**INTRODUCTION**

- Chemotherapy, alone or in combination with immune checkpoint inhibitors, is the standard of care for patients with metastatic triple-negative breast cancer (TNBC).
- However, not all patients with programmed death-ligand 1 (PD-L1)–positive TNBC are appropriate candidates for immune checkpoint inhibitor treatment, and some patients with PD-L1–negative TNBC may not derive clinical benefit.

**TRILACICLIB MECHANISM OF ACTION**

- Trilaciclib is an intravenous (IV) cyclin-dependent kinase (CDK) inhibitor that decreased the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum-based or taxane-containing chemotherapy regimen for metastatic-stage small-cell lung cancer.
- A randomized, open-label, phase 2 trial (NCT02978716) compared trilaciclib prior to gemcitabine plus carboplatin (GCb) with GCb alone in patients with TNBC.
- Although the primary endpoint of myeloprotection was not met, a clinically meaningful improvement in overall survival (OS) was observed in the intention-to-treat population with both PD-L1–positive and -negative tumors.

**PATIENT ELIGIBILITY CRITERIA**

- **Adult patients (≥ 18 years of age)**
- Confirmed locally advanced unresectable or metastatic TNBC
- No PD-L1–I-TP1-L1 inhibitor and no prior therapies in the metastatic setting (cohort 1); prior PD-L1–I-TP1-L1 inhibitor for 2.4 months in duration and documented PD-L1–positive tumor cell expression
- Archival tumor tissue available, or fresh biopsy
- Known hypersensitivity to carboplatin
- Known hypersensitivity to cisplatin
- Known hypersensitivity to paclitaxel
- Known hypersensitivity to oxaliplatin
- Archival tissue is acceptable for use as the baseline sample if no systemic therapy or local radiation has been administered between biopsy and randomization
- Target participation for optional biopsy collection is 80 patients, including ~60 patients from cohort 1 and ~20 patients from cohort 2

**STUDY DESIGN**

- **Primary endpoint**
  - Overall survival
- **Secondary endpoints**
  - TTD-fatigue, as measured by FACIT-F

**STUDY OBJECTIVES**

1. **Primary objective**
   - To evaluate the effect of trilaciclib prior to GCb vs placebo prior to GCb on OS
2. **Key secondary objective**
   - To assess the effect of trilaciclib versus placebo on patients' quality of life, as measured by time to first confirmed deterioration of fatigue (TTDF-tatigue)

**StudY DESIGN**

- **Phase 2 trial** (NCT07492949) is a phase 3, multicenter, randomized, double-blind, placebo-controlled, 2-cohort study evaluating the safety and efficacy of trilaciclib versus placebo administered prior to GCb for triple-negative breast cancer (TNBC).
- **Cohort 1** (n = 170) patients receiving first-line GCb (PD-L1–I-TP1-L1 inhibitor-negative naïve patients)
- **Cohort 2** (n = 80) patients receiving second-line GCb (previously treated with a PD-L1–I-TP1-L1 inhibitor)

**TREATMENT PHASE**

- **Trilaciclib prior to GCb on days 1 and 8 every 21 days**
- **Placebo prior to GCb on days 1 and 8 every 21 days**

**STUDY OUTCOMES**

- **Stratification factors:**
  - PD-L1 status
  - Disease-free interval

- **No stratification factors**

- **End of study**
- **Survival follow-up**

**OPTIONAL BIOPSY COLLECTION**

- To evaluate the impact of trilaciclib on changes to the tumor-associated immune response in TNBC, immunophenotypic changes will be compared between tumor biopsies from patients receiving trilaciclib or placebo prior to GCb.
- For patients who consent to optional biopsy collection, fresh tumor biopsies from a recurrent/metastatic lesion will be collected at baseline and on-treatment, prior to cohort 2.
- Archival tissue is acceptable for use as the baseline sample if no systemic therapy or local radiation has been administered between biopsy and randomization.
- Target participation for optional biopsy collection is 80 patients, including ~60 patients from cohort 1 and ~20 patients from cohort 2.

**STATISTICS**

- Data from each cohort will be analyzed separately.
- An interim analysis for OS will be performed for cohort 1 when ~70% of required events have been observed.
- If the primary analysis of OS is statistically significant, then TTD-fatigue will be analyzed.

**PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; ORR, overall response rate; CBR, clinical benefit rate; TTR, time to response**

- **Estimated date last patient completed:** Q2 2024

- **Estimated date last patient completed:** Q2 2024

**STUDY SITES**

- United States
- Europe
- Russia
- China
- Australia

**Total study sites:** 115

**Estimated date first patient randomized:** Q2 2024

**Estimated date last patient completed:** Q2 2024

**Sponsorships**

- **G1 Therapeutics**
- **Envision Pharma Group**
- **Farhana Burnett, PhD**

**CONTACTS**

- shom.goel@petermac.org
- sjain@g1therapeutics.com

**DISCLAIMER**

- This presentation is the intellectual property of the author/presenter. Copies of this poster obtained through QR (Quick Response) codes are not permitted.

**ACKNOWLEDGMENTS**

- Medical writing assistance was provided by Farhana Burnett, PhD, from Alligent Europe (Envision Pharma Group), funded by G1 Therapeutics.