Preliminary results from a first-in-human trial of AMT-116, a topoisomerase I inhibitor containing antibody-drug conjugate (ADC), in patients with advanced solid tumors.

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Background

CD44v9 is a tumor-associated antigen highly expressed in various solid tumor types including head and neck, lung, esophageal, pancreatic, colorectal, breast, bladder, hepatic, cervical, and gastric cancers. AMT-116 is a first-in-class antibody-drug conjugate (ADC) targeting CD44v9, by conjugating a novel topoisomerase I inhibitor, belotecan derivative named KL610023 (Sichuan Kelun-Biotech) to a humanized anti-CD44v9 immunoglobulin G1 (IgG1) antibody via a hydrolysable linker with an average drug-to-antibody ratio of 7-8..

Aim

Primary Objectives:
- To determine the MTD and the RP2D of AMT-116
- To assess safety and tolerability of AMT-116

Secondary Objectives:
- To evaluate the preliminary anti-tumor activity of AMT-116
- To evaluate the PK profile of AMT-116
- To evaluate the immunogenicity of AMT-116

Exploratory objectives:
- To assess biomarkers related to AMT-116 response, especially CD44v9 expression

Results

As of Feb 1, 2024, eight pts (4 pts at 1.5 mg/kg, 3 pts at 3 mg/kg and 1 pt at 5 mg/kg) have been treated in Australia and pts at 1.5 mg/kg and 3 mg/kg completed the 28-day dose-limiting toxicity (DLT) evaluation period. No DLT events were observed, and the maximum tolerated dose (MTD) has not been reached. Treatment related adverse events (TRAEs) were reported in 5 pts out of 8. The most common TRAEs were fatigue (n=3) and nausea (n=3). Only one Grade 3 TRAE (leukopenia) was reported. There were no Grade 4 or 5 TRAEs or treatment-related SAEs. Seven pts have completed at least one post-treatment tumor assessment. At dose level 3 mg/kg, one pt with anal squamous cell carcinoma achieved unconfirmed PR with a 31% tumor shrinkage and one pt with hepatocellular carcinoma achieved SD with a 23% tumor shrinkage from baseline. Subject enrollment in 5 mg/kg is underway.

Method

This is an ongoing first-in-human, non-randomized, open-label, multicenter, Phase 1 study designed to evaluate the safety, tolerability, pharmacokinetics, and preliminary anti-tumor activity of AMT-116 in patients (pts) with advanced solid tumors, unselected for target expression. Pts received escalating doses of AMT-116 Q2W starting from 1.5 mg/kg guided by the Bayesian logistic regression model (BLRM) following escalation with overdose control (EWOC) principle.

Conclusion

These preliminary data indicate that AMT-116 is well tolerated at the first two dose levels in patients with heavily pretreated advanced solid tumors. Dose escalation is ongoing. Clinical trial information: NCT05725291.

References

Publication: Journal of Clinical Oncology
Volume 42, Number 16_suppl
https://doi.org/10.1200/JCO.2024.42.16_suppl.e15010

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