A phase 1b/2 study of rebastinib and paclitaxel in advanced or metastatic platinum-resistant ovarian cancer

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INTRODUCTION

Rebastinib is a small-molecule inhibitor targeting b-arrestin-dependent MET signaling (Figure 1). The phase 1b/2 trial was designed to evaluate rebastinib and paclitaxel in combination in patients with platinum-resistant ovarian cancer from<br>

METHODS

In Part 1, we observed antitumor activity across multiple tumor types (Table 1). Rebastinib in combination with weekly paclitaxel 80 mg/m² was well tolerated in patients with platinum-resistant ovarian cancer from Part 1 of the study (Figure 2). As new blood vessels form, pericytes stimulated as endothelial cells by Tie2 receptor angiogenesis is further inhibited leading to vascular regression and displacement of TEMs by invasion of new blood vessels (Figure 3).<br>

RESULTS

Inclusion criteria

• Adequate organ function and bone marrow reserve
• History or presence of clinically relevant cardiovascular abnormalities
• Use of systemic corticosteroids within 7 days prior to first dose
• Not recovered from toxicities from prior therapy to Grade 1 (or baseline)
• Patients were treated with rebastinib (50 or 100 mg BID) in combination with 80 mg/m² paclitaxel in patients with platinum-resistant ovarian cancer from Part 1 of the study (Figure 2). Figure 2. Rate of TSE2 in Angiogenesis and Tumor Cell Invasion<br>

PATIENT DISPOSITION AND DEMOGRAPHICS

• In this interim analysis, the safety population was defined on patients with platinum-resistant ovarian cancer who received both rebastinib and paclitaxel in combination with paclitaxel in ≥60% of cycles 1 and 2. In total, 29 patients (100%) were included in the safety population. This included 18 patients with platinum-resistant ovarian cancer from Part 1 of the study (7 patients in Cohort 1, 3 patients in Cohort 2, and 8 patients in Cohort 3) and 11 patients who received rebastinib 50 mg BID, October 2019), and 19 patients reduced to rebastinib 50 mg BID, October 2019) (Figure 3).<br>

Patient disposition

• Reasons for discontinuation include radiological progression (n = 6), clinical progression (n = 6), AE (n = 4), and death (n = 1).<br>

TABLE 2: PATIENT DEMOGRAPHICS AND DISEASE CHARACTERISTICS

• In this study, partial or complete response was confirmed at the 7-week response evaluation visit, and an additional 2 patients had progressive disease (PD) and stable disease (SD) at the 7-week visit. The median time to disease progression (TTP) for the safety population was 4.2 months (range 0.7, 10.2+) (Figure 4).<br>

Drug exposure and safety

• The median number of treatment in the safety population was 4 months (range 1, 19). Median duration of exposure was 8 months (range 1, 22). Overall, 62% of patients received a PARP inhibitor, and 31% received bevacizumab (Table 3).<br>

TABLE 4: TSE2 (%) in % of Patients with Platinum-Resistant Ovarian Cancer

• Inclusion criteria included patients with advanced or metastatic platinum-resistant ovarian cancer from Part 2 of this study has 5 disease levels from baseline that was maintained for at least 28 days (Table 4).<br>

CONCLUSIONS

• In this study, 33 patients received treatment in combination with paclitaxel in the safety population. Rebastinib was well tolerated in patients with platinum-resistant ovarian cancer from Part 2 of this study has 5 disease levels from baseline that was maintained for at least 28 days (Table 4).<br>

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Figure 4. Best Percent Change from Baseline in the Sore of Tumor Lesion (A) and Tissue on Treatment (B)