Reviewer's report

Title: Integrating expert opinion with clinical trial data to extrapolate long-term survival: A case study of CAR-T therapy for children and young adults with relapsed or refractory acute lymphoblastic leukemia

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Reviewer: Elena Critselis

Reviewer's report:

The manuscript entitled "Integrating expert opinion with clinical trial data to extrapolate long-term survival: A case study of CAR-T therapy for children and young adults with relapsed or refractory acute lymphoblastic leukemia" aims to assess the feasibility of formally integrating long-term survival estimates from experts with empirical clinical trial data to provide more credible extrapolated survival curves. To this effect, the authors apply a case study regarding relapsed or refractory B-cell pediatric and young adult acute lymphoblastic leukemia (r/r/ pALL) regarding long-term survival for CTL019 (chimeric antigen receptor T-cell) from which evidence from the phase II ELIANA trial is available up to 1.5 years. Seven pediatric oncologists and hematologists experienced with CAR-T therapies were recruited in a double-blinded manner. Survival rates and related uncertainty at 2, 3, 4, and 5 years were elicited from experts using a web-based application adapted from SHeffield ELicitation Framework. The experts' results were combined with the ELIANA trial data using time-to-event parametric models in a Bayesian framework that accounted for experts' uncertainty in their estimates, producing an overall distribution of survival over time. The authors found that extrapolated survival curves based on ELIANA trial data without expert information were uncertain, differing based on the model choice. Survival estimates between 2 to 5 years also varied between individual experts. However, incorporating their estimates improved the precision in the extrapolated survival curves. The authors conclude that by the proposed methodology expert opinion can be elicited and synthesized with observed survival data using a transparent and formal procedure. The manuscript and proposed approach is of interest and seeks to integrate empirical and experimental data. However, further information is necessary regarding the selection of experts. In particular, selection and recruitment procedures ought to be described in further detail, and a justification of the number of experts included should be provided. Further information regarding discrepancies and differences in expert opinions should be presented. Finally, the proposed methodology ought to be validated in the experimental ELIANA cohort following adequate follow-up, and further replicated in an independent trial.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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