

**Bendamustine plus Rituximab versus CHOP plus Rituximab as First-Line-Treatment in Patients with Indolent Lymphomas and Waldenstrom's macroglobulinemia**

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**Background:** Rituximab plus chemotherapy is first-line standard of care for patients with advanced indolent lymphoma and Waldenstrom's macroglobulinemia (WM). Bendamustine plus rituximab (B-R) has been shown to be effective in relapsed or refractory lymphoma disease. The current multicenter, randomized, phase III study compared B-R and CHOP-R as first-line treatment in variant indolent lymphoma entities including WM.

**Methods:** 549 patients with indolent lymphomas or WM were randomized to B-R or CHOP-R for a maximum of 6 cycles. The primary objective was to compare progression-free survival (PFS) with B-R and CHOP-R.

**Results:** 513 patients were evaluable (260 B-R; 253 CHOP-R). Patient and disease characteristics were well balanced between arms, and the median age was 64 years (range 31–83). At a median follow-up of 35 months, median PFS was significantly prolonged with B-R compared with CHOP-R (54.8 versus 31.2 months; hazard ratio 0.58, 95% confidence interval 0.44–0.76;  $P < 0.0001$ ). The PFS benefit for B-R was maintained in all histological subtypes, except marginal zone lymphoma, where B-R was at least non-inferior compared with CHOP-R. The median PFS for 22 patients with WM randomized to B-R was superior and not yet reached, while the median PFS for 19 patients with WM randomized to CHOP-R was 35 months (hazard ratio 0.21, 95% confidence interval 0.06–0.56;  $P = 0.0024$ ). At the time of analysis 4 relapses (18%) occurred in the B-R group and 11 relapses (58%) in the CHOP-R group, respectively. The B-R regimen was better tolerated than CHOP-R, with no alopecia ( $P < 0.0001$ ), and lower rates of hematotoxicity ( $P < 0.0001$ ), infections ( $P = 0.0004$ ), peripheral neuropathy ( $P < 0.0001$ ) and stomatitis ( $P < 0.0001$ ). Skin toxicity was more common with B-R than CHOP-R ( $P = 0.0122$ ).

**Conclusions:** In patients with previously untreated indolent lymphoma and WM, B-R demonstrates a PFS benefit and improved tolerability compared with CHOP-R. Therefore, B-R should be considered a new standard of care in these indications.