Conclusions Penpulimab was shown to be highly active resulting in a high CR rate in pts with R/R cHL. With longer follow-up, CR rate for penpulimab in R/R cHL could be further increased. Penpulimab demonstrated notably lower rates of SAE, TRAE leading to discontinuation, and Grade ≥3 immune-related AEs in pts with R/R cHL.

Trial Registration NCT03722147

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0791

Abstract 791 Table 1

<table>
<thead>
<tr>
<th>IRC-assessed (N=73)</th>
<th>ORR, % (95% CI)</th>
<th>CR, %</th>
<th>DCR, %</th>
<th>DCR, median (range)</th>
<th>mDoR, median (range)</th>
<th>mPFS, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>83.0% (73.9, 91.2)</td>
<td>49.3%</td>
<td>91.8% (83.0, 96.9)</td>
<td>0% (0, 11.9)</td>
<td>6% (0, 36.5)</td>
<td>82.2% (68.5, 90.6)</td>
</tr>
</tbody>
</table>

Background Specific immune cell responses against oncogenic antigens are major determinants to achieve long-term disease control for HPV-related malignancies. We developed TG4001, a viral based vaccine against the HPV E6 and E7 antigens. Following the demonstration of its safety in phase Ib, we aimed to evaluate the antitumor activity and immune priming effects of TG4001 in combination with the PD-L1 inhibitor avelumab in HPV-related malignancies in phase II (NCT03260023).

Methods Patients (pts) with previously treated R/M HPV-16+ cancers received TG4001 at 5x10⁷ pfu SC weekly for 6 weeks, every 2 weeks up to M6, and every 12 weeks thereafter in combination with avelumab IV at 10mg/kg every 2 weeks. PBMC and tissue samples were collected longitudinally prior to and during the treatment period. Specific T cell response was assessed using ex-vivo IFNg-ELISPOT, and changes in the tumor microenvironment by phenotyping of immune infiltrate and transcriptomic analyses of immune related genes.

Results 34 pts with anal (15), oropharyngeal (8), cervical (6) or vulvar/vaginal (5) cancer, were enrolled. Median age was 61 years; the majority (88%) had received at least 1 prior line of chemotherapy (CT) with 32% having received ≥ 2 lines. 8 pts achieved confirmed response according to RECIST 1.1 (1 CR, 7 PR, ORR 23.5%). Responses were observed in all primary tumor types and across all lines of prior therapy. Liver metastases had a profound impact on outcome: ORR was 34.8% and PFS 5.6 months in pts without liver metastases (n=23) versus 0% and PFS of 1.4 months in pts with liver metastases (n=11). Consistent with phase Ib data, the combination had a favorable safety profile.

11 pts were evaluable for T-cell response at day (D) 43. 7/11 patients had vaccine-induced reactive T cells against E6, E7 or both. In particular, in the patient with CR, lesions disappearance was accompanied by the development of a strong T-cell response against E6 and E7. This response developed as early as D43 and sustained at 6 months after initiation of therapy, consistent with the durable disease-control. Increased infiltrates, expression of immune related genes and higher PD-L1 protein expression were observed across all patients suggesting a remodeling of the tumor microenvironment consistent with a switch toward a ‘hot tumor’ phenotype.

Conclusions Our study suggests that immunotherapeutic combination of TG4001 and avelumab shows valuable tumor activity in pts with previously treated advanced HPV-16+ cancers. These results warrant validation in a larger cohort of patients.

Trial Registration NCT03260023

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0793

TG4001 (TIPAPKINOCENE SOVACIVEC) AND AVELUMAB FOR RECURRENT/METASTATIC (R/M) HUMAN PAPILLOMA VIRUS (HPV)-16+ CANCERS: CLINICAL EFFICACY AND IMMUNOGENICITY

1Christophe Le Toumeau, 2Philippe Cassier, 3Frederic Rolland, 4Sebastien Salas, 5Jean Marc Limacher, 6Olivier Captain, 7Olivier Lantz, 8Ana Lalarne, 9Christina Elewghaara, 10Anne B Tavernaro, 11Hamid Makhloufi, 12Kadre Bendjama, 13Jean-Pierre Delord. 1Institut Curie, Paris, France; 2Centre Leon Bérard, Lyon, France; 3Curie Institute, Paris, France; 4Institut Bergonié, Bordeaux, France; 5CEPCM CLIP2, Toulouse, France; 6CEPCM Hôpital Timone, Marseille, France; 7Hôpitaux Civils de Colmar, Illkirch, France; 8Transgene S.A., Illkirch -Graffenstaden, France; 9IUCT Oncopole Toulouse, Toulouse, France

Background Specific immune cell responses against oncogenic antigens are major determinants to achieve long-term disease control for HPV-related malignancies. We developed TG4001, a viral based vaccine against the HPV E6 and E7 antigens. Following the demonstration of its safety in phase Ib, we aimed to evaluate the antitumor activity and immune priming effects of TG4001 in combination with the PD-L1 inhibitor avelumab in HPV-related malignancies in phase II (NCT03260023).

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Trial Registration NCT03260023

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0793

SAFETY AND EFFICACY RESULTS FROM A PHASE 1/1B STUDY OF INTRATUMORAL MK-4621, A RETINOIC ACID-INDUCIBLE GENE I (RIG-I) AGONIST, PLUS INTRAVENOUS PEMBROLIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

1Víctor Moreno, 2Caroline Gaudy-Marquete, 3Martin Wermke, 4Antoine Italiano, 5Emanuela Romano, 6Aurelien Marabelle, 7Emilee Connors, 7Heng Zhou, 8Konstantin Dobrenkov, 9Ettore Chiratsh, 10Emiliano Calvo*, 11Emiliano Calvo Aller. 1START Madrid-FJD, Hospital Universitario Fundacion Jimenez, Madrid, Spain; 2CEPCM CUP2, Timone’s Hospital, Marseille, France; 3Universitätsklinikum Carl Gustav Carus, Dresden, Germany; 4Institut Bergonié, Bordeaux, France; 5Institut Curie, Paris, France; 6Institut Gustave Roussy, Villejuif, France; 7Merck and Co., Inc., Kenilworth, NJ, USA; 8START Madrid-CIOCC, Centro Integral Onco, Madrid, Spain

Background The oligonucleotide MK-4621 selectively binds RIG-I to activate the RIG-I pathway, inducing a type 1 interferon response. In a first-in-human study (MK-4621-001, NCT03065023), intratumoral MK-4621 resulted in no dose-limiting toxicities (DLTs) and increased circulating chemokine levels and tumor expression of interferon signaling genes in patients with advanced/recurrent solid tumors. We report outcomes from an open-label, dose-escalation phase 1/1b study of intratumoral MK-4621 and intravenous pembrolizumab in patients with advanced solid tumors (MK-4621-002, NCT03739138).

Methods Participants were aged ≥18 years with histologically/cytologically confirmed advanced/metastatic solid tumors, ECOG PS 0/1, cutaneous, subcutaneous, and/or nodal lesions amenable to intratumoral injection and had received, or were intolerant to, all treatments known to
confer clinical benefit. In 3-week cycles, patients received intratumoral MK-4621 0.4, 0.6, or 0.8 mg on days 1, 8, and 15 for 6 cycles (delivered via jetPEI®, Polyplus Transfection, Illkirch, France) plus intravenous pembrolizumab 200 mg on day 1 for 35 cycles. Treatment continued until disease progression or unacceptable toxicity. The primary objective was to establish a preliminary recommended phase 2 dose based on DLTs (cycle-1), AEs, and treatment discontinuations due to AEs; AEs were graded per NCI CTCAE v4.0. Tumor imaging was performed Q9W; response was assessed by the investigator.

Results As of May 14, 2020, 30 participants received therapy with MK-4621 0.4 (n=7), 0.6 (n=5), or 0.8 mg (n=18). Median time on therapy was 57 (range, 1-365) days. The most frequent tumor types were breast (20%) and melanoma (17%); 90% of patients received ≥2 prior lines of therapy. One patient in the 0.8-mg group experienced a DLT (grade 3 treatment-related pleural effusion), which resulted in treatment discontinuation; no other patient discontinued owing to AEs. Grade 3 treatment-related AEs occurred in 1 patient (14%) at the 0.4-mg dose (pyrexia), 1 patient (20%) at the 0.6-mg dose (hypertension), and 5 patients (28%) at the 0.8-mg dose (anemia [n=2], dyspnea/pleural effusion [n=1], lymphopenia [n=1], pyrexia [n=1]). No treatment-related grade 4/5 AEs occurred. Across dose levels, the most frequently occurring treatment-related AEs were pyrexia (63%), chills (37%), cytokine-release syndrome (20%), and nausea (20%). Efficacy outcomes are below (table 1). Significant changes in blood interferon-gamma inducible protein-10 and monocyte chemotactic protein-2 were observed at each dose level, and 5 patients (28%) at the 0.8-mg dose (anemia), and 5 patients (28%) at the 0.8-mg dose (anemia [n=2], dyspnea/pleural effusion [n=1], lymphopenia [n=1], pyrexia [n=1]). No treatment-related grade 4/5 AEs occurred. Across dose levels, the most frequently occurring treatment-related AEs were pyrexia (63%), chills (37%), cytokine-release syndrome (20%), and nausea (20%). Efficacy outcomes are below (table 1). Significant changes in blood interferon-gamma inducible protein-10 and monocyte chemotactic protein-2 were observed at each dose level, and consistent with the mechanism of action of MK-4621.

<table>
<thead>
<tr>
<th>Table: Efficacy Outcomes</th>
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<tbody>
<tr>
<td>MK-4621 0.4 mg + Pembrolizumab (n=7)</td>
</tr>
<tr>
<td>Overall response, n (%)</td>
</tr>
<tr>
<td>CB</td>
</tr>
<tr>
<td>PR</td>
</tr>
<tr>
<td>SD</td>
</tr>
<tr>
<td>ORR, % (95% CI)</td>
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</table>

Conclusions The combination of intratumoral MK-4621 plus intravenous pembrolizumab had a manageable safety profile. At the highest dose level, modest antitumor activity was observed in patients treated with combination therapy.

Trial Registration ClinicalTrials.gov identifier, NCT03739138

Ethics Approval An independent institutional review board or ethics committee approved the protocol at each study site, and the trial is being conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki.

Background Angiosarcoma is a rare cancer of endothelial cells that can be aggressive and carries a high mortality. A subset of angiosarcomas are characterized by high tumor mutational burden (TMB) and UV light exposure DNA mutational signature. Isolated case reports have suggested clinical efficacy of immune checkpoint blockade in angiosarcoma; no prospective studies of immune checkpoint inhibition in angiosarcoma have been reported. We report efficacy analysis results for patients with advanced or unresectable angiosarcoma treated with ipilimumab and nivolumab as a cohort of an ongoing phase II study for rare cancers (NCT02834013).

Methods This is a prospective, open-label, multicenter phase II clinical trial of ipilimumab (1mg/kg IV q6weeks) plus nivolumab (240mg IV q2weeks) for patients with metastatic or unresectable angiosarcoma. Primary endpoint is objective response rate as assessed by RECIST v1.1, including measurable cutaneous disease that can be followed by photography. Secondary endpoints include PFS, OS, stable disease at 6 months, and toxicity. A two-stage design is used with six patients in the first stage and an additional ten patients in the second stage.

Results At data cutoff, 16 patients with angiosarcoma were enrolled. Median age was 68 years (25-81 years). Median number of prior lines of therapy was 2 (0-5). 9 patients had cutaneous primary tumors of any cutaneous site, 7 had non-cutaneous primary tumors. ORR for all patients was 25% (4/16, table 1, figure 1). Subgroup analysis revealed that 60% (3/5) of patients with primary cutaneous tumors of the scalp or face had a confirmed objective response. 6-month PFS was 38%. 75% of patients experienced an adverse event (AE), and 25% experienced a grade 3-4 AE. 68.8% experienced an immune related AE (irAE), and 2 (12.5%) developed grade 3 or 4 irAEs. Grade 3-4 irAEs were ALT and AST increase and diarrhea. There were no grade 5 toxicities.

Conclusions The combination of ipilimumab and nivolumab was well tolerated and had an ORR of 25% in angiosarcoma regardless of primary site, with 3 of 5 patients with cutaneous tumors of the scalp or face responding. Ipilimumab and nivolumab warrant further investigation in angiosarcoma.