**TRITON2: An International, Multicenter, Open-Label, Phase 2 Study of the PARP Inhibitor Rucaparib in Patients with Metastatic Castration-Resistant Prostate Cancer (mCRPC) Associated with Homologous Recombination Deficiency (HRD)**

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**Background:** There are limited treatment options available for patients with advanced mCRPC following androgen deprivation and taxane treatment. Germline or somatic alterations in the homologous recombination genes *BRCA1, BRCA2,* and *ATM* have been observed in ≈20% of patients with mCRPC (Robinson et al. *Cell.* 2015;161:1215-28). These molecular markers are suggestive of HRD and may be used to select patients with mCRPC for targeted treatment with a poly(ADP-ribose) polymerase (PARP) inhibitor. PARP inhibition in cells with HRD results in synthetic lethality, and PARP inhibitors have demonstrated evidence of antitumor activity in patients with mCRPC and a homologous recombination gene mutation (Mateo et al. *N Engl J Med*. 2015;373:1697-708). Preclinical studies of rucaparib, a potent inhibitor of PARP1, PARP2, and PARP3, demonstrated potent cytotoxicity in *BRCA2*- or *ATM*-knockout prostate cancer cell lines. These data provide a compelling rationale for evaluating rucaparib in patients with mCRPC associated with HRD.

**Methods:** TRITON2 (NCT02952534) is a phase 2 study evaluating rucaparib 600 mg BID in patients with mCRPC harboring a deleterious germline or somatic *BRCA1*, *BRCA2*, or *ATM* mutation (per local and/or central testing). An exploratory cohort is enrolling patients with an alteration in any of 12 other prespecified homologous recombination genes (eg, *RAD51C*, *RAD51D*, and *PALB2*). Patients must have progressed on androgen receptor signaling–directed therapy and 1 prior taxane-based chemotherapy for mCRPC. Patients who received prior treatment with a PARP inhibitor, mitoxantrone, cyclophosphamide, or platinum-based chemotherapy are excluded. The primary endpoint is response rate (per modified RECIST v1.1/PCWG3 in patients with soft-tissue disease and prostate-specific antigen response in patients with nonmeasurable disease). Secondary endpoints include duration of response, radiographic progression-free survival, overall survival, clinical benefit rate, and safety. Pretreatment blood samples collected from all patients will enable development of a plasma-based companion diagnostic to select patients for rucaparib treatment. Patients (≈160) will be enrolled at >100 sites worldwide.

**Results:** TRITON2 is currently enrolling patients.

**Conclusions:** TRITON2 will assess the efficacy and safety of rucaparib treatment in patients with mCRPC associated with HRD.

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**Declaration of Interests:**

**WA** has served in a consulting or advisory role for Clovis Oncology; has received honoraria from Caret Healthcare; and has received research funding from AstraZeneca and Zenith Epigenetics.

**AP** has served in a consulting or advisory role for Janssen; and has received research funding from Bristol-Myers Squibb and GlaxoSmithKline.

**CJR** has served in a consulting or advisory role for Bayer and Millennium; has received honoraria from Janssen Oncology and Astellas Pharma; and has received research funding from BIND Biosciences, Karyopharm Therapeutics, Novartis

**SW**, **AS**, **JG**, and **TG** are employees of Clovis Oncology and may own stock or stock options in that company.

**SC** has served in a consulting or advisory role and/or on speakers bureaus for Clovis Oncology, Sanofi, Pfizer, Astellas Pharma, and Janssen; has received honoraria from GlaxoSmithKline and Novartis; and has received research funding from Sanofi and Johnson & Johnson.

**HIS** has served in a consulting or advisory role for AstraZeneca, Astellas Pharma, Bristol-Myers Squibb, Celgene, Endocyte, Exelixis, Endo Pharmaceuticals, Ferring, Foundation Medicine, Genentech, Janssen, OncologySTAT, Palmetto GBA, Pfizer, Sanofi, Takeda, Ventana Medical Systems, BIRB-Copernicus Group, and Medivation; has served on a speakers bureau for WebMD; has received financial support for travel and/or accommodation from Exelixis, Janssen, Sanofi, Endocyte, AstraZeneca, Genentech, Bristol-Myers Squibb, Celgene, Pfizer, Takeda, Ferring, WIRB-Copernicus Group, and Astellas Pharma; has received honoraria from Chugai Pharma; and has received research funding from BIND Biosciences, Exelixis, Janssen, Medivation, and Janssen Diagnostics.

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