Reviewer's report

Title: Optimal and continuous anaemia control in a cohort of dialysis patients in Switzerland

Version: 2 Date: 28 July 2008

Reviewer: Dorothea Nitsch

Reviewer's report:

Major compulsory revision are still needed:

The analysis does not appear to allow for clustering Hb values in individual patients over time and for clustering of patients within in centres. The joint analysis of haemoglobin levels and erythropoietin ignores their correlation within an individual and over time. All this leads to incorrect standard errors, confidence intervals and p-values.

The authors state following aim: To assess "A) if the management of anaemia has improved since previous assessments in dialysed patients in Switzerland". There arise following questions for clarification:

What are the control data that inform on whether the current data on Hb management are better or worse than before? Are these only the ESAM data from the surveys?

If so, are these surveys comparable given the entirely different study designs with regards to follow up? Were patients in the cited comparison surveys treated with the same doses/agents?

The authors write "Exclusion criteria were the following: unstable angina pectoris, untreated uncontrolled hypertension, haemoglobinopathy, haemolysis, gastrointestinal bleeding, acute infection or unstable systemic inflammatory disease, epilepsy, pregnancy, lactation, deficiency of vitamin B12 (<200 ng/L), deficiency of acid folic (<2?g/L), planned surgery during the survey period (except fistula surgery), known hypersensitivity to EPO beta". This text suggests selection to a relatively healthy prevalent group of patients. Are all the other comparison cohorts cited by the authors selected towards a healthy population in the same way? Based on the massive differences in prevalence of peripheral vascular disease when compared to ESAM 2003 this appears not to be the case. Has the historical comparison with the present data been adjusted for changes in case-mix occurring over time?

The authors write "Participating centres were asked to include as many patients as possible, on a voluntary basis, meeting the inclusion/exclusion criteria. Ten dialysis centres included more than 80% of all their patients treated with epoetin beta, and 15 centres in total included more than 60% of their patients receiving epoetin beta, contributing to 71% of the patients included in this survey." Who are
the other 29% of patients who are included in this survey?

The authors state as second aim: To assess "B) if the control of anaemia and its treatment parameters could be maintained over a long period of time ". In the methods they state: ".reasons for the incomplete data were the following: death (33), transplantation (7), unknown reason (1).". "Missing values of patients (Hb, body weight, EPO dose, administration frequency, route of administration), who received at least one survey medication, were replaced by using the last observation carried forward method (LOCF). " This implies dead patients were assumed to have a haemoglobin or treatment dose value despite being dead. Similarly, for transplant patients, who are per definition not on dialysis the dialysis haemoglobin was assumed. This is not a realistic data analysis. Of course, with these assumptions it may be possible for dead people to maintain their haemoglobin. Because all analyses did not take account of clustering of Hb values within patients this may have an effect on the results, depending on the numbers of these partially missing data. The authors’ claim that LOCF is a standard method - it is well known to be an approach to missing data that may be associated with severely biased results[1], [2], and the authors should at least make the effort to investigate whether this approach would have led to biased results or not by conducting sensitivity analyses with another statistical approach.


Level of interest: An article of importance in its field

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

Declaration of competing interests:

'I declare that I have no competing interests