Abstract 304 Table 1 Best ORR With CMP-001 Plus Pembrolizumab and CMP-001 Monotherapy

	Part 1: CMP-001 + Pembrolizumab Escalation and Expansion			Part 2: Monotherapy
	Intent-to-Treat Population (N=159)	CMP-001 PS20 0.01% + pembrolizumab (n=98)	CMP-001 PS20 0.00167% + pembrolizumab (n=61)	CMP-001[a] (N=40)
Best ORR (RECIST v1.1), % (95% CI)	18.9[b] (13.1, 25.9)	23.5 (15.5, 33.1)	11.5 (4.8, 22.3)	17.5[c] (7.3, 32.8)
Best ORR (including post-PD responders), % (95% CI)	23.3 (17.0, 30.7)	27.6 (19.0, 37.6)	16.4 (8.2, 28.1)	NA
Best response, n				
CR	8	7	1	0
PR	22	16	6	7
SD	35	17	19	13
PD	74	46	27	20
Post-PD response	7	4	3	–
Not evaluable[d]	13	8	5	–

CR, complete response; NA, not applicable; ORR, objective response rate; PD, progressive disease; PR, partial response; PS20, polysorbate 20; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; SD, stable disease.
Patients were dosed at CMP-001 starting doses of 1, 3, 5, 7.5, or 10 mg, using one of 2 dosing schedules. In Schedule A, CMP-001 was administered once weekly for 7 weeks, then once every 3 weeks until the patient discontinued treatment. In Schedule B, CMP-001 was administered once weekly for 2 weeks, then once every 3 weeks until the patient discontinued treatment. [a]Includes CMP-001 PS20 0.01% and PS20 0.00167%. [b]Includes 26 confirmed responders. [c]Includes 4 confirmed responders. [d]Discontinued prior to having a follow-up scan.
Data cutoff: June 1, 2020.

6.9%; Part 2: 5.0%). No Grade 5 TRAEs were observed. In Part 1, the best objective response rate (ORR; RECIST v1.1) in patients treated with pembrolizumab and CMP-001 (PS20 0.01%) was 23.5% (23/98), while CMP-001 PS20 (0.00167%) resulted in a lower ORR of 11.5% (7/61). Seven additional patients had a delayed response after initial PD (table 1). The median duration of response was >1 year. In the 37 RECIST v1.1 and post-progression responders, the mean regression in injected and noninjected target lesions was 54.7% and 52.7%, respectively. In Part 2, the best ORR with CMP-001 monotherapy was 17.5% (7/40 patients); the response duration was shorter than in Part 1. Intratumoral CMP-001 PS20 0.01% 10 mg was selected as the RP2D.

Conclusions Intratumoral CMP-001 was well-tolerated and provided both local and distant responses in patients with advanced melanoma with disease progression on prior PD-1 blockade. CMP-001 monotherapy induced systemic tumor regression in some patients, but duration of response was substantially increased by the addition of pembrolizumab.

Acknowledgements This work was supported by Checkmate Pharmaceuticals. Medical writing assistance was provided by Cindy Rigby, PhD, of ApotheCom (San Francisco, CA) and was funded by Checkmate Pharmaceuticals.

Trial Registration NCT02680184

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

Consent N/A

REFERENCES

N/A

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0304

305 TECHNICAL CONSIDERATIONS FOR NORMALIZING DIGITAL SPATIAL PROFILING DATA WITH MULTIPLE WITHIN-PATIENT SAMPLES

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Background NanoString's GeoMx Digital Spatial Profiling (DSP) technology enables profiling of gene or protein expression from fresh or archival tissues. Specific regions of interest (ROIs) are identified via fluorescently labeled visualization markers. Within a given ROI, oligonucleotide tags from labeled, incubated antibodies can be released by area of interest (AOI)-specific exposure to UV light. With DSP, multiple AOIs can be collected within an individual tissue and/or within an individual patient. As with other technologies, technical variation that needs to be accounted before meaningful conclusions can be drawn.[1] Herein, we discuss technical considerations for normalizing and examining DSP data with multiple within-sample observations. We have two goals: 1) determine how different technical artifacts affect raw protein or RNA counts 2) provide guidelines for normalization strategies based on the biological questions of interest. To address these, we examine a recent melanoma dataset to quantify protein expression levels in tumor and stroma AOIs and to determine associations of specific proteins with clinical benefit (CB) from immunotherapy.

Methods Seventy-nine segmented ROIs containing matched tumor and stroma compartments were examined from eight patients at baseline (range: 4–12 ROIs). Five of these patients showed CB, defined as complete response, partial response, or remaining progression-free for 6 months. Following UV cleavage, liberated oligonucleotide tags were collected via microcapillary into a microtiter plate, and then processed using the nCounter Prep Station and Digital Analyzer as per manufacturer instructions.

Results Each AOI included 57 protein counts and six categories of control molecules/metrics (e.g., isotype molecules, AOI-specific cellularity). Before normalization, we examined controls and excluded those showing correlations with CB or segmentation type. We compared different normalization strategies including area and isotype normalization, upper quartile, and RUV.[2] For each strategy, we used linear and negative binominal mixed models to correlate protein expression with CB status, segmentation type, or their interaction. Findings consistent throughout many analysis combinations included higher MART1 expression in the CB group, lower PD-L1 and Ki-67 in the CB group, and lower HLA-DR expression in tumor segments of the CB group.

Conclusions ROIs can vary in size, cellularity, and staining, and normalization is important to account for technical differences when quantifying expression in spatial profiling studies. Normalization choices can affect outcome, and it is important to check whether proposed control proteins are in fact unassociated with the biological factors of interest. Mixed modeling approaches can be used to simultaneously model variation between ROIs within a sample and determine differences between sample groups.

Trial Registration ClinicalTrials. gov NCT02731729

Ethics Approval The study protocol and amendments were approved by the IRB of each participating institute. Written informed consent was obtained from all patients before conducting any study-related procedures.

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http://dx.doi.org/10.1136/jitc-2020-SITC2020.0305