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Phase I/II study of eprenetapopt (APR-246) in combination with pembrolizumab in patients with solid tumor malignancies

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Background

Eprenetapopt is a small molecule that stabilizes the active form of p53 and increases oxidative stress, resulting in tumor cell apoptosis and ferroptosis and alterations in the tumor microenvironment including immune modulation. In preclinical models, eprenetapopt in combination with anti-PD1 therapy significantly improved tumor growth control and survival. We report preliminary safety and efficacy data from the phase 1/2 study of eprenetapopt and pembrolizumab.

Methods

A safety lead-in with a 3+3 dose de-escalation design for patients (pts) with advanced solid tumors with known tumor *TP53* mutation status (mutant and WT are included) is followed by expansion cohorts in pts with NSCLC (prior anti-PD1/PDL1 required), gastric/GEJ (GC) and urothelial cancer (UC) (GC and UC were anti-PD-1/PD-L1 therapy naïve). Primary objective is to establish safety and maximum tolerated dose (MTD) of the combination. Primary endpoints include dose-limiting toxicities (DLTs) and adverse events (AEs).

Results

As of April 7, 2021, 20 pts have been enrolled in the study (6 in the safety cohort and 14 in the expansion cohorts: 2 GC, 2 UC, 10 NSCLC) with 18 pts having at least one *TP53* mutation. Pts received a median of 4 prior lines of therapy; all pts had ECOG PS≤ 2. No DLTs were reported in the safety cohorts. The dose of eprenetapopt of 4.5 g/day IV D1-4 and pembrolizumab 200mg IV D3 Q3W was established as the RP2D. The most common (>4pts) AEs included nausea (7), abdominal pain (5), fatigue (5), dizziness (5), decreased appetite (5). Treatment-related AEs (all grades) (>2pts) included nausea (6), vomiting (4), fatigue (4), dizziness (4), and decreased appetite (3). The majority of advanced grade AEs and SAEs were unrelated and associated with disease progression. There were no treatment discontinuations due to AEs. Two pts with *TP53* mutant NSCLC who received prior anti-PD-1/PD-L1 therapy demonstrated reductions in target lesion size of 27% and 8.2%, respectively, at the first disease assessment.

Conclusions

The combination of eprenetapopt and pembrolizumab is safe and tolerable. Early signals of anti-tumor activity are observed. The expansion cohorts of the trial continue to enroll.

Clinical trial identification

NCT04383938.

Legal entity responsible for the study

Aprea Therapeutics.

Funding

Aprea Therapeutics.

Disclosure

H. Park: Financial Interests, Institutional, Sponsor/Funding: Aprea Therapeutics. X. Gao: Financial Interests, Personal, Advisory Board: Exilixis. D. Hickman: Financial Interests, Personal and Institutional, Full or part-time Employment: Aprea Therapeutcs. P. Gallacher: Financial Interests, Personal and Institutional, Full or part-time Employment: Aprea Therapeutcs. E. Attar: Financial Interests, Personal and Institutional, Full or part-time Employment: Aprea. All other authors have declared no conflicts of interest.