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960 – TROFUSE-032: a phase 3, randomized study of pembrolizumab plus sacituzumab tirumotecan or chemotherapy followed by pembrolizumab plus chemotherapy for early-stage triple-negative breast cancer or hr+/her2– breast cancer

Ruffo Freitas-Junior¹, Peter Schmid¹, Jing Wei¹, Francisco Beca¹, Usha Malhotra¹, Nadia Harbeck¹

¹Universidade Federal de Goiás, Hospital das Clínicas – Goiânia (GO) - Brazil

Introduction: Trophoblast cell surface antigen 2 (TROP2) is highly expressed in triple-negative breast cancer (TNBC) and is associated with poor prognosis. Current standard of care for high-risk, early-stage TNBC is neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab after surgery. The same approach may be used for hormone receptor-low-positive (HR-low+)/human epidermal growth factor receptor 2-negative (HER2–) breast cancer. Patients with TNBC or HR-low+/HER2– breast cancer without a pathologic complete response (pCR) after neoadjuvant therapy have higher risks of recurrence and mortality. Sacituzumab tirumotecan (sac-TMT), a TROP2-directed antibody-drug conjugate with a unique, bifunctional linker that maximizes payload delivery to tumor cells, demonstrated significant progression-free survival and overall survival benefits compared with chemotherapy in metastatic TNBC. TroFuse-032 (NCT06966700) evaluates the efficacy and safety of neoadjuvant pembrolizumab plus sac-TMT or chemotherapy followed by pembrolizumab plus chemotherapy in early-stage TNBC or HR-low+/HER2– breast cancer.

Methods: This phase 3, randomized, open-label study is enrolling participants aged ≥18 years with centrally confirmed untreated, high-risk, early-stage TNBC or HR-low+/HER2– breast cancer per ASCO/CAP guidelines. Participants are randomized 1:1 to neoadjuvant pembrolizumab 200 mg Q3W plus sac-TMT 4 mg/kg Q2W followed by pembrolizumab 200 mg Q3W plus paclitaxel plus carboplatin (arm 1) *versus* pembrolizumab 200 mg Q3W plus paclitaxel plus carboplatin followed by pembrolizumab 200 mg Q3W plus doxorubicin or epirubicin plus cyclophosphamide (arm 2). Surgery is performed 3–6 weeks after the last dose of neoadjuvant treatment. Adjuvant therapy is initiated ≤60 days after surgery, consisting of pembrolizumab 200 mg Q3W or 400 mg Q6W alone (participants with pCR) or with optional treatment at the physician's discretion (participants with residual disease). Primary endpoints are pCR (ypT0/Tis ypN0) at surgery and event-free survival. Secondary endpoints include overall survival, pCR-no DCIS (ypT0 ypN0), distant progression-free or distant recurrence-free survival, patient-reported outcomes, and safety. Enrollment is planned across 352 sites in 41 countries.

Ethics: Research Ethics Committee of Araújo Jorge Cancer Hospital, Association for Cancer Control in Goiás (ACCG; Approval No. 7.838.063; September 15, 2025).

Registry: ClinicalTrials.gov (NCT06966700); European Union Clinical Trials Information System (EU CT) 2024-520190-12.

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Keywords: triple negative breast neoplasms; breast neoplasms; clinical trial; phase III; pembrolizumab.