#3553 A phase 1 dose escalation and expansion study of CUE-102, a novel WT1-pHLA-IL2-Fc fusion protein, in HLA-A*0201-positive patients with WT1-positive recurrent/metastatic cancers.

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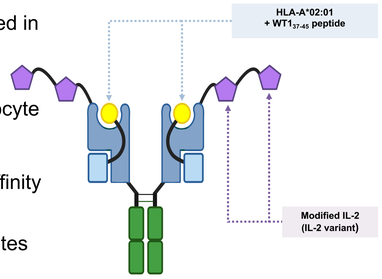
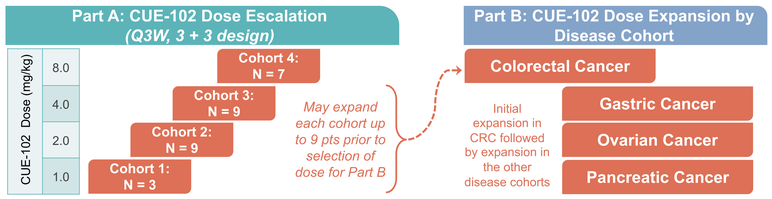
Background

- Wilms' Tumor 1 (WT1) is highly expressed in multiple solid tumor and hematologic malignancies.
- CUE-102 is comprised of a human leukocyte antigen (HLA) complex, HLA-A*0201, a peptide epitope derived from the WT1 protein, and 4 molecules of a reduced affinity human interleukin-2 (IL-2).
- CUE-102 selectively expands and activates WT1-specific CD8 T cells.
- The selective targeting of IL-2 to tumor-specific T cells avoids non-specific T cell activation and toxicity.



CUE-102 Immuno-STAT design

Dose Escalation and Expansion Schema



Key Eligibility Criteria:

- HLA-A*0201 genotype
- WT1+ expressing colorectal, gastric/GEJ, ovarian or pancreatic cancer
  - Part A: Dose Escalation
  - Part B: Dose Expansion
- Measurable disease by RECIST 1.1
- Life expectancy ≥ 12 weeks

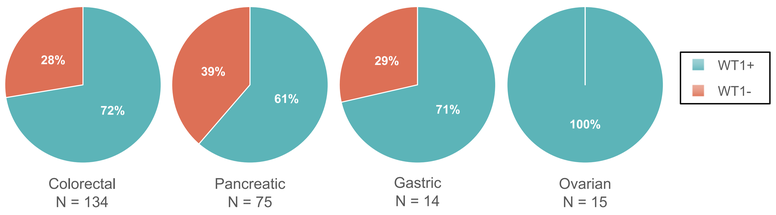
Objectives:

- *Primary:* Safety and tolerability
- *Secondary:* PK/PD, Anti-tumor activity, OS

Biomarkers:

- Immunophenotyping and monitoring of immune cell subsets including WT1-specific CD8+ T cells
- Serum biomarkers and cytokines, cfDNA, and TCR sequencing

WT1 Prevalence by Cancer Type in Prescreened Patients



238 patient tumor samples have been tested for expression of WT1 by IHC as of 03-May-24.

Dose Escalation Patient Enrollment by Indication

Dose/Indication	1 mg/kg	2 mg/kg	4 mg/kg	8 mg/kg	TOTAL
Colorectal	3	4	6	4	**17**
Gastric	0	1	2	0	**3**
Ovarian	0	1	0	1	**2**
Pancreatic	0	3	1	2	**6**
TOTAL	**3**	**9**	**9**	**7**	**28**

Dose Escalation Patient Demographics

Patients		**N = 28**
Age (years)	Mean (range)	59 (36 – 77)
Sex	Male	14 (50%)
	Female	14 (50%)
Race	White	21 (75%)
	Asian	3 (10.7%)
	Black / African American	2 (7.1%)
	Other / Not Reported	2 (7.1%)
Cancer Type	Colorectal	17 (60.7%)
	Liver metastasis	15 (88.2%)
	Pancreatic	6 (21.4%)
	Gastric / GEJ	3 (10.7%)
	Ovarian	2 (7.1%)
ECOG	0	10 (35.7%)
	1	18 (64.3%)
Prior Lines of Therapy	Median (range)	4 (1 – 9)

Data extract 01-May-2024.

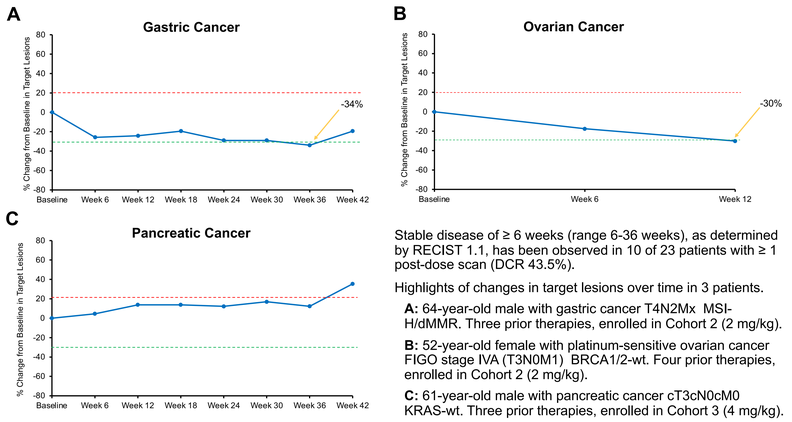
Dose Escalation Safety and Tolerability

	Dose Escalation Patients (N = 28)			
	Treatment-Related Adverse Events		All Adverse Events	
Preferred Term	**≥ Grade 3**	**Any Grade**	**≥ Grade 3**	**Any Grade**
Nausea	0	9 (32.1%)	2 (7.1%)	12 (42.9%)
Vomiting	0	8 (22.2%)	1 (3.6%)	10 (35.7%)
Fatigue	0	5 (17.9%)	0	9 (32.1%)
Infusion related reaction	0	9 (32.1%)	0	9 (32.1%)
Anaemia	0	2 (7.1%)	1 (3.6%)	8 (28.6%)
Pyrexia	0	6 (21.4%)	0	8 (28.6%)
Abdominal pain	0	1 (3.6%)	1 (3.6%)	7 (25.0%)
Decreased appetite	0	1 (3.6%)	0	7 (25.0%)
Chills	0	4 (14.3%)	0	5 (17.9%)
Aspartate aminotransferase inc.	0	1 (3.6%)	1 (3.6%)	4 (14.3%)
Constipation	0	0	0	4 (14.3%)
Cough	0	0	0	4 (14.3%)
Diarrhea	0	0	0	4 (14.3%)
Hypokalemia	0	1 (3.6%)	0	4 (14.3%)
Pleural effusion	0	0	0	4 (14.3%)
Abdominal pain upper	0	1 (3.6%)	0	3 (10.7%)
Ascites	0	0	2 (7.1%)	3 (10.7%)
Alkaline Phosphatase increased	0	1 (5.6%)	1 (5.6%)	3 (10.7%)
Bilirubin increased	0	1 (5.6%)	1 (5.6%)	3 (10.7%)
Dyspnoea	0	0	0	3 (10.7%)
Hypotension	0	1 (5.6%)	1 (5.6%)	3 (10.7%)
Lymphocyte count decreased	2 (7.1%)	3 (10.7%)	2 (7.1%)	3 (10.7%)
Pruritus	0	3 (10.7%)	0	3 (10.7%)
Urinary Tract Infection	0	0	0	3 (10.7%)

Adverse Events occurring at ≥ 10% frequency in all patients treated with ≥1 dose of CUE-102. AEs coded using MedDRA V21.0 and NCI-CTCAE v5.0 as of 10-Apr-2024. At each level of summation patients reporting >1 occurrence of the same AE are counted once at highest toxicity.

- **No dose-limiting toxicities were observed.**
- **No drug related SAEs were reported.**

Preliminary Characterization of CUE-102 Activity



Stable disease of ≥ 6 weeks (range 6-36 weeks), as determined by RECIST 1.1, has been observed in 10 of 23 patients with ≥ 1 post-dose scan (DCR 43.5%).

Highlights of changes in target lesions over time in 3 patients.

A: 64-year-old male with gastric cancer T4N2Mx MSI-H/dMMR. Three prior therapies, enrolled in Cohort 2 (2 mg/kg).

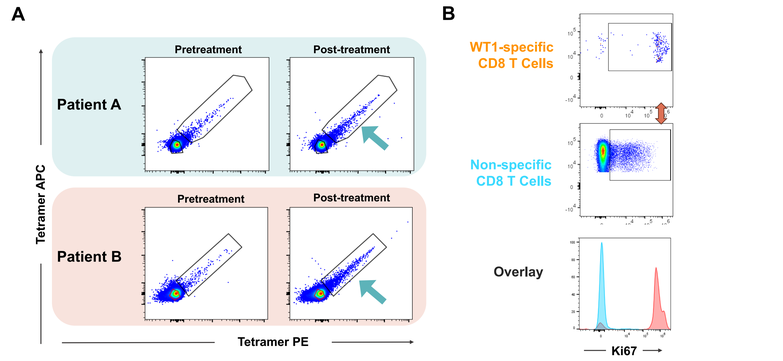
B: 52-year-old female with platinum-sensitive ovarian cancer FIGO stage IVA (T3N0M1) BRCA1/2-wt. Four prior therapies, enrolled in Cohort 2 (2 mg/kg).

C: 61-year-old male with pancreatic cancer cT3cN0cM0 KRAS-wt. Three prior therapies, enrolled in Cohort 3 (4 mg/kg).

Preliminary Characterization of CUE-102 Pharmacokinetics

- Following monotherapy treatment, CUE-102 exhibits approximately dose proportional increases in exposure
- CUE-102 exposures are comparable following repeat administration
- Simultaneous quantificdrugation of two regions of CUE-102 confirm the bioanalytical method is measuring intact in circulation

CUE-102 Treatment Selectively Expands WT1-Specific CD8 T Cells



(A) Increased frequency of WT1-specific CD8+ T cells are observed following CUE-102 treatment. Representative plots are shown from preliminary analyses following direct flow staining of PBMCs from 2 patients. (B) An increase in proliferation, as indicated by Ki67 expression, is noted in WT1-specific CD8 T cells whereas the irrelevant CD8 T cells that do not recognize WT1 exhibit significantly lower expression of Ki67. Representative plots are shown from preliminary analyses following direct flow cytometry analysis of patient PBMCs.

Summary

- CUE-102-01 is a phase 1, open label, two-part dose escalation and expansion study for patients with late-stage colorectal, gastric/GEJ, ovarian, and pancreatic cancers that express WT1.
- Enrollment in dose escalation (Part A) is complete. Patients received 1–8 mg/kg CUE-102 IV every 3 weeks. Following expansion of 2, 4, and 8 mg/kg dose levels, 4 mg/kg was selected for dose expansion (Part B). Following initial dose expansion in colorectal patients, enrollment is now ongoing for all disease-specific cohorts.
- CUE-102 is safe and exhibits a manageable tolerability profile with > 85.6% AEs being CTCAE Grade 1 – 2, no dose-limiting toxicities and no related SAEs.
- Two patients, one with gastric cancer and one with ovarian cancer have demonstrated reduction in tumor burden. Disease control rate (DCR) in Part A = 43.5%. Of the 28 patients treated in Part A, 13 are alive in survival follow-up.
- Preliminary PK and PD analyses demonstrate approximately dose proportional exposure and evidence of selective stimulation and expansion of WT1-specific CD8 T cells.
- The tolerability profile of CUE-102 together with preliminary evidence of selective immune stimulation supports additional testing of CUE-102 in combination regimens in the future.

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