Reviewer's report

**Title:** An Open-label, Sequential, Dose-finding Study of Peginesatide for the Maintenance Treatment of Anemia in Chronic Hemodialysis Patients

**Version:** 1  **Date:** 12 March 2012

**Reviewer:** Holger Schmid

**Reviewer's report:**

The manuscript by Besarab and coworkers entitled “……Dose-finding Study of Peginesatide for Maintenance Treatment of Anemia in Chronic Hemodialysis Patients” is of interest for the the Dialysis community.

Despite a complex study design due to different treatment cohorts, which could be confusing for those readers, who are not so familial with ESA dosing in HD patients, Besarab and coworkers here clearly show that

i) increases in peginesatide dose requirements are less apparent in cohorts in which tiered conversion tables were used and

ii) Hb levels are more stable in those cohorts in which an ESA-free interval was used.

Also additional long-term data in larger groups of patients are necessary. the results presented here are a prerequisite for the phase 3 randomized, active-controlled, openlabel studies EMERALD 1 and EMERALD 2.

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. The majority of the study population were black patients. Do the authors believe that this fact could have any impact on study outcome?

2. Baseline and Demographic characteristics (Table 2, page 26): Are there any significant differences between the analyzed cohorts?

3. Adverse events/Safety (page 9), A high rate of adverse events was reported. “Adverse events were reported in 137 of 164 patients (84%), of which, 93 patients (68%)

had AEs considered mild to moderate in severity….Serious adverse events were reported in 27 of 139 patients (20%)

a. The exact number of patients with AE (139 vs. 137) could be unclear for the reader.

b. Of particular interest, these percentages in dialysis patients are similar to that seen in nondialysis patients, reported by MacDougall and colleagues (Clin J Am Soc Nephrol. 2011 Nov;6(11):2579-86). This is important, as the authors state in the discussion: “The observed SAEs were consistent with events that have been described in dialysis populations with multiple comorbidities”. The authors should clarify this potential ambiguity.
4. A potential discrepancy in trends of median peginesatide doses is obvious between the sections Result (page 7) and Discussion (page 12): …both groups trend towards… vs. …this general trend was not observed in cohorts that used tiered conversion tables…. The authors should clarify this.

5. A Dose-finding study of peginesatide for anemia correction in nondialysis chronic kidney disease patients was recently presented by MacDougall and coworkers MacDougall IC et al. Clin J Am Soc Nephrol. 2011 Nov;6(11):2579-86. The authors should include this study in the Discussion section.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. page 5, last sentence: conversion from instead of to

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
1. Some words regarding potential harms of peginesatide in the Introduction section could be of interest for those readers who are not so familial with investigational ESA

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
'I declare that I have no competing interests.