Background 

Immu-STATM 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 Immu-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 eradication of HPV16-driven cancers. In preclinical studies (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 eradication of HPV16-driven cancers.

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 patients 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), Advarra Pro00037736 (Moffitt Cancer Center), IRB(IRBMED) HUM00165746 (University of Michigan Comprehensive Cancer Center), 2019-087 (Karmanos Cancer Institute), WIRB IRB00112341(Winsip 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 5274 (Stanford University School of Medicine).

REFERENCE 


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Background NKTR-255, an investigational IL-15Rα-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-15Rα and IL-2/IL-15Rβγ 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 antitumor 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(1.5µg/kg:3 patients; 3µg/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 3 event(pyrexia) was reported, resolving <24 hours with 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

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.

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 IFNy-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

<table>
<thead>
<tr>
<th># Participants</th>
<th>Clinical Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ITT Participants (n=19)</td>
<td>SD</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Immune infiltrates N=13 (%)</td>
<td></td>
</tr>
<tr>
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<td>1 (33)</td>
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<tr>
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