

EMAPALUMAB IN TREATMENT-EXPERIENCED PRIMARY HLH: SAFETY, EFFICACY, AND TRANSPLANT OUTCOMES FROM THE OPEN-LABEL, SINGLE-ARM POST-AUTHORIZATION STUDY SOBI.EMAPALUMAB-104 IN CHINESE PATIENTS

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CONCLUSIONS

- The safety and efficacy of emapalumab in Chinese patients with previously treated primary hemophagocytic lymphohistiocytosis (pHLH) were consistent with outcomes in the pivotal NI-0501-04 study¹
- In total, 10/13 (76.9%) patients had an overall response to emapalumab and 9 (69.2%) patients underwent hematopoietic stem cell transplant (HSCT)
- Eleven (84.6%) patients were alive at 12 months post-HSCT, or following last emapalumab infusion, if HSCT was not performed
- Most adverse events (AEs) were mild or moderate in intensity, with infections being the most common AE; no infusion-related reactions or treatment discontinuations because of treatment-related AEs were reported
- The outcomes of this study support emapalumab as a well-tolerated and effective bridge to HSCT in this critically ill population of treatment-experienced Chinese patients with pHLH

INTRODUCTION

- Primary hemophagocytic lymphohistiocytosis is a life-threatening hyperinflammatory syndrome requiring timely transition to HSCT, the only potentially curative therapy²
- Increased interferon gamma (IFN γ) production plays a key role in the pathogenesis of pHLH³
- Emapalumab, a fully human IgG1 anti-IFN γ monoclonal antibody, neutralizes the biologic activity of IFN γ ⁴
- Emapalumab has demonstrated efficacy in patients with pHLH and has a favorable safety profile with no apparent increase in the risk of AEs with greater drug exposure^{1,2,5}
- Emapalumab was approved in China in 2022 for the treatment of pHLH in adult and pediatric patients with refractory, recurrent or progressive disease or intolerance to conventional hemophagocytic lymphohistiocytosis (HLH) therapy⁶

OBJECTIVE

- To assess the safety and efficacy profile of emapalumab in treatment-experienced patients diagnosed with pHLH in China

METHODS

- Sobi.EMAPALUMAB-104 (NCT05744063) was an open-label, single-arm, multicenter, post-authorization study performed in China
- Eligible participants had a confirmed or suspected diagnosis of pHLH and had worsened or reactivated disease, or an unsatisfactory response to conventional therapy, or were unable to continue to receive conventional therapy because of adverse effects
- Patients received an initial intravenous infusion of emapalumab 1 mg/kg every 3–4 days
 - Dosing could be increased up to 10 mg/kg, if required, based on predefined laboratory and clinical response parameters
- Treatment continued until HSCT conditioning or until HSCT was not deemed indicated
- Emapalumab was administered on a background of dexamethasone $\geq$ 5 mg/m²/day, which could be tapered or increased according to physician assessment
- Patients underwent long-term follow up until 12 months post HSCT, or 12 months post last emapalumab infusion, if HSCT was not performed
- Descriptive statistics are provided for the all-treated set (patients who received $\geq$ 1 emapalumab infusion)

Endpoints

- Primary endpoint: treatment discontinuation because of a treatment-related AE, supported by other safety assessments as secondary endpoints
- Key secondary endpoint: overall response (achievement of complete or partial response or HLH improvement) at end of treatment (EOT) or Week 8, whichever occurred earlier
 - A complete response was defined as absence of fever (<37.5°C), normal spleen size, no cytopenia, no hyperferritinemia (<2000 μ g/L), no evidence of coagulopathy, no neurologic or cerebrospinal fluid abnormalities attributable to HLH, and no sustained increase in soluble CD25
 - A partial response was defined as $\geq$ 3 HLH clinical and laboratory abnormalities (including central nervous system [CNS] abnormalities) that met the criteria of complete response and there was no progression of other aspects of HLH disease pathology
 - HLH improvement was defined as an improvement (>50% change from baseline) of $\geq$ 3 HLH clinical and laboratory abnormalities (including CNS involvement)
- Other secondary efficacy endpoints included time to first overall response, cumulative duration of response, glucocorticoid (GC) tapering ($\geq$ 50% reduction from baseline dose for $\geq$ 7 days), survival to HSCT, post-HSCT survival, and overall survival
- Number of patients who underwent HSCT was an exploratory endpoint

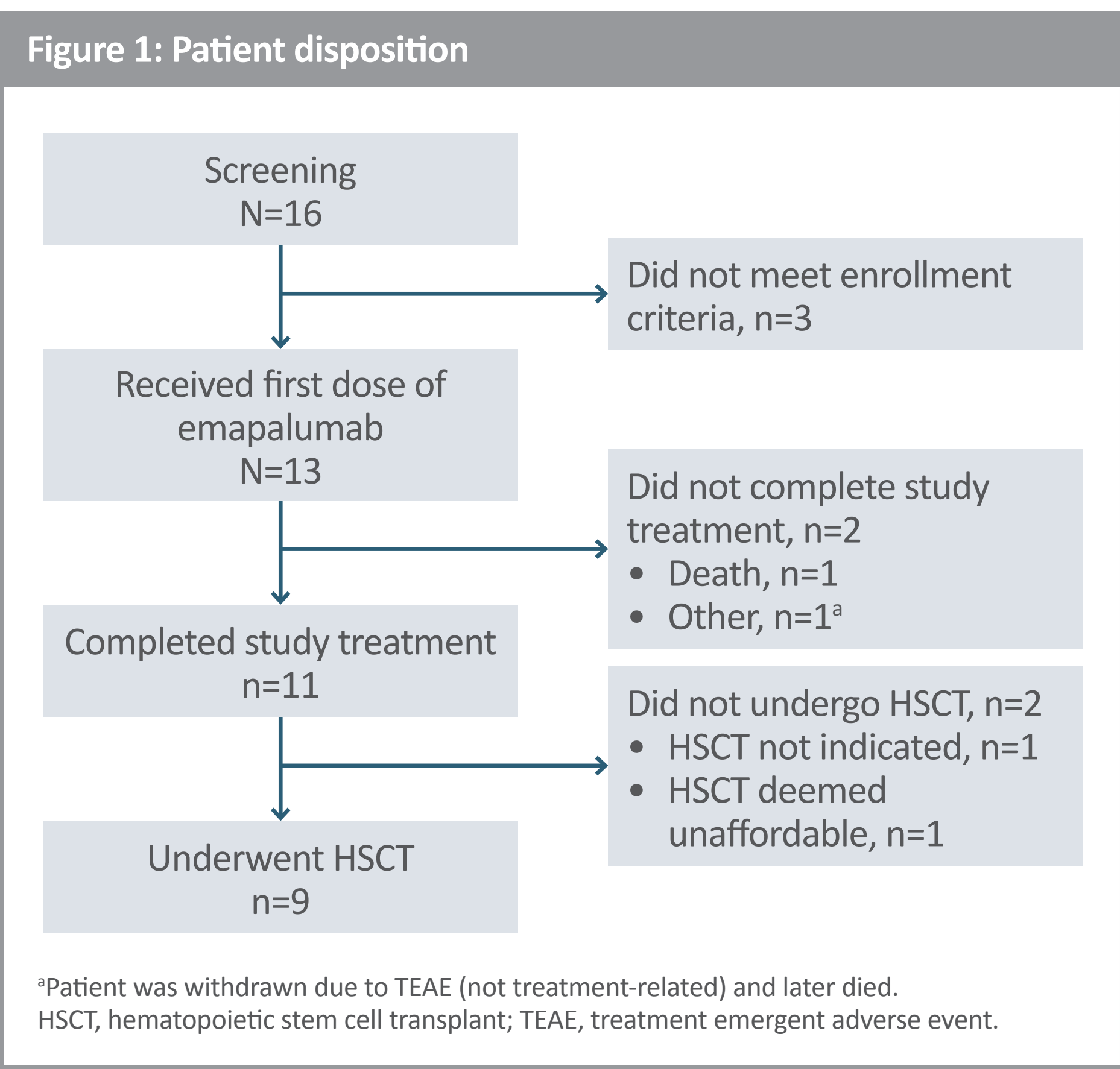
RESULTS

Baseline characteristics and patient disposition

- Thirteen Chinese patients with treatment-experienced pHLH from 7 centers participated in this study between January 29, 2023 and February 21, 2025 (**Table 1**)
- Median total duration of emapalumab dosing was 44 days (interquartile range [IQR], 36–77; range, 1–100)
- All patients received $\geq$ 1 concomitant HLH medication that included GCs
- Eleven (84.6%) patients completed study treatment (**Figure 1**)
- Nine (69.2%) patients underwent HSCT

Table 1: Demographics and baseline characteristics	
	N=13
Age, years, median (range)	7 (3–33)
Age group, n (%)	
<18 years	12 (92.2)
$\geq$ 18 years	1 (7.7)
Sex, male, n (%)	8 (61.5)
pHLH diagnosis, n (%)	
Confirmed	9 (69.2)
Suspected	4 (30.8)
Genetic confirmation of pHLH, n (%) ^a	
PRF1	9 (69.2)
UNC13D	5 (55.6)
STXBP2	4 (44.4)
PALB2	1 (11.1)
Family history, n (%)	
Confirmed pHLH diagnosis	1 (7.7)
Suspected pHLH diagnosis	1 (7.7)
Disease features, n (%)	
CNS involvement	3 (23.1)
Liver involvement	3 (23.1)
Previous pHLH treatment, n (%)	
GCs	13 (100)
Antineoplastic agents	10 (76.9)
Immunosuppressants	9 (69.2)
Concomitant pHLH treatment, n (%)	
GCs	13 (100)
Immunosuppressants	5 (38.5)
Antineoplastic agents	3 (23.1)
Immune sera and immunoglobulins	1 (7.7)

^aPatients could have more than 1 mutation.
CNS, central nervous system; GC, glucocorticoid; pHLH, primary hemophagocytic lymphohistiocytosis.



Safety

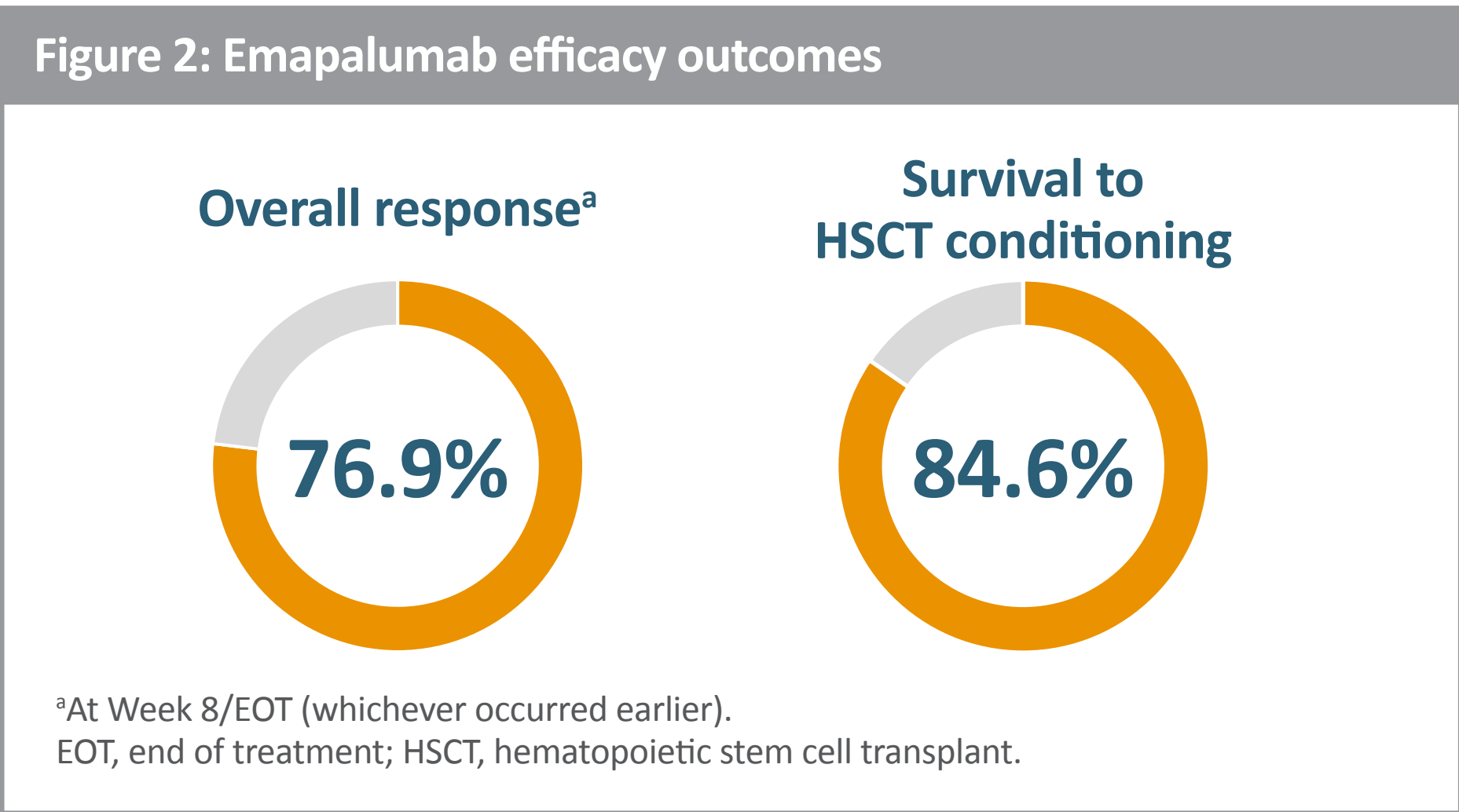
- All patients experienced $\geq$ 1 treatment-emergent adverse event (TEAE) prior to HSCT conditioning; most were mild or moderate in intensity (**Table 2**)
 - Treatment-related TEAEs were observed in 9 (69.2%) patients
- Six (46.2%) patients experienced serious TEAEs
 - Four serious treatment-related TEAEs (pneumonia respiratory syncytial viral [n=2], sepsis [n=1], and pneumonia [n=1]) were experienced by 3 (23.1%) patients
- No patient experienced an infusion-related TEAE
- One patient (7.7%) experienced treatment-related TEAEs that required treatment interruption
- No patient discontinued emapalumab because of a treatment-related AE
- Two (15.4%) patients died prior to HSCT conditioning as a result of pHLH progression

Table 2: Adverse events prior to HSCT		
N=13	Events	n (%)
TEAEs	154	13 (100)
Treatment-related	18	9 (69.2)
Serious TEAEs	8	6 (46.2)
Treatment-related	4	3 (23.1)
Infection TEAEs	28	10 (76.9)
Serious infection TEAEs	4	3 (23.1)
Treatment-related TEAEs leading to treatment interruption	3	1 (7.7)
TEAEs leading to study withdrawal	2	2 (15.4)
TEAEs leading to death ^a	2	2 (15.4)

^aCondition aggravated (n=2); not related to emapalumab.
HSCT, hematopoietic stem cell transplant; TEAE, treatment-emergent adverse event.

Efficacy

- Overall response at Week 8/EOT was achieved by 10 (76.9%) patients (**Figure 2**)
 - Five (38.5%) patients had a complete response, 4 (30.8%) patients had a partial response, and 1 (7.7%) patient had HLH improvement
 - Two (15.4%) patients had no response
 - One (7.7%) patient had missing data due to premature withdrawal from the study
- The median time to first overall response was 4 days (range, 3–5)
- The median cumulative duration of any response, measured until EOT, was 43 days (range, 8–106)
- GC tapering occurred in 6 (46.2%) patients at any time point during the treatment period



- Eleven (84.6%) patients survived to HSCT conditioning (**Figure 2**)
- HSCT was performed in 9 (69.2%) patients
 - Four (30.8%) patients did not progress to HSCT (death, treatment not successful and patient later died, HSCT was deemed unaffordable, HSCT was deemed not needed by investigator [n=1 each])
- Eleven (84.6%) patients remained alive at 12 months follow-up

HSCT outcomes

- Engraftment was achieved in 8/9 (88.9%) patients
- Median donor chimerism was 100% (IQR, 99.4–100; range, 73.1–100)
- One (12.5%) of the 8 patients who achieved engraftment developed graft-versus-host disease
- No patient experienced pHLH reactivation
- Survival at 12 months post-HSCT was 100%

References

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Disclosures

RZ, XZ, and JF have no disclosures. AD is a former employee of Sobi. BP, PH, and RK are employees of Sobi. RK also has a research affiliation with Karolinska Institutet, Stockholm, Sweden. AR and BDJ are employees of Sobi, Inc.

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