Reviewer's report

Title: Epidemiology and Outcome of Pneumocystis Pneumonia in the Recent Era of Highly Active Antiretroviral Therapy: A Cohort Study

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Reviewer: Hansjakob Furrer

Reviewer's report:

General remarks
1. The authors address the issue of outcome (primary endpoint in-hospital mortality) of pneumocystis pneumonia in 292 HIV-infected patients admitted to a large hospital in the era of combination antiretroviral therapy (2000-2003). They also aim to address the impact of HAART on outcome. They do it by retrospective chart review. They conclude that the outcome of PCP has not changed in the HAART era.

2. The data about all in-hospital parameters and outcomes are important contributions to the field.

3. (Major Compulsory Revision) The major weakness of the study is the unacceptable high grade of incompleteness of important descriptive variables regarding pre-hospital time period and HAART. While this is not very important for the overall mortality, all stratified and multivariable analyses are seriously hampered because of losses for the respective analysis. Obviously the authors failed to get insight in outpatient charts of the period prior to admission.
   a. Already a “random loss” of 17% of charts of interest is surprising to me. I doubt that losses are at random.
   b. Duration of HAART prior to admission was only available for 33% of the patients
   c. Crucial markers of HIV infection, prognosis and HAART efficacy (CD4 counts and HIV RNA) were only available for a minority of the patients, even though the authors accepted a (too) wide temporal range of determination of these markers before or after admission date (6 months).

4. (Major Compulsory Revision) There is more information about in-hospital events such as ICU, pneumothorax and analyses of these parameters are more meaningful. However even important in hospital variables are missing such as
   a. PO2 or alveolo-arterial gradient, important prognostic markers of PCP outcome are not reported.
   b. Reports about co-infections, which are likely to be present in a patient with median CD4 counts below 20.

5. (Major Compulsory Revision) The HAART issue cannot be addressed with this paper. According to table 1 none of the HAART patients was “really” HAART, all showing detectable HIV RNA, in fact median viral load (and lower range of viral
load) was higher in the HAART group than in the non-HAART group. In addition, the number of patients starting HAART during hospitalization is too low to allow for meaningful analyses for the important question of whether HAART should be started during PCP treatment.

6. (Major Compulsory Revision) I miss data whether patients have been treated according well established guidelines (adequate dosage, steroids) and whether adhering to this guidelines was associated with lower mortality.

For me the conclusion of this study is the following: In the HAART era there are obviously patients not receiving adequate care (not being on/not taking “real” HAART, not receiving/taking PCP prophylaxis, not being monitored adequately for their HIV infection). Those patients present similar to patients in the pre-HAART era and have similar prognosis.

I propose to drop the HAART section to a great extent because of lack of adequate data and power reasons and concentrate on a shorter contribution with regard to outcome of PCP in hospitalized patients in recent times.

Specific remarks
A. (Minor Essential Revision) Title: The epidemiological part of the study is not enough addressed: No denominator of the population at risk, PCP managed on out-patient basis not included. Something like “Outcome of HIV-associated PCP in hospitalized patients 2000-2003” would be a better choice.

B. (Minor Essential Revision) Abstract: The number of the studied patients should be included. Drop the conclusions about HAART.

C. (Minor Essential Revision) Log transforming of HIV RNA: The authors transform to the basis e (ln) but should log10 transform the data, as is usually done.

D. (Major Compulsory Revision) Data about adequate use of steroids should be given.

E. (Minor Essential Revision) Multivariable models: Please give the number of patients included in each of these multivariable models.

F. (Discretionary Revision) Table 3: LDH consider to give the OR per 100U increase.

G. (Minor Essential Revision) Table 4: I don’t understand how the number of patients that started HAART in hospital can be smaller than the number that started HAART and continued for at least 7 days.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:

No competing interest.