Results from the completed dose-escalation of the ALLOSHRINK phase I study evaluating the allogeneic NKG2D-based CAR T-cell therapy CYAD-101 in metastatic colorectal cancer patients

Hans Prenen 1, Marika Rasschaert 1, Alain Hendliss 2, Leila Shaza 2, Erik Alcantar-Orozco 3, Emilie Cerf 3, Florence Renard 3, Caroline Lomez 3, Anne Flament 3, Jeroen Dekervel 2, Eric Van Cutsem 2

1. University Hospital Antwerp (UZ Antwerp), Antwerp, Belgium; 2. Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; 3. Celyad, Mont-Saint-Guibert, Belgium; 4. University Hospital Leuven (UZ Leuven), Leuven, Belgium

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HP, ML, AH, LS, and ECV are investigators on the ALLOSHRINK trial. EAO, EC, FR, CL, and AF are employed by Celyad SA.
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MAIN RESULTS

- In total 12 mCRC patients have been enrolled in this Phase I study (3 at DL 1, 3 at DL2, and 6 at DL3).
- At the study snapshot (29 October 2019), 6 out of 12 patients reported at least one treatment-related adverse event (AE).
  - All were Grade 1 or 2 (1/2), no patients experienced Grade ≥ 3 AE (Table 2).
- There was no report of dose-limiting toxicity (DLT) or clinical or laboratory evidence of GvHD (Table 3).
- Best overall response included 2 patients with partial response (PR) and 7 patients with stable disease (SD).
  - Including 5 SD ≥ 1 month, with 2 ongoing (out of 12) patients at time of this manuscript submission (Table 4).
- Tumor burden decrease was observed in 4/7 patients achieving SD (Figure 3).
  - All responses were observed at the first tumor assessment scheduled 8-12 days after the second CYAD-101 infusion (Figure 1). There was no obvious correlation to dose-levels or baseline characteristics.
  - The Msd reaction against the allogeneic CYAD-101 cells appears to be controlled by each FOXLX cycle as evidenced by the similar levels of CYAD-101 engraftment after 2nd and 3rd infusions (Figure 3).

CONCLUSIONS

- CYAD-101 is a novel, first-in-class, allogeneic NKG2D receptor-based CAR T-cell therapy.
- ALLOSHRINK Phase I study is the first trial using a non-gene edited, allogeneic CAR T-cell therapy in a solid cancer indication.
- ALLOSHRINK evaluates CYAD-101 with prior FOLFOX as effectively as a preconditioning chemotherapy in advanced metastatic colorectal cancer patients who progressed after previous treatment with oxaliplatin and irinotecan.
- CYAD-101 has been found to have a favorable safety profile at all doses evaluated. No dose-limiting toxicities or GvHD have been reported. No cumulative toxicities were noted with multiple administrations of CYAD-101.
- CYAD-101 cells were detected in the peripheral blood up to 40 days after 1st infusion. A detailed discussion of cell kinetics is presented in poster P147.
- The initial observations of anti-tumor activity of CYAD-101 combined with FOXLX is encouraging in patients with incurable mCRC relapsing after multiple lines of therapy that includes oxaliplatin. In this patient population, the expected clinical response against subsequent oxaliplatin therapy alone is thought to be low.
- Enrollment is ongoing at the dose-level 3 with an extension of the study under consideration.