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

Version: 1 Date: 24 Jul 2018

Reviewer: Paul Gaynon

Reviewer's report:

I am a clinician with some experience in clinical trials and trial design. I am uncertain of your audience.

With regard to Kymriah, only a fraction of eligible patients undergo pheresis, only a fraction of harvested patients have a useful product, and only a fraction of patient with a useful product are actually infused.

You start your analysis from infusion.

I believe that attrition runs about one third.

Thus the subset of patients with a successful infusion differs from the subset of patients enrolled on trial in an uncertain manner,

If you plan to inform bedevilled clinicians such as myself, you will do well to provide further inform about the implications of your various cure models - Weibull and Gompertz.

This is a critical issue as we depend too strongly on the logrank statistic - a measure of time to event and not the eventual cure rate.

Current treatments in ALL have both delayed and decreased relapse.

I understand, I think, your careful refinement of your expert's thoughtful opinions but I see no empiric validation of their consensus.

Are your experts any more accurate than kindergartners or kangaroos?

You offer no validation of your quite reasonable method in other circumstances where such validation may exist.

Figure 3 is too busy - too many curves. Too hard to distinguish the Gompertz curve.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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None

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