Studies Offer Improved Treatments for Diverse Set of Common and Rare Cancers

Research Presented at ASCO’s Annual Meeting Identifies New Targeted Drug for Most Common Breast Cancer Type; Illuminates New, Better Applications of Conventional Therapies for Other Patients

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CHICAGO – Results from five late-breaking studies released today at the American Society of Clinical Oncology’s (ASCO) 51st Annual Meeting provide important new treatment options for patients with common and rare cancers. They include new or refined therapies for melanoma, prostate and breast cancers, which are together diagnosed in more than 500,000 Americans annually. Another study reveals a long-awaited new treatment for patients with certain forms of sarcoma. These soft-tissue cancers account for 1% or less of all cancers diagnosed each year. [1]

“The diversity of these studies represents the vibrancy of cancer research today. We are learning smarter ways to use existing treatments, even as we uncover new drugs that target the biological features that make cancers tick,” said ASCO Expert Don S. Dizon, MD. “Today’s data show that increasing the aggressiveness of treatment with chemotherapy can make a big difference in prostate cancer. In contrast, scaling back surgery strategies for some melanoma patients can spare them from debilitating side effects, with little risk to their survival,” added Dr. Dizon.

Studies include:

- A federally funded phase III study finds the first effective adjuvant chemotherapy for men with localized, high-risk prostate cancer; adding docetaxel to standard therapy improved four-year survival.
- Large, phase III trial shows for the first time that extensive lymph node surgery does not improve survival for certain patients with melanoma, thus potentially reversing a long-time standard practice.
- A phase III trial shows longer overall survival of patients with advanced sarcoma treated with the chemotherapy agent eribulin compared to those treated with standard dacarbazine. This marks the first phase III trial to show an overall survival benefit for patients with this rare cancer of the muscle and fat tissue.
- In postmenopausal women with hormone receptor-positive DCIS, anastrazole offers slightly
higher cancer-free survival than tamoxifen, suggesting that it may represent an effective additional option for preventing new or recurrent breast cancer.

- In a phase III study stopped early due to efficacy, researchers report that adding the novel targeted drug palbociclib to standard hormonal therapy more than doubled progression free survival in women with previously treated, hormone receptor-positive, HER2-negative advanced breast cancer. This is the most common form of breast cancer.

Media Resources:

*Online Annual Meeting Media Resource Center*: Visit ASCO.org/AMMRC for press releases, the press briefing schedule, embargo policies, high-resolution photos, and the Virtual Press Room, an online repository of corporate and institutional press materials from third-party organizations.

*CancerProgress.Net*: ASCO’s interactive website chronicling the progress achieved in clinical cancer research, including an in-depth timeline that tracks major research milestones in 18 of the most common cancers.

*Cancer.Net*: ASCO’s cancer information website for patients, providing doctor-approved information on more than 120 cancer types.


FIRST EFFECTIVE ADJUVANT CHEMOTHERAPY FOR HIGH-RISK, LOCALIZED PROSTATE CANCER

ASCO Perspective

*ASCO Expert Charles J. Ryan, MD*

“Adjuvant chemotherapy has delivered major survival gains to people with several of the most common types of cancer, and now we’re finally seeing the same with prostate cancer. Here we have a powerful new use for a long-established therapy. It’s an advance that would not have been possible without federally funded clinical trials.”

A federally funded phase III study found that adding docetaxel chemotherapy to standard hormone and radiation therapy reduces the risk of death for men with high-risk, localized prostate cancer. At an average follow-up of 5.5 years, four-year overall survival rates were 89% in the standard therapy group vs. 93% in the docetaxel group.

According to the authors, as many as 33,000 men are diagnosed with high-risk, localized prostate cancer in the United States every year.

“This study is the first indication that chemotherapy has a role in the adjuvant treatment of localized prostate cancer, and we also expect to see an even bigger survival advantage over time,” said lead study author Howard Sandler, MD, a professor of radiation oncology at the Cedars-Sinai Medical
Center in Los Angeles, CA. “This finding could improve outcomes for thousands of men. At the same time, chemotherapy carries a modest increase in side effects, so it is important that physicians discuss the balance of benefits and risks with their patients.”

Adjuvant therapy is additional treatment that is given after patients complete the primary treatment for their tumor, such as surgery or radiation. The goal of adjuvant therapy is to lower the risk of recurrence and improve overall survival. Among the most common cancers — lung, breast, colorectal, and prostate — prostate cancer is the only disease without an established adjuvant chemotherapy regimen.

In the study, 562 men with high-risk, locally advanced prostate cancer were randomly assigned to treatment with standard therapy (radiation therapy plus two years of hormone therapy) or standard therapy followed with docetaxel chemotherapy. Docetaxel was given for 18 weeks, starting a month after radiation therapy.

After an average follow-up period of 5.5 years, 52 deaths occurred in the standard therapy group compared to only 36 deaths in the docetaxel group. The four-year overall survival rates were 89% in the standard therapy group compared to 93% in the docetaxel group. Docetaxel also reduced the risk of relapse — the five-year disease-free survival rates were 66% in the standard therapy group vs. 73% in the docetaxel group.

Patient follow-up will continue to determine the long-term benefit of adjuvant chemotherapy in this setting, and an analysis of quality of life data will be performed at a later time. Dr. Sandler noted that future studies will explore the impact of adjuvant therapies among men with high-risk, localized prostate cancer.

This study received funding from The National Institutes of Health, Sanofi, and AstraZeneca.

View the full abstract.

For Your Readers
• Guide to Prostate Cancer
• Chemotherapy

EXTENSIVE LYMPH NODE SURGERY MAY NOT BE NECESSARY FOR SOME PATIENTS WITH MELANOMA

ASCO Perspective

ASCO Expert Lynn Schuchter, MD, FASCO

“This is the first study to offer solid evidence that many patients with melanoma don’t need extensive lymph node surgery. The findings should reduce the use of an approach that we have long assumed to be optimal. This is great news for patients, who can forego extensive surgeries
A randomized study finds that surgical removal of the lymph nodes surrounding a melanoma tumor after a positive lymph node biopsy (melanoma found in node) does not improve survival. The study will likely change practice and conclude a long-standing debate about the role of this approach, called complete lymph node dissection (CLND). More importantly, the new knowledge gained from this study will help spare thousands of patients with melanoma from unnecessary surgery and its significant side effects.

Patients who have cancer detected in the sentinel lymph node upon biopsy are deemed to be at increased risk of melanoma recurrence and metastasis. Worldwide, it is recommended that such patients undergo CLND.

CLND is an extensive surgical procedure that involves removal of entire groups of lymph nodes. It carries the risk of debilitating side effects, including infection, nerve damage and lymphedema. According to the authors, lymphedema can occur in more than 20% of patients and persist long-term in 5-10% of patients.

“I think that our study is the beginning of the end of a general recommendation of complete lymph node dissection for patients with positive sentinel nodes,” said senior study author Claus Garbe, MD, a professor of dermatology at the University of Tübingen in Tübingen, Germany. “However, it is possible that this surgery may provide a smaller survival advantage than this study could detect. So, doctors may want to discuss this finding with their patients to help them decide whether this procedure is right for them.”

Following surgery to remove the primary tumor, 483 patients with stage III melanoma and a positive lymph node biopsy were randomly assigned to observation only or CLND. Patients in the observation group were closely monitored for signs of disease recurrence – they underwent a lymph node ultrasound exam every three months and CT/ MRI or PET scans every six months. Patients in the CLND group followed the same schedule of check-ups after CLND.

Patients had a median follow-up of 35 months. In the observation group, 14.6% of patients developed lymph node regional metastases (near the primary tumor), compared to 8.3% in the CLND group. However, the differences in three and five-year recurrence-free survival, distant metastases-free survival, and melanoma-specific survival were not statistically significant between the two groups. In this study, a survival difference of 10% or higher between the two treatment groups was considered statistically significant based on the study design.

Only patients with tiny, microscopic-size metastases (micrometastases) were included in this study. According to the authors, CLND will continue to be recommended for patients with larger,
clinically detectable metastases (macrometastases).

Another analysis of this study is planned in three years; however, Dr. Garbe stated it is unlikely that the overall findings of the study will change, because prior research has shown that the majority (roughly 80%) of melanoma recurrences happen in the first three years of initial diagnosis.

Another ongoing CLND randomized trial, MSLT-II, is much larger and designed to detect an even smaller (5%) difference in survival. However, the final results from MSLT-II are not expected until 2022.

This study received funding from German Cancer Aid.

View the full abstract.

For Your Readers
• Guide to Melanoma
• What is Cancer Surgery?
• Making Decisions About Cancer Treatment
• Buildup of Fluid or Lymphedema

ERIBULIN EXTENDS OVERALL SURVIVAL FOR PATIENTS WITH ADVANCED LIPOSARCOMA AND LEIOMYOSARCOMA

ASCO Perspective
ASCO Expert Gary K. Schwartz, MD
“In a disease that has been notoriously difficult to treat, even small steps forward are worthwhile. These findings also remind us that our work is far from finished. The survival gain seen with eribulin must be weighed against the burden of side effects patients experienced.”

Findings from a randomized phase III trial point to a promising new therapy for patients with advanced intermediate or high grade liposarcoma or leiomyosarcoma whose disease worsened after two or more lines of initial therapies. Patients treated with the chemotherapy drug eribulin had a two-month increase in median overall survival compared to those treated with the standard drug dacarbazine.

According to the authors, this is the first randomized phase III study to show an improvement in overall survival in patients with this aggressive family of diseases.

“Soft-tissue sarcomas are relatively rare and can be very difficult to treat. The efficacy of available drugs for initial therapy is very unsatisfactory, and patients whose disease progresses despite two or more lines of treatment have a very poor prognosis,” said lead study author Patrick Schöffski, MD,
MPH, Head of Department of General Medical Oncology, University Hospitals Leuven in Leuven, Belgium. “For a disease where such few treatment options exist, a two-month improvement in survival is significant. The more treatments our patients have access to, the better their chances of improving life expectancy.”

An estimated 12,000 people will be diagnosed with soft-tissue sarcoma in the United States this year.\(^1\) Soft-tissue sarcoma is a diverse family of rare diseases, and liposarcomas and leiomyosarcomas are among the more common types. Patients with advanced, metastatic soft-tissue sarcoma have poor outcomes, typically with survival of one year or less. There are currently few treatment options available, particularly at the point the disease worsens or further spreads to other parts of the body despite prior therapy.

In the study, 452 patients with advanced leiomyosarcoma or adipocytic sarcoma, which is also called liposarcoma, were randomly assigned to treatment with eribulin or dacarbazine until disease progression. Leiomyosarcoma (which starts in smooth muscle) and adipocytic sarcoma (which starts in fat tissue) are difficult-to-treat malignancies. All patients had cancers that had worsened upon receiving two or more prior treatments.

The median overall survival was 13.5 months in the eribulin group and 11.5 months in the dacarbazine group. The most common side effects associated with eribulin were low white blood cell counts, fatigue, nausea, hair loss, and constipation, and 8% of patients stopped treatment due to side effects.

Low platelet counts were more common in the dacarbazine group compared to the eribulin group. Grade 3 and 4 treatment-related side effects occurred more frequently with eribulin than dacarbazine.

Eribulin belongs to a class of anticancer drugs known as microtubule inhibitors, which block cell division. It was originally derived from a natural source — a sea sponge. The FDA approved eribulin for the treatment of advanced breast cancer in 2010.

Several additional analyses are ongoing, including quality of life analysis, subgroup analysis and biomarker tests. The results of those analyses will be reported at a later date.

This study received funding from Eisai Inc.


View the full abstract.

For Your Readers
ANASTRAZOLE OFFERS HIGHER BREAST CANCER-FREE SURVIVAL RATES THAN TAMOXIFEN FOLLOWING DCIS

ASCO Perspective

ASCO Expert Don S. Dizon, MD

“Women with DCIS already have several great treatment options, and now they have one more. Aromatase inhibitors offer important advantages, but patients and their doctors should still consider the full range of options, including tamoxifen or even foregoing adjuvant treatment, as every approach carries its own risks and benefits.”

A federally funded phase III trial suggests that postmenopausal women with ductal carcinoma in situ (DCIS) may have an additional option for breast cancer prevention. The study compared the standard five-year treatment of tamoxifen to five years of the aromatase inhibitor anastrazole in more than 3,000 DCIS survivors. The 10-year breast cancer-free survival rates were higher in the anastrazole group than in the tamoxifen group (93.5% vs. 89.2%).

“The good news is tamoxifen and anastrazole are both very effective, but it seems that women have better chances of staying well with anastrazole,” said lead study author Richard G. Margolese, MD, a professor of surgical oncology at The Jewish General Hospital, McGill University in Montreal, Canada. “Women should also consider differences in side effects when discussing treatment options with their doctors.”

Women with DCIS are at increased risk of developing invasive breast cancer, although breast cancer-related death is uncommon following DCIS treated with radiation and lumpectomy.

While both tamoxifen and aromatase inhibitors have been used to prevent recurrences of more advanced forms of breast cancer, this is the first study to compare the two treatments in women with DCIS. In the study, 3,104 postmenopausal patients with hormone receptor-positive DCIS were randomly assigned to daily tamoxifen or anastrazole, each given for five years. Prior to starting hormone therapy, all had undergone lumpectomy and radiation therapy.

After an average follow-up period of 8.6 years, 114 breast cancers were detected in the tamoxifen group compared to 84 in the anastrazole group. This included recurrences of DCIS as well as development of a new breast cancer (DCIS or invasive) in the same or other breast. The 10-year breast cancer-free rates were higher in the anastrazole group than in the tamoxifen group (93.5% vs. 89.2%), and this difference was statistically significant.
There were eight deaths due to breast cancer in the tamoxifen group and five in the anastrazole group. While the 10-year overall survival rates were comparable in the two groups (92.5% for anastrazole and 92.1% for tamoxifen), a subgroup analysis revealed that anastrazole may not be superior to tamoxifen in women older than 60 years.

Hormone receptor-positive breast cancer is dependent on estrogen for growth. Tamoxifen and anastrazole block the estrogen growth signal in different ways. While tamoxifen blocks the estrogen receptor (i.e., access of estrogen to the cancer cells), anastrazole suppresses the manufacturing of estrogen.

Generally, there were no significant differences in the toxicity profiles of these agents. The main side effect of anastrazole is hastening of osteoporosis, which increases the risk of bone fracture. Indeed, anastrazole resulted in a higher rate of bone fractures compared to tamoxifen, though the difference was not statistically significant. In addition, treatment with tamoxifen was associated with higher rates of uterine cancer, though the difference also did not reach statistical significance.

This study received funding from the National Institutes of Health.

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• Guide to Breast Cancer
• Coping With Fear of Recurrence

NOVEL TARGETED DRUG PALBOCICLIB SLOWS PROGRESSION OF HORMONE RECEPTOR-POSITIVE BREAST CANCER

ASCO Perspective

ASCO Expert Don S. Dizon, MD

“For women with advanced breast cancer, it’s remarkable to be able to stall disease progression and stave off the need for chemotherapy for months with a simple pill. In one of the most common forms of advanced breast cancer, palbociclib works in both older and younger women.”

The phase III registration study PALOMA-3 reports that adding the investigational targeted agent palbociclib to standard hormonal therapy (fulvestrant) more than doubled the duration of disease control, delaying disease progression by roughly five months in women with previously treated, hormone receptor-positive, human epidermal growth factor receptor 2 negative (HR+/HER2-) advanced breast cancer.
This trial was stopped early based on efficacy seen in the interim analysis.

Approximately 75% of all breast cancers are hormone receptor-positive (HR+), HER2 negative, and palbociclib in combination with hormonal therapy could become a very effective treatment option after initial hormonal therapy for women with HR+, HER2- advanced breast cancer.

“After initial hormonal therapy stops working in metastatic breast cancer, the next step is typically chemotherapy, which can be effective, but the side effects are often very difficult for women,” said lead study author Nicholas C. Turner, a consultant medical oncologist at The Royal Marsden and a team leader at The Institute of Cancer Research, London, United Kingdom. “This relatively easy-to-take new drug can substantially delay the point when women need to start chemotherapy, making this an exciting new approach for women.”

Palbociclib is a novel, first-in-class oral drug that blocks cyclin dependent kinases (CDKs) 4 and 6. Prior research has shown that CDK4 and CDK6 are among the key proteins that fuel the growth of hormone receptor-positive breast tumors. Strong preclinical evidence supports combining CDK4 and CDK6 inhibitors with hormonal therapy. Fulvestrant is one of the most active hormone therapies for patients with HR+/HER2- advanced breast cancer.

Women with HR+/HER2- breast cancer were randomly assigned to palbociclib with fulvestrant or placebo with fulvestrant. All patients had metastatic disease that had worsened or relapsed after initial hormonal therapy, and 21% were premenopausal. According to the authors, PALOMA-3 is one of the first registration targeted therapy–hormone therapy combination studies in advanced breast cancer to include younger, premenopausal women.

At the time of this interim analysis, the average time to disease progression was 9.2 months in the palbociclib arm compared to 3.8 months in the placebo arm. Comparable benefits were seen in pre- and postmenopausal women. Longer follow-up is needed to determine the effect of palbociclib on overall survival. Quality of life data were collected and will be reported at a later date.

The palbociclib combination was generally well tolerated, with only 2.6% of patients having to stop treatment due to side effects, the most common being blood count abnormalities. Despite frequent occurrences of low white blood cell counts, the rates of a serious complication known as febrile neutropenia were very low (0.6%), the same in both treatment groups.
Another study known as PALOMA-2 is exploring the efficacy of palbociclib as a therapy for advanced breast cancer not previously treated with hormonal therapy. Dr. Turner noted that researchers are also looking at the possibility of using this therapy in women with early-stage hormone receptor-positive breast cancer.

Earlier this year, the FDA granted palbociclib accelerated approval for use in combination with letrozole for women with advanced (metastatic) estrogen receptor positive (ER+), HER2- breast cancer who have not yet received hormonal therapy for their metastatic disease. The approval was granted based on results of a prior phase II study, PALOMA-1.

This study received funding from Pfizer.

1 PALbociclib: Ongoing trials in the Management of breast cAncer

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• Targeted Treatments
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View the disclosures for the 2015 ASCO Annual Meeting News Planning Team.

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