DOSE ESCALATION AND EXPANSION STUDY OF LEROCICLIB (G1T38), AN ORAL CDK4/6 INHIBITOR, DOSED WITH NO DRUG HOLIDAY IN COMBINATION WITH FULVISTEN IN PATIENTS WITH HR+/HER2- ADVANCED BREAST CANCER


Vermont Exploratory Medicine Research Unit, Institute of Oncology, Christchurch, Middlesex; UCL Armona Exploratory Medicine, Thessaloniki; George; J. Crew Cancer Research Institute, London, UK; W1087 for Women Health – Nicola Sand, Sofia, Bulgaria; Cambridge Cancer Centre, Cambridge, UK; The Christie NHS Foundation Trust, Manchester, UK; University of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine & Health, University of Manchester, Manchester, UK; New York University College of Manhattan Hospital Exploratory Research Centre, London, UK; USC Therapeutics, Inc., Research Triangle Park, NC, USA

BACKGROUND

Lerociclib (G1T38) is a potent and selective oral CDK4/6 inhibitor that has consistently demonstrated efficacy in phase 1 studies in both hormone receptor-positive (HR+) and human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer (ABC) patients treated with fulvestrant (FV) as second-line treatment for disease progression.

STUDY OBJECTIVES

- Evaluate the safety, tolerability, and efficacy of lerociclib administered on a fixed dose schedule combined with FV in patients with HR+/HER2- ABC who have failed prior endocrine therapy.

METHODS

- Part 1: open-label, 3+3, parallel-dose escalation of lerociclib 200 mg–850 mg QD and 100 mg–425 mg BID in combination with FV 250 mg BID.
- Part 2: dose expansion and safety study in patients who are enrolled in Part 1 and have progressed on or after 1 prior therapy with FV.

RESULTS

- Median (range) number of cycles per patient: 4.0 (2.5–6.0) in Part 1. Median (range) duration of lerociclib exposure: 6.0 (1.0–31.0) months in Part 1.
- No serious adverse events (AEs) considered related to lerociclib were reported in 6 patients (5.5%).
- One patient (0.9%) discontinued treatment due to an AE: Grade 4 neutropenia at 200 mg QD; this event resolved.
- No cases of QTcF prolongation (≤450 ms) were observed.
- There was generally well-tolerated and showed early evidence of antitumor activity in progression-free survival (PFS) and overall survival (OS).

CONCLUSIONS

- Coadministration of fulvestrant had minimal impact on the PK of lerociclib. The efficacy data are consistent with prior clinical experience with fulvestrant and lerociclib, including the efficacy of the 50 mg QD dose (n = 110).
- Coadministration of fulvestrant had a minimal impact on the PK of lerociclib. The efficacy data are consistent with prior clinical experience with fulvestrant and lerociclib, including the efficacy of the 50 mg QD dose (n = 110).
- Slamon DJ, et al. (2019). Endocrine therapy is the preferred treatment for patients with hormone receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2)-negative breast cancer.
- Coadministration of fulvestrant had a minimal impact on the PK of lerociclib. The efficacy data are consistent with prior clinical experience with fulvestrant and lerociclib, including the efficacy of the 50 mg QD dose (n = 110).
- Slamon DJ, et al. (2019).