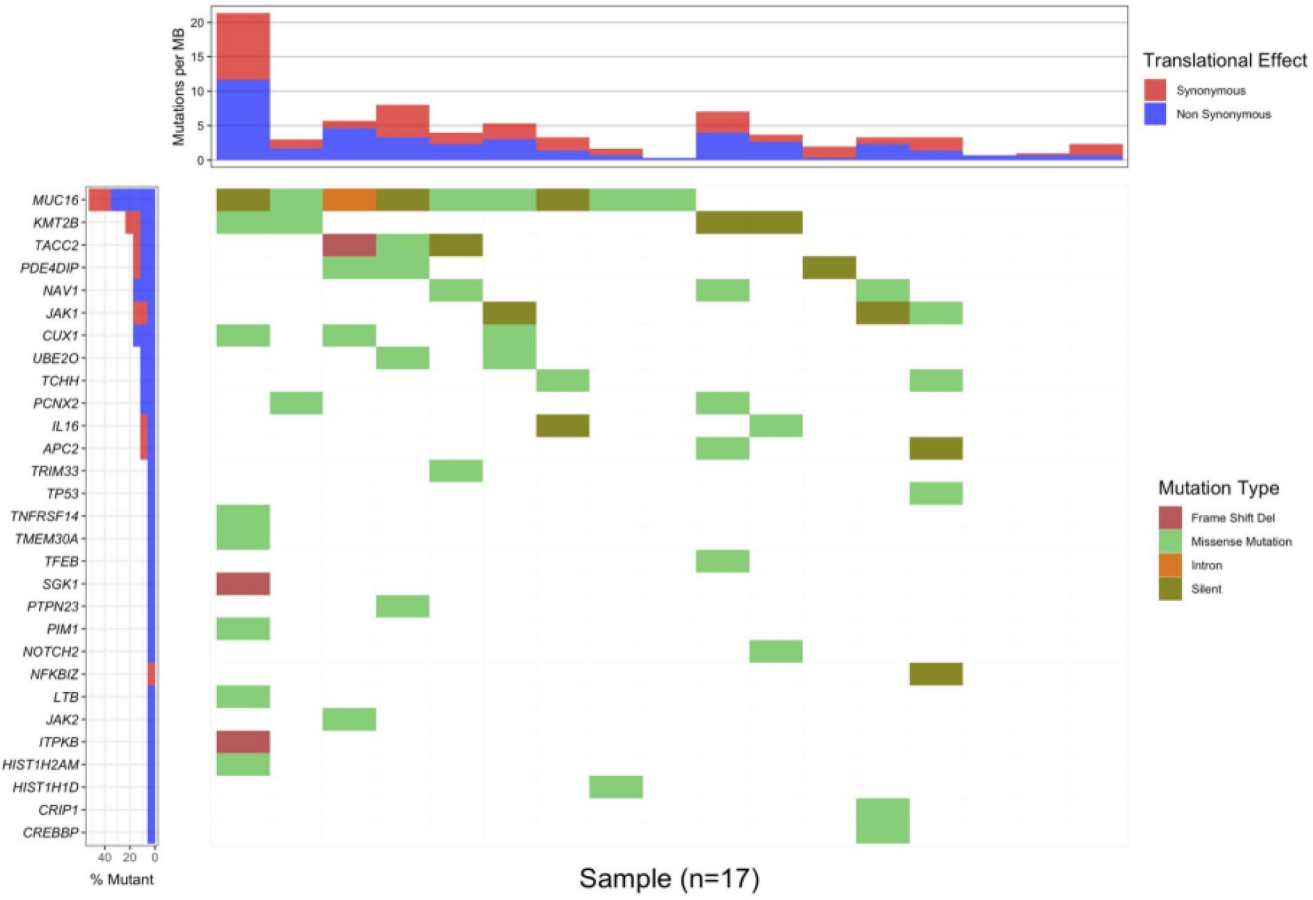

FIGURE 1 Somatic variants (SNVs or InDels) limited to significant genes ($p < 0.05$) following MutSig2CV analysis

displayed somatic variants (SNVs or InDels). Somatic variants were detectable in all patients with a median of 10 mutations per patient (range 1-43). Overall, we identified 29 significantly mutated genes by MutSig2CV analysis (Figure 1). Among the most recurrently mutated genes were *KMT2D* (7 patients), *NFKBIA* (4 patients) and *EP300* (4 patients). The mutated allele frequency was generally low (median 0.95%; range 0.14%-16.00%). *KMT2D* and *KMT2B* mutations had high allele frequencies, suggesting they constitute events early in PCNSL oncogenesis. Surviving patients had significantly lower ctDNA burden measured by average mutated allele frequency than patients who died (1,61% vs. 4,13%; p = 0,011). At the meeting, a full analysis of our cohort including copy number variations and further genotype-phenotype links will be presented.

Conclusions: Our results show that detection of ctDNA in peripheral blood of patients suffering from PCNSL is feasible. Furthermore, we were able to detect several recurrent genetic aberrations that were previously shown to be present in DLBCL as well as PCNSL in tissue genotyping. Despite the fact that the mutated allele frequency was rather low compared to previous reports from DLBCL, our pipeline allowed us to detect genetic aberrations in 100% of cases in our series. Liquid biopsy-based genotyping of PCNSL might offer tremendous advantages for diagnostic approaches, discovery of potential therapeutic targets and assessment of response or early detection of relapse.

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Keywords: Liquid biopsy, Extranodal non-Hodgkin lymphoma, Pathology and Classification of Lymphomas

No conflicts of interest pertinent to the abstract.

156 | SARS-COV-2 INFECTION IN 50 PATIENTS WITH PRIMARY CNS LYMPHOMA: PRESENTATION, EFFECTS ON TUMOR TREATMENT AND OUTCOME IN A SERIES OF THE INTERNATIONAL PCNSL COLLABORATIVE GROUP

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Introduction: COVID-19 is associated with high mortality in cancer patients (pts); its course varies greatly among patient subgroups and tumor status. Herein, we report an international study on pts with primary CNS lymphoma (PCNSL), an aggressive tumor where dose intensity is crucial, and concurrent SARS-CoV-2 infection.

Methods: Data of presentation, management and outcome of pts with PCNSL and SARS-CoV-2 infection were analyzed to define effects of infection on timing of anti-lymphoma treatment and overall outcome. Pts were grouped in 1st and 2nd pandemic waves using July 31, 2020 as cut-off for SARS-CoV-2 diagnosis.

Results: 50 pts from 12 centers of 5 countries were registered (Table): 30 during 1st and 20 at 2nd wave. SARS-CoV-2 was diagnosed before/during 1st-line PCNSL treatment in 35 (70%) pts, with a median time between PCNSL diagnosis and virus detection of 45 days (d) (range -27-179). 26 of these pts (75%) developed pneumonia, were hospitalized (median 22 d; 5-192), 9 admitted to ICU (median 14 d; 1-51); 13/26 (50%), cleared the virus (median time 31 d; 1-69), resumed anti-lymphoma treatment (median treatment delay 27 d; 0-112) and were alive at the last visit. The 13 pts with pneumonia who did not clear virus died of COVID-19 or related infections within 25 d from symptoms onset. 8 of the 9 pts without pneumonia cleared virus and resumed/initiated anti-lymphoma treatment (median delay 16 d; 0-93); none died of COVID-19. Virus clearance and pneumonia were significantly associated with resumption of anti-lymphoma treatment.

5 of 11 pts affected by SARS-CoV-2 during lymphoma follow-up developed pneumonia, required hospitalization (median 25 d; 5-25). All 11 pts cleared virus and are alive. Conversely, the 4 pts infected during salvage anti-lymphoma therapy, interrupted treatment, were unable to clear virus and died of lymphoma or COVID-19.

At a median follow-up since virus detection of 214 d (0-322), 30 (60%) pts are alive, 15 without evidence of lymphoma and 28 cleared virus. SARS-CoV-2 serology was positive in 7/11 assessed survivors.

Patient's characteristics	N= 50
median age (range; years)	68 (22-87)
Males/females	28 / 22
Race: Caucasian/Asiatic/Hispanic	44 / 4 / 2
Disease site	
Brain parenchyma	42 (84%)
Brain + Meninges	6 (12%)
Brain + eyes	1 (2%)
Brain + spinal cord	1 (2%)
IELSG risk	
Low	4 (8%)
Intermediate	18 (36%)
High	16 (32%)
Undefined	12 (24%)
Comorbidity	
High blood pressure	22 (44%)
Hypercholesterolemia	17 (34%)
Vasculopathy/coronaropathy/cardiac arrhythmia	12 (24%)
Obesity/overweight	12 (24%)
Type-II diabetes	10 (20%)
Chronic respiratory disease	5 (10%)
Renal failure	3 (6%)
Hepatitis virus infection/HIV	3 (6%)
Prior solid or hematological tumor	3 (6%)
None	9 (18%)
SARS-CoV-2 detected	
before first-line treatment for PCNSL	8 (16%)
during first-line treatment for PCNSL	27 (54%)
during follow-up	11 (22%)
during salvage treatment (relapsed PCNSL)	4 (8%)
COVID-19 symptoms	
Fever	28 (56%)
Cough	19 (38%)
Dyspnea	17 (34%)
Fatigue	10 (20%)
Pain	1 (2%)
Anosmia	2 (4%)
Ageusia	1 (2%)
Diarrhea	1 (2%)
Treatment of COVID-19	
Hydroxychloroquine	11 (22%)
Antiviral agents (include hyper-immune plasma)	6 (12%)
Dexamethasone	19 (38%)
Anticoagulant therapy or prophylaxis	22 (44%)
Ongoing or prior first-line treatment for PCNSL	
MATRIX or similar regimens	16 (32%)
High-dose methotrexate monotherapy	3 (6%)
High-dose methotrexate plus oral alkylating agent and rituximab	28 (56%)
None	3 (6%)

12 (24%) pts died of COVID-19, 3 of other infections and 4 of lymphoma. The 6-month OS was 63%; virus persistence was independently associated with poor outcome. Mortality among pts in 1st line treatment was significantly higher during the 2nd wave (4-month OS: 75% vs 37%, p = 0.03), and associated with a lower viral eradication rate (75% vs 40%; p = 0.03).

Conclusions: COVID-19 was a strong outcome-defining event, especially in pts receiving anti-PCNSL treatment and those diagnosed during the 2nd wave. Multidisciplinary strategy facilitated eradication of the infection and completion of planned therapy, with acceptable timing and short-term OS rate, in half of pts with pneumonia. For pts in follow up, SARS-CoV-2 infection was not associated with severe symptoms and did not affect OS. Poor results in pts treated during the 2nd wave deserve particular attention.

Keywords: Aggressive B-cell non-Hodgkin lymphoma, Extranodal non-Hodgkin lymphoma

No conflicts of interest pertinent to the abstract.

157 | OLDER PATIENTS WITH PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA (PCNSL): REAL WORLD (RW) OUTCOMES OF POST-INDUCTION THERAPY IN THE MODERN ERA

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Introduction: Treatment of older patients (pts) with PCNSL is challenging due to the prevalence of comorbidities, frailty, and effective delivery of chemotherapy (CT). Optimal induction CT or consolidation for older PCNSL pts are unknown. Moreover, there are a paucity of large-scale prognostication studies available. We analyzed post-induction treatment patterns and outcomes with prognostication across 19 academic centers.

Methods: We conducted a large, RW retrospective study of newly diagnosed PCNSL pts (1/2008-1/2019) ages > 60 years (yrs). Among 525 older pts in the full data set (David KA et al, ASH 2020), 363 pts achieved either complete or partial remission (CR/PR) with induction. Survival rates were estimated by Kaplan-Meier with differences assessed by log rank test. Univariate associations were derived via Cox model with variables $p < 0.05$ entered stepwise into multivariate (MVA) models.

Results: Among 363 pts in PR or CR, mean age was 70 yrs (60-88). 50 (14%) pts underwent consolidative autologous stem cell transplant (ASCT), with mean age 66 yrs (60-77) and ECOG PS 0-1 in 72% ASCT pts. 18 pts (mean age 68, range 62-75) received consolidative radiation therapy (RT). Post-induction maintenance was given to 22% of pts (mean age 72 yrs, 60-86); the most common regimens were temozolomide (28%), methotrexate (19%), and lenalidomide (25%). Among all 363 pts, median progression-free survival (PFS) was 61 months (95% CI 41-72, Figure 1A) and median overall survival (OS) was 70 months (95% CI 56-90, Figure 1B).

In the full data set of 525 pts on MVA analysis, advancing age & worse ECOG PS were associated with inferior PFS, while advancing age, hypoalbuminemia, CIRS-G score & worse ECOG PS were associated with inferior OS. On MVA analysis among the 363 CR/PR pts, factors associated with inferior PFS were advancing age (HR 1.050, p = 0.0004) and anemia (HR 1.13, p = 0.0228), with advancing age (HR 1.057, p = 0.0006), impaired creatinine clearance (1.009, p = 0.0381), and worse ECOG PS (p = 0.0049) associated with inferior OS.

The 3-yr PFS among pts undergoing ASCT was 72% vs. 46% among those who did not (p = 0.002) with 3-yr OS 81% vs. 64%, respectively (p = 0.02); these survival improvements persisted when stratified for the aforementioned prognostic factors (Figure 1C/D). Among pts who received maintenance therapy, 3-yr PFS was 65% vs. 44% with no maintenance (p = 0.02), with 3-yr OS of 83% vs. 61%, respectively (p = 0.0007)), with both remaining significant on stratification (Figure 1E/F). Consolidative RT did not improve survival (data not shown).