[ABSTRACT WM3.10]

Increased incidence of disease transformation and development of MDS/AML in Waldenstrom's Macroglobulinemia (WM) patients treated with nucleoside analogues.

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Background: WM is an indolent B-cell lymphoma. NA are widely used in the treatment of WM, and are considered as appropriate first line agents for the treatment of WM (Gertz et al, Semin Oncol 2003; Treon et al, Blood 2006). Increased incidences of disease transformation and development of MDS/AML have been observed among patients with indolent B-cell malignancies receiving NA. We therefore sought to delineate the incidence for these events in a large population of WM patients treated at our institution. Methods: 326 previously treated patients with the consensus panel definition of WM, who received treatment with (n=173) or without (n=153) a NA were included in this analysis. Baseline characteristics between NA and non-NA treated patients were not significantly different and were as follows: median age 59 years; male/female ratio 1.4; median B2M 2.9 mg/L; serum IgM 3,000 mg/dL; BM involvement 40%; Hct 34%; WBC 5,100/ul, and PLT count 243,000/ul. For patients receiving NA, treatment consisted of either fludarabine (n=117; 68%), cladribine (n=48; 27%) or both (n=8; 5%). For non-NA treated patients, therapy included chlorambucil, rituximab, CVP, CHOP, thalidomide, and cyclophosphamide alone or in combination with rituximab, and alemtuzumab. Median follow-up of patients was 64 (range 10-270) months. Results: Among NA treated patients, 10 (5.7%) patients had transformation to an aggressive NHL (to DLBCL) (n=7; 4%) or developed MDS/AML (n=3; 1.7%). Disease transformation and development of MDS/AML occurred at a median time of 48 (range 7-114), and 48 (range 38-52) months following NA treatment, respectively. In contrast, among non-NA treated patients, only 1 patient demonstrated disease transformation (to DLBCL) at 10 months and no patients developed AML/MDS (p=0.025). Conclusion: These data demonstrate an increased incidence of disease transformation and development of MDS/AML among treated with NA.