Background Immune checkpoint blockade (ICB) has revolutionized cancer treatment; however, most patients fail to achieve the full clinical benefit of ICB. Although anti-PD-1 agents are FDA-approved for non-small cell lung cancer (NSCLC) and hepatocellular carcinoma (HCC), only a minority of patients respond clinically.1,2 This limited response is likely due, in part, to immunosuppressive factors within the tumor microenvironment (TME). Myeloid cells, specifically monocytic-derived macrophages (mo-Macs) and immature granulocytes (iPMNs), make up the majority of leukocytes in the TME and suppress anti-tumor immunity; pre-clinical work has demonstrated to date in metastatic cancer models. In this mouse models, although only modest clinical benefit has been elaborated the specific effects of these agents on the TME and immunity monitoring will be performed using multiplex and single-cell analysis platforms to define the immunodynamic effects of the therapies.

Methods This phase Ila multi-cohort, two-stage trial was designed to assess the clinical efficacy of BMS-813160 (CCR2/5 inhibitor) and BMS-986253 (anti-IL8 antibody) in patients with resectable NSCLC and HCC. The trial contains 2 cohorts (NSCLC and HCC) consisting of 5 arms (figure 1); arms A and B will enroll patients with NSCLC and arms C, D, and E will enroll patients with HCC. Patients will be treated with neoadjuvant nivolumab either alone (arm C) or in combination with BMS-813160 (arms A and D) or BMS-986253 (arms B and E). The patients will then undergo surgical resection, followed by standard-of-care adjuvant therapy in the NSCLC cohort or adjuvant nivolumab therapy in the HCC cohort. The primary endpoint for the NSCLC cohort is major pathologic response, defined as $\leq 10\%$ viable tumor at time of surgery. The primary endpoint for the HCC cohort is significant tumor necrosis, defined as $>70\%$ tumor necrosis at time of surgery. The secondary endpoints are time to surgery, safety and tolerability, radiographic response, progression-free survival, and overall survival. Tissue, blood, and stool will be collected prior to treatment and at the time of surgery. Deep immune monitoring will be performed using multiplex and single-cell analysis platforms to define the immunodynamic effects of the therapies.

Trial Registration NCT04123379

REFERENCES

Ethics Approval This trial obtained approval from the Icahn School of Medicine at Mount Sinai Institutional Review Board (#18-2373); all patients gave informed consent before participating in this trial.

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