## W9: Two Dose Series of High-Dose Influenza Vaccine is Associated with Longer Duration of Serologic Immunity in Patients with Waldenstrom's Macroglobulinemia and Other Plasma Cell Disorders

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**Background:** Infections, such as influenza, are a major source of morbidity and mortality in patients with Waldenstrom's Macroglobulinemia (WM) and other plasma cell disorders (PCDs). Seasonal flu vaccination is routinely administered to patients with PCDs, yet influenza infections remain common.

**Methods:** We conducted a double-blind, randomized clinical trial over the 2015-16 flu season, comparing two doses of FluzoneÒ High-Dose influenza vaccination (separated by 30 days) to standard of care influenza vaccination. Patients were allocated to the experimental arm 2:1. US standard of care influenza vaccination was considered single age-based vaccine (standard dose <65 years, high-dose >65 years) and patients in this arm received a saline placebo injection at 30 days to assist in blinding. HAI titers were analyzed by standardized procedure at four time points, baseline, 30 days following the initial vaccine, 30 days following the second vaccine, and at the end of the flu season.

**Results:** 122 total plasma cell disorder patients were enrolled, including 13 with WM. Forty-eight patients (7 with WM) received a single standard of care influenza vaccination and 74 patients (6 with WM) received two doses of High-Dose vaccine. Median age was 67 years. Following the second vaccine / placebo, rates of total seroprotection (against all 3 flu vaccine strains) were 86.3% following two high dose vaccines and 63.9% following standard vaccination. At the end of the flu season, rates of total seroprotection were 58.5% for patients who received two high dose vaccines and 33.3% for standard vaccination patients. Chi-square testing revealed that patients receiving the two dose vaccine strategy experienced significantly higher rates of total seroprotection following second vaccine ($p<0.05$) . At the end of the flu season rates of seroprotection trended toward significance at the end of the flu season against all 3 vaccine strains ($p=0.07$), against the H3N2 strain ($p=0.05$) and were significantly higher against the H1N1 strain ($p<0.05$). Subgroup analysis of WM patients reveal similar improvement in total seroprotection following a second vaccine (80% vs. 43%) and at the end of the flu season (33% vs 20%) favoring patients receiving the second high-dose vaccine.

**Conclusions:** We previously reported a two dose strategy of high -dose influenza vaccine is safely tolerated in patients with plasma cell disorders and associated with fewer laboratory-confirmed influenza infections (Branagan, et al, ASH 2016). Unexpectedly, the current analysis revealed that protective HAI antibody titers rapidly fall in PCD patients. Typically, HAI titers

slowly decrease following a peak protective response, but are stable for over 6 months. However, PCD patients in this study began to lose HAI seroprotection even as little as 30 days. Interestingly, patients who received the two dose series of high- dose influenza vaccine maintained higher rates of seroprotection at the end of the influenza season. Importantly, these results suggest that a two dose series of high- dose vaccine provides may mitigate loss of vaccine-induced HAI titers and allow more durable serologic protection throughout the flu season. More studies are warranted to help optimize vaccination strategies in WM and other PCD patients.