CR/VGPR attainment following rituximab-based therapy is an important determinant to progression free survival, and is impacted by polymorphisms in the FcγRIIIA Receptor in Waldenstrom's Macroglobulinemia.

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Background: The incorporation of rituximab into various regimens has improved depth of response in Waldenstrom's macroglobulinemia (WM), though the impact of achieving better responses remains to be determined.

Patients and Methods: We examined response depth on progression free survival (PFS) in 159 rituximab-naïve WM patients who received rituximab-based therapy. The median follow-up was 33.5 months, and categorical responses were as follows: CR (8.8%); VGPR (13.2%); PR (50%); MR (18.9%); Non-Responders (8.8%). Sequencing for polymorphic variants at FcγRIIA, FcγRIIB, and FcγRIIIA was performed, and impact on response depth determined.

Results: Achievement of better categorical responses was incrementally associated with improved PFS ($p<0.0001$). No separation was observed between CR and VGPR, and attainment of at least a VGPR was associated with improved TTP. Neither age, serum IgM, hematocrit, platelet count, serum B_2M, WM ISS score, and treatment group predicted for CR/VGPR. Polymorphisms at FcγRIIIA-48 and -158 were associated with improved categorical responses, particularly attainment of CR/VGPR ($p\leq0.03$).

Conclusions: The attainment of CR/VGPR is associated with significantly longer PFS in rituximab-naïve WM patients undergoing rituximab-based therapy, and is predicted by polymorphisms in FcγRIIIA.