>18–64 years old" plus "older adults = 65 years and older". We examined all clinical trials that met the inclusion criteria from January 1st, 2012, through December 31st, 2022. We excluded trials with overlapping terminology that did not enroll patients with mature lymphoid neoplasms, such as precursor b-lymphoblastic lymphoma/leukaemia, anaplastic lymphoma kinase (ALK) non-small-cell lung cancer and trials involving very broad disease categories such as "advanced cancer", "hematological malignancies" or "high risk populations" with the exception when a significant proportion of patients with lymphoma was expected to be enrolled. Difficult cases were discussed and decided at the discretion of the authors.

Results: Our search returned 2085 clinical trials, of those we included 1376 in the analysis according to our inclusion/exclusion criteria. We found that between 2012 and 2022 randomization was performed in 12.8% (177/1376) of interventional phase II clinical trials of adult patients with lymphoma. The histogram (Figure 1) shows that the number of trials increased during the analysis period, but the number of randomized clinical trials remained proportionally low.

Conclusions: A small proportion of interventional phase II clinical trials of adult patients with lymphoma use randomization when assessing efficacy and safety of their interventions. The use of data derived from SANRS for clinical decision making should be used with caution by health providers. Randomization should be encouraged by stakeholders.

Keywords: therapeutics and clinical trials in lymphoma, other

No conflicts of interests pertinent to the abstract.

TRANSLATIONAL STUDIES, LIQUID BIOPSY

514 | GENOMIC ABERRATIONS DETECTED IN CIRCULATING TUMOR DNA FROM CEREBROSPINAL FLUID AND PLASMA OF PATIENTS WITH PRIMARY AND SECONDARY CNS LYMPHOMAS WITH NEGATIVE FLOWCYTOMETRY

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Introduction: Primary or secondary central nervous system lymphomas (PCNSL, SCNSL) represent aggressive malignancies with poor prognosis. Their diagnosis is based on magnetic resonance imaging and brain biopsy or cerebrospinal fluid (CSF) analysis by cytology or flow cytometry (FC). The biopsy is highly invasive, with a risk of complications. Cytology and FC have high specificity but limited sensitivity, showing up to 40% of false negative results. The analysis of circulating tumor DNA (ctDNA) in plasma and CSF has the potential to identify the presence of tumor in CNS. The aim of our work was to map the genomic alterations in ctDNA of CNS lymphoma cases with negative FC results.

Methods: We analyzed paired samples (plasma and CSF) of 7 PCNSL and 5 SCNSL patients. Peripheral blood (20 mL) and CSF (10 mL) were collected in special tubes with stabilizing agent (CELL-FREE DNA BCT®, Streck). After double centrifugation, plasma, CSF pellet, and CSF supernatant were obtained. ctDNA was extracted using the QIAamp Circulating Nucleic Acids kit (QIAGEN) and analyzed by custom NGS panel LYNX (PMID: 34082072) together with DNA from CSF pellets. NGS library was prepared by SureSelectXT HS kit (Agilent Technologies) and sequenced on NextSeq (Illumina). LYNX panel enables analysis of various genomic biomarkers in lymphoproliferative disorders—mutations in 67 genes, genome-wide copy number alterations, antigen receptor rearrangements, and common lymphoma translocations.

Results: Our cohort of 12 patients with CNS lymphoma comprised six men and six females of median age 66.5 years, diagnosed during 2021–2022 at our clinic. Genomic aberrations and clonal immunoglobulin rearrangements detected in ctDNA from plasma and CSF supernatant are summarized in Table 1. At diagnosis, we detected clonal abnormalities only in CSF of PCNSL, whereas in SCNSL, plasma was also infiltrated with ctDNA. In relapse or progression of the systemic disease to SCNSL, ctDNA was detected in CSF, not in plasma. In all PCNSL cases, we found pathogenic *MYD88* L265P mutation (in one patient, CSF pellet but not supernatant was positive), clonal IG rearrangements, and in majority of cases complex chromosomal changes. In ctDNA, we also detected *IGH::BCL2* in two SCNSL patients and a *BCL6::IGH* translocation in one case.

Conclusions: Despite the small number of patients in our cohort, we showed that CSF is the relevant material for the analysis of lymphoma genomic markers in ctDNA, which seems to be a feasible and reliable approach for identifying lymphoma CNS infiltration. Importantly, we were able to confirm the CNS involvement even in samples with negative FC results.

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Keywords: aggressive B-cell non-Hodgkin lymphoma, diagnostic and prognostic biomarkers, liquid biopsy

Conflicts of interests pertinent to the abstract

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