
Safety/tolerability and preliminary 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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Objective:

Sitravatinib, a spectrum-selective tyrosine kinase inhibitor, reduces the number of myeloid-derived suppressor cells and regulatory T cells while increasing the ratio of M1/M2-polarized macrophages, which may overcome an immunosuppressive tumor microenvironment and augment antitumor responses. Tislelizumab, an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, 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 had unresectable or metastatic melanoma refractory/resistant to PD-(L)1 inhibitors and had not received other prior immunotherapy (eg, anti-CTLA-4, -OX40, or -CD137) or anti-BRAF/MEK therapy. Patients received oral sitravatinib 120 mg once daily and tislelizumab 200 mg IV Q3W until a discontinuation criterion was met. The primary endpoint was safety/tolerability; key secondary endpoints included investigator-assessed objective response rate (ORR), disease control rate (DCR), and progression-free survival (PFS).

Results:

As of Oct 13, 2020, 25 patients were enrolled; 16 patients (64%) remained on treatment. All patients received 1 prior line of PD-(L)1 therapy, median age was 51 years (range: 23–79), and baseline histology included cutaneous (n=12; 48%), acral (n=7; 28%), and mucosal (n=4; 16%) subtypes. Median study follow-up was 5.5 months (range: 1.5–13.3).

Adverse events (AEs) were reported in 25 patients (100%); the most commonly reported Grade ≥ 3 AE was hypertension (n=3; 12%). Serious AEs were reported in 4% (n=1/25) of patients. Dose reductions of sitravatinib due to AEs occurred in 13 patients. No AEs led to death. Six patients achieved a confirmed partial response. Confirmed ORR was 24.0% (95% CI: 9.36–45.13); DCR was 88.0% (95% CI: 68.78–97.45). Median PFS was 6.7 months (95% CI: 4.07– not evaluable).

Conclusion:

Sitravatinib + tislelizumab had a manageable safety/tolerability profile and demonstrated antitumor activity in patients with refractory/resistant unresectable or metastatic melanoma previously treated with a PD-(L)1 inhibitor. Further investigation is warranted.