A phase 2 trial of loperamide and granulocyte colony-stimulating factors to improve sacituzumab govitecan tolerability in patients with unresectable locally advanced or metastatic triple-negative breast cancer: PRIMED

BACKGROUND

• Sacituzumab govitecan (SG) is an antibody-drug conjugate that targets Trop-2 to deliver SN-38 (the active metabolite of irinotecan, a topoisomerase I inhibitor) to malignant cells [1].
• SG has demonstrated a benefit in terms of progression-free survival and overall survival in patients with refractory triple-negative and hormone receptor (HR) positive/human epidermal growth factor receptor 2 (HER2) negative advanced breast cancers in comparison with single agent chemotherapy [2,3].
• The most common adverse events related to SG administration include neutropenia and diarrhea, which when severe required treatment delay, toxicity, suppression, or discontinuation [1-3].
• Loperamide and granulocyte colony-stimulating factors (G-CSF) are commonly used to treat and prevent drug-associated diarrhea and neutropenia in cancer patients, respectively [4,7].
• PRIMED hypothesizes that prophylactic administration of loperamide (for diarrhea) and G-CSF (for neutropenia) can help mitigate these undesirable effects related to SG treatment and therefore reduce dose reductions or discontinuations.

STUDY DESIGN

Primary Endpoints
• Co-primary endpoints are incidence of grade ≥2 diarrhea and grade ≥3 neutropenia per NCI-CTCAE v.5.0 at cycle 2.
• Secondary endpoints: Tolerability and safety per NCI-CTCAE v.5.0 at cycle 2.
• Discontinuation and dose reduction rates.
• Efficacy in terms of progression-free survival, objective response rate, clinical benefit rate, time to response, duration of response, and best percentage of change in tumor burden per RECIST v.1.1.

Exploratory Objectives
• Evaluate predictive or prognostic biomarkers associated with disease activity status or response to treatment.
• Identify possible mechanisms of sensitivity/resistance to treatment through the comparative analysis of potential biomarkers from patients pre-treatment and post-progression blood samples and/or tumor samples.

Sample size
• It was based on a Simon’s two-stage design, planned to attain an 80% power at nominal level of one-sided alpha of 0.05 to each endpoint.

Stage I (N=25)
• The trial will continue to final analysis if there are ≤6 patients (P25) with ≥4 grade 2 diarrhea and ≤9 patients (P25) with ≥2 grade 3 neutropenia. Otherwise, the recruitment will continue to achieve 50 patients.

Final stage (≥50)
• The study will be declared positive if any of the following outcomes are achieved:
  1. If there are ≥7 (14%) patients with grade ≥2 diarrhea (expected rate as the null hypothesis 23%)
  2. If there are ≤5 (10%) patients with grade ≥3 neutropenia (expected rate as null hypothesis 40%).

STATISTICS

• Patients ≥18 years with taxane-pretreated advanced breast cancer.
• At least one and up to two prior chemotherapy regimens for advanced disease.
• Earlier treatment in curative setting will be continued as one of the regimens if advanced disease occurred ≥12 months after completion of chemotherapy.
• ECOG performance status 0 or 1.
• Measurable or non-measurable, but evaluable, disease per RECIST v.1.1. Patients with bone-only metastases are also eligible.

BID: Twice a day; Day: ECOCG. Eastern Cooperative Oncology Group; G-CSF: Granulocyte-colony stimulating factor; IV: Intravenous; L: Loperamide; NCI-CTCAE v.5.0: National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0; PO: Orally; QD: Daily; RECIST v.1.1: Response Evaluation Criteria in Solid Tumors version 1.1; SG: Sacituzumab govitecan.

* As of March 14, 2023, the protocol is pending approval of an amendment to also allow the inclusion of patients with HR-positive/HER2-negative advanced breast cancer.

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Figure 1. PRIMED Trial Design

BIBLIOGRAPHY

5. Rugo et al. Annals of Oncology, 2022; 33_suppl, 585B-586B.

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TRIAL ENROLLMENT

PRIMED study was opened to accrual in February 2023 and is currently recruiting in 10 institutions from Spain.