Trilaciclib improves overall survival when given with gemcitabine/codecitabine in patients with metastatic triple-negative breast cancer: final analysis of a randomized phase 2 trial

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INTRODUCTION

Chemotherapy remains the mainstay of treatment for most patients with metastatic breast cancer. However, resistance to current chemotherapy treatments and irradiation is a common problem in metastatic settings, resulting in poor progression-free survival (PFS) and overall survival (OS). In order to maximize treatment efficacy and survival, new and novel agents that target the proliferation and composition of lymphocytes in the tumor microenvironment and improve OS are needed.

Aims: To assess the effect of trilaciclib on the composition of lymphocyte subsets and clonal expansion, and to determine whether trilaciclib delays the onset of PFS and OS among patients treated with chemotherapy in the BRCA family.

METHODS

The study used a phase 2 randomized controlled trial design (NCT02885036). Participants received trilaciclib and gemcitabine/codecitabine (GCb) in a 3:1:1 dosing ratio (cycle 1, 95% CI 0.25–0.75), with 7 of 10 patients on cycle 8 (95% CI 0.25–0.75) receiving gemcitabine/codecitabine in the phase 2 analysis. The study was conducted at 54 sites in 10 countries and 306 patients were enrolled. Patients were randomized to receive trilaciclib 5 mg/kg or placebo 5 mg/kg and chemotherapy as follows: group 1, chemotherapy on days 1 and 8; group 2, trilaciclib and chemotherapy on days 1 and 8; group 3, trilaciclib alone on days 1 and 8. For each group, the primary analysis was performed on per-protocol and intention-to-treat populations.

RESULTS

The primary analysis was performed on 302 participants, 126 in each arm. The median age was 60.8 years and 75% were Black. The study showed a statistically significant improvement in OS among patients with decreased peripheral clonality, with a statistically significant improvement among patients receiving GCb alone (P = 0.0497) and compared with responders receiving GCb alone (P = 0.0021). Eight patients (26.4%) who received trilaciclib in combination with tumor microenvironment-expanded OS among patients with decreased peripheral clonality, with a statistically significant improvement among patients receiving GCb alone (P = 0.0438) compared with responders receiving GCb alone (P = 0.0006). The study was terminated early due to a significant improvement in OS among patients with decreased peripheral clonality, with a statistically significant improvement among patients receiving GCb alone (P = 0.0006) compared with responders receiving GCb alone (P = 0.0006).

CONCLUSIONS

Chemotherapy remains the mainstay of treatment for most patients with metastatic breast cancer. However, resistance to current chemotherapy treatments and irradiation is a common problem in metastatic settings, resulting in poor progression-free survival (PFS) and overall survival (OS). In order to maximize treatment efficacy and survival, new and novel agents that target the proliferation and composition of lymphocytes in the tumor microenvironment and improve OS are needed.

Figure 2C. T2M and T2M associated with increased OS among patients treated with gemcitabine/codecitabine (GCb) in the phase 2 analysis. The study was conducted at 54 sites in 10 countries and 306 patients were enrolled. Participants were randomized to receive trilaciclib 5 mg/kg or placebo 5 mg/kg and chemotherapy as follows: group 1, chemotherapy on days 1 and 8; group 2, trilaciclib and chemotherapy on days 1 and 8; group 3, trilaciclib alone on days 1 and 8. For each group, the primary analysis was performed on per-protocol and intention-to-treat populations.