Current Therapy of Waldenström's Macroglobulinemia – Alkylator based therapy (excluding Bendamustine)

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The recent years have shown amazing progress in the development of innovative therapies for patients with B – cell lymphomas, targeting critical kinases in signaling pathways downstream of the B – cell receptor. Despite the emergence of these new compounds, conventional chemotherapy is still the backbone of treatment in virtually all B – cell lymphomas outside of clinical trials. This in particular true for Waldenström's macroglobulinema (WM), as there are still few data on the safety and efficacy of e.g. BTK and PI3K inhibitors, also due to the low incidence of this disease and the lack of larger clinical trials. Thus, conventional chemotherapy is widely used in this entity. Among the different chemotherapeutical options, alkylator based therapy is still among the most prominent ones as it offers the patient a well tolerated and highly efficient treatment option. When used in a more dose intense regimen such as R-CHOP, it induces high overall response rate of 91% and a long time to treatment failure (TTF) with a median 63 months for R-CHOP as shown in a prospective randomized trial of the 'German Low Grade Lymphoma Study Group'. This regimen is in particular appropriate in younger patients without co-morbidities and in patients with a more aggressive clinical course. Alkylator-based therapy can be also designed as a mild chemotherapy without any major myelosuppressive toxicity: this was demonstrated by the DRC regimen, which induced an objective response in 83% of patients, including 7% with CR, 67% with PR. The 2-year progression-free survival rate for the total patient group was 67 %, for responding patients 80%. This remarking activity was paralleled by only moderate myelotoxicity with only 9% of patients experiencing grade 3 or 4 neutropenia and none experiencing grade 3 or 4 thrombocytopenia. Thus, the DRC regimen might be a very attractive regimen for the treatment of the large group of elderly patient with WM. The 'European Consortium for Waldenström's Macroglobulinemia' (ECWM) currently uses the DRC regimen as a backbone to test the benefit of additional bortezomib in patients with newly diagnosed WM in a large European randomized phase III trial. Thus, this trial documents that alkylator – based therapy is still an important part of our therapeutic concepts and if less dose intense also an ideal partner for novel compounds.