ATLAS: A Phase 2, Open-Label Study of Rucaparib in Patients with Locally Advanced or Metastatic Urothelial Carcinoma (mUC)

INTRODUCTION

- There are limited treatment options for patients with mUC that has progressed during or after platinum (cisplatin or carboplatin)-based chemotherapy and/or immune checkpoint inhibitor treatment.
- Analysis of the bladder cancer dataset from The Cancer Genome Atlas (http://cancergenome.nih.gov) suggests that approximately 60% of bladder tumors have homologous recombination deficiency (HRD), as identified by a deleterious mutation in a homologous recombination repair pathway gene or high genomic loss of heterozygosity (LOH)\(^1\).
- Poly(ADP-ribose) polymerase inhibitors, including rucaparib, have antitumor activity in tumors with HRD through synthetic lethality (Figure 1)\(^2\)\(^4\).
- These data provide a rationale for investigation of rucaparib in patients with locally advanced (unresectable) urothelial carcinoma (UC) or mUC.

ATLAS TRIAL OVERVIEW

- ATLAS (NCT03397394) is an international, multicenter, open-label, phase 2 study evaluating single-agent rucaparib (600 mg twice daily) as treatment for locally advanced (unresectable) UC or mUC previously treated with platinum-based chemotherapy and/or immune checkpoint inhibitors (Figure 2).
- Based on the estimated prevalence of HRD in bladder cancer, approximately 200 patients will be enrolled to enable robust estimates of response in the intent-to-treat population and the population with HRD.
  - Two interim analyses are planned after data are available for 60 and 120 patients.
  - The study has >90% power to reject the null hypothesis (P=0.10) at a 5% significance level if the true response rate for rucaparib is 20%.

Planned Analyses

- Primary endpoints are investigator-assessed objective response rate per Response Evaluation Criteria In Solid Tumors version 1.1\(^5\) in HRD-positive (signature based on tumor genomic LOH) and intent-to-treat populations.
- Secondary endpoints include response duration, progression-free survival, overall survival, safety, and pharmacokinetics.
- Exploratory endpoints include evaluation of molecular biomarkers associated with response and resistance to rucaparib, including changes in plasma and tumor samples, and serial sampling of circulating cell-free tumor DNA.

TRIAL SUMMARY

- The phase 2 ATLAS study aims to assess the safety and efficacy of single-agent rucaparib in patients with locally advanced (unresectable) UC or mUC who have progressed after platinum-based chemotherapy and/or immune checkpoint inhibitor treatment.
- Recruitment of patients is planned in ≈70 sites in 6 countries, with a target enrollment of 200 patients (Figure 3).

REFERENCES


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