Results N/A
Conclusions N/A
Ethics Approval The study was approved by Dartmouth-Hitchcock, Norris Cotton Cancer Center Ethics Board, approval number IRB00012031 The study was approved Sarah Cannon Cancer Research Institute, approval number IORG0000689

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0392

FIRST-IN-HUMAN PHASE 1/2A STUDY OF THE NOVEL INTERLEUKIN-8 Gmokine ligands 9 and 10 and interferon-and the half-life was reached. BMS-986218 exposure increased dose proportionally, toxicities occurred. The maximum tolerated dose has not been grade 5 TRAE (pneumonitis; 2 mg) occurred. Seven patients defined management. No grade 4 TRAEs were reported; 1 patients (12%) had grade 3 TRAEs; most resolved with proto- were pruritus (12%; 0%) and diarrhea (11%; 3%). Eight patients was associated with clinical activity in some patients. Updated part of dose escalation, BMS-986218 monotherapy treatment with paired biopsies, BMS-986218 was associated with an consistent with findings with IPI 10 mg/kg. In a subset of patients was developed to increase the effects of CTLA-4 blockade and 1 prior therapy received BMS-986218 2–70 mg intravenously Q4W. Safety, tolerability, pharmacokinetics, and pharmacodynamics were evaluated.

Results As of December 12, 2019, 65 patients (median age, 61 years [range, 24–85 years]) received BMS-986218 monotherapy. TRAEs occurred in 52% of patients; most were grade 1–2. The most common (≥10%) TRAEs (any grade; grade 3) were pruritus (12%; 0%) and diarrhea (11%; 3%). Eight patients (12%) had grade 3 TRAEs; most resolved with protocol-defined management. No grade 4 TRAEs were reported; 1 grade 5 TRAE (pneumonitis; 2 mg) occurred. Seven patients (11%) discontinued treatment due to TRAEs; 4 dose-limiting toxicities occurred. The maximum tolerated dose has not been reached. BMS-986218 exposure increased dose proportionally, and the half-life was ∼2 weeks. Increased levels of serum chemokine ligands 9 and 10 and interferon-γ indicate that pharmacodynamic changes occurred at the lowest dose tested (2 mg =0.03 mg/kg), similar to previous findings with IPI 3 mg/kg, and at higher doses (40–70 mg =0.06–1 mg/kg), consistent with findings with IPI 10 mg/kg. In a subset of patients with paired biopsies, BMS-986218 was associated with an increased gene signature linked to CD8+ T-cell infiltration and inflammation. In a highly heterogeneous population, as part of dose escalation, BMS-986218 monotherapy treatment was associated with clinical activity in some patients. Updated data based on a September 2020 data cutoff will be presented.

Conclusions BMS-986218 monotherapy demonstrated an acceptable safety profile and signs of clinical benefit in this heterogeneous patient population with select advanced cancers. Preliminary pharmacodynamic activity was consistent with enhanced effects of CTLA-4 blockade. Data from continuing dose escalation of BMS-986218 ± NIVO along with preclinical results provide support for ongoing monotherapy expansions and for BMS-986218 + NIVO expansions in patients with advanced cancer.

Acknowledgements The authors acknowledge Dr Charles Drake while at Columbia Medical Center, New York, NY, USA, for his contributions to the study.

Trial Registration NCT03110107

Ethics Approval This study was approved by the WCG Independent Review Board, approval number 20170464

REFERENCE

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0393

INTERLEUKIN-8-NEUTRALIZING MONOCLONAL ANTIBODY BMS-986253 PLUS NIVOLUMAB (NIVO) IN BIOMARKER-ENRICHED, PRIMARILY ANTI-PD-(L)1– EXPERIENCED PATIENTS WITH ADVANCED CANCER: INITIAL PHASE 1 RESULTS

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Background Interleukin 8 (IL-8) is a C-X-C chemokine that exerts protumorigenic effects in the tumor microenvironment, including recruiting immunosuppressive PMN-MDSCs and promoting angiogenesis.1–3 Elevated serum IL-8 (sIL-8) is a negative prognostic indicator in patients with solid tumors and may have predictive value in patients treated with immunotherapies.2 4 5 BMS-986253, a fully human-sequence IgG1 anti-IL-8 monoclonal antibody, binds IL-8 and prevents signaling through CXCR1/CXCR2 and has been shown to be safe in patients with advanced cancers.3 We present initial results of BMS-986253 + NIVO from a phase 1/2a trial in patients with advanced cancers who had detectable sIL-8 levels, the majority of whom had progressed on/after prior anti-PD-(L)1 (NCT03400332).

Methods During safety evaluation/dose exploration, patients with advanced metastatic solid tumors (melanoma, NSCLC, SCCHN, RCC, or UCC) and detectable sIL-8 (>10 pg/mL at screening) received BMS-986253 600 (n=16), 1200 (n=15), or 2400 mg (n=18) Q4W, or 1200 (n=12) or 2400 mg (n=59) Q2W, + NIVO 480 mg intravenously Q4W. Safety, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity were evaluated (investigator-assessed, RECIST v1.1).