950 **FINAL ANALYSIS: PHASE 1B STUDY INVESTIGATING INTRATUMORAL INJECTION OF TOLL-LIKE RECEPTOR 9 AGONIST VIDUTOLIMOD ± PEMBROLIZUMAB IN PATIENTS WITH PD-1 BLOCKADE–REFRACTORY MELANOMA**

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Background There are limited therapeutic options for patients with progressive disease (PD) on or after PD-1–blocking antibody therapy. Vidutolimod (CMP-001) is a first-in-class, immunostimulatory virus-like particle containing a CpG-A Toll-like receptor 9 (TLR9) agonist. This phase 1b study evaluated the safety and clinical activity of intratumoral vidutolimod with and without pembrolizumab in patients with refractory melanoma.

Methods This two-part, open-label, multicenter, phase 1b study (NCT02680184) enrolled adults with histologically confirmed metastatic or unresectable cutaneous melanoma who had stable disease after ≥12 weeks or PD on anti−PD-1 treatment, measurable disease per RECIST v1.1, ECOG PS 0/1, and ≥1 lesion accessible for intratumoral injection. Part 1 evaluated vidutolimod + pembrolizumab and Part 2 evaluated vidutolimod monotherapy. Key objectives included assessment of safety and clinical activity, and exploratory analyses were performed on available tumor biopsies using immunohistochemistry and RNAseq.

Results At data cutoff (August 17, 2021), 159 patients had enrolled in Part 1 and 40 patients in Part 2. The median age was 64 years in Part 1 (range, 30-90) and 68 years in Part 2 (range, 30-89). Most patients had PD as their last response to prior anti–PD-1 therapy (Part 1, 93.1%; Part 2, 80.0%). Grade 3/4 treatment-related adverse events (TRAEs) occurred in 37.1% of patients treated with vidutolimod + pembrolizumab and in 22.5% of patients treated with vidutolimod monotherapy. No treatment-related deaths occurred. Based on the efficacy data presented in Table 1, vidutolimod polysorbate 20 (PS20) A was selected for further development as this formulation in combination with pembrolizumab had a best objective response rate (ORR; RECIST v1.1) of 23.5%, with a median duration of response (DOR) of 25.2 months. Vidutolimod monotherapy had an ORR of 20.0%, with a median DOR of 5.6 months. Exploratory translational analyses identified association of unique biomarkers with response among patients with T cell–inflamed versus non-T cell–inflamed tumors at baseline.

Abstract 950 Table 1 Safety and clinical activity of vidutolomod ± pembrolizumab

	Part 1: Vidutolimod + Pembrolizumab (Dose Escalation and Expansion)			Part 2: Vidutolimod Monotherapy
	Intention-to-Treat Population n=159	Vidutolimod PS20 A + Pembrolizumab n=98	Vidutolimod PS20 B + Pembrolizumab n=61	Vidutolimod n=40
Safety[a]				
TRAE grade 3, n (%)	55 (34.6)	37 (37.8)	18 (29.5)	9 (22.5)
TRAE grade 4, n (%)	4 (2.5)[b]	3 (3.1)	1 (1.6)	0
TRAE grade 5, n (%)	0	0	0	0
Clinical Activity				
Best ORR per RECIST v1.1, % (95% CI)	18.9 (13.1-25.8)	23.5 (15.5-33.1)	11.5 (4.7-22.2)	20.0 (9.1-35.6)
Best ORR, including postprogression responders, % (95% CI)	23.3 (16.9-30.6)	27.6 (19.0-37.5)	16.4 (8.2-28.1)	22.5 (10.8-38.5)
Responders, n (%)				
Complete response	8 (5.0)	7 (7.1)	1 (1.6)	0
Partial response	22 (13.8)	16 (16.3)	6 (9.8)	8 (20.0)
Postprogression partial response	7 (4.4)	4 (4.1)	3 (4.9)	1 (2.5)
Median DOR, months (95% CI)	19.9 (9.6-NE)	25.2 (8.7-NE)	11.4 (5.4-19.9)	5.6 (3.1-NE)

NE, not estimable; PS20 A, vidutolimod formulation with polysorbate 20 at 0.01%; PS20 B, vidutolimod formulation with polysorbate 20 at 0.00167%.
[a]Patients are reported for their highest-grade TRAE only.
[b]Grade 4 TRAEs were alanine aminotransferase increased, aspartate aminotransferase increased, blood creatine phosphokinase increased, hypotension, and platelet count decreased (n=1 [0.6%] each).

Conclusions Promising clinical activity was observed with vidutolimod + pembrolizumab and vidutolimod monotherapy in patients with PD-1 blockade–refractory melanoma. A manageable safety profile was observed. The DOR with vidutolimod + pembrolizumab was substantially longer than with vidutolimod monotherapy. Clinical studies to confirm the efficacy of vidutolimod + PD-1 blockade in patients with previously untreated unresectable/metastatic melanoma (phase 2/3, NCT04695977) or PD-1 blockade–refractory melanoma (phase 2, NCT04698187) are ongoing.

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Trial Registration NCT02680184

Ethics Approval This study was approved by the WCG-WIRB; WIRB approval tracking number: 20152597.

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