690 **HIGH SAFETY AND EFFICACY OF CRISPR-BASED NON-VIRAL PD1 LOCUS SPECIFIC INTEGRATED ANTI-CD19 CAR-T CELLS (BRL-201) IN TREATING RELAPSED OR REFRACTORY NON-HODGKIN'S LYMPHOMA: FIRST-IN-HUMAN PHASE I STUDY**

[1]Biao Zheng*, [2]YongXian Hu, [1]Jiqin Zhang, [3]Mingming Zhang, [1]Wei Li, [2]Wenjun Wu, [2]Jiazhen Cui, [3]Guoqing Wei, [1]Bing Du, [1]Mingyao Liu, [2]He Huang. *[1]BRL Medicine Inc., Shanghai, China; [2]The First AffiliatedHospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China; [3]Zhejiang Province Engineering Laboratory for Stem Cell andImmunity Therapy, Hangzhou, Zhejiang, China*

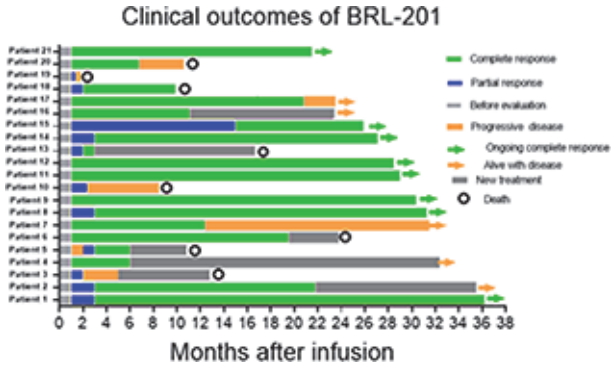
Background We developed a novel approach to generate non-viral, genome-specific integrated CAR-T cells through CRISPR/Cas9, thereby breaking through both virus usage and random integration simultaneously. Here, we update the newest data of phase I trial of non-viral PD1 locus specifically integrated anti-CD19 CAR-T cells (BRL-201) in patients with relapsed/refractory (r/r) Non-Hodgkin's lymphoma (NCT04213469).

Methods Adult patients with r/r B-NHL underwent leukapheresis and a lymphodepletion chemotherapy with cyclophosphamide (500mg/m^2, D -3 to -2) and fludarabine (30mg/m^2, D -4 to -2) before BRL-201 infusion. Dose escalation are based on 3+3 escalation rule, including three cohorts: 2×10^6/kg, 4×10^6/kg, 6×10^6/kg. The primary endpoint was the incidence of dose-limiting toxicities (DLT) and secondary endpoint was the objective response rate (ORR) at 3 months.

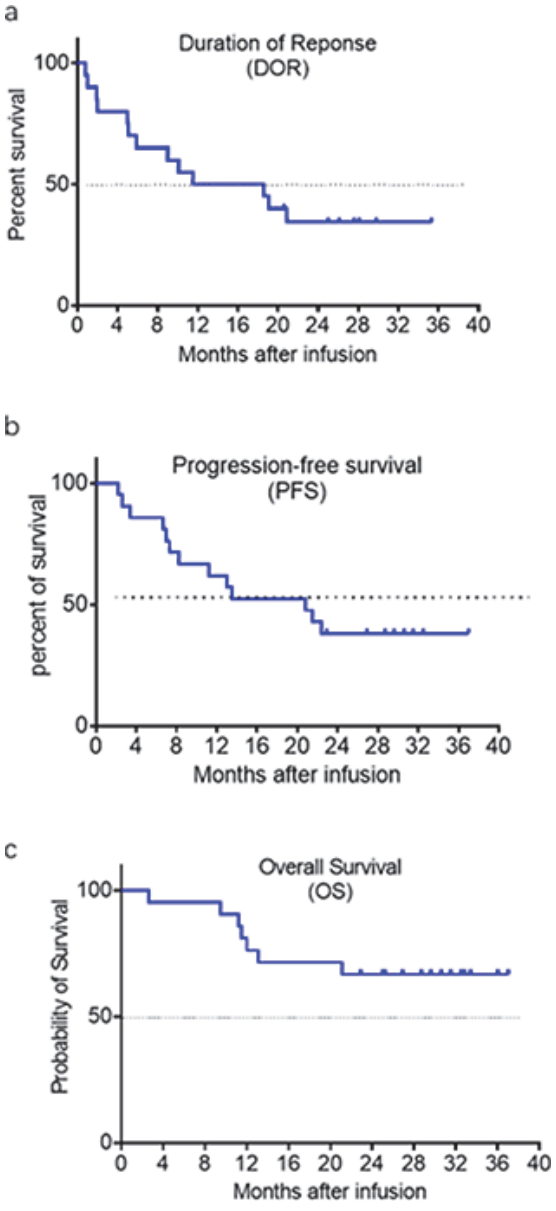
Results Between May 3, 2020 and August 10, 2021, 25 patients with r/r B-NHL were enrolled and 21 received BRL-201 with a median age of 56 years (34–70) and a median of 4 (1–9) prior lines of therapy. Among all the treated patients, 17 patients (93.8%) were diagnosed with disease stage III or IV, and 13 patients (81.3%) were assessed with intermediate to high risk according to IPI or aaIPI score assessment.

As of May 17, 2023, the median follow- up was 29.0 months (21.5–36.2 m). All of 21 (100%) patients had an objective response to BRL-201 and 18 (85.7%) patients had a complete response (CR) as best response (figure 1). 7 patients maintained CR at data cut-off date. The median duration of response(DOR) for all 21 patients was 15.1 months (95%CI: 5.9, NA) (figure 2A). The median progression free survival (PFS) was 20.8 (95%CI: 8.2, NA) months (figure 2B), while the median overall survival (OS) was not reached, 12-month OS rate was 76.2% (95% CI: 60%, 96.8%) (figure 2C). 14 patients (66.7%) experienced grade 1–2 cytokine release syndrome (CRS) and only one patient received tocilizumab. 4 patients (19.0%) experienced grade 1–2 immune effector cell-associated neurotoxicity syndrome (ICANS). No grade 3–4 CRS and ICANS were observed.

Conclusions This is a first-in-human study of a novel type of non-viral genome specific targeted CAR-T cells in heavily treated r/r B-NHL in China. BRL-201 demonstrated durable response with a median PFS of 20.8 months and 12-month OS rate of 76.2%, and a manageable safety profile. These data continues supporting the compelling clinical benefit-risk profile of BRL-201for r/r B-NHL patients.



Abstract 690 Figure 1 Swimming plots of BRL-201 treatment duration, response and clinical outcomes.



Abstract 690 Figure 2 DOR, PFS and OS.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0690