

The efficacy and safety of eutideron, etoposide, and bevacizumab in patients with brain metastases from breast cancer.

Bishal Tiwari, Yehui Shi, Roshan Afshan; Nassau University Medical Center, East Meadow, NY; Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; Detroit Medical Center, Wayne State University, Detroit, MI

Background: Brain metastases (BM) from breast cancer (BC) are a significant therapeutic challenge, with limited systemic treatment options capable of crossing the blood-brain barrier (BBB). Median overall survival (OS) ranges from 4 to 16 months, influenced by molecular subtype and treatment modality. Triple-negative and HER2-positive subtypes are associated with higher BM incidence. There is a crucial need to explore systemic therapies that address both intracranial and extracranial disease. Eutideron, a novel small-molecule inhibitor with robust CNS penetration, has demonstrated activity against metastatic BC models involving the brain. Early clinical studies suggest its efficacy in advanced BC, with intracranial activity and manageable toxicity. Combining eutideron with etoposide, a cytotoxic agent, and bevacizumab, an anti-VEGF monoclonal antibody, may enhance therapeutic outcomes. Bevacizumab, known for reducing BM-associated edema and improving quality of life, has shown promise in combination regimens but has not been evaluated alongside eutideron and etoposide. This Phase II trial investigates this novel three-drug regimen in patients with recurrent BC and measurable BM. **Methods:** This open-label, single-arm Phase II trial evaluates the efficacy and safety of eutideron, etoposide, and bevacizumab in female patients aged ≥ 18 years with recurrent metastatic BC and measurable BM. Eligible patients had an ECOG performance status of 0–2, life expectancy ≥ 12 weeks, and progressed untreated or previously treated BM not requiring immediate local treatment. Baseline brain MRIs confirmed at least one measurable CNS lesion per RANO-BM criteria. The treatment regimen includes eutideron (30 mg/m²/day, IV, Days 1–5 of a 21-day cycle), etoposide (30 mg/m²/day, IV, Days 1–3 of a 21-day cycle), and bevacizumab (10 mg/kg, IV, Days 1 and 21 of each cycle). After 4–6 cycles, responders continued bevacizumab maintenance until progression or intolerable toxicity. Primary endpoint: CNS Objective Response Rate (CNS-ORR) per RANO-BM. Secondary endpoints: CNS Clinical Benefit Rate, CNS Progression-Free Survival, Overall Survival, and systemic ORR by RECIST 1.1. Safety was monitored using CTCAE v5.0. The trial, targeting 43 patients across Chinese centers, aims to inform future strategies for BC patients with BM. Clinical trial information: NCT05781633. Research Sponsor: None.