Two Years Rituximab Maintenance Vs. Observation after First Line Treatment with Bendamustine Plus Rituximab (B-R) in Patients with Waldenström's Macroglobulinemia (MW): Results of a Prospective, Randomized, Multicenter Phase 3 Study (the StiL NHL7-2008 MAINTAIN trial)

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Background:

The StiL NHL1-2003 trial demonstrated that Bendamustine-Rituximab (B-R) is a highly effective treatment for patients with WM achieving a median PFS of 69.5 months. Rituximab (R) maintenance is part of a standard treatment for follicular lymphoma. In WM, however, the role of R maintenance is unclear. In this study we compared the effect of 2 years R maintenance vs. observation after first-line treatment with B-R in patients with previously untreated WM.

Methods:

Patients needed to have advanced stage of disease with indication for treatment (e.g. B-symptoms, anemia, hyperviscosity syndrome, etc.). Primary endpoint was progression free survival (PFS). Secondary endpoints included response rates, overall survival (OS), and toxicity. All patients were treated with up to 6 cycles of B-R plus 2 additional R cycles. Only patients responding to B-R were randomized to either R maintenance (q 2 months for 2 years) or observation.

Results:

Of 293 registered patients, 5 were excluded due to lack of data and other reasons. Median time of follow-up was 70.2 months at the time of this analysis (July 2019). 257 of 288 patients with a median age of 67 years were evaluable for response evaluation. The median baseline value of IgM was 31.3 g/l, and of Hb 10.1 g/dl. Median PFS for all patients (intention to treat) was 78.0 months. The median OS was not yet reached, with an estimated 5-year-survival of 78%. A total of 38 secondary malignancies were recorded, with 1 AML during observation and 1 MDS in R maintenance. 235 patients (91.4%) responded to B-R induction, with the majority of patients (231, 89.9%) achieving a partial remission. Of 218 randomized patients, 109 (50%) were randomized to R maintenance and 109 (50%) to observation. Median age of randomized patients was 67 years, patient characteristics were comparable for both groups. The 2-year R maintenance provided a better disease control with a median PFS of 101 months in the R maintenance group compared to the median PFS of 83 months in the observation group, however, this difference was not statistically significant with a hazard ratio of 0.80 (95% CI 0.51 – 1.25, $p = 0.32$). The median PFS of the group of all patients receiving treatment with B-R induction only was 65.3 months and is consistent with the results of the previous StiL NHL1-2003 trial (69.5 months). This group of 179 patients includes both non-randomized patients (B-R non-responder, not randomized for any reason) and patients randomized to observation. There was no difference in OS with the median not yet reached for both R maintenance and observation.

Conclusions:

We confirmed that induction with B-R is a highly effective treatment for WM. After a median observation time of 5.9 years the results could not demonstrate an improvement in PFS or OS after a 2-year R-maintenance when compared with observation after B-R induction in patients with WM.