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

Human papillomavirus (HPV) is associated with a significant global cancer burden. The early development of HPV vaccines has reduced cervical cancer incidence, reducing mortality. A growing body of evidence supports the therapeutic potential of HPV vaccines in HPV-positive cancers, including head and neck squamous cell carcinoma (HNSCC). However, the impact of HPV on HNSCC is complex, and the role of HPV in cancer pathogenesis remains uncertain. The therapeutic potential of HPV vaccines in HNSCC has yet to be explored, and it is not known whether HPV has a significant role in HNSCC pathogenesis.

Methods

Parts A and B of this Phase 1, open-label, 3-part study aim to characterize the safety, tolerability, PK, PD, and preliminary antitumor activity of CUE-101, a HPV16 E7-pHLA-IL2-Fc fusion protein designed to target and activate HPV-positive cancer cells. The study was conducted in two parts, CUE-101 and CUE-101 CIN, with CUE-101 CIN to follow CUE-101 if tolerated.

Safety

In CUE-101, 15 patients remained on study for a total of 3 cycles at 8-week intervals. Following a review of data from the first 21 patients, the following were observed: non-serious adverse events (AEs) were observed in 100% of patients, with the most common AEs being fatigue, rash, and hypotension. Serious AEs were observed in 40% of patients, with the most common being fatigue (12.5%). The incidence of thrombocytopenia was 50% of patients, with the most common AEs being fatigue, rash, and hypotension. The incidence of hypotension was 50% of patients, with the most common AEs being fatigue, rash, and hypotension. The incidence of thrombocytopenia was 50% of patients, with the most common AEs being fatigue, rash, and hypotension. The incidence of hypotension was 50% of patients, with the most common AEs being fatigue, rash, and hypotension.

Pharmacokinetics

Serum CUE-101 concentrations over time are determined using a validated hybrid capture liquid chromatography-tandem mass spectrometry (LC-MS/MS) method. The assay measures CUE-101 and its metabolites, CUE-101 C1 and CUE-101 C2, over a period of 24 hours. The assay is sensitive to CUE-101 concentrations of 0.1 ng/mL, with a coefficient of variation of 10% at 1 ng/mL. The assay is specific for CUE-101, and does not detect other HPV16 E7-pHLA-IL2-Fc fusion proteins. The assay is validated for CUE-101 concentrations over time.

Pharmacodynamics

Assessment of the potential to generate on-target immunity response with CUE-101 treatment is an important secondary objective of the trial. Blood samples are collected prior to dosing and at several different time points post-dosing, including before and after therapy. The samples are analyzed for HPV16 E7-specific T-cell responses using standard methods.

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Summary

CUE-101 is a first-in-human (FIH) phase 1 study in patients diagnosed with HPV16+ HNSCC who have failed prior line of therapy. The study was designed to evaluate the safety, tolerability, PK, PD, and preliminary antitumor activity of CUE-101 in patients with recurrent/metastatic HNSCC. The trial was conducted in two parts, CUE-101 and CUE-101 CIN, with CUE-101 CIN to follow CUE-101 if tolerated.

Preclinical data from preclinical pharmacodynamic and tumor imaging studies have shown early signals of expression of HPV16 E7-specific T-cell responses. The study is supported by Cue Biopharma and the collaboration with partners is being performed in collaboration with biomarkers.