

Artificial intelligence (AI)-based membrane specific PD-L1 and immune subtypes as predictive biomarkers for danburstotug in relapsed or refractory extranodal NK/T cell lymphoma (R/R ENKTL): Insights from the phase II trial (DISTINKT)

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INTRODUCTION

- Danburstotug, a fully human anti-PD-L1 recombinant monoclonal antibody, enhances T-cell activation and proliferation. It also maintains Fc effector function to stimulate antibody-dependent cellular cytotoxicity.
- Preliminary efficacy and safety data from the phase 2 study of danburstotug have been reported, demonstrating high effectiveness in patients with R/R ENKTL and a well-tolerated safety profile.
- This study further explored AI-based PD-L1 membrane specificity (MS) and tumor immune microenvironment (TIME) as potential predictive biomarkers.

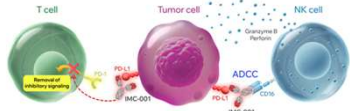


Figure 1. Mechanism of Action of Danburstotug

AIM & METHODS

- Primary Endpoint:** ORR by the centralized independent review
- Secondary Endpoints:** PFS, OS, PK, safety, and biomarkers

Key Inclusion Criteria

- Histologically confirmed R/R ENKTL per WHO classification (2016)
- At least 1 previous line of systemic therapy
- At least 1 measurable disease as per the Lugano criteria (2014)

Figure 2. Study Design and Treatment

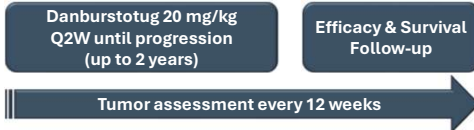


Figure 3. Biomarker Assessment using Tumor Tissue

3-A. AI-based Membrane Specificity

Lunit SCOPE[®] universal IHC analyzer

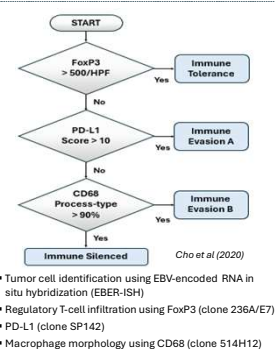
- A subcellular analysis model segmented cells (membrane, cytoplasm, nucleus) and quantified compartment intensity (0-100%)

PD-L1 (clone 28-8)

$$\text{Membrane Specificity} = \frac{\text{Membrane Intensity}}{\text{Membrane} + \text{Cytoplasm} + \text{Nucleus Intensity}}$$

- Non-specific cell proportion: number of cells with (Mb intensity ≥ 0.1 and Mb specificity < 0.35) divided by the number of cells with Mb intensity ≥ 0.1
- MS-High: Non-specific cell proportion $< 40\%$
- MS-Low: Non-specific cell proportion $\geq 40\%$

3-B. TIME Subtypes



- Tumor cell identification using EBV-encoded RNA in situ hybridization (EBER-ISH)
- Regulatory T-cell infiltration using FoxP3 (clone 236A/E7)
- PD-L1 (clone SP142)
- Macrophage morphology using CD68 (clone 514H12)

Danburstotug Shows Robust and Durable Efficacy with a Predictive Biomarker

- High and Durable Response:** ORR 79% and CR 63% in relapsed/refractory ENKTL
- Sustained Survival Benefit:** mPFS 29.4 mo and mOS 40.2 mo
- Clinical benefit observed across IT, IE-A, and IE-B with lower PD-L1 expression**
- PD-L1 Membrane Specificity identified as a potential predictive biomarker**

RESULTS

From Oct 2020 to Aug 2025, a total of 23 patients were enrolled and treated with danburstotug. Four patients were considered inevaluable due to absence of post-baseline tumor assessments, leaving 19 patients eligible for the efficacy analysis.

Table 1. Baseline Characteristics

Characteristics	ITT (N=23)	FAS (N=19)	Characteristics	ITT (N=23)	FAS (N=19)
Age, years*	58 (33-79)	57 (33-79)	Immune subtype	1 (4)	1 (5)
Sex, male	20 (87)	16 (84)	Immune tolerance	10 (43)	9 (47)
ECOG PS 0	15 (65)	13 (68)	Immune evasion A	9 (39)	7 (37)
Asian	23 (100)	19 (100)	Immune evasion B	0	0
Ann Arbor disease stage			Immune silenced	3 (13)	2 (11)
I/II	13 (57)	13 (68)	Unknown	11 (48)	11 (58)
IV	10 (43)	6 (32)	PD-L1 membrane specificity	7 (30)	3 (16)
Non-nasal type	6 (26)	4 (21)	High	5 (22)	5 (26)
EBV DNA in blood	17 (74)	13 (68)	Low	19 (83)	15 (79)
PINK/PINK-E			Unknown	5 (22)	5 (26)
Low/Intermediate	14 (61)	14 (74)	Prior systemic therapy ≥ 3	7 (30)	6 (32)
High	9 (39)	5 (26)	Prior anti-PD-1	5 (22)	5 (26)
Disease status, relapsed	16 (70)	15 (79)	Prior L-asparaginase regimen	19 (83)	15 (79)
Serum LDH, normal	18 (78)	16 (84)	Previous radiotherapy	17 (74)	15 (79)

number of patients (%), *median, ITT (intent-to-treat set; all enrolled subjects), FAS (full analysis set; at least one post-baseline efficacy assessment)

Efficacy Result

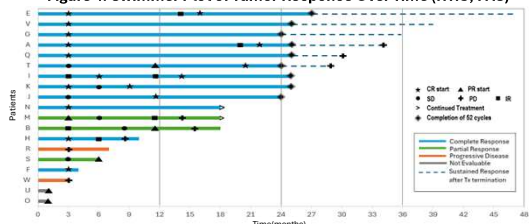
- ORR and CR rates by independent review were 79% and 63%, respectively.
- Among twelve patients who received treatment for over one year, nine completed two years of therapy.

Table 2. Tumor Response by ITRC (FAS)

Endpoints	Results	Endpoints	Results
Objective response	15 (79)	Duration of response*	NR
Best overall response	12 (63)	1-year rate	77%
Complete response	3 (16)	2-year rate	77%
Partial response	0	Duration of complete response*	NR
Stable disease	2 (11)	1-year rate	91%
Progressive disease	2 (11) ^a	2-year rate	91%
Not evaluable	2 (11) ^a	Time to response*	3 mo.

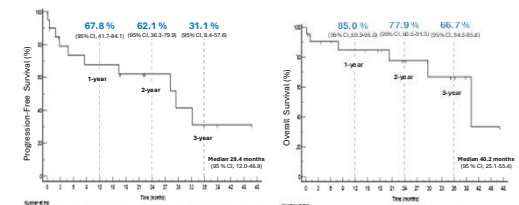
number of patients (%), ^aPR but maintained for less time than the minimum duration of 6 weeks, *median, ITRC (independent tumor review committee), NR (not reached yet)

Figure 4. Swimmer Plot of Tumor Response Over Time (ITRC, FAS)



Median PFS was 29.4 months and median OS was 40.2 months, indicating durable efficacy.

Figure 5. Kaplan-Meier Curve of PFS and OS (ITT)



Biomarkers Result

High PD-L1 MS was significantly associated with improved response and longer PFS compared with low PD-L1 MS.

Figure 6. Tumor Response by PD-L1 MS

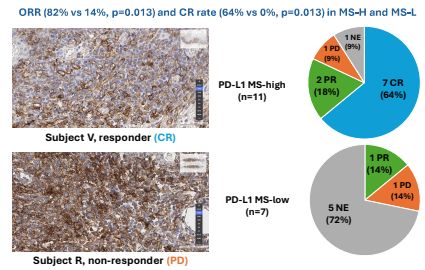
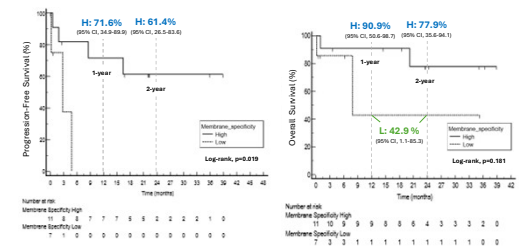


Figure 7. Kaplan-Meier Curve of PFS and OS by PD-L1 MS



Clinical benefit was observed across the IT, IE-A, and IE-B TIME subtypes, regardless of PD-L1 expression level.

Figure 8. Tumor Response by TIME Subtypes

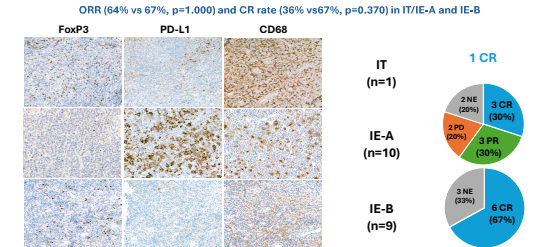


Figure 9. Kaplan-Meier Curve of PFS and OS by TIME Subtypes

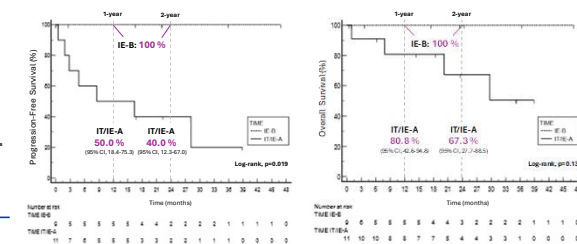
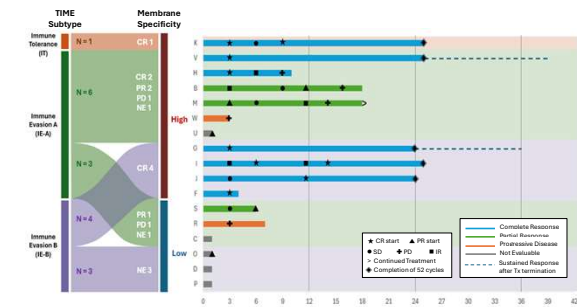


Figure 10. Distribution of TIME Subtypes by AI-based Membrane Specificity



CONCLUSIONS

- Danburstotug demonstrated robust and durable efficacy with manageable safety profile in relapsed/refractory ENKTL.
- Clinical benefits were observed across IT and IE subtypes, including IE-B despite lower PD-L1 expression.
- PD-L1 membrane specificity (MS) emerged as a predictive biomarker for response to danburstotug.

ACKNOWLEDGEMENT

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