An Open-Label, Multicenter, Phase 2 Study to Evaluate the Antitumor Activity and Safety of Pamiparib in the Treatment of Metastatic HER2-Negative Breast Cancer Patients With *BRCA* Mutation 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 proteins 1 and 2 (PARP1/2) are involved in DNA damage repair, and their inhibition is cytotoxic for cells with homologous recombination deficiency (HRD). Breast cancers with germline *BRCA1/2* mutation, including triple negative (TNBC) and hormone receptor-positive (HR+)/HER2 negative (HER2-), have been shown to respond to PARP1/2 inhibitors. Pamiparib is a selective PARP 1/2 inhibitor with potent PARP trapping ability that can cross the blood-brain barrier and has demonstrated antitumor activity in both *in vitro* and *in vivo* nonclinical tumor models harboring *BRCA* gene mutations and other homologous recombination deficiencies. In early phase clinical studies in Caucasian and Chinese patients (NCT02361723; NCT03333915), pamiparib was generally well tolerated and showed preliminary antitumor activity. These studies also established 60 mg orally twice daily (PO BID) as the recommended pivotal dose.

Methods This open-label, multicenter, phase 2 study (CTR20171623) was designed to evaluate the efficacy, safety, and tolerability of pamiparib in Chinese patients with advanced TNBC or HR+/HER2- breast cancer harboring germline *BRCA1/2* mutation. All eligible patients are being enrolled into one of two cohorts. Cohort 1 is enrolling patients with locally advanced or metastatic TNBC with confirmed either deleterious or suspected deleterious germline *BRCA1/2* mutation. Cohort 2 is enrolling patients with HR(+)/HER2(-) and confirmed either deleterious or suspected deleterious germline *BRCA1/2* mutation. Patients in both cohorts will receive pamiparib 60 mg PO BID starting on Day 1 of Cycle 1, in 28-day treatment cycles until disease progression. The primary endpoint is objective response rate; secondary endpoints will include progression-free survival, overall survival, best overall response, safety, and tolerability. Exploratory endpoints include identification of predictable biomarkers and determining the pharmacokinetic profile.