Reviewer's report

Title: Increased financial burden among patients with chronic myelogenous leukaemia receiving imatinib in Japan: A retrospective survey study

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Reviewer: Lina Eliasson

Reviewer's report:

This paper is reporting a retrospective study which quantified the financial burden of Japanese CML patients who have been prescribed imatinib. It is an interesting paper which adds value to the discussion regarding affordability of cancer drugs, access to drugs and health policy. The research question is well defined, methods are appropriate and the data seems sound - although I have included two compulsory revisions I struggled somewhat with deciding whether they would have been more appropriate as minor essential revisions (and thus been able to accept the paper).

However, the discussion could be strengthened and the authors need to have the article edited by someone with English proficiency. I have included some suggestions for editing, but have not included grammar mistakes and unsuitable use of words. The comments regarding language are also relevant to Table 1.

Major Compulsory Revisions

1. Clarify why cost/financial burden of imatinib was assessed in 2000, when sales started in Japan in December 2001 (p.9 last paragraph)? The patients who received imatinib at this time, where did they get it from? Did patients pay for it? Was it reimbursed according to the same scheme as after it has gone on sale? Is data collected from before imatinib was sold directly comparable to data collected in 2005 and 2008?

2. p.11 In terms of the multivariate analysis, since co-payment is dependent on patients age and upper-limit of co-payments are dependent on household income and age (see background p.5 second paragraph) these factors should all be highly correlated and I therefore question whether it is appropriate to include all three in the model and also wonder if this contributed to these 3 factors all being found to be significant to predict patients considering discontinuing imatinib (because of their interactions)?

I am not a statistician though, so please seek further advice on this.

Minor Essential Revisions

3. It is stated that one of the aims were to assess patients thoughts about their financial burdens over time – I expected more qualitative data because of this wording and I am not convinced patients’ “thoughts” can be assessed
satisfactory by the single item “Do you feel the financial burden of your medical expenses [YES/NO]” (Supp. Table 2) and then whether they have stopped or consider stopping imatinib because of high costs (Supp. Table 1). I assume this may be a translation issue though, so maybe it just needs to be reformulated?

4. I suggest replacing all instances of “taken” with “prescribed” – e.g. on p.6, instead of writing “In this study we focused on CML patients who have TAKEN imatinib”, write ...CML patients who have BEEN PRESCRIBED imatinib” – because patients may be prescribed imatinib but not take it as directed...

5. p.5 please clarify in what way co-payments vary with age and income – e.g. does higher age mean higher or lower co-payments (in particular to help interpreting the multivariate analysis)?

6. p.6 final paragraph – replace “cooperated with our survey” with “participated in our survey”

7. p.6 final paragraph – it is unclear if the nine associations agreed to take part in the survey or not?

8. p.7 first paragraph – replace “patients filled-in questionnaire forms” with “patients completed the questionnaires”

9. I would also write that “Two patients were excluded...//... never been PRESCRIBED imatinib.” (unless the case was that they had been prescribed but never actually took the imatinib?)

10. p.10 second paragraph – Clarify if the “medical expenses” that were felt to be a heavy burden by the 28 pts in 2000 was directly due to cost of imatinib?

11. p.11 I would like to know how many patients were not considering stopping imatinib and how many considered doing so due to side effects?

12. p.12 end of first paragraph – A thought: can imatinib still be considered to be “newly developed” having been approved as first line for 11 years and coming off US patent in 3?

13. Elaborate more on what can be done to address high cost of drugs in last sentence – in what way do medical insurance programs need to be different to the medical insurance programs these patients already have? Same comment applies to end of second paragraph on page 14.

14. p.12 last paragraph – Rephrase first sentence – maybe by adding “many” or “most” as not all CML patients had financial problems: i.e. “This study showed that most CML patients did not have enough financial resources...”

15. p.14 – rephrase sentence stating that the ratio of patients discontinuing imatinib treatment due to monetary constraints in this study only being 10% of that reported by Darkow et al 2007. As far as I can see, Darkow did not report the ratio of patients stopping imatinib specifically due to monetary constraints?
16. Clarify the sentence regarding noting that the universal insurance system guarantees all Japanese citizens access to hospitals, regardless of income or insurance policy. In what way is this sentence linked to the previous arguments and in what way is this linked to patients’ access to or affordability of imatinib?

17. p.14 last paragraph – rephrase the sentence “Since the summer of 2007, the association has given members an idea of three-month prescription…” In fact, I find this whole paragraph a little difficult to follow.

18. p.15 paragraph on limitations – I am not convinced dose level in itself is the only and most important difference between Japan, Europe and USA that make generalizability of the study difficult (in particular as 63% of study sample was prescribed 400mg or more)?

19. p.25 Table 4 – the classifications are confusing, I think it may be because of the use of both the # “less than or equal to” sign and the < “less than” sign? Also think about not having values that overlap and I assume 74,423 should be marked with the # “equal to or more than” sign?

20. p.26 – Change “Odds rate” to “Odds ratio” – write out the exact p-values instead of “n.s.”

21. Supplement p.4 Table 3 – Change “Odds rate” to “Odds ratio” and add the confidence intervals

Discretionary Revisions

22. I think some mentioning of patients-access schemes may be appropriate?

23. Maybe interesting for European and US readers to have some mentioning of access/cost of second line treatments nilotinib/dasatinib - are these available, are they reimbursed?

**Level of interest:** An article of importance in its field

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

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I have received honoraria from Novartis and Bristol-Myers Squibb. I have no other competing interest to declare.