Pharmacodynamics and Genomic Profiling of Patients Treated With Cabiralizumab + Nivolumab Provide Evidence of On-Target Tumor Immune Modulations and Support Future Clinical Applications

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Abstract: This study evaluated patients with advanced malignancies treated with cabiralizumab + nivolumab and provided evidence of on-target tumor immune modulations and gene expression changes. CSF-1 concentration increased in treated patients, while nonclassical monocytes decreased. TMB was low in responders. Gene expression profiling revealed on-target immune modulations. These findings support further clinical development of cabiralizumab + nivolumab.

Methods: Patients (N = 282) with advanced solid tumors were treated with cabiralizumab (1 mg/kg Q2W) + nivolumab (3 mg/kg Q2W). Pharmacodynamics and gene expression were assessed, with treatment-related adverse events monitored (March 1, 2018, data cutoff). Immune modulations were measured in peripheral blood mononuclear cells (PBMCs).

Results: CSF-1 concentration increased in patients treated with cabiralizumab doses ≥ 4 mg/kg + nivolumab 3 mg/kg Q2W. Nonclassical monocytes decreased consistently with the Q2W regimen but varied with the Q3W regimen. Tumor pharmacodynamic changes were observed, with increases in CSF-1R, CD163, and CD68. Gene expression profiling demonstrated changes in immune-related genes.

Conclusions: This study provided evidence of on-target tumor immune modulations with cabiralizumab + nivolumab. Gene expression changes supported further clinical development of this combination in advanced malignancies.

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