Reviewer's report


Version: 2 Date: 8 December 2010

Reviewer: Gordon Doig

Reviewer's report:

This is a very well written protocol paper describing a major undertaking. It is detailed and explicit. Congratulations. I wish you all the best in your clinical trial. Please address the following very minor issues with regards to improving the validity and transparency of reporting of your trial:

1. You report a limited number of subgroup analysis. Please report how you will test for sub-group differences. For example, I assume some form of test of interaction will be used. Please be specific. Since a test of interaction is accepted to have unconventionally lower power than other direct tests, you should also stipulate the interaction p-value that will be accepted to indicated the presence of a meaningful sub-group difference.

2. In your section on Safety Endpoints, you explicitly report the intent to use chi-square analysis to analyze landmark ICU and hospital discharge vital status (dead/alive). Throughout the remainder of the manuscript you infer that you also have access to information reporting time to vital status at Day 90. Day 90 may be longer than hospital discharge status, and may not be biased by discharges to other hospitals as discharge status from the primary study hospital may be. There is information in this field (NICE SUGAR study) to suggest important safety information may be captured by Day 90 vital status. Please include the analysis of Day 90 vital status (dead/alive) as a Safety Endpoint to be reported and analyzed as per ICU and hospital discharge status.

3. There is no need to report 'current recruitment'. Reporting of completion date is sufficient.