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## **S226: EFFICACY OF ANTI-PD1 THERAPY IN RELAPSED OR REFRACTORY EXTRANODAL NK/T CELL LYMPHOMA: A MATCHED COHORT ANALYSIS FROM THE LYSA**

Amira Marouf, Sammara Chaubard, J.M. Michot, Julien Rossignol, Camille Golfier, Olivier Allangba, Laure Philippe Walter, Benoît Tessoulin, Adrien Chauchet, Benedicte Deau, et al.

► **To cite this version:**

Amira Marouf, Sammara Chaubard, J.M. Michot, Julien Rossignol, Camille Golfier, et al.. S226: EFFICACY OF ANTI-PD1 THERAPY IN RELAPSED OR REFRACTORY EXTRANODAL NK/T CELL LYMPHOMA: A MATCHED COHORT ANALYSIS FROM THE LYSA. HemaSphere, 2023, HemaSphere, 7 (S3), pp.e41118bf. 10.1097/01.hs9.0000967816.41118.bf . hal-04406218

**HAL Id: hal-04406218**

**<https://hal.science/hal-04406218>**

Submitted on 19 Jan 2024

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## S226 EFFICACY OF ANTI-PD1 THERAPY IN RELAPSED OR REFRACTORY EXTRANODAL NK/T CELL LYMPHOMA: A MATCHED COHORT ANALYSIS FROM THE LYSA

**Topic:** Aggressive lymphoma - Clinical, non-CAR-T

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### Background:

Extranodal NK/T cell lymphoma (ENKTCL) nasal type is a rare subset of peripheral T lymphoma characterized by a constant association to Epstein Barr Virus (EBV). Asparaginase containing regimen is the current standard of care in this pathology. Despite recent improvements in the therapeutic strategy, patient's prognosis remains poor, especially for those who experienced relapsed or refractory (R/R) disease. Recent studies highlighted that immune escape mechanisms are involved in ENKTCL pathogenesis. Particularly, the frequent PD-L1 upregulation led to assess the efficacy of anti-PD1 (aPD1) therapy in small cohorts of R/R ENKTCL patients, with encouraging results. Thus, immune checkpoint blockade represents a promising approach for R/R ENKTCL to date.

### Aims:

Our study aims to evaluate the efficacy of aPD1 therapy alone or in combination in 37 patients with R/R ENKTCL. We also performed a comparative analysis with a historic cohort of 38 patients treated for R/R ENKTCL before immunotherapy era.

### Methods:

37 patients from 24 French centers, with R/R ENKTCL treated with at least one cycle of aPD1 as salvage therapy between 2017 and 2022 were analyzed in this study. Among them, 12 were included in the prospective ACSE Unicancer study and received aPD1 as monotherapy.

The historic cohort used for the comparative analysis was established from the ENKTCL national observatory

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(DRC Limoges) and composed of 38 R/R ENKTCL patients who received at least one cycle of first salvage therapy without aPD1 between 2006 and 2019.

All patients were treated with Asparaginase-containing regimen as frontline therapy.

### Results:

Patient characteristics were as follows: median age of 52 years (19-79), sex ratio M/F of 2/1, disseminated stage in 57% of the cases, high PINK score in 41% of the cases.

The overall response rate (ORR) at the last follow-up was 40.5% (15 patients) in the aPD1 group. With a median follow-up time of 6.5 months for the whole cohort and 23.4 months for survivors, at 2 years progression free survival (PFS) was 22.4% and overall survival (OS) was 50.2%. Median PFS was 6.9 months and median OS was unreached.

Among the 22 patients who experienced progression or relapse after the initiation of aPD1 therapy, 14 patients (64%) received salvage therapy, mostly containing gemcitabine in association with immunotherapy continuation.

Regarding prognostic factors at relapse, we identified that patients with performance status (PS)  $\geq 2$ , B symptoms and  $\geq 2$  extranodal sites involved at relapse had significantly worse OS in univariate analysis. Only patients with  $\geq 2$  extranodal sites involved at relapse had significantly decreased OS in multivariate analysis.

This cohort was then compared to the historic cohort after matching on a propensity score using the greedy nearest neighbor 1:1. 23 patients in each group were included in this analysis. Both groups had a comparable PFS ( $p=0.16$ ) but OS was significantly improved in patients treated with aPD1 as salvage therapy alone or in combination (48.4% versus 23.1%,  $p=0.011$ ).

### Summary/Conclusion:

We report here the largest cohort of R/R ENKTCL treated with aPD1. Our study confirms the efficacy of aPD1 therapy in R/R ENKTCL and highlights its superiority as compared to other types of salvage therapy used in this setting before immunotherapy era.

Our results will prompt us to now prospectively evaluate the benefit of aPD1 therapy as first line therapy in patients with high risk disseminated stage of ENKTCL, in combination with chemotherapy agents able to enhance anti-tumor immune response.

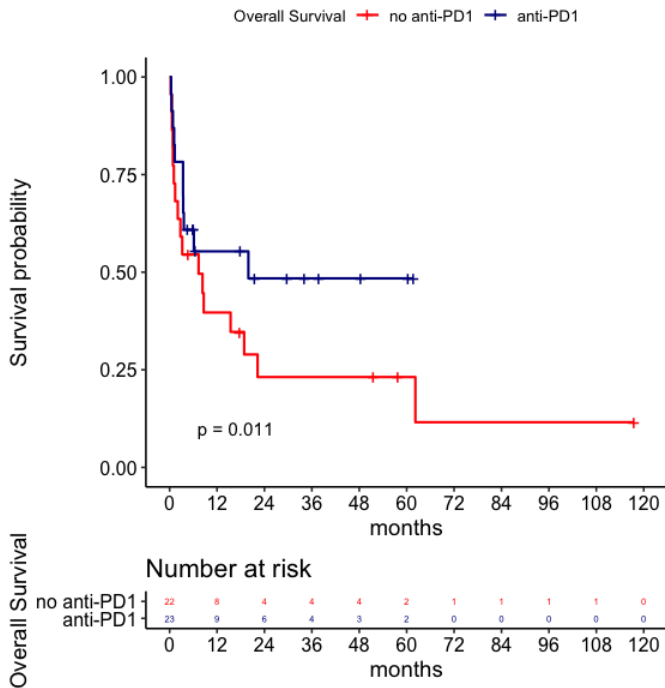
To improve response to immunotherapy, it is also crucial to decipher mechanisms underlying immune escape mechanisms in ENKTCL and to identify biomarkers predictive of response or resistance to immune checkpoint blockade.

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