Reviewer's report

Title: Rationale and study design of PROVHILO - a worldwide multicenter randomized controlled trial on protective ventilation during general anesthesia for open abdominal surgery

Version: 2 Date: 10 March 2011

Reviewer: Gordon Doig

Reviewer's report:

This is a very well designed clinical trial and well written protocol paper. I wish you all possible success in your undertaking. Could you please address the following issues:

1. Page 7, "Randomization is performed using a dedicated website. Randomization is balanced per center.". I assume you meant 'stratified' by center, not 'balanced'. Please also provide details regarding how the randomization sequence was generated (blocked, variable size blocks or minimization). There is no need to report the block size if blocking was used. Knowledge of block size may aid researchers to guess the randomization sequence. Was blocking applied to any other trial factors? Please also report whether the study web site is password protected and encrypted. Please report the level of encryption.

2. Provide methodological references to support your thresholds for interim analysis. It is very interesting that you have a strict p-value for your primary outcome (0.0005) yet you allow consideration for stopping early due to other 'complications' which may not be as clinically important as your primary outcome at the first interim analysis with a lax p-value (0.022). You need to resolve this issue by explicitly defining your primary outcomes and these other 'complications' or reconsidering your stopping rules. Please address this issue and justify your decisions in your Discussion.

3. Please expand your statistical analysis section. Please explicitly state the analytical model that will be used to assess your primary outcome. Report the key variables that will be assessed for baseline imbalance, how imbalance will be defined and what will be done in the presence of imbalance. You report your intention to use a Proportional Hazards model to assess 'time dependent' variables. I believe you meant 'time to event' variables. Please list all variables you intend to assess as 'time to event' variables.