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Abstract CT008: First-in-human study of SYS6010, a novel EGFR targeting antibody drug conjugate (ADC) for patients with advanced solid tumors FREE

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Abstract

Background:

SYS6010 is a novel ADC comprising of an anti-epidermal growth factor receptor (EGFR) humanized IgG1 monoclonal antibody conjugated to topoisomerase I inhibitor JS-1 via a cleavable glycine-glycine-phenylalanine-glycine tetrapeptide linker.

Methods:

This multicenter, open-label, phase 1 study evaluated the safety, tolerability and preliminary efficacy of SYS6010 in patients with advanced solid tumors who had failed or were intolerant to standard treatment. The study consisted of two parts, dose escalation, PK expansion (part 1) and dose expansion (part 2), part 1 used a 3+3 dose-escalation design with six dose levels of SYS6010 (0.6, 1.8, 3.6, 4.8, 5.6 and 6.4 mg/kg) administered intravenously every 3 weeks and PK expansion. Part 2 was dose expansion at effective doses identified in part 1. The primary endpoints were safety, maximum tolerated dose (MTD) and recommended phase II dose (RP2D).

Results:

As of December 26, 2024, 232 patients received ≥ 1 dose of SYS6010. Most frequent cancer type was non-small cell lung cancer (NSCLC, n=137). The median (range) prior anti-cancer drug therapy regimen was 3 (1-11). One dose-limiting toxicity (grade 4 thrombocytopenia) occurred at 6.4 mg/kg. MTD was not reached. 213 (91.8%) patients had treatment-related adverse events (TRAEs) with ≥ grade 3 TRAEs at 47%. The most common (all grade/≥ grade 3) TRAEs were

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leukopenia (47.8%/20.7%), anemia (46.1%/7.3%), nausea (46.1%/0.9%), thrombocytopenia (44.8%/13.8%), neutropenia (42.7%/23.7%), decreased appetite (41.8%/1.7%), asthenia (41.8%/2.2%), vomiting (33.2%/1.3%), rash (26.3%/0.4%), and alopecia (22.8%/0%). 174 patients were efficacy evaluable. The objective response rate (ORR) and disease control rate (DCR) were 32.8% (95% CI 25.85-40.27) and 86.2% (95% CI 80.18-90.96), respectively. The ORR and DCR in ≥ 4.8 mg/kg groups were 39.1% (45/115) and 78.3% (90/115), respectively. The ORR and DCR in ≥ 4.8 mg/kg groups in EGFR-mutant nonsquamous NSCLC (nsq-NSCLC) were 50% (27/52) and 92.3% (48/52), respectively. In the EGFR-mutant NSCLC subjects who failed prior EGFR tyrosine kinase inhibitors (TKIs), the ORR and DCR were 90% (9/10) and 100% (10/10), respectively, and the ORR and DCR were 41.5% (17/41) and 90.2% (37/41) for those who failed prior EGFR TKI as well as a platinum-based chemotherapy. In EGFR wild-type nsq-NSCLC patients who failed both immunotherapy and chemotherapy, the ORR and DCR were 50% (3/6) and 83.3% (5/6) in ≥ 4.8 mg/kg groups, respectively. The Cmax and AUC of JS-1 were significantly lower than those of ADC and total antibody, indicating SYS6010 was stable in the circulation. The Cmax and AUC of ADC increased linearly with doses ranging from 0.6 to 6.4 mg/kg.

Conclusions:

SYS6010 demonstrated a tolerable safety profile with promising efficacy in patients with advanced solid tumors, particularly in nsq-NSCLC subjects with EGFR TKI resistance or EGFR wild type.

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