Background Humanized IgG1 mAb NEO-201 binds core 1 O-glycans and showed antibody-dependent cell-mediated cytotoxicity (ADCC) activity against cancer cells expressing core 1 O-glycans. NEO-201 kills 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. Elevated neutrophil-to-lymphocyte ratio (NLR) correlates with poor prognosis. We evaluated post-treatment NLR and depletion of gMDSCs as prognostic markers in patients treated with NEO201 and pembrolizumab.

Methods PBMCs and serum from cancer patients on the Phase II trial combining NEO-201 with Pembrolizumab (NCT03476681) were used to evaluate the percentage of circulating gMDSCs (flow cytometry) and arginase-1 levels (ELISA). Patients with chemoresistant solid tumors, who were resistant to prior checkpoint inhibitor therapy, received NEO-201 1.5mg/kg every 2 weeks with pembrolizumab 400mg IV every 6 weeks (1 cycle), and were imaged for response every 2 cycles. gMDSCs percentage in PBMCs and Arginase-1 levels in serum were analyzed before treatment (C1D1), 14 days after first infusion with NEO-201 (C1D15), before cycle 2 (C2D1), and before of cycle 3 (C3D1). gMDSC population was defined as HLA-DR+/CD33+/CD15+/CD14-/CD66b+. Results We compared cancer patients with SD and PD at first radiological assessment. Among patients with SD, 1 patient (SD > 8 months) showed reduced gMDSCs (93.86%) at C3D1 compared to baseline (0.014% vs 0.228%) (figure 1). Similarly, another patient with SD showed a marked reduction of gMDSCs (87.42%) at C1D15 compared to C1D1 PRE (0.074% vs 0.588%). The other patient with SD > 8 months showed initial increase of gMDSCs at C1D15 and C2D1 compared to C1D1 but trended down at C3D1 (0.146% vs 0.114%). On the other hand, there was a general uptrend of circulating gMDSCs in patients with PD. Additionally, patients with PD had NLR >10 at C2D1, suggesting moderate to severe physiological stress compared to patients with SD who had NLR level <10 (table 1).

Conclusions Recent studies highlight the host’s inflammatory response in tumor development and progression of various cancers. In our study, patients with SD had a downtrend of circulating gMDSCs, arginase-1 levels and normal to mild NLR compared to patients with PD, suggestive of good prognosis for treatment with NEO-201 and pembrolizumab (figures 1 and 2). Ongoing enrollment in this clinical trial will validate these findings in larger cohorts.

Trial Registration Clinical trial information NCT03476681

REFERENCES


Ethics Approval The study was approved by NCI, NIH, Institutional Review Board (protocol code NCT03476681, first approved 2/26/2018; combination of NEO-201 and pembrolizumab approved 10/5/2021; latest update 02/13/2023) and all participants signed a written informed consent.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Abstract 879 Figure 1 Comparison of the percentage of circulating gMDSCs (HLA-DR+/CD33+/CD15+/CD14+/CD66b+) cells between 3 cancer patients with stable (SD) and 3 cancer patients with progressive disease (PD) at different time points by flow cytometry analysis. gMDSCs were gated from alive PBMCs. Data are presented as median of percentage of viable cells expressing gMDSCs markers. Positivity was determined by using fluorescence-minus-one controls.
Abstract 879 Figure 2  Comparison of the serum levels arginase-1 between 3 cancer patients with stable (SD) and 3 cancer patients with progressive disease (PD). Data are presented as median of arginase-1 serum levels.

Abstract 879 Table 1  Neutrophil-to-lymphocyte ratio (NLR). Absolute Neutrophil Count (ANC)/Absolute Lymphocyte Count (ALC) [NLR]. Correlation between NLR and physiological stress levels: 1–3 — normal, 6–8 — mild, 9–18 — moderate, and >18 — severe. Progressive disease (PD). Stable disease (SD).

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