Envaflolimab (KN035) in advanced tumors with mismatch-repair deficiency

Lin Shen1, Jian Li1, Yanhong Deng2, Weijie Zhang3, Aiping Zhou4, Weijian Guo5, Jianwei Yang5, Ying Yuan5, Lianjuan Zhu5, Shukui Qin5, Silong Xiang6, Haolan Lu1, John Gong7, Ting Xu8, and David Liu1
1Beijing Cancer Hospital, Beijing, China; 2The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; 3The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; 4Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China; 5Fudan University Shanghai Cancer Center, Shanghai, China; 6Fujian Provincial Cancer Hospital, Fuzhou, China; 7The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China; 8Liangang Cancer Hospital Nanyang, China; 9The 81 Hospital of the Chinese people’s Liberation Army, Nanyang, China; 103Medicones Co. Ltd, Sichuan, China; 11Alphanab Co. Ltd, Suzhou, China.

Background:
- Envaflolimab (KN035), a novel subcutaneously administered PD-L1 single domain antibody, showed acceptable safety and encouraging antitumor activity in preclinical and early clinical studies.
- Microsatellite instability-high or mismatch repair deficient (MSI-H/dMMR) results in exceptionally high number of mutations/mutant neoantigens and predicts sensitivity to PD-(L)1 blockade regardless of cancers’ tissue of origin.
- Patients with advanced MSI-H/dMMR cancer who failed standard of care have no satisfactory alternative treatment options and poor prognosis.
- Pembrolizumab and nivolumab have been approved for the treatment of patients with previously treated dMMR/MSI-H advanced cancers. However, no PD-(L)1 inhibitors has been approved in China.

Methods:
- This is a single arm, pivotal, multicenter, phase 2 study performed in China to evaluate efficacy and safety of envaflolimab in subjects with previously treated dMMR/MSI-H advanced cancer.

Key Eligibility Criteria
Age ≥ 18 years
Locally advanced or metastatic solid tumor
Centrally confirmed MSI-H for colorectal cancer (CRC) and gastric cancer (GC).
Centrally confirmed dMMR for other tumors
ECOG PS 0–1
At least 1 line of therapy prior to study entry
No concomitant treatment with another immunotherapy
No prior systemic therapy

The primary efficacy population (PEP) included subjects with CRC who had failed fluoropyrimidine (F), oxaliplatin (O), and irinotecan (I) plus those with advanced GC who had failed at least one prior systemic treatment.

The report is based on a pre-planned analysis after the first 50 subjects in the PEP had at least two on-study tumor assessments (PEP).

Results:
- From August 22, 2018 to December 5, 2019, 103 subjects with MSI-H/dMMR advanced cancers were enrolled at 25 centers.
- The PEP included 39 subjects with CRC and 11 with GC, with a median follow-up of 7.5 months. The median number of prior systemic treatment was 3.

- The overall population (n=103) included 65 subjects 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 median number of prior systemic treatment was 2.
- The confirmed ORR (BIRC) was 34.0% (35/103, 5 CRs and 30 PRs) in overall population.

Table 1. Efficacy results in subjects who had completed ≥2 on-study tumor assessments

Table 2. Drug Related TEAEs

Conclusion:
- Envaflolimab demonstrated robust durable antitumor activity in patients with previously treated advanced MSI-H/dMMR cancer, a population with high unmet need for effective treatment options in China.
- Confirmed ORR was 30.0%, 35.0% and 34.0% in PEP, other tumors and overall population, respectively.
- Median DoR not reached with 6-month DoR of 71.9%, 100% and 84.1% in PEP, other tumors, and overall population, respectively.
- Median OS not reached with 12-month OS rates of 63.7%, 76.8% and 72.4% in PEP, other tumors, and overall population, respectively.
- Safety profile was similar to other PD-L1 antibodies but without infection reactions. No colitis or pneumonitis case was reported in the study.
- The data support envaflolimab as a new promising and convenient treatment option with durable benefit for patients with heavily previously treated advanced MSI-H/dMMR cancer.

References
• Li ET al. 2018 ASCO annual meeting, Abstract 2609.
• Shimizu T et al. 2019 ASCO annual meeting, Abstract 2609.

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