Abstract 347 Table 1 Summary of response observations among patients with ovarian cancer

Patient	Age (years)	Prior Therapies	Max. Reduction of Target Lesions (%)	OR ^a	CA125 (U/mL) Response From Baseline	Time on ALKS 4230 (Weeks)
1	48	CBP/PAC/BEV, CDDP/GEM, CBP/PLD, PCA, CBP/DOC	70.0	CR ^b	Normalized from 282 to 24.5 at cycle 4	81 ^{+c}
2	83	CBP/PAC/DOC, CBP/DOC/NIR/TAM	76.3	PR	Normalized from 125 to 16 at cycle 4	23 ^{+c}
3	60	CBP/PAC, CBP/PLD, CBP/BEV, PAC/BEV, BEV, PLD	44.7	uPR	Reduced from 1400 to 260 at cycle 4	34
4	75	CBP/PAC, PLD/BEV, CBP/GEM, TOP, NIR	21.9	SD	Reduced from 493 to 245 at cycle 5	14 ^{+c}
5	83	CBP/PAC, CBP, CBP/PAC/CAP, CBP/PLD, CBP/PLD	18.3	SD	Normal at baseline at 10.6	21 ^{+c}

^aAs assessed by the investigator.^bCR due to node shrinkage to <10 mm short axis, which is considered normal.^cPatient is currently ongoing in the trial.

BEV, bevacizumab; CAP, capecitabine; CBP, carboplatin; CDDP, cisplatin; CR, confirmed response; DOC, docetaxel; GEM, gemcitabine; max, maximum; NIR, niraparib; OR, objective response; PAC, paclitaxel; PCA, paclitaxel albumin; PD, progressive disease; PLD, pegylated liposomal doxorubicin hydrochloride; SD, stable disease; TAM, tamoxifen; TOP, topotecan; uPR, unconfirmed partial response.

Abstract 347 Figure 1 Increased markers of lymphocyte tumor infiltration

An increase in CD3+CD8+ T cells (A, red = CD3; blue = CD8; purple = CD3+CD8+; teal = tumor marker), GranzymeB (B, red = CD8; green = granzymeB; yellow = granzymeB+CD8+; teal = tumor marker), and PD-L1 (C, red = PD-L1; blue = tumor marker) in the tumor microenvironment of a single patient was observed after the patient received monotherapy ALKS 4230

presented include antitumor activity (RECIST v1.1) and safety as of 7/24/2020. To evaluate changes in tumor microenvironment (TME), baseline and on-treatment biopsies were collected.

Results Fourteen 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.

Acknowledgements The authors would like to thank all of the patients who are participating in this trial and their families. The trial is sponsored by Alkermes, Inc. Medical writing and editorial support was provided by Parexel and funded by Alkermes, Inc.

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), TRIAL20190090 (Cleveland Clinic), and 0000097 (ADVARA).

REFERENCES

- Lopes JE, Fisher JL, Flick HL, Wang C, Sun L, Ernstoff MS, et al. ALKS 4230: a novel engineered IL-2 fusion protein with an improved cellular selectivity profile for cancer immunotherapy. *J Immunother Cancer* 2020;**8**:e000673. doi: 10.1136/jitc-2020-000673.
- Vaishampayan UN, Muzaffar J, Velcheti V, Winer I, Hoimes CJ, Rosen SD, et al. 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.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0347>

348

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)

¹Brian Slomovitz*, ²Bradley Monk, ³Katherine Moxley, ⁴Nadeem Ghali, ⁵Justyna Fronczek Sokol, ⁶Chuan Tian, ⁷Nawel Bourayou, ⁸Jalid Sehouli. ¹Florida International University, Fort Lauderdale, FL, USA; ²Saint Joseph's Hospital and Medical Center, Phoenix, AZ, USA; ³University of Oklahoma Health Sciences, Oklahoma City, OK, USA; ⁴Incyte Corporation, Wilmington, DE, USA; ⁵Incyte Biosciences International Sàrl, Morges, Switzerland; ⁶Medical University of Berlin, Berlin, Germany

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 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.

*Patients eligible to retifanlimab monotherapy will first be considered for Group A until fully enrolled, unless they don't meet MSI-H criteria.
†Patients in Group A or Group B who experience disease progression on retifanlimab monotherapy may be eligible for further treatment with one of the combination regimens in Group C or Group D.
CPI, checkpoint inhibitor therapy; dMMR, mismatch repair deficient; FGFR, fibroblast growth factor receptor; MSI-H, microsatellite instability high; POLE, DNA polymerase epsilon.

Abstract 348 Figure 1 POD1UM-204 study design

Results N/A

Conclusions N/A

Acknowledgements This study is sponsored by Incyte Corporation (Wilmington, DE).

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

REFERENCES

- Mittica G, Ghisoni E, Giannone G, et al. Checkpoint inhibitors in endometrial cancer: preclinical rationale and clinical activity. *Oncotarget* 2017;**8**:90532–544.
- Di Tucci C, Capone C, Galati G, et al. Immunotherapy in endometrial cancer: new scenarios on the horizon. *J Gynecol Oncol* 2019;**30**:e46.
- Brooks R, Fleming G, Lastra R, et al. Current recommendations and recent progress in endometrial cancer. *CA Cancer J Clin* 2019;**69**:258–79.
- Makker V, Rasco D, Vogelzang N, et al. Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer: an interim analysis of a multicentre, open-label, single-arm, phase 2 trial. *Lancet Oncol* 2019;**20**:711–8.
- Marabelle A, Le D, Ascierto P, et al. Efficacy of Pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair-deficient cancer: results from the phase II KEYNOTE-158 study. *J Clin Oncol* 2020;**38**:1–10.
- Oaknin A, Duska L, Sullivan R, et al. Preliminary safety, efficacy, and pharmacokinetic/pharmacodynamic characterization from GARNET, a phase I/II clinical trial of the anti-PD-1 monoclonal antibody, TSR-042, in patients with recurrent or advanced MSI-h and MSS endometrial cancer. *Gynecol Oncol* 2019;**154**(suppl 1):17 [Abstract 33].
- Mehner JM, Joshua AM, Lakhani N, et al. First-in-human phase 1 study of INCMGA00012 in patients with advanced solid tumors: interim results of the cohort expansion phase. *J Immunother Cancer* 2018;**6**(suppl 1):115 [Abstract P669].

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0348>

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)

¹Alain Algazi*, ²William Smith, ³Timothy Panella, ⁴Dong Shin, ⁵Marie-Louise Fjaellskog, ⁵John Celebi, ⁵Alice Drumheller, ⁵Jean Campbell, ⁵Robert Pierce, ⁶Michael Guarino.
¹University of California – San Francisco, San Francisco, CA, USA; ²New Orleans Clinical Research, Knoxville, TN, USA; ³University of Tennessee, Knoxville, TN, USA; ⁴Emory University, Atlanta, GA, USA; ⁵Sensei Biotherapeutics, Boston, MA, USA; ⁶Christiana Hospital, Newark, DE, USA

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 NanostringTM, multiplex immunohistochemistry, and correlate with clinical outcomes. Blood