Preliminary Safety and Efficacy of Rovalpituzumab Tesirine in Patients With Delta-Like Protein 3-Expressing Advanced Solid Tumors

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OBJECTIVES
- To determine the safety, tolerability, and antitumor activity of Rova-T™ in patients with Delta-Like Protein-3 (DLL3)-expressing advanced solid tumors
- Preliminary studies have shown that in addition to SCLC, DLL3 is expressed in neuroendocrine carcinomas (NEC), with minimal to no expression in normal tissue
- DLL3 has a role in development and cell fate decisions
- DLL3 is expressed in the cell surface, making it accessible to monoclonal antibodies
- Rova-T is an antibody-drug conjugate (ADC) targeting DLL3
- In vitro studies in DLL3-expressing neuroendocrine tumors and other solid tumors
- This is a Phase 1, open-label, multicenter study in patients with histologically confirmed, unresectable, DLL3-expressing advanced solid tumor
- The primary mechanism of action of Rova-T is the binding of the ADC to DLL3 on target-expressing cells, internalization of the complex, and release of the payload via protein-protein degradation in late endosomes, leading to intracellular DNA cross-linking and cell death
- A Phase 1 study of Rova-T monotherapy in small cell lung cancer (SCLC) (D6.5/SC-DR002) showed a dose-related increase in tumor-specific events in patients with DLL3 expression, a manageable safety profile, and was well-tolerated
- Improved efficacy in high DLL3-expressing tumors suggests that DLL3 expression may help identify patients for clinical trials
- Rova-T is currently being evaluated for efficacy and safety in patients with extensive stage SCLC in multiple Phase 3 studies

BACKGROUND
- Delta-like protein 3 (DLL3) is an atypical Notch receptor family member that is highly expressed in high-grade neuroendocrine carcinomas (NEC), with minimal to no expression in normal tissue

METHODS
- This is a Phase 1, open-label, multicenter study in patients with histologically confirmed, unresectable, DLL3-expressing advanced solid tumor
- Key inclusion criteria
  - Histologically confirmed, unresectable, DLL3-expressing advanced solid tumor
- Key exclusion criteria
  - Prior systemic therapy; surgically/medically castrated
  - Eastern Cooperative Oncology Group (ECOG) performance score (PS) ≥ 2
  - Patient has received > 1 prior systemic therapy

RESULTS
- As of 30 June 2017, 63 treated patients had data available (D6.5/SC-DR002)
- The last cleared dose was 0.3 mg/kg Rova-T and the MTD has not been reached

PATIENT DISPOSITION AND DOSES
- Full Dose Escalation: 21 patients (33%)
- Dose Escalation: 12 patients (19%)
- Expansion cohorts: 30 patients (47%)

SAFETY
- An adverse event (AE) is shown in Table 5
- 45 patients had at least one AE (Table 5)

PATIENT CHARACTERISTICS
- Median age (range): 62 (21-82)
- Sex: Male, 41 (65%)
- Female, 22 (35%)
- ECOG PS: 0, 45 (71%)
- 1, 14 (22%)
- Key inclusion criteria
- Histologically confirmed, unresectable, DLL3-expressing advanced solid tumor
- Key exclusion criteria
- Prior systemic therapy; surgically/medically castrated
- ECOG PS ≥ 2
- ≥ 1 prior systemic therapy

CONCLUSIONS
- Rova-T is tolerated at the doses tested so far and the antitumor activity observed in Phase 1 with SCLC
- Continuous reduction in tumor burden and confirmed responses in DLL3-expressing advanced solid tumors beyond SCLC
- Preliminary safety and efficacy data of Rova-T warrant continued study in these disease populations

REFERENCES
- Corresponding author email: rahulagarwal5@ms cuffs.com
- Additional information in electronic supplementary information

ACKNOWLEDGEMENTS
- The MTD has not been reached in any disease cohort and dose escalation is ongoing
- Reduction in tumor burden and confirmed responses have been observed for Rova-T in DLL3-expressing advanced solid tumors beyond SCLC
- Preliminary safety and efficacy data of Rova-T warrant continued study in these disease populations

Table 1. Patient Demographics

Table 2. Patient Characteristics

Table 3. Dosing Cohorts

Table 4. Overview of AEs

Table 5. Overall AEs

Table 6. Serious AEs

Table 7. Characteristics of Exemplary Patients