Elevating Precision Medicine in Breast Cancer Care

Key Takeaways

- Sacituzumab govitecan efficacy in first-line metastatic TNBC appears biomarker-agnostic across TROP-2, BRCA, and HER2-0/low, reinforcing broad applicability in both PD-L1-ineligible and PD-L1-positive paradigms.
- PersevERA failed to show statistically significant PFS or tolerability improvements for giredestrant plus palbociclib versus letrozole plus palbociclib, limiting near-term justification for premium-priced oral SERDs first line.
- Palbociclib's diminished first-line role complicates translation of PersevERA results, increasing interest in oral SERD combinations with ribociclib or abemaciclib in ongoing trials.
- PALMARES-2 suggests selected patients with oligoprogression can continue endocrine therapy plus CDK4/6 inhibition with local-regional therapy, achieving notably longer post-progression PFS and OS versus switching systemic regimens.
- REDUSE supports denosumab 120 mg q12w after lead-in as non-inferior for skeletal-related event prevention, with reduced hypocalcemia and osteonecrosis of the jaw versus q4w dosing.

New breast cancer trial insights reshape metastatic care: sacituzumab benefits broadly, oral SERDs lag, denosumab every 12 weeks suffices.

Breast cancer is the most common cancer in women in the United States, accounting for approximately 30% of all new female cancers each year.[1] Treatments continue to evolve across various challenging subtypes—and with their evolution comes growing complexity. The deeper we dig into disease pathology, the more avenues for therapeutic intervention appear. With so many potential paths to take, the challenge is no longer finding options—it's knowing which one to choose, for which patient, and when.

"I think the biggest struggle we have in metastatic disease in breast cancer is we have an embarrassment of riches," said Allison Butts, PharmD, BCOP, Pharmacist Manager, Oncology, Breast Oncology, and Clinical Pharmacy Specialist, UK Markey Cancer Center in Kentucky. "We have so many treatments—and I think the sequencing is the big challenge that we all face."[2]

At the 2026 Oncology Pharmacists Connect meeting in Austin, Texas, pharmacy experts discussed the practice-changing, actionable takeaways behind key breast cancer clinical trial data presented at the 2026 American Society of Clinical Oncology Annual Meeting in Chicago, Illinois.

Guiding Treatment Decisions With Biomarker Testing

Both ASCENT-03 (NCT05382299) and ASCENT-04/KEYNOTE-D19 (NCT05382286) included a focused biomarker program examining TROP-2 expression—the target of sacituzumab govitecan (SG, Trodelvy; Gilead Sciences, Inc)—alongside tumor *BRCA* status and HER2 expression, specifically HER2-0 by IHC and HER2-low tumors. The intent was to determine whether specific subgroups derived more or less benefit from SG, or whether the agent should be considered broadly across the first-line metastatic triple-negative breast cancer (TNBC) population.[2]

"Anytime there's a first line setting treatment that comes out, I think it's important to kind of think back," said Butts. "Are there any biomarkers that could help us maybe determine who really benefits from this new therapy? Should we be using it across the board?"[2]

The findings pointed clearly toward broad use of SG in this population. Across both trials, benefit was observed regardless of TROP-2 expression level, *BRCA* mutation status, or HER2 category. No single biomarker subgroup emerged as uniquely driving the efficacy signal, nor was any subgroup excluded from benefit. In ASCENT-03, which enrolled PD-L1-ineligible patients without pembrolizumab, all evaluated subgroups favored SG over chemotherapy. ASCENT-04/KEYNOTE-D19, which added pembrolizumab (Keytruda; Merck) to both arms in PD-L1-positive patients, showed the same pattern across the same biomarker panel.[2]

These findings carry meaningful clinical implications. Rather than narrowing the indication to a biomarker-defined niche, the data support broad use of SG in first-line metastatic TNBC—spanning both PD-L1-ineligible and PD-L1-positive settings. Treatment decisions are therefore more likely to hinge on PD-L1 status for immunotherapy eligibility, patient fitness, tolerability, and logistical considerations than on TROP-2, *BRCA*, or HER2 testing as currently analyzed. That said, overall survival data remain immature, and the speakers noted that more refined predictive biomarkers may yet emerge as the field continues to investigate this space.[2]

Combining CDK4/6 Inhibitors and Oral SERDs

The arrival of oral selective estrogen receptor degraders (SERDs) has reshaped how clinicians think about endocrine therapy in hormone receptor-positive metastatic breast cancer. Paired with CDK4/6 inhibitors—already the backbone of first-line hormone receptor-positive (HR+) treatment—oral SERDs represent an attempt to build on that foundation with agents designed to more completely block estrogen receptor signaling. The persevERA trial (NCT04546009) tested that premise, investigating whether replacing a traditional aromatase inhibitor with an oral SERD could meaningfully advance outcomes in the first-line metastatic setting.[2]

The trial included patients with HR+ metastatic breast cancer who had not received prior oral SERD therapy and who were randomized to giredestrant (GIRE; Roche) plus palbociclib (Ibrance; Pfizer) or letrozole plus palbociclib, with progression-free survival (PFS) as the primary end point. Numerically, giredestrant showed improvements in both PFS and duration of response

compared to letrozole, but neither reached statistical significance. Overall survival data remain immature and showed no clear advantage for the giredestrant arm.[2]

A central critique was the trial's use of palbociclib, which is no longer the preferred CDK4/6 inhibitor in this setting—ribociclib (Kisqali; Novartis) and abemaciclib (Verzenio; Eli Lilly and Company) have since accumulated stronger evidence and largely supplanted it in clinical practice. That context makes the results difficult to act on, since the combination being tested does not reflect how most clinicians are treating first-line HR+ metastatic disease today.[2]

Compounding that concern, oral SERDs were in part hoped to reduce the musculoskeletal and vasomotor toxicities associated with aromatase inhibitors—arthralgias, hot flashes, and the like—but persevERA trial did not clearly deliver on that either. For panelists weighing a premium-priced oral SERD against a well-established aromatase inhibitor, a numerically but not statistically significant PFS improvement with similar tolerability is a difficult case to make.[2]

From a practical standpoint, the current data do not compel a switch from letrozole in the first-line setting, and payer scrutiny around the oral SERD class—with 2 PDUFA dates in 2026 for giredestrant on the horizon—is expected to intensify. The more meaningful question may be where giredestrant and other oral SERDs ultimately land in later lines of therapy and how they perform when paired with ribociclib or abemaciclib, trials for which are already underway. persevERA trial opens the door, but the data as they stand suggest the field is still waiting for the combination and the context that will make oral SERDs a clear first-line choice.[2]

Navigating Treatment Continuation Decisions

One of the most common dilemmas in managing HR+ metastatic breast cancer is what to do when a patient on first-line endocrine therapy and a CDK4/6 inhibitor shows signs of progression. The instinct is often to switch—but the PALMARES-2 trial (NCT06805812) challenges that reflex with real-world data suggesting that, for the right patient, staying the course may be the more effective decision.[2]

The analysis drew from over 2400 patients who experienced disease progression on first-line endocrine therapy plus a CDK4/6 inhibitor. Approximately 18% were kept on that same regimen, with the majority receiving concurrent local-regional treatment—most commonly radiation—to address the site of progression. Critically, this strategy was not applied to patients with diffuse, widespread disease but to those with a mixed response picture: bone-only or oligoprogression, with the remainder of disease still controlled.[2]

The outcomes were striking. Real-world progression-free survival after documented progression exceeded 10 months, and overall survival reached over 71 months in patients who continued first-line therapy compared to approximately 44 months in those who switched. Patients with high ER/PR expression, low Ki-67, good performance status, and disease amenable to focal intervention derived the greatest benefit.[2]

For clinicians already making this call intuitively, PALMARES-2 provides the evidence to support it. The data do not endorse a blanket continuation strategy, and questions remain around treatment gaps and timing. But for patients with favorable biology and focal progression, the case for continuing first-line therapy—and investing in the local-regional infrastructure to make it feasible—is now well-supported.[2]

Determining Denosumab Dosing Intervals

For patients with HR+ metastatic breast cancer, bone metastases and skeletal-related events represent a significant source of morbidity—and the agents used to prevent them carry their own toxicity burden. The SAKK 96/12 REDUSE trial (NCT02051218) addressed the question: does denosumab need to be given every 4 weeks, or can the interval be safely extended?[2]

REDUSE enrolled patients with at least 3 bone metastases, randomizing them to standard denosumab 120 mg every 4 weeks or 4 monthly lead-in doses followed by every 12-week dosing. Extended-interval dosing was non-inferior for SRE prevention and came with a cleaner safety profile—lower rates of both hypocalcemia and osteonecrosis of the jaw. A formal health-economic analysis is pending, but with similar efficacy and fewer adverse events, the cost-effectiveness case for quarterly dosing is expected to follow.[2]

“The financial analysis is ongoing, but if I were a betting gal, I would say it's probably going to be favorable to do every 12-week dosing instead, knowing that the outcomes are similar,” explained Kelly Romo, PharmD, BCOP, manager of Oncology Medical Drug Management and Customer Initiatives at Blue Cross Blue Shield of Michigan.[2]

The data presented across this session reflect a field grappling productively with complexity—not just in terms of what works, but also who benefits, when to act, and how to make evidence-driven decisions sustainable in practice. From sequencing oral SERDs with CDK4/6 inhibitors, to rethinking progression as a signal to pause rather than pivot, to optimizing bone-health regimens long governed by habit, the throughline is consistent: precision in breast cancer care now extends beyond the molecular to the operational, the financial, and the deeply individual. The session closed not with definitive answers but with a sharper set of questions—and in a disease this complex, that may be the most honest measure of progress.

REFERENCES

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