Reviewer’s report

Title: Exploring the characteristics of patients with mesothelioma who chose active symptom control over chemotherapy as first-line treatment: a prospective, observational, single centre study

Version: 0 Date: 27 May 2017

Reviewer: Charles B. Simone

Reviewer’s report:

The authors performed a 200 patient query into reasons why patients chose active symptom control over chemotherapy for malignant mesothelioma. This is an interesting and novel study, as it is the first such analysis to describe the characteristics of mesothelioma patients who chose active symptom control. These findings are important and have implications for discussions with patients regarding decision making, as well as the design and implementation of future systemic therapy trials.

Abstract

1) In the background section, the authors state that "the only treatment that extends survival is chemotherapy." There have not been phase III trials in surgery, radiation therapy, or currently used immunotherapy agents, so this statement cannot be said. I suggest changing the sentence to something more along the lines of 'chemotherapy is the current standard of care to improve survival.'

Introduction

1) The authors state that "chemotherapy with pemetrexed and cisplatin is the only treatment that has been shown to extend survival." In fact, in the past year, results of the phase III MAPS trial have demonstrated that the addition of bevacizumab significantly prolongs survival. The authors cite this trial later in the Background section. Perhaps reword to clarify something to the order of 'chemotherapy has been the only treatment that has consistently been shown to improve survival for mesothelioma' and not limit the statement to pemetrexed and cisplatin.

2) It is implied that chemotherapy offers only a 2.8 month median survival benefit, but time is the benefit of adding pemetrexed to cisplatin. Please reword to clarify that the actual magnitude of chemotherapy over no chemotherapy is greater than 2.8 months.

3) Replace "the alternative to chemotherapy" with "an alternative to chemotherapy" given that a standard and likely preferred alternative treatment to chemotherapy is clinical trial enrollment.
Methods

1) The authors call this a prospective longitudinal study, but the reasons for choosing active symptom control were obtained retrospectively by review of the medical record system. Clarify what was actually performed prospectively and if (and which) an institutional review board or ethics committee approved of the study.

2) Why was survival censored nearly a full year ago when the median survival is so limited in this cohort? Valuable data could be missed and should be updated.

Results

1) Add actual quantitative information on the performance status for both groups in the manuscript text in addition to the \( p \) value that is already listed.

2) Among the 22 patients who chose active symptom control after discussion with a respiratory physician, how many saw a medical oncologist?

3) For both the 24 and 22 patients that are quoted in the text, I suspect that several were seen by both providers. Clarify how patients who saw both providers were stratified for the decision analysis.

4) Explain fewer than one-third of medical records contained the reason for treatment decision, as I would have thought this standard of care decision should be in every single patient's medical record regardless of clinical trial participation.

5) How did previous negative experiences of chemotherapy influence the decision to receive chemotherapy? Did these patients have a prior cancer for which they received chemotherapy? Did they receive chemotherapy for their mesothelioma previously and now refuse second or third line chemotherapy?

6) Furthermore, clarify that the decision point being assessed in this study is for first line chemotherapy vs. active symptom control or if any refusal of chemotherapy at any line is counted as refusal.

7) \( PS \geq 2 \) is listed as a factor associated with poor survival, but according to Table 1, there are no patients with a \( PS > 2 \). Clarify or review to \( PS = 2 \) and not \( \geq 2 \).

8) Survival is listed, but the median follow-up and follow-up range are not provided.

Table 1

1) Classify all stage I patients as IA or IB
Discussion

1) Again, the authors misinterpret the findings in reference #5. The survival difference of 7.2 months seen in their study should not be equated to the survival difference of adding pemetrexed to cisplatin since both arms of reference #5 received chemotherapy.

2) Discuss that among patients for whom there were able to report on reasons for a treatment decision, these reasons were not defined a priori and/or asked to patients, and that the reasons were strictly identified by a chart review that introduces inherent bias.

Figure 1

1) The median survival for active symptom control patients appears to be 9.9 months, not 6.7 months that is listed in the manuscript text for this cohort. The 9.9 months is what is listed in the manuscript text as the median survival for all 200 patients

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:
1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal