**BACKGROUND**

- TSR-042 is an investigational humanized anti-programmed death 1 (PD-1) monoclonal antibody that binds with high affinity to the PD-1 receptor and effectively blocks its interaction with the PD-1 ligands PD-L1 and PD-L2.
- TSR-042 is the only anti-PD-1 therapy administered as a monotherapy every 3 weeks (Q3W) for 4 doses then every 6 weeks (Q6W) until disease progression.
- In clinical trials, preliminary data show that TSR-042 has activity and safety profiles similar to approved anti-PD-1 therapies.
- The ongoing GARNET trial (NCT02715284) is evaluating TSR-042 as monotherapy in patients with advanced solid tumors.
- GARNET included a weight-based dose escalation study (part 1A) and a fixed-dose safety study (part 2A), both completed.
- Here, we present safety, efficacy, and biomarker data from the previously treated recurrent or advanced NSCLC cohort.

**OBJECTIVES**

- **Primary**
  - To evaluate the clinical activity of TSR-042 at the RP2D in patients with previously treated recurrent or advanced NSCLC.
- **Secondary**
  - To further characterize the pharmacokinetic (PK) profile of TSR-042.

**METHODS**

**Patients**

- Subjects with previously treated recurrent or advanced NSCLC.
- Key exclusion criteria included:
  - Prior therapy with agents targeting PD-1, PD-L1, or PD-L2.
  - Uncontrolled central nervous system metastases and/or carcinomatous meningitis, or additional malignancy that progressed or required active treatment within the last 2 years.

**Study Design**

- GARNET is a multicenter, open-label, first-in-human phase 1 dose escalation study with expansion cohorts designed to assess the safety, PK, pharmacodynamics, and clinical activity of the PD-1 inhibitor TSR-042 in patients with advanced solid tumors (Figure 1).

**RESULTS**

- **SAFETY**
  - TEAEs were reported in 62 patients with previously treated recurrent or advanced NSCLC (85.5%, Table 3).
- **PK AND PHARMACODYNAMIC SUMMARY**
  - The C3 for the 500 mg Q3W and 1000 mg Q6W dosing were shown to be equivalent (Table 2).

**CLINICAL ACTIVITY**

- At the October 25, 2018 cutoff date, 47 patients with previously treated recurrent or advanced NSCLC had at least 1 tumor assessment or discontinued treatment prior to first postbaseline tumor assessment due to AEs or withdrawal of consent. The best overall tumor response by rIRCST is shown in Table 5.
- **Overall response rate** 95% CI
  - ORR 13.7% (95% CI 9.1, 18.4)
  - Disease control rate 95% CI
  - DCR 46.2 (95% CI 34.3, 58.0)

**CONCLUSIONS**

- TSR-042 is an anti-PD-1 monoclonal antibody that binds with high affinity to the PD-1 receptor.
- TSR-042 is administered at 500 mg Q3W for the first 4 cycles and 1000 mg Q6W thereafter, which is less frequent than approved PD-1 inhibitors.
- At this unique dosing schedule, TSR-042 achieved serum concentrations sufficient for full RO throughout the dosing cycle.
- TSR-042 was well tolerated; the safety profile was characteristic of approved PD-1 inhibitors.

**REFERENCES**


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