

## **Pamiparib, an Investigational PARP1/2 Inhibitor, for the Treatment of Patients With HER2-Negative Metastatic Breast Cancer Harboring Germline *BRCA1/2* Mutations: An Open-label, Multicenter, Phase 2 Trial in China**

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**Objective** Breast cancer is the most prevalent malignancy among women in China and one of the main causes of tumor-related death. Poly (ADP-ribose) polymerase 1 and 2 proteins (PARP1/2) are involved in DNA damage repair and their inhibition can lead to an accumulation of double-strand DNA breaks and cell toxicity. Breast cancers with germline *BRCA1/2* mutations, including triple negative (TNBC) and hormone receptor–positive (HR+)/HER2 negative (HER2-), have been shown to respond to PARP1/2 inhibitors. Pamiparib is an investigational PARP1/2 inhibitor that was designed to exploit *BRCA*-like homologous recombination deficiencies (HRD) by trapping PARP-DNA complexes and preventing DNA repair. Pamiparib demonstrated antitumor activity in both in vitro and in vivo nonclinical tumor models harboring *BRCA* gene mutations and other HRD. In early phase clinical studies (NCT02361723; NCT03333915), pamiparib was generally well tolerated, showed preliminary antitumor activity, and 60 mg orally twice daily (PO BID) was determined as the recommended phase 2 dose.

**Methods** This open-label, multicenter, phase 2 study (NCT03575065) was designed to evaluate the efficacy, safety, and tolerability of pamiparib in Chinese patients (pts) with advanced HER2- breast cancer harboring germline *BRCA1/2* mutations. Approximately 75 female pts are being enrolled into one of two cohorts. Patients with locally advanced or metastatic TNBC are being enrolled into Cohort 1 and Cohort 2 is enrolling pts with HR+/HER2- metastatic breast cancer. All pts must have confirmed either deleterious or suspected deleterious germline *BRCA1/2* mutations. Patients in both cohorts will receive pamiparib 60 mg PO BID in 28-day cycles starting on Day 1 of Cycle 1 until disease progression or unacceptable toxicity. The primary endpoint is objective response rate (ORR) by independent radiology review (IRR); key secondary efficacy endpoints will include OS, investigator-assessed ORR, as well as PFS and duration of response as assessed by investigator and IRR. The incidence and severity of AEs are also being evaluated as a secondary endpoint.