Effect of chemotherapy on cellular kinetics of NKG2D-based CAR T-cells in metastatic colorectal cancer patients

Erik Alcantar-Orozco1, Eytan Brennan1, Marie-Sophie Dheur1, Eric Van Cutsem2, Alain Hendil2, Jean-Luc Canon3, Jean-Pascal H. Machiels3, Hans Preven3, Sylvie Rottey,4 Kunle Odunsi2, Solmaz Sahebjam8, Ahmad Awada2, Fabian Borghese1, Emilie Cerf1, Nathalie Braun1, Caroline Lonez1, Anne Flamant1, Frédéric Lehmann1
1. Celyad, Mont-Saint-Guibert, Belgium; 2. Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; 3. Service d’OncoLogie-Hématologie, Site Notre-Dame, Grand Hôpital de Charleroi (GHAC), Charleroi, Belgium; 4. Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium; 5. University Hospital Antwerp (UZ Antwerp), Antwerp, Belgium; 6. Gheni University Hospital, Gheni, Belgium; 7. Roswell Park Comprehensive Cancer Center, Buffalo, NY; 8. Moffitt Cancer Center, Tampa, FL

MAIN RESULTS

Table 1: Baseline characteristics of mCRC patients included in the trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>NKG2D CAR T-cells</th>
<th>Clinical Trial</th>
<th>Chemotherapy</th>
<th>NKG2D CAR T-cells</th>
<th>Clinical Trial</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYAD-01</td>
<td>CYAD-101</td>
<td>CYAD-01</td>
<td>CYAD-101</td>
<td>CYAD-01</td>
<td>CYAD-101</td>
<td></td>
</tr>
<tr>
<td>CYAD-01 (automologous)</td>
<td>CYAD-01</td>
<td>CYAD-01</td>
<td>CYAD-01</td>
<td>CYAD-01</td>
<td>CYAD-01</td>
<td></td>
</tr>
</tbody>
</table>

In three trials, a total of 35 patients received NKG2D based CAR T-cells at increasing doses (1x10^8, 3x10^8 or 1x10^9) including 23 patients with CYAD-01 (autologous) and 12 patients with CYAD-101 (allogeneic). No occurrence of graft vs. host disease (GvHD) was observed in patients treated with CYAD-101 (see Table 1).

In the THNK trial (NCT03018405), CYAD-01 is injected without preconditioning chemotherapy or CyFlu. In the SHINK trial (NCT03310008), FOLFOS (methotrexate (folic acid), fluorouracil and oxaliplatin) is given before CYAD-01 injections (Information on CYAD-01 in Poster P313).

In our knowledge, the kinetics of cell engraftment autologous and allogeneic CAR T-cells employing the same CAR have not been reported. Herein we compare the engraftment between autologous and allogeneic CAR T-cells injected as monotherapy, after FOLFOX or after CyFlu preconditioning is also presented.

In the ALLOGHON trial (NCT03366429), in ALLOGHON, CYAD-01 is injected before CAR T-cell injections (Information on CYAD-101 in Poster P313).

To our knowledge, the kinetics of cell engraftment autologous and allogeneic CAR T-cells employing the same CAR have not been reported.

CONCLUSIONS

We observed similar cell kinetics parameters between autologous and allogeneic CAR T-cells in mCRC patients concomitantly treated with FOLFOX chemotherapy.

Persistence of allogeneic CYAD-101 CAR T-cells administered after CyFlu preconditioning shows similar cell kinetics parameters (Figure 3) as CYAD-01 (Figure 2).

To our knowledge, the kinetics of cell engraftment autologous and allogeneic CAR T-cells employing the same CAR have not been reported. Herein we compare the engraftment between autologous and allogeneic CAR T-cells injected as monotherapy, after FOLFOX or after CyFlu preconditioning is also presented.

Herein we compare the engraftment between autologous and allogeneic CAR T-cells injected as monotherapy, after FOLFOX or after CyFlu preconditioning is also presented.

We observed similar cell kinetics parameters between autologous and allogeneic CAR T-cells in mCRC patients concomitantly treated with FOLFOX chemotherapy.

Persistence of allogeneic CYAD-101 CAR T-cells suggests control of immune reaction against allogeneic product is achieved as expected. It is hypothesized that FOLFOX chemotherapy could play a role in the control of HvsG reaction through a transient lymphodepleting effect.

CyFlu-based preconditioning chemotherapy enhances the engraftment of NKG2D-based CAR T-cells in an autologous setting in mCRC patients in a manner that appears similar to that observed for other CAR T-cell therapies.

ACKNOWLEDGEMENTS & DISCLOSURES

1. Celyad thanks patients & families, principal investigators, and study teams at all participating centers of the THNK, SHINK and ALLOGHON trials for their dedicated efforts.
2. EAD, B, MD, RF, LB, NL, CB, and FL are employees of Celyad SA.
3. This paper was submitted for information only. The information represents those of the authors and not necessarily those of the organizations with which they are affiliated.