Breast Cancer: 2021 ASCO Annual Meeting Highlights for the Advanced Practitioner

Sheeba Cantanelli, MPAS, PA-C, of UT Southwestern Medical Center, Simmons Comprehensive Cancer Center, discusses results from studies evaluating adjuvant therapy with a PARP inhibitor in *BRCA*-mutated HER2-negative metastatic breast cancer; immunotherapy in the treatment of early-stage triple-negative breast cancer; adjuvant capecitabine after neoadjuvant chemotherapy in triple-negative breast cancer; the addition of palbociclib to fulvestrant in HR-positive, HER2-negative advanced breast cancer; and the impact of vitamin D levels on outcomes. Reporting is provided by *The ASCO Post*.

Abstract LBA1

OlympiA Trial: Adjuvant Olaparib Extends Disease-Free Survival in *BRCA*-Mutated Early Breast Cancer

By Alice Goodman

Visit https://meetinglibrary.asco.org/record/196707/abstract to read the full abstract and view author disclosures.

Adjuvant therapy with the PARP inhibitor olaparib for 1 year extended disease-free survival in patients with high-risk early-stage HER2-negative breast cancer with *BRCA1/2* germline (inherited) mutations, according to a prespecified interim analysis of the phase III OlympiA trial presented at the 2021 ASCO Annual Meeting.[1] These findings were presented by lead author Andrew Tutt, MB, PhD, MBChB, Director of Breast Cancer Bow at the Toby Robins Research Centre, Institute of Cancer Research Unit at Guy's Hospital, King's College, London.

At 24 months of follow-up, 85.9% of patients treated with adjuvant olaparib were alive and free of recurrent invasive cancer and new second cancer (ie, invasive disease–free survival) compared with 77.1% of placebo-treated patients. The estimated 3-year distant disease–free survival rate was 87.5% with olaparib vs 80.4% with placebo.

"The OlympiA study results—the first reporting the effect of a PARP inhibitor as adjuvant therapy on survival endpoints in early *BRCA1/2*-mutated breast cancer or any adjuvant setting—suggest a possible addition to the standard of care for patients with germline *BRCA1/2* mutation–associated early breast cancer who have levels of risk requiring neoadjuvant or adjuvant chemotherapy," stated Dr. Tutt.

"Patients who received adjuvant olaparib were more likely to be alive without cancer and avoid metastasis at 3 years of follow-up. These findings support adjuvant olaparib for 1 year after

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standard-of-care treatment in patients with high-risk BRCA-mutated disease," he added.

"These results are so important! This study demonstrates a significant reduction after 1 year of olaparib in invasive recurrences, second cancers, and distant events. Of note, these results support germline testing in increasing numbers of patients with breast cancer and may even open the door for more trials of PARP inhibitors in other *BRCA*-associated cancers as adjuvant therapy," said 2020–2021 ASCO President Lori J. Pierce, MD, FASTRO, FASCO, at a premeeting press conference where the findings were previewed.

BRCA mutations are associated with 5% to 10% of breast cancers. Newly diagnosed patients with breast cancers associated with these mutations may present with aggressive, high-risk disease. After completion of multimodality therapy, recurrence rates can be high, and additional effective adjuvant therapies are needed.

Olaparib is a PARP inhibitor that targets a DNA repair defect in these cancers. It is already approved for treatment of patients with germline *BRCA*-mutated HER2-negative breast cancer.

Study Details

The double-blind OlympiA trial included 1,836 patients with high-risk early breast cancer that was HER2-negative, and *BRCA1/2*-positive, including triple-negative and hormone receptor–positive breast cancers. Following surgery, radiation therapy, and chemotherapy if needed, patients were randomly assigned to receive either 1 year of adjuvant olaparib or placebo.

"We used stringent criteria for invasive disease–free survival and distant disease–free survival," Dr. Tutt explained. "At the planned interim analysis, these criteria were met for early reporting." The primary endpoint of invasive disease–free survival was defined as the time from randomization until the first occurrence of ipsilateral invasive breast tumor, locoregional invasive disease, distant recurrence, contralateral invasive breast cancer, second primary invasive cancer, or death from any cause.

Key Results and Toxicity

For the primary results, compared with placebo, adjuvant olaparib reduced the risk of invasive disease–free recurrence (ie, local recurrence, metastatic recurrence, other new cancers) by 42% compared with placebo ($P < .0001$). At 3 years, the rate of invasive disease–free survival was 85.9% with olaparib vs 77.1% with placebo, an absolute difference of 8.8%.

Compared with placebo, olaparib achieved a 43% reduction in distant disease–free survival (ie, risk of metastatic breast cancer [$P < .0001$]). The difference between treatment arms was 7.1% at 3 years.

Overall survival is still immature, but fewer deaths occurred in the olaparib arm. "At this early timepoint [median of 2.5 years], given a stringent test for statistical superiority, there is no significant difference between treatment arms," Dr. Tutt noted. The estimated 3-year overall survival rate was 92% for the olaparib-treated group and 88.3% for the placebo group. Follow-up for survival is ongoing.

The side effects were consistent with the safety profile of olaparib, and no new safety signals emerged during the trial. Olaparib did not increase the rate of serious adverse events, including hospitalization, leukemias, or other cancers. Adverse events of grade 3 or higher more common with olaparib included anemia, lower white blood cell count, and fatigue, but the rates were low.

Charles L. Shapiro, MD, Director of Translational Breast Cancer Research and Cancer Survivorship and Professor of Medicine, Mt. Sinai's Icahn School of Medicine, New York City, said that OlympiA will be "practice-changing" for adjuvant therapy for *BRCA1/2*-positive breast cancer. "If it is fast-tracked to the FDA, olaparib will be the new standard of care," he predicted. "Also, olaparib could be a reasonable choice in the prevention setting for *BRCA1/2*-positive patients."

Reference

1. Tutt A, Garber JE, Kaufman B, et al: OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer. 2021 ASCO Annual Meeting. Abstract LBA1. Presented June 6, 2021

The Advanced Practitioner Perspective

Sheeba Cantanelli, MPAS, PA-C
UT Southwestern Medical Center,
Simmons Comprehensive Cancer Center

The OlympiA trial is a phase III trial that evaluated the use of adjuvant olaparib (Lynparza) in patients with germline *BRCA* mutations and high-risk, early-stage triple-negative or hormone receptor–positive HER2-negative breast cancer. Patients who were eligible for the study had > pT2 or > pN1 disease prior to adjuvant anthracycline-cyclophosphamide and taxane (ACT) or had neoadjuvant ACT and did not have a pathologic complete response. The patients were randomized 1:1 to receive adjuvant olaparib 300 mg po twice daily vs. placebo for 1 year.

The results of the study demonstrated an increase in invasive disease-free survival (85.9% vs. 77.1%) and distant disease-free survival (87.5% vs. 80.4%) with olaparib vs. placebo at 3 years. Overall survival data are still maturing, but the estimated overall survival at 3 years is higher in the olaparib vs. placebo group (92% vs. 88.3%).

The results of this phase III trial are pivotal, as about 5% to 10% of breast cancers are associated with *BRCA* mutations, and breast cancers associated with these mutations typically have a higher risk of recurrence. It is also the first trial to report survival data with PARP inhibitors in the adjuvant treatment of breast cancer in this patient population. In addition, these data could potentially lead to clinical trials in the adjuvant setting of other *BRCA*-mutated cancers.

The data should prompt advanced practitioners to be diligent in obtaining genetic testing in breast cancer patients who meet criteria, as there are now known prognostic data and information on the adjuvant therapeutic benefits with PARP inhibitors in this patient group. It is also important for the advanced practitioner to be knowledgeable of the potential adverse effects of grade 3 or higher anemia, leukopenia, and fatigue that can be associated with PARP inhibitors.

Disclosure: Ms. Cantanelli has no conflicts of interest to disclose.

Abstract 506

Triple-Negative Breast Cancer: Improving Long-Term Outcomes With Durvalumab

By The ASCO Post Staff

Visit https://meetinglibrary.asco.org/record/196389/abstract to read the full abstract and view author disclosures.

Sibylle Loibl, MD, PhD, of the German Breast Group, discusses results from the phase III GeparNUEVO study, which investigated neoadjuvant durvalumab in addition to anthracycline/taxane-based neoadjuvant chemotherapy in patients with early triple-negative breast cancer. A summary of her interview with *The ASCO Post* follows.

The GeparNUEVO study presented at this year's ASCO meeting is a neoadjuvant trial in 174 patients with triple-negative breast cancer. It looked at the addition of durvalumab as part of the neoadjuvant therapy to nab-paclitaxel, followed by epirubicin/cyclophosphamide (EC). The primary endpoint of this trial was the pathologic complete response rate, which has already been published. Although we did not observe any increase in the pathological complete response rate, which was substantial, it was just 9% when durvalumab, a PD-L1 inhibitor was added to the chemotherapy compared with the placebo group, we are awaiting the long-term outcome.

Before we discuss the results, I want to highlight some specificities of this trial. The trial had a running phase where patients received one dose of durvalumab or placebo before they started chemotherapy, and they continued with the chemotherapy up to surgery and then were operated on. There was no additional treatment after surgery pre-planned, at the discretion of the investigators.

After 170 patients were enrolled, this running phase was stopped because the time between the histological confirmation to the start of the chemotherapy within the trial was in the median of 7 weeks, and it was felt to be too long. So we effectively had two cohorts—the cohort with the window and the cohort without the window.

When we initially looked at the pathologic complete response (pCR) data, we saw an about 20% difference in the pCR rate in the window cohort, so it looks like there was some priming and there was no difference in the non-window cohort. But this is hypothesis generating, and therefore we need to await long-term outcome data. Something else we saw was that generally in high-risk patients, the addition of durvalumab resulted in a higher pCR rate than with the placebo.

Study Findings

Now, we have a 43-month follow-up in the median, and we looked at invasive disease-free survival (iDFS), distant disease-free survival (DDFS), and the overall survival (OS) and observed that in all three time-to-event endpoints, there was significant improvement in iDFS, DDFS, and OS by the addition of durvalumab compared with the placebo arm, with a hazard ratio of 0.48 for the iDFS and even smaller hazard ratio in the other subgroups.

Of interest was when we looked at the subgroups of pCR patients and patients without pCR, where we normally see the main difference in long-term outcomes, then we saw that also the pCR patient benefited with the addition of durvalumab. I think these are extremely interesting data in the light of other checkpoint inhibitor data where they all continue with the checkpoint inhibitor after surgery, like we do in HER2+ breast cancer, but here we stopped at surgery and still saw this dramatic difference.

Safety was expected and published previously. There were no long-term safety issues captured. So, we hope that these data will be transferred to larger endeavors and that we have the chance to investigate whether we need checkpoint inhibitor therapy at all after surgery in our patients or if there is something else we can do for these patients.

The Advanced Practitioner Perspective

Sheeba Cantanelli, MPAS, PA-C
UT Southwestern Medical Center, Simmons Comprehensive Cancer Center

The GeparNuevo trial assessed the benefit of adding durvalumab (Imfinzi), an anti–PD-L1 checkpoint inhibitor, to neoadjuvant chemotherapy in early-stage (cT1b–cT4a-d) triple-negative breast cancer. Durvalumab or placebo was given as monotherapy for the first 2 weeks (window phase), and then continued every 4 weeks during neoadjuvant chemotherapy with nab-paclitaxel followed by epirubicin and cyclophosphamide. Durvalumab was not planned as adjuvant therapy in this trial. The window phase of the trial was eventually stopped due to a concern that it led to a prolonged time to start of chemotherapy. The study was designed to primarily assess pathologic complete response (pCR). The secondary endpoints of the study were invasive disease-free survival, distant disease-free survival, and overall survival.

Although the trial did not show a clinically significant increase in pCR in the durvalumab treatment arm as a whole, there was a small benefit in pCR in patients who received durvalumab alone prior to the start of chemotherapy. In addition, there were significant improvements in invasive disease-free survival, distant disease-free survival, and overall survival at 3 years in all of the durvalumab treatment arms (window phase and non-window phase cohorts).

Given the results, future clinical trials with a larger patient cohort with durvalumab in the neoadjuvant setting and continued in the adjuvant setting is a consideration. It is important for advanced practitioners to be aware of the emerging data of immunotherapy in the treatment of early-stage triple-negative breast cancer in order to inform patients and appropriately screen patients for future clinical trials in this context.

Disclosure: Ms. Cantanelli has no conflicts of interest to disclose.

Abstract 605

EA1131 Trial: Platinum Not Equal to Capecitabine for Residual Disease in Triple-Negative Breast Cancer

By Caroline Helwick

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In patients with triple-negative breast cancer who have residual disease after neoadjuvant chemotherapy, adjuvant capecitabine remains the standard of care. In the multicenter randomized noninferiority EA1131 trial, which included primarily basal tumors, noninferiority of adjuvant platinum over capecitabine could not be demonstrated, according to Ingrid A. Mayer, MD, MSCI, of Vanderbilt University, Nashville, who presented the findings at the 2021 ASCO Annual Meeting.[1]

"The available data show that platinum agents are unlikely to be noninferior or superior to capecitabine in improving invasive disease–free survival, regardless of intrinsic subtype," Dr. Mayer said. "The study definitely reinforces the role of capecitabine in this high-risk group."

Of note, the 3-year invasive disease–free survival rate was lower than expected, regardless of study treatment: 42% in the platinum arm and 49% in the capecitabine arm. In the CREATE-X trial, which established the value of adjuvant capecitabine for residual disease, the 5-year disease-free survival was 70% with capecitabine and 56% with observation.[2]

"The event rate was much higher than expected, as the patient population we selected was at the highest possible risk," Dr. Mayer explained. "Not only did 78% of participants have basal-like tumors—which have worse biologic behavior—but regarding residual disease, all patients had an RCB [residual cancer burden] score of 2 or 3. In CREATE-X, about 40% had an RCB score of 1."

It is important to evaluate novel approaches in such a high-risk population, she emphasized, because that is precisely the population most in need of better strategies. "We don't know how much capecitabine is helping that high-risk group because we don't have a real comparator. However, we don't know how to do anything better. Thus, for now, capecitabine remains the standard of care for these high-risk patients, although better strategies are definitely needed."

About EA1131

Patients with triple-negative breast cancer left with residual disease after neoadjuvant chemotherapy have a very high risk for recurrence that may be reduced by adjuvant capecitabine.[2] In the basal intrinsic subtype, preclinical models support the use of platinum agents.[3] EA1131 tested the hypothesis that, for this subtype of triple-negative disease, treatment with a platinum rather than capecitabine may improve the odds of not recurring, but it was not proven.

EA1131 enrolled 410 patients with clinical stage II or III triple-negative breast cancer with residual disease ≥ 1 cm in the surgical specimen (breast or nodes) after standard neoadjuvant chemotherapy. Using the PAM50 assay, the researchers found 78% of the patients had the basal subtype, and this subgroup constituted the primary analysis population. Most tumors were high grade, and approximately half the patients had lymph node involvement. Residual tumors were primarily ypT1 (approximately 37%) and ypT2 (44%).

The study initially assigned patients randomly to a platinum agent or observation, but the trial was soon amended to include capecitabine as the control arm, based on the CREATE-X results. Patients received carboplatin AUC 6 or cisplatin at 75 mg/m^2 every 3 weeks for four cycles or capecitabine (1,000 mg/m^2 BID on days 1–14) every 3 weeks for six cycles. Radiotherapy prior to or after treatment could be given at the provider's discretion and was required in some situations.

A noninferiority design (hazard ratio [HR] noninferiority margin of 1.154) with a superiority alternative (alternative HR of 0.754) was chosen, assuming a 4-year invasive disease–free survival of 67% for the capecitabine arm. Noninferiority was tested first. If noninferiority was shown, a formal test for superiority of the platinum compared with capecitabine would be conducted.

At the fifth interim analysis, the hazard ratio for platinum/capecitabine was 1.09 (95% repeated confidence interval [CI] = 0.62–1.90), and the

observed outcome in EA1131 was deemed "inconclusive." Therefore, the data safety and monitoring committee recommended stopping the trial in March 2021, since it was unlikely to show noninferiority or superiority of the platinum arm and the grade 3 and 4 toxicities were more common with platinum agents.

Noninferiority Not Proven

"For patients with triple-negative breast cancer and residual disease after preoperative taxane plus anthracycline chemotherapy, the results of EA1131 suggest there is no role for adjuvant platinum agents," Dr. Mayer reported.

After a median follow-up of 20 months, 120 invasive disease–free survival events had occurred among the basal subtype cohort, including 90 distant recurrences and 15 locoregional recurrences. Their 3-year invasive disease–free survival rates were 42% with adjuvant platinum (95% CI = 30%–53%) and 49% (95% CI = 39%–59%) with adjuvant capecitabine (HR for platinum vs capecitabine = 1.06 [95% repeated CI = 0.62–1.81]). By intrinsic subtype, the 3-year invasive disease–free survival was 46% (95% CI = 38.1%–53.2%) for the basal subtype and 55% (95% CI = 38.6%–69.5%) for the nonbasal subtype, Dr. Mayer reported.

For the basal subtype, recurrence-free survival at 3 years was 46% with platinum and 49% with capecitabine (Table 1), and overall survival was 58% and 66%, respectively, she added.

Overall toxicity rates were similar in both arms (82%), but there were more severe hematologic adverse events with platinum agents, including grade ≥ 3 anemia (7% vs 0%) and leukopenia (10% vs 3%). Overall grade ≥ 3 adverse events were observed in 25% vs 15%. No deaths related to treatment were reported.

The main reason for early platinum discontinuation was the occurrence of adverse events (n = 21), whereas most patients discontinued capecitabine early for disease progression (n = 22).

Adjuvant Platinum Remains Experimental

"The adjuvant use of platinum agents in addition to taxane/anthracycline chemotherapy after upfront surgery remains investigational, and adjuvant trials with survival as the primary endpoint are ongoing (NRG BR-003). Better strategies are needed," Dr. Mayer said.

The investigators are now performing correlative analyses of residual tissue; they are correlating surgical tissue profiling, circulating tumor cells, and cell-free DNA with recurrence-free survival and collecting patient-reported outcomes. "EA1131 provides a richly annotated biobank for discovery efforts," she added.

References

1. Mayer IA, Zhao F, Arteaga CL, et al: A randomized phase III post-operative trial of platinum-based chemotherapy versus capecitabine in patients with residual triple-negative breast cancer following neoadjuvant chemotherapy: ECOG-ACRIN EA1131. 2021 ASCO Annual Meeting. Abstract 605. Presented June 6, 2021.
2. Masuda N, Lee SJ, Ohtani S, et al: Adjuvant capecitabine for breast cancer after preoperative chemotherapy. *N Engl J Med* 376:2147-2159, 2017.
3. Lehmann BD, Bauer JA, Chen X, et al: Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. *J Clin Invest* 121:2750-2767, 2011.

TABLE 1: 3-Year Invasive Disease–Free Survival From EA1131 Trial

Intrinsic Subtype	Capecitabine	Platinum	Hazard Ratio (95% Confidence Interval)
Basal subtype	49%	42%	1.06 (0.62–1.81)
Nonbasal subtype	69%	46%	1.94 (0.69–5.45)

The Advanced Practitioner Perspective

Sheeba Cantanelli, MPAS, PA-C
UT Southwestern Medical Center
Simmons Comprehensive Cancer Center

Clinical trial EA1131 evaluated cisplatin in the adjuvant setting for patients with clinical stage II/III triple-negative breast cancer who had more than 1 cm residual disease in the surgical specimen after standard neoadjuvant chemotherapy. The trial was designed to evaluate for noninferiority and, if noted, then superiority of platinum chemotherapy in comparison to current standard of care, capecitabine, in this patient population. Patients received adjuvant carboplatin AUC 6 or cisplatin 75 mg/m^2 every 3 weeks for 4 cycles vs. capecitabine 1,000 mg/m^2 twice daily on days 1 to 14 every 3 weeks for 6 cycles.

The clinical trial was stopped as the data suggested treatment with adjuvant platinum therapy was unlikely to demonstrate noninferiority to capecitabine in this setting. In addition, grade 3 and 4 toxicities in the patients who received platinum were higher, with increased hematologic adverse effects, including anemia and leukopenia.

In patients with triple-negative breast cancer and clinically significant residual disease after standard neoadjuvant therapy, adjuvant capecitabine remains the standard of care. To maximize the potential benefit of adjuvant capecitabine, advanced practitioners should focus on patient compliance in taking this oral regimen as recommended and assess for side effects that may cause early discontinuation. In addition, advanced practitioners involved in the management of these patients need to continue to monitor for and encourage patient enrollment in clinical trials when available.

Disclosure: Ms. Cantanelli has no conflicts of interest to disclose.

Abstract 1000

Breast Cancer: Updated Analysis on Palbociclib Plus Fulvestrant

By The ASCO Post Staff

Visit https://meetinglibrary.asco.org/record/198379/abstract to read the full abstract and view author disclosures.

Massimo Cristofanilli, MD, of the Feinberg School of Medicine at Northwestern University, discusses updated overall survival data from the phase III PALOMA-3 trial of palbociclib plus fulvestrant in women with hormone receptor–positive, HER2-negative advanced breast cancer. A summary of his interview with *The ASCO Post* follows.

PALOMA-3 was a multicenter clinical trial enrolling patients who had been treated with prior endocrine therapy and also one line of chemotherapy. It randomized 2:1 the combination of palbociclib and fulvestrant or placebo and fulvestrant. The primary endpoint was progression-free survival, and the secondary endpoint was overall survival.

The first analysis of overall survival, prespecified per protocol at 44.8 months of follow-up, was already presented and published showing a superiority of palbociclib and fulvestrant (34.9 months vs. 28 months). At this ASCO meeting, we presented updated overall survival based on the follow-up of 73 months. The purpose of this study was to identify potential loss of benefit in patients treated with this combination.

Study Findings

We demonstrated that the benefit is maintained, as well as the difference in overall survival between the two groups, with a hazard ratio of 0.81. This trend was observed in most patient subgroups, except those in which patients were endocrine-resistant or had previous chemotherapy for advanced breast cancer.

We looked at the mutations detected as cell-free DNA in the plasma in the patients who consented to the study, and identified *ESR1*, *PIK3CA*, and *RB1* mutations as the most important for treatment resistance and endocrine resistance.

This study demonstrated that the combination of palbociclib and fulvestrant in patients who fail prior endocrine therapy is superior to single agent, and associated with improved PFS

and OS irrespective of endocrine resistant mutations or any treatment-resistant mutations that can be detected at time of study entry during the evaluation of cell-free DNA. This is a new standard of care continuing to show that this combination remains the most effective treatment we have for hormone receptor–positive metastatic breast cancer.

The Advanced Practitioner Perspective

Sheeba Cantanelli, MPAS, PA-C
UT Southwestern Medical Center, Simmons Comprehensive Cancer Center

The initial results of PALOMA-3, which reported progression-free survival and overall survival benefits of palbociclib (Ibrance) and fulvestrant in comparison to fulvestrant alone in women with hormone receptor–positive, HER2-negative advanced breast cancer, were practice changing. The patients were previously treated with endocrine therapy and one line of chemotherapy. The current update of the PALOMA-3 trial, based on a follow-up at 73 months, revealed ongoing overall survival benefit in most patient subgroups. The subgroups that did not have ongoing benefit were those previously treated with chemotherapy and those with endocrine-resistant disease. Endocrine resistance was associated with mutations in *ESR1*, *PIK3CA*, and *RB1* detected on cell-free DNA testing noted in the plasma of these patients.

This update indicates that the current standard-of-care treatment with palbociclib and fulvestrant in this population remains superior to single-agent endocrine therapy. It is also clinically important that there were no additional safety concerns reported with the update. Advanced practitioners providing care for this patient population should be thinking about next-generation sequencing, as it seems to be one of the most important predictors of endocrine resistance and duration of treatment response.

Disclosure: Ms. Cantanelli has no conflicts of interest to disclose.

Abstract 10510

Does Vitamin D Supplementation Improve Prognosis for Patients With Breast Cancer?

By The ASCO Post Staff

Visit https://meetinglibrary.asco.org/record/196871/abstract to read the full abstract and view author disclosures.

A research team has found that sufficient vitamin D levels at the time of diagnosis may be associated with improved outcomes among people with breast cancer. These findings were presented by Yao et al during the 2021 ASCO Annual Meeting (Abstract 10510).

These findings are based on Kaiser Permanente Northern California's Pathways Study—a large prospective study in patients with breast cancer that has been underway since 2006.

"Consistent with results from randomized trials and meta-analyses, our findings from this large, observational cohort of breast cancer survivors with long follow-up provide the strongest evidence to date for maintaining sufficient vitamin D levels in [patients with] breast cancer, particularly among Black women and patients with more advanced-stage disease," noted first study author Song Yao, MD, a molecular epidemiologist and Professor of Oncology in the Department of Cancer Prevention and Control at Roswell Park Comprehensive Cancer Center.

"These findings highlight not just the role of vitamin D in breast cancer prognosis, but also the contribution of and need for prospective studies in cancer survivors to complement clinical trials," added senior study author Lawrence Kushi, ScD, Director of Scientific Policy at the Kaiser Permanente Northern California Division of Research.

Measuring Levels of Vitamin D and Their Effects

The research team measured 25-hydroxyvitamin D (25[OH]D) levels from 3,995 women with breast cancer who were enrolled in the Pathways Study, using blood serum samples collected at the time of diagnosis. They examined potential determinants of 25(OH)D levels, including polygenic score. Vitamin D supplement intake, body

mass index (BMI), and race/ethnicity were the most influential factors on serum 25(OH)D levels, while genetic variants had only a limited impact, noted Dr. Yao.

The study categorized vitamin D levels based on clinical cutoffs: deficient (< 20 ng/mL), insufficient (20 to < 30 ng/mL), or sufficient (≥ 30 ng/mL). Dr. Yao and colleagues then evaluated these levels in relation to overall survival, breast cancer–specific survival, recurrence-free survival, and invasive disease–free survival after a median follow-up of 9.6 years. The researchers built Cox proportional hazards models adjusting for nonclinical, clinical, and treatment factors that were further stratified by stage, estrogen receptor status, and BMI.

"Having clinically sufficient vitamin D levels at the time of breast cancer diagnosis is associated with better outcomes," Dr. Yao stated. "While these results are consistent with our earlier analysis based on a subset of the study population, it's significant that we saw the same trends in this much larger, longer-term data set—suggesting an ongoing benefit for patients who maintain sufficient levels through and beyond breast cancer treatment."

The team also observed that associations were similar by estrogen receptor status and found that the association between vitamin D levels and breast cancer outcomes appeared to be stronger among study participants diagnosed at more advanced stages or with lower BMI. Black women had the lowest vitamin D levels, which might contribute to their generally poorer outcomes after breast cancer diagnosis.

"In the context of supportive data from recent randomized trials and meta-analyses, our findings support the use of daily vitamin D supplementation to maintain sufficient vitamin D levels after breast cancer diagnosis, particularly among Black women and patients diagnosed with later-stage disease," said senior author Christine Ambrosone, PhD, Co-Principal Investigator of the Pathways Study and Senior Vice President of Population Sciences and Chair of Cancer Prevention and Control at Roswell Park.

The Advanced Practitioner Perspective

Sheeba Cantanelli, MPAS, PA-C
UT Southwestern Medical Center,
Simmons Comprehensive Cancer Center

In this large observational study over a course of 9.6 years with a cohort of 3,995 breast cancer patients, serum vitamin D levels (25-hydroxyvitamin D) at initial diagnosis were measured and then monitored on an ongoing basis. Vitamin D levels of < 20 ng/mL were classified as deficient, 20 to 30 ng/mL were classified as insufficient, and > 30 ng/mL were classified as sufficient. The most important factors associated with vitamin D levels were vitamin D intake, body mass index (BMI), and race/ethnicity, with Black women found to have the lowest vitamin D levels. Vitamin D levels were then evaluated in relation to invasive disease-free survival, recurrence-free survival, breast cancer–specific survival, and overall survival.

The analysis showed patients with sufficient vitamin D levels at the time of breast cancer diagnosis had overall improved outcomes. The findings also suggested maintaining adequate vitamin D levels had a positive impact on the long-term outcomes in breast cancer patients, especially those with advanced stage breast cancer or with a lower body mass index.

The findings of this study should prompt advanced practitioners involved in providing health care to women within any specialty to assess and adequately manage vitamin D levels to improve outcomes. Monitoring and adequately treating vitamin D levels should be a routine part of survivorship care for breast cancer patients, with focused attention in those at a higher risk of vitamin D deficiency, including Black women, women with lower BMI, as well as those with advanced-stage breast cancer.

Disclosure: Ms. Cantanelli has no conflicts of interest to disclose.