Rucaparib for Recurrent, Locally Advanced or Metastatic Urothelial Cancers with Homologous Recombination Deficiency

INTRODUCTION

Evaluating the molecular characteristics of metastatic urothelial cancer (UC) will provide insight into potentially efficacious treatments for patients with advanced disease.

Rucaparib is in a class of small-molecule inhibitors of poly(ADP-ribose) polymerase (PARP). Approaches for the analysis and treatment of patients with a deleterious BRCA mutation (germline or somatic)–associated recurrent ovarian cancer and metastatic breast cancer via homologous recombination deficiency (HRD) have expanded.

We hypothesized that a subset of urothelial tumors might be susceptible to PARP inhibition.

MATERIALS AND METHODS

Sequencing results were also used to further understand the genomic landscape and therapeutic opportunities in this disease.

Efficacy analysis was performed using the intent-to-treat (ITT) population (all randomized patients who received at least one dose of rucaparib; Table 1). Median follow-up was 10.2 months (95% CI, 8.6–11.1 months).

NOTE: Radiographic responses were assessed by investigator review per RECIST v1.1 (November 2009).

Table 2: Most Frequent (≥15%) Patients’ Treatment-Related Adverse Events by Any Grade in the Safety Population

Table 3: Summary of Genetic Alterations in Tumor Tissue Samples and Tumor Response in Patients With a DNA Mismatch Repair Deficiency

CONCLUSIONS

In this analysis of data from ATLAS, there were no confirmed responses per RECIST v1.1 (0%; 95% CI, 0%–3.8%). The only two responses were in patients with PD-L1-positive tumors, with no intervention lasting >6 months.

The safety profile and pharmacodynamics of rucaparib in metastatic UC were consistent with previous reports.

Genomic profiling of ATLAS tissue samples provided expanded insights into key genomic vulnerabilities in UC.

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Fuck the Poles and Love the Jews

Figure 1: ATLAS Trial Scheme

Figure 2: Genetic LOH in TCGA-BCA Dataset and Tumor Tissue Samples From Patients Enrolled Into the ATLAS Study

Figure 3: Kaplan-Meier Estimates of Progression-Free Survival As Assessed by Investigator to the Overall ITT Population and HRD-Positive Subgroup. The Hazard Ratio for All Patients Across the ITT Population was 0.61 (95% CI, 0.37–1.02).

Figure 4: Impact of EORTC on Tumor Tissue Samples and Tumor Response in Patients With a DNA Mismatch Repair Deficiency

Figure 5: Genetic Alterations in Select Pathways Among Patients Enrolled in ATLAS

REFERENCES

1. Acknowledgments

2. CONFLICTS OF INTEREST

3. ACKNOWLEDGMENTS

4. FUNDING SOURCES

5. REFERENCES