Author’s response to reviews

Title: Treatment of gastrointestinal stromal tumours in paediatric and young adult patients with sunitinib: a multicentre case series

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Author’s response to reviews:

Dr Dafne Solera
Executive Editor
BioMed Central Cancer
Floor 6, 236 Gray's Inn Road.
London WC1X 8HB
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12th July 2017

Dear Dr Solera,

Re: Treatment of gastrointestinal stromal tumours in paediatric and young adult patients with sunitinib: a multicentre case series

On behalf of my co-authors, I would like to thank you for the constructive feedback provided on the above submitted manuscript. The manuscript has been updated accordingly and responses are provided below.
Editor Comments

1) The manuscript as presented should be submitted as a Research article. Please re-format the manuscript accordingly.

Response: The manuscript has been reformatted as requested.

2) Ethics approval: we understand that the study was a retrospective analysis of patient clinical data. You have provided conflicting statements regarding ethical approval under Ethics and consent and Consent to publish statements, please clarify whether ethical approval was sought and obtained from the local IRBs, and include their full names here. In the UK, this type of study would still require ethical approval, so if this was not required based on local legislation, then a reference to this legislation must be provided.

Response: The ethics statements have been amended to reflect the fact that ethical approval was sought and provided for collection and reporting of patient data at each of the participating centres (Page 14 Ethics approval and consent to participate; Page 15 Consent for Publication).

3) Consent to participate: this is required for the publication of individual patient data, such as in Table 1. If you have not obtained consent to publish for the patients and/or legal guardians, then this table must be removed or amended so that data such as gender, date of diagnosis and age are presented as a range.

Response: It was not possible to seek or obtain permission from all patients (only a proportion) for publication of their data. Table 1 has been amended and age, diagnosis and gender data summarised in the results section (Page 8, Results, Para 1).

Kuniaki Shirao (Reviewer 1): This manuscript is very valuable data as the reference for molecular target therapy and chemotherapy against pediatric GIST. This paper is well written as a case series report.

1) What is the reason why sunitinib as second line is effective?

Response: The clinical activity of sunitinib in this patient population is consistent with its pharmacology as a multi-tyrosine kinase inhibitor with activity against a variety of ligands including VEGFR, PDGFR and KIT, including WT KIT. This has been clarified in the discussion section (Page 12, Discussion, Para 2).
2) Isn't there any data on other treatments of second line setting that can be compared with sunitinib of second line?

Response: Sunitinib is the only agent to have been approved for second-line use in GIST. This and the subsequent third-line option of regorafenib are detailed in the introduction.

Özgür Ekinci (Reviewer 2):

1) Not all of the patients are of pediatric age and the text flows rather liberally for this matter, which is unacceptable. The authors have to decide to report only on patients of pediatric age or not. If some patients are to be named "young adults", this should be throughout the text, not when needed; a reader can detect the otherwise.

Response: The text has been amended throughout to clarify that the data set included paediatric and young adult patients. The results section has also been updated to bring out the greater number of patients aged ≤18 years (Page 8, Results, Para 1).

2) Even if there is a negligence of the pathological diagnostic parameters for a concise treat on sunitinib, the mutational analyses - at least some - of the patients should be included. There seems to be a sharp declaration of these GISTs being wild-type for KIT and PDGFRA. Any reader interested in the field would request a figure of these tests. Besides, I would recommend the names of the mutational analytic methods to be provided in a table with full brand names.

Response: The mutational status of the patients' tumours are presented in Table 1. The manuscript has now been reformatted at the request of the Editor as a Research Article. Consequently, a new methods section has been added with details of the mutational analysis conducted with an appropriate reference (Page 7, Methods, Para 1).

Yoshito Komatsu, Ph.D.,M.D. (Reviewer 3):

1) Please note that there is no description about the physique (body surface area etc.) of the patient.
Response: Body surface area at the start of sunitinib therapy (where available) has been added to Table 2. Bodyweight, height and body surface area have been summarised (Page 8, Results, Para 1), at the request of the Editor, to maintain patient anonymity.

2) Please explain the relationship between physique, dosage and side effects.

Response: Physicians treating patients in our case series did not specifically select a sunitinib dose based on bodyweight or body surface area, although these aspects were considered when deciding on dose selection. Retrospective analysis of dose by body surface area at baseline (where available) and outcome (efficacy or toxicity) showed no obvious correlation in this small sample. A statement reflecting this has been added (Page 11, Discussion, Para 2).

I trust the above responses meet with your approval and I look forward to hearing from you in due course.

Yours sincerely,

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