

**Abstract Title: The rationale for the combination of the monoclonal antibody NEO-201 with Immune Checkpoint Inhibitors (ICI)**

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NEO-201 is a humanized IgG1 mAb which binds core 1 O-glycans and has demonstrated antibody-dependent cell-mediated cytotoxicity (ADCC) activity against cancer cells expressing core 1 O-glycans. NEO-201 has been shown to both target and kill cancer cells, neutrophils, and immune suppressor cells (iSCs), including regulatory T cells (Tregs) and granulocytic myeloid-derived suppressor cells (gMDSCs) via ADCC and complement-dependent cytotoxicity. Resistance to PD-1/PDL1 blockade may be due to accumulation of iSCs in the tumor microenvironment. In Phase I clinical trial we observed that NEO-201 also binds to circulating regulatory T cells (cTregs) and cause a reduction of the quantity of cTregs in cancer patients with stable disease (SD). One of the reasons of the low response rates and resistance to PD-1/PD-L1 blockade in solid cancers may be due to the activity of Tregs in the tumor microenvironment (TME). The reduction in the percentage of cTregs following NEO-201 treatment supported the rationale of the ongoing phase II clinical trial at the National Cancer Institute (NCI), evaluating the efficiency of the combination of NEO-201 with pembrolizumab in adults with checkpoint inhibitors treatment-resistant solid tumors. Based on the preliminary data evaluating both Tregs and gMDSCs pre and post NEO-201 therapy, additional studies combining NEO-201 with other ICI's are being explored in tumor types including gastric cancer.