Abstract #213773

Pharmacodynamics (PD) and genomic profiling of pts treated with cabiralizumab (cabira) + nivolumab (NIVO) provide evidence of on-target tumor immune modulations and support future clinical applications.

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Background: Colony stimulating factor 1 receptor (CSF-1R) signaling supports recruitment, development, and maintenance of immune suppressive macrophages within the tumor. Combining anti-CSF-1R with anti-PD-1 showed enhanced efficacy in preclinical models. Cabira, a humanized IgG4 monoclonal antibody, disrupts CSF-1R binding to ligands CSF-1 and IL-34, thus blocking receptor activation. We report immunohistochemistry (IHC) and transcriptomic evidence of on-target PD effects of cabira + NIVO in treated pts, as well as the first insight into genotypic characteristics of pancreatic tumors exhibiting durable PRs with cabira + NIVO (Wainberg et al. J Immunother Cancer 2017;5(suppl 2) [abst O42]).

Methods: PD activity of cabira + NIVO in pts with advanced tumors treated in a ph 1a/b trial (NCT02526017) was evaluated using peripheral and tumor biomarkers.

Results: Cabira + NIVO induced increases in serum CSF-1 and decreases in peripheral nonclassical monocytes sustained during the 2-week dose interval. IHC analysis of pre- and on-treatment biopsies across tumor types showed increases in CD8 T-cell infiltrates and decreases in macrophage markers CSF-1R and CD163. Transcriptomes of paired biopsies showed increased CD8 and cytolytic gene signatures with concurrent increased expression of M1 macrophage-associated genes, supporting blockade of CSF-1R–driven M2 responses. Genomic analyses demonstrated 91 of 94 pts with low tumor mutation burden (TMB) below 10 mutations/megabase with only 1 microsatellite instability tumor identified. Responses were observed across tumor types. Of note, in the 4 PRs observed in pts with pancreatic cancer, all were microsatellite stable (MSS) and low TMB.

Conclusions: Orthogonal IHC and transcriptome-wide analyses demonstrated cabira-mediated CSF-1R blockade in the periphery and tumor microenvironment in pts with advanced cancer. Ongoing analyses include identification of transcriptomic signatures associated with response. These data support further clinical development of cabira + NIVO in multiple indications, including MSS pancreatic cancer (NCT03336216).

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