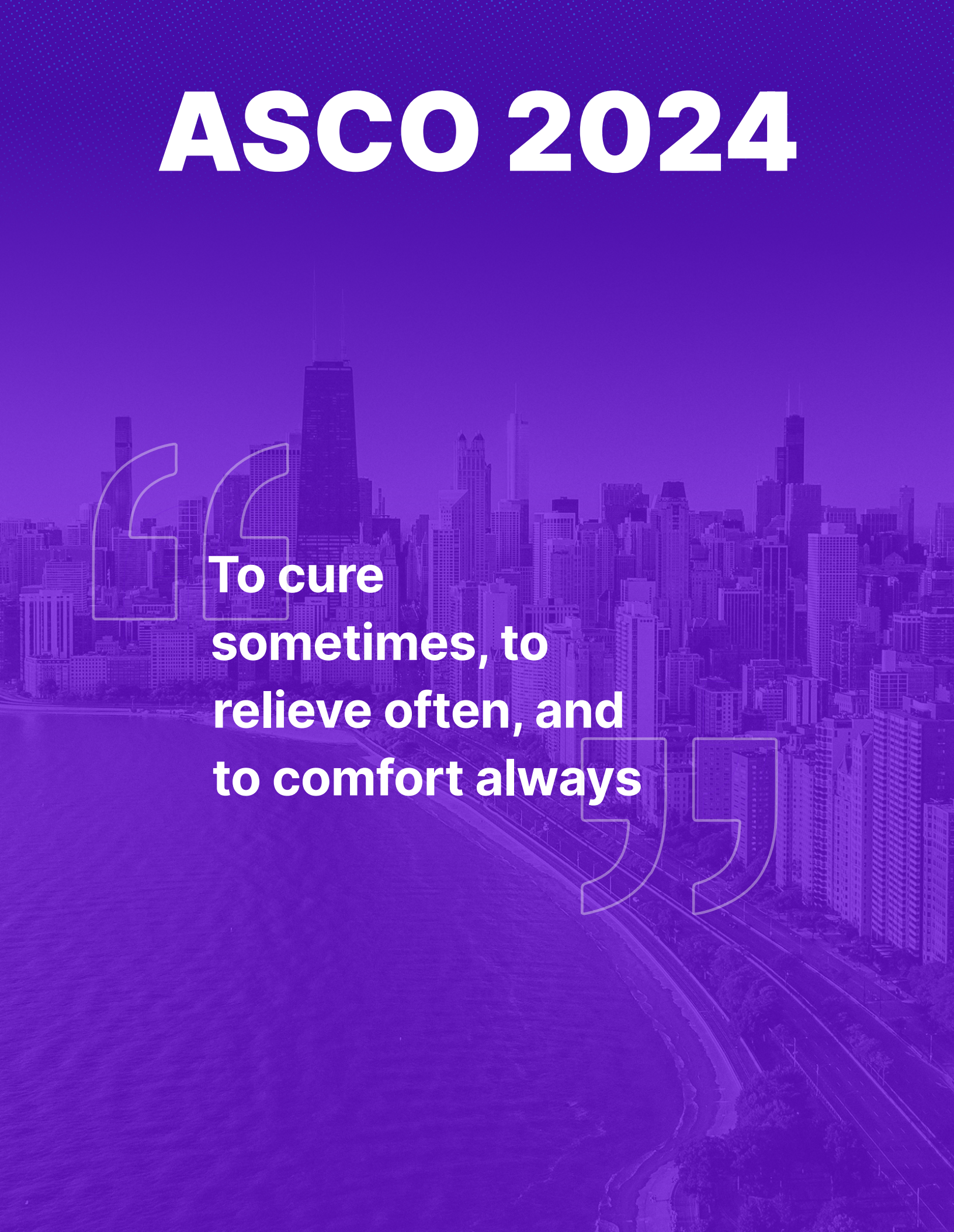
ASCO 2024



"To cure sometimes, to relieve often, and to comfort always"

Congress Review

Review of the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting

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THE ART of cancer care, the "human side of human medicine", involves engaging with patients and their families with deep compassion and integrating supportive or palliative care as a crucial part of all treatment.

The opening words of the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting by Congress President Lynn Schuchter stressed the importance of patient care and equitable access to healthcare. "While we continue advancing oncology science and fully leveraging the new and latest technologies, we must ensure these innovations benefit all patients," she stated. As an expert in melanoma, a cancer that was once considered hopeless, Schuchter has witnessed the transformation of the melanoma treatment landscape over the last decades, with the advent of powerful immunotherapies and targeted therapies, such as PD-1 antibodies and BRAF inhibitors, that have drastically improved patient outcomes.

For the first time in 25 years, the ASCO presidential theme touched on palliative care. Schuchter advocated for meaningful patient support throughout the cancer experience, and honoring patients' and families' preferences. She drew on her personal experience with a young patient who, unfortunately, did not survive a year after her melanoma diagnosis. Re-emphasizing a fundamental concept of medicine, she quoted Hippocrates: "To cure sometimes, to relieve often, and to comfort always, is all that may be reasonably expected of medicine." Comfort is not optional, and it involves the delicate communication of extremely difficult information. According to recent research, oncologists deliver bad news to patients an average of 35 times per month. Furthermore, patients often interpret a 20% response rate as a 20% cure rate, unless given more explicit information. Schuchter emphasized the need for better training of clinicians in patient communication, to avoid misunderstandings, allow patients to cope with information, and best allow for advanced care planning.

This year, ASCO has been committed to helping its members become just as skilled in the art of care as they are in the science. The 2024 program includes educational sessions, communications workshop, and a plenary session on how to deliver quality palliative care through telemedicine. Schuchter stressed that integration of palliative care globally is more important than ever: "We are facing a worldwide health crisis in oncology." By 2040, the World Health Organization (WHO)

estimates 29.5 million new cancer diagnoses per year, and cancer-related deaths will skyrocket to a projection of >16 million.

> **ASCO's goal is to lower cancer-related mortality, and ease patient suffering through education, research, and professional development**

To tackle this crisis, ASCO's goal is to lower cancer-related mortality, and ease patient suffering through education, research, and professional development. This 2024 was a record year, with more than 7,000 abstracts submitted, and 44,000 in-person and virtual attendees. Furthermore, over the past 5 years, ASCO has created regional councils in Asia Pacific, Latin America, sub-Saharan Africa, and Central and Eastern Europe to address region-specific cancer challenges. Free ASCO membership is also being provided to all oncology care professionals from low- and lower-middle income countries.

Closing her talk, Schuchter reminded the audience that, in a new era where AI algorithms can analyze complex brain MRIs in minutes, assess a tumor's genetic makeup, or identify the best treatment avenue for patients, "no machine can explain to a patient, with human compassion, what their choices are, and what their future may hold."

Read on for key insights from ASCO 2024, and come back next year for our coverage of ASCO 2025, also taking place in Chicago, from May 30–June 3.

Asciminib: Promising First-Line Treatment for Chronic Myeloid Leukemia

A NEW study presented at ASCO 2024 highlights asciminib as a promising treatment for newly diagnosed chronic phase chronic myeloid leukemia (CML).

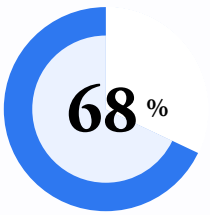
Asciminib, a 'Specifically Target the ABL Myristoyl Pocket' (STAMP) drug, has shown superior efficacy and a more favorable safety profile compared to current standard tyrosine kinase inhibitors (TKI). The Phase III ASC4FIRST trial involved 405 patients with recently diagnosed chronic phase CML, randomly assigned to receive either asciminib (201 patients) or an investigator-selected TKI (204 patients), such as imatinib or a second-generation TKI. The median age of participants was 52 years, and the study included a diverse patient population from cancer centers in 29 countries.

After 48 weeks, 68% of patients treated with asciminib achieved a major molecular response (MMR), compared to 49% in the TKI group. Additionally, 39% of asciminib patients reached a deep molecular response, suggesting potential for treatment-free remission. Subset analyses showed that asciminib was more effective than both imatinib and second-generation TKIs. For instance, 69% of patients in the imatinib subset who received asciminib achieved MMR, compared to 40% in the imatinib group. Similarly, 66% of those in the second-generation TKI subset who received asciminib achieved MMR, versus 58% in the corresponding TKI group.

Asciminib's safety profile was notable, with fewer adverse events and lower rates of treatment discontinuation compared to TKIs. Common side effects in the asciminib group included low platelet and neutrophil counts, but severe side effects like blood clots were rare, occurring in only 1% of participants. This combination of high efficacy and better tolerability positions asciminib as a potential first-line treatment for chronic phase CML.

The study's lead author, Timothy Hughes, emphasized that asciminib's potency and safety could enable more patients to achieve treatment-free remission, the goal of CML therapy. Researchers will continue to monitor long-term outcomes, including overall survival, progression-free survival, and the potential for treatment-free remission, to further establish asciminib's role in CML therapy.

After 48 weeks,



of patients treated with asciminib achieved a major molecular response

Longest Progression-Free Survival Reported in Advanced Non-small Cell Lung Cancer with Lorlatinib

NEW research presented at ASCO 2024 by lead study author Benjamin Solomon, Head of Lung Medical Oncology at the Peter MacCallum Cancer Center in Melbourne, Australia, revealed unprecedented progression-free survival (PFS) in advanced non-small cell lung cancer (NSCLC) with the use of lorlatinib, paving the way for new treatment outcomes.

Only 4 out of 114

patients in the lorlatinib group who did not present with brain metastases at the beginning of the study developed brain metastases within the first 16 months of treatment

The study demonstrated how lorlatinib, a third-generation anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitor (TKI), provided the longest progression-free survival ever recorded in patients with advanced ALK-positive NSCLC.

The Phase III CROWN clinical trial included 296 participants (59.1% female; 43.9% Asian; median age: 59 years) with advanced, previously untreated ALK-positive NSCLC, who were randomly assigned to receive either lorlatinib (149 patients) or crizotinib (147 participants). In the beginning of the study, 25% of the participants had brain metastases.

As of October 31st 2023, results showed that 50% of participants in the lorlatinib group were still receiving treatment, compared to just 5% in the crizotinib group. The median PFS for the lorlatinib group has not yet been reached, indicating that more than half of the patients have not experienced disease progression. In contrast, the median PFS was only 9.1 months for the crizotinib group. Additionally, the 5-year PFS rate was reported at 60% in the lorlatinib group, which was significantly higher than the crizotinib group at 8%.

Notably, only 4 out of 114 patients in the lorlatinib group who did not present with brain metastases at the beginning of the study developed brain metastases within the first 16 months of treatment. Additionally, the median time to disease progression in the brain had not yet been reached with lorlatinib, whereas it had with crizotinib at 16.4 months.

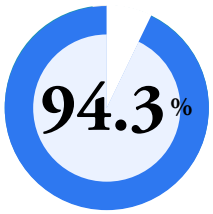
Treatment-related adverse events occurred in 77% of patients in the lorlatinib group and in 57% of patients in the crizotinib group, with 5% discontinuing lorlatinib and 6% discontinuing crizotinib. Reported adverse events included edema, high cholesterol, and hyperlipidemia.

Lorlatinib has demonstrated an unprecedented duration of disease control in patients with ALK-positive NSCLC, included those with brain metastases. The findings of this study indicate that lorlatinib offers significant advantage over second-generation ALK TKIs, providing better possibilities for long-term management of NSCLC. The study will continue to monitor the participants to determine if lorlatinib also leads to longer overall survival compared to crizotinib, and to establish the median PFS for lorlatinib.

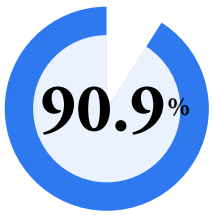
Novel Combination Therapy Minimizes Adverse Side Effects in Hodgkin Lymphoma

NOVEL combination anti-cancer therapy is effective at reducing the risk of advanced-stage classic Hodgkin lymphoma progression, relapse, or disease, resulting in a high 4-year progression-free survival rate of 94.3%.

Progression-free survival was higher for patients receiving BrECADD at



compared to



for patients receiving BEACOPP

The standard intensive chemotherapy regimen, BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone), is an effective curative treatment for classic Hodgkin lymphoma, comprising seven anti-cancer drugs. However, patients often experience acute, chronic, and potentially long-lasting adverse side effects. Researchers presented findings on an open-label Phase III clinical trial evaluating a novel combination therapy's side effects and effectiveness at ASCO 2024.

The GHSG-HD21 study was a multicenter, randomized clinical trial composed of 742 patients receiving the novel BrECADD therapy (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, and dexamethasone) and 740 receiving BEACOPP. Patients in the BrECADD regimen group had individualized treatment adapted to the patient's risk profile. Patients enrolled in the study were ≤60 years old with a diagnosis of advanced-stage classic Hodgkin lymphoma (average age: 31 years). Researchers used PET to determine the number of treatment cycles patients should receive, ranging from four to six.

Results from the study revealed that at a 4-year follow-up, an equivalent number of patients receiving BreCADD and BEACOPP (64%) were eligible for fewer treatment cycles. Progression-free survival was higher for patients receiving BrECADD at 94.3% compared to 90.9% for patients receiving BEACOPP. Disease progression in the BrECADD group was significantly reduced by 34% compared to the BEACOPP group. Moreover, the individualized treatment with BrECADD enabled 64% of patients in the BrECADD group to finish their treatment cycles in 3 months. Severe blood-related side effects arose in 31% of BrECADD group compared to 52% in the BEACOPP group, with almost all patients in the BrECADD group fully recovering from adverse events within 1 year.

These results led the authors to conclude that novel BrECADD treatment is associated with improved survival outcomes and reduced severe side effects in patients with advanced-stage classic Hodkin lymphoma compared to BEACOPP. The researchers aim to increase treatment efficacy without contributing to side effects, possibly by adding PD-1 inhibitors to BrECADD, thus reducing the number of treatment cycles.

Impact of Lymphadenectomy on Advanced Ovarian Cancer Outcomes

A randomized Phase III clinical trial called the CARACO trial has demonstrated that patients undergoing surgery for advanced ovarian cancer may avoid additional lymph node removal without compromising survival outcomes.

This research, presented at ASCO 2024, underscores efforts to reduce surgical morbidity while maintaining efficacy in cancer treatment. The study focused on advanced epithelial ovarian cancer, evaluating the necessity of lymphadenectomy during primary cancer surgery. Traditionally, lymphadenectomy was part of the standard treatment protocol, which included tumor removal followed by chemotherapy. However, findings from previous clinical trials indicated that omitting lymphadenectomy did not adversely affect survival rates.

Conducted between December 2008–March 2020, the Phase III CARACO trial involved 379 participants with advanced epithelial ovarian cancer, none of whom showed lymph node involvement before or during surgery. Participants were randomly assigned to either undergo lymphadenectomy (181 participants) or not (187 participants). Approximately 75% of participants received neoadjuvant chemotherapy before surgery.

The study's primary outcomes revealed no significant differences in survival between the two groups. Median progression-free survival was 14.8 months for those without lymphadenectomy compared to 18.5 months for those with the procedure. Median overall survival was 48.9 months versus 58 months, respectively. These differences were not statistically significant. Participants who underwent lymphadenectomy experienced higher rates of post-operative complications, such as additional surgeries to address bleeding or fluid buildup (8.3% versus 3.2%) and transfusions (34% versus 25%). The mortality rate within 60 days of surgery was similar between groups (1.1% versus 0.5%).

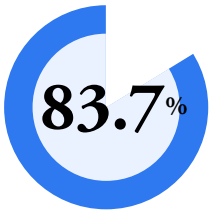
The CARACO trial reinforces the findings of a 2019 clinical trial termed the LION trial, suggesting that lymphadenectomy can be safely omitted in advanced ovarian cancer surgeries, thereby reducing surgical complications without affecting survival outcomes. This approach may enhance post-operative recovery and resource allocation. Jean-Marc Classe, Institut de Cancerologie de l'Ouest, Nantes University, France, emphasized the trial's significance in informing surgical practices post-neoadjuvant chemotherapy. Future research will focus on assessing lymphadenectomy's role in patients with evident lymph node involvement prior to surgery. The CARACO study marks a critical step in refining surgical strategies for advanced epithelial ovarian cancer.

> **This research underscores efforts to reduce surgical morbidity while maintaining efficacy in cancer treatment**

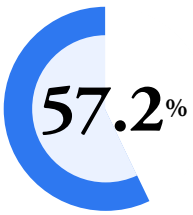
Neoadjuvant Immunotherapy Significantly Improves Outcomes in Stage III Melanoma

ADMINISTRATION of immunotherapy for melanoma before surgery has been shown to significantly improve outcomes for patients with Stage III melanoma compared to post-surgical immunotherapy.

At 12 months



of neoadjuvant therapy patients were event-free, compared to



of adjuvant therapy patients

Disease recurrence is a common phenomenon in patients receiving standard therapeutic lymph node dissection followed by adjuvant therapy to treat their melanoma. Researchers presented the NADINA Phase III trial results at the 2024 ASCO Annual Meeting. The trial compared outcomes between patients receiving the combined immunotherapy before surgery and those receiving standard post-surgical immunotherapy.

The NADINA Phase III trial was a multicenter study comprised of 423 patients from Europe and Australia, with 212 participants receiving neoadjuvant therapy, and 211 receiving adjuvant therapy. The patients who enrolled had cancer that had spread to the lymph nodes and required surgery. Patients were treated with ipilimumab and nivolumab before surgery, and monitored for a median of 9.9 months. If the tumor response was insufficient, they received additional adjuvant therapy post-surgery.

The results showed significantly fewer disease-related events in the neoadjuvant group compared to the adjuvant group (28 versus 72 events). At 12 months, 83.7% of neoadjuvant therapy patients were event-free, compared to 57.2% of adjuvant therapy patients. Furthermore, around 60% of patients in the neoadjuvant group required no additional adjuvant therapy after achieving a major pathological response. The trial also assessed outcomes based on the presence of a *BRAF* mutation. Among patients with a *BRAF* mutation, 83.5% of those receiving neoadjuvant therapy were event-free at 12 months, compared to 52.2% of those receiving adjuvant therapy. For patients without a *BRAF* mutation, the event-free survival rates were 83.9% for the neoadjuvant group and 62.4% for the adjuvant group.

Researchers noted that, although the neoadjuvant approach showed increased efficacy, it also came with higher rates of severe side effects (29.7% versus 14.7% in the adjuvant group), including infections, diarrhea, abnormal blood counts, rash, fever, and fatigue. The authors concluded that NADINA underscores the potential of neoadjuvant immunotherapy to improve survival outcomes in Stage III melanoma, supporting the shift towards personalized and response-driven treatment strategies. The NADINA trial is the first Phase III trial to assess and demonstrate the superiority of neoadjuvant immunotherapy for Stage III melanoma.

Osimertinib Revolutionizes Treatment for Locally Advanced EGFR-Mutated NSCLC

Research presented at ASCO 2024 by lead study author Suresh Ramalingam, Winship Cancer Institute of Emory University, Atlanta, Georgia, USA, suggests that osimertinib significantly improves progression-free survival in patients with unresectable Stage III epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer (NSCLC).

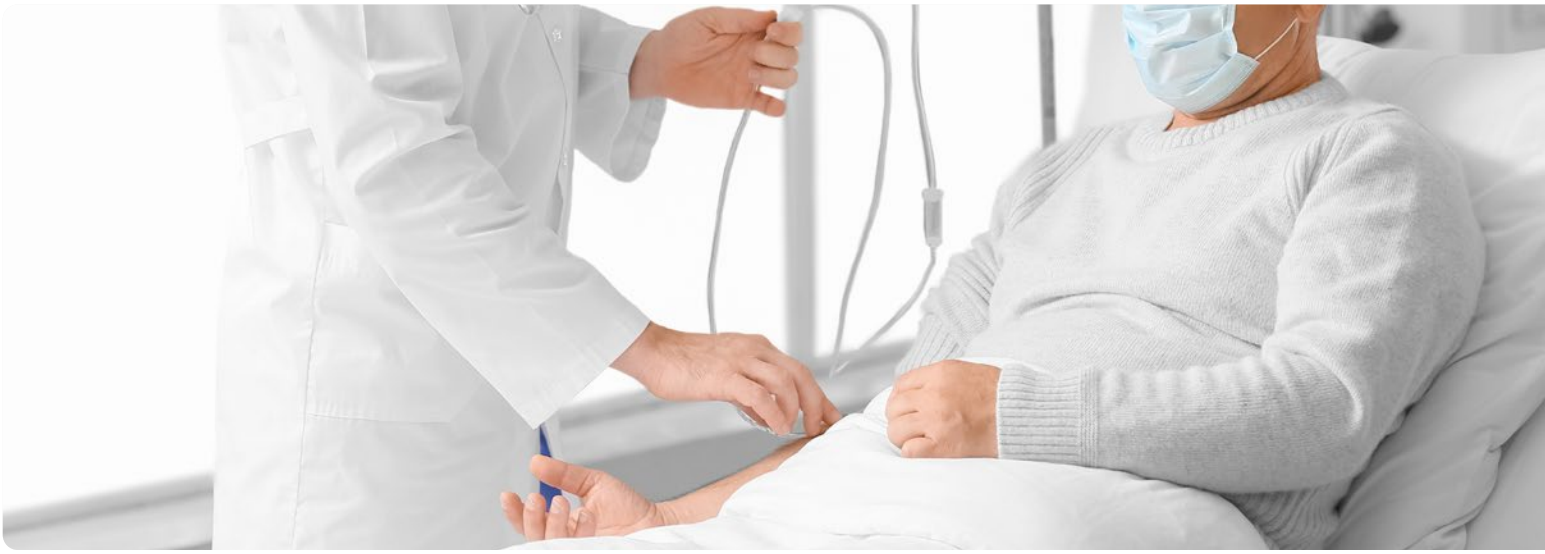
The Phase III LAURA trial enrolled patients with unresectable Stage III NSCLC with EGFR mutations who showed no disease progression during or after definitive platinum-based chemoradiotherapy. Patients were randomly assigned in a 2:1 ratio to receive either osimertinib (143 patients) or placebo (73 patients). Key patient characteristics included a median participant age of 62 years in the osimertinib group and 64 years in the placebo group; 63% female in the osimertinib group and 58% female in the placebo group; and 63% with no history of smoking in the osimertinib group, and 67% in the placebo group.

> **Results showed that osimertinib significantly reduced progression-free survival (PFS), with a median PFS of 39 months versus only 6 months in the placebo group**

Results showed that osimertinib significantly reduced progression-free survival (PFS), with a median PFS of 39 months versus only 6 months in the placebo group. Additionally, in the osimertinib group, 74% of participants had no cancer growth after 12 months, and 65% after 24 months, compared to the placebo group (22% versus 13%). Osimertinib also showed a higher objective response rate, reducing cancer size by at least 30% with the treatment, compared to placebo (57% versus 33%). Additionally, the rate of new brain metastases was significantly lower in the osimertinib group at 8%, compared to placebo at 29%.

Common side effects associated with osimertinib occurred in both study groups. These side effects included radiation pneumonitis, diarrhea, and rash. However, it was reported that most patients presented with mild cases of radiation pneumonitis. Due to severe adverse events, 13% of patients discontinued therapy in the osimertinib group, and 5% in placebo.

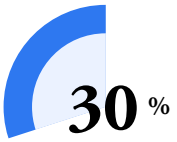
The study will continue to follow the participants to evaluate the impact of osimertinib on overall survival, brain metastases, and other outcomes. Ongoing monitoring will help to determine the long-term benefits of osimertinib for patients with locally advanced EGFR-mutated NSCLC.



Improving Esophageal Cancer Outcomes with Post-operative Chemotherapy

NEW insights into the treatment of locally advanced esophageal adenocarcinoma have revealed that administering chemotherapy before and after surgery (the FLOT protocol) significantly improves patient survival compared to the traditional approach of pre-operative chemoradiotherapy (the CROSS protocol), according to research presented at ASCO 2024.

FLOT recipients experienced a



lower risk of dying within this period [3 years]

The results were obtained from a Phase III ESOPEC clinical trial conducted across 25 centers in Germany. The trial involved 438 patients, predominantly male, with a median age of 63 years, all diagnosed with locally advanced, resectable esophageal adenocarcinoma. The participants were divided into two groups: 221 patients received the FLOT protocol, while 217 patients were treated with the CROSS protocol. Key findings revealed that 403 participants started treatment, and 371 proceeded to surgery. Post-surgery, 4.3% of the patients had died within 90 days (3.2% in the FLOT group versus 5.6% in the CROSS group). After a median follow-up of 55 months, 218 participants had died (97 from the FLOT group and 121 from the CROSS group). The median overall survival was notably higher for the FLOT group at 66 months, compared to 37 months for the CROSS group. Three-year survival rates were 57% for FLOT and 51% for CROSS, with FLOT recipients experiencing a 30% lower risk of dying within this period.

The results demonstrate that in patients with resectable esophageal adenocarcinoma, a combination of pre-operative and post-operative chemotherapy (FLOT) provides better outcomes than pre-operative chemoradiotherapy alone (CROSS). Researchers plan to explore if surgery can be avoided in patients who achieve a complete pathological response to FLOT or CROSS treatments, and show no cancer growth during active surveillance. This approach could preserve the esophagus, significantly enhancing the patient's quality of life. These findings may influence national and international treatment guidelines, potentially establishing the FLOT protocol as the preferred standard of care for locally advanced, resectable esophageal cancer.

Early Palliative Care Boosts Outcomes in Patients With Lung Cancer

RESEARCH shows that early palliative care enhances outcomes for patients with advanced non-small cell lung cancer, including survival.

Telehealth has the potential to significantly lessen the burden on patients, clinicians, and healthcare resources, while preserving quality care. The findings of this study presented at ASCO 2024 emphasizes the crucial need for healthcare systems and policymakers to integrate telehealth more widely into evidence-based palliative care standards.

This randomized comparative effectiveness trial included 1,250 patients recently diagnosed with advanced non-small cell lung cancer. Patients attended palliative care sessions every 4 weeks, conducted through video visits for those in the telehealth group and in person for those in the traditional care group. These sessions addressed physical and psychological symptoms, coping, illness, understanding care preferences, and treatment decisions. The mean age of patients was 65.5 years, with 54.0% identifying as women, and 66.7% being married or partnered. The racial diversity in the study was 10.4% African American or Black, 5.2% Asian, 82.7% White, and 4.8% Hispanic or Latino.

Patient quality-of-life scores were statistically similar between the telehealth and in-person groups (99.67 versus 97.67 on a scale of 0–136) at 24 weeks. Caregiver participation was significantly lower in the telehealth group compared to the in-person group (36.6% versus 49.7%). There were no significant differences between the two groups in patient-reported depression, anxiety, or coping skills.

> **Research shows that early palliative care enhances outcomes for patients with advanced non-small cell lung cancer**

The researchers in the future plan to investigate whether particular patient subgroups benefit more from telehealth or in-person care, including assessments based on age and proficiency in technology. Additionally, they plan to study the effects of both care delivery methods on the quality of end-of-life care, especially regarding patient-clinician communication about care preferences, to further refine and optimize palliative care protocols.

Trastuzumab Deruxtecan Enhances Progression-Free Survival in Patients with Breast Cancer

RESEARCH presented at ASCO 2024 by Giuseppe Curigliano, University of Milan and European Institute of Oncology in Milan, Italy, has shown that trastuzumab deruxtecan benefits patients with human epidermal growth factor receptor 2 (HER2)-low and HER2-ultra-low metastatic cancer, and significantly improves progression-free survival in patients with metastatic breast cancer that was previously treated with endocrine therapy.

This has the potential to improve treatment strategies, and utilize treatment earlier in the management of HER+ metastatic breast cancer, especially in patients who did not previously benefit from targeted therapies post-endocrine treatment.

The study included 866 participants with metastatic breast cancer, categorized into patients with either HER2-low (713 participants) or HER2-ultra-low (153 participants) cancers. HER2-low cancer group had an immunohistochemistry score of 1+ or 2+, indicating moderate HER2 protein expression, while HER2-ultra-low cancer group had a score >0 but <1+. All participants had received at least one prior endocrine treatment, and nearly 90.4% has also received targeted therapy with a cyclin-dependent kinase 4/6 inhibitor. Patients were randomly assigned to receive either trastuzumab deruxtecan (436 participants) or a physician's choice of chemotherapy (430 participants), including capecitabine, nab-paclitaxel, or paclitaxel.

Results showed that progression-free survival for patients with HER2-low cancer was 13.2 months with trastuzumab deruxtecan versus 8.1 months in patients who underwent chemotherapy. Similar events were noted in the HER2-ultra-low group. Patients with HER2-low cancer who received trastuzumab deruxtecan had a 38% lower chance of cancer progression compared to those on chemotherapy. The objective response rate was 56.5% for trastuzumab deruxtecan versus 32.3% for chemotherapy in patients with HER2-low cancer. For HER2-ultra-low cancer, the objective response rate was 61.8% with trastuzumab deruxtecan versus 26.3% with chemotherapy.

In terms of side effects and treatment duration, trastuzumab deruxtecan treatment lasted longer than chemotherapy (median of 11 months versus 5.6 months respectively), with fewer side effects. Serious side effects occurred in about 41% of patients on trastuzumab deruxtecan versus 31% on chemotherapy. Interstitial lung disease was noted in 11% of patients, consistent with previous research, leading to treatment discontinuation in about 5% of cases, and three deaths.

The study will continue to monitor the patients to evaluate overall survival outcomes and analyze additional secondary endpoints, including patient-reported outcomes; the authors will also undertake exploratory translational analyses to further understand the impact of these drugs.

The findings of this study have the potential to transform treatment options for metastatic breast cancer and offer new options for patients who have exhausted other endocrine and targeted therapy options.

Progression-free survival for patients with HER2-low cancer was

13.2 months

with trastuzumab deruxtecan versus

8.1 months

in patients who underwent chemotherapy

Belantamab Mafodotin: An Effective Addition to Multiple Myeloma Treatment

DISEASE progression and mortality rates are significantly reduced in patients with relapsed or refractory multiple myeloma when belantamab mandolin is incorporated into the treatment regimen, according to recent findings from the DREAMM-8 clinical trial.

The DREAMM-8 trial, presented at ASCO 2024, evaluated the efficacy of belantamab mafodotin combined with pomalidomide and dexamethasone (BPd), compared to the current standard regimen of pomalidomide, bortezomib, and dexamethasone (PVd). The study included 302 patients with relapsed or refractory multiple myeloma. After a median follow-up of 22 months, the trial demonstrated that the median progression-free survival (PFS) was not reached for patients treated with BPd, whereas it was 12.7 months for those on the PVd regimen. One year into the study, 71% of patients receiving BPd remained free of disease progression compared to 51% of those receiving PVd. The overall response rate was higher in the BPd group at 77% versus 72% in the PVd group, with 40% of BPd-treated patients achieving a complete or better response compared to 16% in the PVd group.

Both treatment groups experienced high rates of side effects, with over 99% of BPd recipients and 96% of PVd recipients reporting adverse effects. Eye-related side effects, including corneal changes and blurred vision, were notably more common in the BPd group (89%) than in the PVd group (30%). These side effects were generally manageable through dose adjustments or temporary discontinuation of belantamab mafodotin, allowing most patients to continue benefiting from the treatment.

> **The DREAMM-8 trial evaluated the efficacy of belantamab mafodotin combined with pomalidomide and dexamethasone**

The findings from the DREAMM-8 trial demonstrate that belantamab mafodotin, combined with pomalidomide and dexamethasone is more effective than the standard PVd regimen. Lead study author Suzanne Trudel, Princess Margaret Cancer Centre, Toronto, Canada, proposed that the addition of belantamab mafodotin should be a standard treatment option for patients with multiple myeloma at first relapse and for subsequent relapses. The researchers will continue to monitor participants to determine long-term outcomes, including overall survival and the duration of response in those treated with BPd. These findings could potentially lead to a new standard of care for relapsed or refractory multiple myeloma, offering hope for better management of the disease.

Addressing Chemotherapy Toxicity Disparities

RACIAL and ethnic differences in chemotherapy toxicity have been observed but are often understudied due to low minority enrolment in clinical trials.

Trials in the USA particularly lack Black participants, which concerns racial disparities in cancer outcomes. Black patients with breast cancer face higher mortality rates and more severe toxicity. This study presented at ASCO 2024 demonstrates the successful enrolment of females with African ancestry with early-stage breast cancer to evaluate a germline predictor of taxane-induced peripheral neuropathy, and compare toxicity between two taxane drugs in this population.

> **Black patients with breast cancer face higher mortality rates and more severe toxicity**

Research has shown that Black patients with breast cancer experience significantly more treatment-induced peripheral neuropathy (TIPN) than other races, with specific genetic differences influencing this risk. Higher rates of TIPN often lead to chemotherapy dose reductions and lower cure rates. To address this, the ECOG-ACRIN Cancer Research Group designed the EAZ171 trial to validate genetic predictors of neuropathy and determine the optimal taxane drug, focusing on side effects and potential dose reductions for Black patients with early-stage breast cancer. The trial's design and patient recruitment involved collaboration with Black patient advocates, including Indianapolis-based 'Pink-4-Ever – Ending Disparities'. A strong social media campaign, featuring Black females with breast cancer, was developed for recruitment. Many participants were enrolled through the National Cancer Institute's Community Oncology Research Program (NCORP), not just from academic settings.

In the study, 249 Black females with early-stage breast cancer were treated with either weekly paclitaxel or tri-weekly docetaxel. Of these, 121 received at least one dose of paclitaxel and 118 received docetaxel.

Black patients with breast cancer treated with docetaxel experienced less TIPN and fewer dose reductions compared to those on paclitaxel. Inherited gene alterations were more common in patients with TIPN, but this was not statistically significant. Physician-reported that Grade 2–4 neuropathy rates did not differ significantly between high- and low-risk gene alteration groups. However, Grade 2–4 neuropathy was significantly higher in patients on paclitaxel by both physician reports (44% versus 29%) and patient reports (40% versus 24%). Patients on paclitaxel required more dose reductions due to peripheral neuropathy (28% versus 9%) or any cause (39% versus 25%).

The researchers plan another trial to further optimize therapy for Black patients with breast cancer.

ADRIATIC Trial: Durvalumab as Consolidation Treatment

FINDINGS from the ADRIATIC trial were presented in a plenary session at ASCO 2024.

The median OS for the durvalumab group was **59.9 months** compared to **33.4 months** for the placebo group

The interim results were from a Phase III study exploring the efficacy of durvalumab as a consolidation treatment for patients with limited-stage small-cell lung cancer (LS-SCLC) who had not progressed following concurrent platinum-based chemoradiotherapy (cCRT).

The ADRIATIC trial was a randomized, double-blind, placebo-controlled study. It involved 730 patients who were eligible with a WHO performance status of 0 or 1 with Stage I–III LS-SCLC. The patients were randomized to receive either durvalumab (1,500 mg) plus placebo, durvalumab (1,500 mg) plus tremelimumab (75 mg), or placebo plus placebo every 4 weeks for four cycles. Maintenance doses of durvalumab or placebo were administered every 4 weeks until disease progression or intolerable toxicity, for a maximum of 24 months. Randomization was stratified by disease stage and whether patients had received prophylactic cranial irradiation.

The interim analysis showed statistically significant improvements in the dual primary endpoints, overall survival (OS) and progression-free survival (PFS), for patients treated with durvalumab compared to placebo.

The median OS for the durvalumab group was 55.9 months compared to 33.4 months for the placebo group (hazard ratio [HR]: 0.73; 95% CI: 0.57–0.93; P=0.0104). The 24-month OS rate was 68.0% for durvalumab versus 58.5% for placebo, and the 36-month OS rate was 56.5% versus 47.6%, respectively. The median PFS was 16.6 months for durvalumab compared to 9.2 months for placebo (HR: 0.76; 95% CI: 0.61–0.95; P=0.0161). The 18-month PFS rate was 48.8% for durvalumab versus 36.1% for placebo, and the 24-month PFS rate was 46.2% versus 34.2%.

Durvalumab was generally well tolerated. Grade 3/4 adverse events occurred in 24.3% of the durvalumab group versus 24.2% in the placebo group. Discontinuation due to adverse events was higher in the durvalumab arm (16.3% versus 10.6%), and the incidence of pneumonitis/radiation pneumonitis was also higher (38.0% versus 30.2%). The safety profile of durvalumab remained consistent with previous studies.

The ADRIATIC trial's interim results demonstrated the potential of durvalumab as a new standard of care for patients with LS-SCLC post-cCRT. Ongoing analysis of the durvalumab plus tremelimumab arm will shed more light on the role of combination immunotherapy in this setting, offering survival benefits to patients without introducing new safety concerns.