Safety/tolerability and antitumor activity of sitravatinib plus tislelizumab in patients with PD-(L)1-refractory/resistant unresectable or metastatic melanoma from a Phase 1b study

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Background:
Sitravatinib, a selective multiple-target tyrosine kinase inhibitor, reduces the number of myeloid-derived suppressor and regulatory T cells and increases the ratio of M1/M2-polarized macrophages, which may augment antitumor responses. Tislelizumab, an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages, has shown clinical activity in patients with advanced solid tumors, including melanoma. This Phase 1b study assessed safety/tolerability and antitumor activity of sitravatinib + tislelizumab in advanced solid tumors (NCT03666143). We report results from the melanoma cohort.

Methods:
Eligible patients (pts) had unresectable or metastatic melanoma that progressed on or after prior first-line anti-PD-1/PD-L1 monotherapy. Pts received oral sitravatinib 120 mg once daily and tislelizumab 200 mg IV Q3W until disease progression, unacceptable toxicity, death or withdrawal. The primary endpoint was safety/tolerability and key secondary endpoints were investigator-assessed objective response rate (ORR), disease control rate (DCR), and progression-free survival (PFS).

Results:
As of March 29, 2021, 25 pts were enrolled; 10 pts (40.0%) remained on treatment. Median study follow-up was 9.6 months (range: 5.6–18.8). Median age was 51 years (range: 23–79), 52.0% of pts were male and all pts received one prior line of PD-(L)1 treatment. Treatment-emergent adverse events (TEAEs) of any Grade/≥ Grade 3 were reported in 100.0%/52.0% of pts. Serious TEAEs were observed in 12.0% of pts (n=3) and no TEAE led to death. The most common ≥ Grade 3 TEAE was hypertension (n=4;16.0%). Confirmed ORR was 36.0% (95% CI 18.0–57.5) with one pt

achieving a complete response and eight pts a partial response. DCR was 88.0% (95% CI 68.8–97.5) and median PFS was 6.7 months (95% CI 4.1– not evaluable).

Conclusions:

With a longer follow-up period, the combination of sitravatinib + tislelizumab showed a manageable safety/tolerability profile and demonstrated antitumor activity in patients with R/R unresectable or metastatic melanoma previously treated with a PD-(L)1 inhibitor.