Reviewer's report

Title: Comparison of darbepoetin alfa dosed weekly (QW) vs. extended dosing schedule (EDS) in the treatment of anemia in patients receiving multi-cycle chemotherapy in a randomized, phase 2, open-label trial

Version: 2 Date: 10 March 2010

Reviewer: Angel Cronin

Reviewer's report:

This is a well written paper with proper design and overall the statistical analyses are appropriate. There are some improvements, particularly in the presentation of results, which should be made.

Major Compulsory Revisions:

1. It appears that the p-values presented are for a superiority test, that is, testing the null hypothesis that there is no difference between groups. However, this study was designed as a non-inferiority study and as such the null hypothesis is that the EDS group is inferior to the QW group. The investigators should include p-values that test the null hypothesis of inferiority.

2. The analyses for achieving hemoglobin > 11 and hematopoietic response are conducted appropriately using time to event methods. However, the investigators must give the time frame of their Kaplan-Meier estimates (13 months? 25 months?). The investigators should remove the crude percentages since they do not account for loss to followup. It should be clarified what subgroup was included in a particular analysis and why. For example, why are only 190 QW and 178 EDS patients included in the analysis of hematopoietic response?

Minor Essential Revisions:

3. The method of analysis for the primary endpoint (linear regression with the change score as the dependent variable and randomization strata as covariates) should be included in the statistical analysis section.

4. The results currently shown in graphical format in figure 3 would be better presented in table format with the following columns: mean change for QW group, mean change for EDS group, mean difference between groups, confidence interval for difference between groups (which may be a one-sided confidence interval, by study design), and p-value; the shaded area in the figure 3 has no statistical meaning since the outcome is a continuous variable. Similar comment applies to the results shown in figure 5 – these results would be easier to interpret in table format.

5. The investigators state that the p-values in table 2 were obtained using the stratified chi-square test. Please clarify whether this was the log rank test.

6. When reporting the mean values for the primary endpoint, the authors should
use an additional significant figure, e.g. mean difference 0.14 instead of 0.1.

7. On page 9, first paragraph, the investigators state “If the upper limit of the 95% CL for the difference in mean change...is not more than 0.75 g/dL, then the conclusion from this study would be that EDS is non-inferior to QW and that the efficacy of EDS is greater than placebo.” The latter conclusion – that the efficacy of EDS is greater than placebo – is not appropriate and should be omitted.

Discretionary Revisions:

8. It is encouraged for the authors to follow the CONSORT statement for reporting of randomized controlled trials. For example, there is no mention of whether the study was blinded; presumably it was not blinded due to the study design, but this should be mentioned.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.