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ORAL ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Isatuximab and Cemiplimab in Relapsed or Refractory Extranodal Natural Killer/T-Cell Lymphoma: A Multi-Center, Open-Labeled Phase II Study (CISL2102/ICING study)

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Introduction

Extranodal NK/T-cell lymphoma (ENKTL), an Epstein-Barr virus (EBV) associated lymphoid malignancy is a rare but aggressive non-Hodgkin lymphoma (NHL). The prognoses of patients with relapsed or refractory (R/R) ENKTL are still poor because there is limited treatment option for R/R ENKTL. The expression of PD-L1 (Programmed Death Ligand-1) is common in ENKTL because EBV could induce the PD-L1 expression. Thus, PD1 and PD-L1 inhibitors have been tried as salvage treatments, but their single-agent activities in previous studies were not satisfactory. CD38 has been considered as another potential therapeutic target in ENKTL because tumor cells of ENKTL could express CD38. CD38 expression was also reported to be related with the resistance to PD1 inhibitors. Thus, we conducted a phase II study with the combination of cemiplimab (PD1 inhibitor) and isatuximab (monoclonal anti-CD38 antibody) in patients with R/R ENKTL.

Methods

We aimed to analyze the efficacy of isatuximab (anti-CD38 monoclonal antibody) and cemiplimab (anti-PD1 monoclonal antibody) in patients with R/R ENKTL. Patients eligible for this study had relapsed or refractory disease at least one line of treatment. The induction treatment consisted of cemiplimab 250mg (day 1 and 15) and isatuximab 10mg/kg (day 2 and 16) intravenous administration every 4 weeks for 6 cycles. After that, responders received cemiplimab 250mg and isatuximab 10mg/kg once every 3 weeks up to 24 months or until progression, death, or study withdrawal. The primary end point was complete response (CR) rate and secondary end points were objective response rate (ORR) consisting of CR and partial response (PR), progression-free survival (PFS), and safety. The target CR rate was designated as 40% (P1). Considering 20% (P0) of CR rate after conventional salvage therapies and 10% of drop-out rate, 37 patients were planned to be enrolled.

Results

Between June 2021 and May 2023, we enrolled 37 patients. At enrollment, 29 (78%) patients had stage IV disease and 26 (70%) belonged to the high-risk of prognostic index of NK lymphoma (PINK-E, Table 1). Prior to the participating in the study, 19 (51%) patients had received $\geq$ 2 lines of systemic therapy. At the time of enrollment, 10 (27%) patients were refractory to their previous treatments whereas the remaining patients had relapsed diseases. After the first day of first cycle, all patients completed at least one cycle of treatment. The response rate was determined by the best response during treatment. As 16 patients achieved CR, the CR rate was 43% (16/37). Thus, the primary end point was met in the study. The ORR was 65% (24/37) consisting of 16 CR and 8 PR. The responders could maintain their treatments up to 32 cycles, and the median PFS of responders was 21.0 months (95% CI: 7.8-34.2 months, Figure 1). The comparison of characteristics between responders

and non-responders showed stage at enrollment was significantly associated with response (P = 0.032, Table 1). Thus, eight patients with stage I/II at enrollment responded to the treatment (100%, 8/8) whereas 55% (16/29) patients in stage III/IV responded to the treatment. The risk of PINK-E and other unfavorable parameters were not related with treatment response. Furthermore, the PD-L1 expression showed an association with response (Table 1), thus, 83% of patients (15/18) achieved CR or PR. Most treatment-emergent adverse events were grade 1-2 in severity. Only one patient with CR withdrew from the study due to neuropathic pain that was related with the patient's previous treatments. The hematologic and non-hematologic grade ≥ 3 events were reported in 12 (32%) patients including pneumonia. However, they were manageable, and there was no treatment-related death.

Conclusions

The combination of isatuximab with cemiplimab showed durable antitumor activity and manageable safety profiles in R/R ENKTL. Especially, patients with PD-L1 expression showed better outcomes than patients with low PD-L1 expression. Further study with a larger study population should be warranted to confirm our findings.

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OffLabel Disclosure: Isatuximab (CD38 antibody) and cemiplimab (PD1 inhibitor) is applied for relpased or refractory NK/T-cell lymphoma.

Table 1. Characteristics of patients at enrollment

Characteristics	Total	Responders	Non-responders	
	n (%)	*n* (%)	*n* (%)	*p**
Age (years)				
≤ 60	26 (70)	15 (63)	11 (85)	0.262
> 60	11 (30)	9 (37)	2 (15)	
Sex				
Male	22 (59))	15 (63)	7 (53)	0.730
Female	15 (41)	9 (37)	6 (47)	
Performance status				
ECOG 0	29 (78)	19 (79)	10 (77)	> 0.999
ECOG 1	8 (22)	5 (21)	3 (23)	
Stage				
I/II	8 (22)	8 (33)	0 (0)	**0.032**
III/IV	29 (78)	16 (67)	13 (100)	
Disease status				
Relapsed	27 (73)	19 (79)	8 (62)	0.275
Refractory	10 (27)	5 (21)	5 (38)	
PINK-E risk				
Low	7 (19)	7 (29)	0 (0)	0.069
Intermediate	4 (11)	3 (13)	1 (7)	
High	26 (70)	14 (58)	12 (93)	
PDL1 score				
≤ 10	16 (43)	7 (29)	9 (69)	**0.050**
> 10	18 (49)	15 (63)	3 (23)	
Not available	3 (8)	2 (8)	1 (8)	
Number of previous treatments				
< two	18 (49)	13 (54)	5 (38)	0.495
≥ two	19 (51)	11 (46)	8 (62)	
Previous radiotherapy				
Not done	18 (49)	9 (37)	9 (69)	0.091
Done	19 (51)	15 (63)	4 (31)	
Previous autologous SCT				
Not done	32 (87)	22 (92)	10 (77)	0.321
Done	5 (13)	2 (8)	3 (23)	

ECOG=Eastern Cooperative Oncology Group

PINK-E=Prognostic Index for Natural Killer-EBV; SCT=Stem cell transplantation

*p**: Chi-square test for responders and non-responders

Figure 1. Progression-free survival of responders

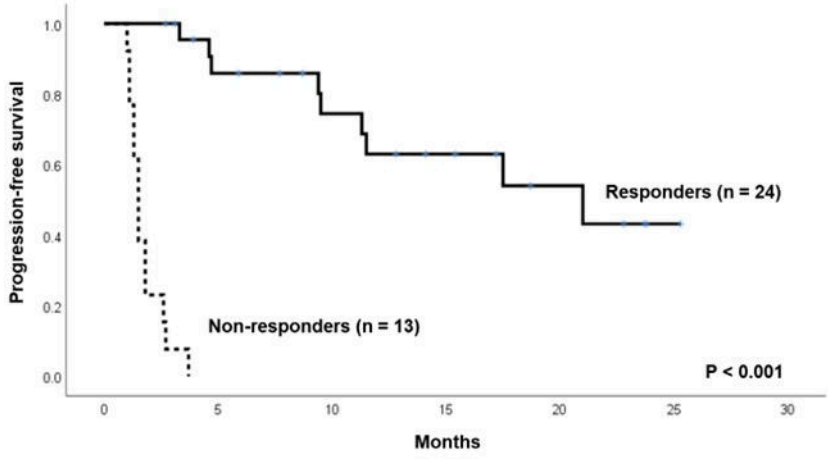

Figure 1

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