Long-term follow-up of bendamustine plus rituximab (BR) regimen in 69 treatment-naïve (TN) patients with Waldenström Macroglobulinemia, a study on behalf of the French Innovative Leukemia Organization (FILO).

Eveillard JR, Chaoui D, Cavalieri D, Dartigeas C, Willems L, Le Calloch R, Roos-Weil D, Merabet, F, Roussel X, Bareau B, Tricot S, Dupuis J, Poulain S, Laribi K, Leblond V

Bendamustine-rituximab (BR) is a first-line option for treatment-naïve (TN) patients with Waldenström macroglobulinemia (WM), more effective than other immunochemotherapies used in this setting. The FILO group has followed 69 patients with BR-Treated TN-MW patients (*Laribi K, BJH 2018, BJH 2024*). Here, updated information of this cohort is provided, after a median observation time of 97 months (interquartile range [IQR] 83-110 months). Median OS is still not reached (NR), and median progression-free survival (PFS) is 82.2 months (95% confidence interval [CI] 69.7-93.1). For *MYD88 wild-type* patients, median OS is 27.37 months (95%CI 23.47-79.17) vs. NR for mutated patients (p=0.004). Median survival is NR whatever the *CXCR4* status. Seventeen (24.6%) patients relapsed. Fifteen received second line therapy (BTK-inhibitor, n=9, chemoimmunotherapy n=6) or supportive care (n=2). After second-line treatment, median PFS is 20.99 months (range 9.13-NR), yet 44.98 months (9.13-NR) for patients who received BTKi. Twenty-six patients died, 8 from progression, 2 from therapy-related AML, 7 from second solid tumors, 7 from non-related cause and 2 from unknown cause. Median EFS defined as death, relapse or second cancer is 81.47 months (62.43-98.67). The cumulative incidence of second cancer is 2.90%, 5.80%, 10.49%, and 17.6% at 12, 24, 48, and 96 months. In multivariate analysis, only age at first therapy remains a significant risk factor (p: 0.008). In conclusion the BR regimen is very efficient in patients with TN-WM with long term responses. Secondary cancers should be monitored.