571 PENPULIMAB FOR RELAPSED/REFRACTORY (R/R) CLASSICAL HODGKIN'S LYMPHOMA (CHL): EXTENDED FOLLOW-UP OF THE MULTICENTER, SINGLE-ARM, PHASE 2 STUDY

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Background Nearly all anti-PD-1 antibodies are of the IgG4 isotype which may possess residual crystallizable fragment (Fc) gamma receptor (FcγR) effector functions and are also associated with immune tolerance and escape due to instability of the CH3 domain and Fc-Fc interaction. Penpulimab is a novel IgG1 anti-PD-1 antibody that has a good stability and reduced host cell protein residue. Penpulimab was engineered to eliminate Fc-mediated effector function that compromises anti-tumor immune cell function. Penpulimab also showed numerous contacts with N58 glycosylation on the BC loop of PD-1 which may contribute to slower binding off-rate. In this trial, we examined the efficacy and safety of penpulimab in patients (pts) with R/R cHL. Here we report results from up to 30 months follow-up.

Methods AK105-201 (NCT03722147) is a multicenter, single-arm, open-label study of penpulimab in R/R cHL. Adult pts (≥18 years of age) received penpulimab 200 mg once biweekly until progression or unacceptable toxicities. Eligible pts had prior autologous stem cell transplant (ASCT) or at least 2 lines of prior chemotherapy. The primary endpoint was ORR based on the Lugano 2014 criteria as assessed by an independent review committee (IRC). Key secondary endpoints included complete response (CR) rate, progression-free survival (PFS), overall survival (OS), treatment-related adverse events (TRAEs) and immune-related adverse events (irAEs).

Results A total of 94 patients were enrolled. As of the data cutoff date (Dec 31, 2021), the median follow-up was 29.5 months. Median number of treatment cycles was 26.1 (range 2–36). 85 patients meted the definition of primary efficacy population-IRC. Efficacy data is presented in (table 1). TRAEs (with unlikely related events included) occurred in 98.9% of pts (≥ G3 in 28.7% [27/94], treatment discontinuation in 6.4% [6/94]). Treatment related serious adverse event (SAEs) occurred in 12.8%. Most frequent TRAEs were hypothyroidism (33.0%), upper respiratory tract infection (26.6%), fever (24.5%), and ALT elevations (24.5%). Grade ≥3 TRAEs reported in ≥3 pts were platelet count decreased (3.2%), hyperlipemia (3.2%), rash (3.2%). In addition, 52 (55.3%) patients experienced an irAEs. The most frequent irAE was hypothyroidism (51.1%), and 4 (4.3%) patients developed grade 3 irAEs. No grade 4 or 5 irAEs were reported. No new safety signals were observed.

Conclusions Penpulimab was well tolerated, with a good safety profile in long-term use in R/R cHL pts. It demonstrated promising therapeutic activity and continued PFS and OS benefit.

Trial Registration NCT03722147

Ethics Approval The study was approved by relevant ethic committees and institutional review boards.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Abstract 571 Table 1 Efficacy data evaluated by IRC based on 2014 Lugano classification in the full analysis set (FAS; n=85)

	IRC-evaluated N=85
Confirmed ORR, n (%) (95% CI)	77 (90.6) (82.3, 95.8)
DCR, n (%) (95% CI)	83 (97.6) (91.8, 99.7)
CR, n (%)	42 (49.4)
PR, n (%)	35 (41.2)
SD, n (%)	6 (7.1)
PD, n (%)	2 (2.4)
Not evaluable, n (%)	0
TTR (month), median (range)	1.8 (1.4, 6.9)
PFS (month) [a]	
Median (95% CI)	33.2 (18.6, -)
12-mo rate (%) (95% CI)	76.9 (66.2, 84.6)
30-mo rate (%) (95% CI)	51.3 (39.0, 62.3)
OS (month) [a]	
Median (95% CI)	NR (NE, NE)
18-mo rate (%) (95% CI)	100.0 (100.0, 100.0)
36-mo rate (%) (95% CI)	96.1 (88.2, 98.7)

Abbreviations: CI, confidence interval; CR, complete response; DoR, duration of response; IRC: Independent Review Committee; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease; TTR, time to tumor response.

[a] Kaplan-Meier method; [b] some cases were censored.

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