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.

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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 HPV16 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.

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

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Background NKTR-255, an investigational IL-15R α -dependent polymer-conjugated recombinant human IL-15 (rhIL-15) agonist, maintains the full spectrum of IL-15 biology and provides sustained pharmacodynamic (PD) responses without the need for daily dosing. NKTR-255 engages IL-15R α and IL-2/IL-15R β leading to natural killer(NK) and CD8⁺ T-cell expansion, proliferation and activation. In preclinical studies, NKTR-255 enhanced antibody-dependent cellular cytotoxicity(ADCC) of each of daratumumab, rituximab, trastuzumab and cetuximab, resulting in synergistic anticancer activity. This ongoing phase 1 trial (NCT04136756) evaluates NKTR-255 in patients with hematologic malignancies.

Methods Heavily pretreated patients with relapsed/refractory multiple myeloma(MM) or non-Hodgkin lymphoma(NHL) received escalating doses of NKTR-255 intravenously q3w. Patients were observed for 3 weeks following the first NKTR-255 dose for dose-limiting toxicity(DLT). Preliminary safety, PK and PD were evaluated in all patients and bone marrow biopsy was evaluated in one patient. NKTR-255-mediated activation of the immune system was assessed by flow cytometry and plasma cytokine analysis.

Results As of June 25, 2020, 4 patients were dosed(1.5 μ g/kg:3 patients; 3 μ g/kg:1 patient). NKTR-255 was well tolerated. Most common treatment-related adverse events(AEs): flu-like symptoms, muscle stiffness, and myalgia. One Grade 3 event(pyrexia) was reported, resolving <24 hours with over-the-counter medications. No NKTR-255-related DLTs or serious AEs occurred. Clinical activity was observed in 2/4 patients(NHL and MM). The NHL patient achieved reduced metabolic activity in all prespecified target lesions after 5 cycles. The MM patient achieved stable disease after 3 cycles on NKTR-255 monotherapy. This 63 y/o male had high-risk recurrent stage III MM with complex cytogenetics (relapsing after VRd, DRd, and carfilzomib plus dexamethasone). Preliminary PK analyses(1.5 μ g/kg) showed mean half-life of >24 hours with no accumulation following repeat dosing. NKTR-255 at 1.5 μ g/kg expanded NK and CD8⁺ T-cells in peripheral blood, with peak fold-changes in cell numbers of ~5-fold and ~3-fold respectively, maintained during the cycle. Bone marrow biopsy data indicate 7-fold(cycle 5) to 13-fold (cycle 9) increase from baseline in the CD56⁺ population in the MM patient. Proliferative capacity for NK and CD8⁺ T-cells was maintained across multiple treatment cycles. NKTR-255-dependent changes in inflammatory cytokines, including MCP-1 and IL-6, peaked by 6 hours and resolved to baseline levels by 24 hours, further supporting the safety of NKTR-255.

Conclusions In heavily pretreated patients with hematologic malignancies, NKTR-255 is biologically active and demonstrated sustained increases in NK and CD8⁺ T-cells. NKTR-255 was well tolerated, with minimal treatment-related toxicities. Our preclinical and preliminary clinical data provide evidence of synergistic effects enhancing ADCC and support continued dose escalation of NKTR-255.

Trial Registration NCT04136756

Ethics Approval The study was approved by the institutional review board of each participating site.

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BASELINE PD-L1 EXPRESSION AND TUMOR IMMUNE INFILTRATION IS ASSOCIATED WITH CLINICAL RESPONSE IN PATIENTS WITH R/R DLBCL TREATED WITH DPX-SURVIVAC, LOW-DOSE CYCLOPHOSPHAMIDE AND PEMBROLIZUMAB

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Background Treatment of recurrent/refractory (r/r) DLBCL remains an unmet clinical need, and new effective and well-tolerated treatments are required. DPX-Survivac is a unique T cell activation therapy that targets survivin-expressing tumor cells and has shown anti-tumor activity in clinical trials. This trial is evaluating a novel immunotherapy combination with DPX-Survivac, intermittent low dose CPA and pembrolizumab.

Methods 'SPiReL' is a Phase 2 non-randomized, open label, efficacy and safety study of a novel immunotherapy combination with DPX-Survivac (a unique T cell activation therapy that targets survivin-expressing tumor cells), intermittent low dose CPA and pembrolizumab, treatment regimen as described in figure 1. Subjects with r/r incurable DLBCL and survivin expression are eligible for participation. This study was approved by the Ontario Cancer Research Ethics Board, approval number 0981. ORR is assessed by modified Cheson criteria. For translational analyses, baseline and on-treatment PBMCs, along with tumor biopsy samples are collected from each subject. Survivin-specific systemic T cell responses are assessed using IFN γ -ELISPOT assay and tumour immune-infiltrate profile by multiplex-IHC.

Results Twenty-two subjects have been enrolled to date, 19 are included in the intent to treat (ITT) population and 11 subjects are evaluable in the per protocol (PP) population. In the PP, the ORR is 63.6% including 3 CRs (27.3%), 4 PRs (36.4%) and the DCR is 81.8% (9/11). In the ITT, the ORR is 35% (7/19), and DCR is 52.0% (10/19). Preliminary results

Abstract 356 Figure 1 SPiReL treatment regimen

Abstract 356 Table 1 Data summary of results

# Participants	Clinical Response		
	SD	PR/CR	No Response
All ITT Participants (n=19)	3	7	9
Immune Infiltrates N=11 (%)			
PDL1+	1 (33)	6 (86)	4 (44)
CD4+	1 (33)	6 (86)	4 (44)
CD8+	2 (66)	5 (71)	4 (44)
Positive ELISpot Response	1 (33)	6 (86)	1 (11)