

Waldenström Macroglobulinaemia (WM) is an indolent lymphoma still primarily managed with chemo-immunotherapy in first-line.

The aim of our study was to evaluate and compare efficacy and safety of different frontline chemo-immunotherapeutic regimens. A retrospective analysis was conducted on 447 WM patients treated between 2008-2022: 245 received BR (bendamustine-rituximab), 116 DRC (dexamethasone-rituximab-cyclophosphamide), and 86 R-chemo (other chemo-immunotherapies).

We obtained a 4-y progression free survival of PFS 80% for BR, 68% for R-chemo, 60% for DRC; the difference is significant between BR and DRC ( $p<0.001$ ). Overall survival OS curves did not differ among the three schemes.

A significant dose reduction was recorded in terms of total bendamustine dose administered, using the percentage of the relative dose intensity (RDI).

A bendamustine starting dose of 70 mg/m<sup>2</sup> is not inferior in terms of PFS to 90 mg/m<sup>2</sup>. A dose with a RDI reduction <30% allows to maintain adequate treatment intensity, obtaining long PFS. A RDI reduction >30% was associated to age superior to 75 years and CrCl inferior to 70 mmol/L.

This is the largest Italian, retrospective, real-life study on treatment naive WM patients with excellent outcomes. The long-term follow-up confirmed better PFS for BR-treated patients, while OS remained comparable between BR and DRC.