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Envafolimab (KN035) in advanced tumors with mismatch-repair deficiency.

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Abstract Disclosures

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Background:
KN035 is a novel fusion protein of humanized anti-PD-L1 single domain antibody and human IgG1 Fc formulated for subcutaneous injection. This open-label phase II study evaluated the safety and antitumor activity of KN035 in patients with advanced microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) cancer.

Methods:
The study included patients aged ≥18 years with previously treated MSI-H/dMMR colorectal cancer (CRC) or other advanced solid tumors. MSI-H/dMMR status was assessed centrally for CRC and gastric cancer (GC) and locally for other tumors. KN035 was administered at 150 mg once weekly until progression, unacceptable toxicity, or withdrawal. Tumor assessments were every 8 weeks. The primary endpoint was the objective response rate per RECIST v1.1 by independent radiology review. The primary efficacy population (PEP) included patients with CRC who failed fluoropyrimidine (F), oxaliplatin (O), and irinotecan (I) plus those with advanced GC who had failed at least one prior systemic treatment. Th Print a planned interim analysis performed after the first 50 patients in the PEP had at least two on-study tumor assessments (PEP_i).

Results:
As of December 17, 2019, 103 patients with MSI-H/dMMR advanced cancers were enrolled at 25 centers in China. The PEP_i included 39 patients with CRC and 11 with GC, with a median follow-up of 7.5 months. The overall population included 65 patients with CRC (24 had prior therapy with F and O or I), 18 with GC, and 20 with other tumors, with a median follow-up of 6.7 months. The confirmed objective response rate was 30% (95% CI: 17.9%, 44.6%) in the PEP_i, 54.2% (95% CI: 32.8%, 74.4%) in the CRC patients who had prior therapy with F and O or I, and 34.0% (95% CI: 24.9%, 44.0%) in the overall population. Of patients who had an objective response at the interim analysis, 80% of those in the PEPi, 84.6% of CRC patients who had prior therapy with F and O or I, and 85.7% of those in the overall population were still responding at the time of data cutoff. Median progression-free survival was 6.6 months in both the PEP_i and the overall population. Median overall survival was not

reached in either population. Fourteen (13.6%) patients had grade 3–4 treatment-related adverse events. No grade 5 treatment-related adverse events, pneumonitis, or colitis were reported. Local injection-site reactions, all grade 1 or 2, were reported in nine patients.

Conclusions:

Envafolimab demonstrated durable anti-tumor activity with a manageable safety profile in patients with previously treated advanced MSI-H/dMMR cancer. Clinical trial information: NCT03667170.