Pamiparib, an investigational PARP inhibitor, in patients with metastatic castration-resistant prostate cancer (mCRPC) and a circulating tumor cell (CTC) homologous recombination deficiency (HRD) phenotype or *BRCA* defects: A trial in progress.

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Background:
Men with mCRPC who have a *BRCA1/2* mutation (*BRCA1/2*^{mut}) or mutations in other genes resulting in HRD have a poor prognosis. A novel liquid biopsy test (EPIC Sciences) identifies CTCs with an HRD phenotype. Preliminary studies showed that these men may respond to treatment with a PARP inhibitor. Pamiparib, an investigational PARP1/2 inhibitor, has shown brain penetration and potent PARP–DNA complex trapping in nonclinical studies. In early phase clinical studies (NCT02361723; NCT03333915), pamiparib was generally well tolerated and showed preliminary antitumor activity; 60 mg orally twice daily (BID) was established as the recommended investigational dose.

Methods:
This open-label, global, phase 2 study (NCT03712930) evaluates the antitumor activity and safety/tolerability of pamiparib in mCRPC patients (pts) with CTC-HRD, assessed by the CTC-HRD assay, or deleterious germline/somatic mutations in *BRCA1/2*. Patients must have progressed on/after ≥1 androgen receptor-targeted therapy, received ≥1 taxane-based therapy, and have prostate-specific antigen (PSA) progression per PCWG3 criteria. Four cohorts of pts will receive pamiparib 60 mg BID in 28-day cycles. Cohort 1 will include ~50 pts with CTC-HRD^{+} +/- *BRCA1/2*^{mut} mCRPC with measurable metastatic disease; Cohort 2 will include ~30 pts with CTC-HRD^{+} +/- *BRCA1/2*^{mut} mCRPC with bone-only disease; Cohorts 3 & 4 will include ~20 pts with CTC-HRD$^{-/unk}$ + *BRCA1/2*^{mut} mCRPC with measurable metastatic disease (Cohort 3), or bone-only disease (Cohort 4). Disease status will be assessed every 8 wks for 24 wks, then every 12 wks; PSA levels will be tested every 4 wks. Co-primary endpoints are radiographic ORR assessed by IRC (pts with measurable disease) and confirmed PSA response rate per PCWG3 criteria (pts +/- measurable disease). Secondary endpoints include ORR, time to PSA response/progression, duration of PSA response, time to symptomatic skeletal event, radiographic progression-free survival, overall survival, and safety. As of 05 December 2018, this study is actively enrolling.
Clinical trial information: NCT03712930