Reviewer's report

Title: Comparison of the safety of pegaptanib sodium in the treatment of age-related macular degeneration in subjects with or without diabetes mellitus: A retrospective, pooled data analysis

Version: 2 Date: 12 March 2012

Reviewer: Michael Stewart

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Major Compulsory Revisions:

1. Were the patient populations similar? Is the gender difference significant? Race? These should be calculated and mentioned.

2. Three patients in the non-diabetic groups discontinued due to the development of choroidal neovascularization. This sound strange since patients were receiving an anti-VEGF drug for AMD. Please explain in more detail.

3. Under early discontinuation of treatment, the diabetic patients had 3 thromboembolic events whereas the non-diabetic patients experienced 1. Is this significant?

4. Why was the ruptured aneurysm considered treatment related whereas the the MIs and CVAs were not? Were these purely at the discretion of the PI?

5. The introductory Background section contains a long discussion about ant-VEGF injections for DME. This suggests that the authors are investigating pegaptanib safety in AMD patients with diabetes so that the results can be generalized to patients who receive pegaptanib for DME. The authors have already concluded that pegaptanib is generally safe for patients with AMD (see Discussion) so subanalyzing the AMD patients by diabetes or not adds little. However, AMD patients with diabetes and diabetics receiving pegaptanib for DME likely represent 2 very different diabetic populations. Patients with DME generally have had diabetes for years and have more generalized microvascular disease. AMD patients with diabetes, on the other hand, probably have only had diabetes for a short period of time as the presence of diabetic retinopathy would probably have excluded them from entering the AMD studies. Therefore this study does little to establish the systemic safety of pegaptanib for patients with DME. If the authors only goal is to establish safety in AMD patients with diabetes then they need to completely rewrite the Background section to delete the references to DME.

Minor Essential Revisions

1. Background, second sentence: move the parentheses phrase to after "off-label". In it's current position it sounds as though ranibizumab is not effective.

Level of interest: An article of limited interest
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
Regeneron: Research support, consultant
Bayer: Research support
Allergan: Consultant