# Application of the Proposed Immunohistochemistry Algorithm for the Prognostication of GATA3 and TBX21 Subtypes of Peripheral T-cell Lymphoma, Not Otherwise Specified

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## Background

- Peripheral T-cell lymphomas , Not otherwise specified (PTCL, NOS) are an aggressive group of hematolymphoid malignancies accounting for less than 5% of the total lymphomas
- Recent molecular studies have indicated the varied oncogenic pathways resulting in the subtypes of PTCL, NOS, (GATA3 and TBX21) which affect the prognosis and may have predictive value.
- Amador et al established an immunohistochemical algorithm with validation using gene expression profiling
- PTCL-GATA3 was shown to associated with phosphatidylinositol 3 kinase (PI3K)-mammalian target of rapamycin (mTOR) pathway with a worse clinical outcome and PTCL-TBX21 showed activation of NF-kB pathway

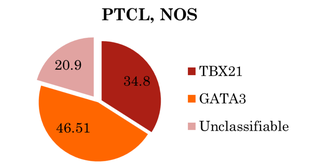
## Objectives

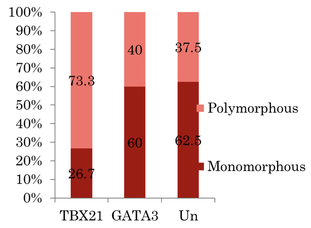
- To evaluate the immunohistochemistry (IHC) algorithm (Amador et al.) for the subtyping of the PTCL, NOS and to ascertain their relevance with correlation to the clinicopathological profile.

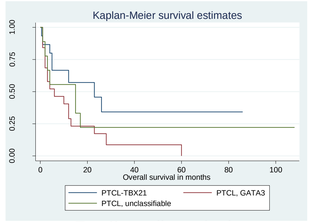
## Materials and Methods

- This 7-year (2015–2021) was an ambispective study over including 43 patients with diagnoses of PTCL, NOS from the archives of the Department of Pathology
- IHC for transcription factors- GATA3 (>50% immunopositivity considered positive) and, TBX21 (>20%) and their target proteins- CCR4 (>50%) and CXCR3 (>20%) was performed followed by subtyping by two pathologists
- Main Outcome Measures: The association between the subtypes and clinical factors (demographics, performance status, organomegaly, IPI/PIT score, stage, marrow involvement), histologic features, and was analyzed.

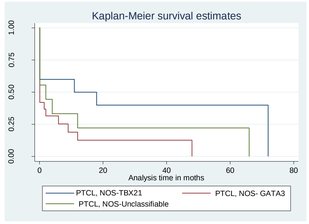
## Results



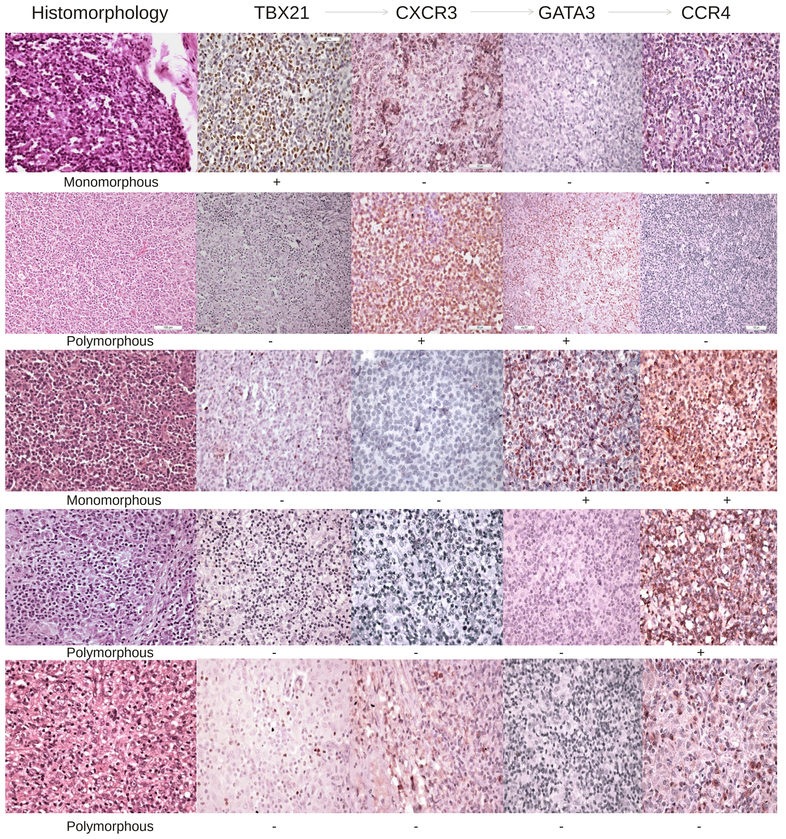




For Overall survival




For Progression free survival




PTCL, NOS-TBX21 (11)

PTCL, NOS-TBX21 (4)

PTCL, NOS-GATA3 (15)

PTCL, NOS-GATA3 (5)

PTCL, NOS-Unclassifiable (8)

Hepatosplenomegaly was found in association with PTCL , NOS unclassifiable (p-value of 0.028)

## Summary

- The cases were categorized into the subtypes- GATA3 (20), TBX21 (15), and unclassifiable (8)
- There was no significant association observed with the clinical parameters of the subtypes except hepatosplenomegaly
- An increased proportion of TBX21-subgroup cases showed a polymorphous population in comparison to the GATA3 -subgroup with monomorphous population, no significant p-value was found (p value=0.111); Two of the Lennert lymphomas were categorized in the GATA3 subgroup
- On multivariate analysis, though no significant difference was present for the overall survival (p value=0.105) and the progression- free survival (p value=0.0509) among the subtypes; the trends suggest that the GATA3 -subgroup having has a worse overall and progression- free survival.

## Discussion and Conclusion

- The IHC-derived subtypes of GATA3 and TBX21 may have a role in prognostication aiding patient management and for targeted therapeutics
- The IHC profile indicates the plausible biological basis
- The algorithm is reproducible, however some of the cases may be left unclassifiable and require further work up and gene -expression profiling
- The results trend toward the GATA3 -subgroup having a monomorphous population with a worse overall prognosis, requiring a larger sample size for validation
- The application of this algorithm in routine practice can help in risk stratification of the patients.

## References

1. Amador C, Greiner TC et al. Reproducing the molecular subclassification of peripheral T-cell lymphoma-NOS by immunohistochemistry. Blood. 2019 Dec 12;134(24):2159-2170. doi: 10.1182/blood.2019000779.

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