INTRODUCTION

Rucaparib in Patients with Metastatic Castration-Resistant Prostate Cancer Associated with Homologous Recombination Deficiency

TRITON2 TRIAL OVERVIEW

- TRITON2 is a phase 2 trial evaluating rucaparib in patients with mCRPC associated with HRD, including those with mutations in BRCA1/2, ATM, and/or other HR genes
- Patients will be randomized to one of three treatment arms
- The primary endpoint is centrally assessed ORR defined as CR or PR using Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST 1.1) in 45 and 18 patients in Cohorts A and B, respectively, for a planned total of 42 patients in each cohort
- Secondary endpoints include PSA and ctDNA response, duration of response, and time to progression

STUDY OBJECTIVES

Primary Objectives
- Assess the efficacy of rucaparib based on the response rate in mCRPC patients with HRD
- Assess the time to progression based on the use of objective radiographic response (by modified RECIST 1.1) in patients with non-clear cell, metastatic urothelial carcinoma
- Assess the time to progression in patients with non-clear cell, metastatic urothelial carcinoma

Key Exclusion Criteria
- Active secondary malignancy, with exception of in situ carcinoma
- Liver metastases
- New or active infection
- Active, untreated second malignancy
- Pre-existing or untreated second malignancy
- History of clinically significant hepatobiliary disease
- Uncontrolled pain from metastatic disease
- Patients with prior therapy not considered for continued treatment

Key Inclusion Criteria
- ECOG Performance Status of 0 or 1
- Evidence of disease progression after prior therapy for mCRPC
- Presence of HRD, including in those with mutations in BRCA1/2, ATM, or other HR genes
- PSA response will be evaluated by the local laboratory during screening (baseline), on day 1 of week 1, and every 4 weeks thereafter
- Vital signs, and electrocardiogram parameters will be assessed throughout the study
- Plasma samples will be collected 1 hour before rucaparib dose on day 1 of weeks 5, 9, 13, and 17
- Patients will be evaluated for safety throughout the trial

PLASMA-BASED COMPANION DIAGNOSTIC

- TRITON2 will also explore the development of a diagnostic based on ctDNA from plasma samples
- A commercially available, retrospective analysis will be performed to determine the concordance between HR gene alterations identified in tumor tissue samples and ctDNA obtained from plasma
- These results may provide insight into the benefits and limitations of ctDNA testing for monitoring response and resistance to PARP inhibition

TRIAL SUMMARY

Patients with mCRPC may harbor mutations in HR genes and could benefit from treatment with a PARP inhibitor such as rucaparib

The phase 2 TRITON2 study aims to determine the response rate with rucaparib in patients with mCRPC who have HRD, assessed on both AR-targeted therapy and taxane-based chemotherapy

- Approximately 157 patients will be enrolled at more than 100 sites worldwide

REFERENCES

1. Wassim Abida, 2 Simon Chowdhury, 2 Simon Watkins, 3 Darrin Despain, 3 Chris Karlovich, 3 Tony Goloski, 3 Howard Scher 1
1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Guy’s Hospital, London, UK; 3. Clovis Oncology, Inc., Boulder, CO

EVALUATIONS

Effectiveness of Safety Analysis
- Tumors will be assessed during screening (baseline), every 8 weeks up to 24 weeks, and every 12 weeks thereafter using appropriate imaging techniques (PET, CT, MRI, and/or mammography) and radiology will be evaluated on modified RECIST criteria
- Bone lesions will be evaluated based on Prostate Cancer Clinical Trials Working Group 3 criteria
- PSA response will be evaluated by the local laboratory during screening (baseline), on day 1 of week 1, and every 4 weeks thereafter

Safety Analyses
- Adverse events, incidence, type, seriousness, and severity, clinical laboratory parameters, vital signs, and electrocardiogram parameters will be assessed throughout the study

PLASMA-BASED COMPANION DIAGNOSTIC

- ctDNA testing could provide additional information about tumor genetic status
- ctDNA analysis could be used to monitor patients for response and resistance to PARP inhibition

Figure 1. TRITON2 Study Design

TRITON2 patients with mCRPC associated with HRD

PATIENT ELIGIBILITY

Key Inclusion Criteria

- Presence of HRD, including in those with mutations in BRCA1/2, ATM, or other HR genes
- PSA response will be evaluated by the local laboratory during screening (baseline), on day 1 of week 1, and every 4 weeks thereafter

Key Exclusion Criteria

- Active secondary malignancy
- Liver metastases
- New or active infection
- Active, untreated second malignancy
- History of clinically significant hepatobiliary disease
- Uncontrolled pain from metastatic disease
- Patients with prior therapy not considered for continued treatment

Table 1. Key Patient Inclusion/Exclusion Criteria

<table>
<thead>
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