Genomic Landscape of Primary Thyroid Lymphoma (PTL): CD79B/MYD88 Alterations and Implications for Polatuzumab-Based Therapy

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INTRODUCTION

Primary thyroid lymphoma (PTL) is a rare extranodal lymphoma with limited genomic characterization and unclear applicability of targeted therapies. Given the emerging role of CD79B-directed therapy in diffuse large B-cell lymphoma (DLBCL), understanding MYD88/CD79B-associated molecular alterations in PTL may help identify biologically relevant therapeutic targets.

METHOD

A structured literature review was performed evaluating studies reporting molecular characteristics, cell-of-origin (COO), MYD88/CD79B alterations, and outcomes associated with polatuzumab-based therapy in PTL and related DLBCL cohorts.

CONCLUSIONS

PTL demonstrates substantial molecular heterogeneity with variable MYD88/CD79B reporting, recurrent BCR-pathway associated alterations, and overlap with aggressive DLBCL molecular subtypes. Emerging evidence suggests that CD79B-associated and non-GCB molecular profiles may predict enhanced responsiveness to polatuzumab-based therapy. Comprehensive genomic profiling may therefore improve risk stratification and guide precision-based therapeutic selection in PTL.

RESULTS

Results - Clinicopathologic and Molecular Characteristics

Study	N	Median Age	Cell of Origin (COO)	Hashimoto Assoc.	CD Markers	Molecular Notes
Numata et al	21	70	57% GCB / 43% ABC	67%	CD20+	MYD88 0%; CD10 83%; MUM1 83%; Ki-67 80–100%
Hamada et al	45	71	NR	82%	CD20+	NR
Guidobaldi et al	1	NR	NR	NR	CD20+, CD79b+	High MYD88; MCD-relevant; A20 mutation present
Sharma et al	1	82	ABC	Yes	CD79b+	Ki-67 >80%; IPI 2–5
Zhu et al	879	65	GCB + ABC	NR	CD20+, CD79b+	~79% high IPI
Matsuura et al	53	72	22 GCB / 22 ABC	NR	CD20+, CD79b+	56% had high IPI
REALYSA	645	66	44% GCB	NR	NR	NR
Pyke et al	62	67	NR	High	CD20+	Stage II disease included
Zemni et al	NR	76.2	NR	40%	CD20+, CD79b+	IPI 3
Gao et al	1	78	ABC	Yes	CD79b+	IPI >3
Sanjuro et al	80	68	Non-GCB predominant	NR	NR	NR

N = cohort size; COO = cell of origin; GCB = germinal-center B-cell; ABC = activated B-cell; IPI = International Prognostic Index; NR = not reported.

Results - Efficacy and Toxicity of Polatuzumab-Based Regimens

Study	ORR	CR %	12-mo PFS	Pola-Specific Toxicity	Rationale for Pola
Numata et al (control)	81%	81%	85%	NA	NA – R-CHOP control arm
Hamada et al	NA	NA	NA	NA	NA
Guidobaldi et al	NA	NA	NA	NA	Molecular profiling
Sharma et al	100%	100%	NA	Well tolerated	CD79b expression
Zhu et al	88%	78%	84%	Peripheral neuropathy, neutropenia	Superior PFS over R-CHOP
Matsuura et al	81.1%	71.7%	73.1%	Neutropenia	Real-world effectiveness in elderly
REALYSA	80%	76–81%	79.8%	Peripheral neuropathy, neutropenia	Validates POLARIX
Pyke et al	NA	NA	NA	NA	NA
Zemni et al	NA	20%	NA	NA	NA
Gao et al	100%	100%	NA	Grade 1 neuropathy	Targeted CD79b in PTL
Sanjuro et al	99%	70%	88%	Standard profile	High-risk frontline success

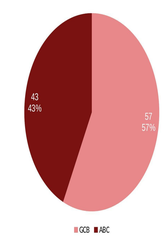
ORR = overall response rate; CR = complete response; PFS = progression-free survival; NA = not reported/not applicable.

Results - Summary of Included Studies

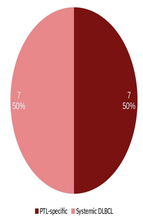
Study	Year	Setting	N	Cell of Origin (COO)	Pola-Based Tx	Key Outcome
Sharma et al	2024	PTL	1	ABC	Yes	Rapid tumor response
Numata et al	2024	PTL	21	57% GCB / 43% ABC	No	5-yr OS 83%
NGS Thyroid study	2024	PTL	10	NR	No	CR in most cases
Peng et al	2025	Systemic	55	Predominantly ABC	No	Poor outcomes; aggressive
Gao et al (SEER)	2025	PTL	1469	Predominantly ABC	No	Prognostic model derived
Tzoni et al	2025	PTL	80–90	Mostly GCB	No	CR in several cases
Guidobaldi et al	2023	PTL	1	NR	No	Partial remission
Munz et al	2025	Systemic	9 (cell lines)	ABC + GCB	Yes (in vitro)	Low CD79B → resistance
Scheffer et al	2026	Systemic	740	Non-GCB	Yes	ORR 59.7% vs conventional
GO29365	2022	Systemic	192	GCB + ABC	Yes	ORR 62.5%; OS HR 0.4
POLARIX	2022	Systemic	879	GCB + ABC	Yes	CR 78%; PFS HR 0.73
Berhan et al	2025	Systemic	NA	ABC vs GCB	NA	Molecular classification
Kim et al	2024	Systemic	52	NR	Yes	ORR 51.9% (bridge 61.5%)
Zhao et al	2024	PTL	1	GCB	No	CR, no recurrence

PTL = primary thyroid lymphoma; COO = cell of origin; GCB = germinal-center B-cell; ABC = activated B-cell; NR = not reported.

COO Distribution (Reported Cohort)



Study Setting (n = 14)



Therapeutic Regimen (n = 14)