

PREDICTIVE MODELING FOR EVENT ACCRUAL AND ENROLLMENT RATES IN ONGOING CLINICAL TRIAL

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Introduction Predicting the landmark date when a specific number of events will occur or the target number of patients will be enrolled is crucial to evaluate the feasibility and for the operational, statistical success of a clinical trial with time-to-event endpoints. For ongoing clinical trials (with patients already enrolled and events already observed), this type of forecasting becomes a vital resource for monitoring, statistics and ethical considerations.

Objectives We introduce a method for predicting event occurrences and subject enrollment in clinical trials using advanced statistical techniques, applicable to both closed and ongoing accrual statuses. We developed an R function to compute the point prediction of the landmark date and the Bayesian prediction intervals.

Methods The input data include for each subject: identifier, start date (i.e. randomization/registration date), event status, dropout status, event date (if occurred), date of last observation and cutoff date (the date from which the predictions are performed). Patients are categorized by their follow-up status: lost to follow-up, event-free at the cutoff date, or having experienced the event of interest. The function calculates the time-to-event in days for each patient; three time-to-event models (exponential, Weibull [1], log-normal) are then computed and evaluated using the Akaike Information Criterion (AIC) to identify the optimal fit. Dropout events are similarly modeled if occurrences are sufficient at the cutoff date. For studies with ongoing accrual the enrollment numbers are modeled according to time-decay and Poisson models [2] and the two models are compared with the AIC. The landmark date and the prediction intervals are derived using Bayesian simulative methods proposed by Emilia Bagiella and Daniel F. Heitjan [3].

Results We applied the method to generate predictions for the final Overall Survival analysis of AtTEnd/ENGOT-en7 trial, a clinical trial evaluating the efficacy and safety of atezolizumab combined with paclitaxel and carboplatin in women with advanced or recurrent endometrial cancer [4]. The aim of our predictions was to estimate the date for reaching the target events of Overall Survival (294 deaths). We performed the prediction once the accrual was already closed and after the observation of 269 deaths. According to the prediction, the 294th event will be observed on January 24th 2025 with a 95% prediction interval ranging from October 27th 2024 to June 3rd 2025. The landmark date is consistent with the planned end of the study.

Conclusions This method enhances the ability to manage clinical trials effectively by providing accurate and timely predictions of key milestones. This function supports the operational and statistical aspects of clinical trials, contributing to their overall success.

Bibliography

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