Reviewer's report

Title: The efficacy and safety of Shaoyao Shujin tablet for knee osteoarthritis: study protocol for a multicenter randomized, double-blind, placebo-controlled trial

Version: 2
Date: 30 July 2015
Reviewer: Kent Johnson

Reviewer's report:

All of these are major compulsory revisions.
I believe the trial is fundamentally sound regarding trial population, intervention, outcomes, and analysis, but the awkward, sometimes almost incoherent use of English and the propensity to make claims (to editorialize) without substantive evidence undermine the effort. Thus, I suggest the following:

1- Have a native English speaking science writer carefully edit the entire manuscript.
2- Rewrite all sections that make claims without substantive standards of evidence (well-controlled, randomized trials) – for example lines 103-105. The language needs to be much more nuanced – the science editor should be able to help here. The text needs to reflect the design used in ref 6, and it needs to reflect that delay in degeneration claim has been shown only in animal models (ref 7 & 8). In another area, lines 245-250, without a careful, critical review of the claims made, I think this material amounts to editorializing and should be deleted.
3- Line 100 – these are only a small part of the toxicity that is seen in the elderly.
4- Need a discussion of the duration – 6wk treatment only. Is there any longer term follow-up planned?
5- Blinding (line 205): Are the treating physicians/health care workers also blinded. This needs to be made explicit. If they are not, then the design is inappropriate.
6- Lines 182-187 – The abstract says rescue medication use is also a secondary outcome, yet it is not mentioned here.
7- Statistical analysis: Elaborate on the multi-level regression model to assess rescue medication use. Where did the 18.2 come from – ref 13/Table 2 shows 19.8 to be the overall SD of the total WOMAC score (although this won’t change the sample size much)? In the discussion you need to address the possibility that a success conclusion in the primary endpoint analysis might be undermined by the conclusion in the rescue medication analysis - i.e., the SST herbal medicine may win by the WOMAC but if the rescue medication analysis shows more rescue use in the SST herbal medicine patients, then the WOMAC win may not be due to the SST herbal medicine use but to a greater ibuprofen use.
8- Why are electrocardiograms being done? Is there any good evidence on the toxicity profile of SST?
Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests’