Abstract: P668

Title: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) WITH CENTRAL NERVOUS SYSTEM INVOLVEMENT (CNSI)

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

CNSi of CLL is a rare condition with heterogeneous clinical manifestations and diagnostic challenges.

Aims:

Here we describe 16 patients (pts) with CNSi identified from a systematic analysis of a large, single-institution CLL database.

Methods:

We conducted a comprehensive chart review of pts followed by both lymphoma and neuro-oncology divisions of Dana-Farber Cancer Isntitute. CNSi was defined by documented neurologic symptoms and the presence of either: 1) histologically confirmed CNSi with a biopsy or flow cytometry (FC) of CNS tissue or cerebrospinal fluid (CSF), or 2) infiltrative CNS lesions detected on imaging in the absence of other compelling explanation for the lesion.

Results:

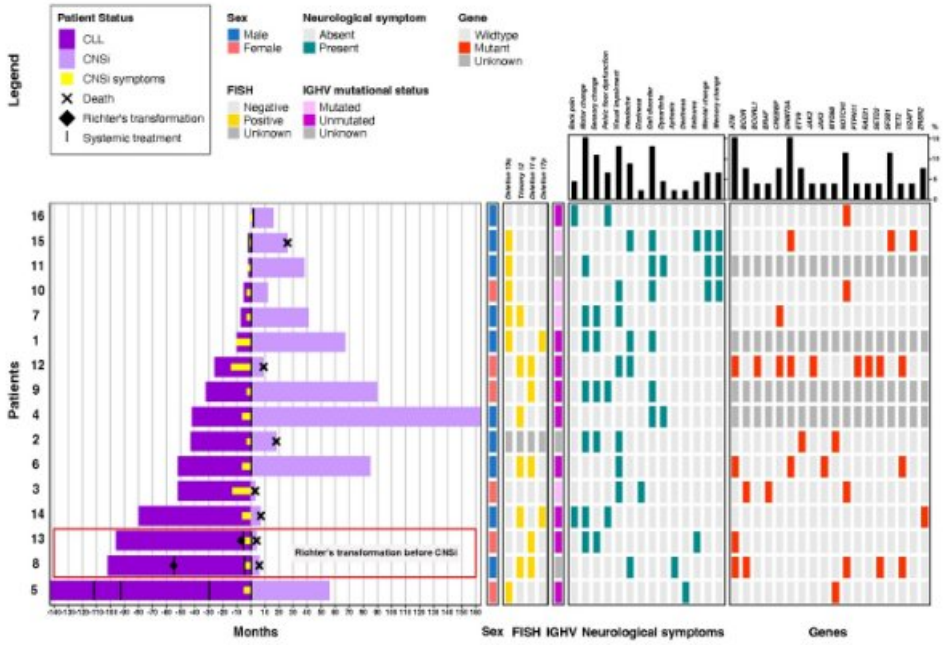
Of 3,580 pts included in the analysis, 81 (2.3%) had documented neurologic symptoms and 16 (0.4%) met the predefined criteria for CNSi of CLL. Of 16 pts, two were diagnosed with Richter's transformation before CNSi (6.0 and 54.6 months (mos) before CNSi) and three had MBL prior to CLL. The median age at CLL diagnosis was 67 years (range 47–88), 62.5% were male. A total of 56.3% had unmutated *IGHV*, 31.3% had del11q, and 12.5% had del17p without *TP53* mutation. Four pts (25%) had complex karyotype (≥3 abnormalities). Frequently detected mutations on the targeted next-generation sequencing platform were *ATM* and *NOTCH1* (25% each), followed by *TET2* and *DNMT3A* (18.8% each). Twelve pts had other malignancies, contributing to high CIRS score (median 11, range 5–18). FC of CSF was done for 13 pts (median % CD5+CD19+cells: 19%). Biopsy of the CNS lesions was performed in 8 pts, and imaging confirmation of leptomeningeal disease was available in 16 pts. Interestingly, systemic disease progression at the time of CNSi diagnosis was uncommon, found in only 3 pts (19%). Most pts (69%) were on observation and had not received prior CLL-directed therapy before CNSi.

Time from CLL diagnosis until the first onset of neurological symptoms was highly variable from 0 to 140 mos (median 35). Median time from the onset of neurological symptoms to the diagnosis of CNSi of CLL was 2 mos (range 0–11). The most common neurologic symptoms were motor dysfunction (n=7), followed by visual (n=6), gait (n=6), and sensory changes (n=5). Multiple neurologic symptoms frequently co-occurred (median 3).

The median time from the diagnosis of CNSi to treatment initiation was 0.5 mos (range 0–5.3) CNSi-directed therapy included: 1) covalent Bruton's tyrosine kinase inhibitor (cBTKi) monotherapy (n=7); 2) high-dose methotrexate plus rituximab +/- cBTKi (n=5); 3) obinutuzumab with acalabrutinib or venetoclax (n=2); 4) corticosteroids (n=1). Four pts received radiation as an adjunct to systemic therapy. Resolution or improvement of neurologic symptoms was reported from 12 of 14 pts who received CNSi-directed therapy. At the median follow-up of 80 mos, 7 of 16 pts died including 3 deaths due to disease progression. Median overall survival (OS) was 69 mos (range 13–206) from CLL diagnosis, and 21 mos (range 0.3–164) after CNSi diagnosis.

Summary/Conclusion:

The prevalence of CNSi with CLL was 0.4% in our cohort, which likely underestimated the true prevalence of this condition given the diagnostic challenges and the stringent disease-defining criteria used in this study. Most pts with CNSi of CLL frequently had no prior CLL-directed therapy (69%) and no evidence of systemic disease progression (81%). Sensory motor deficits resolved or improved with CNSi-directed therapy in 86% of treated pts. 43% died at a median of 21 mos after the diagnosis of CNSi, indicating the poor prognosis of this condition.



Keywords: CNS, B-CLL, Bruton’s tyrosine kinase inhibitor (BTKi), Chronic lymphocytic leukemia