

## ANSWERING REVIEWERS

Dear reviewer

We corrected all data which you are demanded in the points 1-8.

Point 9 answer: Chemotherapy regimens which contains anti –VEGF may attenuate CEA expression or shedding by tumour cells<sup>1</sup>, and 5FU can increase CEA expression and shedding<sup>2</sup>. On the other hand CEA cut-off calculation is based on RECIST 1.1 criteria, and in regimens which contains anti-VEGF lack of association between radiological response and outcome was described<sup>3,4</sup>. In our study due to small number of regimens with anti- VEGF drugs, and other biological agents also, we have not plan to consider this analysis now. In the future research we will consider this analysis.

## References

- 1.Abuqayyas L, Balthasar JP. Pharmacokinetic mAb-mAb interaction: anti-VEGF mAb decreases the distribution of anti-CEA mAb into colorectal tumor xenografts. *AAPS J.* 2012;14(3):445–455.
- 2.Aquino A, Formica V, Prete SP, et al. Drug-induced increase of carcinoembryonic antigen expression in cancer cells. *Pharmacol Research.* 2004;49(5):383–396.
- 3.Grothey A, Hedrick EE, Mass RD, et al. Response-independent survival benefit in metastatic colorectal cancer: a comparative analysis of N9741 and AVF2107. *JCO.* 2008;26(2):183–189.
4. Mizard T, Boonsirikamchai P, Overman MJ, et al. Comparison of early radiological predictors of outcome in patients with colorectal cancer with unresectable hepatic metastases treated with bevacizumab. *Gut.* 2018;67(6):1095–1102.