8.8 months, 14 patients had responded, and nine more had SD.

The median duration of response was not reached at the time of data cutoff, and responses were ongoing for 13 of 15 patients, which Krop called "highly encouraging."

Although 98% of patients experienced treatment-emergent adverse events (TEAE), about half were grade 1 or 2. The most common TEAEs were nausea and stomatitis, predominantly grade 1 or 2.

Lisa Carey, MD, of the University of North Carolina Lineberger Comprehensive Cancer Center in Chapel Hill, noted that the number of patients in the trial was small and just "an early look at activity," but she deemed the study findings "very compelling."

As with the phase III ASCENT trial of sacituzumab govitecan, patients enrolled in the trial were not tested for TROP2 expression because it is expressed across all breast cancer subtypes. Also, because this was the first trial of Dato-DXd, researchers didn't know the minimum level of TROP2 expression likely to generate responses. "It was felt prudent to allow an unselected group of patients on this initial study, and then retrospectively assess if there was a clear relationship between level of TROP2 expression and effectiveness," Krop explained.

That's data that Sherene Loi, MBBS, PhD, of Peter MacCallum Cancer Centre in Melbourne, Australia, would like to see. "It is always better to have a good predictive biomarker, especially given [that] other ADCs are [or] will be available in the near future, and the side effect profile may not be tolerable for some patients," she said.

"These promising results warrant further investigation ... in phase III clinical trials," said Leisha Emens, MD, PhD, of the University of Pittsburgh Hillman Cancer Center in Pennsylvania. To that end, researchers are planning a phase III trial in TNBC. In the meantime, they have launched BEGONIA, an ongoing trial in TNBC to evaluate the efficacy and safety of Dato-DXd plus durvalumab (Imfinzi; AstraZeneca), and TROPION-Breast01, a phase III trial in HR-positive/HER2-negative breast cancer. *–Suzanne Rose* ■

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Novel SERD Has PFS Edge against Breast Cancer

For patients with advanced or metastatic ER-positive/HER2-negative breast cancer who experience disease progression after treatment with endocrine therapy and a CDK4/6 inhibitor, the investigational oral selective estrogen receptor degrader (SERD) elacestrant could offer some benefit. In the phase III EMERALD trial, the novel drug provided a brief but statistically significant improvement in progression-free survival (PFS) compared with standard endocrine monotherapy. However, some experts have wondered about the drug's value.

Results of the trial were presented at the 2021 San Antonio Breast Cancer Symposium in Texas, December 7–10.

Investigators enrolled 470 postmenopausal women and seven men with metastatic ER-negative/HER2-positive breast cancer whose disease recurred after one or two endocrine therapies, one of which was given with a CDK4/6 inhibitor. Patients could have had one prior line of chemotherapy.

Participants were randomly assigned to receive elacestrant or investigators' choice of fulvestrant or an aromatase inhibitor (AI). In all, 70% of patients in the standard-of-care arm received fulvestrant because they had initially had an AI plus a CDK4/6 inhibitor.

In the intention-to-treat population, the median PFS was 2.8 months for patients treated with elacestrant compared with 1.9 months for patients treated with standard care, a 30% improvement, reported Aditya Bardia, MD, MPH, of Massachusetts General Cancer Center in Boston.

Of note, the PFS with elacestrant was higher among the 228 patients with tumors harboring an *ESR1* mutation, which can cause resistance to endocrine therapy. For them, elacestrant yielded a median PFS of 3.8 months, compared with 1.9 months for those who received standard care—a 45% improvement in the risk of disease progression or death.

"Elacestrant is the first oral SERD that has demonstrated an improvement in clinical outcome as compared to standard-of-care endocrine therapy in a phase III clinical trial for patients with ER-positive, HER2-negative metastatic breast cancer," Bardia said.

Patients generally tolerated elacestrant well, with nausea and vomiting being the most common adverse events. Treatment discontinuation due to adverse events occurred in just 6.3% of patients taking elacestrant and 4.4% assigned to standard of care.

Overall survival data aren't mature, but an interim analysis shows a trend in favor of elacestrant, Bardia said.

Despite the PFS improvements, some oncologists were disappointed by the relatively small benefit.

"An early and rapid drop-off in the progression-free survival occurs at the first restaging, reflecting that many of these patients have endocrine-resistant disease," commented discussant David Cescon, MD, PhD, of Princess Margaret Cancer Centre in Toronto, Ontario, Canada.

"So how do we move from EMERALD to everyday management of ER-positive disease? Again, [it's] important to emphasize that in the post-CDK4/6 inhibitor–resistant setting, a majority of patients do very poorly with endocrine monotherapy, and thus identifying that group and identifying alternative strategies is critical," Cescon said.

"Please look at the absolute results, not just to hazard ratio," said presentation attendee Fatma Cardoso, MD, of Champalimaud Clinical Center in Lisbon, Portugal. "Is this really a positive trial? ... For many patients, fulvestrant had been previously used, which means that there was at least partial resistance to this drug."

Hope Rugo, MD, from the University of California, San Francisco, questioned whether the cost of elacestrant was worth the modest difference in PFS.

Bardia acknowledged that if elacestrant is approved, it would likely be more expensive than generic fulvestrant, but he suggested that the overall 12-month PFS rate of 22.3% for elacestrant, compared with 9.4% for standard care, might tip the scales in the SERD's favor. *–Neil Osterweil* ■

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Tumor Profiling Improves Breast Cancer PFS

Genomic profiling of tumors can improve progression-free survival (PFS)