Updated Data from the alloSHRINK Phase 1 First-in-Human Study Evaluating CYAD-101, an Innovative Non-Gene-Edited Allogeneic CAR-T, in Metastatic Colorectal Cancer

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BACKGROUND

- Effective therapeutic options for patients with refractory unresectable metastatic colorectal cancer (mCRC) are limited.
- Chimeric antigen receptor (CAR) T-cell treatments has shown clinical efficacy in patients with advanced B-cell malignancies but, to date, has failed to deliver a clinically relevant impact on solid tumor indications.
- Most CAR T-cell therapies use the patients' own T-cells (autologous) as the source material which brings major operational and medical issues. Allogeneic CAR T-cell treatments using healthy donor T-cells provides an 'off the shelf' solution that circumvents many of these challenges.

**Figure 1. Best overall responses and case studies**

**Figure 2. Treatment schedule**

**Figure 3. Luminex score evolution per dose-level**

**Figure 4. Luminex profile at baseline**

**CONCLUSIONS**

- At the highest CYAD-101 dose level, six of nine patients have shown some evidence of tumor control by RECIST 1.1 criteria.
- Within this limited dataset, in the patients achieving SD or PR, there was evidence of new T-cell clones entering the hyper-expanded TCR repertoire post-treatment. Moreover, an interesting upregulation of Luminex score was observed in the patient with durable partial response after first and second infusions of CYAD-101.
- Pre-clinical studies have shown that CAR T-cell treatment employing the NK92CD16 receptor (CAR) utilizes both direct anti-tumor activity and induces the host endogenous immune response. Our observations imply that modulation of the endogenous immune response may be an important mechanism of action of CYAD-101 in mCRC patients. Further testing will be pursued in the on-going exploratory phase of the alloSHRINK clinical study to confirm findings.
- The clinical evaluation of CYAD-101 with therapeutic modalities possessing complementary mechanisms of action, such as checkpoint inhibitors, is strongly warranted, given the promising results and is now being pursued in the KEYNOTE-B79 clinical study due to initiate in 2021.

**RESULTS**

- The waterfall plot of patients in the alloSHRINK study shows the relative change of target lesions from baseline by RECIST 1.1 criteria (Figure 1A).
- The median progression-free survival and overall survival were 3.94 months (range: 1.2-8.1 months) and 10.58 months (range: 8.1-16.7 months), respectively.
- Four patients treated with the CYAD-101 dose of 1x109 cells/infusion but showing differential responses by RECIST 1.1 criteria (patient 08: PR; patients 14 and 16: SD for 5 months; patient 15: progressive disease, PD) were assessed for changes in their peripheral blood TCR repertoire and cytokine and chemokine (Luminex) profiles (Figure 1A).
- TCR repertoire (baseline versus 3 to 4 months post CYAD-101 treatment) (Figure 1B):
  - For patients 08 (PR), 14 and 16 (SD), there was evidence of changes in the overall TCR repertoire post-treatment as determined by CD80 amino acid (aa) length frequency analysis. For patient 15 (PD), pre- and post-treatment curves largely overlap suggesting no change in clone frequencies between both timepoints.
  - The changes in frequency of CD80 as length for patients 08, 14 and 16 were mirrored in the analysis of hyper-expanded TCR clones (frequency >1%) where the number of new clone entries post-treatment was 11 for patient 08, 21 for patient 14 and 14 for patient 16. By contrast, there was only a new clone observed for patient 15 (PD).
- Luminex profile (Figure 1B):
  - Patient 08 (PR) showed a Luminex score peak approximately 4 days after the first and second CYAD-101 infusions with a reduced peak after the third. These peaks appear to be concomitant with a relative increase in the contribution of inflammatory cytokines. For patients 14 and 16 (SD), no clear peaks in Luminex score were seen. However, both patients presented apparent changes in the relative contribution of chemo-attractive cytokines after each CYAD-101 infusion.
  - There was little evidence of change in the Luminex profile after each CYAD-101 infusion for patient 15 (PD).
- Luminex profile across all patients (Figures 3 and 4):
  - There was high variability in the baseline Luminex profile among patients, with a higher contribution of inflammatory cytokines compared to healthy donors (driven primarily for higher concentrations of IL-7. Figure 4). While the two PR patients both showed a high baseline Luminex score, the high degree of variability among patients means that greater normalisation across CYAD-101 dose levels (Figure 3). Patient 08 (PR, DL: 1x109 cells/infusion) stood out with clear peaks after the first and second CYAD-101 infusions (Figure 3C).

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1. UZ Antwerp, Antwerp, Belgium. 2. UZ Leuven, Leuven, Belgium. 3. Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium. 4. Cellect Oncology, Middelbourg-Guille, Belgium. Cellect Oncology owns certain of the patents, patent families, physicians, and study teams at all participating centers. This study was funded and supported by Cellect Oncology SA - ClinicalTrials.gov Identifier: NCT03692429). 4. PD, PR, AA and EVC are investigators on the alloSHRINK study. This poster is published for information only. The views expressed are those of the authors and not necessarily those of the organizations named herein. The data are based on those received from the participating sites as of the data cut-off of Oct 28, 2020 (uncleaned database).

**REFERENCES**