First-in-human, first-in-class study of the CD44v6 inhibitor AMC303 as monotherapy in patients with advanced epithelial tumors

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Background: CD44v6 is an isoform of the CD44 family of transmembrane glycoproteins. High CD44v6 expression in epithelial cancer correlates with tumor growth, invasion, metastasis, and recurrence. CD44v6 is a co-receptor of the receptor tyrosine kinases c-Met, RON and VEGFR-2. Inhibition of CD44v6 blocks RTK activation and intracellular signaling processes. AMC303 is a highly selective inhibitor of CD44v6 with strong in vivo and in vitro anti-tumor activity.

Methods: This is a Phase I/Ib open label, non-randomized, multi-center study for intracellular signaling processes. AMC303 is a highly selective inhibitor of CD44v6 with strong in vivo and in vitro anti-tumor activity.

Results: 26 patients with a total of 11 different cancer types were treated in 6 dose levels with colorectal cancer as most frequent type. AMC303 infusions were very well tolerated, most drug-related AEs were grade 1 and 2 (in 46% of patients). No related SAEs were reported. Most frequently reported related events were infusion related reactions and hypersensitivity (grade 1-2, in 22% of patients), followed by nausea, diarrhea and fatigue. MTD was not achieved. PK analysis revealed a linear dose-exposure relationship. AMC303 was demonstrated to be well-tolerated with a favorable PK profile. A comprehensive biomarker program with paired tumor biopsies and plasma samples was established.

Conclusions: AMC303 was demonstrated to be well-tolerated with a favorable PK profile. Part 2 is designed to test anti-tumor activity, including patients with high expression of CD44v6 in specific tumor types.

Clinical trial identification: NCT03009214.

Legal entity responsible for the study: Amcure GmbH.

Funding: Amcure GmbH.

Disclosure: P. Ehmer: Employee: Pharmaceutus GmbH. A. Martin, H.K. Bender, K. Dembowski: Employee: Amcure GmbH. All other authors have declared no conflicts of interest.