A Phase 2 study of pamiparib in the treatment of patients with locally advanced or metastatic HER2-negative breast cancer with germline *BRCA* mutation.

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Background:

Breast cancer is the most common cancer among women, with up to 37% of patients (pts) harboring germline *BRCA1/2* mutations (g*BRCA1/2*m) that appear to be sensitive to poly (ADP-ribose) polymerase proteins 1 and 2 (PARP1/2) inhibition. Pamiparib is an orally administered selective PARP1/2 inhibitor that has the potential to cross the blood-brain barrier. This study evaluated the efficacy and safety of pamiparib in pts with locally advanced/metastatic human epidermal growth factor receptor 2-negative (HER2-) breast cancer, with deleterious or suspected deleterious g*BRCA1/2*m, who received ≤ 2 prior lines of chemotherapy.

Methods:

In this open-label, Phase 2, multi-center study in China (NCT03575065), pts with locally advanced/metastatic HER2- breast cancer with deleterious or suspected deleterious g*BRCA1/2*m triple negative breast cancer (TNBC cohort) or hormone receptor-positive (HR+)/HER2- breast cancer (HR+ cohort) were enrolled. Pts received pamiparib 60 mg orally twice daily in 28-day cycles. The primary endpoint was objective response rate (ORR; RECIST v1.1) by independent review committee (IRC). Secondary endpoints included duration of response (DOR) and progression free survival (PFS) by IRC, overall survival (OS), safety and tolerability.

Results:

88 pts were enrolled (median age 45.5 years), 76 pts (TNBC cohort n = 55; HR+ cohort n = 21) had measurable disease at baseline per IRC. 60 pts (68.2%) received 1 or 2 prior lines of chemotherapy; 42 pts (47.7%) were treated with platinum previously. Median follow-up was 13.77 months (TNBC cohort, 10.87 months; HR+ cohort, 18.45 months). In the TNBC cohort: confirmed ORR was 38.2% (95% CI: 25.4–52.3); median DOR (mDOR) was 6.97 months (95% CI: 3.94–not estimable[NE]); median PFS (mPFS) was 5.49 months (95% CI: 3.65–7.33); median OS (mOS) was 17.08 months (95% CI:13.70–NE). In the HR+ cohort: confirmed ORR was 61.9% (95% CI: 38.4–81.9); mDOR was 7.49 months (95% CI: 5.55–14.75); mPFS was 9.20 months (95% CI: 7.39–11.93); mOS was not reached (NR; 95% CI 18.10–NE). ≥ Grade 3 treatment emergent adverse events (TEAEs) occurred in 54 pts (61.4%); anemia was the most common TEAE, occurring in 77 pts (87.5%). Dose reduction due to TEAEs occurred for 57 pts (64.8%); discontinuations due to TEAEs occurred for 2 pts (2.3%).

Conclusions:

Pamiparib showed a promising response in pts with locally advanced/metastatic HER2- breast cancer with a g*BRCA1/2*m. The safety profile of pamiparib was considered acceptable and was generally consistent with therapies in the same class.

Efficacy by cohort:

	TNBC (N = 62)	**HR(+)/HER2(-)** (N = 26)
Efficacy Evaluable Analysis Set, N	55	21
ORR by IRC, n (% [95% CI])	21 (38.2% [25.4–52.3])	13 (61.9% [38.4–81.9])
mDOR by IRC, months (95% CI)	6.97 (3.94–NE)	7.49 (5.55–14.75)
mPFS by IRC, months (95% CI)	5.49 (3.65–7.33)	9.20 (7.39–11.93)
mOS, months (95% CI)	17.08 (13.70–NE)	NR (18.10–NE)