Clinical trials in progress

A PHASE 1 EVALUATION OF TEBOTELIMAB, A BISPECIFIC PD-1 X LAG-3 DART® MOLECULE, IN COMBINATION WITH MARGETUXIMAB IN PATIENTS WITH ADVANCED HER2+ NEOPLASMS

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Methods This study characterizes safety, PK/PD, and preliminary antitumor activity of tebotelimab plus margetuximab in patients with advanced HER2+ malignancies. A one-step 3+3 dose escalation phase of tebotelimab (300 and 600 mg) combined with margetuximab 15 mg/kg, both every 3 weeks, was followed by cohort expansion of patients with breast, gastric or gastroesophageal, and other HER2+ tumors.

Results At data-cutoff, 31 patients (2.0 median lines of prior therapy; 64.5% with prior HER2-directed therapy) were treated. Median duration of treatment is 10.3 weeks with 17 patients remaining on treatment. No maximum tolerated dose was defined. Treatment-related adverse events (TRAEs) occurred in 23/31 (74.2%) patients, most commonly diarrhea (n=6), nausea, ALT increased (n=5, each), AST increased, and myalgia (n=4, each). The rate of Grade 3 TRAEs was 19.4%, with no Grade 4–5 TRAEs observed. Immune-related AEs were consistent with events observed with anti-PD-1 antibodies and were manageable with supportive treatment. Among 20 response-evaluable patients (i.e., received on-treatment scan), 8 objective responses (6 confirmed) per RECIST v1.1 have been observed, including a confirmed complete response (cholangiocarcinoma) and 7 partial responses (breast [2], microsatellite stable colorectal cancer [2], esophageal adenocarcinoma [1], ovarian cancer [1], and microsatellite stable gastroesophageal junction carcinoma). Immunohistochemistry (IHC) of available baseline tumor specimens (n=17) demonstrated low PD-L1 expression with combined positive scores of either 0 (n=16) or 1 (n=1, colorectal cancer). Investigations into other potential correlative biomarkers, including LAG-3 and PD-1 by IHC and gene expression profiling by NanoString, remain ongoing.

Conclusions Tebotelimab in combination with margetuximab has demonstrated an acceptable safety profile and encouraging early evidence of anti-tumor activity, with a preliminary overall response rate (ORR) of 40% (8/20) [including unconfirmed responses] among late-line patients with various advanced HER2+ malignancies.

Trial Registration NCT03219268

Ethics Approval This study was approved by each Institution’s Ethics Board prior to enrollment of subjects.

REFERENCE


A193