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Clinical Trial

Efficacy and safety of GLS-010 (zimberelimab) in patients with relapsed or refractory classical Hodgkin lymphoma: A multicenter, single-arm, phase II study

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Abstract ***Background:*** GLS-010 (zimberelimab) is a novel, fully human, anti-programmed death-1 monoclonal antibody that shows promising efficacy and safety in advanced solid tumors. This trial aimed to evaluate the efficacy and safety of GLS-010 (zimberelimab) in Chinese patients with relapsed or refractory classical Hodgkin lymphoma (r/r-cHL).
Methods: This phase II, single-arm, open-label, multicenter clinical trial was conducted at 24 centers in China and enrolled patients with r/r-cHL after two or more lines of therapy. The patients were administered intravenous GLS-010 (zimberelimab) (240 mg, once every 2 weeks) until progression, death, unacceptable toxicity, or consent withdrawal. The primary end-point was the objective response rate assessed by an independent radiology review committee (IRC). This study was registered (NCT03655483).
Results: Eighty-five patients were enrolled between August 2018 and August 2019. The median follow-up was 15.8 months. Seventy-seven patients (90.6%; 95% confidence interval [CI] 82.3–95.9) had an IRC-assessed objective response. The complete response rate was 32.9% (n = 28). The 12-month progression-free survival and overall survival rates were 78% (95% CI 67.5–85.6) and 99% (95% CI 91.9–99.8), respectively. Treatment-related adverse events (TRAEs) were observed in 92.9% of participants. Grade III or IV TRAEs occurred in 24 (28.2%) of the 85 participants. The most common grade III or IV TRAEs were abnormal hepatic function (5.9%), hyperuricemia (4.7%), decreased neutrophil count (3.5%), and increased weight (3.5%). Only one grade V AE, gastrointestinal infection, occurred.
Conclusions: GLS-010 (zimberelimab) appears to be effective and safe for the treatment of Chinese patients with r/r-cHL. Long-term follow-up is required to confirm these clinical benefits.

1. Introduction

Hodgkin lymphoma (HL) is a rare hematologic malignancy originating in the lymphatic system [1–3]. HL has a bimodal incidence distribution by age (peaks at ages 15–34 years and ≥55 years) and is slightly more common in men [1–4]. In China, the incidence of lymphoma is 4.2 per 100,000 individuals, with 8.6–13.0% of all cases being HL [5]. Most patients with HL achieve a complete response (CR) after the initial treatment and long-term disease control, but a relapse may occur in 10–15% of HL patients with early-stage disease (stages I and II) and 15–30% in those with more advanced disease [6–12]. In addition, 10–15% of patients have a refractory disease that does not respond to the initial therapy or progresses after an initial partial response (PR) [6–12]. The standard treatment option for relapsed or refractory classical Hodgkin lymphoma (r/r-cHL) is salvage chemotherapy, and in case of negative positron emission tomography (PET) results, autologous stem cell transplantation (ASCT) is followed by brentuximab vedotin maintenance [1]. Still, some cases cannot undergo ASCT or relapse after ASCT. The treatment of r/r-cHL remains challenging, and patients still have high unmet needs for treatment.

cHL is characterized by the presence of malignant Reed–Sternberg cells, which are tumor-initiating cells accompanied by immune cell infiltration and changes in chromosome 9p24.1 [13,14]. These genetic changes lead to increased programmed death (PD)-1 ligand (PD-L1) expression; therefore, PD-1 inhibitors can be used to target the PD-1/PD-L1 axis to treat patients with cHL [13,14]. Clinical trials revealed that monotherapy with nivolumab or pembrolizumab is effective for r/r-cHL; most of the participants in these trials had a high expression of PD-L1, but about one-third of them did not achieve a CR or PR in the CheckMate 205 [15],

KEYNOTE-013 [16,17], KEYNOTE-087 [17], and KEYNOTE-204 [1] trials. ASCT is not reimbursed by medical insurances in China [5,18,19]; therefore, only one-third of patients in the ORIENT-1 trial received ASCT, and approximately 25% did not achieve CR or PR [20]. The anti-PD-1 drugs tested in China for r/r-cHL include camrelizumab [21], sintilimab (ORIENT-1) [20], and tislelizumab [22]. Therefore, new PD-1 inhibitors with high efficacy and low rates of adverse events (AEs) are needed.

GLS-010 (zimberelimab) is a novel, fully human, anti-PD-1 monoclonal antibody with high affinity and selectivity for PD-1. It is an antibody drug that undergoes natural selection and affinity maturation in transgenic rats. The S228P mutation in the immunoglobulin G4 (IgG4) core-hinge area was introduced to prevent Fab-arm exchange, while the mutation in the N95S region in the CDR3 area of the light chain prevents the glycosylation of the antigen-binding domain. It is expected to be the first fully human antibody drug from a transgenic rat platform to be marketed. Preclinical studies showed that the analogous function of T cell activation and antitumor activity were similar to those of other anti-PD-1 drugs. Previous phase I trials suggest promising efficacy and acceptable safety of GLS-010 (zimberelimab) in patients with advanced solid tumors [23,24]. The preliminary results of GLS-010 (zimberelimab) in the treatment of r/r-cHL suggest high efficacy and safety [25].

This phase II, single-arm, open-label, multicenter clinical study aimed to investigate the efficacy and safety of GLS-010 (zimberelimab) in patients with r/r-cHL.

2. Materials and methods

2.1. Study design and participants

This phase II, single-arm, open-label, multicenter clinical study was conducted at 24 centers in China. The study was approved by the ethics committee of each participating center. All participants provided signed informed consent before any study procedure. This trial was registered on ClinicalTrials.gov (#NCT03655483).

The inclusion criteria were as the following: (1) male or female ≥18 years of age; (2) histologically confirmed cHL; (3) r/r-cHL (relapse, confirmed PD after the most recent treatment; refractory, no CR or PR after the most recent treatment); (4) relapse/progression after salvage chemotherapy followed by ASCT or impossibility to perform ASCT (because of chemotherapy failure, age, or any other factor); (5) first-line chemotherapy being systemic multidrug combination chemotherapy; (6) subsequent chemotherapies including at least one systemic multidrug combination chemotherapy, and the last two cycles not achieving PR, the last four cycles not achieving CR, or the last cycle showing PD; (7) at least one measurable lesion according to Lugano 2014 [26]; (8) Eastern Cooperative Oncology Group performance status of 0–1; (9) expected survival >12 weeks; and 10) adequate organ function.

The key exclusion criteria were the following: (1) known lymphoma in the central nervous system; (2) allogeneic hematopoietic stem cell transplantation; (3) ASCT within 100 days before the initial administration of GLS-010 (zimberelimab); (4) symptomatic autoimmune disease; (5) systemic corticosteroids (dose equivalent ≥10 mg/d of prednisone) or other immunosuppressive drugs administered within 14 d before enrollment or during the study; or (6) a history of treatment with the anti-PD-1 antibody, anti-PD-L1 antibody, anti-PD-L2 antibody, anti-CD137 antibody, anti-CTLA-4 antibody, or any antitumor biological agents.

2.2. Treatment

All eligible participants received an injection of 240 mg of GLS-010 (zimberelimab) (fixed dose) for continuous treatment once every 2 weeks (a treatment cycle was 4 weeks), until confirmed PD, death, intolerable side-effects, or withdrawal from the study, for a maximum of 2 years. Dose adjustments were not allowed. When the administration was suspended because of immune-related adverse reactions or other reasons, the suspension time could not exceed 28 d; otherwise, the treatment was discontinued. Participants with PD diagnosed for the first time continued to undergo treatment according to investigators' judgment, receiving GLS-010 (zimberelimab) injection until PD was confirmed by imaging within 4–12 weeks.

2.3. Assessment

According to the Lugano 2014 evaluation criteria [26], the antitumor efficacy was evaluated by computed tomography (CT) and/or PET-CT until definite disease progression, initiation of new anticancer treatment, consent withdrawal, death, loss to follow-up, or end of the study, whichever occurred first. If contrast agents were contraindicated, whole-body magnetic resonance imaging/CT plain scan was allowed. Imaging examinations in the screening period were performed within 28 days before the first dose. Tumor assessments during the treatment phase were carried out during the 9th, 17th, 29th, 41st, and 53rd weeks, and every 16 weeks afterward (including the follow-up period if the patient did not have disease progression at the end of the treatment) (±1 week time window). PET-CT was performed during the screening period, in weeks 9 and 17, in case of clinical or CT suspected PD or to confirm a possible CR.

AEs were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 and coded using the Medical Dictionary for Regulatory Activities (version

20.0). Treatment-related AEs (TRAEs) were defined as related, possibly related, or uncertain AEs, by the investigators.

2.4. Pharmacokinetics

Blood was collected 1 h before administration on the 1st and 15th day of the 1st, 2nd, and 3rd treatment cycles, and 1 h before administration on the 1st day of every two cycles (every 8 weeks), thereafter. The serum concentration of GLS-010 (zimberelimab) was determined by electrochemiluminescence assay. The lower limit of quantification and the upper limit of quantification were 7.81 and 800 ng/mL, respectively.

2.5. End-points

The primary end-point was objective response rate (ORR): CR + PR, assessed by the independent radiology review committee (IRC) based on CT or PET-CT and according to Lugano 2014 [26].

Secondary end-points included ORR assessed by the investigator, progression-free survival (PFS), overall survival (OS), disease control rate (DCR) (participants with CR, PR, and stable disease [SD] divided by the total number of participants), duration of response (DOR), time to response (TTR), safety, pharmacokinetics (PK) characteristics, and the correlation between PD-L1 expression and efficacy. Treatment-emergent AEs were defined as AEs occurring between the first dose and 28 days after the last dose of GLS-010 (zimberelimab).

2.6. Statistical analysis

Assuming that the ORR of a historical control monotherapy was 40%, the ORR of GLS-010 (zimberelimab) in this study was estimated at 60%; the one-sided significance level was 0.025 and the dropout rate was 15%. Therefore, recruiting 85 participants would be necessary to achieve a power of 90% to test the statistical significance of the difference between GLS-010 (zimberelimab) and historical controls.

The full analysis set (FAS) was used for efficacy analysis and included all participants who met or did not meet the dropout criteria, and received at least one dose of the investigational drug. The safety set (SS) was used for safety analysis, including all participants who administered the drug at least once after enrollment and had data on post-drug safety assessment. The PK set was used for the PK analysis, including those who received at least one drug treatment and had assessable PK data.

The primary efficacy end-point was the ORR assessed by the IRC. The number, percentage, and 95% confidence interval (CI) of patients achieving an objective response (PR + CR) were determined. The binomial exact test was used to compare the investigational drug's ORR with historical control monotherapy (set at 40%). In case the 95% CI's lower limit of the investigational drug ORR was greater than that of the historical control monotherapy, the superiority of the investigational drug over the historical control monotherapy was established. The median PFS and its 95% CI were estimated, based on the Kaplan–Meier survival curve. In the absence of PD or death before PD, the date of the last imaging assessment was used for censoring. DCR, DOR, and their 95% CI were calculated, respectively.

For the PK analysis, the blood concentration–time curve was plotted according to the time point of blood collection and average or individual levels. Mean concentration–time curves were plotted linearly and semi-logarithmically according to the planned blood sample collection time. In the linear proportional graph, one or more below quantification limits (BQLs) were presented as 0 before the first measurable blood concentration, whereas other BQLs were presented as missing after the first measurable blood concentration. All analyses were performed using SAS Enterprise Guide version 7.1 (SAS Institute, Cary, NC).

3. Results

3.1. Characteristics of the participants

From August 2018 to April 2019, 85 participants were enrolled in the FAS and SS. As of 18th April 2020, 62 participants were still receiving treatment, and 23 of them discontinued. The causes of treatment discontinuation were PD (n = 13, 15.3%), AEs (n = 8, 9.4%), participant's request (n = 1, 1.2%), and other reasons (n = 1, 1.2%). One (1.2%) participant died. Ten patients continued the treatment after PD. Of these, two achieved SD, and others remained in PD. In patients who continued the treatment after PD, the average time from the first PD to treatment discontinuation was 5.7 months.

The baseline characteristics of the patients are presented in Table 1. All patients had received second- or further-line treatment. There were 49 (57.6%) males. HL was stage II in 12 (14.1%) participants, stage III in 19 (22.4%), and stage IV in 48 (56.5%). Twelve (14.1%) patients underwent ASCT and 2 (2.4%) received brentuximab vedotin.

3.2. Best overall response

In the IRC assessment, 28 participants (32.9%) had CR, 49 (57.6%) had PR, 5 (5.9%) had SD, and 3 (3.5%) had PD. A total of 77 participants achieved an objective response, for an ORR of 90.6% (95% CI 82.3–95.9%) (Table 2). The lower 95% CI limit (82.3%) was greater than the ORR (40%) of the historical control monotherapy ($p < 0.0001$). The ORR of investigators'

Table 1
Baseline characteristics.

	Patients with r/r-cHL (n = 85)
Age (years), median (min, max)	31 (18, 59)
Sex, n (%)	
Male	49 (57.6)
Female	36 (42.4)
Current tumor stage, n (%)	
II	12 (14.1)
III	19 (22.4)
IV	48 (56.5)
Other	6 (7.1)
ECOG, n (%)	
0	54 (63.5)
1	31 (36.5)
Previous therapies, n (%)	
Chemotherapy	85 (100)
Autologous stem cell transplantation	12 (14.1)
Brentuximab vedotin	2 (2.4)
Targeted drug[a]	10 (11.8)
Lines of prior therapy, n (%)	
2	48 (56.5)
3	25 (29.4)
4-6	12 (14.1)

ECOG, Eastern Cooperative Oncology Group; r/r-cHL, relapsed or refractory classical Hodgkin lymphoma
[a] Targeted drugs included HMLP-689 (PI3K inhibitor), lenalidomide, thalidomide, and verbutuximab.

Table 2
Best overall response.

	Assessed by IRC (n = 85)	Assessed by the investigator (n = 85)
Complete response, n (%)	28 (32.9)	31 (36.5)
Partial response, n (%)	49 (57.6)	46 (54.1)
Stable disease, n (%)	5 (5.9)	5 (5.9)
Progressive disease, n (%)	3 (3.5)	3 (3.5)
Objective response rate, n (%)	77 (90.6)	77 (90.6)
95% CI	(82.3–95.9)	(82.3–95.9)

Objective response = complete response + partial response.
IRC, independent radiology review committee; CI, confidence interval.

assessment is the same but with more CR (Table 2). A decrease in the sum of diameters of target lesions from baseline was observed in all evaluable cHL cases (Fig. 1).

3.3. Survival

The median follow-up was 15.8 (range 1.1–19.9) months. As of April 2020, the IRC assessed 9 (10.6%) participants with PD and one case of death before PD. The PFS rate at 6 months was 90% (95% CI 80.0–94.7). The 12-month PFS rate was 78% (95% CI 67.5–85.6), and the 12-month OS rate was 99% (95% CI 91.9–99.8). Median DOR, median PFS, and median OS were not reached (Fig. 2).

3.4. Pharmacodynamic analysis

For pharmacokinetics, a total of 664 serum samples from 85 participants were tested. According to the GLS-010 (zimberelimab) average serum concentration time curve, the average serum drug concentration increased with the number of doses. Starting with the fifth cycle, serum drug amounts reached a steady state, with average levels ranging from 77.304 to 93.250 μg/ml (Fig. 3).

3.5. Adverse events

AEs were observed in 85 participants (100%) and TRAEs were found in 79 participants (92.9%). The overall incidence rate of TRAE was greater than 10.0% including hypothyroidism (n = 18, 21.2%), decreased neutrophil count (n = 17, 20.0%), increased alanine aminotransferase (n = 17, 20.0%), decreased white blood cell count (n = 16, 18.8%), increased weight (n = 11, 12.9%), increased blood bilirubin (n = 10, 11.8%), increased aspartate aminotransferase (n = 9, 10.6%), pyrexia (n = 9, 10.6%), upper respiratory tract infection (n = 9, 10.6%), pruritus (n = 9, 10.6%), abnormal hepatic function (n = 9, 10.6%), and anemia (n = 9, 10.6%). A total of 19 participants (22.4%) developed CTCAE grade III TRAE, including abnormal hepatic function (n = 4, 4.7%), decreased neutrophil count (n = 3, 3.5%), increased weight (n = 3, 3.5%), hypertriglyceridemia (n = 2, 2.4%), and upper respiratory tract infection (n = 2, 2.4%). CTCAE grade IV TRAEs occurred in 5 participants (5.9%), including 4 cases of hyperuricemia (4.7%), 1 of abnormal hepatic function (1.2%), 1 of hypokalemia (1.2%), and 1 of increased blood creatine phosphokinase (1.2%), whereas 1 grade V TRAE (gastrointestinal infection) occurred in a single patient (Table 3).

Immune-related adverse events were observed in 41 participants (48.2%), including hypothyroidism (n = 16, 18.8%), increased alanine aminotransferase (n = 8, 9.4%), pruritus (n = 7, 8.2%), abnormal hepatic function (n = 6, 7.1%), and increased blood bilirubin (n = 5, 5.6%).

4. Discussion

GLS-010 (zimberelimab) is a novel, fully human, anti-PD-1 monoclonal antibody that shows promising efficacy and safety in advanced solid tumors. This phase II trial of GLS-010 (zimberelimab) strongly suggested the efficacy and safety of GSL-010 for r/r-cHL. In 85 patients with r/r-cHL, the ORR was 90.6%, and the CR rate was 33%, as assessed by IRC. The PFS at 6 months was 90%. Although TRAEs were observed in nearly all participants (92.9%), grade III–IV TRAEs occurred in only 22%. This phase II trial suggests that the ORR and 6-month PFS rate of GLS-010 (zimberelimab) in the

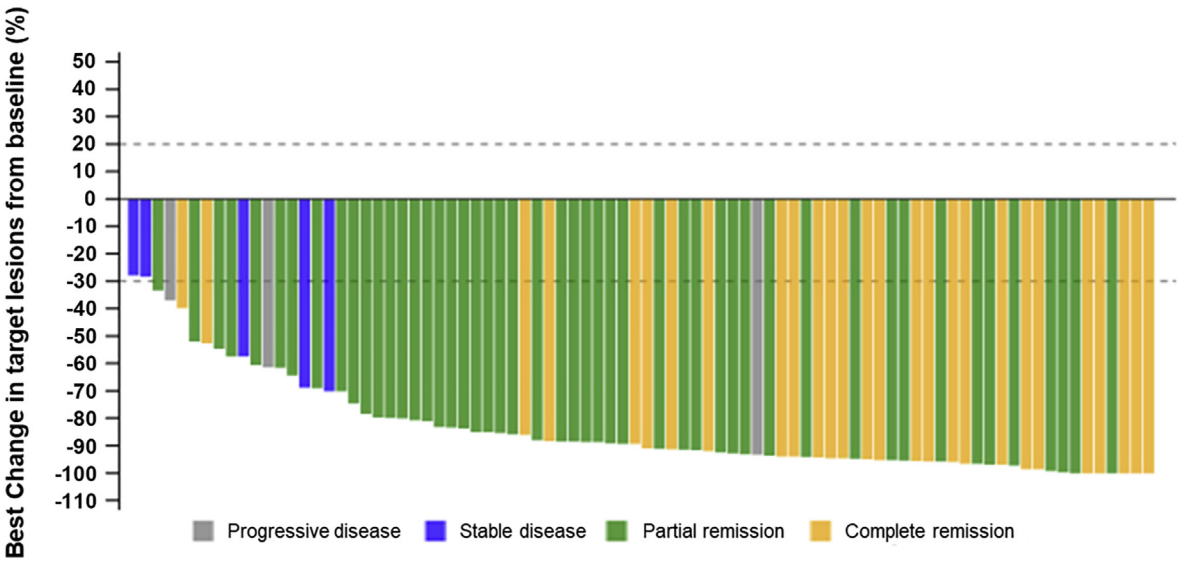

Fig. 1. Waterfall plot of the evaluation of the best overall response by the independent review committee (n = 85).

treatment of r/r-cHL are high, and the safety profile was acceptable.

In the present study, GLS-010 (zimberelimab) achieved an ORR of 90.6%, which was higher than the estimated 40% for the historical control and the preplanned 60% for GLS-010 (zimberelimab) in the power analysis, and similar to the ORR reported in the preliminary results (88%) [25]. This ORR was numerically higher than in previous studies of other anti-PD-1/PD-L1 therapies in the CheckMate 205 (nivolumab, 69%) [15], KEYNOTE-013 (pembrolizumab, 65%) [16,17], KEYNOTE-087 (pembrolizumab, 72%), and KEYNOTE-204 (pembrolizumab, 65.6%) [1,17] trials, and similar to those of the ORIENT-1 (sintilimab, 90%) [20], camrelizumab (80%) [21], and tislelizumab (87.1%) [22] trials. The 6-month PFS rate (90%) was also higher than in previous studies of various anti-PD-1 drugs (pembrolizumab, nivolumab, and tislelizumab) [15–17,22]. Nevertheless, a further follow-up is needed to determine the exact clinical benefit because the median PFS and OS were not reached.

There are major differences in the participants of the above studies between Western countries and China that prevent direct comparison of ORRs among different anti-PD-1 drugs. In Western countries, almost all patients were administered brentuximab vedotin before exposure to an anti-PD-1 therapy as second line [1]. Furthermore, ASCT is a fairly common procedure in r/r-cHL patients in Western countries [1]. Brentuximab vedotin had not been approved for marketing when the participants were enrolled, and hence, only few patients treated using brentuximab vedotin were enrolled in this study. Nevertheless, these results could partly explain the higher CR rate among patients who were less heavily pretreated. Furthermore, most participants in this study did not receive ASCT because it is expensive and not covered by medical insurance in China, leading to only a small number of patients being able to afford it [5,18,19]. Nevertheless, GLS-010 (zimberelimab) might be a good treatment option for individuals who could not receive or refused ASCT, or for patients eligible for ASCT as a bridge-to-transplant. Of the 12 participants who received ASCT, 4 had a CR, 6 had a PR, and 2 had SD. The two participants who received brentuximab vedotin had a PR, and the ORR remained significant even after excluding these two participants. Brentuximab vedotin is indicated for previous r/r-cHL and maintenance therapy after ASCT, with ORRs of 36–54% in heavily pretreated patients with r/r-cHL or improving median survival from 24.1 months (placebo) to 42.9 months (brentuximab vedotin) [27]. Nevertheless, brentuximab vedotin and GLS-010 (zimberelimab) do not have the same targets nor the same mechanisms of action, and both drugs could have additive or synergistic effects. PD-1 inhibitors such as GLS-010 (zimberelimab) block the immune escape of cancer cells, while brentuximab vedotin use CD30 to enter cancer cells and deliver the cytotoxic agent. More studies are required to evaluate the efficacy of GLS-010 (zimberelimab) in cases with progression after ASCT and brentuximab vedotin treatment.

The safety profile of GLS-010 (zimberelimab) was acceptable and similar to those of other PD-1/PD-L1 inhibitors as there were no unexpected or off-target safety signals similar to nivolumab [15], pembrolizumab [1,16,17], camrelizumab [21], and tislelizumab [22], along with GLS-010 (zimberelimab) in solid tumors [23,24]. TRAEs occurred in 92.9% of participants, most of which were grade I–II AEs. Grade III–IV TRAEs occurred in 22.4% of participants. Only one patient had a grade V TRAE, which was an intestinal infection that occurred after 3 months of treatment. The patient

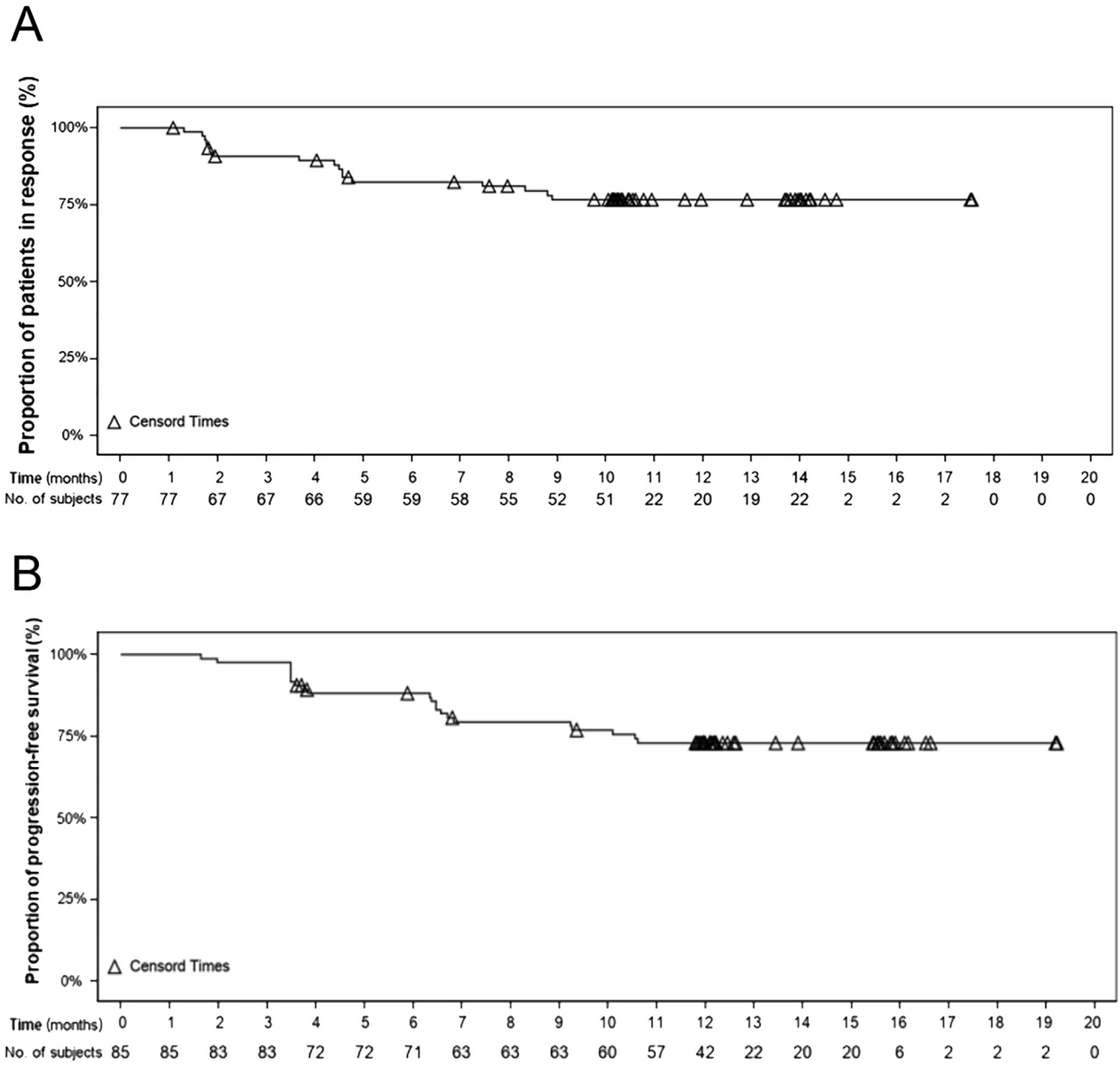

Fig. 2. Survival analysis. (A) Duration of response. (B) Progression-free survival.

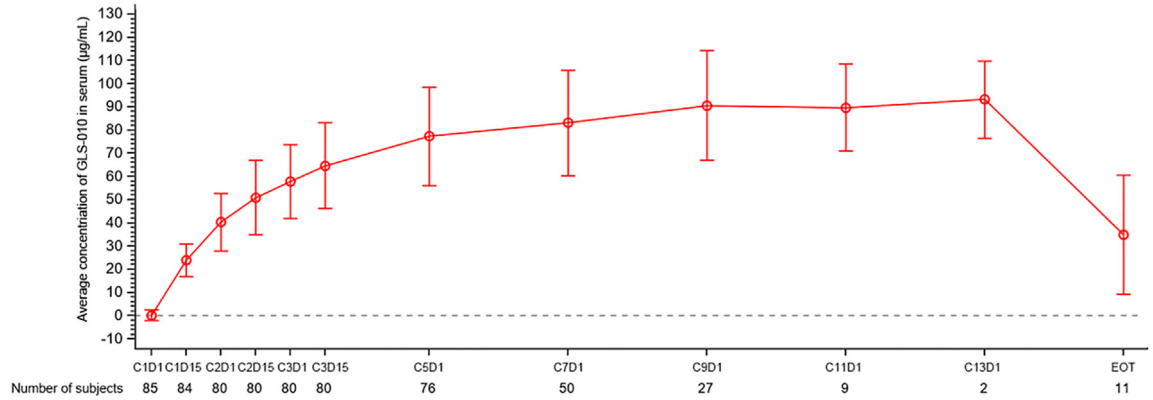

Fig. 3. Pharmacodynamic analysis of GLS-010 (zimberelimab) for relapsed/refractory classical Hodgkin lymphoma. The baseline represents the limit of detection of GLS-010 (zimberelimab) in serum, that is, 0.0078 μg/ml. C, cycle; D, day; EOT, end of treatment.

Table 3
Adverse events with an incidence >10%.

Adverse events	TEAEs (n = 85)		TRAEs (n = 85)	
	Any grade	Grade III–IV	Any grade	Grade III–IV
	n (%)	n (%)	n (%)	n (%)
Upper respiratory tract infection	44 (51.8)	3 (3.5)	9 (10.6)	2 (2.4)
Pyrexia	31 (36.5)	1 (1.2)	27 (31.8)	1 (1.2)
Weight increased	27 (31.8)	3 (3.5)	11 (12.9)	3 (3.5)
Neutrophil count decreased	23 (27.1)	4 (4.7)	17 (20.0)	3 (3.5)
White blood cell count decreased	21 (24.7)	0	16 (18.8)	0
Hypothyroidism	20 (23.5)	1 (1.2)	18 (21.2)	1 (1.2)
Alanine aminotransferase increased	18 (21.2)	0	17 (20.0)	0
Urinary tract infection	15 (17.6)	0	4 (4.7)	0
Hypertriglyceridemia	15 (17.6)	2 (2.4)	7 (8.2)	2 (2.4)
Pruritus	14 (16.5)	0	9 (10.6)	0
Anemia	14 (16.5)	0	9 (10.6)	0
Blood bilirubin increased	12 (14.1)	0	10 (11.8)	0
Hyperuricemia	11 (12.9)	4 (4.7)	6 (7.1)	4 (4.7)
Proteinuria	11 (12.9)	0	3 (3.5)	0
Lymphocyte count decreased	10 (11.8)	2 (2.4)	7 (8.2)	1 (1.2)
Aspartate aminotransferase increased	10 (11.8)	0	9 (10.6)	0
Cough	10 (11.8)	0	3 (3.5)	0
Hepatic function abnormal	10 (11.8)	5 (5.9)	9 (10.6)	5 (5.9)
Hypokalemia	9 (10.6)	1 (1.2)	2 (2.4)	1 (1.2)
Rash	9 (10.6)	0	5 (5.9)	0

One grade V TRAE occurred.
TEAEs, treatment-emergent adverse events; TRAEs, treatment-related adverse events.One grade 5 TRAE occurred.

received seven doses of GLS-010 (zimberelimab) (240 mg q 2 weeks) before the AE occurred and died in another hospital 2 d after the diagnosis. Because of the missing information of treatment in that hospital, the AE was categorized as 'possibly related' to GLS-010 (zimberelimab). This short-term safety profile is similar to those observed in other trials of GSL-010 [23–25] and anti-PD-1/PD-L1 drugs in general [15–17,21,28,29]. Nevertheless, the follow-up was relatively short, and long-term safety analysis remains to be studied.

The PK data showed that the serum concentration of GLS-010 (zimberelimab) steadily increased from the beginning of the treatment period until cycle 5, after which it remained relatively stable until the end of the treatment, where a sharp decrease was observed. This suggests that the dose of GLS-010 (zimberelimab) at each cycle was adequate to maintain the serum concentration, without accumulation in the body. In addition, no immunogenicity against GSL-010 was observed. Indeed, fully human antibodies usually have low immunogenicity [30]. These characteristics suggest that GLS-010 (zimberelimab) could be a novel, effective, and safe strategy for r/r-cHL treatment. The surface plasmon resonance assay showed that the K_d values of GLS-010 and sintilimab were both 10^{-10} M, while that of nivolumab was 10^{-9} M [31]. The cynomolgus monkey PK study showed that the $AUC_{0\text{-last}}$ was around 20,000 (21,300 and 19,773 h × μg/ml) at a dose of 6 mg. Receptor occupancy (RO) analysis also showed that the RO was >95% at saturation (preclinical data of GLS-010, unpublished at this time). These data indicate that GLS-010 and sintilimab may have similar pharmacokinetics, but both drugs might have a higher affinity to PD-1 and also a stronger inhibitory effect compared with nivolumab.

This trial had some limitations. First, only a few patients had received ASCT, and the efficacy of GLS-010 (zimberelimab) after ASCT needs further study. Second, this is a single-arm clinical trial without a direct comparator. A control group will be planned in future trials. In addition, as discussed, direct comparisons with previous studies are difficult because of the differences in study populations. Finally, the follow-up time was short, and clinical benefit and safety require long-term analysis.

5. Conclusion

The ORR and 6-month PFS rate of GLS-010 (zimberelimab) for the treatment of r/r-cHL were high. The safety profile was acceptable. Our results suggest that GLS-010 (zimberelimab) could serve as a novel, highly effective, and safe therapeutic approach for r/r-cHL. Long-term follow-up is required to confirm the above clinical benefits.

Authors' contributions

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Conflict of interest statement

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jiman Zhu: President of Guangzhou Gloria Biosciences Co., Ltd. Other authors declare no conflict of interest.

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