A Phase 2 study of pamiparib in patients with locally advanced/metastatic HER2-negative breast cancer with germline BRCA mutation

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Introduction

In 2020, female breast cancer was the leading cause of cancer incidence and mortality in women worldwide, with up to 23% of patients harboring a germline BRCA1/2 mutation 

Clinical guidance recommends PARP inhibitors (PARI) for patients with metastatic human epidermal growth factor receptor 2 (HER2) negative breast cancer (BBC), who were positive for chemotherapy in the neoadjuvant, adjuvant, or metastatic setting.

In China, platinum containing chemotherapy is the preferred first line chemotherapy for triple-negative breast cancer (TNBC). However, there are currently no approved targeted therapies for TNBC with gBRCA mutation. In order to meet the need for more efficacious treatment options in this patient population, we conducted this phase 2 study of pamiparib in patients with advanced solid tumors, including breast cancer, harboring gBRCA1/2 mutation, who had progressed on or were unsuitable for endocrine therapy, or for whom no standard therapy exists

Methods

Study design and patient population

- Study design and endpoints are summarized in Figure 1. Treatment was administered by intravenous infusion for 60 minutes every 21 days to patients with locally advanced/metastatic HER2-negative breast cancer harboring gBRCA1/2 mutation

Results

- A total of 88 patients were enrolled into the study and received 1 dose of pamiparib (safety population)

- 76 patients (TNBC cohort n=55; HR[+]/HER2[−] cohort n=21) had measurable disease at baseline per RECIST v1.1 (efficacy population)

- Prior chemotherapy: n (%) 62 (100.0) 26 (100.0) 88 (100.0)

- Female: n (%) 62 (100.0) 26 (100.0) 88 (100.0)

- Median age, n (%) 62 (100.0) 26 (100.0) 88 (100.0)

- Number of metastatic sites: n (%) 62 (100.0) 26 (100.0) 88 (100.0)

- History of brain metastasis: n (%) 6 (9.7) 0 (0.0) 6 (6.8)

- Prior platinum therapy: n (%) 6 (9.7) 0 (0.0) 6 (6.8)

- Prior anthracycline and/or taxane: n (%) 33 (54.8) 10 (38.5) 43 (49.1)

- Prior endocrine therapy: n (%) 60 (96.8) 24 (92.3) 84 (95.5)

- Prior anti-HER2 therapy: n (%) 13 (20.9) 6 (23.1) 19 (21.6)

- Prior anti-angiogenic therapy: n (%) 35 (55.7) 14 (53.8) 50 (57.1)

- Prior immunotherapy: n (%) 22 (35.5) 11 (42.3) 33 (38.0)

- Prior radiotherapy: n (%) 47 (75.8) 17 (65.4) 64 (73.9)

- Total Cycles: n (%) 2 (3.8) 1 (3.8) 3 (3.3)

- Safety

- Number of patients with any treatment-related TEAE: 88 (100.0)

- TEAE grade ≥ 3: n (%) 18 (20.5) 6 (23.1) 24 (27.3)

- Treatment-emergent AE: n (%) 76 (86.3) 26 (100.0) 102 (115.9)

- No treatment-related TEAEs leading to death were reported

- Treatment-emergent adverse events (TEAEs) and treatment-related TEAEs are summarized in Table 2

- The most common Grade 3–4 adverse events include anemia, decreased white blood cell count, and decreased neutrophil count

- 2 patients experienced TEAEs leading to treatment discontinuation (1 patient in each cohort). All other patients remained on treatment at the pre-planned dose modification criteria

- In the TNBC cohort, median duration of treatment was 3.8 months (range: 0.7–19.4) in the TNBC cohort and 9.6 months (range: 0.7–19.4) in the HR[+]/HER2[−] cohort

- Conclusions

- Treatment with pamiparib demonstrated meaningful and durable clinical activity in patients with locally advanced/metastatic HER2-negative breast cancer harboring gBRCA1/2 mutation

- Observed ORR of 32.2% (TNBC cohort) and 61.9% (HR[+]/HER2[−] cohort)

- The safety profile observed for patients treated with pamiparib in the TNBC cohort was consistent with that observed with pamiparib in other solid tumor types

- The results demonstrate that pamiparib may be a promising potential treatment option in patients with locally advanced/metastatic HER2-negative breast cancer harboring gBRCA1/2 mutation

- Table 2. Efficiency endpoints by IRC (efficacy population)

- Table 3. Number of patients with Grade 3–4 adverse events

- Table 5. Demographics and baseline characteristics (safety population)

- Figure 2. DfR by IRC in the (A) TNBC cohort and (B) HR[+]/HER2[−] cohort

- Figure 3. PPS by IRC in the (A) TNBC cohort and (B) HR[+]/HER2[−] cohort

- Figure 4. GSR in the (A) TNBC cohort and (B) HR[+]/HER2[−] cohort

- References

- Acknowledgements

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