

Trial in progress: ENCORE—Multicenter prospective registry of sequential antibody drug conjugates (ADCs) in HER2 negative metastatic breast cancer (MBC) (TBCRC-067).

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Background: Antibody–drug conjugates (ADCs) have demonstrated substantial improvement in progression free survival (PFS) and overall survival (OS) in phase III clinical trials in patients with metastatic triple negative breast cancer (mTNBC) and hormone receptor positive/HER2–negative (HR+/HER2–) metastatic breast cancer (MBC), offering an effective new treatment strategy. Several outstanding questions impact the use of these drugs clinically, and prospective real–world data is needed. First, it is important to understand the safety and efficacy of these agents in a real–world population with diverse patient characteristics. Second, it is critical to understand the safety and efficacy of these ADCs in sequence. Third, it is essential to identify biomarkers that can help clarify mechanisms of response and resistance to ADCs, which may inform future sequencing and treatment strategies. **Methods:** This is a multicenter prospective registry study of patients with HER2–negative MBC who are treated with sequential ADCs per standard of care (SOC) with the goal to understand the safety and efficacy of sequential ADCs in a real–world setting (NCT06774027). A total of 100 participants with HER2–negative MBC will be enrolled in this study, either prior to starting their first ADC per SOC (cohort 1 = HR+/HER2–; cohort 2 = mTNBC) or prior to starting their second ADC per SOC (cohort 3 = HR+/HER2–; cohort 4 = mTNBC). The dual primary endpoints are real–world progression free survival (rwPFS) of ADC1 and rwPFS of ADC2. Secondary endpoints include overall response rate (ORR), duration of response (DOR), best overall response (BOR), disease control rate (DCR), and real–world overall survival (rwOS), and safety for each ADC. Exploratory endpoints include translational correlates of response/resistance to ADCs (e.g., circulating tumor DNA, circulating tumor cells, and tissue spatial correlates) and patient–reported outcomes (PROs). rwPFS and rwOS will be estimated by the Kaplan–Meier method. Statistics will be descriptive. Enrollment to start in the first quarter of 2025. Clinical trial information: NCT06774027. Research Sponsor: Gilead.