A Phase II Study of Penpulimab, an IgG1 Anti-PD-1 Antibody, in Patients With Relapsed or Refractory Classical Hodgkin Lymphoma (cHL)

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Background

- For classical Hodgkin lymphoma (cHL), programmed death-1 (PD-1) is a well-recognized target.
- Most available anti-PD-1 antibodies are of IgG4 isotype, which have residual antibody dependent-cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and antibody-dependent cytokine release (ADCR) activities.[1]
- Moreover, it has been reported that due to instability of Fc and Fc-Fc interaction, IgG4 is associated with immune tolerance and immune escape, which might have a negative impact on immunotherapy.[2]
- Penpulimab is a novel IgG1 anti-PD-1 antibody engineered to eliminate binding to FcγRIa, and FcγRIIIa receptors and so avoid ADCC, ADCP and reduce ADCR.

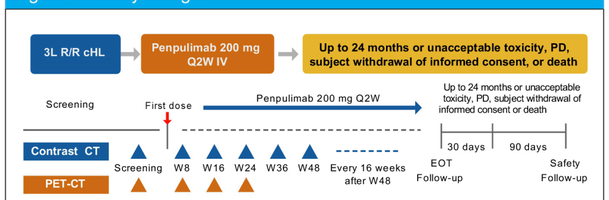
Objectives

- To assess the anti-tumor activity of penpulimab in patients with relapsed or refractory (R/R) cHL.
- To assess the safety and tolerability of penpulimab in R/R cHL.

Methods

- AK105-201 (NCT03722147) is a multicenter, single-arm, open-label phase I/II clinical study of penpulimab in the treatment of R/R cHL (Figure 1). Here we report the updated phase II study results.[3]
- Eligible patients had histopathologist-assessed R/R cHL following autologous hematopoietic stem cell transplantation (ASCT), or ≥2 lines of prior chemotherapy, and had not received PD-1/CTLA-4 antibody treatment.
- Patients received penpulimab 200 mg IV every 2 weeks until progression or unacceptable toxicity.
- The primary endpoint was objective response rate (ORR) based on the Lugano 2014 classification of positron emission tomography (PET), PET-computed tomography (CT) treatment response[4] as assessed by an independent review committee (IRC).
- Key secondary endpoints included complete response (CR) rate, disease control rate (DCR), progression-free survival (PFS), duration of response (DoR), safety, and tolerability.

Figure 1. Study design



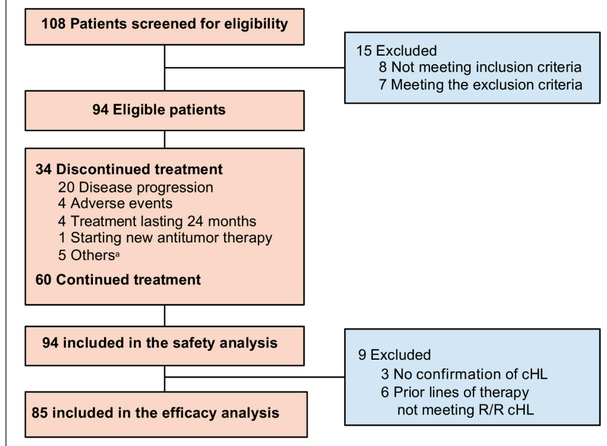
3L, third-line treatment; EOT, end of treatment; IV, intravenous infusion; PD, progressive disease; Q2W, every 2 weeks; W, week.

Results

Patients

- At the time of data cutoff (8 November 2020), there were 94 patients in the safety analysis set and 85 in the full analysis set (Figure 2). Median follow-up was 15.8 months (range, 12.1 to 26.9); 60 patients are still receiving therapy. Baseline characteristics are shown in Table 1.

Figure 2. Patient disposition



[a]3 patients discontinued treatment due to the COVID-19, 2 patients refused treatment due to personal reasons.

Table 1. Baseline characteristics - full analysis set

Characteristic	N=85	Characteristic	N=85
Age, years	32 (18–67)	Bone marrow involvement	21 (24.7)
Sex		Current histology	
Male	52 (61.2)	NSHL	58 (68.2)
Female	33 (38.8)	MCHL	20 (23.5)
ECOG PS		LRCHL	4 (4.7)
0	63 (74.1)	Unknown	3 (3.5)
1	22 (25.9)	Prior lines of therapy	3 (2–11)
B-symptoms	32 (37.6)	≥3	45 (52.9)
Clinical stage		Prior therapy	
Stage I[a]	1 (1.2)	Cancer surgery	7 (8.2)
Stage II	13 (15.3)	Radiotherapy	41 (48.2)
Stage III	16 (18.8)	ASCT	14 (16.5)
Stage IV	55 (64.7)	Transplantation	
Diagnosis to first administration, months	24 (3.4–290.7)	Brentuximab vedotin	0

Values are shown as median (range), or n (%). [a]One subject with stage I was in stage III when diagnosed, relapsed after CR treatment, and was reassessed as stage I. ECOG, Eastern Cooperative Oncology Group performance status; LRCHL, lymphocyte-rich classical Hodgkin lymphoma; MCHL, mixed-cellularity Hodgkin lymphoma; NSHL, nodular sclerosing Hodgkin lymphoma.

Efficacy

- Among the 85 evaluable patients, ORR was 89.4% (95% confidence interval [CI], 80.8%–95.0%) and 40 patients (47.1%) achieved CR. Median duration of response was not reached (Table 2).

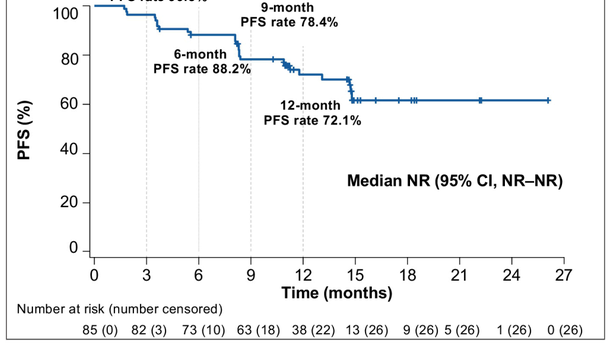
Table 2. Efficacy measurements

	Evaluable patients (N=85)	
ORR	76 (89.4%)	(95% CI, 80.8%–95.0%)
CR	40 (47.1%)	
PR	36 (42.4%)	
SD	6 (7.1%)	
PD	3 (3.5%)	
DCR	82 (96.5%)	(95% CI, 90.0%–99.3%)
DoR, months	NR (1.7–24.5+)	
12-month PFS	72.1%	(95% CI, 60.5%–80.8%)

Values are shown as median (range), or n (%). NR, not reached; PR, partial response; SD, stable disease.

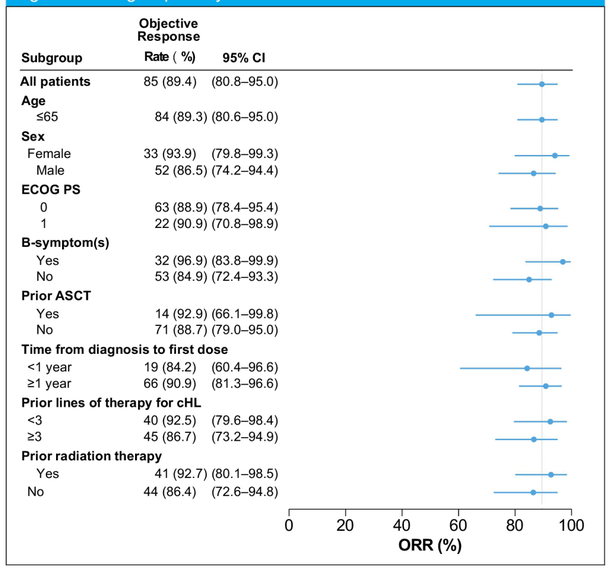
- Median PFS was not reached; 3, 6, 9, and 12-month PFS (95% CI) rates were 96.5%(89.5%, 98.8%), 88.2%(79.2%, 93.5%), 78.4%(67.9, 85.5%) and 72.1%(60.5%, 80.8%), respectively (Figure 3). 18-month overall survival (OS) was 100% and median OS was not reached.

Figure 3. Progression-free survival



- Subgroup analysis of ORR (Figure 4) to explore the prognostic value of baseline characteristics on survival showed that age, sex, ECOG score, B-symptoms, previous lines of therapy, time from initial diagnosis to first dose, previous radiotherapy, and prior ASCT had no significant effect on ORR.

Figure 4. Subgroup analysis



Safety

- Treatment-related adverse events (TRAEs) occurred in 95.7% of patients (Grade 3 in 26.6% [25/94], treatment discontinuation in 5.3% [5/94]). Most frequent TRAEs (≥15%) were hypothyroidism (31.9%), upper respiratory tract infection (25.5%), fever (24.5%), ALT elevations (23.4%), hypertriglyceridemia (19.1%), white blood cell count decreased (18.1%), weight increase (18.1%), hyperuricemia (18.1%), and rash (16.0%).
- Immune-related AEs (irAEs) were reported in 54.3% of patients (Grade 3 in 4.3%, Grade 4/5 in none, serious irAEs in 3.2%, and treatment discontinuation in 4.3% of patients). Excluding thyroid disease, irAEs were reported in 17.0% of patients.

Table 3. Immune-related AE (≥Grade 3) – safety analysis set (N=94)

Preferred term	Grade 3 n (%)	Grade4/5 n (%)
Rash	1 (1.1)	0 (0)
Psoriasis	1 (1.1)	0 (0)
Neutrophil count decreased	1 (1.1)	0 (0)
IgA nephropathy	1 (1.1)	0 (0)

Conclusions

- Penpulimab is an Fc-engineered IgG1 anti-PD-1 antibody that has been shown to be highly active, resulting in a high overall response rate and a favorable immune-related safety profile in patients with R/R cHL.

References

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