Reviewer's report

Title: Early increase in circulating carbonic anhydrase IX during neoadjuvant treatment predicts favourable outcome in locally advanced rectal cancer

Version: 2
Date: 12 May 2015
Reviewer: Nigel Brockton

Reviewer's report:

Peer Review: Hektoen 2015
This manuscript describes the measurement of circulating cleaved extracellular domain of the CAIX enzyme in locally advanced rectal cancer (LARC) and its response to neoadjuvant oxaliplatin-containing chemotherapy (NACT). The study is well described and framed within a robust prospective clinical trial. The methods are appropriate but coefficients of variation for the assay should be presented. The cohort is small but limitations of statistical power have been addressed appropriately. Some discussion of the mechanism of ectodomain shedding in response to therapy/induced cell-death would be helpful.

Major Compulsory Revisions: None

Minor Essential Revisions:
1) Background, Page 3, line 67-68: “hypoxia...important hallmark of the tumour microenvironment”; while I certainly agree that hypoxia is important, it cannot be considered a hallmark of the tumour microenvironment because there are tumours and tumour microenvironments that do not exhibit hypoxia. Suggest “important feature of the tumour microenvironment.”
2) Report assay performance metrics (Inter and intra-assay % CVs).
3) #NACT in PFS Prediction, Page 9; line 220: delete “seen”
4) Discussion: it would be helpful if the authors would describe or propose the mechanism which leads to the increased shedding of CAIX extracellular domain into the circulation in response to NACT.
5) Discussion, page 11, line 260: Delete neoadjuvant since this word is within the abbreviation; i.e. change “but not of the full neoadjuvant treatment of NACT and CRT” to “but not full treatment with NACT and CRT”.
6) Discussion, page 13, line 298: Insert “an” in “The role of oxaliplatin as [an] additional...”
7) Discussion, page 13, lines 312-313: “lack of evidence-based data”; data constitutes the evidence but the way it is currently written suggests that available data is not evidence-based? Suggest change to “lack of evidence-based research on which to base treatment decisions”.

Discretionary Revisions: None
Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.