Exposure Response Analysis of Safety of Elotuzumab in Patients with Multiple Myeloma

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Objectives: Elotuzumab (ELO) is a humanized anti-SLAMF7 IgG1 monoclonal antibody approved in combination with lenalidomide/dexamethasone (Len/Dex) for treatment of relapsed/refractory (R/R) multiple myeloma (MM). Exposure-response (E-R) analyses was conducted to describe relationship between ELO exposure and safety, and impact of covariates in R/R MM patients.

Methods: E-R analysis of time to first occurrence of Grade 3+ AEs and time to AEs leading to discontinuation/death was conducted in MM patients from study CA204004 who received Len/Dex with/without 10 mg/kg ELO with estimates of ELO exposure from PPK analysis (N = 629). The E-R was characterized by two separate semi-parametric Cox Proportional Hazards (CPH) models relating ELO exposures (measured by individual predicted time-dependent average concentrations over dosing interval). A full covariate model was developed by incorporating following predictor variables in the base CPH model: body weight, age, race, gender, lactate dehydrogenase (LDH), ECOG score, albumin, absolute lymphocyte count, serum M-protein, and β2-microglobulin. E-R models were evaluated by visual predictive check.

Results: Risk of Grade 3+ AEs and AEs leading to discontinuation/death does not increase with increasing ELO exposure. Risk of Grade 3+ AEs and AEs leading to discontinuation/death is higher for patients with elevated levels of baseline β2-microglobulin and baseline LDH. Risk of Grade 3+ AEs is higher in patients with baseline ECOG score of 2 compared with patients whose ECOG score is 0 or 1, and in patients with lower baseline albumin. Risk of AEs leading to discontinuation/death is higher in patients with lower baseline serum M-protein.

Conclusion: Risk of Grade 3+ AEs and AEs leading to discontinuation/death do not increase with increasing ELO exposure over the range of exposures achieved with the 10 mg/kg dosing regimen.

References: