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Enhancing the Ability to Diagnose, Interpret and Apply Best Treatment Options for Cutaneous Lymphomas

Prognostic factors for primary cutaneous anaplastic large cell lymphoma: a multicenter retrospective study from Japan

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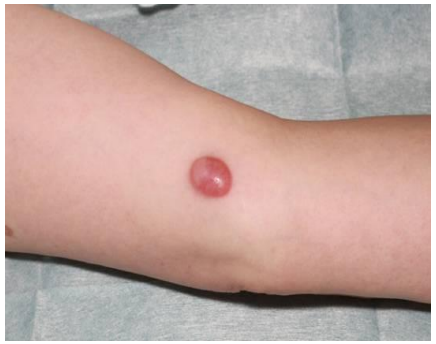
Disclosures

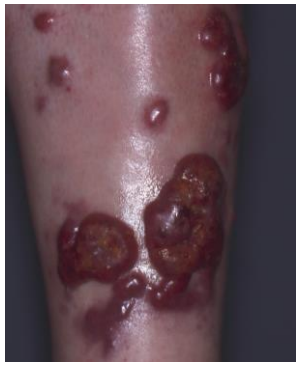
- I do not have any relevant financial relationships.

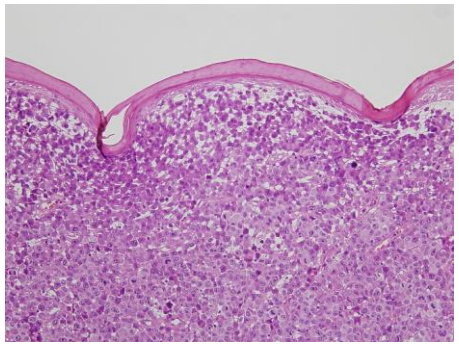
This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Primary cutaneous anaplastic large cell lymphoma (pcALCL)

- The second most common form of cutaneous T-cell lymphoma (CTCL).
- Clinically characterized by solitary, grouped, or multifocal tumors or subcutaneous nodules
- Pathologically characterized by nodular sheet-like infiltration of CD30-positive large lymphoid cells







T	
T1:	Solitary skin involvement
	T1a: a solitary lesion <5 cm diameter
	T1b: a solitary >5 cm diameter
T2:	Regional skin involvement: multiple lesions limited to 1 body region or 2 contiguous body regions*
	T2a: all-disease-encompassing in a <15-cm-diameter circular area
	T2b: all-disease-encompassing in a >15- and <30-cm-diameter circular area
	T2c: all-disease-encompassing in a >30-cm-diameter circular area
T3:	Generalized skin involvement
	T3a: multiple lesions involving 2 noncontiguous body regions
	T3b: multiple lesions involving ≥3 body regions

Kim YH et al., Blood 2007

The prognosis of pcALCL

- 5-year overall survival (OS): 75-87%
- 5-year disease specific survival (DSS): 86-95%
- Extracutaneous progression was observed

  in 15% of all cases after median time of 18 months

  in 10% of T1 cases and 21% of T2-3 cases after median time of 47 months

Willemze R et al., Blood 2019
Benner MF et al., Acrh Dermatol 2009
Hapgood G et al., Br J Haematol 2017
Fernández-de-Misa R et al., JEADV 2020
Safraz H et al., Clin Exp Dermatol 2021

Prognostic factors in pcALCL

- Higher T stage
- Nodal progression
- Older age
- Leg involvement, extensive limb disease

Benner MF et al., Acrh Dermatol 2009
Fernández-de-Misa R et al., JEADV 2020
Safraz H et al., Clin Exp Dermatol 2021

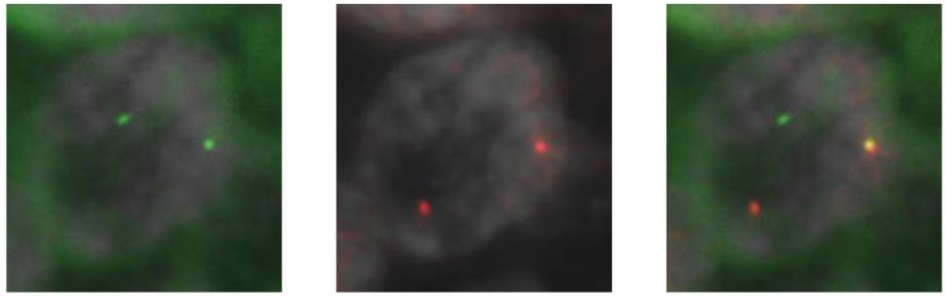
DUSP22-IRF4 rearrangement

- Identified in 30% of ALK-negative systemic ALCL (sALCL) patients, 20-57% cases with pcALCL, and a small portion of lymphomatoid papulosis (LyP) and mycosis fungoides with large cell transformation (MF-LCT) cases.

- In ALK-negative sALCL, *DUSP22* rearrangement indicates a favorable prognosis. Lymphoid enhancer-binding factor (LEF1) overexpression was associated with the presence of *DUSP22* rearrangement in ALK-negative sALCL.

- No impact on the prognosis of pcALCL based on the analysis of 23 patients in France.

Downstream of *DUSP22* Upstream of *DUSP22* Merge



Feldman AL et al., Leukemia 2009
Pham-Ledard A et al., J Invest Dermatol 2010
Wada DA et al., Mod Pathol 2011
Parrilla Castellar ER et al., Blood 2014
Fauconneau A et al., Br J Dermatol 2015
Ravindran A et al., Am J Surg Pathol 2021

Objectives

- To examine prognostic factors of pcALCL and the clinical implication of *DUSP22* rearrangement in pcALCL in Japan.
- To explore the association between *DUSP22* rearrangement and LEF1 expression pattern in pcALCL.

Methods

- Patients with pcALCL, LyP, and CD30-positive MF-LCT diagnosed and treated at six large tertiary hospitals in Japan from January 1, 2000 to December 31, 2018, were enrolled.
- Clinical and histopathological data were collected.
- The immunohistochemical analysis of common molecules and LEF1 and FISH for *DUSP22* rearrangement were performed using skin samples at the diagnosis.
- The OS and DSS were estimated by the Kaplan-Meier method, and the differences in survival between the two groups were assessed by the log-rank test.
- The medical ethical committee of each hospital approved all described studies, and the study was conducted according to the Declaration of Helsinki Principles.

Patient characteristics

- 22 pcALCL, 17 LyP and 11 MF-LCT patients were enrolled.
- pcALCL

  male: female: 13 (59.1%): 9 (40.9%)

  median age: 64 years (range: 36-88 years)

  T stage: T1: 10 (45.5%), T2: 5 (22.7%), and T3: 7 (31.8%)

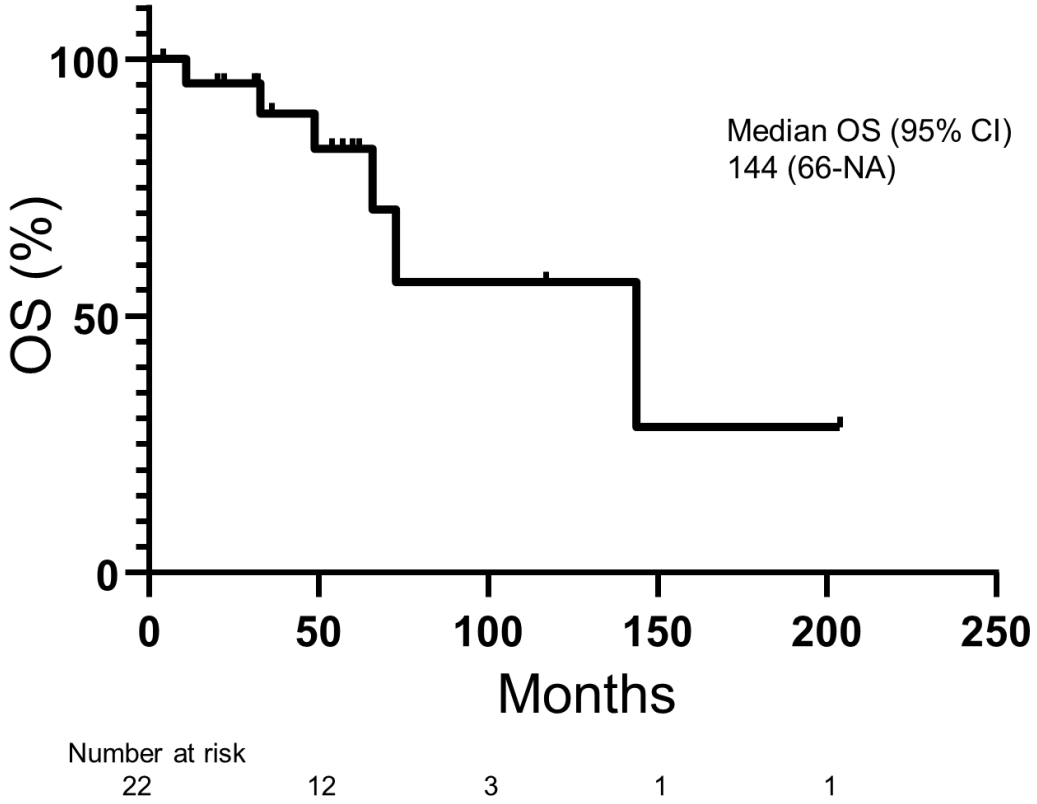
  Distribution: head/neck: 13 (59.1%), arm: 9 (40.9%), trunk: 7 (31.8%), and leg: 7 (31.8%)

  Nodal involvement: 4 (18.2%), Ulcer formation: 9 (40.9%)

DUSP22 rearrangement frequency and its association with clinical and pathological findings

- *DUSP22* rearrangement was found in 11 pcALCL patients (50%).
- No LyP and MF-LCT patients showed *DUSP22* rearrangement.
- *DUSP22*-rearranged pcALCL patients did not tend to form ulcers ($p = 0.081$), but there was not statistically significant difference.
- No other clinical and pathological findings including LEF1 expression pattern were associated with *DUSP22* rearrangement.

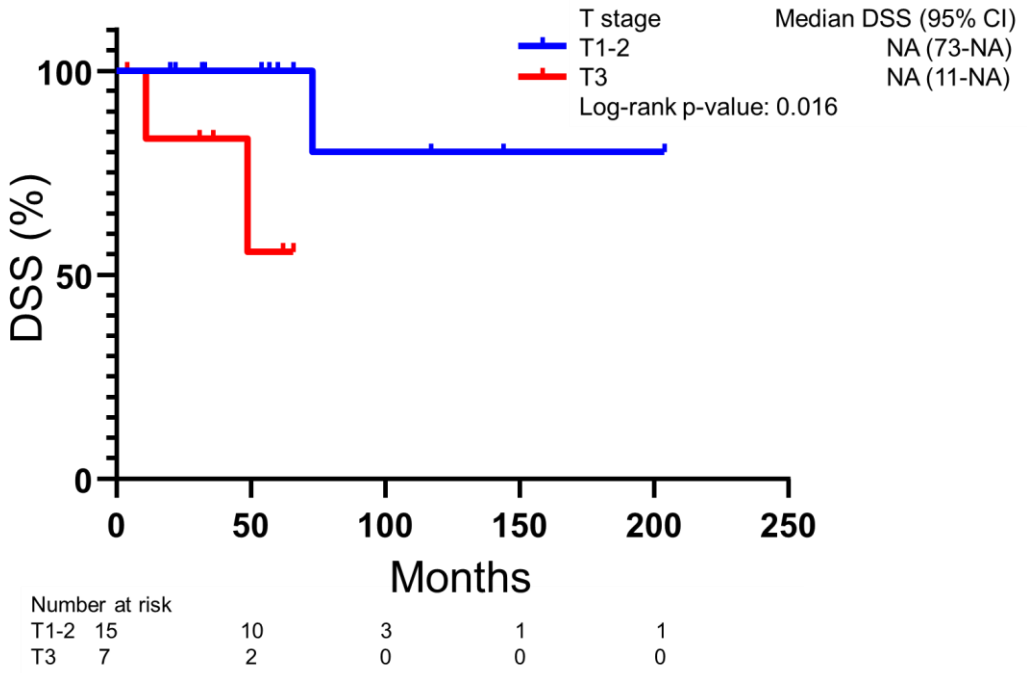
The prognosis of pcALCL

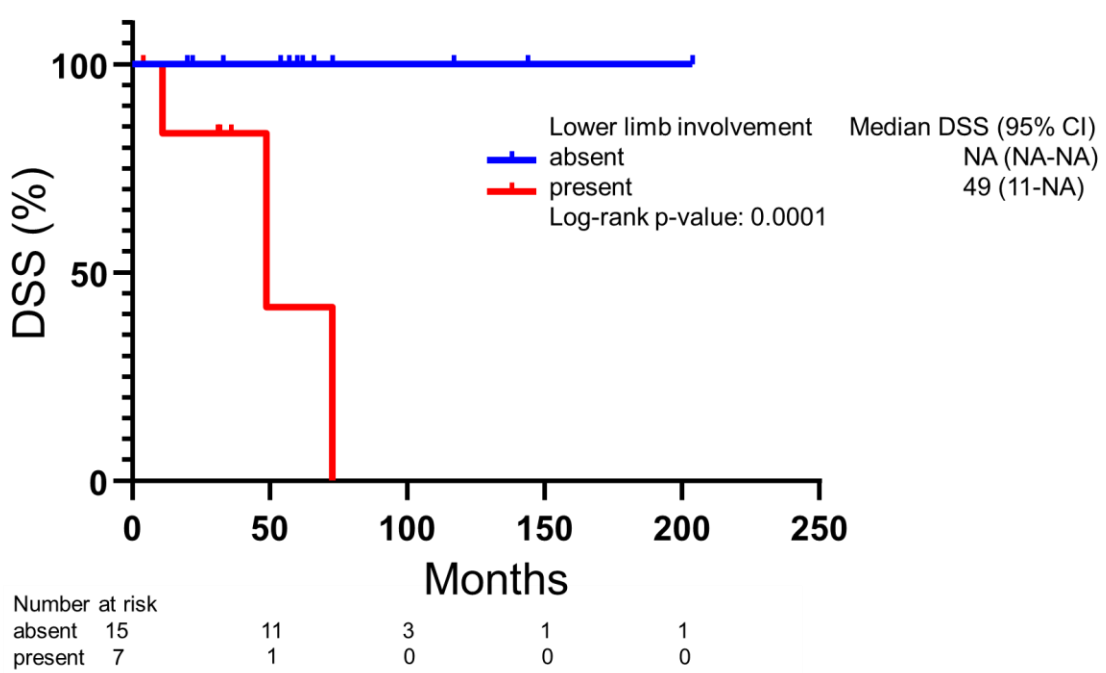


- The median follow-up: 55.5 months (range: 4-204 months)
- The median OS: 144 months (range 66 months-not available)
- 5-year OS: 82.4%
- The median DSS: not reached (range 73 months-not available)
- 5-year DSS: 87.9%
- 3 patients died due to pcALCL and 3 patients died due to other causes.

The prognostic factors in pcALCL

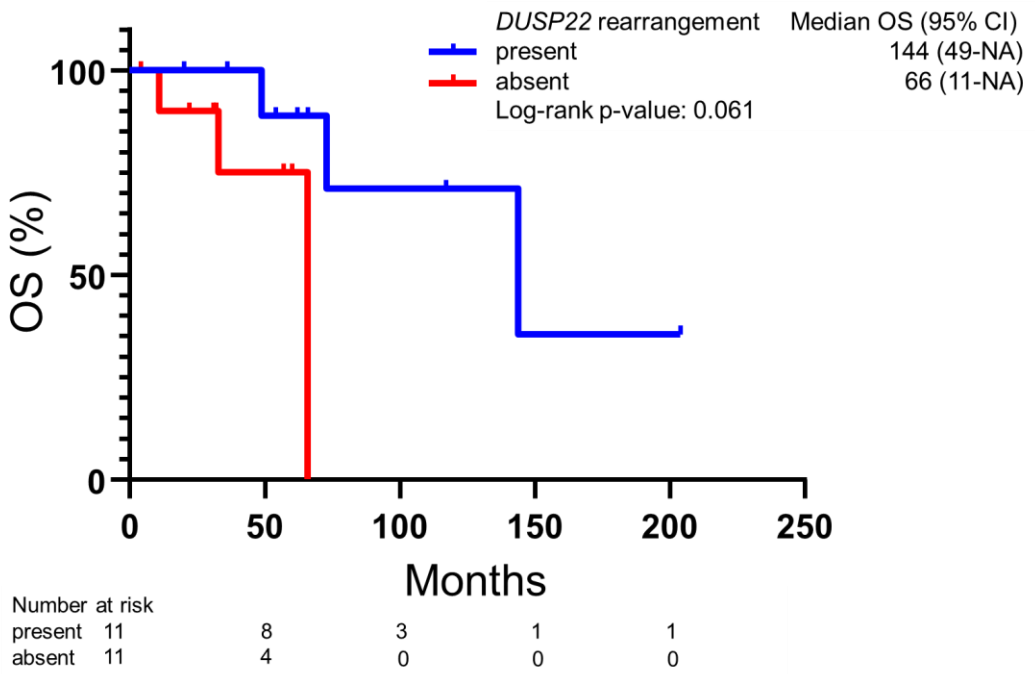
- T3 stage and leg involvement were associated with both shorter OS and DSS.
- Other clinical characteristics including lymph node involvement and the older age showed no impact on the prognosis.

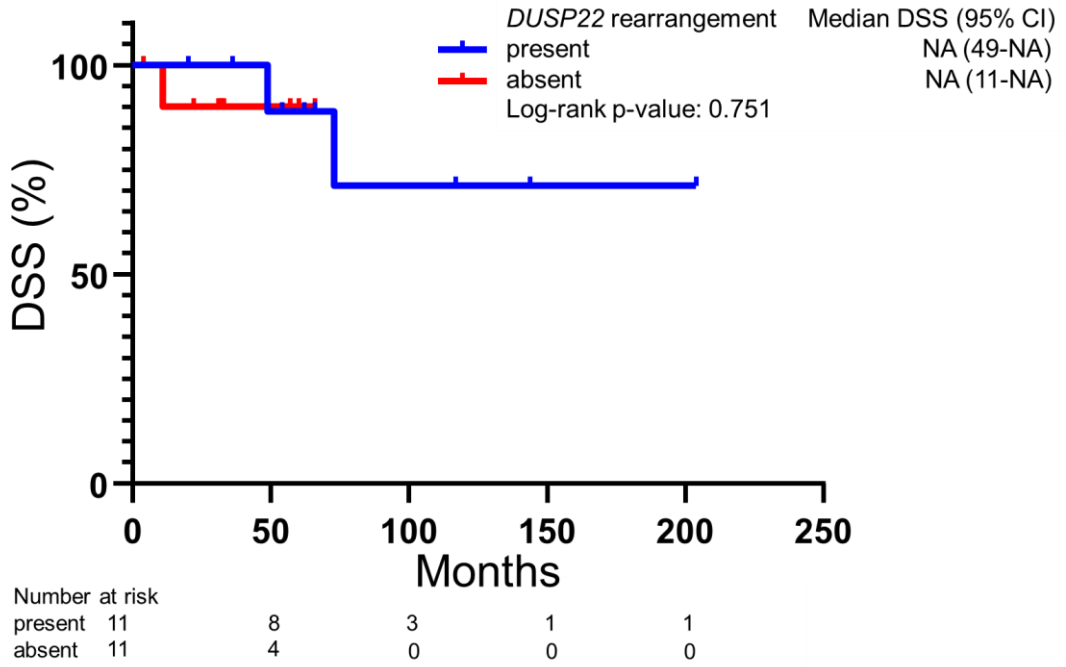




DUSP22 rearrangement and the prognosis

- *DUSP22* rearrangement tended to be associated with longer OS (p = 0.061), but it had no effect on DSS.





Conclusion 1

- *DUSP22* rearrangement was detected in 50% of pcALCL patients, which was within the ranges of previous studies.
- 5-year OS and DSS were 82.4% and 87.9%, respectively, which were also within the ranges in previous studies.
- T3 stage and leg involvement were associated with the decreased DSS, which was similar to findings in previous reports.

There may not be large racial differences in the characteristics of pcALCL between Caucasians and Asians.

Conclusion 2

- *DUSP22* rearrangement was not associated with LEF1 expression in pcALCL, different from ALK-negative sALCL.

- Similarly, *DUSP22* rearrangement did not predict a good prognosis in pcALCL, which was also different from ALK-negative sALCL.

The clinical and pathological implication of *DUSP22* rearrangement may be different between pcALCL and ALK-negative sALCL.

The favorable prognosis in pcALCL compared to sALCL may diminish the impact of *DUSP22* rearrangement on the prognosis.

Limitations

- This was a retrospective study that potentially includes several biases.
- The number of enrolled patients was small.
- Patients were treated in different centers, causing diversity in treatment strategies.
- Brentuximab vedotin was approved in Japan last year, and most patients in this study did not have the option of receiving the drug.

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Thank you!

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