Reviewer’s report

Title: First-line single-agent regorafenib in frail patients with metastatic colorectal cancer: A pilot phase II study of the Spanish Cooperative Group for the Treatment of Digestive Tumours (TTD)

Version: 0 Date: 12 Mar 2019

Reviewer: Mei-Chin Hsieh

Reviewer's report:

This is a an open-label single-arm phase II clinical trial study that exams the efficacy and safety of the first-line single-agent chemotherapy drug regorafenib in the frail patients with advanced colorectal cancer.

Comments:

1. The main issue with this study is the small sample size. Because results generated from small sample size studies are usually neither stable nor reliable, a concrete conclusion cannot be made at. However, authors were aware of this issue and addressed it in their study limitation. I suggest changing the "phase II" in the study title to the "pilot phase II."

2. It is not clear whether the advanced stage of colorectal cancer was identified at the same time the cancer diagnosed or the colon cancer patients later progressed or developed metastases to distant site(s). In the methods, it mentioned patients with microscopically confirmed advanced colorectal adenocarcinoma who were not amenable to curative surgery and were not previously treated for advanced disease. However in the results section, authors described other patients as having surgery and receiving previous adjuvant chemotherapy.

3. In the Results section (line 218) complete response was achieved by one patient with a partial response observed in two patients. Did all of these subjects receive the full dose 160mg/day over the 3+1 week schedule OR did any receive the reduced dose? If so, it would be helpful to indicate that for clarity.

4. Other minor issues includes:

  a. Remove the repeated words "colorectal cancer" from the first sentence of abstract.
b. Proper use of abbreviations: abbreviated words should be spelled out for the first time with the corresponding abbreviation in parenthesis, e.g. progression-free survival (PRS) rate.

c. Remove "percent" after 5% from the second sentence under "Safety and post-study treatments".

d. Tables and figure: Tables 2 and 3 should be cited with the mention of relevant statistical results and not at the end of the paragraph. Figure 1 was not mentioned in the results at all.

e. Suggest to carefully read through the paper and fix other glitches before resubmission.

**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 am able to assess the statistics

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

Needs some language corrections before being published

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