Trial of RucaparIb in ProsTate IndicatiONs-2 (TRITON-2): A Multicenter, Open-Label Phase 2 Study of the PARP Inhibitor Rucaparib in Patients with Metastatic Castration-Resistant Prostate Cancer Associated with Homologous Recombination Deficiency (HRD)

Wassim Abida[1], Simon Chowdhury[2], Simon Watkins[3], Darrin Despain[3], Chris Karlovich[3], **Tony Golsorkhi[3]**, Howard I. Scher[1]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]Guy's Hospital, London, UK; [3]Clovis Oncology, Inc., Boulder, CO

Background: Germline and somatic mutations in *BRCA1*, *BRCA2*, and other homologous recombination (HR) DNA-repair genes are frequently identified in advanced prostate cancer, including metastatic castration-resistant prostate cancer (mCRPC). Poly(ADP-ribose) polymerase (PARP) inhibitors are a promising class of agents that are synthetically lethal to cells with homologous recombination deficiency (HRD). In one study, 14 of the 16 patients with advanced mCRPC who responded to the PARP inhibitor olaparib had a tumor alteration in an HR DNA-repair gene, including *BRCA1*, *BRCA2, ATM*, and *PALB2* (Mateo et al. *N Engl J Med*. 2015;373:1697-708). Those data provide a rationale for further investigation of PARP inhibitors in patients with mCRPC and alterations in HR genes, including *BRCA1*, *BRCA2*, and *ATM*.

Methods: This phase 2 study is evaluating rucaparib (starting dose: 600 mg BID) in patients with mCRPC associated with a genetic alteration in *BRCA1*, *BRCA2*, *ATM*, or other HR gene. All patients will be required to have progressed on prior androgen receptor (AR)-targeted therapy (eg, abiraterone acetate, enzalutamide, or investigational AR-targeted agent). Patients must have progressed after 1 prior taxane-based chemotherapy for mCRPC. Patients who received prior treatment with PARP inhibitors, mitoxantrone, cyclophosphamide, or platinum-based chemotherapy are excluded. The primary objective of this study is to evaluate the investigator-assessed response rate (modified RECIST version 1.1/PCWG3, and/or prostate-specific antigen response). Secondary objectives include duration of response, radiologic progression-free survival, overall survival, clinical benefit rate, safety, and tolerability. Exploratory objectives include response in circulating tumor cells and patient reported outcomes.

Results: Approximately 157 patients will be enrolled at up to 125 sites worldwide.

Conclusions: This study is investigating the efficacy of rucaparib in patients with mCRPC associated with HRD. Initial results are anticipated in 2018.

Disclosures:

Simon Watkins, Darrin Despain, Chris Karlovich, and Tony Golsorkhi are employees of Clovis Oncology, Inc. and may own stock or stock options in that company.

Wassim Abida, Simon Chowdhury, and Howard I. Scher have served on advisory boards for Clovis Oncology, Inc. and have received funding support from Clovis Oncology, Inc. for clinical studies.