

Conclusions LN-145 can be safely combined with pembrolizumab in patients with metastatic HNSCC. LN-145 plus pembrolizumab shows early signs of improved efficacy particularly when compared with literature reports of pembrolizumab alone in a comparable patient population. Enrollment is ongoing and updated data will be presented.

Trial Registration NCT03645928

Ethics Approval The study was approved by Advarra Institutional Review Board, under protocol number: Pro00035064.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0353>

354

A PHASE 1 TRIAL OF CUE-101 A NOVEL HPV16 E7-PHLA-IL2-FC FUSION PROTEIN IN PATIENTS WITH RECURRENT/METASTATIC HPV16+ HEAD AND NECK CANCER

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Background Immuno-STATs™ are novel, modular fusion proteins designed to selectively activate tumor-antigen-specific CD8+ T cells. Human papillomavirus (HPV) associated cancers serve as a model system to assess the safety and efficacy of the Immuno-STAT platform. CUE-101 is comprised of human leukocyte antigen (HLA) complex, HLA A*0201, a peptide epitope derived from the HPV type 16 E7 protein, and 4 molecules of a reduced affinity human interleukin-2 (IL2) designed to bind and activate HPV-specific T cells for eradication of HPV16-driven cancers. In preclinical studies CUE-101 demonstrated selective binding, activation, and expansion of HPV16 E7-specific CD8+ T cells, which translated into anti-tumor activity.¹

Methods CUE-101-01 is a first-in-human (FIH) phase 1 study in patients diagnosed with HPV16+ recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) refractory to one or more lines of therapy. Trial eligibility includes MHC class I type HLA-A*0201 and a diagnosis of an HPV16+ HNSCC, as assessed by p16 IHC and confirmed by HPV16 mRNA ISH. CUE-101 is administered intravenously over 60 minutes every 21 days. Objectives include determination of safety, pharmacodynamics (PD), pharmacokinetics (PK), recommended phase 2 dose (RP2D), and preliminary anti-tumor activity. The safety results from treated participants will be presented.

Results 19 participants have received CUE-101 monotherapy as of August 7, 2020. Doses ranging from 0.06 to 1 mg/kg were determined to be safe and well-tolerated, enabling dose escalation to 2 mg/kg. Preliminary PK data demonstrate dose-dependent increases in drug exposure which are sustained upon repeat dosing, and low inter-subject variability. Preliminary data from systemic blood analyses show

early signals of expansion of HPV-16 E711-20-specific CD8+ T cells. Stable disease (SD), as determined by RECIST 1.1, was observed in several participants in these early dose cohorts, with one subject maintaining SD up to 19 weeks. The maximum tolerated dose (MTD) has not yet been reached. As of May 14, 2020 (the development safety update report (DSUR) data-lock date), no dose limiting toxicities and the following adverse events were observed in the first 12 patients treated with CUE-101: fatigue (n=3), decreased appetite (n=1), arthralgia (n=1), muscular weakness (n=1), parasthesia (n=1), bullous pemphigoid (n=1), and infusion-related reactions (n=1).

Conclusions CUE-101 is a novel agent that is demonstrating acceptable tolerability, favorable PK, and preliminary PD signals that support selective activation of tumor-specific T cells. Neither the MTD nor the monotherapy RP2D have been established. PD and PK analyses are ongoing as dose escalation continues.

Acknowledgements The authors would like to thank all the patients who are participating in this study. The study is sponsored by Cue Biopharma.

Trial Registration ClinicalTrials.gov NCT03978689

Ethics Approval This study was approved by Ethics and Institutional Review Boards (IRBs) at all study sites; IRB reference numbers: DF/HCC IRB# 19-374 (Massachusetts General Hospital), HRPO# 201905108 (Washington University School of Medicine), IRB 191714 (Vanderbilt University Medical Center Vanderbilt-Ingram Cancer Center), Advarra Pro00037736 (Moffitt Cancer Center), IRB(IRBMED) HUM00165746 (University of Michigan Comprehensive Cancer Center), 2019-087 (Karmanos Cancer Institute), WIRB IRB00112341 (Winship Cancer Institute/Emory University), WIRB 2000026098 (Yale Cancer Center), WIRB STUDY00008948 (University of Washington, Seattle), WIRB 1908869642 (University of Arizona Cancer Center, IRB 20-073 (Memorial Sloan Kettering Cancer Center), 2019-0578 (The University of Texas MD Anderson Cancer Center), IRB 52744 (Stanford University School of Medicine).

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<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0354>

355

FIRST-IN-HUMAN PHASE I STUDY OF NKTR-255 IN PATIENTS WITH RELAPSED/REFRACTORY HEMATOLOGIC MALIGNANCIES

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