Author's response to reviews

Title: Guidelines for the use and management of long-acting injectable antipsychotics in serious mental illness

Authors:

Pierre Michel Llorca (pmllorca@chu-clermontferrand.fr)
Mocrane Abbar (mocrane.ABBAR@chu-nimes.fr)
Philippe Courtet (philippe.courtet@univ-montp1.fr)
Sebastien Guillaume (s-guillaume@chu-montpellier.fr)
Sylvie Lancrenon (s.lancrenon@sylia-stat.fr)
Ludovic Samalin (lsamalin@chu-clermontferrand.fr)

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Author's response to reviews: see over
To: Chief Editor
BMC Psychiatry

Sir,

Please, find enclosed a revised version of manuscript entitled "Guidelines for the use and management of long-acting injectable antipsychotics in serious mental illness" for publication in BMC Psychiatry. Answers to the comments and suggestions raised by the reviewers can be found in separate sheets.

Hoping to hear from you soon, I remain

Sincerely Yours

Ludovic Samalin
« Abstract, section “results and discussion”

From the current wording it is not possible to differentiate the outcomes of the survey reported and the interpretation / additional information coming from the panel. The authors may more clearly label where the respective data comes from. The last paragraph of this section is not understandable and needs some language revision. »

RESPONSE: We have completed the section « Method » by a sentence for more clarity about the recommendations presented in the section « Results ».

p2: « The following results summarize the key recommendations from the guidelines after data analysis and interpretation of the results of the survey by the scientific committee. »

The section « Results » presents only recommendations from data analysis of the survey without additional information from the authors.

We have change the last paragraph of this section.

p3: « Recommendations for medication management when switching oral antipsychotics to LAI antipsychotics are proposed. Recommendations are also given for the use of LAI in specific populations. »

« Materials and methods, section “questionnaire development”

The authors should briefly list the compounds listed in France as SGA and FGA LAIs respectively here (page 7 of the PDF). Referring to table 1 is too complicated as it lists a lot of different compounds holding a marketing authorization in European countries. As France was the target of the current survey only the current situation regarding available LAIs in this very country is key for interpretation of the data. »

RESPONSE: We have change Table 1 (and title) which lists only the available LAIs in France.
« Materials and methods, section “data analysis”

The statement “What’s more, if at least 20% of the experts replied in zone 0 and a first-line or second-line treatment could be selected, the question was considered as non-consensual.” seems to be redundant as this was already stated just some lines before. The corresponding table needs revision in the last line as a rating of “0” exceeding 20% already led to a non-consensus statement. »

RESPONSE: We have removed these sentences of the section « data analysis » and have added sentence according to the corresponding table.

p9: « For all other cases the question was considered as non-consensual. »

« Results, section “indications”

The authors switch back and forth between listing indications or compound groups (FGA or SGA LAI). Reporting the results either based on “indication” or “compound group” (as in the corresponding table) would be a lot easier to grasp. Mixing the reference point may lead to confusion. »

RESPONSE: We have listed indications based on compound group (FGA/SGA LAI).

p10:

« LAI SGA are recommended (in monotherapy or combination):

- as 1st line treatment in schizophrenia, delusional disorder and schizoaffective disorder
- as 2nd line treatment in bipolar disorder and personality disorders

They are contraindicated in organic mental disorders with behavioural disorders (Alzheimer’s disease, vascular dementia...).

LAI FGA are recommended (in monotherapy or combination):

- as 2nd line treatment in schizophrenia, delusional disorder, schizoaffective disorder and personality disorders

They are contraindicated in recurrent depressive disorder and in organic mental disorders with behavioural disorders.

»
Results, section “introduction period”

The statement “can be used from the first psychotic episode” is not in line with the categories of ratings mentioned in the methods section of the manuscript. With all results in this section of the manuscript the authors should clearly state the respective rating as otherwise interpretation/speculations/opinions mix with survey results.

Also in the tables referring to these outcomes the wording is not in line with the categories. A uniform way of presenting the outcomes is recommended.

RESPONSE: We have change all results in this section using the categories of rating mentioned in the method section. Also, the terms « first-line/second-line/ third-line intention » in the section « Method » (p8, Figure 1 and Table 2) was replaced by « first-line/second-line/ third-line treatment/strategy ». We used exactly the same terms in the section « Results » to uniform the presentation of our recommendations.

p 11: « They can be used are recommended from the first psychotic episode. »

p 13: « * LAI SGA and LAI FGA may be proposed are recommended (as 2nd line treatment) for clinical forms where positive symptoms prevail.

* Only LAI SGA may be proposed is recommended (as 2nd line treatment) in cases of predominant negative symptoms. »

p 14: « LAI SGA may be offered are recommended as a 1st line treatment (in monotherapy or in combination).

These patient may receive LAI SGA are recommended as 2nd line treatment. »

p 16: « First-line strategy is to start preferentially with the antipsychotic oral form for the length of time required to obtain an effective dose and good tolerance before switching to the LAI form. »

p 17: « First–line strategy is to introduce introduction of the new LAI antipsychotic will be made after the discontinuation of the current LAI FGA or LAI SGA. »

« In 2nd line strategy, the switch from the current LAI FGA or LAI SGA to the new LAI SGA is recommended can be considered directly after having given an oral test dose of the newly introduced SGA LAI in order to eliminate any hypersensitivity. »

« In order to help with the acceptance and understanding of the benefits of an LAI treatment, it is unanimously recommended by the experts (strategy of choice) to convey to the patient specific information concerning both the advantages and inconveniences of the FGA and SGA LAI which are being considered, in the framework of shared decision-making. »

The other changes are highlighted in the text of the manuscript.
« Results section, general concern

As the respective concrete questions of the survey are not reported upon the reader cannot assess how the questions were posed. This leaves a lot of room for speculation. The authors do publish a link to the questionnaire to my understanding (as the complete questionnaire is surely too elaborate to be published) but 1 or 2 examples of how questions were phrased would still be helpful. With a lot of presented results it remains unclear how they derive from the questionnaire (categories do not match; additional information is sometimes reported with certain questions but it is somehow unclear if this was part of the questionnaire or reflects the authors view). The entire results section needs profound revision. »

RESPONSE: We have added 4 examples of questions with the answers of the experts’ panel in the different parts of the section « Results ». These examples are presented with a graphic in the Figures 2,3,4,5 and mentioned in the text of manuscript (p10, 15, 19, 28).

We have revised entire results section. All results in this section use the categories of rating mentioned in the method section and derive from the data analysis of the survey. None additional information was reported. Some sentences, that were opinions from scientific committee, have been removed:

p14 : « Note: Owing to the fact that other drug classes are available for bipolar disorder (lithium and antiepileptic drugs) there was a lower level of consensus than the one found for schizophrenic patients. »

p18/19 : « The experts did not reach a decision on a preferential site of injection, in so far as it depends, first of all, on the patient’s preference. »

p 27 : « With neuroleptic treatment, particular attention must be given to the risk of malignant syndrome. »

« Discussion

The authors do refer to the expert consensus programs already published but do not present their data in the same way. As the concrete questions are not published the outcomes are hardly interpretable for the reader (and they cannot be differentiated from mere opinion coming from the authors rather than the surveyed experts) »
RESPONSE: The section « Discussion » have been completed using the term « experts’ panel » to facilitate the differentiation between the discussion/opinion from the authors with the recommendations from the surveyed experts.

The current guidelines are not homogeneous recommendations about LAI antipsychotics. Table 9 was an interpretation of the recommendations from these guidelines by authors of the manuscript. We have choose to remove Table 9 because was confusing.

« Quality of written English: Needs some language corrections before being published »

RESPONSE: English has been revised by PRS Proofreading Services.

REVIEWER 2

No question or comment