

Pre-therapy serum IgM levels predict clinical response to extended rituximab in Waldenstrom's macroglobulinemia.

Steven P Treon, MD PhD 1, Christos A Emmanouilides, MD PhD 2, Eva Kimby, MD PhD 3, Andrew Branagan, BA 1, Constantine Mitsiades, MD 1, Kenneth C Anderson, MD 1 and Stanley R Frankel, MD 4. 1Medical Oncology, Dana Farber Cancer Institute, Boston, MA, United States; 2Hematology Oncology, UCLA Medical Center, Los Angeles, CA, United States; 3Hematology Oncology, Karolinska Institutet, Stockholm, Sweden and 4Hematology Oncology, Greenebaum Cancer Center, Baltimore, MD, United States.

We undertook a prospective, multicenter phase II study to determine the activity of extended rituximab therapy in Waldenstrom's macroglobulinemia (WM). Twenty-nine patients with a median age of 65 (range 43-90 yrs), and median prior treatments of 1 (range 0-2) were enrolled. 26 patients completed the intended therapy which consisted of receiving 4 infusions of rituximab (375 mg/m² weekly), followed by 4 additional infusions of rituximab (375 mg/m² weekly) at week 12, if they demonstrated a response or had stable disease (SD) following the first course of therapy. Overall, treatment was well tolerated. One patient died of sepsis and another patient experienced neutropenia, both events deemed by their treating physicians to be unrelated to protocol treatment. One patient experienced significant diffuse joint pains after 4 infusions of rituximab which resolved after steroid therapy. Best overall responses following rituximab for 26 patients who completed protocol therapy are as follows: partial response (PR; > 50% decline in IgM) in 12 patients (46.1%) and minor response (MR; > 25% decline in IgM) in 7 patients (26.9%). The overall response rate (ORR) was 73.0% and 3 (11.5%) patients demonstrated stable disease (SD). The median time to treatment failure for responding patients has not been reached with a median follow-up of 20 months (range 7-30+ months). Analysis of baseline serum IgM levels and clinical response to rituximab showed that 18/20 (90.0%) patients with an IgM level under 6,000 mg/dL responded, whereas only 1/6 (16.6%) patients with an IgM level of over 6,000 mg/dL had a response (p=0.002). No correlation with pre-therapy bone marrow involvement and clinical response to rituximab was seen. These data therefore show that extended rituximab therapy is highly active in WM patients and produces durable responses. WM patients with serum IgM levels of <6,000 mg/dL are more likely to benefit from extended rituximab therapy. The mechanism for this finding is currently under investigation in our laboratory.