Methods Patients (pts) with unselected PD-L1 expression were recruited into 3 cohorts: part A; 1st line, immunotherapy naïve NSCLC; part B; 2nd line, immunotherapy refractory NSCLC and part C; 2nd line immunotherapy naïve HNSCC. The study uses a Simon’s 2-stage design, with objective response rate (ORR) by iRECIST as the primary endpoint (EP). Secondary EPs include tolerability, disease control rate (DCR), progression free survival (PFS), overall survival (OS), PK, PD and immunogenicity. Fifty-eight (58) pts were recruited into stage 1. Up to additional 51 pts will be recruited if a pre-specified ORR threshold is met for the respective part. Efti is administered as 30 mg subcutaneous injection every 2 wks for 8 cycles and then every 3 wks for 9 cycles; pembrolizumab is administered at 200 mg intravenous infusion every 3 wks for up to 2 yrs. The study was approved by ethic committees and institutional review boards.

Results Between Mar 2019 and Jul 2020 88 pts were enrolled. The median age was 67 yrs (range 53-84) and 70% were male. ECOG PS 0:1 was 42% and 58% respectively. Pts from all PD-L1 tumor expression subgroups were recruited. Pts received a median of 4 (1-25) pembrolizumab and 5.5 (1-22) efti administrations. The most common (≥ 15%) treatment emergent adverse events (TEAEs) were asthenia (28%), cough (27%), decreased appetite (22%), dyspnea (21%), fatigue (18%) and diarrhea (15%). Three (3) pts discontinued due to treatment related AEs. The ORR (acc. to iRECIST) of the 58 patients enrolled into stage 1 is shown in (table1). PK profiles after the first or repeated efti dosing were in line with previous studies, with a mean Cmax at 7 ng/ml reached £ 24h. Circulating TH1 biomarkers 2 weeks after the last efti administration were increased (3 months vs. baseline) by a mean 61% and 209% for CXCL10 (Student paired t-test, p=0.02, n=31) and IFN-γ(p= 0.02, n=19), respectively.

Conclusions Efti plus pembrolizumab is safe and shows encouraging antitumor responses in NSCLC and HNSCC patients

Trial Registration NCT03625323

Ethics Approval The study was approved by relevant ethic committees and institutional review boards.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0790

Abstract 790 Table 1

ORR (acc. to iRECIST) of the 58 patients enrolled into stage 1

<table>
<thead>
<tr>
<th>Response parameter</th>
<th>Part A (1st line NSCLC, PD-1-naive)</th>
<th>Part B (2nd line NSCLC, PD-1 refractory)</th>
<th>Part C (2nd line HNSCC, PD-1-naive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>23</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>Median follow-up, months</td>
<td>24.4</td>
<td>5.5</td>
<td>9.5</td>
</tr>
<tr>
<td>ORR (n, %) (95% CI)</td>
<td>9 (52.9; 77.0)</td>
<td>1 (4.4%; 21.9)</td>
<td>7 (38.9; 64.3)</td>
</tr>
<tr>
<td>CR (n, %)</td>
<td>1 (5.3%)</td>
<td>0 (0% )</td>
<td>2 (11.1% )</td>
</tr>
<tr>
<td>DCR (n, %)</td>
<td>14 (76.5%)</td>
<td>7 (30.4%)</td>
<td>9 (50.0%)</td>
</tr>
<tr>
<td>Responses with low PD-L1 (n, %)</td>
<td>4 (44.4%; 50% PD-L1 79%)</td>
<td>0 (0% )</td>
<td>1 (25.0%; 15% PD-L1 79%)</td>
</tr>
<tr>
<td>Median PFS, months (95% CI)</td>
<td>3.6 (1.6-10.0)</td>
<td>2.1 (1.8-3.0)</td>
<td>4.26</td>
</tr>
<tr>
<td>OS rate at 9/12/15 months</td>
<td>85% / 71% / 64%</td>
<td>not yet reached</td>
<td>67% / 50% / not yet reached</td>
</tr>
</tbody>
</table>

Background Penpulimab is a humanized IgG1 mAb that blocks PD-1 binding to PD-L1. Penpulimab was engineered to eliminate FcR binding and ADCC/ADCP completely, as compared to majority of marketed IgG4 PD-1 antibodies with ADCC/ADCP activity. ADCC/ADCP effects can induce T-cell apoptosis and clearance and then compromise anti-tumor activity. The removal of FcR binding eliminates Fc receptor mediated immune-cell recruitment and activation and could potentially reduce immune-related adverse reactions. Penpulimab demonstrated a slower PD-1 antigen binding off-rate than marketed IgG4 PD-1 antibodies with ADCC/ADCP activity. ADCC/ADCP effects can induce T-cell apoptosis and clearance and then compromise anti-tumor activity. The removal of FcR binding eliminates Fc receptor mediated immune-cell recruitment and activation and could potentially reduce immune-related adverse reactions. Penpulimab demonstrated a slower PD-1 antigen binding off-rate than marketed PD-1 antibodies, which result in better cellular activity and higher receptor occupancy. Penpulimab also showed numerous contacts with N58 glycosylation on the BC loop of PD-1 which could be an advantage to facilitate interaction of PD-1 antibody and may contribute to slower binding off-rate. These structural differentiations offer more robust biological effect and enhance anti-tumor activity of penpulimab.

Methods AK105-201 (NCT03722147) is a multicenter, single-arm, open-label study of penpulimab in R/R chL. All pts received penpulimab 200 mg q2w until progression or unacceptable toxicity. Eligible pts had R/R chL after ASCT, or at least 2 lines of prior chemotherapy. The primary endpoint was ORR based on the Lugano 2014 criteria as assessed by an independent review committee (IRC). Key secondary endpoints included CR rate, DCR, PFS, duration of response (DoR), safety, and tolerability.

Results As of 10 January, 2020, the median follow-up was 6.3 months (range, 3.5 to 17.0). The anti-tumor activity of penpulimab in the 73 pts evaluable for efficacy (defined as pts who had
an opportunity to be followed for at least 16 weeks) is shown in the table 1. At data cutoff, 91.8% of responders remained ongoing and still on treatment. Treatment-related adverse events (TRAEs) occurred in 93.6% of pts (G3 in 13.8% [13/94], no G4 or G5, treatment discontinuation in 2.1% [2/94]). Treatment-related SAEs occurred in 3.2%. Most frequent TRAEs (≥15%) were fever (24.5%), hypothyroidism (21.3%), upper respiratory tract infection (18.1%), and ALT elevations (17.0%). Grade ≥3 TRAEs reported in ≥2 pts were platelet count decreased (2.1%). Immune-related AEs were reported in 42.6% of pts (G3 in 2.1%; psoriasis [n=1], IgA nephropathy [n=1]).

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

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

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Background Specific immune cell responses against oncoligogenic 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 phase Ib. Patients with advanced/recurrent solid tumors. We report outcomes from an open-label, dose-escalation phase 1/ib study of intratumoral MK-4621 and intravenous pembrolizumab in patients with advanced solid tumors. These results warrant validation in a larger cohort of patients.

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

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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/ib 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