Central Nervous System Involvement in Patients with Richter Transformation: The Mayo Clinic Experience

Poster #: 1601

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BACKGROUND

- Richter transformation (RT) refers to transformation of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) to an aggressive lymphoma, most commonly diffuse large B-cell lymphoma (DLBCL).
- Central nervous system (CNS) involvement in patients with RT is a rare complication and is understudied.
- We sought to investigate the clinical characteristics, treatment, outcomes, and prognostic factors in RT with CNS involvement.

METHODS

- Patients with biopsy-confirmed RT (DLBCL and HGBCL histology) diagnosed between 1/2005 and 8/2024 who developed either biopsy- or imaging-confirmed CNS involvement were identified via Mayo Clinic CLL Database.
- Clinical characteristics, treatment, and follow-up data were abstracted.
- Primary endpoint of interest was overall survival (OS), defined as the time from CNS involvement detection to death from any cause, and analyzed using the Kaplan-Meier method.

RESULTS

TABLE 1. BASELINE CHARACTERISTICS

Phase of disease	Patients with RT and CNS involvement (N=36)	
Chronic Lymphocytic Leukemia (CLL)	**Age at CLL diagnosis (years)**	Median 63 (34-78)
	Sex	Male, n=21 (58%)
	***IGHV* mutation**	Unmutated, 8 out of 15 (53%)
	***TP53* alteration (del(17p) and/or *TP53* somatic mutation)**	Positive, 12 out of 25 (48%)
	CLL treatment status prior to RT	Untreated, n=24 Treated, n=12 (median 1.5 lines) • CIT only, n=4 • Novel only, n=4 • CIT+novel, n=4
Richter Transformation (RT)	**Time to transformation (months)**	Median 17.3 (range 0-277.4)
	Histology	DLBCL, n=33 HGBCL, n=3
	MYC/BCL-2 double expressor (IHC)	Positive, n=10
	***MYC/BCL2* rearrangement**	Positive, n=2
	Clonal relatedness with CLL*	Related, n=12 Likely related, n=8 Likely unrelated, n=4 Unrelated, n=4 Missing, n=8
	Lines of treatment for RT before CNS involvement in treated (n=14)	Median 1 (range 1-5)
CNS involvement of Richter Transformation (RT)	**Age at CNS RT diagnosis (years)**	Median 69 (range 46-80)
	Timing of CNS involvement of RT	At RT diagnosis, n=22 At RT progression, n=14
	Time from RT diagnosis to CNS involvement (months) in patients with CNS involvement at progression (n=14)	Median 11.1 months (range 1-41.6)
	Extent of CNS involvement	Isolated, n=19 Combined CNS and systemic, n=17
	CNS biopsy or imaging confirmation	Tissue biopsy, n=16 CSF, n=5 Vitreous fluid, n=3 Imaging, n=12
	Site of CNS involvement**	Parenchymal only, n=12 Parenchymal + others, n=11 Others, n=13

*Twelve (42.9%) were classified as related by identical immunoglobulin gene rearrangement. Eight (28.6%) were likely related (6 [21.4%] by PD-1 positivity; 2 [7.1%] by CD5+, same light chain restriction and similar FISH). Four (14.3%) were likely unrelated by PD-1 negativity and 4 (14.3%) were unrelated by discordant immunoglobulin gene rearrangement.
**Parenchymal + others: parenchymal + leptomeningeal, cranial nerve roots, or ocular disease; Others: leptomeningeal, ocular, cranial or spinal nerve roots, and skull base lesions.

RESULTS

FIGURE 1. TIMING AND PATTERN OF CNS INVOLVEMENT

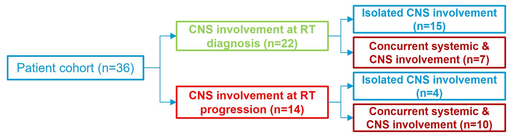


TABLE 2. FIRST LINE TREATMENT AFTER CNS INVOLVEMENT DETECTION IN PATIENTS WITH RT

CNS and systemic involvement	First-line treatment
isolated CNS involvement (n=19)	**Methotrexate-based regimens, n=15** • HD-MTX, n=1 • MR, n=8 • MRT, n=5 • MATRIX, n=1
	Other regimens, n=2 • High-dose steroids, n=1 • Rituximab + temozolamide, n=1
	No treatment, n=1
	Unknown treatment, n=1
Concurrent systemic and CNS involvement (n=17)	**Methotrexate-based regimens, n=6** • HD-MTX, n=3 • MR, n=2 • MRT, n=1
	Anthracycline-based plus CNS directed therapy, n=8 • MR-CHOP, n=5 • R-mini-CHOP + intrathecal MTX, n=1 • WBRT + R-CHOP, n=1 • Hyper-CVAD, n=1
	Other regimens, n=1 • Steroids + obinutuzumab + venetoclax, n=1
	No treatment, n=2

FIGURE 2. OS AFTER CNS INVOLVEMENT

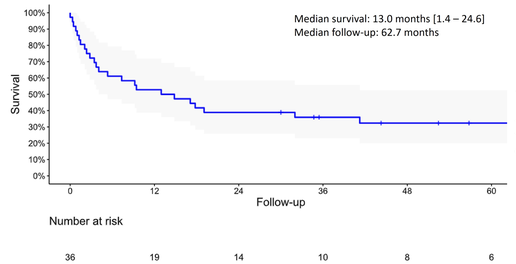


FIGURE 3. OS BY TIMING AND EXTENT OF CNS INVOLVEMENT

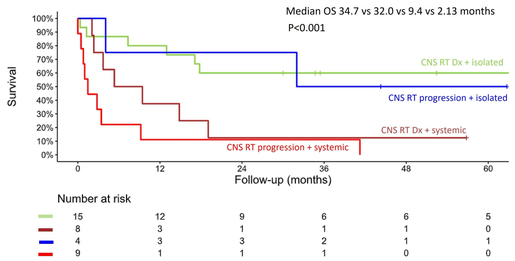


FIGURE 4. OS BY PREVIOUS CLL THERAPY

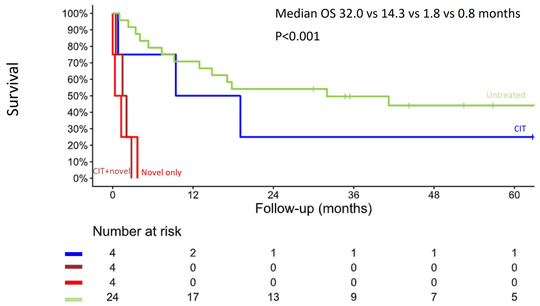


FIGURE 5. OS BY CNS TREATMENT STRATIFIED BY EXTENT OF CNS INVOLVEMENT (ISOLATED VS CONCURRENT SYSTEMIC)

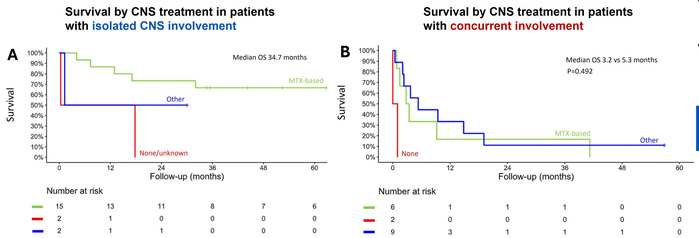


FIGURE 6. OS BY CLONAL RELATIONSHIP

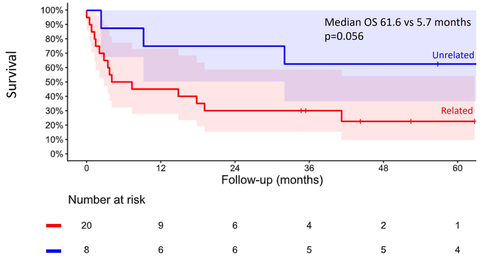
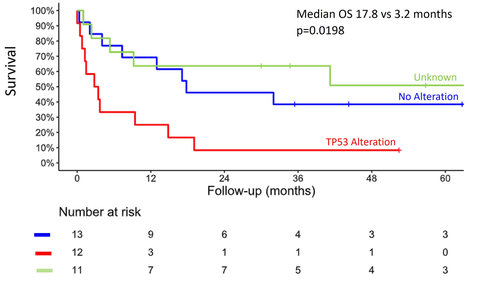


FIGURE 7. OS BY *TP53* ALTERATION



CONCLUSIONS

- CNS involvement in patients with RT has heterogenous presentations and poor overall survival outcomes.
- Adverse prognostic features included concurrent systemic disease, CNS involvement at RT progression, prior CLL treatment, clonal relatedness to CLL, and *TP53* alterations.
- These findings highlight the need for a tailored approach to management and continued investigation into novel therapies.
- Prospective and larger studies are needed to guide optimal treatment strategies.

CONTACT

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