Author’s response to reviews

Title: Memory loss during lenalidomide treatment: a report on two cases

Authors:

Adeline Rollin-sillaire (adeline.rollin@chru-lille.fr)
Xavier Delbeuck (xavier.delbeuck@chru-lille.fr)
Marianne Pollet (marianne.pollet@chru-lille.fr)
Marie-Anne Mackowiak (marie-anne.mackowiak@chru-lille.fr)
Pierre Lenfant (pierre.lenfant@chru-lille.fr)
Marie-Pierre Noel (marie-pierre.noel@chru-lille.fr)
Thierry Facon (thierry.facon@chru-lille.fr)
Xavier Leleu (xavier.leleu@chru-lille.fr)
Florence Pasquier (florence.pasquier@chru-lille.fr)
Emilie Lerhun (emilie.lerhun@chru-lille.fr)

Version: 4 Date: 15 May 2013

Author’s response to reviews: see over
Dear Christopher Morrey,

Please find enclosed a new revised manuscript (MS: 1429284928705049) that we wish to publish as a Case report in the BMC Pharmacology and Toxicology which is entitled “Memory loss during lenalidomide treatment: a report on two cases”. We describe the case of two patients who developed a severe and rapidly progressive cognitive impairment, involving mostly episodic memory with loss of independence in activities of daily living during lenalidomide-based treatment for multiple myeloma. Chemo-brain induced by lenalidomide may induce particular cognitive disorders. This is a possible unusual side effect of this medication; no major cognitive impairment with impact on activities of daily living was described so far with lenalidomide. The drug’s putative neurotoxicity is probably promoted by specific risk factors (such as previous chemotherapy, prior mild cognitive impairment, age and the presence of cerebrovascular lesions). The publication of this Case report in your journal will contribute to the better medical knowledge of possible lenalidomide’s side effects and could change clinical practice.

All co-authors have participated in the work, all have seen and agree with the content of the manuscript. We take full responsibility for the data. We have full access to all of the data.

Xavier Leleu received grant support, lecture fees and board honoraria from Celgene. Thierry Facon received lecture fees and board honoraria from Celgene. The others co-authors do not disclose any financial conflict.

We certify that this manuscript is not under review at any other publication.

We hope this article would be now suitable for publication in the BMC Pharmacology and Toxicology.
The point-by-point response is as follows:

Dear Editorial Advisor,

We would like to thank Editorial Advisor her/his useful comments. We hope to have addressed each point adequately.

Since there are no prior case reports of toxicity with this drug, I believe that publication of a case report is useful to the field. I do not believe that substantial revision is necessary. However, I do have a few comments/questions on the manuscript:

a) Did the authors ask the manufacturer of lenalidomide if there have been reports of such reactions? I realize data on file cannot be cited, but it would be worth looking into and stating if such reactions have been reported in postmarketing surveillance.

We thank you for this very relevant comment. We have asked to Celgene laboratory if there have been reports of such reaction. There are few cases of cognitive impairment reported during lenalidomide administration (the exact number cannot be diffused due to confidential reasons). In addition, these cases are not considered directly related to the lenalidomide administration due to lack of evidence or other etiologies. We have not insert this comment in the manuscript because data are not enough precise.

b) The last sentence of the discussion is not a complete sentence. (Starts, "As with chemo brain in general..."

We have now modified the sentence as asked: “As with chemo brain in general, the mechanism of lenalidomide’s putative neurotoxicity is not clear. Several mechanisms could be suspected: direct neurotoxic effect of the drug, oxidative stress and DNA damage, induced hormonal changes, immune dysregulation, cytokine release, vascular injury and blood clotting in small vessels and a genetic predisposition.”

c) In the conclusion, third sentence, "patient profiles" cannot be vulnerable. I would restate as, "...some patients may be particularly vulnerable..."

We have now modified the sentence as asked.

Yours sincerely,

Adeline Rollin-Sillaire, MD
Emilie Le Rhun, MD