

Using simulated individual patient data (IPD) from published registry and IPD from the SEER-Medicare registry to extrapolate results from randomised clinical trials (RCTs) in metastatic melanoma (MM)

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Background: Pre-marketing authorisation estimates of survival are generally restricted to those observed directly in randomised clinical trials (RCTs). However, for regulatory and Health Technology Assessment (HTA) decision-making a longer time horizon is often required than is studied in RCTs. Therefore, extrapolation is required to provide long-term evidence of treatment effect. Registry data can provide evidence to support extrapolation of treatment effects. The aim of this work is to use real world data (RWD) and non-linear regression models to evaluate long term survival.

Methods: IPD was simulated from published survival curves of patients with MM in real world. Additionally, SEER-Medicare registry data were combined with RCT data to estimate long-term survival of patients with MM. Exponential, Weibull, Gompertz, log-logistic, log normal parametric survival models and a non-parametric model were fit to the RCT data, and used to extrapolate the data from 48 months to 72 months. A naive extrapolation was applied as well as extrapolation based on simulated IPD, summary data and SEER-Medicare data. Adequacy of the models was assessed through comparisons of the log-likelihood, whilst treatment effects were estimated using the restricted Area under the Curve (AUC). Reliability was assessed through visual inspection of the fit to the long-term data.

Results: Blending RCT and registry data allowed for reliable estimation of long term survival of patients with MM using a log-logistic, lognormal model and non-parametric model. The log-logistic and lognormal model estimated long term survival with reduced uncertainty when including the SEER-Medicare database compared to a naive extrapolation approach.

Conclusions: The results showed that the use of the SEER-Medicare registry decreased the uncertainty in long term prediction of overall survival in patients with MM. The use of registry data may be an

acceptable approach for pharmaceutical companies, regulatory and HTA decision bodies for assessing long term survival of cancer treatments.