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P3.319: Clinicopathological features of DLL3 expression and tumor-infiltrating T-cells in large cell neuroendocrine lung carcinoma(LCNEC)

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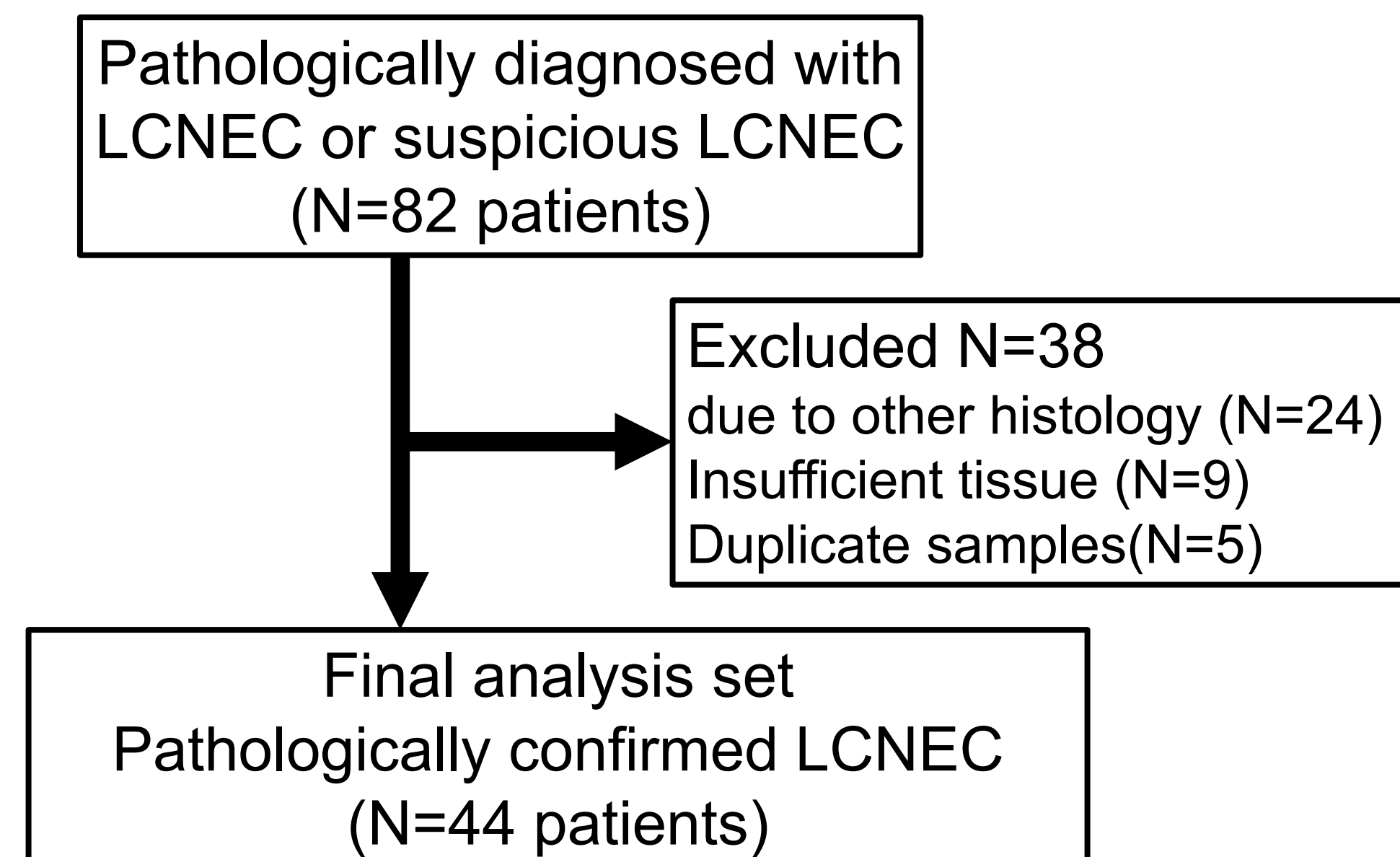
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INTRODUCTION

- Large-cell neuroendocrine lung carcinoma (LCNEC) is a rare, aggressive tumor with poor prognosis, similar to SCLC¹.
- DLL3-targeted BiTEs (tarlatamab) show marked efficacy in SCLC², with clinical trials ongoing in LCNEC.
- We evaluated DLL3 expression and CD8+ TILs in LCNEC.

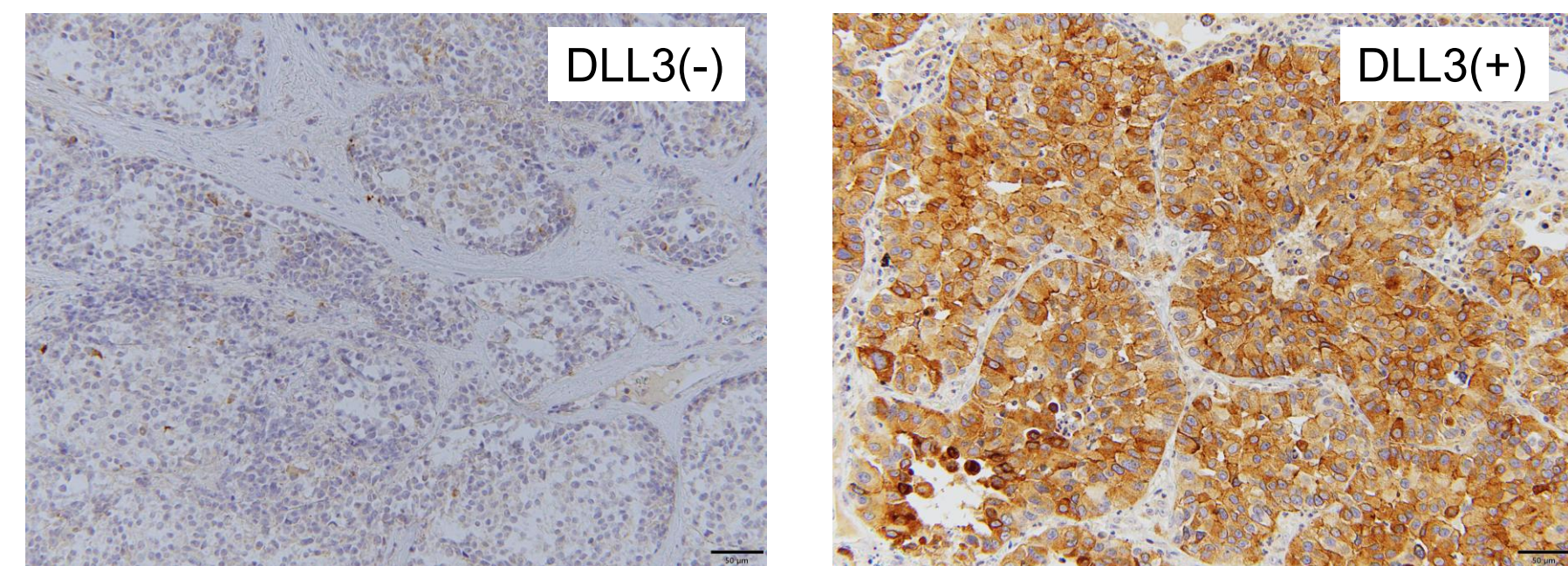
METHODS



- Immunohistochemistry (IHC):** Evaluated for DLL3 (clone SP347, Ventana) and CD8 (clone C8/144B, Dako).

Scoring Criteria

DLL3: Positive ($\geq 1\%$ tumor cells) vs. Negative ($< 1\%$)



CD8+ TIL density: Graded from 0 to 2+
0, < 30 cells/HPF; 1+, 30–69 cells/HPF; and 2+, ≥ 70 cells/HPF

Evaluation:

Assessed by two independent pathologists blinded to clinical data.

REFERENCES

- REFERENCES**
- [1] Nicholson AG, et al. *J Thorac Oncol.* 2022;17(3):362-387.
 - [2] Ahn MJ, et al. *N Engl J Med.* 2023;389(22):2063-2075.
 - [3] Hermans BCM, et al. *Lung Cancer.* 2019;138:102-108.
 - [4] Patel SA, et al. *JTO Clin Res Rep.* 2024;5(10):100712.

Note: AI-assisted tools were used in part for Japanese-to-English translation in the preparation of this poster.

RESULTS

Table 1. Patient characteristics (N=44)

	Number of patients (%)
Median age (range)	75 (51-84)
Sex, male / female	36 (81.8%) / 8 (18.2%)
Smoking history, (+) / (-)	43 (97.7%) / 1 (2.3%)
PS at diagnosis, 0 / 1 / 2 / 3 / 4 / unknown	28 (63.6%) / 10 (22.7%) / 2 (4.6%) / 1 (2.3%) / 1 (2.3%) / 2(4.6%)
Specimens, biopsy / surgical resection	16 (36.4%) / 28 (63.6%)
Sample, primary lesion / metastatic site	40 (90.9%) / 4 (9.1%)
Stage at diagnosis, I / II / III/ IV	22 (50.0%) / 4 (9.1%) / 6 (13.6%) / 12 (27.3%)
Histology, pure LCNEC / combined LCNEC	31 (70.5%) / 13 (29.5%)
Initial Treatment, Curative treatment / Palliative chemotherapy	30 (68.2%) / 14 (31.8%)

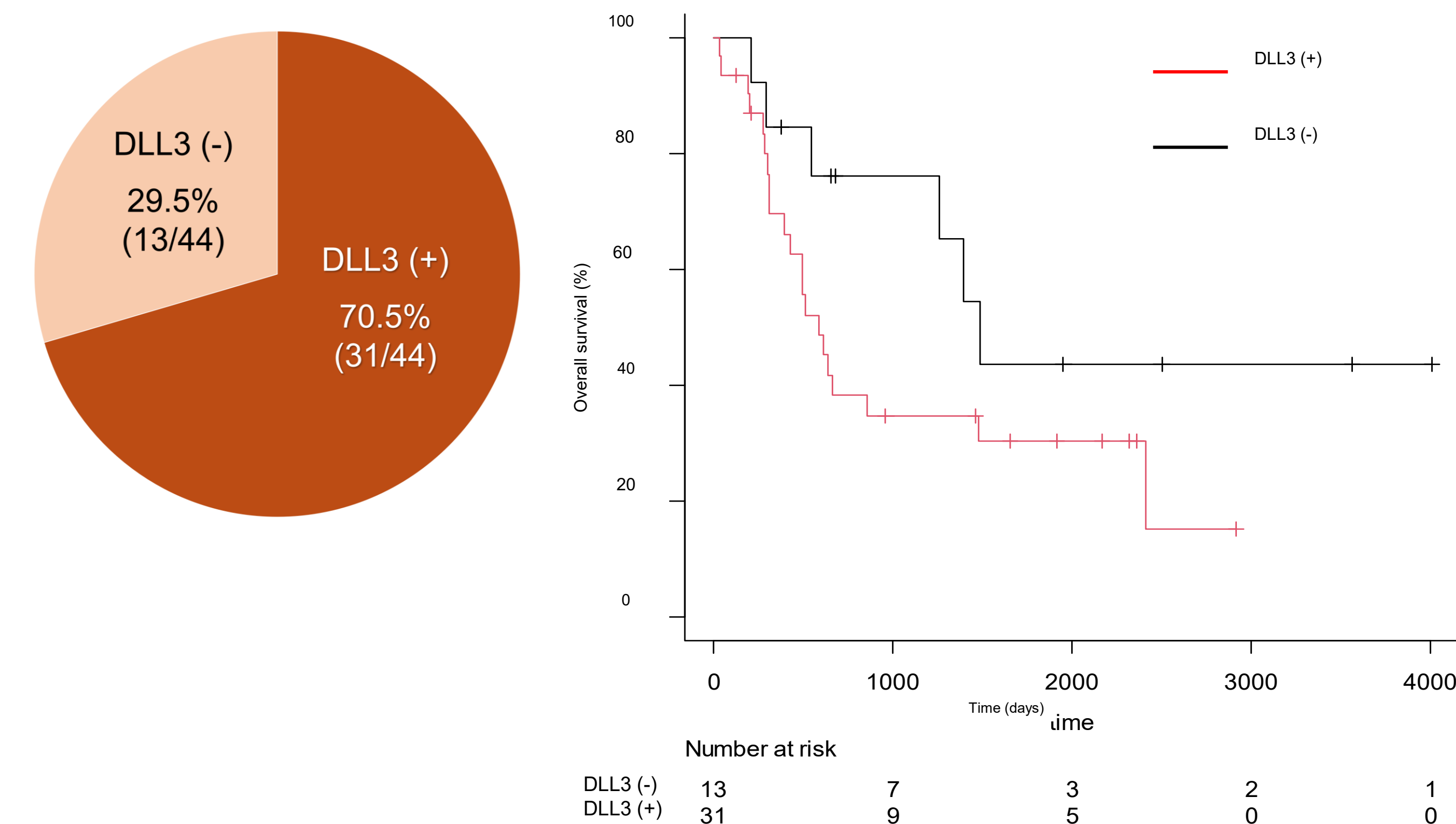


Figure 1. DLL3 expression and overall survival.

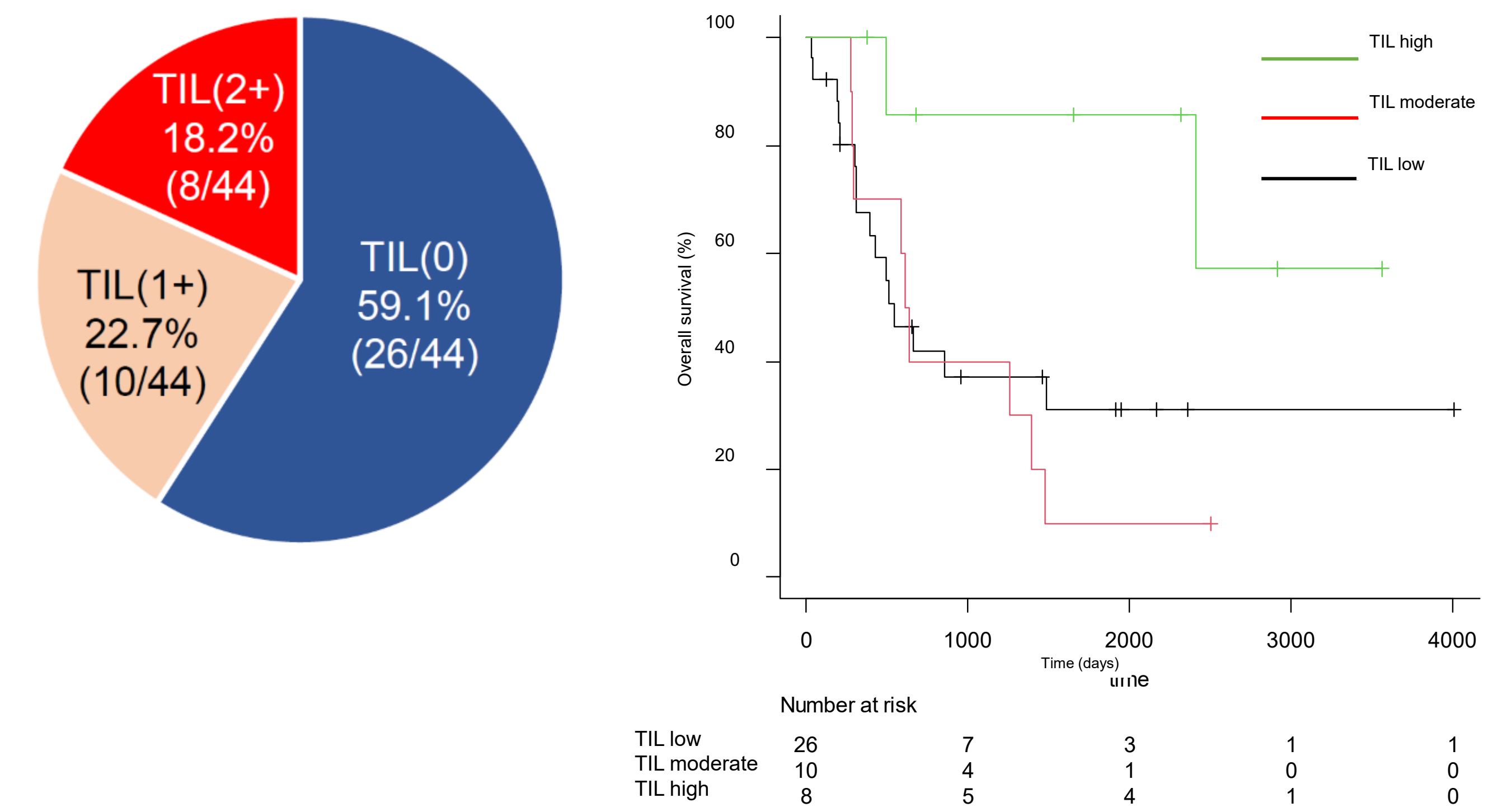
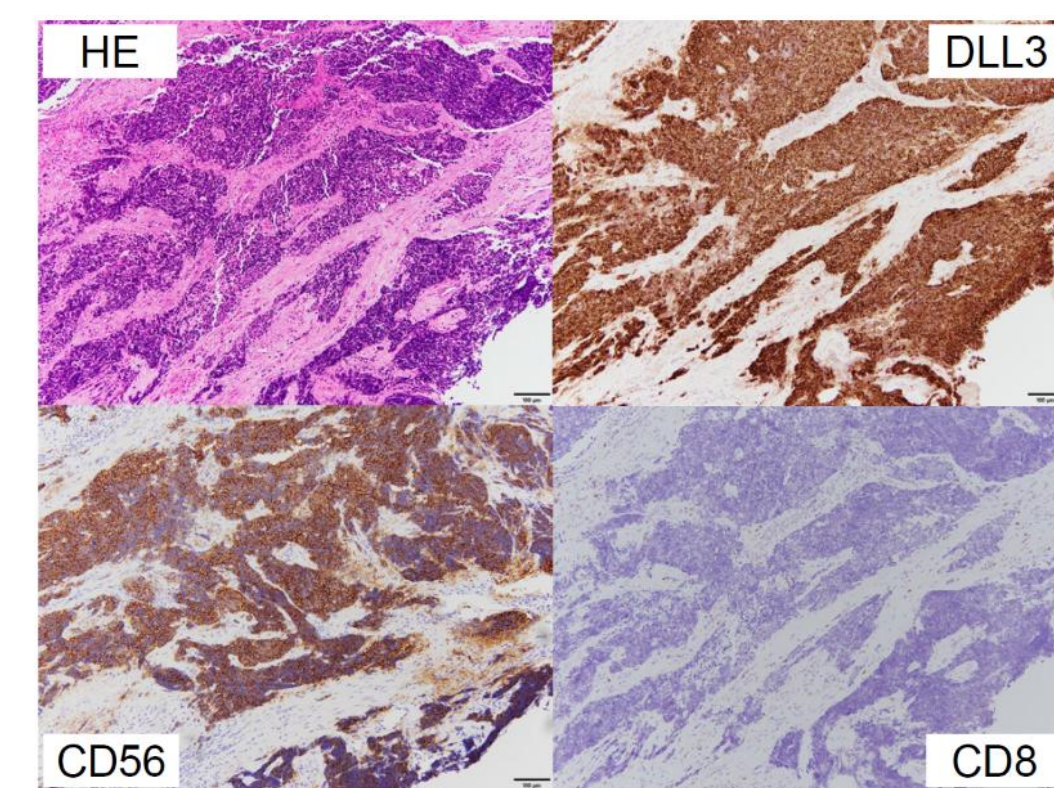


Figure 2. CD8+ TIL infiltration and overall survival

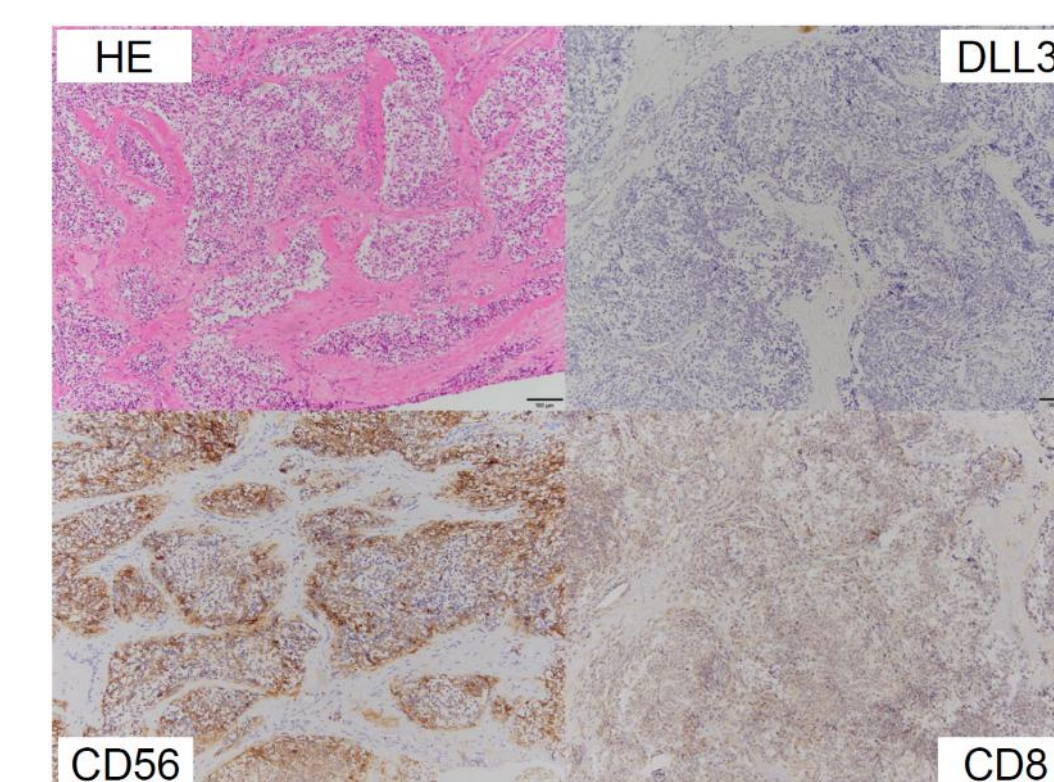
Case1

73 y.o.
Female
DLL3(+)
CD8 TILs(0)

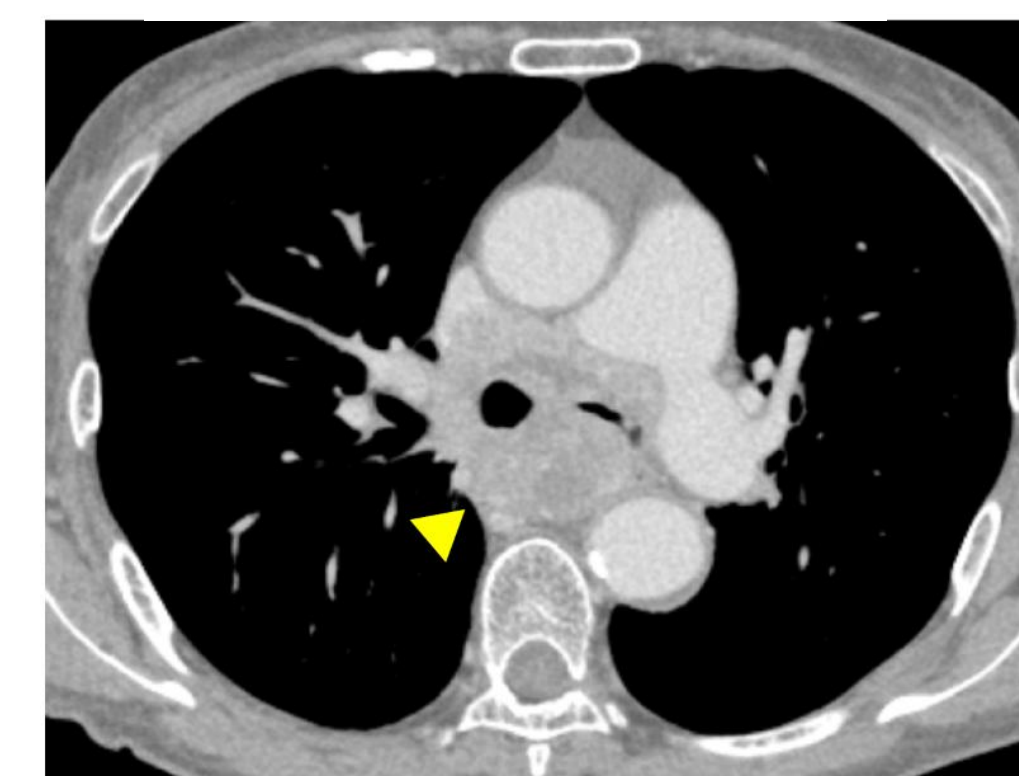


Case2

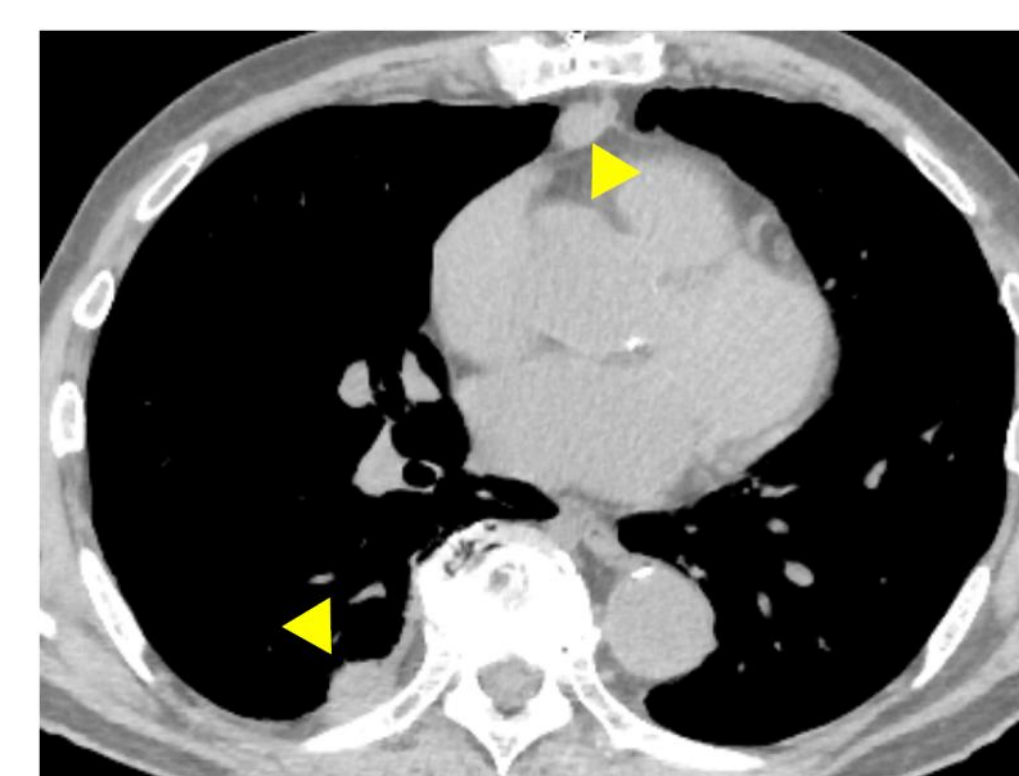
76 y.o.
Male
DLL3(-)
CD8 TILs(0)



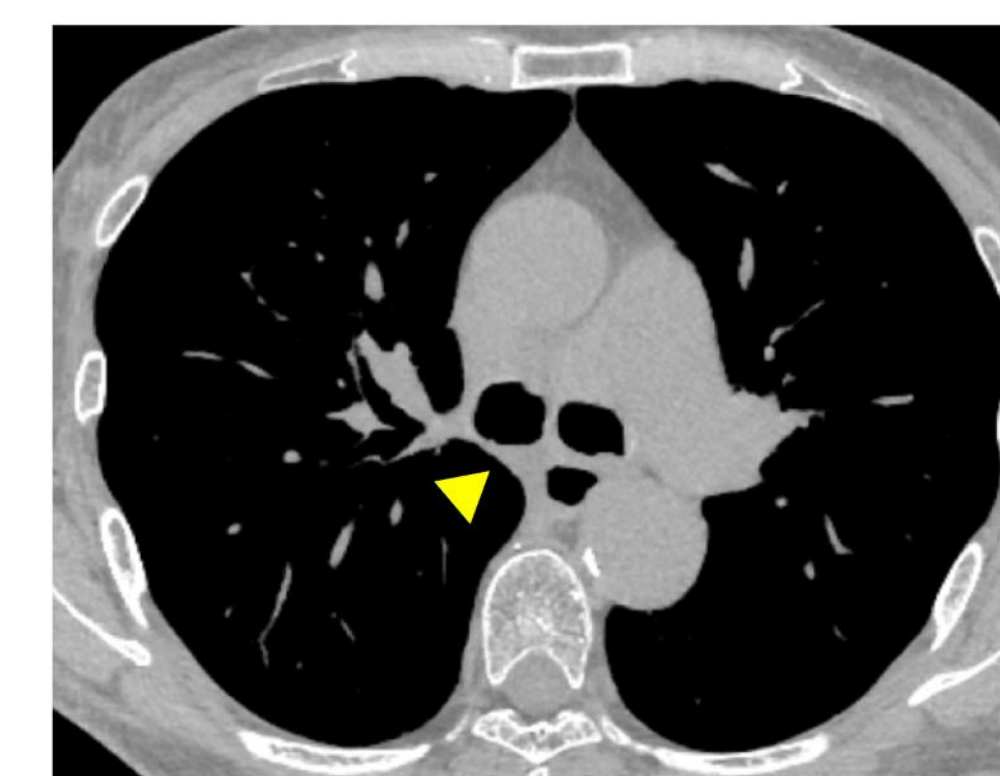
Before tarlatamab



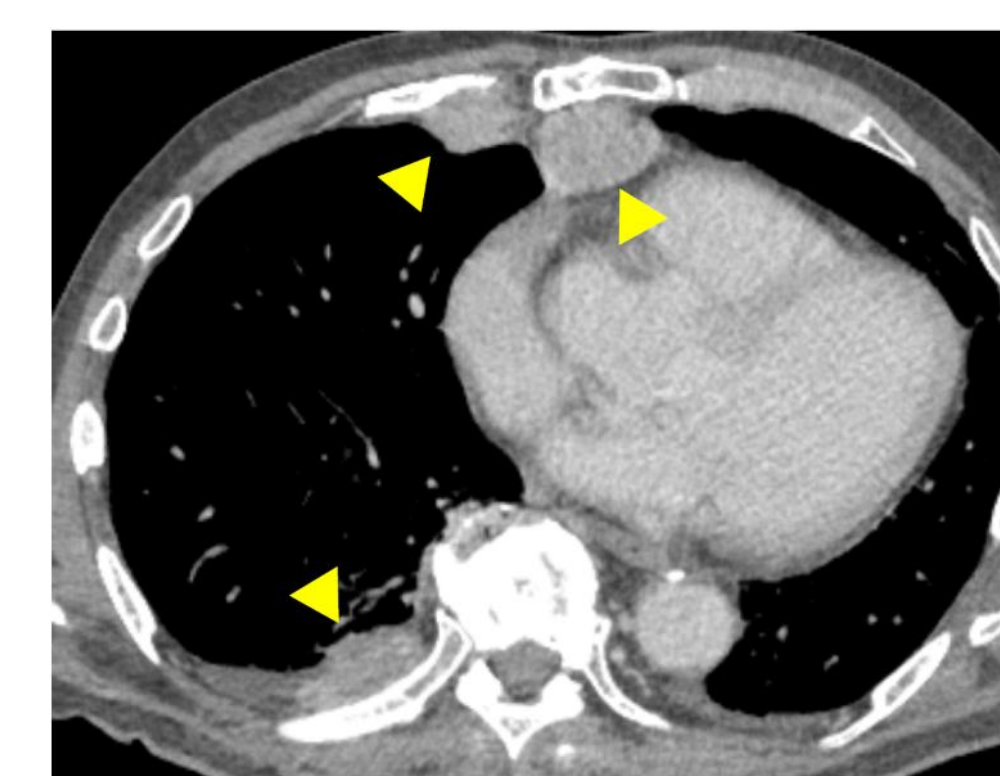
Before tarlatamab



After tarlatamab



After tarlatamab



DISCUSSION AND CONCLUSION

Actionable Take Away Message

- DLL3 Expression in LCNEC:** DLL3 expression was observed in 70.45% (31/44) of LCNEC cases.
- Immune-Desert Phenotype:** An immune-desert tumor microenvironment (CD8 score 0) was identified in 59.1% (26/44) of cases.
- Therapeutic Potential:** Our findings support a biological rationale for the use of DLL3-BiTE agents in DLL3-positive LCNEC.