Session VI: Treatment of Waldenström’s Macroglobulinemia

Abstract 132

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Fludarabine-based Combination therapies for Waldenström’s Macroglobulinemia. Enrica Morra, Dept. of Hematology, Niguarda Ca’ Granda Hospital, Milano, ITALY.

Fludarabine (F) has been extensively used in WM, either alone or in combination. Most trials with F as a single agent in previously treated patients were small phase II studies with different inclusion and response criteria. The overall response rate (RR) ranged from 30% to 50%, being higher in patients responsive to first line therapy. In a randomized trial in pretreated patients, F was compared with a combination of cyclophosphamide (C), doxorubicin, and prednisone (Leblond et al, 2001). Patients receiving F obtained higher RR and longer duration of response. F as first-line therapy produced 38% to 100% RR, depending on the characteristics of patients and on the criteria used for response. Purine analogues and alkylating agents are known to be synergistic. With F + C, RRs of 85% in previously treated, and of 55% to 89% in relapsed/refractory patients have been reported. The addition of Rituximab to F + C (FCR) increased the overall RR to 80% - 90%. In our experience FCR induced high percentages of good quality responses, with 42% of patients achieving near CR (defined as complete resolution of symptoms, regression of adenopathy/organomegaly on CT scan, absence of BM infiltration, with persistence of positive serum immunofixation). Major toxicity was neutropenia, which in a few patients persisted for weeks after the end of therapy. With FCR, responses occurred within 3-6 months. The majority of responses improved over time, up to 6-12 mos from the end of treatment (Tedeschi et al, 2007). The major adverse events after F-containing regimens are myelosuppression and immunosuppression. The risk of opportunistic infections should be considered and anti-infective prophylaxis is recommended. Risk of development of MDS/AML and increased incidence of transition to high grade lymphoma have been reported. Impairment of peripheral stem cell (PSC) collection may occur after purine analogues. Therefore, these drugs should be avoided in patients eligible for autologous stem cell transplant. F-based combinations including R (FCR) may be appropriate second-line treatment for patients with short remission or resistant to frontline therapy. The high rate of good quality responses warrants their use as first line treatment for patients with advanced disease.