A phase 3, randomized study of adjuvant sacituzumab tirumotecan plus pembrolizumab vs treatment of physician's choice in participants with triple-negative breast cancer who received neoadjuvant therapy and did not achieve a pathologic complete response at surgery.

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Background: Trophoblast cell surface antigen 2 (TROP2) expression is higher in triple-negative breast cancer (TNBC) vs other breast cancer subtypes, and high expression is associated with poor prognosis. Sacituzumab tirumotecan (sac-TMT; also known as MK-2870/SKB264) is a novel antibody-drug conjugate composed of anti-TROP2 antibody coupled to a cytotoxic belotecan derivative via a novel linker (average drug/antibody ratio, 7.4). In a prior phase 3 study (OptiTROP-Breast01), sac-TMT alone improved PFS (HR, 0.31; 95% CI, 0.22-0.45; $P < 0.00001$) and OS (HR, 0.53; 95% CI, 0.36-0.78; $P = 0.0005$) vs chemotherapy in participants with heavily pretreated advanced TNBC. The current standard of care (SOC) for patients with newly diagnosed, high-risk, early-stage TNBC is neoadjuvant pembrolizumab + chemotherapy followed by adjuvant pembrolizumab after surgery. Patients who do not achieve a pathologic complete response (pCR) with the current SOC have higher rates of recurrence and mortality vs patients who achieve pCR. This study (NCT06393374) evaluates adjuvant sac-TMT + pembrolizumab vs treatment of physician's choice (TPC; pembrolizumab ± capecitabine) in participants with TNBC who received neoadjuvant therapy and did not achieve pCR at surgery.
Methods: This phase 3, multicenter, open-label study is enrolling participants ≥18 years old with centrally confirmed TNBC per most recent American Society of Clinical Oncology/College of American Pathologists guidelines. Participants have non-pCR after ≥5 cycles of neoadjuvant pembrolizumab + chemotherapy, including ≥1 cycle of anthracycline-based neoadjuvant therapy. Participants must provide tissue from the surgical specimen for central TROP2 assessment and be able to continue on adjuvant pembrolizumab. Randomization must be conducted ≤12 weeks from surgical resection (window may be extended in consult with sponsor). Participants are randomized 1:1 to pembrolizumab 400 mg Q6W for 5 doses + sac-TMT 4 mg/kg Q2W for 12 doses or TPC with pembrolizumab 400 mg Q6W for 5 doses ± capecitabine 1000-1250 mg/m^2 BID on days 1-14 and days 22-35 every 42 days for 4 cycles until completion of therapy or disease recurrence, unacceptable toxicity, or withdrawal. Randomization is stratified by residual tumor and lymph node status, TROP2 expression, and intention to use capecitabine. Primary endpoint is invasive disease-free survival. Secondary endpoints are OS, distant recurrence-free survival, patient-reported outcomes, and safety. Enrollment began Q2 2024. Clinical trial information: NCT06393374. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.