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CD52 ANTIGEN EXPRESSION IN WALDENSTRÖM'S MACROGLOBULINAEMIA AND ACTIVITY OF ALEMTUZUMAB IN PATIENTS WITH RELAPSED / REFRACTORY DISEASE.

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Alemtuzumab is highly effective treatment for patients with chronic lymphocytic leukemia who have previously received a purine analogue. Little however is known about its activity in other B-cell lymphoproliferative disorders. In order to assess its applicability in WM we used three-colour flow cytometry (CD19-PE/Cy5 vs CD52-PE vs CD59-FITC) to assess antigen expression in a series of 32 patients. Antigen expression was demonstrable in all cases with a median of 99.5% of cells (range 92.9-100%) expressing the antigen compared to the isotype control. Antigen density was very similar to that seen in CLL (mean fluorescence intensity 748, range 162-4022).

We therefore proceeded with a phase II trial of intravenous alemtuzumab in a series of 9 pts with heavily pre-treated WM. The cohort consisted of 7 men and 2 women with a median age of 58 years (range 50-82) all of whom had evidence of bone marrow infiltration and IgM monoclonal gammopathy (median 40g/l). Lymphadenopathy was documented in 2 pts while 5 had evidence of bone marrow failure. All pts were heavily pre-treated receiving a median of 4 previous therapies (range 1-5) which included purine analogues (9 pts), alkylators (8 pts), anthracycline containing regimens (5 pts) and rituximab either alone or in combination (5 pts). 6 pts were considered to be refractory to their most recent therapy while 3 were treated in untested relapse. Alemtuzumab was given according to the standard schedule of 30mg IV on three days per week for a maximum of 12 weeks. Pts received a median of 10 weeks of therapy (range 2-12 weeks) and all received prophylaxis against pneumocystis and herpes infection. Weekly PCR was used to monitor for CMV reactivation and bone marrow examination was performed every 4 weeks during therapy to assess response.

8 pts are currently evaluable for response (treatment is ongoing in the remaining pt) using the criteria proposed at the Athens Workshop. Responses were documented in 6 of the 8 evaluable pts and consisted of 1CR and 5PR. A further pt had stable disease while the remaining pt was considered to have failed when treatment was stopped at 2 weeks because of severe bacterial sepsis. The median duration of response was 7 months from the completion of therapy (range 1-48 months). Infective complications were common and consisted of CMV reactivation (4 pts), bacterial infection (5 pts), herpes simplex, varicella zoster, tuberculosis and aspergillosis (1 case each). Of the responding pts 4 have died, 2 from infective causes, 1 from progressive disease and 1 from an unrelated cause whilst still in PR. 2 responding pts remain in PR at 3 and 48 months post therapy.

We would therefore conclude that CD52 is expressed at high levels in WM and that alemtuzumab shows promising activity in patients with relapsed / refractory disease. However infectious complications are common and further studies are warranted to define the exact role of alemtuzumab in the treatment of WM.