INTRODUCTION

Recent data have shown that a deleterious germline and/or somatic mutation in BRCA1, BRCA2, ATM, or other homologous recombination (HR) repair genes is present in patients with advanced prostate cancer (including mCRPC) at frequencies of up to 25% or higher. These molecular markers may be used to select patients with mCRPC who are most likely to benefit from targeted treatment with poly(ADP-ribose) polymerase (PARP) inhibitors, which have been shown to be synthetically lethal to cells with HRD.

- In a phase 2 study of the PARP inhibitor olaparib (NCT01682772) in patients with mCRPC, 16 of 49 evaluable patients who had progressed on ≥1 prior chemotherapy responded to olaparib treatment; 14 of the 16 patients had a tumor alteration in an HR gene, including BRCA1, BRCA2, or ATM.
- These data provide a rationale for further investigation of rucaparib in patients with mCRPC that harbors an alteration in an HR gene.

PLASMA-BASED COMPANION DIAGNOSTIC

There are significant challenges in collecting and analyzing biopsy specimens from patients with mCRPC. TRITON3 will explore the use of circulating tumor DNA (ctDNA) purified from blood as a companion diagnostic. Pretreatment blood samples will be collected from all patients and analyzed for BRCA1, BRCA2, and ATM mutations in ctDNA (Figure 2).

A central retrospective analysis is planned to evaluate the agreement between HR gene alterations identified in tumor tissue samples and ctDNA obtained from plasma.

TRIAL SUMMARY

- Deleterious mutations in BRCA1, BRCA2, or ATM have been identified in patients with mCRPC.
- Patients with a deleterious mutation in an HR DNA-repair gene may potentially benefit from treatment with the PARP inhibitor rucaparib.
- TRITON3 is actively recruiting patients, with a goal of enrolling approximately 400 patients from >100 sites worldwide.

ACKNOWLEDGMENTS

The study is funded by Clovis Oncology, Inc. Medical writing and editorial assistance were provided by Nathan Yardley and Shannon Davis of Ashfield Healthcare Communications and provided by Luke Passler – May 2020.

REFERENCES