**INTRODUCTION**

- There are limited treatment options for patients with metastatic urothelial carcinoma who have progressed on prior platinum-based chemotherapy and first-line immunotherapy.
- Poly(ADP-ribose) polymerase (PARP) inhibitors are approved in ovarian and breast cancer; however, there are limited data on PARP inhibitors in urothelial cancer.
- Non-small cell lung cancer has shown that PARP inhibitor rucaparib has antitumor activity through a mechanism called synthetic lethality in tumors with homologous recombination (HR) deficiency (HRD) (Figure 1).

**Tumour Tissue Collection and Analyses**

- **Blood sample collection**: The trial has >90% power to reject the null hypothesis (P=0.10) at a 5% significance level if the true response rate is 24.7% or lower.
- **Optimal archival tumour tissue**: The trial is enrolling patients with or without tumours associated with HRD status.

**BIOMARKER ASSESSMENT**

- The trial is enrolling tissue unselected for tumours with HRD status.
- PAS: Potential biomarker of rucaparib sensitivity and resistance (Figure 4). Collecting these data allows for the comprehensive characterization of tumour evolution.

**Tumour tissue samples to be collected:**

- **Optional archival tumour tissue:**
  - Patients receiving clinical benefit may continue treatment beyond progression.
  - All patients will be followed every 12 weeks for survival and secondary end points.

**RESULTS**

- Approximately 200 patients will be enrolled.
- Results from the analysis indicated that many urothelial tumours have high genomic LOH (Figure 2).
- Genomic LOH is a specific type of DNA damage indicative of HRD and sensitivity to PARP inhibitors.

- Research has shown that many urothelial tumours have high genomic LOH.
- The ATLAS trial is enrolling tissue unselected for tumours with HRD status.

**PRIMARY ENDPOINTS**

- Objective response rate
- Duration of response
- Overall survival
- Pharmacokinetics

**SECONDARY ENDPOINTS**

- Duration of response
- Overall survival
- Pharmacokinetics

**Figure 1. Schematic of Rucaparib-Induced Dysfunction in Cells with HRD**

**Figure 2. Genomic LOH in Bladder, Ovarian, and UC Tumours**

**Figure 3. ATLAS Trial Scheme**

**Figure 4. ATLAS Biomarker Assessments Schedule**

**Figure 5. Countries Participating in ATLAS**

**ATLAS TRIAL OVERVIEW**

- **ATLAS** (NCT03869991; 2017-09-21): an international, open-label phase 2 trial evaluating multiple agents and tumour genotypes in patients with locally advanced (stage T3b-4) or metastatic urothelial carcinoma pre-treated with 1 or 2 platinum treatments for advanced/metastatic disease (Figure 5).

- Eligible patients are not required to have tumours associated with HRD because rucaparib may potentially benefit patients with HRD-associated tumours.

- Approximately 200 patients will be enrolled.

- Two interim analyses planned after data are available for 60 and 120 patients.

- **Primary objective**: To evaluate objective response rate in the intent to treat and molecularly defined HRD-positive populations.

- **Secondary objectives**: Evaluation of duration of response, progression-free survival, overall survival, safety and tolerability, and steady state pharmacokinetics of rucaparib (Figure 3).

- The trial has 33% power to rule out the null hypothesis (P=0.15) at a 5% significance level if the true response rate for rucaparib is 20%.

**REFERENCES**

- 3. Cancer Campus, Villejuif, France.