

PRESENTATION: ORAL PRESENTATION (GENERAL SESSION)

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938 – TROFUSE-011: a phase 3, randomized, open-label study of sacituzumab tirumotecan with or without pembrolizumab versus treatment of the physician's choice for previously untreated, locally recurrent, unresectable, or metastatic triple-negative breast cancer with PD-L1 CPS<10

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Introduction: The standard first-line therapy for most previously untreated, locally recurrent, unresectable, or metastatic triple-negative breast cancer (TNBC) with programmed death-ligand 1 (PD-L1) combined positive score (CPS)<10 is chemotherapy alone. New therapeutic options with superior efficacy are needed. Sacituzumab tirumotecan (sac-TMT) is a trophoblast cell surface antigen 2 (TROP-2)-directed antibody-drug conjugate with a unique, bifunctional linker that maximizes delivery of a belotecan-derived topoisomerase I inhibitor payload to tumor cells. Sac-TMT monotherapy has shown promising efficacy with a manageable safety profile in metastatic TNBC. There is a strong biologic rationale supporting the combination of an antibody-drug conjugate with pembrolizumab regardless of PD-L1 expression.

Objective: The TroFuse-011 study (NCT06841354) evaluates sac-TMT with or without ($\pm$) pembrolizumab *versus* treatment of the physician's choice (TPC) in participants with previously untreated locally recurrent unresectable or metastatic TNBC with PD-L1 CPS<10.

Methods: Eligible participants (≥ 18 years) with centrally confirmed locally recurrent unresectable or metastatic TNBC, measurable disease per RECIST v1.1, ECOG performance status 0 or 1, and a tumor tissue sample evaluable for central PD-L1 and TROP-2 testing were randomized 2:1:2 to receive sac-TMT 4 mg/kg Q2W (Arm A), sac-TMT 4 mg/kg Q2W + pembrolizumab 400 mg Q6W (Arm B), or TPC (Arm C). TPC consists of one of the following: paclitaxel, nab-paclitaxel, or gemcitabine plus carboplatin. Primary endpoints are progression-free survival per RECIST v1.1 as assessed by blinded independent central review (Arm A *vs.* C and Arm B *vs.* C) and overall survival (Arm A *vs.* C). Secondary endpoints are progression-free survival (Arm B *vs.* A), overall survival (Arm B *vs.* C and Arm B *vs.* A), objective response rate (Arm A *vs.* C and Arm B *vs.* C), duration of response, patient-reported outcomes, and safety. Tumor imaging is performed at baseline, every eight weeks after randomization until week 48, and every 12 weeks thereafter.

Results: Enrollment is ongoing across 254 sites in 33 countries.

Conclusion: Not applicable.

Registry: ClinicalTrials.gov, NCT06841354; European Union Clinical Trials Information System (EU CT) 2024-516834-36

Previous Publications: <https://doi.org/10.1158/1557-3265.SABCS25-PS5-08-18>; [https://www.annalsofoncology.org/article/S0923-7534\(25\)01964-7/fulltext](https://www.annalsofoncology.org/article/S0923-7534(25)01964-7/fulltext)

Keywords: clinical trial phase III; randomized controlled trial; pembrolizumab; triple-negative breast cancers.