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, or SD. 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

302 A PHASE I TRIAL OF INTRATUMORAL PVSRIPO IN PATIENTS WITH UNRESECTABLE TREATMENT REFRACTORY MELANOMA

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Background While PD-1/PD-L1 antagonists have improved the prognosis for many patients with melanoma, the majority fail therapy. PVSRIPO is a novel immunotherapy consisting of a non-neurovirulent rhinovirus:poliovirus chimera that activates tumor-associated plasmacytoid dendritic cells (pDC) via TLR9 inducing type I interferons and anti-tumor immunity to facilitate a targeted anti-tumor immune response. MMP-3 and CD8+ T cells. CMP-001/pembrolizumab produces durable benefit, and increased circulating activated CD8+ T cells. Preclinical data show that PVSRIPO 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 PVSRIPO 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 PVSRIPO. 12 patients in 4 cohorts received a total of 1, 2 (into 2 different lesions) or 3 (same lesion 3x or 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 pruritus most common at 58%), with all but 2 PVSRIPO-related TEAEs localized to the injected or adjacent lesions (n=1 G1 hot flash, 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

303 PHASE II TRIAL OF NEOADJUVANT NIVOLUMAB (NIVO) AND INTRA-TUMORAL (IT) CMP-001 IN HIGH-RISK RESECTABLE MELANOMA (NEO-C-NIVO): FINAL RESULTS

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Background Neoadjuvant PD-1 blockade produces major pathological responses (MPR) in ~30% of patients (pts) with high-risk resectable melanoma (MEL) with durable relapse-free benefit, and increased circulating activated CD8+ T cells. 1, 2 CMP-001 is a type A CpG packaged within a virus-like particle that activates tumor-associated plasmacytoid dendritic cells (pDC) via TLR9 inducing type I interferons and anti-tumor CD8+ T cells. CMP-001 pembrolizumab produces durable anti-tumor responses in PD-1 refractory melanoma. 3 We previously reported preliminary evidence of efficacy of neoadjuvant IT CMP/Nivo in high-risk resectable MEL; and herein present final results on 30 evaluable patients.

Abstract 301 Table 1 PFS and OS outcomes with A+V+C vs P+V+C by BOR per RECIST v1.1

<table>
<thead>
<tr>
<th></th>
<th>A+V+C</th>
<th>P+V+C</th>
<th>HR for A+V+C vs P+V+C (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>NR (20.3-NE)</td>
<td>NR (23.3-NE)</td>
<td>0.83 (0.40-1.72)</td>
</tr>
<tr>
<td>PR</td>
<td>18.4 (15.3-24.5)</td>
<td>12.3 (10.4-14.7)</td>
<td>0.64 (0.46-0.87)</td>
</tr>
<tr>
<td>SD</td>
<td>4.6 (3.6-6.5)</td>
<td>5.5 (4.6-7.4)</td>
<td>0.91 (0.61-1.36)</td>
</tr>
</tbody>
</table>

Abstract 302 Table 1 PVSRIPO anti-tumor response relative to ICI administration and post-study disease status

<table>
<thead>
<tr>
<th>Time to last ICI administration</th>
<th>ORR per irRC</th>
<th>Proportion treated with ICI</th>
<th>Proportion-free post-PVSRIPO alone or PVSRIPO followed by ICI</th>
<th>Median duration of follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30 days</td>
<td>69% (3/4)</td>
<td>89% (4 of 5)</td>
<td>69% (3 of 5)</td>
<td>9 months</td>
</tr>
<tr>
<td>&gt; 30 days</td>
<td>14% (1 of 7)</td>
<td>95% (6 of 7)</td>
<td>47% (3 of 7)</td>
<td>14 months</td>
</tr>
</tbody>
</table>

2 patients had pathologic complete response in biopsied lesions.
Methods 30 pts with stage III B/C/D MEL were enrolled. Preoperatively, 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: 46% (complete response, blinded by pathologists based on residual volume of tumor and overall survival (OS). Pathological response was scored 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: 46% (complete response, blinded by pathologists based on residual volume of tumor and overall survival (OS). Pathological response was scored.

Results 30 pts with regionally advanced MEL were enrolled, of stages IIIb (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%), pMRR 3 (10%), 3 pPR (10%); only 9 (30%) had pNR. Pathological responders (pCR/pMRR) 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/pMRR); median RFS is 9 months (among pNR/pPR) and not reached (among pCR/pMRR). 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

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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: