PFS and OS was observed with A+V+C vs P+V+C in patients with PR, with 2-year PFS rates of 42.1% vs 24.6% and 2-year OS rates of 69.1% vs 56.1% with A+V+C vs P+V+C (table 1). In patients with CR, median PFS and OS were not yet reached in either arm, with 2-year PFS rates of 64.6% vs 59.8% and 2-year OS rates of 82.6% vs 82.8% with A+V+C vs P+V+C. PFS and OS outcomes were poor in both treatment arms in patients with SD, with 2-year PFS rates of 10.7% vs not estimable (NE) and 2-year OS rates of 36.6% vs 29.3% with A+V+C vs P+V+C.

Conclusions PFS and OS improvement was observed for A+V+C vs P+V+C for patients who achieved PR. CR is associated with improved PFS and OS with both A+V+C and P+V+C. Further follow-up is required to determine the impact of A+C+V vs P+V+C on survival outcomes.

**Trial Registration** ClinicalTrials.gov, NCT02908672

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0301

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3 different lesions) injections of PVSRIPO monotherapy, 21 days apart.

**Results** PVSRIPO injections were well tolerated with no SAEs or DLTs reported; all TEAEs were grade (G) 1 or 2 (grade 1 pruritis most common at 38%), with all but 2 PVRISPO-related TEAEs localized to the injected or adjacent lesions (n=1 G1 hot flush, n=1 G1 fatigue). Despite the limited number of PVSRIPO treatments relative to the overall lesion burden (67% patients > 5 lesions), 4 of 12 patients (33%) achieved an objective response per irRC, including 4/6 (66%) who received 3 injections (maximum administered). Pathologic complete response (ie, no viable tumor detected in injected and non-injected lesions biopsied) was observed in 2 of 4 (50%) patients with in-transit disease. PVSRIPO response relative to time since prior anti-PD-1 exposure is summarized in table 1. Following study completion/PVSRIPO therapy, 10/12 patients (83%) again received immune checkpoint inhibitor (ICI)-based therapy and 6/12 patients (50%) remained progression free at the data cutoff.

**Conclusions** Intratumoral PVSRIPO was well tolerated. When taken together with preclinical data, the anti-tumor responses observed relative to prior or subsequent ICI therapy suggests that PVSRIPO, either alone or in combination with anti-PD-1, may be an effective treatment in anti-PD-1 refractory melanoma. An amendment exploring higher PVSRIPO dose levels is ongoing and a phase 2 study with and without anti-PD-1 in the refractory population is initiating.

**Ethics Approval** This study (NCT03712358) was approved by WIRB; ID 20181772.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0302

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**Background** While PD-1/PD-L1 antagonists have improved the prognosis for many patients with melanoma, the majority fail therapy. PVRISPO is a novel immunotherapy consisting of a non-neurovirulent rhinovirus:poliovirus chimera that activates innate immunity to facilitate a targeted anti-tumor immune response. Preclinical data show that PVRISPO plus anti-PD-1 therapy leads to a greater anti-tumor response than either agent alone, warranting clinical investigation.

**Methods** An open-label phase I trial of intratumoral PVRISPO in patients with unresectable melanoma (AJCC version 7 stage IIIIB, IIIC, or IV) was performed. Eligible patients failed at least prior anti-PD-1 and BRAF/MEK (if BRAF mutant) therapy. The primary objective was to characterize the safety and tolerability of PVRISPO. 12 patients in 4 cohorts received a total of 1, 2 (into 2 different lesions) or 3 (same lesion 3x or
Methods 30 pts with stage III B/C/D MEL were enrolled. Pre-operatively, CMP-001 was dosed at 5 mg subcutaneous (SC, 1st), then 10 mg IT (2nd-7th) weekly; Nivo was dosed 240 mg q2 weeks for 3 doses – both agents given for 7 weeks. Post-operatively, Nivo was dosed 480 mg q4 weeks with CMP-001 5 mg q4 weeks SC for 48 weeks. Primary end-points included major pathologic response rate (MPR), and incidence of dose-limiting toxicities (DLT). Secondary end-points were radiographic response, relapse-free survival (RFS) and overall survival (OS). Pathological response was scored blinded by pathologists based on residual volume of tumor (RVT) using prior specified cutoffs: 4 0% (complete response, pCR); 0%<rvt<rvt50% (non-response, pNR). Radiographic response was assessed using RECIST v1.1. Sequential blood draws and tumor biopsies were collected and analyzed for CD8+ T cell infiltrate (TIL), multiparameter flow cytometry (MFC) and multiplex immunofluorescence (mIF).

Results 30 pts with regionally advanced MEL were enrolled, of stages IIIIB (57%), IIIC (37%), IIID (7%). 29/30 (97%) of pts completed 7 weeks of neoadjuvant Nivo/CMP; while 1 pt had a delay in surgery related to a pre-operative infection unrelated to therapy. No DLTs were reported; grade 3/4 irAE were reported in 3 pts (11%) leading to CMP-001 discontinuation in 2 pts (7%). Radiographic responses were seen in 13 pts (43%), while 9 pts (30%) had stable disease and 8 pts (27%) had progressive disease. Pathological responses (RVT <50%) were seen in 70% of pts: pCR 15 (50%), pMR 3 (10%), pPR (10%); only 9 (30%) had pNR. Pathological responders (pCR/ pMR) had increased CD8+ TIL and CD303+ pDC intra-tumorally by mIF; and peripherally activated PD1+-Ki67+ CD8+ T cells by MFC.

Conclusions Neoadjuvant CMP/Nivo has acceptable toxicity and promising efficacy. MPR is 60% in 30 pts. 1-year RFS was 82% (all pts) and 89% (among those with pCR/pMR); median RFS is 9 months (among pNR/pPR) and not reached (among pCR/pMR). Response is associated with evidence of immune activation intra-tumorally and peripherally. IT CMP001 increases clinical efficacy of PD-1 blockade with minimal additional toxicity in pts with regionally advanced MEL. Further study of this combination in high-risk resectable MEL is planned.

Acknowledgements We thank Dr. Jagjit Singh and the pathology grossing room staff for their assistance and Checkmate Pharmaceuticals for funding and CMP-001.

Trial Registration Clinical trial information: NCT03618641

Ethics Approval The study was approved by University of Pittsburgh’s Institutional Review Board, approval number MOD19040237-002.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

REFERENCES

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0303

304 INTRATUMORAL INJECTION OF CMP-001, A TOLL-LIKE RECEPTOR 9 (TLR9) AGONIST, IN COMBINATION WITH PEMBROLIZUMAB REVERSED PROGRAMMED DEATH RECEPTOR 1 (PD-1) BLOCKADE RESISTANCE IN ADVANCED MELANOMA


1University of Iowa, Iowa City, IA, USA; 2University of Pittsburgh Medical Center, Pittsburgh, PA, USA; 3Dana-Farber Cancer Institute, Boston, MA, USA; 4University of Colorado Denver, Aurora, CO, USA; 5University of California San Francisco, San Francisco, CA, USA; 6University of California Los Angeles, Los Angeles, CA, USA; 7Banner MD Anderson Cancer Center, Gilbert, AZ, USA; 8Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; 9City of Hope, Duarte, CA, USA; 10Fox Chase Cancer Center, Philadelphia, PA, USA; 11The Angeles Clinic and Research Institute, Los Angeles, CA, USA; 12Thomas Jefferson University, Philadelphia, PA, USA; 13University of Arizona, Tucson, AZ, USA; 14Checkmate Pharmaceuticals Inc., Cambridge, MA, USA; 15Prelude Therapeutics Inc., Wilmington, DE, USA

Background Therapeutic options are limited for patients with advanced melanoma that is refractory to PD-1 blockade. This study was performed in this patient population to assess the safety and antitumor activity of CMP-001, a CpG-A TLR9 agonist packaged within a virus-like particle.

Methods Patients were eligible for this 2-part, open-label, multicenter, phase 1b study if they had metastatic/unresectable melanoma and stable disease after ≥12 weeks or progressive disease (PD) on/after anti-PD-1 therapy. Part 1 evaluated CMP-001 plus pembrolizumab dose-escalation and dose-expansion. Part 2 evaluated CMP-001 monotherapy. Accessible lesion(s) were injected intratumorally with CMP-001, at a polysorbate 20 (PS20) concentration of either 0.01% or 0.00167%. The Part 1 primary objective was to identify the recommended phase 2 dose (RP2D) and schedule of CMP-001 plus pembrolizumab, while the Part 2 primary objective was to assess the safety of CMP-001 monotherapy. Secondary objectives for both parts were a preliminary assessment of antitumor activity of CMP-001 plus pembrolizumab and CMP-001 monotherapy, and the overall safety profile and pharmacodynamics of the combination.

Results In Part 1 (N=159) and Part 2 (N=40), 93.1% and 80.0% of patients had PD as their last response to prior anti-PD-1 therapy, respectively. The most common treatment-related adverse events (TRAEs; ≥25%) were flu-like symptoms (Parts 1 and 2) and injection-site reactions (Part 1). Grade 3/4 TRAEs were reported in 36.5% (Part 1) and 22.5% (Part 2) of patients, the most common being hypotension (Part 1: A186