

CAR T-cell therapy for central nervous system lymphomas: blood and cerebrospinal fluid biology, and outcomes

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SUPPLEMENTARY MATERIAL

Supplementary Table

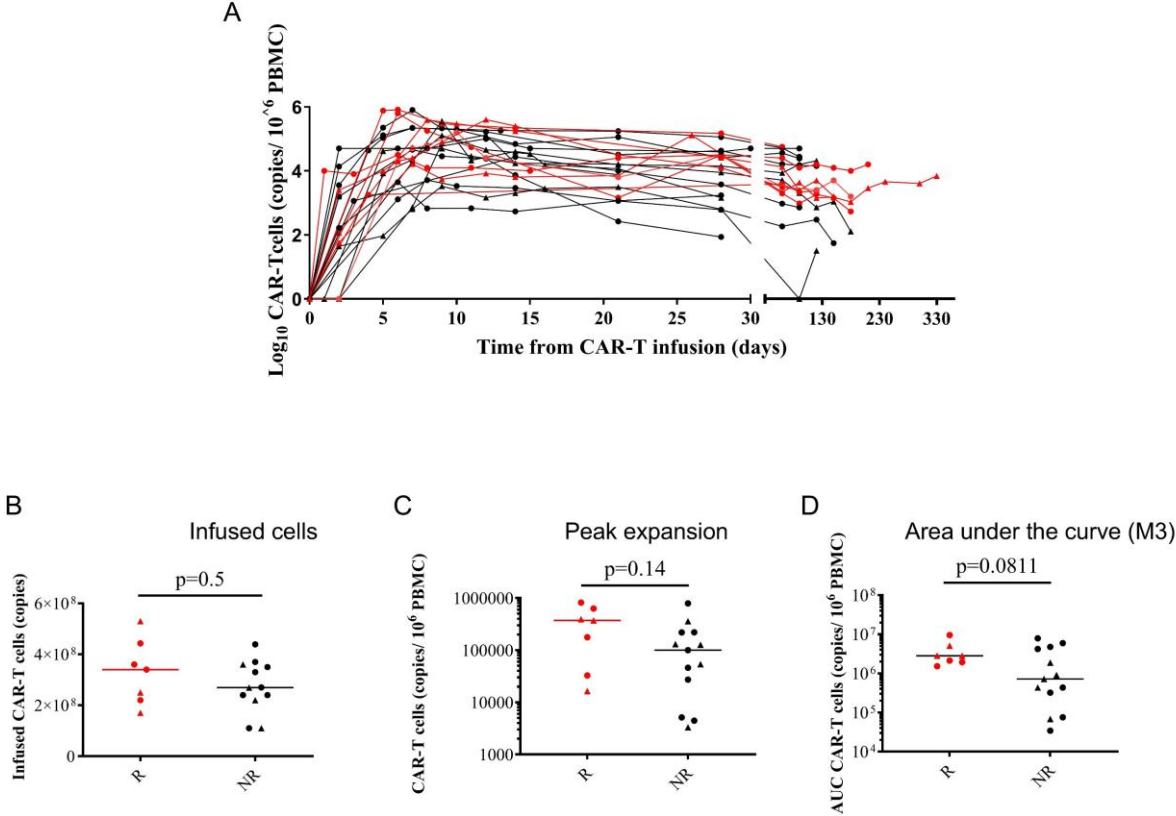
Table 1. Clinical characteristics, responses and outcomes.

| Sex | Age (years) | Disease localization at time of CAR-T infusion | CSF involvement at time of CAR-T infusion | Number of lines of prior therapy | Previous ASCT | Bridging therapy | Status of disease after bridging therapy | Infused CAR-T cells product | CRS | ICANS | Response at M1 | Response at M3 | Subsequent status | Follow-up (mo) |
|-----|-------------|--|---|----------------------------------|---------------|------------------|--|-----------------------------|---------|----------|----------------|----------------|--|----------------|
| F | 73 | PCNSL | No | 4 | Yes | Yes | PD | Axicabtagene ciloleucel | Grade 2 | Grade 4o | PR | PR | Persistent PR | 26 |
| F | 71 | SCNSL | Yes | 2 | Yes | Yes | PD | Tisagenlecleucel | Grade 2 | No | PR | PR | Persistent PR | 29 |
| F | 67 | PCNSL | Yes | 2 | Yes | Yes | PR | Tisagenlecleucel | Grade 3 | No | CR | CR | Persistent CR | 21 |
| F | 49 | PCNSL | No | 3 | Yes | Yes | PR | Tisagenlecleucel | Grade 1 | No | CR | CR | Persistent CR | 22 |
| M | 75 | SCNSL | No | 3 | No | Yes | PR | Tisagenlecleucel | Grade 2 | Grade 2 | PR | PR | Persistent CR | 19 |
| M | 68 | PCNSL | Yes | 4 | Yes | Yes | PR | Tisagenlecleucel | Grade 2 | No | CR | CR | Persistent CR | 12 |
| F | 72 | PCNSL | Yes | 2 | No | Yes | PR | Tisagenlecleucel | Grade 1 | No | CR | CR | Persistent CR | 13 |
| F | 67 | SCNSL | No | 3 | No | Yes | CR | Tisagenlecleucel | No | No | CR | CR | Persistent CR | 12 |
| F | 62 | PCNSL | Yes | 4 | Yes | Yes | PD | Tisagenlecleucel | No | Grade 3o | CR | CR | IL-10 increase at M4; start of lenalidomide. Relapse at M8 Death. | 21 |
| M | 46 | SCNSL | No | 2 | Yes | Yes | PR | Tisagenlecleucel | Grade 2 | No | PR | Relapse | Death | 15 |
| F | 69 | PCNSL | No | 3 | Yes | No | PD | Tisagenlecleucel | No | 0 | PR | Relapse | Death | 10 |
| F | 44 | SCNSL | Yes | 4 | No | Yes | PD | Axicabtagene ciloleucel | Grade 2 | No | PR | Relapse | Death | 8 |
| M | 70 | PCNSL | Yes | 4 | No | Yes | PD | Tisagenlecleucel | Grade 2 | No | PR | Relapse | Death | 7 |
| M | 48 | SCNSL | No | 5 | Yes | Yes | PD | Tisagenlecleucel | No | Grade 1 | PR | Relapse | Death | 6 |
| M | 50 | PCNSL | No | 4 | Yes | Yes | PD | Tisagenlecleucel | Grade 2 | Grade 1 | PD | PD | Death | 20 |

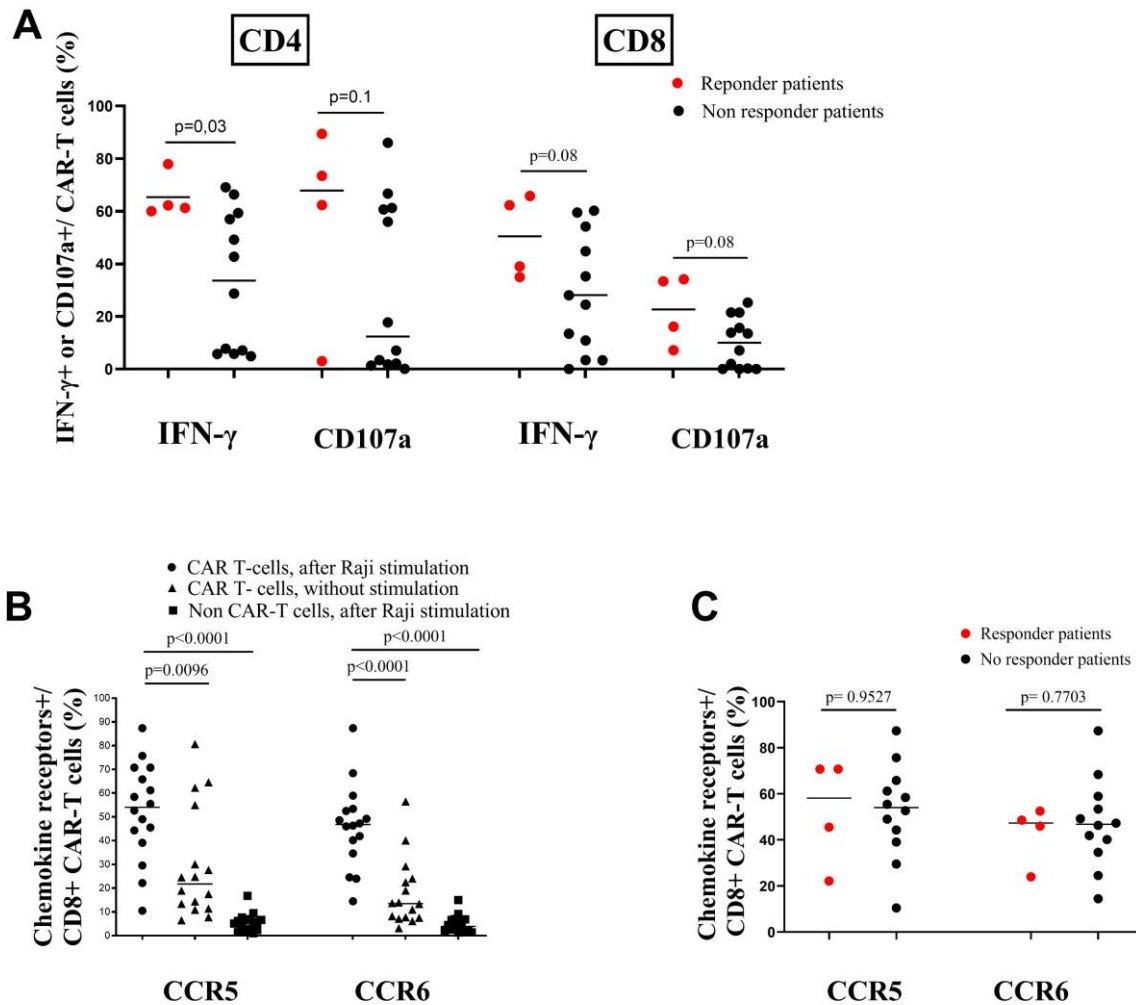
| | | | | | | | | | | | | | | | |
|---|----|-------|-----|---|-----|-----|----|------------------|---------|---------|----|--|----------|-------|----|
| F | 70 | PCNSL | No | 2 | Yes | Yes | PD | Tisagenlecleucel | Grade 2 | Grade 2 | PD | PR* after the start of ibrutinib at M2 because of positive CSF | PD at M8 | Death | 14 |
| F | 33 | PCNSL | Yes | 2 | Yes | Yes | PD | Tisagenlecleucel | Grade 1 | No | PD | PD | Death | Death | 6 |
| M | 64 | SCNSL | No | 3 | Yes | No | PD | Tisagenlecleucel | Yes | 0 | PD | PD | Death | Death | 5 |
| M | 51 | PCNSL | Yes | 3 | Yes | Yes | SD | Tisagenlecleucel | Grade 2 | Grade 2 | PD | PD | Death | Death | 6 |
| M | 74 | SCNSL | No | 3 | Yes | Yes | PD | Tisagenlecleucel | No | 0 | PD | Death | Death | Death | 1 |
| M | 52 | PCNSL | No | 4 | Yes | Yes | PD | Tisagenlecleucel | Grade 2 | No | PD | Death | Death | Death | 1 |

Abbreviations: Mo: month; M; month; CSF: cerebrospinal fluid; ASCT: autologous stem cell transplantation; CRS: cytokine release syndrome; ICAN: immune effector cell-associated neurotoxicity syndrome; M: month; PCNSL; primary central nervous system lymphoma; SCNSL: secondary central nervous system lymphoma; CR: complete response; PR: partial response; PD: progressive disease.

Supplementary Figures



Supplementary Figure 1. Peripheral CAR-T cell expansion. **A.** Individual profiles of CAR-T cells expansion (\log_{10} copies/ 10^6 PBMC) for each patient, **B.** Infused CAR-T cells copies number in R and NR patients, **C.** CAR-T cells expansion peak (copies/ 10^6 PBMC) in R and NR patients, **D.** Area under the curve (AUC) of CAR-T cells (copies/ 10^6 PBMC) during the first 3 months in R and NR patients. *Mann-Whitney test*. Red color denotes R patients, circle plots denote the patients with PCNSL and triangle plots the patients with SCNSL. R, responder patients; NR; non responder patients; AUC, area under the curve. The responder patients were defined with CR or PR at M3 without new treatment.



Supplementary Figure 2. CAR-T cell functionality and homing markers expression. The thawed PBMC of 16 patients on the day of the expansion peak were stimulated with Raji cell line during 5 hours and were then stained with anti: CD107a APC-R700, biotin-PE, CD3-APC780, CD8-BV605, CCR5-BV650, CCR6-BV700 and CD69-PE-CF594. The intracellular cytokine staining and the expression of CD107a were evaluated on CD8⁺ (gated on CD3⁺CD8⁺ cells) and CD4⁺ (gated on CD3⁺CD8⁻ cells) T cells after subtraction of the negative control. **A.** Production of IFN- γ and expression of CD107a by CD4⁺ (left panel) and CD8⁺ (right panel) CAR-T cells. **B.** Expression of CCR5 (left panel) or CCR6 (right panel) on CD8⁺ CAR-T cells after stimulation with Raji cells (circle plots), on non-CAR-T cells after stimulation with Raji cells (square plots) or on CAR-T cells without any stimulation (triangle plots). For the stimulation with Raji cells, thawed PBMC were stimulated during 5 hours.

Mann-Whitney test. C. Expression of CCR5 (left panel) and CCR6 (right panel) on CD8⁺ CAR-T cells depending on response status. Red color denotes responder patients, black color denotes non responder patients. R: responder patients, NR: non responder patients