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: 04 Mar 2019

Reviewer: Eric Chen

Reviewer's report:

Carrato et al conducted a single-arm phase II of regorafenib in a patient population often excluded from clinical trials: frail patients with advanced colorectal cancer. Their findings contribute to the literature. This manuscript may benefit from additional clarifications.

1. Forty-seven patients were enrolled in the study. It is not clear how many patients were screened.

2. Authors claimed that patients who participated in this study were frail or unfit for chemotherapy (lines 140-141), yet
   a. 64% patients were of ECOG 0-1
   b. 19/47 patients received subsequent chemotherapy, some as many as 6 lines.

3. Response assessment was based on investigator assessment, and there was no central review. This might have contributed to the PFS at 6 months of 45%.

4. The median time to treatment failure was only 2.1 months, quite different from median time to progression of 5.6 months. The difference should be explained and discussed fully.

5. The effect of post-progression treatment on overall survival was not discussed.

6. The incidence of grade 3/4 AEs is high and according to authors, these grade 3/4 AEs mainly occurred in the 1st cycle. It is not clear how these events affected quality of life of these patients.

7. Authors argued for further investigation of regorafenib in this patient population, despite the fact that the primary endpoint was not met, and significant toxicities.

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.  

No

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

No

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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