# What IgM MGUS and Smoldering WM Patients are at Risk for Progression to Symptomatic Waldenstrom's Macroglobulinemia?

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The short answer is that all patients with IgM MGUS and smoldering WM are at risk for progression to symptomatic Waldenstrom's Macroglobulinemia. IgM Monoclonal Gammopathy of Undetermined Significance (MGUS) is characterized by the presence of a serum IgM monoclonal protein < 3.0 g/dL, bone marrow lymphoplasmacytic infiltration < 10% if done and the absence of symptomatic anemia, lymphadenopathy, hepatosplenomegaly or hyperviscosity in addition to the absence of constitutional symptoms such as fever, night sweats, fatigue or weight loss. In a cohort of 213 IgM MGUS patients from Southeastern Minnesota a total of 29 patients progressed to non-Hodgkin's lymphoma (N=17), Waldenstrom's Macroglobulinemia (N=6), AL amyloidosis (N=3) and CLL (N=3) with an overall increased relative risk of 15.9-fold based on the Iowa SEER registry. The risk of progression to WM or a related disorder was 8% at 5 years, 12% at 10 years and 18% at 15 years. Smoldering Waldenstrom's Macroglobulinemia (SWM) is defined as the presence of a serum IgM monoclonal protein ≥ 3 g/dL and/or lymphoplasmacytic infiltration of ≥ 10% in the bone marrow and the absence of symptomatic anemia, lymphadenopathy, hepatosplenomegaly or hyperviscosity and no systemic constitutional symptoms. The 48 patients with SWM had a median follow-up of 15.4 years. Thirty-six of the 48 SWM patients have died. Progression consisted mainly of WM (N=34) and only one each of lymphoma or AL amyloidosis. Progression of smoldering WM to symptomatic WM, AL or lymphoma was 39% at 3 years, 59% at 5 years and 68% at 10 years follow-up. The cumulative probability of progression was 12% per year for the first 5 years and then 2% per year for the next 5 years for the entire group. The major risk factors for progression were percentage of lymphoplasmacytic cells in the bone marrow, size of the serum M-spike and the hemoglobin value. The progression rate in those with both an M-spike ≥ 3 g/dL and a bone marrow containing ≥ 10% lymphoplasmacytic infiltration was 61% at 5 years and 72% at 10 years. Ninety-two percent of SWM patients with ≥ 50% lymphoplasmacytic bone marrow infiltration progressed at 5 years. The median survival of symptomatic Waldenstrom's Macroglobulinemia in this study from January 1, 1974 to December 31, 1995 was 5.1 years.