local tariffs from US, Canada, UK, France, Sweden, Belgium, Netherlands, Portugal and Australia. ***Results:*** Among all combinations of distributions considered for the BH MCM, the exponential-exponential fit adequately captured the observed survival trends for both endpoints with reasonable goodness-of-fit measures and shared LTS rates which were (95% credible intervals) 46.3% (32.8%, 62.6%) for nivolumab+ipilimumab, 37.8% (21.6%, 55.7%) for nivolumab, and 15.1% (6.8%, 26.0%) for ipilimumab. For each arm, shared LTS-rates were in between individually-estimated LTS rates from the OS and PFS data in the frequentist MCMs. Compared to frequentist MCMs, over 20-years BH MCMs produced higher incremental QALY gains for nivolumab+ipilimumab and nivolumab versus ipilimumab with differences ranging from 0.30-0.48 and 0.17-0.26, respectively. ***Conclusions:*** Our BH MCM framework can alleviate the disparity between individually estimated OS- and PFS-based LTS rates, and allow for more robust clinical inference and extrapolations.

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JOINT MODELLING MEASURABLE TARGET LESIONS, EQ5D/UTILITY AND OVERALL SURVIVAL: DO WE STILL NEED PARTITIONED SURVIVAL MODELS?

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Objectives: The biologic effect of treatment is typically analyzed using tumor burden or PFS, the latter often leads to loss of information due to being based on the categorization of RECIST criteria. Whereas, tumor burden is complete and rational summarization of the process which captures data on the primary mechanism through which most treatments are expected to act. The objective of this study is to estimate overall survival using joint model which simultaneously models patient's longitudinal tumor burden (TB) trajectory, EQ-5D/utility and survival by accounting for the association between the three outcomes. ***Methods:*** We simulated data based on a clinical trial (n=110), repeated measure (940 observations). Tumor burden is defined as sum of the longest diameters of measurable prespecified target lesions. Joint model using current value association structure and several distribution was fitted to predict survival. Time was included as a random effect. No covariates were included in the model. We compared joint model with independently fitted models for OS and PFS. ***Results:*** The median follow-up visit was 25 months (range: 22-29 months). Joint model showed a positive statistical association to TB, indicating that a higher value of TB increases the risk of death and a negative statistical association to EQ-5D/utility, indicating that proximity to death is linked to lower utility values. While the restricted mean estimates did not show differences between independently fitted models and the joint model, the overall uncertainty around long-term outcomes is dramatically reduced. ***Conclusions:*** Multivariate Joint modelling is a powerful tool which can simultaneously model multiple longitudinal biomarkers and survival that are relevant in economic evaluation and leads to more efficient treatment effect. Given the limitations associated with partitioned survival model, i.e. the structural assumptions that survival functions modeled are independent, this approach provides a new way to conduct cost-effectiveness analysis for metastatic oncology treatments.

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ACCURACY OF LIFE YEAR GAINS PREDICTIONS FOR CAR-T THERAPY IN THE LONG TERM: AN ANALYSIS FOR AXICABTAGENE CILOLEUCEL IN REFRACTORY LARGE B-CELL LYMPHOMA

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Objectives: Survival profiles for chimeric antigen receptor T cell (CAR-T) therapies commonly exhibit a plateau that may indicate a cure. This leads to challenges predicting long-term outcomes for novel CAR-T therapies when trial data are immature. This study retrospectively analysed the accuracy of overall survival (OS) extrapolations from interim data cuts in predicting realised long-term life years (LYs) for axicabtagene ciloleucel in patients with refractory large B-cell lymphoma. ***Methods:*** Published OS data for axicabtagene ciloleucel from successive data cuts of ZUMA-1 (median follow-ups of 15.4, 27.1 and 51.1 months) were digitised. Standard parametric, spline (1–2 knots; normal, odds and hazard) and mixture cure models (MCMs) were fitted to the first two data cuts. Statistical fit was tested using Akaike and Bayesian information criteria (AIC and BIC). Cumulative LYs were estimated for each model over a 58-month time horizon, corresponding to the longest duration of published OS data. These projected LYs were then compared to realised LYs over this period. ***Results:*** At the earliest data cut, MCMs provided the best predictions of realised LYs, with a mean absolute difference of 6.8% between predicted and realised LYs across MCM models (range: 0.5%–10.7%). Standard parametric extrapolations considerably underestimated realised LYs (mean absolute difference: 19.2%; range: 9.9%–28.0%), whilst spline models offered a mean absolute difference of 8.3% (range: 1.4%–13.2%). Similar findings were observed for extrapolations based on the second data cut (representing 11.7 months additional follow-up), but differences between model classes were less pronounced. ***Conclusions:*** MCMs may offer the best predictions of long-term survival for CAR-T therapies, particularly when only short-term data are available. Standard parametric models may be inappropriate to predict survival when extrapolating immature data, failing to capture the plateau in survival typical of CAR-T therapies. Further research is required to determine whether these findings are generalisable across CAR-T therapies and indications.

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COMPETING RISK AND MULTISTATE MODEL COMPARED TO PARTITIONED SURVIVAL MODEL IN METASTATIC NON-SMALL CELL LUNG CANCER

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Objective: Partitioned survival analysis (PartSA) is commonly used for economic evaluations in oncology. We compare PartSA to a competing risk semi-markov multistate model (MSM) and investigate differences in estimated cost-effectiveness in metastatic non-small cell lung cancer from a French perspective. ***Methods:*** To populate both models, pooled data from Checkmate 017 and 057 was digitized to reconstruct patient-level data from overall survival, progression-free survival and post-progression survival Kaplan Meier curves. Models consisted of three states: progression-free, progressed disease and death. Statistical analysis was performed under *R* to fit parametric survival models for the PartSA and to estimate state transitions for the MSM (package "mstate"). Costs and utilities were integrated in the model using values from nivolumab's French HTA submission. Outcomes were discounted at 2,5% per annum over a 7-year time horizon. ***Results:*** Both models produced similar results during trial period (15 months) but showed discrepancies during extrapolation, inducing different costs and quality-adjusted life years (QALYs) over time. Incremental life years gained (LYG) of nivolumab versus docetaxel were 1,11 LYG (PartSA) and 0,88 LYG (MSM). However, both incremental cost effectiveness ratios (ICER) were similar, 88 979€/QALY (PartSA) and 90 148€/QALY (MSM). Scenarios assessing different parametric extrapolations produced an average of 112 496€/QALY (PartSA) and 113 085€/QALY (MSM) with coefficients of variation (CV) estimated at 19,0% (PartSA) and 16,3% (MSM). Probabilistic ICER results were similar between models with CV estimated at 21,8% (PartSA) and 23,2%(MSM). ***Conclusions:*** This study provides new evidence on structural uncertainty. The MSM produced similar results to the PartSA for a 15 months follow-up. Ideally, both models should be tested to validate extrapolations and to ensure that the structural uncertainty is limited. However, when the time horizon is short (<10 years), the impact of the model choice on the ICER seems limited.

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BLENDED SURVIVAL CURVES: A NEW APPROACH TO EXTRAPOLATION FOR TIME-TO-EVENT CLINICAL TRIAL DATA IN HEALTH TECHNOLOGY ASSESSMENT

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Objectives: Survival extrapolation is generally required in the cost-effectiveness analysis to estimate the survival benefit of a new intervention, due to the limited duration of randomized controlled trials (RCTs). Current techniques of extrapolation often assume constant treatment effect beyond the observed period in the RCT, which is implausible and highly influential in survival estimates for resource allocation decisions. The objective of this study is to develop a novel methodology based on "blending" survival curves as a possible solution. ***Methods:*** We mixed a flexible Cox semi-parametric model conducted in Bayesian setting to fit the observed data and a parametric model either by prior assumptions or external data on the long-term expected behavior of the underlying survival curves. The two are "blended" into a single survival curve that is equivalent to the Cox model over the follow-up intervals and gradually approaching to the parametric model over the extrapolation period based on a weight function. The weight function and mixing area of the blended curve control the way the internal and external data sources influence the estimated survival. ***Results:*** A 4-year follow-up RCT of rituximab in combination with fludarabine and cyclophosphamide (RFC) v. fludarabine and cyclophosphamide alone (FC) for the first-line treatment of chronic lymphocytic leukemia is used to illustrate the method. Two kinds of prior information, registry data and summary of clinical knowledge were respectively used for the long-term estimate. ***Conclusions:*** Long-term extrapolation with various assumptions of treatment effect may give significantly different estimated mean survival gains. The blending process allows a consideration of plausible scenarios, abandoning the over-optimistic constant treatment effect and provides sufficient flexibility. Not only internal but also external validity could be carefully considered since a wide range of external evidence can be used to inform the long-term estimate, including hard data from real world and clinical expert opinion.