Reviewer's report

Title: Capecitabine and bevacizumab for non-resectable metastatic colorectal cancer patients: Final results from phase II AIO KRK 0105 trial.

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Reviewer: Timothy Price

Reviewer's report:

This is a well written report of a phase II trial investigating the combination of capecitabine and bevacizumab in a predefined population representing the subgroup who have asymptomatic mCRC and who are not suitable for surgery. Patients who were symptomatic were also included as far as I can tell from the discussion, so it was purely based on non resectability. This I think is not truly the group 3 as indicated. Group 3 should also be low volume asymptomatic. We may have higher volume and symptomatic here and this should be further expanded on. These patients I do not think fit into group 3.

Major comments: This trial was completed some time back and as the authors note there is now 2 randomised trials assessing this regimen, the MAX trial and AVEX. The strength as such is that this trial targets definite non resectable patients and as above included more symptomatic/higher volume patients.

Regarding age, it is suggested I think that this is an older group. MAX was also in its inclusion/exclusion also directing clinicians to the same group, and was thus also aimed at an older population, which is supported by the older med age. AVEX specifically excluded those under 70 and thus was definitively an older group. Ultimately the patient groups under investigation are therefore likely to be similar.

I note the high PS 1 (ie >50% were symptomatic) proportion and also the synchronous group is high, both factors will lead to a poorer outcome potentially and this may be worth exploring in the discussion.

The other difference that is important is that this trial uses full dose capecitabine which is different to AVEX, and also MAX. The authors are partly incorrect in stating MAX used full dose, 66% in fact had the lower dose as per AVEX based on investigator choice. So here we have evidence of tolerance of the full dose. The diarrhoea rate in particular is low given this fact. This may reflect patient selection for the study.

In the discussion first paragraph I think it should comment that cap/bev has "become a standard first line treatment for patients with mCRC" who have the features of group 3, ie better define the group it can be considered for.

The discussion raises the difference in 2nd and 3rd line therapy between AVEX and this trial. It should also include the lower rates in MAX as well in comparison.

Minor comments: The subgroup 3 alluded to is reasonable, but should also note
low volume important. I think if someone has high volume but asymptomatic disease, they would be likely to receive combination chemotherapy and this is not noted in the definition. AGIT should be AGITG. page 7, "on" should be "one".

Overall, this study only adds to that already available now we have 2 randomised trials. The main difference is the inclusion potentialy of more symptomatic patients and all patients were treated with full dose capecitabine. this could be highlighted further to build on this difference.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

uncompensated Ad board for Roche.