605 NEOADJUVANT VIDUTOLIMOD (VIDU) AND NIVOLUMAB (NIVO) RESULTS IN MPR AND IMMUNE ACTIVATION IN HIGH-RISK RESECTABLE MELANOMA (MEL): FINAL PHASE II CLINICAL TRIAL RESULTS

[1]Arivarasan Karunamurthy, [1]Joe-Marc Chauvin, [1]Robert Morrison, [1]Yulong Bai, [1]Jie Sun, [1]Hong Wang, [1]Douglas Hartman, [2]Julie Stein, [1]Christopher Deitrick, [1]Riyue Bao, [1]Jagjit Singh, [1]Quanquan Ding, [1]Wentao Gao, [1]Drew Hurd, [1]Ornella Pagliano, [1]Amy Rose, [1]Yana Najjar, [1]Jason Luke, [3]David Mauro, [3]Arthur Krieg, [3]James Wooldridge, [3]Dmitri Bobilev, [1]John Kirkwood, [2]Janis Taube, [1]Hyun Jung Park, [1]Hassane Zarour, [1]Diwakar Davar*. *[1]University of Pittsburgh Medical Center Hillman Cancer Center, Pittsburgh, PA, United States; [2]Johns Hopkins University, Baltimore, MD, United States; [3]Checkmate Pharmaceuticals, Cambridge, MA, United States*

Background Neoadjuvant PD-1 blockade produces major pathological responses (MPR) in ~30% of patients (pts) with high-risk resectable MEL with durable relapse-free benefit, and increased circulating activated CD8+ T cells.[1,2] Vidutolimod (vidu) comprises a CpG-A oligodeoxynucleotide packaged within a virus-like particle (VLP) and is designed to activate tumor-associated plasmacytoid dendritic cells (pDC) via TLR9, inducing an IFN-rich tumor microenvironment and anti-tumor CD8+ T cell responses. Vidu/anti-PD-1 resulted in durable tumor responses in PD-1 refractory MEL.[3] This phase II study evaluated the pathological, clinical and immunological activities of neoadjuvant vidu/nivo in high-risk stage III B/C/D resectable MEL.

Methods Vidu/nivo was administered over 7 weeks (vidu 10mg IT Q1W x7, nivo 240mg Q2W x3) pre-surgery. Post-surgery, vidu/nivo (vidu SC 5mg, nivo 480mg Q4W) was continued for 48 weeks. Primary endpoints included MPR rate, and incidence of DLT. Secondary endpoints were radiographic response, relapse-free survival (RFS), distant metastasis-free survival (DMFS) and overall survival (OS). Pathological response assessment was performed to evaluate % residual volume of tumor (RVT) per consensus criteria[4-6] by 3 blinded dermatopathologists: 0% (pCR); 0%50% (pNR). Radiographic response assessed using RECIST v1.1. Serial blood, tumor and stool were collected for correlative analyses.

Results 31 pts were enrolled, of whom 30 evaluable for per-protocol (PP) analyses as 1 pt progressed pre-surgery. No DLTs were observed. 8 Gr3 TRAE, including hypertension (7/8) and colitis (1/8) were observed; no delays in surgery occurred. ORR by BICR was 45% (all) and 47% (PP). In PP population, MPR was observed in 57% (17/30) including 47% pCR (14/30) and 10% pMR (3/30). With median follow-up of 26.5 months, median RFS was not reached (table 1). Post-treatment, MPR was associated with increased CD8+ tumor infiltrating lymphocytes ($p<0.0001$), and peripheral immune activation and pDC activation by multiparameter flow cytometry ($p < 0.001$). Spatial investigation of immune cell infiltrates by mIHC revealed significantly immune cell infiltrates ($p<0.05$) and higher pDC ($p=0.053$) within tumor (but not stroma) of MPRs post-treatment (figure 1a,b). Deconvoluted RNAseq confirmed these findings compared to a control cohort of PD-1 treated MEL.

Conclusions Neoadjuvant vidu/nivo has minimal tox and demonstrated promising activity with 47% pCR rate and 57% MPR rate. MPR was associated with improved 1-/2- year RFS (94%/88%), and 1-/2- year DMFS (94%/94%) and 2-year OS (100%). MPR is associated with pDC and immune infiltrate (figure 1c). Further evaluation of this combination is ongoing in an ongoing randomized phase II trial (EA6194, NCT04708418).

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Trial Registration Clinical trial information: NCT03618641.

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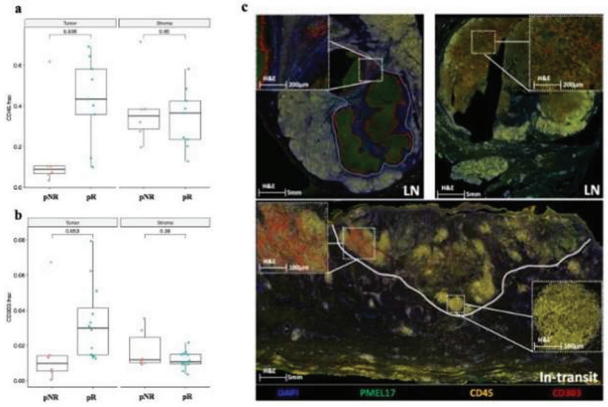
Ethics Approval The study was approved by University of Pittsburgh's Institutional Review Board, approval number MOD19040237-002.

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.

Abstract 605 Table 1 Breakdown of pathologic response categories and associated survival

Pathologic Response Breakdown – % (N, 95% CI)	Median RFS (months)	Landmark Survival		
		1-/2-year RFS	1-/2-year DMFS	1-/2-year OS
MPR including pCR and pMR in 57% (17/30, 95% CI 37-75%)	Unreached	94%/88%	94%/94%	100%/100%
pPR in 10% (3/30, 95% CI 2-27%)	23.0 months	100%/33%	100%/33%	100%/100%
pNR in 33% (10/30, 9% CI 17-53%)	6.0 months	40%/40%	40%/40%	60%/60%



Abstract 605 Figure 1 Multiplex IHC (mIHC) Analysis of Post-treatment Samples by GeoMx Spatial Analysis

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