Estimating patient long-term survival outcomes and characterizing uncertainty associated with enzyme replacement therapy (ERT) treatment for Hunter Syndrome

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ABSTRACT

Introduction: Recent application of reconstructing individual-patient data underlying published Kaplan-Meier curves represents a methodological breakthrough where quantitative data are scarce in rare disease research. This approach was utilized to; (1) estimate a pooled hazard ratio using meta-analysis and combined reconstructed survival data; (2) simulate the progression-free survival (PFS) curve for the treatment arm using the survival statistics obtained from (1) for a disease progression model; (3) estimate the treatment-related life-year gained in comparison to standard-of-care. **Methods:** A partitioned survival model was characterized by four health states (stable, pre-progression, post-progression, and death) based on the selected outcome measures. Time-delayed progression was assumed when estimating PFS by applying the hazard ratio (HR) to the overall survival. The good fit of Weibull and Gompertz parametric models was contrasted to account for the survival plausibility beyond the observed period. The associated uncertainty was generated using the bootstrapped procedure. The probabilities of being in the different disease states were determined using the area under the curve method. Finally, the clinical experts validated the modelled progression. All steps were conducted in R-platform. **Results:** The treatment group demonstrated a 64% lower risk of death (pooled HR [95% CI]: 0.36 [0.25-0.51]). The patients' movement was graphically represented to illustrate the treatment's potential in attaining longer survival years (95% CI) consistent with current observation for the following states: stable 0.38 (0.01-1.01), pre-progression 3.18 (1.30-4.75) and post-progression 0.88 (0.05-2.38). **Conclusion:** The model can be used to evaluate the changes in the quantity (mortality) and quality (morbidity) of life composite outcomes for future cost-effectiveness assessments.