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Product Development Scientific Support Department

Treatment effect measures when using recurrent event endpoints – Qualification Opinion List of Issues regarding provided simulation exercises

Additional list of issues to be addressed in writing by 12 Oct 2018:

Thanks for the latest set of results as shown in table A. Some of the results seen are not initially intuitive and for the purposes of a qualification it is considered important to understand the reasons for the various patterns seen, for example why the analytical estimand values for in table A are above 0.7 when there is no treatment effect on mortality, why they vary in the way they do with changing mortality rate, and why the values for estimand 2 are so large for the equal-weighted rate based estimand. To aid this understanding we make a request for a simplified version of table A.

In this table we would ask that it is assumed that there are no treatment discontinuations (either informative or non-informative) so patients stay on trial either until the end of follow-up or until death. Under this simplified scenario could table A be repeated, and a discussion provided explaining the values and patterns seen. Could additional HRcv scenarios, i.e. HRcv=0.666, 0.8, 1, 1.25, 1.5 be included in order to better understand trends?

Could follow-up time also be varied - the current table has a fixed 3.5 year follow-up time - maybe repeated tables with 1.25 and 7 year follow-up could also be included?

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