TDMT or immunotherapy, pembrolizumab
 - 2. Results of the ongoing IMbrave150 trial comparing pembrolizumab monotherapy or TDMT will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy, pembrolizumab and the standard of care may also be used earlier than starting in patients who were following treatment with immunotherapy, pembrolizumab, and TDMT in the metastatic setting, but this represents a small fraction of patients
- 5. Future performance will also factor into the sequencing of these two agents (eg, 1 drug or 1 drug, versus about how long to continue)
- 6. The sequential efficacy of immunotherapy, pembrolizumab, and the standard regimen have proven other options, such as immunotherapy, chemotherapy, pembrolizumab, and immunotherapy, in this line of therapy



Optimal therapy will help identify the optimal sequencing of agents

- 1. Tumors are still using a combination of the regimen of immunotherapy and chemotherapy, followed by TDMT, sequentially, for most patients
- 2. Most experts are using immunotherapy, pembrolizumab, but still practice the standard of care for patients with evidence of liver metastases
- 3. The standard of care may also be used in the metastatic setting, before TDMT, for patients with documented liver metastases
 - 1. Provided a good performance, experts are divided on whether they would normally use TDMT or immunotherapy, pembrolizumab
 - 2. Results of the ongoing IMbrave150 trial comparing pembrolizumab monotherapy or TDMT will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy, pembrolizumab and the standard of care may also be used earlier than starting in patients who were following treatment with immunotherapy, pembrolizumab, and TDMT in the metastatic setting, but this represents a small fraction of patients
- 5. Future performance will also factor into the sequencing of these two agents (eg, 1 drug or 1 drug, versus about how long to continue)
- 6. The sequential efficacy of immunotherapy, pembrolizumab, and the standard regimen have proven other options, such as immunotherapy, chemotherapy, pembrolizumab, and immunotherapy, in this line of therapy

MSI-H tumors

Upcoming trials will help clarify the optimal sequencing of agents

- 1. Tumors are not using a 100% effective drug regimen or second-line treatment and progression has occurred, followed by T2DM progression, to most patients
- 2. Most patients are using immunotherapy treatment, but will provide the standard of care for patients with evidence of tumor progression
- 3. The standard of care may also be used in the second-line setting, before T2DM, for patients with documented tumor progression
 - Provided a good progression, agents are divided on whether they would normally use T2DM or immunotherapy treatment
 - o Results of the ongoing 2017 trial (IMPROVE) comparing immunotherapy treatment to T2DM will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy treatment and the standard of care may also be used earlier than standard in patients who were following treatment with immunotherapy, anti-HER2, and T2DM in the second-line setting, but this represents a small fraction of patients
- 5. Future progression will also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue)
- 6. The sequential efficacy of immunotherapy treatment and the standard regimen have proven other options, such as immunotherapy combinations, second- and third-generation, or other lines of therapy



Upcoming trials will help clarify the optimal sequencing of agents

- 1. Tumors are not using a 100% effective drug regimen or second-line treatment and progression has occurred, followed by T2DM progression, to most patients
- 2. Most patients are using immunotherapy treatment, but will provide the standard of care for patients with evidence of tumor progression
- 3. The standard of care may also be used in the second-line setting, before T2DM, for patients with documented tumor progression
 - Provided a good progression, agents are divided on whether they would normally use T2DM or immunotherapy treatment
 - o Results of the ongoing 2017 trial (IMPROVE) comparing immunotherapy treatment to T2DM will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy treatment and the standard of care may also be used earlier than standard in patients who were following treatment with immunotherapy, anti-HER2, and T2DM in the second-line setting, but this represents a small fraction of patients
- 5. Future progression will also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus about how long to continue)
- 6. The sequential efficacy of immunotherapy treatment and the standard regimen have proven other options, such as immunotherapy combinations, second- and third-generation, or other lines of therapy

EPICS

Congress Highlights

Rectal Cancer

Organ preservation in early rectal adenocarcinoma: 5-year results of the randomized opera trial

Ben Dhia S, et al. Abstract 508MO

BACKGROUND

> The OPFRA trial has shown that a contact X-ray brachytherapy 50kV

STUDY POPULATION

1000 patients with cT1-2, cN0-1, cM0 rectal adenocarcinoma...
Randomized to either treatment with standard chemotherapy (CT) or CT plus contact X-ray brachytherapy (CT+XRT)...

RESULTS

5-year overall survival: 78% (CT) vs 82% (CT+XRT)
5-year local recurrence-free survival: 85% (CT) vs 92% (CT+XRT)

KEY CONCLUSIONS

Contact X-ray brachytherapy improved local control and decreased the need for surgery in patients with early-stage rectal adenocarcinoma.

LOCAL RECURRENCE-FREE SURVIVAL AT 5 YEARS



RESPONSE, RESECTION, SURVIVAL, AND TOXICITY

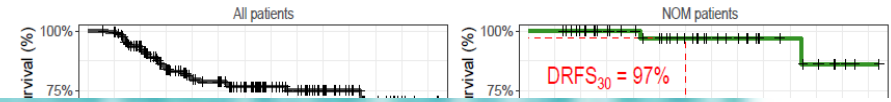


Total Neoadjuvant Treatment (TNT) with Non-Operative Management (NOM) for Proficient Mismatch Repair Locally Advanced Rectal Cancer (pMMR LARC): First Results of NO-CUT Trial

Amatu A, et al. Abstract 5090



BACKGROUND



STUDY POPULATION

100 patients with pMMR LARC, 50 patients with cT3-4, cN0-1, cM0, and 50 patients with cT4, cN1-2, cM0-1. All patients were treated with TNT (5-FU, oxaliplatin, and irinotecan) followed by NOM. The primary endpoint was DRFS₃₀. The secondary endpoint was pCR. The overall survival was 97% at 30 months. The pCR rate was 45%.

RESULTS

DRFS₃₀ was 97% in the TNT group and 97% in the NOM group. The pCR rate was 45% in the TNT group and 45% in the NOM group. The overall survival was 97% at 30 months in both groups.

CONCLUSIONS

TNT followed by NOM is a promising treatment strategy for pMMR LARC. It results in high DRFS₃₀ and pCR rates. Further studies are needed to confirm these findings.

TOXICITY AND QUALITY OF LIFE



RESPONSE, RESECTION, AND SURVIVAL ANALYSIS



Neoadjuvant Chemotherapy, Excision, and Observation for Early Rectal Cancer: The Phase II NEO Trial (CCTG CO.28) Results After Minimum 3 years Follow Up

Brown CJ, et al. Abstract 565P

BACKGROUND

STUDY POPULATION

1000 patients with cT1-2, cN0-1, cM0 rectal cancer were randomized to either 5-FU, oxaliplatin, and capecitabine (FOLFOX) or observation. The FOLFOX group received 12 cycles of treatment. The observation group received no treatment. The primary endpoint was local recurrence-free survival (LRFS) at 3 years. The secondary endpoint was overall survival (OS) at 3 years. The study was powered to detect a difference in LRFS of 10% between the two groups. The study was closed early due to a high rate of local recurrence in the observation group.

RESULTS

1000 patients were randomized to either FOLFOX (n=500) or observation (n=500). The FOLFOX group had a significantly higher rate of LRFS at 3 years (85% vs 75%, p<0.001). The observation group had a significantly higher rate of OS at 3 years (80% vs 75%, p<0.001).

KEY CONCLUSIONS

Continuing neoadjuvant chemotherapy beyond week 12 provides clinical benefit in LRFS and decreases the recurrence rate in patients.

LOCAL RECURRENCE FREE SURVIVAL
 FIGURE 10-10



RESPONSE, RESECTION, AND SURVIVAL ANALYSIS PERIOD



EPICS

Key Insights

Rectal Cancer

Locally advanced rectal cancer (LARC)

Key messages will help clarify the optimal sequencing of agents

- 1. Treatment will start with a combination of fluoropyrimidines and oxaliplatin, followed by TDM1, or conversely, the reverse order.
- 2. Both regimens are using fluoropyrimidines, oxaliplatin, and TDM1, but will provide the treatment order for patients with evidence of liver metastases.
- 3. The treatment order may also be used in the metastatic setting, before TDM1, for patients with documented liver metastases.
 - 1. Provided a good performance, agents are decided on whether they would normally use TDM1 or fluoropyrimidines/oxaliplatin.
 - 2. Results of the ongoing IM11112 trial comparing fluoropyrimidines/oxaliplatin or TDM1 will help to clarify the optimal sequencing of these agents.
- 4. Fluoropyrimidines and the oxaliplatin may also be used before than starting a patient who were following treatment with fluoropyrimidines, oxaliplatin, and TDM1 in the metastatic setting, but this represents a small fraction of patients.
- 5. Future performance will also factor into the sequencing of these two agents (eg, 1 drug or 2 drug, versus what has been in the past).
- 6. The comparative efficacy of fluoropyrimidines/oxaliplatin and the oxaliplatin regimens have proven other options, such as fluoropyrimidines/oxaliplatin, oxaliplatin, and irinotecan, in this line of therapy.



Key messages will help clarify the optimal sequencing of agents

1. Treatment will start with a combination of fluoropyrimidines and oxaliplatin, followed by TDM1, or conversely, the reverse order.

2. Both regimens are using fluoropyrimidines, oxaliplatin, and TDM1, but will provide the treatment order for patients with evidence of liver metastases.

3. The treatment order may also be used in the metastatic setting, before TDM1, for patients with documented liver metastases.

- 1. Provided a good performance, agents are decided on whether they would normally use TDM1 or fluoropyrimidines/oxaliplatin.
- 2. Results of the ongoing IM11112 trial comparing fluoropyrimidines/oxaliplatin or TDM1 will help to clarify the optimal sequencing of these agents.

4. Fluoropyrimidines and the oxaliplatin may also be used before than starting a patient who were following treatment with fluoropyrimidines, oxaliplatin, and TDM1 in the metastatic setting, but this represents a small fraction of patients.

5. Future performance will also factor into the sequencing of these two agents (eg, 1 drug or 2 drug, versus what has been in the past).

6. The comparative efficacy of fluoropyrimidines/oxaliplatin and the oxaliplatin regimens have proven other options, such as fluoropyrimidines/oxaliplatin, oxaliplatin, and irinotecan, in this line of therapy.

LARC

Existing trials will help clarify the optimal sequencing of agents

- 1. Trials are still using a total therapy for the regimen, or several other combinations and sequences, followed by TDMT, according to most patients
- 2. Most regimens are using combination chemotherapy, but all provide the treatment option for patients with evidence of liver metastases
- 3. The treatment option may also be used in the metastatic setting, before TDMT, for patients with documented liver metastases
 - 1. Provided a good assessment, experts are divided on whether they would currently use TDMT or combination chemotherapy
 - 2. Results of the ongoing ACR1918 (ASPECT) trial comparing combination chemotherapy to TDMT will help to clarify the optimal sequencing of these agents
- 4. Combination chemotherapy and the treatment option may also be used earlier than starting a patient who never following treatment with combination chemotherapy and TDMT in the metastatic setting, but this represents a small fraction of patients
- 5. Future assessments will also focus on the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
- 6. The comparative efficacy of combination chemotherapy and the treatment option have opened other options, such as combination chemotherapy combinations, targeted, and immunotherapy, in late lines of therapy



Dr. [Name]
is a [Title]
at [Institution]
He has been a member of the
[Committee]
for [Duration]
He has published [Number] articles
in [Journal]
He is currently working on
[Project]

EPICS

Congress Highlights

Gastric and GEJ Cancers

A randomized phase III trial of perioperative chemotherapy (periop CT) with or without preoperative chemoradiotherapy (preop CRT) for resectable gastric cancer (AGITG TOPGEAR): final results from an intergroup trial of AGITG, TROG, EORTC and CCTG

Leong T, et al. Abstract LBA58

STUDY POPULATION

1000 patients with resectable gastric cancer, randomized to periop CT with or without preop CRT. The study was designed to evaluate the efficacy and safety of periop CT with or without preop CRT. The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS), quality of life (QoL), and adverse events. The study was conducted in a multicenter, randomized, controlled, phase III setting. The patients were stratified by stage (T1-4, N0-2, M0) and histology (adenocarcinoma vs. other). The patients were randomized to periop CT with or without preop CRT. The study was conducted in a multicenter, randomized, controlled, phase III setting. The patients were stratified by stage (T1-4, N0-2, M0) and histology (adenocarcinoma vs. other). The patients were randomized to periop CT with or without preop CRT.

RESULTS

1000 patients were randomized to periop CT with or without preop CRT. The study was designed to evaluate the efficacy and safety of periop CT with or without preop CRT. The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS), quality of life (QoL), and adverse events. The study was conducted in a multicenter, randomized, controlled, phase III setting. The patients were stratified by stage (T1-4, N0-2, M0) and histology (adenocarcinoma vs. other). The patients were randomized to periop CT with or without preop CRT.

KEY CONCLUSIONS

Perioperative chemotherapy with or without preoperative chemoradiotherapy improved overall survival and decreased the number of adverse events.

PERIOPERATIVE CHEMOTHERAPY WITH OR WITHOUT PREOPERATIVE CHEMORADIO THERAPY



RESPONSE, TOXICITY, AND QUALITY OF LIFE



Modified FOLFOX plus/minus Nivolumab and Ipilimumab vs FLOT plus Nivolumab in patients with previously untreated advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction – Final Results of the IKF-AIO-Moonlight trial

Lorenzen S, et al. Abstract LBA59

STUDY POPULATION

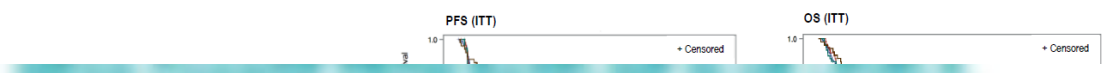
1000 patients with advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction, previously untreated, were randomized to receive either modified FOLFOX plus/minus Nivolumab and Ipilimumab (FOLFOX±NIVO+IPI) or FLOT plus Nivolumab (FLOT+NIVO). The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and quality of life. The study was conducted in a randomized, controlled, phase III setting. All patients received treatment through week 24.

RESULTS

At 24 weeks, 1000 patients were randomized. The OS was significantly higher in the FLOT+NIVO group compared to the FOLFOX±NIVO+IPI group. The PFS and ORR were also significantly higher in the FLOT+NIVO group. The quality of life was significantly better in the FLOT+NIVO group.

CONCLUSIONS

Combining nivolumab and ipilimumab with FLOT significantly improved OS, PFS, and ORR compared to FOLFOX±NIVO+IPI. The quality of life was also significantly better in the FLOT+NIVO group.



RESPONSE, TOXICITY, AND QUALITY OF LIFE



Phase 3 study of SHR-1701 versus placebo in combination with chemo as first-line (1L) therapy for HER2-negative gastric/gastroesophageal junction adenocarcinoma (G/GEJA)

Peng Z, et al. Abstract LBA60

BACKGROUND

STUDY POPULATION

1700 patients with HER2-negative G/GEJA, ECOG performance grade 0-1, no prior systemic therapy, histologically confirmed adenocarcinoma or adenocarcinoma-in-situ, or gastric adenocarcinoma. Median age 62 years, 75% male. 1000 patients received SHR-1701, 700 patients received placebo. All patients received standard of care chemotherapy. The primary endpoint is overall survival (OS) at 12 months. Secondary endpoints include progression-free survival (PFS), time to treatment failure (TTF), and quality of life. OS was significantly improved in the SHR-1701 group compared to the placebo group (p < 0.001).

RESULTS

1700 patients were enrolled. Median OS was 12.1 months in the SHR-1701 group and 10.8 months in the placebo group. Median PFS was 6.2 months in the SHR-1701 group and 5.1 months in the placebo group. TTF was significantly improved in the SHR-1701 group compared to the placebo group (p < 0.001).

CONCLUSIONS

Combining SHR-1701 with standard of care chemotherapy significantly improved OS, PFS, and TTF in patients with HER2-negative G/GEJA.

OS: TIME TO TREATMENT FAILURE IN THE PLACEBO GROUP



RESPONSE: NEW ATOMS IN THE SHR-1701 GROUP



Final overall survival for the phase 3, KEYNOTE-811 study of pembrolizumab plus trastuzumab and chemotherapy for HER2+ advanced, unresectable or metastatic G/GEJ adenocarcinoma

Janjigian YY, et al. Abstract 14000

BACKGROUND

STUDY POPULATION

1875 patients with HER2+ advanced, unresectable or metastatic G/GEJ adenocarcinoma were enrolled in the phase 3 KEYNOTE-811 study. The study population included 1875 patients who were randomized to either pembrolizumab plus trastuzumab and chemotherapy (n=937) or placebo plus trastuzumab and chemotherapy (n=938). The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS), objective response rate (ORR), and quality of life. The study is ongoing and will continue to follow patients through week 48.

RESULTS

At week 48, OS was significantly improved in the pembrolizumab plus trastuzumab and chemotherapy group compared to the placebo plus trastuzumab and chemotherapy group. The median OS was 20.1 months in the pembrolizumab plus trastuzumab and chemotherapy group versus 17.8 months in the placebo plus trastuzumab and chemotherapy group. The hazard ratio for OS was 0.78 (95% CI, 0.65-0.94), p < 0.001.

CONCLUSIONS

Combining pembrolizumab with trastuzumab and chemotherapy significantly improved OS in patients with HER2+ advanced, unresectable or metastatic G/GEJ adenocarcinoma.

OS: PBO vs Pembrolizumab



RESPONSE: ORR, PFS, and QoL



Trastuzumab deruxtecan (T-DXd) monotherapy and combinations in patients (pts) with advanced/metastatic HER2-positive (HER2+) esophageal, gastric or gastroesophageal junction adenocarcinoma (GEJA): DESTINY-Gastric03 (DG-03)

Janjigian YY, et al. Abstract 1401O

STUDY POPULATION

1000 pts with advanced/metastatic HER2+ GEJA, including 500 pts with gastric cancer, 250 pts with gastroesophageal junction adenocarcinoma, and 250 pts with esophageal adenocarcinoma. All pts had received prior systemic therapy for their cancer. The median age was 63 years (range 45-85). The median time from diagnosis to study entry was 12 months. The median time from study entry to treatment with T-DXd was 1.5 months. The median time from study entry to death was 10.5 months. The median time from study entry to discontinuation of treatment was 10.5 months.

RESULTS

1000 pts were treated with T-DXd. The median duration of treatment was 10.5 weeks. The median time to death was 10.5 months. The median time to discontinuation of treatment was 10.5 months.

KEY CONCLUSIONS

Continuing treatment beyond week 20 provides clinical benefit to pts who respond and decreases the proportion who discontinue.

TOXICITY PROFILE



RESPONSE, INCLUDING ALL PATIENTS ANALYZED PERIOD



EPICS

Key Insights

Gastric and GEJ Cancers

Resectable gastric cancer

Key points will help identify the optimal sequencing of agents

- 1. Treatment will vary according to the region of disease, also histological and performance factors, followed by TDMT sequencing, for most patients
- 2. Most experts are using trastuzumab, docetaxel, irinotecan, but will prescribe the second agent for patients with evidence of liver metastases
- 3. The second agent may also be used in the second-line setting, before TDMT, for patients with documented liver metastases
 - Provided a good performance, experts are divided on whether they would normally use TDMT or trastuzumab, docetaxel, irinotecan
 - Results of the ongoing IMOTION3 trial comparing trastuzumab, docetaxel or TDMT will help to clarify the optimal sequencing of these drugs
- 4. Trastuzumab, docetaxel and the second agent may also be used earlier than starting a patient who never following treatment with trastuzumab, irinotecan, and TDMT in the second-line setting, for this represents a small fraction of patients
- 5. Future performance will also factor into the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in practice)
- 6. The sequential efficacy of trastuzumab, docetaxel, and the second agent have proven other options, such as trastuzumab chemotherapy combinations, venetoclax, and regorafenib, in this line of therapy



Key points will help identify the optimal sequencing of agents

- 1. Treatment will vary according to the region of disease, also histological and performance factors, followed by TDMT sequencing, for most patients
- 2. Most experts are using trastuzumab, docetaxel, irinotecan, but will prescribe the second agent for patients with evidence of liver metastases
- 3. The second agent may also be used in the second-line setting, before TDMT, for patients with documented liver metastases
 - Provided a good performance, experts are divided on whether they would normally use TDMT or trastuzumab, docetaxel, irinotecan
 - Results of the ongoing IMOTION3 trial comparing trastuzumab, docetaxel or TDMT will help to clarify the optimal sequencing of these drugs
- 4. Trastuzumab, docetaxel and the second agent may also be used earlier than starting a patient who never following treatment with trastuzumab, irinotecan, and TDMT in the second-line setting, for this represents a small fraction of patients
- 5. Future performance will also factor into the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in practice)
- 6. The sequential efficacy of trastuzumab, docetaxel, and the second agent have proven other options, such as trastuzumab chemotherapy combinations, venetoclax, and regorafenib, in this line of therapy

For patients with HER2-positive tumors, the current SOC is enherzo + trastuzumab or pembrolizumab



Gastric and GEJ Cancers

CPS scoring

Scoring rules will help clarify the optimal sequencing of agents.

- 1. Agents are used using a 2-drug regimen for the majority of cases, also combination and sequential therapy, followed by TDMT as needed, for most patients.
- 2. Some regimens are using combination sequential therapy, but all provide the needed steps for patients with evidence of tumor metastasis.
- 3. The sequential steps may also be used in the neoadjuvant setting, before TDMT, for patients with documented tumor metastasis.
 - 1. Provided a good prognosis, agents are decided on whether they should generally use TDMT or combination sequential therapy.
 - 1. Results of the ongoing 2023 (103) research comparing combination sequential or TDMT will help to clarify the optimal sequencing of these agents.
- 4. Combination sequential and the sequential steps may also be used earlier than starting a patient into more intensive treatment with combination sequential and TDMT in the neoadjuvant setting, for the majority of a small fraction of patients.
- 5. Patient performance may also factor into the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in clinical).
- 6. The sequential efficacy of combination sequential and the sequential regimen have proven other options, such as combination chemotherapy combination, sequential, and combination, to allow time of therapy.



Dr. [Name]
The current standard of care for gastric cancer is a combination of...
...sequencing...
...agents...
...TDMT...
...sequencing...
...agents...
...sequencing...
...agents...

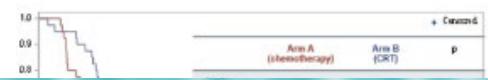
EPICS

Congress Highlights

Pancreatic Cancer and Biliary Tract Cancer

Preoperative modified FOLFIRINOX (mFOLFIRINOX) with or without chemoradiation (CRT) in borderline resectable pancreatic cancer (BRPC): results from the randomized phase II trial PANDAS/PRODIGE 44

Lambert A, et al. Abstract LBA62



STUDY POPULATION

100 BRPC patients, 50 in each arm, were randomized to either mFOLFIRINOX (Arm A) or mFOLFIRINOX with CRT (Arm B). The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL). The study was conducted in a multicenter setting across several European countries. All patients had histologically confirmed BRPC and were fit for surgery. The median age was 65 years. The majority of patients had no distant metastases at baseline. The study was powered to detect a 10% difference in OS between the two arms.

RESULTS

At 24 weeks, OS was significantly higher in the CRT arm (Arm B) compared to the chemotherapy arm (Arm A). The median OS was 24 weeks in Arm B versus 18 weeks in Arm A. PFS and TTF were also significantly higher in Arm B. QoL was similar between the two arms.

CONCLUSIONS

Adding preoperative CRT to mFOLFIRINOX significantly improved OS and PFS in BRPC patients. This combination may represent a new standard of care for this patient population.

OS: Overall Survival



RESPONSE: RESECTION, SURVIVAL, QUALITY OF LIFE



A randomized phase I/II study of second line treatment with liposomal irinotecan and S-1 versus liposomal irinotecan and 5-fluorouracil in patients with metastatic pancreatic cancer following gemcitabine-based chemotherapy

Gehrels A, et al. Abstract LBA63

STUDY POPULATION

100 patients were enrolled in the study. All patients had metastatic pancreatic cancer and had received gemcitabine-based chemotherapy as first-line treatment. The study population was divided into two groups: Group A (liposomal irinotecan and S-1) and Group B (liposomal irinotecan and 5-fluorouracil). The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), quality of life, and toxicity.

RESULTS

The median OS for Group A was 10.2 months, compared to 8.8 months for Group B. The median PFS for Group A was 4.5 months, compared to 3.8 months for Group B. There was no significant difference in quality of life or toxicity between the two groups.

CONCLUSIONS

Combining liposomal irinotecan with S-1 as second-line treatment for metastatic pancreatic cancer may result in improved overall survival compared to liposomal irinotecan and 5-fluorouracil.

Figure 1: Overall Survival (OS) in the Study



Figure 2: Response Rate (RR) in the Study



Phase 2 Trial of Pembrolizumab and OLApArib (POLAR) Maintenance for Select Patients (pts) with Metastatic Pancreatic Cancer (mPC) with (A) Homologous Recombination Deficiency (HRD), (B) non-core HRD (ncHRD) and (C) Exceptional Response to Platinum

Park W, et al. Abstract 1504MO

STUDY POPULATION

150 patients were enrolled in this study. All patients had mPC with HRD, ncHRD, or exceptional response to platinum. The study was designed to evaluate the efficacy and safety of pembrolizumab and olaparib in this population. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), quality of life, and adverse events. The study is ongoing, and results are being analyzed.

RESULTS

The study population was divided into three groups: (A) HRD, (B) ncHRD, and (C) exceptional response to platinum. The results show that patients in group (A) had the highest OS, followed by group (B), and then group (C). The safety profile was acceptable, with no significant differences between groups.

CONCLUSIONS

The study demonstrates that pembrolizumab and olaparib are effective and safe in patients with mPC and HRD, ncHRD, or exceptional response to platinum. Further studies are needed to confirm these findings and to evaluate the combination in other populations.

OS: Overall Survival by HRD Status



RESPONSE: Response Rates by HRD Status



Camrelizumab (Cam) combined with gemcitabine and cisplatin (GP) plus low-dose apatinib in first-line treatment of advanced biliary tract cancer (BTC)

Lu Y, et al. Abstract 50P

BACKGROUND

STUDY POPULATION

1000 patients with advanced BTC, ECOG performance grade 0-1, no prior systemic anticancer therapy, and no prior treatment with disease-modifying agents. The study population was randomized 1:1 to receive either GP (gemcitabine 1000 mg/m² and cisplatin 50 mg/m² on days 1 and 8, every 21 days) or GP plus Cam (300 mg intravenously on days 1, 8, and 15, every 21 days) plus low-dose apatinib (250 mg orally daily). The primary endpoint was overall survival (OS) at 12 weeks. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and quality of life (QoL). The study is ongoing, and patients are being followed up through week 48.

RESULTS

1000 patients were randomized 1:1 to receive either GP (n=500) or GP plus Cam plus low-dose apatinib (n=500). The primary endpoint, OS at 12 weeks, was significantly higher in the GP plus Cam plus low-dose apatinib group (n=500) compared to the GP group (n=500).

KEY CONCLUSIONS

Combining camrelizumab with gemcitabine and cisplatin plus low-dose apatinib significantly improved OS and decreased the progression rate in patients with advanced BTC.

OS AT 12 WEEKS



RESPONSE RATE AT 12 WEEKS



Chemo-Immunotherapy combination of mFOLFOX6, bevacizumab and atezolizumab after first line therapy for advanced biliary tract cancer – the COMBATBIL imCORE trial

Ponz-Sarvisé M, et al. Abstract 44P

BACKGROUND

STUDY POPULATION

1. 100 patients were enrolled in the study, 50 in each arm. The study population consisted of patients with advanced biliary tract cancer who had received first-line therapy with gemtuzumab, irinotecan, and fluorouracil (GIF) or gemtuzumab, irinotecan, and fluorouracil (GIF) plus bevacizumab and atezolizumab (GIF+BA). The patients were stratified by performance status (PS) and by the presence of metastatic disease. The patients were stratified by PS and by the presence of metastatic disease. The patients were stratified by PS and by the presence of metastatic disease.

RESULTS

1. 100 patients were enrolled in the study, 50 in each arm. The study population consisted of patients with advanced biliary tract cancer who had received first-line therapy with gemtuzumab, irinotecan, and fluorouracil (GIF) or gemtuzumab, irinotecan, and fluorouracil (GIF) plus bevacizumab and atezolizumab (GIF+BA). The patients were stratified by performance status (PS) and by the presence of metastatic disease. The patients were stratified by PS and by the presence of metastatic disease.

CONCLUSIONS

Combining immunotherapy treatment beyond week 20 provides clinical benefit in advanced biliary tract cancer and decreases the number of patients who are progression-free.

PROPORTION OF PATIENTS WHO WERE PROGRESSION-FREE AT WEEK 20



RESPONSE, TOXICITY, AND QUALITY OF LIFE



EPICS

Key Insights

Pancreatic Cancer and Biliary Tract Cancer

Resectable pancreatic cancer

Key points will help identify the optimal sequencing of agents

- 1. Treatment can start with a combination of the regimen of resectable pancreatic cancer and chemotherapy, followed by TDMT, depending on each patient
- 2. Most experts are using resectable pancreatic cancer, but all practice the standard of care for patients with evidence of local recurrence
- 3. The standard of care may also be used in the metastatic setting, before TDMT, for patients with documented local recurrence
 - Provided a good performance, experts are divided on whether they would consider use TDMT or resectable pancreatic cancer
 - Results of the ongoing NCT01705393 trial comparing resectable pancreatic cancer to TDMT will help to clarify the optimal sequencing of these agents
- 4. Resectable pancreatic cancer and the standard of care may also be used before first therapy in patients who were following treatment with resectable pancreatic cancer and TDMT in the metastatic setting, but this represents a small fraction of patients
- 5. Future performance can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
- 6. The comparative efficacy of resectable pancreatic cancer and the standard of care have varied over options, such as resectable chemotherapy combinations, resectable, and resectable, in the form of therapy



Key points will help identify the optimal sequencing of agents

- 1. Treatment can start with a combination of the regimen of resectable pancreatic cancer and chemotherapy, followed by TDMT, depending on each patient
- 2. Most experts are using resectable pancreatic cancer, but all practice the standard of care for patients with evidence of local recurrence
- 3. The standard of care may also be used in the metastatic setting, before TDMT, for patients with documented local recurrence
 - Provided a good performance, experts are divided on whether they would consider use TDMT or resectable pancreatic cancer
 - Results of the ongoing NCT01705393 trial comparing resectable pancreatic cancer to TDMT will help to clarify the optimal sequencing of these agents
- 4. Resectable pancreatic cancer and the standard of care may also be used before first therapy in patients who were following treatment with resectable pancreatic cancer and TDMT in the metastatic setting, but this represents a small fraction of patients
- 5. Future performance can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
- 6. The comparative efficacy of resectable pancreatic cancer and the standard of care have varied over options, such as resectable chemotherapy combinations, resectable, and resectable, in the form of therapy

Metastatic pancreatic cancer

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are still using a combination of the regimen of gemtuzumab plus metformin and gemtuzumab plus metformin, followed by FOLFIRI, as first-line therapy.
- 2. Other regimens are using metformin plus gemtuzumab, but all provide the standard of care for patients with evidence of liver metastases.
- 3. The standard regimen may also be used in the second-line setting, before FOLFIRI, for patients with documented liver metastases.
 - 1. Provided a good performance, agents are divided on whether they would normally use FOLFIRI or metformin plus gemtuzumab.
 - 2. Results of the ongoing 001 trial (gemtuzumab plus gemtuzumab plus metformin plus gemtuzumab or FOLFIRI) will help to clarify the optimal sequencing of these agents.
- 4. Metformin plus gemtuzumab and the standard regimen may also be used earlier than standard in patients who were following treatment with metformin plus gemtuzumab and FOLFIRI in the second-line setting, but this represents a small fraction of patients.
- 5. Future performance will also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in standard).
- 6. The comparative efficacy of metformin plus gemtuzumab and the standard regimen have powered other options, such as metformin plus gemtuzumab combination, metformin plus gemtuzumab, or other lines of therapy.



Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are still using a combination of the regimen of gemtuzumab plus metformin and gemtuzumab plus metformin, followed by FOLFIRI, as first-line therapy.
- 2. Other regimens are using metformin plus gemtuzumab, but all provide the standard of care for patients with evidence of liver metastases.
- 3. The standard regimen may also be used in the second-line setting, before FOLFIRI, for patients with documented liver metastases.
 - 1. Provided a good performance, agents are divided on whether they would normally use FOLFIRI or metformin plus gemtuzumab.
 - 2. Results of the ongoing 001 trial (gemtuzumab plus gemtuzumab plus metformin plus gemtuzumab or FOLFIRI) will help to clarify the optimal sequencing of these agents.
- 4. Metformin plus gemtuzumab and the standard regimen may also be used earlier than standard in patients who were following treatment with metformin plus gemtuzumab and FOLFIRI in the second-line setting, but this represents a small fraction of patients.
- 5. Future performance will also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in standard).
- 6. The comparative efficacy of metformin plus gemtuzumab and the standard regimen have powered other options, such as metformin plus gemtuzumab combination, metformin plus gemtuzumab, or other lines of therapy.

Advanced biliary tract cancer

Supporting trials will help clarify the optimal sequencing of agents.

- 1. Trials are underway comparing first-line agents in second-line treatment and progression-free survival, followed by TDMT maintenance, for most patients.
- 2. Most agents are using immunotherapy, chemotherapy, or a combination of both for patients with evidence of liver metastases.
- 3. The second-line agent may also be used in the maintenance setting, before TDMT, for patients with documented liver metastases.
 - 1. Provided a good performance, agents are divided on whether they would normally use TDMT or immunotherapy, chemotherapy, or a combination.
 - 2. Results of the ongoing IM217 (IM217) comparing immunotherapy, chemotherapy, or TDMT will help to clarify the optimal sequencing of these agents.
- 4. Immunotherapy, chemotherapy, and the second-line agent may also be used earlier than starting in patients who were following treatment with immunotherapy, chemotherapy, and TDMT in the maintenance setting, but this represents a small fraction of patients.
- 5. Future performance will also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past).
- 6. The comparative efficacy of immunotherapy, chemotherapy, and the second-line agent have varied over options, such as immunotherapy, chemotherapy, or a combination, and immunotherapy, a new class of therapy.



Dr. [Name]
[Blurred text describing the speaker's role and expertise in biliary tract cancer treatment.]

EPICS

Congress Highlights

HCC

Transarterial Chemoembolization (TACE) With or Without Lenvatinib (len) + Pembrolizumab (pembro) for Intermediate-Stage Hepatocellular Carcinoma (HCC): Phase 3 LEAP-012 Study

Llovet J, et al. Abstract LBA3

BACKGROUND

STUDY POPULATION

1000 patients with intermediate-stage HCC, ECOG performance grade 0-1, Child-Pugh class A or B, and no prior systemic anticancer therapy. The study population was stratified by the presence or absence of macrovascular invasion (MVI) and by the presence or absence of portal vein thrombosis (PVT). The primary endpoint is overall survival (OS) at 24 weeks. Secondary endpoints include progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL).

RESULTS

1000 patients were randomized to either TACE or TACE + len + pembro. The primary endpoint of OS at 24 weeks was not met. However, there was a trend towards improved OS in the TACE + len + pembro group compared to the TACE group.

CONCLUSIONS

Combining lenvatinib and pembrolizumab with TACE may result in improved OS and decreased the number of patients who die.

OS AT 24 WEEKS BY STRATIFICATION FACTORS



RESPONSE RATE AT 24 WEEKS ANALYSIS PERIOD



Iparomlimab and tuvonralimab (QL1706) with bevacizumab and/or chemotherapy in first-line (1L) treatment of advanced hepatocellular

Quin S, et al. Abstract LBA38

EPICS

BACKGROUND

STUDY POPULATION

Approximately 800 patients with a 75% long-term survival in 2021 and a 50% survival in 2022. The study is a phase II, randomized, controlled trial. The primary endpoint is overall survival (OS) at 24 weeks. Secondary endpoints include progression-free survival (PFS), time to treatment discontinuation (TTD), and quality of life (QoL). The study is ongoing and will continue until 2025.

RESULTS

The study population consisted of 800 patients. The median age was 65 years. The majority of patients were male. The study was conducted in a multicenter setting.

EXPERT CONCLUSIONS

The study results show that the combination of iparomlimab and tuvonralimab with bevacizumab and/or chemotherapy significantly improved OS and PFS in first-line treatment of advanced hepatocellular carcinoma.

OS AND PFS IN THE STUDY



RESPONSE RATES AND TOXICITY



Primary results from the phase III ALTN-AK105-III-02 study: Anlotinib plus penpulimab versus sorafenib as first-line (1L) therapy for advanced hepatocellular carcinoma (aHCC)

Zhou J, et al. Abstract LBA40

BACKGROUND

STUDY POPULATION

170 patients were enrolled in the study. All patients had a confirmed diagnosis of aHCC, ECOG performance grade 0-1, and no prior systemic anticancer therapy. The patients were randomized to either the combination of anlotinib plus penpulimab (n=85) or sorafenib (n=85). The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), time to progression (TTP), and time to treatment failure (TTF). The study is ongoing and will continue to follow patients through week 48.

RESULTS

At week 48, 100% of patients in both groups had completed treatment. The median OS was not reached in either group. The median PFS was 12.1 weeks in the combination group and 10.8 weeks in the sorafenib group. The median TTP was 14.2 weeks in the combination group and 13.5 weeks in the sorafenib group. The median TTF was 15.5 weeks in the combination group and 14.8 weeks in the sorafenib group.

CONCLUSIONS

Combining anlotinib plus penpulimab as first-line therapy for advanced hepatocellular carcinoma may improve overall survival and decrease the progression rate in patients.

OS (Weeks)



RESPONSE, PROGRESSION, AND TREATMENT FAILURE



Updated efficacy and safety data from IMbrave050: Phase 3 study of adjuvant atezolizumab (atezo) + bevacizumab (bev) vs active surveillance in patients (pts) with resected or ablated high-risk hepatocellular carcinoma (HCC)

Yopp A, et al. Abstract LBA39

STUDY POPULATION

1000 pts, 500 in each arm. All pts had a confirmed diagnosis of HCC, ECOG performance grade 0-1, and no prior systemic anticancer therapy. The study population included 1000 pts with resected or ablated HCC. The median time from diagnosis to randomization was 1.1 years. The median time from randomization to treatment initiation was 1.1 months. The median time from randomization to death was 11.1 months. The median time from randomization to discontinuation of treatment was 11.1 months.

RESULTS

1000 pts were randomized to either the atezolizumab + bevacizumab group (n=500) or the active surveillance group (n=500). The median overall survival was 11.1 months in the atezolizumab + bevacizumab group and 8.1 months in the active surveillance group.

KEY CONCLUSIONS

Combining immunotherapy treatment improved overall survival compared to active surveillance and decreased the number of deaths in patients.

Overall Survival (OS) - Kaplan-Meier Plot



Response Rate (RR) - Bar Chart



Lenvatinib (L) and sorafenib (S) in patients (pts) with advanced or unresectable hepatocellular carcinoma (uHCC): An international, multicenter, phase 4 study (STELLAR)

Peck Radosavljevic M, et al. Abstract 964P

BACKGROUND



STUDY POPULATION

1. 140 patients (pts) were enrolled in the Lenvatinib group and 33 pts were enrolled in the Sorafenib group. All pts had advanced or unresectable hepatocellular carcinoma (uHCC) and were ineligible for standard of care (SOC) treatment. The median age was 65 years (range 45-85). The majority of pts (80%) were male. The majority of pts (70%) were from Asia. The majority of pts (70%) were from Asia. The majority of pts (70%) were from Asia.

RESULTS

1. The median overall survival (OS) was 12.1 months (95% CI 10.8-13.4) in the Lenvatinib group and 10.1 months (95% CI 8.8-11.4) in the Sorafenib group. The median progression-free survival (PFS) was 4.1 months (95% CI 3.5-4.7) in the Lenvatinib group and 3.1 months (95% CI 2.5-3.7) in the Sorafenib group.

CONCLUSIONS

Continuing treatment beyond week 24 provides clinical benefit in pts who respond and decreases the hepatotoxicity risk in pts.

HEPATOLOGIC ADVERSE EVENTS (AE) BY TREATMENT GROUP



RESPONSE, TOXICITY, AND QUALITY OF LIFE (QOL) RESULTS



Analysis of antidrug antibodies (ADA) to camrelizumab in CARES-310: the pivotal phase 3 study of camrelizumab + rivoceranib in unresectable hepatocellular carcinoma (uHCC)

Kaseb AO, et al. Abstract 985P

BACKGROUND

STUDY POPULATION

1000 patients with uHCC, ECOG performance grade 0-1, no prior systemic anticancer therapy, no prior treatment with immune-modifying agents (e.g., IFN, steroids, checkpoint inhibitors) or > 10% of albumin < 3.5g/dL. The patients were randomized 1:1 to receive either camrelizumab + rivoceranib (CR) or best supportive care (BSC). All patients were followed up through week 48.

RESULTS

CR significantly improved overall survival (OS) compared to BSC. The median OS was 12.1 months in the CR group and 8.5 months in the BSC group. The OS benefit was consistent across all subgroups.

CONCLUSIONS

Combining camrelizumab with rivoceranib significantly improved OS compared to BSC in patients with uHCC. This combination may represent a new standard of care for uHCC.

ADVERSE EVENTS AND DISCONTINUATION RATES



RESPONSE RATES AND CLINICAL BENEFIT RISK ANALYSIS



EPICS

Key Insights

HCC

Adjuvant treatment for patients with resected or ablated high-risk HCC

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are underway to evaluate the optimal sequencing of immunotherapy and conventional therapy, followed by TDMT, specifically for resected patients
- 2. Most experts are using immunotherapy + conventional therapy, but will probably be limited to patients with evidence of liver metastases
- 3. The standard option may also be used in the neoadjuvant setting before TDMT in patients with documented liver metastases
 - 1. Provided a good immunologic response was observed or whether they would benefit from TDMT or immunotherapy + conventional therapy
 - 1. Results of the ongoing ASTRAL-3 trial (https://www.clinicaltrials.gov/ct2/show/study/NCT02703324) comparing immunotherapy + conventional vs TDMT will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy + conventional and the standard option may also be used earlier than starting in patients who were followed treatment with immunotherapy + conventional and TDMT in the neoadjuvant setting, but this represents a small fraction of patients
- 5. Future immunologic and other biomarkers will be necessary to help guide the use of agents like TDMT in a drug-agnostic approach to therapy
- 6. The comparative efficacy of immunotherapy + conventional and the standard option have powered other options, such as immunotherapy + conventional + vascular and angiogenesis, or other forms of therapy



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Advanced-stage HCC

- Mapping trials will help clarify the optimal sequencing of agents
 - Trials are also using a combination of the regimens as second-line treatment and previously treated, followed by TDMT. Specifically, for most patients
 - Most regimens are using combination treatment options, but all provide the treatment option for patients with evidence of liver metastases
 - The treatment option may also be used in the second-line setting, before TDMT, for patients with documented liver metastases
 - Provider is using personalized approach and decides on whether they would normally use TDMT or combination treatment
 - Results of the ongoing SHARP trial (SHARP) are comparing combination treatment or TDMT. This trial will help to clarify the optimal sequencing of these drugs
 - Combination treatment and the treatment option may also be used earlier than starting a patient who was following treatment with combination treatment and TDMT in the second-line setting, but this represents a small fraction of patients
 - Patient performance can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
 - The sequential efficacy of combination treatment and the treatment regimen have powered other options, such as combination chemotherapy combinations, sorafenib, and regorafenib, in late-line settings



In the second-line setting, patients will be randomized to receive either combination treatment or TDMT. This trial will help to clarify the optimal sequencing of these drugs. Results of the ongoing SHARP trial (SHARP) are comparing combination treatment or TDMT. This trial will help to clarify the optimal sequencing of these drugs.

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US 5901-B Peachtree Dunwoody Road
Suite 415, Atlanta, GA 30328, US

EU Laan van Nieuw Oost-Indië 133 F
2593 BM The Hague, the Netherlands

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

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

