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. This limited response is likely due, in part, to immunosuppressive factors within the tumor microenvironment (TME). Myeloid cells, specifically monocye-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 revealed that tumor-derived CCR2 ligands and interleukin-8 (IL-8) play a key role in recruiting mo-Macs and iPMNs, respectively, to the TME. Disrupting these signaling pathways appears to potentiate the role of PD-1 blockade in mouse models, although only modest clinical benefit has been demonstrated to date in metastatic cancer models. In this "window-of-opportunity" trial, patients will receive neoadjuvant nivolumab monotherapy or neoadjuvant nivolumab in conjunction with a CCR2/5 inhibitor or an anti-IL8 antibody prior to surgical resection, providing a unique opportunity to elaborate the specific effects of these agents on the TME and to identify factors that may allow clinicians to better predict response in the future.

Methods This phase Ia 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 (confirmation of the primary endpoint for the NSCLC cohort and if this cohort demonstrates ≥10% objective response rate (ORR)).

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Trial Registration NCT04123379

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.