Reviewer's report

Title: A randomized, placebo-controlled, double-blind trial of UdenafiL Therapy to Improve symptomology, exercise Tolerance and hemodynamics in Patients with chronic Systolic Heart Failure [ULTIMATE- SHF trial]: Rationale and Design

Version: 1 Date: 29 May 2013

Reviewer: Erik Cobo

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I read the paper from Dr. Kyung-Hee Kim et al. “A randomized, placebo-controlled, double-blind trial of UdenafiL Therapy to Improve symptomology, exercise Tolerance and hemodynamics in Patients with chronic Systolic Heart Failure [ULTIMATE- SHF trial]: Rationale and Design” and I think it is suitable for publication in Trials.

But before recommending publication, I would like authors to address the 2 following suggestions.

1.- You specify an intention to treat analysis, that requires including in the analysis all randomized patients (see CONSORT 2010, E&E). Also, in order to protect patient rights, you allow dropping out in several parts of your manuscript (“will be dropped from the trial”, P8L24; “patients will be permitted to request withdrawal”, P9L18; and “allowing a loss of 10%”, P10L24). Please note that patients may drop out of the treatment but still continue in the trial in order to obtain their final outcome value. You will find useful advice in the NEJM recommendations to prevent and treat missing data: (http://www.nejm.org/doi/full/10.1056/NEJMsr1203730).

2.- To avoid reporting bias, it is usually preferred to fully specify the statistical analysis without any ambiguity. As treatment effects are expected to change the mean but not the outcome shape, you may already choose a concrete statistical analysis. Please, also note that a t-test would fully agree with your sample size formula. You may also consider improving your efficiency and power by adjusting for baselines in the final analysis (see, for example, chapter 7 in “Statistical Issues in Drug Development”, by Stephen Senn, Ed Wiley). If so, please consider changing P11L2-3 to “The differences between the treatment groups in the main outcome will be assessed using an unpaired t-test adjusted by baseline values (ANCOVA).”