CUE-102 Selectively Activates and Expands WT1-Specific T Cells for the Treatment of Patients with WT1+ Malignancies

CUE-102 Series Immuno-STATs

- **Immunostimulatory (I/S) Threates (A)**: selectively engineered biologic composed of a biotinylated peptide-MHC complex and multivalent co-stimulatory molecules built on a FC-carrier to enable stability, valuation favoring PK and manufacturability.
- CUE-102 series I/S are designed to selectively deliver altered intercellular (IL-2) to tumor-specific CD8+ T cells (Quayle 2020). Sadiqi 2021.
- **Wnt1 tumor (WT)** was previously selected as the highest priority antigen for therapeutic targeting in an effort by the National Cancer Institute (Cheever 2019).
- Development of novel modalities targeting WT provide a significant opportunity to address high unmet medical need in WT patients including AML, ovarian, endometrial, breast, lung, gastric, colorectal and pancreatic cancer.
- CUE-102 is being developed as a novel therapeutic fusion protein to selectively activate tumor antigen-specific T cells to treat WT1-positive cancers.

CUE-102 Selectively Activates Antigen-Specific CD8+ T Cells in Blood and Tumor

- **B**: Decreased expression of antigen-specific CD8+ T cells in blood and tumor of tumor-bearing mice treated with vehicle control compared to tumor-bearing mice treated with CUE-102 (Day 0 vs. Day 10).
- **C**: Increased expression of antigen-specific CD8+ T cells in blood and tumor of tumor-bearing mice treated with CUE-102 compared to tumor-bearing mice treated with vehicle control (Day 0 vs. Day 10).

CUE-102 Expands Polyfunctional and Cytolytic WT1+Specific CD8+ T Cells from Human PBMCs

- **A**: Increased frequency of polyfunctional and cytolytic WT1+specific CD8+ T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.
- **B**: Increased frequency of polyfunctional and cytolytic WT1+specific CD8+ T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.

CUE-102 Selectively Expands WT1+Specific CD8+ T Cells from Human PBMCs

- **A**: Increased frequency of WT1+specific CD8+ T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.
- **B**: Increased frequency of WT1+specific CD8+ T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.

CUE-102 Selectively Expands Tumor Relevant T Cells

- **A**: Increased frequency of tumor-relevant T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.
- **B**: Increased frequency of tumor-relevant T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.

CUE-102 Selectively Expands In Vivo by CUE-102 are Polyfunctional and Cytolytic

- **A**: Increased frequency of polyfunctional and cytolytic WT1+specific CD8+ T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.
- **B**: Increased frequency of polyfunctional and cytolytic WT1+specific CD8+ T cells in human PBMCs treated with CUE-102 compared to treatment with vehicle control.

CUE-102 Ist Muret Surrogate (mCUE-101) Expands Antigen-Specific CD8+ T Cells in Blood and Tumor

- **A**: Increased frequency of antigen-specific CD8+ T cells in blood and tumor of tumor-bearing mice treated with mCUE-101 compared to tumor-bearing mice treated with vehicle control.
- **B**: Increased frequency of antigen-specific CD8+ T cells in blood and tumor of tumor-bearing mice treated with mCUE-101 compared to tumor-bearing mice treated with vehicle control.

CUE-102 First-in-Human Clinical Trial

- **A**: Eligibility criteria for CUE-102 clinical trials. (1) Patients with selected malignancy (e.g., LHD-1701, LHD-412) and progression or intolerance to conventional therapy. (2) Presence of WT1+ T cells. (3) Adequate hematologic and organ function. (4) Written informed consent. (B) Dose levels for CUE-102 clinical trials. (1) 0.3 mg/kg CUE-102. (2) 3 mg/kg CUE-102. (3) 10 mg/kg CUE-102.

Conclusions

- **CUE-102**, developed in collaboration with LG Chem (Korea), is a novel fusion protein designed to selectively deliver altered IL-2 to tumor-specific CD8+ T cells. CUE-102 demonstrates selective binding, activation, and expansion of polyfunctional and cytolytic WT1+specific primary human CD8+ T cells from healthy and cancer patient samples.
- Treatment of naive HL-A2+ transgenic mice with CUE-102 elicits and selectively expands WT1+specific CD8+ T cells that are polyfunctional and cytolytic in vivo.
- The novel mechanism of action of CUE-102, namely targeted activation of tumor-antigen-specific CD8+ T cells by delivery of robust affinity mAbs, supports its potential for anti-cancer efficacy in a Phase I clinical trial in WT1+ myeloid neoplasms/cancers.

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