Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background: The efficacy of rituximab in Primary CNS Lymphoma (PCNSL) is still under debate. We performed an international randomized phase III study to investigate the efficacy of rituximab when added to methotrexate, BCNU, teniposide and prednisolone (MBVP) in PCNSL. The primary endpoint, event-free survival (EFS) at one year, was similar in both treatment groups and was previously reported (Bromberg et al, Lancet Oncology 2019; 20: 216-228).

Aims: Here we present long-term follow up results with a median follow-up of 82 months.

Methods: Between August 2010 and May 2016 200 newly-diagnosed, non-immunocompromised patients with PCNSL aged 18-70 years and WHO performance status 0-3 were randomized between treatment with MBVP chemotherapy with (arm B) or without (arm A) rituximab. The rituximab was given weekly in the first MBVP cycle, fortnightly in the second (in total 6 rituximab administrations). Responsive patients received consolidation with high-dose cytarabine, and patients aged ≤ 60 were subsequently treated with low-dose WBRT if in CR/CRu; in case of PR with an additional boost on the tumor. Patients > 60 were not irradiated. All patients gave written informed consent.

Results: The modified intention-to-treat (m-ITT) population consisted of 199 eligible patients, 55% were men. The median age was 61 yrs (range 26-70), the median WHO performance status 1 (range 0-3). The primary endpoint EFS at one year was 49% (95% CI 39-58) (MBVP) vs 55% (95% CI 44-64) (R-MBVP). The EFS at 5 years was 25% (17-34) vs 36% (27-46) respectively, hazard ratio (HR) 0.85, 95% CI 0.61-1.18, p=0.33 (adjusted for age and WHO performance status). The progression-free survival (PFS) at one and 5 years were 58% (47-67) and 29% (21-39) (MBVP) and 65% (54-73) and 43% (33-53) (R-MBVP) (HR 0.73, 95% CI 0.52-1.02, p=0.07).

80 patients were still alive. Overall survival (OS) at 5 years for MBVP and R-MBVP was 49% (39-59) and 53% (43-63) respectively. The median OS was 57 months (95% CI 38-75) in the MBVP arm and 85 months (95% CI 43-104) in the R-MBVP arm (HR 0.87, 95% CI = 0.61-1.26, p=0.47). A total of 111 patients had progression or relapse, 63 after MBVP and 48 after R-MBVP. 79% of these patients received further treatment. The median OS after progression/relapse was 9.7 months (5.9-19.9) in the MBVP arm, and 6.1 months (2.4-13.1) in the R-MBVP arm (HR 1.25, 95% CI 0.83-1.87, p=0.29).

119 patients died, 64 in the MBVP arm and 55 in the R-MBVP arm. Causes of death were PCNSL in 69% of the patients (both arms), complication of treatment (6% vs 5%), secondary malignancy (5% vs 2%) and other or...
unknown causes (20% vs 24%). Age was the strongest prognostic factor for EFS, PFS and OS in multivariate analysis.

An unplanned subgroup analysis by age (≤60 vs > 60 yrs) showed a significant different EFS at one year for younger patients with R-MBVP, not found in patients > 60 yrs (Bromberg et al, 2019). With longer follow up the 5-year EFS in the younger group was 28% (16-41) (MBVP) vs 55% (40-68) (R-MBVP), HR 0.48, 95% CI 0.28-0.81, p=0.006. 5-year PFS was 31% (18-44) versus 57% (42-70), HR 0.47, 95% CI 0.27-0.81, p=0.007. The OS at 5 years was 54% (39-68) vs 70% (55-81) respectively (HR 0.65, 95% CI 0.36-1.19, p=0.16).

Image:

![Graph showing overall survival](image)

**Overall survival**

HR=0.87, 95% CI 0.61-1.28, P=0.47

**Summary/Conclusion:** In the modified-ITT population we found no statistically significant benefit of the addition of rituximab to MBVP on EFS, PFS and OS in patients with PCNSL, even after a long follow-up of median 82 months. Therefore, the results of this study do not support the use of rituximab with MBVP in the treatment of primary CNS lymphoma.