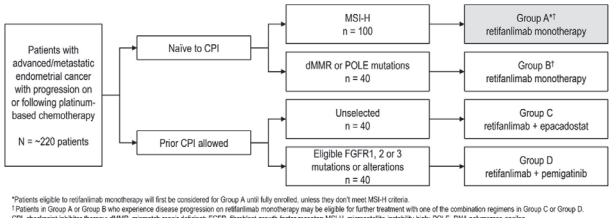
antibody against programmed cell death 1 (PD 1). In POD1UM-101, retifanlimab monotherapy demonstrated acceptable tolerability and durable clinical benefit in multiple advanced tumor types, including pretreated endometrial cancer.[7] POD1UM-204 is designed to further investigate efficacy and safety of 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.



Abstract 348 Figure 1 POD1UM-204 study design

Results N/A

Conclusions N/A

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Trial Registration ClinicalTrials. gov Identifier: NCT04463771; EudraCT 2020-000496-20

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

Consent N/A

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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)

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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 β-hydroxylase (ASPH), a tumor associated antigen overexpressed in multiple tumor types. SNS-301 is a self-adjuvanted vaccine consisting of λ-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 Nanostring™, multiplex immunohistochemistry, and correlate with clinical outcomes. Blood

samples are collected to evaluate T cell responses using flow cytometry, ELISA, ELISPOT.

Results As of July 23, 2020, 9 patients were enrolled. Median duration of ongoing anti-PD therapy was 37 weeks (range 20–101). The combination was well-tolerated with no DLTs and mostly Grade 1–2 unrelated adverse events. Two Grade 3 events were reported: hypertension (not related) and dehydration (related), the later reported as serious adverse event. Of seven patients eligible for efficacy analysis, one patient with PD-L1 negative disease had a partial response with a reduction of 29% at week 6 with deepening of the response to 43% at week 12 and one patient with progressive disease at study entry had stabilization of disease at week 6 and 12. Another two patients had stable disease for 30+ weeks and three patients had PD. Additional efficacy and immunological analyses are ongoing.

Conclusions Early data show that the combination of SNS-301 and pembrolizumab has manageable toxicity and capacity to achieve long-term disease stability and objective tumor responses.

Trial Registration NCT04034225

Ethics Approval This study has been approved by WIRB (20190628) as well as several institutional IRBs.

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351 PEMBROLIZUMAB PLUS LENVATINIB VS CHEMOTHERAPY AND LENVATINIB MONOTHERAPY FOR RECURRENT/METASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA THAT PROGRESSED ON PLATINUM THERAPY AND IMMUNOTHERAPY: LEAP-009

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Background Pembrolizumab alone and in combination with platinum-based chemotherapy have become standard first-line treatment options for recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC), and there is a growing unmet need for safe and efficacious treatment options for R/M HNSCC that has progressed on or after platinum-based chemotherapy and immunotherapy. Data from Study 111/KEYNOTE-146 showed promising antitumor activity and acceptable safety for the PD-1 inhibitor pembrolizumab given in combination with the multikinase inhibitor lenvatinib in patients with metastatic HNSCC.[1] LEAP-009 (NCT04428151), a global, randomized, open-label, phase 2 trial, will assess the efficacy and safety of pembrolizumab in combination with lenvatinib versus SOC chemotherapy, as well as the efficacy and safety of lenvatinib monotherapy, in patients with R/M HNSCC that has progressed after platinum-based chemotherapy and a PD-(L)1 inhibitor.

Methods Eligible patients are adults with histologically confirmed, locally incurable R/M HNSCC of the oral cavity, oropharynx, hypopharynx, or larynx, disease progression at any time during or after platinum-containing chemotherapy (with or without cetuximab), disease progression within 12 weeks from the last dose of treatment with ≥2 doses of a PD-(L)1 inhibitor, measurable disease based on RECIST v1.1 as confirmed by BICR, ECOG performance status of 0 or 1, and no major blood vessel invasion/infiltration. Patients will be randomized 3:3:2 to pembrolizumab (200 mg IV Q3W for up to 35 cycles) plus lenvatinib (20 mg orally once daily), investigator's choice of SOC chemotherapy (docetaxel, paclitaxel, cetuximab, or capecitabine), or lenvatinib monotherapy (24 mg orally once daily). Randomization will be stratified by PD-L1 tumor proportion score (<50% versus ≥50%) and ECOG performance status (0 versus 1). Treatment will continue until centrally verified disease progression, unacceptable toxicity, or decision to withdraw. Patients in the chemotherapy and lenvatinib monotherapy arms may be eligible to receive pembrolizumab plus lenvatinib upon disease progression. The primary endpoint is ORR according to modified RECIST v1.1 as assessed by BICR. Secondary endpoints include PFS, OS, DOR, and safety. Interim futility analysis will be conducted for the lenvatinib monotherapy arm. Tumor imaging by CT or MRI will be performed 6 weeks after randomization, every 6 weeks through year 1, and every 9 weeks thereafter. Safety will be monitored throughout the study and for 30 days after treatment end (90 days for serious AEs if no new anticancer treatment is initiated, and at any time if the AE is considered treatment-related). Recruitment is ongoing; Planned enrollment is ~400 patients.

Results N/A

Conclusions N/A

Trial Registration ClinicalTrials. gov Identifier, NCT04428151

Ethics Approval The study and protocol were approved by the Institutional Review Board or ethics committee at each site.

Consent All patients provided written informed consent to participate in the clinical trial.

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352 UPDATED CLINICAL DATA FROM THE SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (SCCHN) EXPANSION COHORT OF AN ONGOING PH1/1B STUDY OF EGANELISIB (FORMERLY IPI-549) IN COMBINATION WITH NIVOLUMAB

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Background Eganelisib is a first-in-class, oral, selective PI3K-γ inhibitor. Preclinically, eganelisib reprograms macrophages/myeloid derived suppressor cells (MDSCs) from an immune-suppressive to an immune-activating phenotype and enhances efficacy of checkpoint inhibitors. Efficacy of eganelisib + nivolumab in patients with SCCHN resistant to immediate prior anti-PD(L)1 therapy is presented.