Model-based meta-analysis (MBMA) for relapsed/refractory multiple myeloma (RRMM): Application of a quantitative drug-independent framework for efficient decisions in oncology drug development

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Objectives: The failure rate for phase 3 trials in oncology is high, and quantitative predictive approaches are needed. We developed an MBMA framework to predict progression-free survival (PFS) from overall response rates (ORR) in RRMM.

Methods: A linear relationship was developed between ORR and PFS using data from four Phase 3 RRMM trials (PANORAMA, N=768\(^1\); ENDEAVOR, N=929\(^2\); ELOQUENT-2, N=646\(^3\); ASPIRE, N=792\(^4\)) to predict PFS based on ORR. A Bayesian analysis was used to predict the probability of technical success (PTS) for achieving desired phase 3 PFS targets from phase 2 reports of ORR. An external validation of this MBMA framework was done by comparing predicted to observed PFS for ixazomib plus lenalidomide-dexamethasone (IRd) in RRMM patients from the phase 3 TOURMALINE-MM1 study.

Results: Based on the strongly correlated (\(R^2=0.90\)) linear relationship between ORR and PFS (Figure), MBMA predicted a PFS of 20 months based on an observed ORR of 78% with IRd in TOURMALINE-MM1. This is consistent with the reported PFS of 20.6 months\(^5\). As a representative application of the framework, MBMA predicted that an ORR of approximately 70% would be needed in a phase 2 study to achieve a target PFS of 15.8 months. Estimation of PTS for achieving PFS targets based on ORR using a Bayesian analysis will be illustrated.

Conclusions: A quantitative drug-independent framework for RRMM has been developed to predict PFS based on an earlier endpoint (ORR). This model can be used to enhance proof-of-concept assessment and estimate PTS to enable objective decision-making.

References: