Author’s response to reviews

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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Author’s response to reviews:

Dear Editor,

Thank you very much for reviewing our manuscript, ‘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’ (BMRM-D-17-00515R1). We also greatly appreciate the reviewers for their thoughtful comments and suggestions. We have revised the manuscript based on their feedback and included point-by-point responses to their comments below. We hope that you find our responses satisfactory and that the manuscript is now acceptable for publication in BMC Medical Research Methodology.

Sincerely,

Shannon Cope
Reviewer reports:

Paul Gaynon (Reviewer 1):

Abstract
"where evidence" should be "with evidence"
Response: Thanks for catching this error. We have revised the abstract accordingly.

Results or opinions?
Response: We have revised to the abstract to: ‘Estimates from each expert’ (rather than ‘Results from each expert’).

line 115: Outcome after relapse depends strongly on the mix of actual patients entered - relapse or refractory and time to relapse.
The EIIANA study included many conventionally unfavorable patients who were judged well enough to enroll on study
Response: We agree this is an important challenge to acknowledge and have added to the list so that the sentence now reads as: “In the context of relapsed or refractory (r/r) pALL, the challenge of extrapolating survival data is compounded by the young age of patients, differences among patients in terms of relapse or refractory disease and treatment history, limited evidence regarding best supportive care, the absence of randomized controlled trials (RCTs) for tisagenlecleucel (i.e. single-arm trials only), the possibility of curing patients, and the innovative nature of the new treatment.”

line 144 The proportion of patients cured after relapse is not large!!
Sun et al have recently published data on survival after second and subsequent relapse
Response: We agree and have revised the sentence in above response to as: “the possibility of curing patients”.

Elena Critselis, MPH PhD (Reviewer 2): The authors have successfully addressed all previous comments. It is recommended that the authors report in the study limitations sections that a validation cohort was not applied within the context of the present investigation.

Response: We have revised the discussion paragraph as follows to highlight this limitation: “Ultimately, a validation cohort was not evaluated within the current study, which reflects a limitation of the study.”