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ASCO 2023 edition

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highlights from the #ASCO23 scientific meeting

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BEST OF ASCO 2023

Under the presidential theme "Partnering with Patients: The Cornerstone of Cancer Care and Research," ASCO23 will bring together oncologists, researchers, industry professionals, and patient advocates in Chicago and online. This highly anticipated event will feature over 2,900 abstracts and more than 2,600 poster presentations, highlighting groundbreaking scientific advancements, innovative therapies, and emerging trends in cancer research. In this report, we aim to provide a comprehensive overview of the most impactful abstracts presented at ASCO23, offering insights into the latest developments and promising breakthroughs that hold the potential to revolutionize the field of oncology.

As an organization deeply committed to advocating for cancer patients, the chosen theme for this year's ASCO is both exciting and concerning. While it emphasizes the importance of partnering with patients, it is disheartening to acknowledge that a significant portion of the studies being presented may not have been developed in true collaboration with patients. It is our sincere hope that the Annual Meeting will serve as a catalyst for change, igniting a renewed sense of purpose among attendees and inspiring them to prioritize the active engagement of patients as essential partners in scientific discovery. Together, we can strive for a future where patient-centered research is at the forefront, driving meaningful progress in cancer care and improving outcomes for all individuals affected by this disease

CONTENTS

LUNG CANCER

Adjuvant Osimertinib Extends Survival in Lung Cancer Patients with EGFR Mutations LBA3

Key Points:

1. Adjuvant osimertinib significantly improved overall survival (OS) and reduced the risk of death by half compared to placebo in patients with EGFR-mutated non-small cell lung cancer (NSCLC).
2. The OS benefit was consistent across all patient subgroups, including different stages of the disease and regardless of prior adjuvant chemotherapy.
3. These results reinforce adjuvant osimertinib as the standard of care for patients with resected EGFR-mutated stage IB to IIIA NSCLC.

BACKGROUND

- The ADAURA trial aimed to evaluate whether targeted therapy with osimertinib could improve outcomes for patients with early-stage EGFR-mutated NSCLC.
- Osimertinib is a third-generation EGFR tyrosine kinase inhibitor (TKI) with high efficacy and lower resistance compared to earlier-generation TKIs.
- The trial included 682 patients with completely resected stage IB to IIIA nonsquamous NSCLC harboring EGFR exon 19 deletion or L858R mutation.

RESULTS

- Adjuvant osimertinib significantly improved OS compared to placebo after approximately 5 years of follow-up.
- Among patients with stage II to IIIA disease, osimertinib reduced the risk of death by 51% and had a 5-year survival rate of 85% compared to 73% in the placebo arm.
- The OS benefit was observed consistently across all subgroups, regardless of disease stage or prior adjuvant chemotherapy.

CLINICAL IMPLICATIONS

- Adjuvant osimertinib is currently the only EGFR TKI to show a statistically significant improvement in disease-free survival and OS in a phase 3 trial.
- Testing all patients with early-stage lung cancer for EGFR mutations is essential to determine the optimal treatment strategy and facilitate multidisciplinary management.
- Patients with resected tumours and EGFR mutations should receive adjuvant therapy.

NEXT STEPS

- Additional long-term survival data and the effects of treatments in the context of recurrence are necessary to further evaluate the efficacy of adjuvant osimertinib.
- Ongoing studies are exploring osimertinib in different EGFR-mutated NSCLC settings, such as stage IA disease, neoadjuvant treatment, and longer durations of adjuvant therapy.
- The success of osimertinib in early-stage NSCLC may pave the way for targeted therapies directed at other molecular targets, such as ALK and RET, to improve outcomes in early-stage NSCLC

Clinical trial information: NCT02511106

adjuvant osimertinib shows that it can help people with NSCLC with an EGFR mutation live longer after surgery to remove the tumour

HEMATOLOGIC MALIGNANCIES

Promising Results of CARTITUDE-4 Trial: Ciltacabtagene Autoleucel Benefits Lenalidomide-Refractory Multiple Myeloma Patients LBA106

KEY POINTS

- Ciltacabtagene autoleucel (cilta-cel), a CAR T-cell therapy, showed significant improvement in progression-free survival (PFS) for lenalidomide-refractory multiple myeloma (MM) patients after their first relapse.
- During the study, patients receiving cilta-cel had a 76% 12-month PFS rate compared to 49% for those receiving standard of care (SOC).
- Cilta-cel also demonstrated higher overall response rates and measurable residual disease negativity rates compared to SOC, with a positive trend towards improved overall survival.
- Lenalidomide-based therapies, commonly used as frontline treatments for MM, often result in lenalidomide refractoriness, necessitating new treatment options for patients at an early stage of the disease.

BACKGROUND

- MM patients typically experience relapse after each line of therapy, leading to shorter remission periods and reduced quality of life.
- Lenalidomide-refractory disease poses a challenge, requiring effective therapies to be used early in the treatment journey.
- Cilta-cel was approved by the FDA in 2022 for treating relapsed or refractory MM after multiple lines of therapy.

RESULTS

- The phase 3 CARTITUDE-4 trial included 419 lenalidomide-refractory MM patients who had received 1-3 prior lines of therapy.
- Patients were randomly assigned to receive either cilta-cel or SOC.
- After a median follow-up of 15.9 months, cilta-cel demonstrated superior 12-month PFS rates (76% vs. 49% for SOC).
- Cilta-cel showed significant improvements in overall response rate, complete response rate, and measurable residual disease negativity rate compared to SOC.
- Adverse events were experienced by all patients in both treatment arms, with hematologic treatment-emergent AEs being the most common.

CLINICAL IMPLICATIONS

- Cilta-cel has the potential to become a new standard of care for lenalidomide-refractory MM patients after their first relapse.
- The efficacy benefits of cilta-cel were consistent across various patient subgroups, including those with high-risk disease factors.
- Cilta-cel's efficacy, safety, and limited treatment duration suggest it may replace continuous treatments and impact the treatment paradigm for MM.
- Further studies, including CARTITUDE-5 and CARTITUDE-6, are investigating cilta-cel as frontline therapy for MM.

Expert Discussion

- Experts view cilta-cel as a valid and important therapy for MM patients based on the significant PFS benefit and high percentage of patients achieving MRD-negative disease.
- The study's findings may lead to CAR T-cell therapy being preferred in early-line therapy instead of later-line therapy.
- Concerns exist regarding access to this treatment approach, especially for vulnerable and minority patients, as well as the high costs associated with it.
- The study's results offer hope for treating MM earlier in the disease course, with high response rates and a potential for molecular remission

Clinical trial information: NCT04181827

Axicabtagene Ciloleucel Improves Survival in Relapsed/Refractory Large B-cell Lymphoma: RESULTS from ZUMA-7 Study LBA107

KEY POINTS

1. Axicabtagebe ciloleucel (axi-cel) demonstrated a significant improvement in overall survival compared to SOC therapy.
2. The survival benefit with axi-cel was consistent across various patient subgroups, including age, disease characteristics, and treatment history.
3. Axi-cel also showed a significant improvement in progression-free survival compared to standard of care (SOC) therapy.

BACKGROUND

- Patients with early relapsed or refractory large B-cell lymphoma (R/R LBCL) have limited treatment options and poor outcomes.
- The ZUMA-7 study aimed to compare the effectiveness of axi-cel with SOC therapy in these patients.

RESULTS

- The study included 359 patients, with 180 receiving axi-cel and 179 receiving SOC therapy.
- At a median follow-up of 47.2 months, axi-cel showed a statistically significant improvement in overall survival compared to SOC.
- Median OS was longer with axi-cel vs SOC (not reached vs 31.1 mo, respectively); 48-mo OS estimates were higher with axi-cel (54.6% vs 46.0%, respectively).
- Axi-cel also demonstrated better progression-free survival rates compared to SOC therapy.

CLINICAL IMPLICATIONS

- Axicabtagene ciloleucel offers a significant survival advantage over standard-of-care therapy for patients with early relapsed/refractory LBCL.
- These findings highlight the potential of axi-cel as an effective treatment option in improving outcomes for this patient population.
- Axi-cel should be considered as a valuable therapeutic approach for patients with limited treatment options and poor prognosis in R/R LBCL.

Clinical trial information: NCT03391466.

SWOG-S1826: Nivolumab Plus AVD Chemotherapy as New Standard of Care for Advanced-Stage Hodgkin Lymphoma LBA4

KEY POINTS

1. Nivolumab plus AVD significantly prolonged progression-free survival and was better tolerated when compared with brentuximab vedotin plus AVD in patients with advanced-stage Hodgkin lymphoma ≥ 12 years of age.
2. Overall, < 1% of patients in the trial received end-of-treatment radiation therapy.
3. Nivolumab plus AVD is poised to become a new standard of care for the treatment of classic Hodgkin lymphoma and marks a key step toward harmonizing the management of pediatric and adult patients.

BACKGROUND

- Adding brentuximab vedotin (BV) to initial chemotherapy has shown improved overall survival in adults and progression-free survival in pediatric patients with advanced-stage HL. However, BV's use adds toxicity, radiation therapy is often necessary for pediatric patients, and a portion of patients experience relapsed or refractory HL.
- The PD-1 pathway plays a central role in HL's development, and blocking PD-1 has been effective in treating relapsed or refractory HL.
- The SWOG-S1826 trial, conducted by the adult and pediatric cooperative groups of the National Clinical Trials Network, aimed to compare N-AVD and BV-AVD in newly diagnosed advanced-stage HL patients. A potentially better-tolerated and more effective treatment option.
- The trial included over 1,000 centers across the National Clinical Trials Network, making it the largest study of advanced-stage Hodgkin lymphoma and the first prospective collaboration between adult and pediatric groups.

RESULTS

- A total of 994 eligible patients were enrolled and randomized into the N-AVD (n=489) or BV-AVD (n=487) groups.
- The median age was 27 years, with a diverse patient population in terms of gender and ethnicity.
- At the interim analysis, N-AVD demonstrated superior progression-free survival, with a lower number of progression events compared to BV-AVD.
- N-AVD also showed a favorable safety profile, with fewer grade ≥ 3 hematologic adverse events and a lower mortality rate due to adverse events.
- Rates of febrile neutropenia, pneumonitis, ALT elevation, and colitis were similar between the two groups, while hypothyroidism/hyperthyroidism and peripheral neuropathy differed.

- The effectiveness of nivolumab/AVD in treating Hodgkin lymphoma surpassed the predetermined statistical threshold set by the study protocol, leading the independent data monitoring committee to suggest revealing the results earlier than planned.

CLINICAL IMPLICATIONS

- Nivolumab-enhanced treatment (N-AVD) significantly improved progression-free survival in patients with advanced-stage Hodgkin lymphoma, surpassing the outcomes of brentuximab vedotin and AVD (BV-AVD).
- N-AVD demonstrated a more favorable safety profile, reducing immune-related adverse events and the need for radiation therapy.
- Longer follow-up is required to assess overall survival and patient-reported outcomes.
- The S1826 study represents a crucial milestone in harmonizing treatment approaches for advanced-stage HL in both pediatric and adult populations.
- This breakthrough provides a foundation for further research and the potential to enhance personalized treatment strategies for advanced Hodgkin lymphoma.
- This is a practice-changing study given the favorable efficacy and toxicity associated with nivolumab/AVD
- This study included children, adolescents, adults, and elderly patients, all of whom benefited from nivolumab/AVD

Clinical trial information: NCT03907488.

↳ Treatment with nivo + chemo reduced the risk of cancer related deaths for people with newly diagnosed stage III or IV HL when compared to current SoC

MELANOMA

A Promising Personalized Cancer Vaccine Approach in Melanoma LBA9503

KEY POINTS

1. The phase 2b KEYNOTE-942 trial showed that the combination of an mRNA cancer vaccine and an immune checkpoint inhibitor (ICI) can improve upon the rates of recurrence free survival in melanoma previously achieved by PD-1 blockade alone.
2. Challenges associated with mRNA vaccine development include their relative instability and the potential for easy degradation, which can complicate in vivo delivery.

3. The safety and efficacy of mRNA vaccines are currently being explored in different cancer types including melanoma, liver, prostate, ovarian and pancreatic cancers, and other advanced solid tumours.

BACKGROUND

- mRNA-4157 is an innovative mRNA-based personalized cancer vaccine that encodes up to 34 patient-specific tumour neoantigens.
- The Phase 2 mRNA-4157-P201/KEYNOTE-942 trial aimed to evaluate the efficacy of mRNA-4157 in combination with pembrolizumab compared to pembrolizumab monotherapy in patients with resected high-risk stage IIIB/C/D and IV melanoma.
- The trial met its primary endpoint of improved recurrence-free survival (RFS), demonstrating a significant benefit of the combination therapy over pembrolizumab monotherapy.

RESULTS

- A total of 157 patients were enrolled, with 107 receiving the combination therapy and 50 receiving pembrolizumab monotherapy.
- The combination therapy showed a statistically and clinically significant improvement in DMFS compared to pembrolizumab monotherapy, with a reduction in distant recurrence or death by 65.3%.
- At the primary analysis, the 18-month DMFS rates were 91.8% in the combination arm and 76.8% in the monotherapy arm.
- The RESULTS also revealed favorable RFS rates, with a 18-month rate of 78.6% in the combination arm and 62.2% in the monotherapy arm.

CLINICAL IMPLICATIONS

- The combination of mRNA-4157 with pembrolizumab as adjuvant therapy for resected high-risk melanoma demonstrated a significant prolongation of DMFS compared to pembrolizumab monotherapy.
- These findings provide further support for the potential benefits of personalized neoantigen approaches in cancer treatment.
- A Phase 3 randomized study will be initiated to validate the efficacy of mRNA-4157 in patients with melanoma.

Clinical trial information: NCT03897881

TUMOUR AGNOSTIC

T-DXd Shows Promise Across HER2-Expressing Solid tumours: DESTINY-Pantumours-02 Interim Results LBA3000

KEY POINTS

1. Interim RESULTS of the phase 2 trial DESTINY-Pantumour-02 show that T-DXd has broad activity across tumour types and a toxicity profile consistent with previous studies.
2. T-DXd had the lowest activity in pancreatic cancer, and this cohort was stopped early.
3. Responses were especially high among patients who had cervical, endometrial, and ovarian cancers.

BACKGROUND

- T-DXd is an antibody-drug conjugate composed of trastuzumab and deruxtecan, approved for specific HER2-positive cancers.
- DESTINY-Pantumours-02 is an international, open-label study including 267 patients across different tumours cohorts, including urothelial bladder, biliary tract, cervical, endometrial, ovarian, and pancreatic cancers, as well as a rare tumour cohort that included a range of tumours types for which T-DXd is currently either not available or not being investigated (including head and neck cancers and intestinal adenocarcinoma)

RESULTS

- T-DXd had a compelling objective response rate (ORR) of 37.1%, with durable responses in a substantial number of patients at 12 months.
- Patients who responded to treatment showed a long duration of response, with nearly 50% maintaining response at 12 months.
- The confirmed HER2 IHC2+ and IHC3+ subgroups had response rates of 27.2% and 61.3%, respectively.
- Responses were observed in all tumour types, with lower activity observed in pancreatic cancer.
- High response rates were noted in cervical, endometrial, and ovarian cancers.
- Additionally, 41.6% of patients had stable disease, meaning their condition did not worsen.

✳ T-Dxd has revolutionized the treatment of HER2 positive (HER2 Low) mBC - this trial shows the efficacy in other types of HER2 positive cancers - representing a huge step forward for patients.

CLINICAL IMPLICATIONS

- The study's responses indicate a potential shift in clinical practice, suggesting T-DXd as a compelling treatment option for various tumour types expressing HER2.
- Safety findings were consistent with previous studies, and no new safety concerns were identified.
- Routine HER2 IHC testing may increase due to the study's outcomes and the availability of an effective treatment option for HER2-expressing tumours.
- Further analysis of overall survival and progression-free survival is underway.

FUTURE CONSIDERATIONS

- The positive results may lead to an increase in the frequency of HER2 testing for these tumour types.
- It would be interesting to further investigate the effectiveness of T-DXd in patients with differing HER2 status between central and local testing.
- The use of next-generation sequencing (NGS), alongside immunohistochemistry (IHC) testing, could provide additional information for tumours-type agnostic approaches.

Clinical trial information: NCT04482309

GYNECOLOGIC CANCERS

Interim Analysis Shows Immunotherapy's Survival Benefit in Advanced Ovarian Cancer: DUO-O Trial LBA5506

KEY POINTS

- DUO-O assessed safety and efficacy of maintenance therapy with bevacizumab monotherapy versus bevacizumab in combination with durvalumab and olaparib in patients with newly diagnosed advanced ovarian cancer and no BRCA mutations.
- PFS with the triplet maintenance therapy was significantly greater than with bevacizumab monotherapy.
- 35% of the patients in the triplet arm experienced adverse events leading to discontinuation of 1 or more of the triplet drugs.
- Final analysis data are awaited to fully assess the overall clinical benefit.

BACKGROUND

- Most cases of ovarian cancer are diagnosed at an advanced stage, and relapse is common within 10 to 18 months.
- Maintenance therapy with olaparib, alone or in combination with bevacizumab, has become a standard option to reduce the likelihood of disease recurrence.
- Previous studies showed improved PFS with PARP inhibitors in newly diagnosed advanced ovarian cancer, regardless of BRCA mutation status.
- Combining PARP inhibitors with immune checkpoint inhibitors (ICIs) has shown promising results in maintenance therapy.
- The MEDIOLA trial demonstrated better disease control rates and longer PFS with olaparib, durvalumab, and bevacizumab compared to olaparib and durvalumab alone.

RESULTS

- The DUO-O trial evaluated the safety and efficacy of bevacizumab monotherapy versus bevacizumab plus durvalumab and olaparib in advanced ovarian cancer patients without BRCA mutations.
- PFS was significantly greater with the triplet maintenance therapy in the intent-to-treat (ITT) population and HRD-positive population.
- The effect was consistent across clinical subgroups, including HRD-negative patients.
- Median PFS was numerically greater with bevacizumab plus durvalumab compared to bevacizumab monotherapy, but statistical significance was not reached.
- The safety and tolerability of these combinations are broadly consistent with that observed in prior clinical trials and the known profiles of the individual medicines
- For the first time, the DUO-O trial demonstrated a clinical benefit among patients who are historically challenging to treat and HRD negative against an active control arm

CLINICAL IMPLICATIONS

- The DUO-O trial results suggest that the triplet maintenance therapy has the potential to improve outcomes for advanced ovarian cancer patients.
- The combination of olaparib and durvalumab may enhance the efficacy of treatment.
- DUO-O is the first phase 3 clinical trial to meet its primary endpoint in ovarian cancer using an immuno-oncology agent—in this case, durvalumab—in combination with a PARP inhibitor for this population.

- Further analysis, including overall survival data, is necessary to fully understand the clinical benefit.
- The study opens possibilities for exploring immunotherapy options in ovarian cancer management, particularly in historically challenging-to-treat and HRD-negative patients

Clinical trial information: NCT03737643.

Groundbreaking Study Reveals Significant Survival Benefits of Pembrolizumab in First-Line Treatment of Cervical Cancer abstract 5500

KEY POINTS

1. The KEYNOTE-826 trial shows that adding pembrolizumab to chemotherapy with or without bevacizumab provides significant overall survival (OS) and progression-free survival (PFS) benefits in patients with persistent, recurrent, or metastatic cervical cancer.
2. No new safety concerns were observed during over 3 years of follow-up.
3. The study supports the use of pembrolizumab plus chemotherapy, with or without bevacizumab, as a new standard of care for this patient population.

BACKGROUND

- In the KEYNOTE-158 trial, pembrolizumab demonstrated benefits for patients with advanced cervical cancer who had experienced progression on or after chemotherapy.
- KEYNOTE-826 was conducted to evaluate the addition of pembrolizumab to chemotherapy with or without bevacizumab as a first-line treatment for cervical cancer.

RESULTS

- After a median follow-up of 39.1 months, pembrolizumab added to chemotherapy with or without bevacizumab continued to show significant improvements in OS and PFS.
- The OS improvement was observed in the overall population and in patients with tumours PD-L1 expression levels (CPS) ≥1 and CPS ≥10.
- PFS outcomes also favored the pembrolizumab-containing regimen in all three patient groups.

CLINICAL IMPLICATIONS

- The updated findings confirm the previous data and support the use of pembrolizumab plus chemotherapy, with or without bevacizumab, as the new

standard of care for patients with persistent, recurrent, or metastatic cervical cancer.
- Pembrolizumab provides a therapeutic option for patients who are not eligible for bevacizumab.
- Ongoing research aims to explore the role of pembrolizumab and other immune checkpoint inhibitors in earlier stages of cervical cancer, in combination with radiation therapy and chemotherapy, to achieve the best outcomes with minimal side effects.

NEXT STEPS
- Further investigation is needed to determine the optimal incorporation of immunotherapy into the treatment of early-stage cervical cancer, balancing efficacy and toxicity.
- Additional trials, such as the KEYNOTE-A18 trial, are evaluating the potential benefits of pembrolizumab in combination with chemoradiotherapy for locally advanced cervical cancer.

Clinical trial information: NCT03635567

GASTROINTESTINAL CANCERS

Transcriptional Metabolic Profiling in Young Onset Colorectal Cancer (CRC) Patients abstract 3509

KEY POINTS
1. Younger colorectal cancer (CRC) patients (<50 years) present with more advanced disease and exhibit distinct transcriptional profiles compared to older patients (>50 years).
2. The younger group showed enrichment in metabolic pathways, such as amino acids and lipids, as well as oncogenes like MYC targets and NRAS targets. The older group demonstrated enrichment in methylation, histone modification, immune response, and other metabolic pathways.
3. Metabolic pathway analysis revealed consistent alterations in steroid hormone metabolism and kynurenine metabolism, predominantly upregulated in the older group. Pathways associated with response to CTLA4 and PDL1 treatment were also upregulated in the older group, indicating potential differences in clinical outcomes and therapeutic response.

BACKGROUND

- Younger CRC patients (<50 years) often experience more advanced disease and face poorer treatment response and clinical outcomes.
- Understanding the transcriptional profiles and metabolic differences between younger and older CRC patients is crucial to address the unmet need for improved therapeutic strategies.

RESULTS

- Comparisons between younger and older groups revealed a significant number of differentially expressed transcripts and enrichment in distinct metabolic pathways, oncogenes, and cellular processes.
- Metabolic pathway analysis identified consistent alterations in steroid hormone metabolism and kynurenine metabolism, predominantly upregulated in older patients.
- Additionally, pathways associated with response to CTLA4 and PDL1 treatment were mostly upregulated in the older group.

CLINICAL IMPLICATIONS

- This study highlights the differences in transcriptional metabolic profiles and immune profiles between younger and older CRC populations.
- The identified transcriptional signatures may provide insights into distinct clinical outcomes and therapeutic response, suggesting potential avenues for targeted treatment approaches, particularly in younger CRC patients.
- Further exploration of these biological differences could lead to new strategies for the treatment of younger CRC populations, ultimately improving their clinical outcomes.

Promising RESULTS: Trastuzumab Deruxtecan Shows Potential in Treating HER2-Positive Metastatic Colorectal Cancer abstract 3501

KEY POINTS

1. Trastuzumab deruxtecan (T-DXd) demonstrated promising antitumour activity in patients with HER2-positive metastatic colorectal cancer, regardless of RAS mutation status and prior anti-HER2 therapy.
2. The study showed a confirmed objective response rate of 37.8% for the 5.4 mg/kg T-DXd dose and 27.5% for the 6.4 mg/kg T-DXd dose, indicating significant tumour shrinkage in both treatment arms.
3. Overall, the safety profile of T-DXd was consistent with previous knowledge, with fewer adverse events observed in the 5.4 mg/kg dose group compared to the 6.4 mg/kg group.

BACKGROUND

- HER2-positive mCRC is a rare but unique molecular subset found in 2-3% of patients
- T-DXd demonstrated antitumor activity in pts with HER2+ mCRC in DESTINY-CRC01
- The DESTINY-CRC02 study aimed to assess the efficacy and safety of T-DXd in patients with HER2-positive metastatic colorectal cancer.
- This multicenter phase 2 study included patients with centrally confirmed HER2-positive metastatic colorectal cancer.
- Patients with both RAS wild-type and mutant tumours were eligible.

RESULTS

- At the data cutoff, the majority of patients in both T-DXd arms had HER2 IHC 3+ tumours and a median of 3 to 4 prior lines of therapy.
- The confirmed objective response rates were 37.8% for the 5.4 mg/kg dose and 27.5% for the 6.4 mg/kg dose.
- The duration of response and progression-free survival were similar between the two dose groups.
- Grade ≥3 treatment-emergent adverse events occurred in 49.4% of patients in the 5.4 mg/kg arm and 59.0% of patients in the 6.4 mg/kg arm.
- Serious adverse events were observed in 24.1% of patients in the 5.4 mg/kg arm and 30.8% of patients in the 6.4 mg/kg arm.

CLINICAL IMPLICATIONS

- Trastuzumab deruxtecan demonstrated promising antitumour activity in patients with HER2-positive metastatic colorectal cancer, regardless of RAS mutation status and prior anti-HER2 therapy.
- The safety profile of T-DXd was favorable, with fewer adverse events observed in the 5.4 mg/kg dose group.
- These findings highlight the potential of T-DXd as a treatment option for HER2-positive metastatic colorectal cancer patients.
- Further research and clinical trials are warranted to validate these RESULTS and explore the long-term benefits and safety of T-DXd in this patient population.

Clinical trial information: NCT04744831.

Breakthrough Treatment for Pancreatic Cancer: NALIRIFOX Outperforms Standard Therapy in Survival Rates abstract 4006

KEY POINTS

1. NALIRIFOX, a combination therapy of liposomal irinotecan, 5-fluorouracil/leucovorin, and oxaliplatin, demonstrated significantly improved overall survival compared to the standard treatment of nab-paclitaxel and gemcitabine in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC).
2. Patients treated with NALIRIFOX also experienced longer periods without disease progression, indicating better disease control compared to the standard therapy.
3. NALIRIFOX showed a higher overall response rate, indicating a greater proportion of patients experiencing tumour shrinkage, compared to the standard therapy.

BACKGROUND

- Few treatment options are available for mPDAC
- NALIRIFOX is a combination therapy approved for mPDAC patients who have previously received gemcitabine-based treatment.
- Early-phase studies demonstrated promising anti-tumour activity of NALIRIFOX in patients with mPDAC as a first-line treatment.
- The NAPOLI 3 trial (NCT04083235) aimed to compare the efficacy and safety of NALIRIFOX with nab-paclitaxel and gemcitabine as the initial treatment for mPDAC.
- The phase 3 study included treatment-naive patients with histopathologically/cytologically confirmed mPDAC.
- Overall survival, progression-free survival, overall response rate, and safety were evaluated as primary and secondary endpoints.

RESULTS

- A total of 770 patients were included in the study, with 383 receiving NALIRIFOX and 387 receiving the standard therapy.
- The median follow-up was 16.1 months, and 544 events were observed.
- Patients treated with NALIRIFOX had a median overall survival of 11.1 months compared to 9.2 months in the standard therapy group.
- The median progression-free survival was 7.4 months for NALIRIFOX and 5.6 months for the standard therapy.
- The duration of response was longer in patients receiving NALIRIFOX compared to the standard therapy.

- Grade 3/4 adverse events, such as diarrhea, nausea, hypokalemia, anemia, and neutropenia, were more common in the NALIRIFOX group but generally manageable.

CLINICAL IMPLICATIONS

- First-line treatment with NALIRIFOX demonstrated significant improvements in overall survival and progression-free survival compared to the standard therapy for mPDAC.
- The safety profile of NALIRIFOX was consistent with the individual components of the regimen and generally manageable.
- These findings highlight NALIRIFOX as a breakthrough treatment option with potential CLINICAL IMPLICATIONS for improving outcomes in patients with metastatic pancreatic ductal adenocarcinoma.
- Further research and clinical trials are needed to validate these RESULTS and explore the long-term benefits and safety of NALIRIFOX in this patient population.

Clinical trial information: NCT04083235.

PROSPECT Trial: Multiple Paths for High Cure Rate in Locally Advanced Rectal Cancer LBA2

KEY POINTS

1. Neoadjuvant FOLFOX with selective use of 5-FU chemoradiotherapy (5-FU CRT) was noninferior to 5-FU CRT in participants with locally advanced rectal cancer.
2. The 2 strategies achieved nearly identical disease-free survival outcomes, and at 5 years, the overall survival rates were similar.
3. Findings indicate that either treatment from the PROSPECT trial could be administered, giving patients options and the ability to be empowered in their treatment selection.

BACKGROUND

- Locally advanced rectal cancer (LARC) is typically treated with radiation and fluoropyrimidine (5FUCRT) to improve disease-free survival.
- However, this standard treatment has associated short- and long-term toxicities.
- The PROSPECT trial compares FOLFOX chemotherapy with selective use of 5FUCRT to 5FUCRT alone as neoadjuvant treatment before total mesorectal excision (TME) for LARC.

RESULTS

- The trial involved 1,194 participants who were randomly assigned to receive either modified FOLFOX6 or chemoradiation.
- After a median follow-up of 58 months, the 5-year disease-free survival rate was 80.8% in the FOLFOX group and 78.6% in the 5-FU CRT group.
- The neoadjuvant FOLFOX approach was shown to be noninferior to 5-FU CRT, meeting the criterion for noninferiority.

CLINICAL IMPLICATIONS

- The PROSPECT trial provides evidence that the neoadjuvant approach using FOLFOX is a viable treatment option for rectal cancer.
- The chemotherapy-first option is beneficial for those with limited access to radiation therapy and for younger patients prioritizing fertility preservation and bowel and sexual function.
- The trial's results emphasize the importance of presenting information to patients in a transparent and accurate manner to enable informed decision-making. Either treatment strategy can be administered based on patient preference and toxicity profiles.
- Further analysis of trial data and follow-up studies are planned to refine and personalize therapies for rectal cancer.

Some patients with locally advanced rectal cancer can safely avoid radiation therapy

Clinical trial information: NCT01515787.

BREAST CANCER

Ribociclib and Endocrine Therapy in Early Breast Cancer: Primary RESULTS from NATALEE Trial LBA500

KEY POINTS

1. NATALEE was designed to evaluate the combination of ribociclib plus endocrine therapy in patients with early breast cancer.
2. There was a trend toward improved OS with ribociclib plus endocrine therapy, and a 3-year treatment duration of ribociclib 400 mg showed a predictable safety profile that was more favorable than the 600 mg dose of ribociclib used in the metastatic setting.
3. Follow-up data is still being collected, and further quality-of-life results will be provided later in the year.

BACKGROUND

- Recurrence of ER-positive breast cancer can occur, often at advanced stages, necessitating the prevention of recurrences.
- Previous research indicated the effectiveness of ribociclib plus endocrine therapy in advanced breast cancer, leading to the evaluation of this combination in early-stage disease.
- NATALEE study aims to enlarge the patient population with access to CDK4/6 inhibitors if the FDA acknowledges the data.

RESULTS

- The NATALEE trial included 5,101 men and pre- or postmenopausal women with early breast cancer, NATALEE included a broad population of patients, representing 70% of stage II and 100% of stage III HR-positive/HER2-negative early breast cancer patients.
- Patients were randomized to receive ribociclib + ET or ET alone.
- Patients receiving ribociclib plus endocrine therapy showed a 26.1% reduced risk for distant disease-free survival.
- A trend toward improved overall survival was observed with ribociclib plus endocrine therapy.
- Ribociclib + ET demonstrated significantly longer iDFS compared to ET alone, with a 3-year iDFS rate of 90.4% versus 87.1%.
- Secondary endpoints, including overall survival and recurrence-free survival, consistently favored ribociclib.
- Patient follow-up is ongoing to evaluate long-term outcomes and extended follow-up will provide better understanding of how ribociclib treatment affects both early and late disease recurrences.
- Quality-of-life results are expected to be reported later in the year.

CLINICAL IMPLICATIONS

- Adding ribociclib to standard-of-care endocrine therapy offers a meaningful improvement in disease-free survival for patients with HR+/HER2- early breast cancer.
- The NATALEE RESULTS support the use of ribociclib + ET as the preferred treatment option for a broad range of patients with stage II or III HR+/HER2- early breast cancer, including those with no nodal involvement.
- Ribociclib, in combination with endocrine therapy, provides a well-tolerated treatment approach with potential clinical benefits.
- Ribociclib plus endocrine therapy should be considered alongside BRCA testing for patients with high-risk early breast cancer and a BRCA mutation.

* if NATALEE shows ribociclib to be an appropriate alternative in this setting, it will change SoC - allowing for a choice between CDK4/6 inhibitors in this vulnerable patient population and allow more patients in the high risk early setting to gain more benefit

- Easily identifiable population of patients at risk of recurrence, the tolerability of ribociclib, and the clinically meaningful reduction in the risk of recurrence seen in this study, which is consistent across patients with different disease features, these landmark results have fundamental clinical impact and could help streamline decisions for how patients with stage II and III early breast cancer are treated

Clinical trial information: NCT03701334.

Telephone-Based Weight Loss Intervention and Weight Change in Breast Cancer: RESULTS from the BWEL Trial ABstract 12001

KEY POINTS

1. The telephone-based weight loss intervention (WLI) resulted in a significant decrease in weight compared to the control group.
2. Patients who received the WLI lost an average of 4.8% of their baseline body weight at 12 months, while the control group experienced a weight gain of 0.8%.
3. The WLI induced weight loss across different patient groups, including menopausal status, race/ethnicity, and hormone receptor status.

BACKGROUND

- Obesity is known to have a negative impact on the prognosis of early breast cancer.
- The BWEL trial aimed to evaluate the effects of a telephone-based WLI on invasive disease-free survival in breast cancer patients with a BMI of 27 kg/m2.
- This report focuses on the impact of the WLI on weight change.

RESULTS

- A total of 3,181 women with stage 2-3 HER2-negative breast cancer were randomized.
- The WLI group achieved a significant decrease in weight, with an average weight loss of 4.8% at 12 months, while the control group experienced a weight gain of 0.8%.
- The WLI's effectiveness was observed across various demographic and tumour factors, including menopausal status, race/ethnicity, and hormone receptor status.

* being overweight or obese is associated with worse outcomes in early BC. If this tel/web intervention can be replicated on a larger scale it could PREVENT reoccurrence and reduce the impact of other obesity associated diseases as well

CLINICAL IMPLICATIONS

- The telephone-based WLI demonstrated a significant and clinically meaningful weight loss in breast cancer patients with overweight and obesity.

- Tailoring the WLI to address the specific needs of Black and younger patients could enhance weight loss outcomes.
- Further analysis of the BWEL trial will determine whether the WLI improves disease outcomes.
- These findings highlight the importance of implementing weight loss interventions in the management of breast cancer, potentially improving patients' overall prognosis and quality of life.

Clinical trial information: NCT02750826

BRAIN TUMOURS

Vorasidenib Delays Chemotherapy and Radiotherapy in IDH-Mutant Low-Grade Glioma: Key Findings from the INDIGO Trial LBA1

KEY POINTS

1. The INDIGO trial is the first randomized phase 3 study exploring a targeted therapy for grade 2 IDH1/2-mutated glioma.
2. Vorasidenib reduced the risk of tumours progression or death by 61% and significantly delayed the need for more toxic treatments compared to placebo.
3. Vorasidenib exhibited a manageable safety profile, with elevated transaminase levels and diarrhea being the most common adverse events.
4. This marks the first significant therapeutic breakthrough in low-grade glioma treatment in over 20 years, providing improved outcomes for patients.

BACKGROUND

- Grade 2 IDH-mutant gliomas are slow-progressing but incurable brain tumours associated with disability and premature mortality.
- Current standard treatment involves monitoring with MRIs followed by chemotherapy and radiotherapy, which carry significant toxicities.
- Vorasidenib, an IDH1/2 inhibitor, has shown promise in penetrating the blood-brain barrier and targeting the mutant enzymes driving tumours growth.

RESULTS

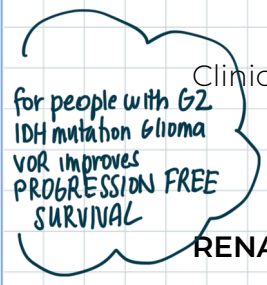
- The INDIGO trial enrolled patients with grade 2 IDH1/2-mutated oligodendroglioma or astrocytoma who had not received prior treatment.
- Vorasidenib demonstrated a remarkable improvement in median progression-free survival (27.7 months) compared to placebo (11.1 months).

- The time to the next intervention was significantly longer with vorasidenib, with 83.4% of patients not requiring additional treatment at 24 months, compared to 27.0% with placebo.
- Adverse events such as increased transaminase levels and diarrhea were more common with vorasidenib, but overall, it had a manageable safety profile.

CLINICAL IMPLICATIONS

- Vorasidenib has been granted fast-track designation by the FDA for the treatment of IDH-mutant gliomas, addressing unmet needs in these patients.
- Early use of vorasidenib can delay the need for aggressive therapies, potentially revolutionizing treatment approaches for young patients with low-grade gliomas.
- The approval of vorasidenib will offer a precise and less toxic therapeutic option, contributing to a paradigm shift in the management of this disease.
- The impact of vorasidenib on overall survival and its integration into clinical practice for different patient populations remain subjects of ongoing research and discussion

Clinical trial information: NCT04164901.



RENAL AND BILIARY TRACT CANCERS

Atezolizumab and Cabozantinib Combo Falls Short in Treating Advanced Kidney Cancer abstract LBA4500

KEY POINTS

1. Median PFS, OS and response rates were no different between patients with advanced RCC who received cabozantinib alone or combined with atezolizumab after progression on immune checkpoint inhibition.
2. Toxicity was greater in the combination arm versus monotherapy.
3. The data highlight the need for randomized prospective assessment of rechallenge with checkpoint inhibitors and PD-1/PD-L1 inhibitors in RCC and other tumour types.

BACKGROUND

- Immune checkpoint inhibitor (ICI)-based regimens are the standard initial treatment for metastatic clear cell renal cell carcinoma (ccRCC) (ipi+nivo).
- Limited treatment options are available when disease progression occurs during or after ICI therapy, with single-agent ICI (nivo) being commonly used.

- The CONTACT-03 study aimed to assess the efficacy and safety of adding the anti-PD-L1 agent atezolizumab to cabozantinib compared to cabozantinib alone in patients with metastatic RCC who experienced progression after prior ICI treatment.

RESULTS

- A total of 522 patients were randomized, with 263 receiving atezolizumab plus cabozantinib and 259 receiving cabozantinib alone.
- The combination therapy did not demonstrate significant improvements in progression-free survival or overall survival compared to cabozantinib alone.
- Both treatment groups had a similar overall response rate of 41%, and the duration of response was comparable between the two arms.
- However, the combination therapy resulted in higher rates of grade 3/4 adverse events and treatment withdrawal compared to cabozantinib alone.
- These findings indicate that the addition of atezolizumab to cabozantinib did not provide clinical benefits and increased the risk of toxicity in patients with RCC who had previously received ICI treatment.

CLINICAL IMPLICATIONS

- The combination of atezolizumab and cabozantinib did not show improved clinical outcomes in patients with metastatic renal cell carcinoma who experienced disease progression after prior immune checkpoint inhibitor (ICI) treatment.
- The study RESULTS suggest caution when considering the continuation of PD-(L)1 inhibitors in combination with standard treatments.
- Although CONTACT-03 failed to meet its primary endpoint, it is nevertheless informative in that an emerging practice in the treatment of mRCC and other cancers is the rechallenge of immune checkpoint inhibition after initial progression
- Further research is needed to explore alternative treatment approaches for this patient population.

Clinical trial information: NCT04338269.

Breakthrough Treatment Option for Aggressive Biliary Tract Cancer: TUCATRAS Shows Promise in Previously Treated Patients abstract 4007

KEY POINTS

1. The combination of tucatinib (TUC) and trastuzumab (Tras) demonstrated a confirmed objective response rate (cORR) of 46.7%, with significant tumour

shrinkage observed in patients with previously treated HER2-positive (HER2+) metastatic biliary tract cancer (BTC).
2. Patients who responded to the TUCATRAS combination experienced a median duration of response of 6.0 months, indicating sustained effectiveness of the treatment.
3. The 12-month overall survival rate was 53.8%, suggesting a potential shift in the historically poor outcomes associated with metastatic BTC.

BACKGROUND

- Biliary tract cancer (BTC) is a highly aggressive cancer type with limited treatment options, especially in advanced stages.
- Tucatinib (TUC) is a targeted therapy approved for HER2-positive metastatic breast and colorectal cancer, showing potential for HER2-overexpressing BTC cases.
- This study aimed to assess the efficacy and safety of TUC combined with trastuzumab (Tras) in patients with previously treated HER2-positive metastatic BTC.
- The SGNTUC-019 trial (NCT04579380) was an open-label phase 2 study evaluating the effectiveness, safety, and tolerability of TUC and Tras in patients with HER2-altered solid tumours, including BTC.
- Primary and secondary endpoints included objective response rate, overall survival, disease control rate, duration of response, progression-free survival, and safety assessments.
- Patients in the BTC cohort had received prior systemic therapy for metastatic disease and demonstrated HER2 positivity.

RESULTS

- The BTC cohort included 30 patients, with a median follow-up of 8.3 months.
- The confirmed objective response rate was 46.7%, with 14 patients showing either a complete or partial response to treatment.
- The median duration of response was 6.0 months, and the disease control rate was 76.7%.
- Median progression-free survival was 5.5 months, and the 12-month overall survival rate was 53.8%.
- The most common treatment-emergent adverse events were pyrexia (fever) and diarrhea, with manageable grade ≥3 adverse events reported in a subset of patients.
- Treatment discontinuation due to adverse events was observed in a small number of patients, and no deaths were attributed to treatment-related adverse events.

CLINICAL IMPLICATIONS:

- The combination of TUC and Tras demonstrated favorable tolerability and exhibited promising antitumour activity in previously treated HER2-positive metastatic BTC patients.
- These RESULTS suggest that TUCATRAS could serve as a potential chemotherapy-free treatment option for a patient population with historically poor outcomes.
- Further research and clinical trials are needed to validate these findings and explore the long-term benefits and safety of TUCATRAS in this specific population.

Clinical trial information: NCT04579380.

Groundbreaking RESULTS: Zani Provides Hope for Previously-Treated HER2-Amplified Biliary Tract Cancer abstract 4008

KEY POINTS

1. Zanidatamab (Zani), a HER2-targeted bispecific antibody, demonstrated a confirmed objective response rate (cORR) of 41% in patients with HER2-amplified biliary tract cancer (BTC), with ongoing responses and a median duration of response of 12.9 months.
2. Promising Efficacy: Among the responders, 82% experienced a duration of response of at least 16 weeks, indicating sustained effectiveness of Zani in a subset of patients.
3. Manageable Safety Profile: Zani showed a manageable safety profile, with diarrhea and infusion-related reactions being the most common treatment-related adverse events.

BACKGROUND

- Locally advanced/metastatic biliary tract cancer (BTC) has limited treatment options and poor survival outcomes after first-line therapy.
- Zanidatamab (Zani), a HER2-targeted bispecific antibody, showed promising responses in a subset of patients with BTC in a Phase 1 trial.
- This Phase 2b study aimed to evaluate the efficacy and safety of Zani in previously treated patients with HER2-amplified BTC.
- The HERIZON-BTC-01 trial (NCT04466891) was an open-label, global Phase 2b study that included patients with HER2-amplified, locally advanced unresectable or metastatic BTC.
- Efficacy was assessed based on confirmed objective response rate (cORR) by independent central review (ICR), with other efficacy and safety outcomes as secondary endpoints.

RESULTS

- A total of 87 patients were enrolled (Cohort 1: n=80; Cohort 2: n=7).
- In Cohort 1, the cORR was 41%, with a median duration of response of 12.9 months.
- Among the responders, 49% had ongoing responses, and 82% had a duration of response of at least 16 weeks.
- No responses were observed in Cohort 2.
- Treatment-related adverse events occurred in 72% of patients, with diarrhea and infusion-related reactions being the most common.
- Grade 3 treatment-related adverse events occurred in 18% of patients, with diarrhea and decreased ejection fraction being the most common.
- Two patients discontinued Zani due to adverse events.
- Serious treatment-related adverse events occurred in seven patients.
- No Grade 4 adverse events or deaths related to Zani were reported.

CLINICAL IMPLICATIONS

- The pivotal HERIZON-BTC-01 study demonstrated that Zanidatamab (Zani), a HER2 bispecific antibody, led to rapid and durable responses with a manageable safety profile in previously treated patients with HER2-positive biliary tract cancer.
- These promising RESULTS support the further development of Zani as a treatment option for HER2-positive BTC patients.

Clinical trial information: NCT04466891.

MENTAL HEALTH

Empowering Mental Health: A Digital Therapy for Anxiety and Depression in Cancer Patients abstract 1507

KEY POINTS

1. Patients who used the digitized Cognitive Behavioral Stress Management (CBSM) app, called "attune," experienced significant reductions in anxiety and depression symptoms compared to those using a control app.
2. At the end of the study, participants using attune reported a greater improvement in their anxiety and depression symptoms, indicating significant clinical progress.

participation in a digitized cognitive behavioural program significantly reduced anxiety and depression - SUGGESTING that we may be able to harness technology to compensate for the shortage of mental health providers and manage anxiety & depression in vulnerable populations

3. Digitizing psychological interventions like CBSM provides an opportunity to democratize access to evidence-based mental health support for cancer patients.

BACKGROUND

- Patients with cancer often face elevated distress levels, including anxiety and depression.
- Psychological interventions, such as CBSM, have demonstrated benefits in improving distress, quality of life, and long-term health outcomes.
- These interventions are not widely available or easily accessible, leading to the exploration of digital solutions to increase access to cancer-focused mental health care.

RESULTS

- The study involved 449 patients with non-metastatic and hematological cancers receiving or recently completing systemic treatment.
- Patients were randomized to either the attune app (digitized CBSM) or the control app (health education) in a double-blind manner.
- Participants using attune showed significantly greater reductions in anxiety and depression symptoms over the 12-week study period compared to the control group.
- At the end of the study, a higher proportion of attune users reported mild or no symptoms of anxiety and depression.
- Participants using attune also expressed a greater sense of improvement in their anxiety and depression symptoms.

CLINICAL IMPLICATIONS

- Digital therapeutics, such as the attune app, have the potential to enhance access to evidence-based psychological treatments for anxiety and depression in cancer patients.
- The study demonstrates that using attune leads to significant reductions in anxiety and depression symptoms, indicating its clinical effectiveness.
- Future efforts will focus on implementing strategies to maximize the benefits and accessibility of this cancer-specific digital therapy, ensuring its widespread use in supporting the mental well-being of cancer patients.

Clinical trial information: NCT05227898.

SPECIAL TOPICS

The Importance of Comprehensive Genomic Profiling in Precision Oncology

In the field of precision oncology, access to comprehensive genomic profiling (CGP) and CGP-directed therapies is of paramount importance, particularly for patients diagnosed with non-small cell lung cancer (NSCLC) and metastatic colorectal cancer (mCRC). Recent studies presented at the 2023 ASCO Annual Meeting shed light on the crucial role of CGP and its impact on treatment decisions in these cancer types. In the study focused on NSCLC, researchers discovered that negative single gene testing (SGT) conducted prior to CGP resulted in a significant increase in CGP test cancellations and failures in DNA extraction. SGT had previously been commonly employed to quickly identify specific mutations, such as EGFR or ALK. However, tissue availability for subsequent biopsies proved to be a major challenge for patients who failed frontline therapies selected based on SGT. The limitations of SGT prompted the need for broader molecular testing using CGP, which revealed a more comprehensive range of potential therapeutic targets.

In the study analyzing mCRC, the significance of CGP in guiding treatment decisions was highlighted. In this retrospective analysis, nearly half of the screened mCRC patients had actionable biomarkers identified through CGP, making them eligible for targeted therapy or immunotherapy. The analysis included patients enrolled in the U.S. Department of Veterans Affairs (VA) National Precision Oncology Program (NPOP), which emphasizes CGP as part of its care approach. The findings showed that CGP effectively identified actionable biomarkers, irrespective of gender or geography, ensuring equitable access to treatment options for female veterans and those residing in underserved areas.

However, certain disparities were observed in treatment administration based on age and race. Younger patients were more likely to receive FDA-approved CGP-directed therapies, possibly due to concerns about the potential toxicity of certain treatments in older patients. Additionally, Black patients were more likely to receive CGP-directed therapies compared to White patients, indicating a need to ensure equal access and treatment opportunities for all patient populations.

The study also revealed that a significant proportion of patients with MSI-high disease did not receive immune checkpoint inhibitors (ICIs). This highlights an opportunity to improve treatment outcomes for patients with this specific biomarker. Similarly, a considerable number of patients with NRAS/KRAS/BRAF wild-type disease did not

receive anti-EGFR antibodies, which underscores the importance of educating healthcare providers on appropriate treatment options based on CGP RESULTS.
In conclusion, the studies presented at the ASCO Annual Meeting underscored the indispensable role of comprehensive genomic profiling in precision oncology. The limitations of single gene testing became apparent, prompting a transition towards CGP to facilitate personalized therapy. To optimize patient outcomes, healthcare professionals need to be well-informed about the benefits of CGP and the potential therapeutic opportunities it presents. Efforts should be directed towards promoting widespread adoption of CGP and improving access to targeted therapies and immunotherapies based on actionable biomarkers, ultimately advancing precision oncology care.

KEY POINTS

- Access to comprehensive genomic profiling (CGP) and CGP-directed therapies is crucial for patients with non-small cell lung cancer (NSCLC) and metastatic colorectal cancer (mCRC).
- Negative single-gene testing before CGP in NSCLC led to increased CGP test cancellations and DNA extraction failures.
- CGP in mCRC identified actionable biomarkers in almost 50% of patients, highlighting the need for targeted therapy and immunotherapy prescriptions.

BACKGROUND

- Comprehensive genomic profiling (CGP) and CGP-directed therapies play a vital role in the treatment of NSCLC and mCRC.
- Previous single-gene testing strategies may hinder CGP effectiveness and turnaround time.

RESULTS

1. Single Gene Testing and CGP in NSCLC

- NSCLC patients undergoing negative single gene testing (SGT) before CGP experienced increased CGP test cancellations and DNA extraction failures.
- Limited tissue availability after frontline therapy selected based on SGT poses challenges for subsequent biopsies.
- CGP offers a broader scope for molecular testing, enabling the identification of therapeutic opportunities.

2. CGP in mCRC

- CGP screening of mCRC patients identified actionable biomarkers in nearly 50% of cases, making them eligible for targeted therapy or immunotherapy.

- No significant disparities were observed in FDA-approved treatment administration based on gender or geography.
- Younger patients and Black patients were more likely to receive CGP-directed therapies.
- A significant minority of patients with MSI-high disease did not receive immune checkpoint inhibitors (ICIs), highlighting the need for improved treatment for this biomarker.

CLINICAL IMPLICATIONS:

- Transitioning away from single gene testing towards comprehensive genomic profiling is crucial for timely and effective personalized therapy.
- Increased education and awareness are needed to promote the prescription of targeted therapies and immunotherapies based on actionable biomarkers.

Note: The information provided is based on two studies presented during the 2023 ASCO Annual Meeting, highlighting the importance of CGP in NSCLC and mCRC. Abstract 6506 and Abstract 3602

Focus on Disparities in Cancer Care

Researchers, led by Dr. Eric Chen, examined the effectiveness of rideshare services in facilitating timely completion of radiation therapy for patients who faced barriers such as transportation limitations, financial constraints, and inadequate social support. They analyzed data from approximately 2,900 patients who underwent radiation therapy, with 58 of them utilizing a free hospital-provided rideshare service.

The study found that those who utilized the free rideshare service were generally younger and more likely to identify as Black or African American compared to non-users. They also had higher socioeconomic disadvantages and traveled shorter distances for their treatment. Interestingly, rideshare service users had a higher proportion of radiation therapy with curative intent, longer treatment durations, and a higher number of prescribed treatment fractions. The matched-cohort analysis revealed that rideshare utilizers had significantly higher radiation therapy completion rates compared to non-rideshare utilizers, particularly among patients undergoing curative radiation therapy.

The key takeaway message from this study is that hospital-provided free rideshare services can be beneficial in improving radiation therapy completion rates, especially for patients facing barriers to accessing treatment. It underscores the importance of

addressing transportation challenges and providing support services to ensure timely and successful completion of radiation therapy, particularly in the curative setting.
In a different study, titled "Trends and Disparities in Oncology Telehealth after the Initial Pandemic Era," Dr. Michael Lee and colleagues investigated the continued utilization of telehealth in oncology practices after the pandemic and examined potential demographic differences among its users. The study analyzed over 340,000 hematology oncology visits in 22 Kaiser Permanente Northern California clinics between October 2020 and June 2022.

The findings showed that telehealth visits, including office, video, and telephone visits, remained popular even after the initial pandemic period. Video visits were the most commonly utilized form of telehealth. However, there were disparities in telehealth use among different demographic populations. Video visits were more prevalent among individuals under 45 years old, primary English speakers, patients with commercial insurance, and non-Hispanic Whites and Asians. In contrast, Hispanic, White, and Black patients, as well as those living in deprived neighborhoods, had lower utilization of video visits.

The key takeaway is that while telehealth continued to be widely used in oncology practices post-pandemic, there are disparities in its utilization, particularly among underprivileged populations. Addressing barriers to accessing telehealth for these populations should be a priority to ensure equitable healthcare delivery.
Abstract 6530

Using mRNA Vaccines to Fight Cancer: Promising Advances and Current Status

mRNA vaccines are a new and promising tool in the fight against cancer. They have shown potential in improving the rates of survival without recurrence in melanoma when combined with immune checkpoint inhibitors (ICIs) compared to ICIs alone. However, there are challenges in developing mRNA vaccines, such as their relative instability and the risk of easy degradation, which can make delivery inside the body complex. Currently, researchers are exploring the safety and effectiveness of mRNA vaccines in various types of cancer, including melanoma, liver, prostate, ovarian, and pancreatic cancers, as well as other advanced solid tumours.

A recent trial conducted by Moderna evaluated the mRNA-4157/V940 vaccine in combination with pembrolizumab in patients with advanced resected melanoma. The trial showed a significant reduction in the risk of disease recurrence or death compared to pembrolizumab alone. This is the first time that a combination of an

mRNA cancer vaccine and an ICI has demonstrated improved recurrence-free survival rates. The success in melanoma opens up possibilities for testing mRNA vaccines with other ICIs and in different types of cancer.

mRNA technology has been under development as a cancer therapy for the past decade, but it gained significant attention during the COVID-19 pandemic with the rapid development of mRNA vaccines against the SARS-CoV-2 virus. mRNA vaccines have advantages such as good tolerability, the ability to induce both humoral and cell-mediated immunity, and relatively fast and cost-effective production methods. They are easily degraded by cells, do not integrate into the host genome, and cannot cause infections. These characteristics make mRNA vaccines suitable for repeat administration.

In cancer treatment, mRNA vaccines work differently from ICIs. Once taken up and translated by dendritic cells, mRNA vaccines trigger an immune response against cancer cells while sparing healthy cells. They can target multiple antigens and potentially include immune stimulatory proteins to enhance efficacy.

Currently, mRNA vaccines are being tested mostly in advanced metastatic cancer, but promising results have also been seen in the adjuvant setting. Ongoing clinical trials are exploring the safety and effectiveness of mRNA vaccines in various types of cancer, with melanoma being the main focus. However, other cancers with high mutational loads and high expression of neoantigens or shared antigens could also benefit from mRNA vaccines.

Challenges remain in the production and administration of mRNA vaccines, including improving stability and ease of delivery. Different vectors, such as nonviral, viral, and cell-based systems, are used for in vivo delivery. Finding the most potent epitopes to include in the vaccines is also an important consideration.

Future research will focus on finding the optimal combination of mRNA vaccines with existing cancer therapies. While monotherapy trials of vaccines have not shown significant clinical efficacy in the past, the recent randomized trial with mRNA vaccines and ICIs has demonstrated added effectiveness.

Ongoing Clinical Trials of mRNA Cancer Vaccine Candidates in Different Cancers

NCT number	Agent	Indication	Phase	Status	Trial title
NCT05198752	SW1115C3 neoantigen personalized mRNA vaccine	Advanced malignant solid tumors	1	Recruiting	A Study of Neoantigen mRNA Personalized Cancer Vaccine in Patients With Advanced Solid Tumors
NCT05192460	Neoantigen cancer vaccine with or without PD-1/L1	Advanced gastric cancer, esophageal cancer and liver cancer	N/A	Recruiting	Safety and Efficacy of Personalized Neoantigen Vaccine in Advanced Gastric Cancer, Esophageal Cancer and Liver Cancer
NCT03897881	mRNA-4157 + pembro	High-risk melanoma	1	Active, not recruiting	An Efficacy Study of Adjuvant Treatment With the Personalized Cancer Vaccine mRNA-4157 and Pembrolizumab in Participants with High-Risk Melanoma (KEYNOTE-942)
NCT03313778	mRNA-4157 + pembro	Unresectable solid tumors	1	Active, not recruiting	Safety, Tolerability, and Immunogenicity of mRNA-4157 Alone in Participants With Resected Solid Tumors and in Combination With Pembrolizumab in Participants With Unresectable Solid Tumors (KEYNOTE-603)
NCT04382898	BNT112 +/- cemiplimab	Prostate cancer	1/2	Recruiting	PRO-MERIT (Prostate Cancer Messenger RNA Immunotherapy) (PRO-MERIT)
NCT04163094	W_ova1 vaccine + (neo) adjuvant chemo	Ovarian cancer	1	Active, not recruiting	Ovarian Cancer Treatment With a Liposome Formulated mRNA Vaccine in Combination With (Neo-)Adjuvant Chemotherapy (OLIVIA)
NCT01197625	Dendritic cell vaccine	Prostate cancer	1/2	Active, not recruiting	Vaccine Therapy in Curative Resected Prostate Cancer Patients
NCT05714748	EBV mRNA vaccine	Advanced malignant tumors	1	Recruiting	Application of mRNA Immunotherapy Technology in Epstein-Barr Virus-related Refractory Malignant Tumors
NCT05738447	HBV mRNA vaccine	Liver cancer Hepatocellular carcinoma	1	Recruiting	Application of mRNA Immunotherapy Technology in Hepatitis B Virus-related Refractory Hepatocellular Carcinoma
NCT00639639	pp65-LAMP mRNA-loaded dendritic cells +/- autologous lymphocyte transfer	Malignant neoplasms of the brain	1	Active, not recruiting	Vaccine Therapy in Treating Patients With Newly Diagnosed Glioblastoma Multiforme (ATTAC)
NCT01686334	Dendritic cell vaccine	Acute myeloid leukemia	2	Recruiting	Efficacy Study of Dendritic Cell Vaccination in Patients With Acute Myeloid Leukemia in Remission (WIDEA)
NCT04573140	Autologous total tumor RNA and pp65-LAMP mRNA-loaded DOTAP liposome vaccine	Adult glioblastoma	1	Recruiting	A Study of RNA-lipid Particle (RNA-LP) Vaccines for Newly Diagnosed Pediatric High-Grade Gliomas (pHGG) and Adult Glioblastoma (GBM) (PNOC020)
NCT04911621	Dendritic cell vaccine + temozolomide-based chemo or dendritic cell vaccine + conventional therapy	High-grade glioma (phase 1) Diffuse intrinsic pontine glioma (phase 2)	1 & 2	Active, not recruiting	Adjuvant Dendritic Cell Immunotherapy for Pediatric Patients With High-grade Glioma or Diffuse Intrinsic Pontine Glioma (ADDICT-pedGLIO)

Source. Clinical advances and ongoing trials of mRNA vaccines for cancer treatment

CAR T Therapy Shows Promise In Solid Tumours

CAR T therapy, a groundbreaking treatment that has shown success in blood cancers, is now making its way into the realm of solid tumours, specifically colorectal cancer. A recent phase I study titled "A Phase I Dose-escalation Study of GCC19 CAR T: A Novel Coupled CAR Therapy for Patients with Metastatic Colorectal Cancer" has provided encouraging results, offering hope for patients with refractory metastatic colorectal cancer who have exhausted other treatment options.

While CAR T therapy has been effective in treating lymphoma and other blood cancers, its application in solid tumours has been challenging. To date, there hasn't been enough evidence to support its use in solid tumours. This phase I study

represents an important step toward exploring the potential of CAR T therapy in solid tumours, particularly colorectal cancer.
The study included 13 patients with metastatic colorectal cancer who had undergone at least two lines of therapy, rendering them refractory to treatment. The researchers administered two doses of CAR T therapy, with the higher dose demonstrating more promising outcomes. The lower dose showed a progression-free survival (PFS) of approximately 1.9 months, while the higher dose exhibited a PFS of 6.3 months. These results are particularly meaningful for patients in the refractory setting, where treatment options are limited.

The median overall survival for the lower dose group was 13 months, which is notable considering the challenging circumstances these patients face. The higher dose group showed an even better median overall survival of 18 months. Although the study involved a small number of patients, its findings serve as a proof of concept, indicating that CAR T therapy can be effective in solid tumours like colorectal cancer.

Importantly, the therapy was generally well-tolerated by the patients, with no unexpected or severe side effects reported. This safety profile adds to the growing evidence that CAR T therapy holds promise for the treatment of solid tumours. While the study's sample size is limited, it highlights the potential of CAR T therapy in addressing the unmet needs of refractory metastatic colorectal cancer patients. The successful implementation of CAR T therapy in solid tumours opens up new possibilities for patients who are looking for the next step in their treatment journey.

Further research and larger-scale trials are needed to validate and expand upon these initial findings. As the medical community continues to explore the potential of CAR T therapy in colorectal cancer and other solid tumours, the ultimate goal is to provide improved outcomes and enhanced quality of life for patients who face limited treatment options.
Abstract 3547

ABSTRACTS

Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC) Abstract LBA3

First phase 3 RESULTS from CARTITUDE-4: Cilta-cel versus standard of care (PVd or DPd) in lenalidomide-refractory multiple myeloma. Abstract LBA106

Primary overall survival analysis of the phase 3 randomized ZUMA-7 study of axicabtagene ciloleucel versus standard-of-care therapy in relapsed/refractory large B-cell lymphoma. Abstract LBA107

SWOG S1826, a randomized study of nivolumab(N)-AVD versus brentuximab vedotin(BV)-AVD in advanced stage (AS) classic Hodgkin lymphoma (HL). LBA4 Trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-overexpressing/amplified (HER2+) metastatic colorectal cancer (mCRC): Primary RESULTS from the multicenter, randomized, phase 2 DESTINY-CRC02 study. LBA4

Distant metastasis-free survival RESULTS from the randomized, phase 2 mRNA-4157-P201/KEYNOTE-942 trial. Abstract LBA9503

Efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) interim results. Abstract LBA3000

Efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-expressing solid tumours: DESTINY-Pantumour02 (DP-02) interim RESULTS. Durvalumab with paclitaxel/carboplatin (PC) and bevacizumab (bev), followed by maintenance durvalumab, bev, and olaparib in patients (pts) with newly diagnosed advanced ovarian cancer (AOC) without a tumour BRCA1/2 mutation (non-tBRCAm): RESULTS from the randomized, placebo (pbo)-controlled phase III DUO-O trial. LBA5506

KEYNOTE-826: Final overall survival RESULTS from a randomized, double-blind, phase 3 study of pembrolizumab + chemotherapy vs placebo + chemotherapy for first-line treatment of persistent, recurrent, or metastatic cervical cancer. Abstract 5500

Transcriptional metabolic profiling in young onset colorectal cancer (CRC) patients. Abstract 3509

Trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-overexpressing/amplified (HER2+) metastatic colorectal cancer (mCRC): Primary results from the multicenter, randomized, phase 2 DESTINY-CRC02 study. Abstract 3501

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PROSPECT: A randomized phase III trial of neoadjuvant chemoradiation versus neoadjuvant FOLFOX chemotherapy with selective use of chemoradiation, followed by total mesorectal excision (TME) for treatment of locally advanced rectal cancer (LARC) (Alliance N1048). Abstract LBA2

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Effect of a telephone-based weight loss intervention (WLI) on weight at 12-months in women with early breast cancer: RESULTS from the Breast Cancer Weight Loss (BWEL) trial. Abstract 12001

INDIGO: A global, randomized, double-blinded, phase 3 study of vorasidenib versus placebo in patients with residual or recurrent grade 2 glioma with an IDH1/2 mutation. Abstract LBA1

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