A PHASE 2 UMBRELLA STUDY OF RETIFANLIMAB (INCMGA00012) ALONE OR IN COMBINATION WITH OTHER THERAPIES IN PATIENTS WITH ADVANCED OR METASTATIC ENDOMETRIAL CANCER (POD1UM-204, GOG 3038, ENGOT-EN12/NOGGO)

Background Management of advanced endometrial cancer after failure with platinum therapy remains a challenge. Tumors characterized by DNA repair abnormalities are associated with high numbers of neoantigens; immunotherapy is promising in this setting as demonstrated in studies with checkpoint inhibitors (CPI). 1-6 Overcoming emerging resistance to CPI through novel combinations is a focus of research. Retifanlimab is an investigational humanized immunoglobulin G4 monoclonal antibody that targets the programmed cell death protein 1 (PD-1) receptor on T cells and inhibits its interaction with the PD-L1 and PD-L2 ligands, thereby increasing markers of lymphocyte infiltration in the tumor microenvironment. 7 8 Retifanlimab has demonstrated antitumor activity in various tumor types and has an acceptable safety profile. 

Objectives The primary objectives of this phase 2, open-label, single-arm, umbrella study were to evaluate antitumor activity (RECIST v1.1), safety, and tolerability of ALKS 4230 monotherapy and in combination with pembrolizumab (pembro) in patients (pts) with refractory solid tumors (ARTISTRY-1). Oral presentation at: European Society for Medical Oncology Annual Meeting; September 2020; virtual.

METHODS 14 heavily pretreated patients with OC were enrolled. Patients received a median of 5 (range, 2–11) prior regimens and all were previously treated with platinum based therapy. Among 13 evaluable patients with ≥1 assessment, 9 experienced disease control and 4 experienced disease progression; median treatment duration was approximately 7 weeks. Three patients experienced an objective response, including 1 complete response, 1 partial response (PR), and 1 unconfirmed PR; all were platinum resistant and negative for BRCA mutations. Five patients experienced tumor burden reductions (table 1). Treatment-related adverse events at the doses tested have generally been transient and manageable, with the majority being grade 1 and 2 in severity. Overall, based on preliminary data, the combination with ALKS 4230 did not demonstrate any additive toxicity to that already established with pembrolizumab alone. Additional safety and efficacy data are being collected in ongoing cohorts. In the monotherapy dose escalation portion of the study, ALKS 4230 alone increased markers of lymphocyte infiltration in 1 paired melanoma biopsy (1 of 1; on treatment at cycle 2); CD8+ T cell density and PD-L1 tumor proportion score increased 5.2- and 11 fold, respectively, supporting evidence that ALKS 4230 has immunostimulatory impact on the TME and providing rationale for combining ALKS 4230 with pembrolizumab (figure 1).

Conclusions The combination of ALKS 4230, an investigational agent, and pembrolizumab demonstrates an acceptable safety profile and provides some evidence of tumor shrinkage and disease stabilization in some patients with heavily pretreated OC. This regimen could represent a new therapeutic option for these patients.

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Trial Registration ClinicalTrials.gov NCT02799095

Ethics Approval This trial was approved by Ethics and Institutional Review Boards (IRBs) at all trial sites; IRB reference numbers 16–229 (Dana-Farber Cancer Institute), MOD00003422/PH285316 (Roswell Park Comprehensive Cancer Center), 20160175 (Western IRB), i15-01394_MOD23 (New York University School of Medicine), TRIAL20190909 (Cleveland Clinic), and 000097 (ADVARRA).

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antibody against programmed cell death 1 (PD-1). In POD1UM-101, retifanlimab monotherapy demonstrated acceptable tolerability and durable clinical benefit in multiple advanced tumor types, including pretreated endometrial cancer. POD1UM-204 is designed to further investigate efficacy and safety of retifanlimab alone or in combination with other immunotherapy or targeted agents in patients with advanced/metastatic endometrial cancer.

Methods POD1UM-204 is a phase 2, multicenter, nonrandomized, open-label, umbrella study in women =18 years of age, with histologically confirmed diagnosis of advanced/metastatic endometrial cancer that has progressed on or after platinum-based chemotherapy. Patients must have an ECOG performance status =1, at least 1 measurable tumor lesion by Response Evaluation Criteria in Solid Tumors v1.1, and provide tumor tissue at baseline. Approximately 220 patients will be enrolled into 4 treatment groups: Group A–patients with MSI-H (microsatellite instability high) endometrial cancer and no prior CPI therapy (up to 100 patients) receiving retifanlimab monotherapy; Group B–patients with dMMR (deficient DNA mismatch repair) or POLE (DNA polymerase epsilon) endometrial cancer and no prior CPI therapy (up to 40 patients) receiving retifanlimab monotherapy; Group C–patients with unselected endometrial cancer and regardless of prior CPI treatment (up to 40 patients) receiving retifanlimab plus epacadostat (indoleamine 2,3-dioxygenase inhibitor); and Group D–patients with endometrial cancer and activating fibroblast growth factor receptor (FGFR1, 2 or 3) mutations or alterations outside of the kinase domain and regardless of prior CPI treatment (up to 40 patients) receiving retifanlimab plus pemigatinib (FGFR1, 2, 3 inhibitor) (figure 1). Patients can receive up to 26 treatment cycles if they continue to derive benefit and have not met criteria for withdrawal. The primary study objective is evaluating retifanlimab monotherapy antitumor activity (objective response rate [ORR] determined by independent central review [ICR]) in Group A. Secondary study objectives include assessing additional efficacy measures (duration of response, disease control rate and progression-free survival by ICR, and overall survival) in Group A; determining clinical activity (ORR by the investigator) in Groups B, C and D; and evaluating safety and tolerability of retifanlimab.

Results N/A

Conclusions N/A

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Ethics Approval The study was approved by institutional review boards or independent ethics committees of participating institutions.

Consent N/A

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Abstract 348 Figure 1 POD1UM-204 study design

349 EARLY SAFETY AND EFFICACY OF A PHASE 1/2 OPEN-LABEL, MULTI-CENTER TRIAL OF SNS-301 ADDED TO PEMBROLIZUMAB IN PATIENTS WITH ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (SCCHN)

Background Efficacy of anti-PD-1 therapy is attributed to the presence of infiltrating antigen-specific CD8+ T-cells. Despite the success of anti-PD-1 therapy, many patients with SCCHN present with immune desert or immune excluded tumors and only 13–18% of patients achieve tumor reductions. Given this low response rate, it is imperative to combine agents that generate or expand anti-tumor T cells, such as vaccines, with anti-PD-1 therapies. SNS-301 is a first-in-class, bacteriophage-based immune activating agent targeting human aspartate beta-hydroxylase (ASPH), a tumor associated antigen overexpressed in multiple tumor types. SNS-301 is a self-adjuvanted vaccine consisting of ASPH-bacteriophage engineered to express an immunogenic fragment of ASPH fused to the phage gpD coat protein, previously shown to be well tolerated and generate an immune response (Phase 1, NCT03120832). The objectives of this trial are to evaluate safety, immunogenicity and preliminary efficacy of SNS-301 in combination with pembrolizumab in patients that did not achieve tumor reductions on anti-PD-1/PD-L1 therapy alone.

Methods The study consists of an initial safety-run-in followed by a two-stage design. SNS-301 is delivered intradermally in addition to pembrolizumab in up to 30 patients with locally advanced unresectable or metastatic/recurrent SCCHN. Patients must have actively received anti-PD-1 therapy for ≥12 weeks, with a best response of stable disease (SD) or unconfirmed progressive disease (PD) per iRECIST. Patients provide pre, on-treatment and biopsies at PD (optional) to characterize the tumor microenvironment using NanoStringTM, multiplex immunochemistry, and correlate with clinical outcomes. Blood