Reviewer's report

Title: Randomized phase III clinical trial comparing the combination of capecitabine and oxaliplatin (CAPOX) with the combination of 5-fluorouracil / leucovorin and oxaliplatin (modified FOLFOX6) as adjuvant therapy in patients with operated high risk stage II or stage III colorectal cancer

Version: 3
Date: 14 March 2015
Reviewer: Gunnar Folprecht

Reviewer's report:

The authors answered the questions to the study design and the patient number, but the conclusions drawn should be modified accordingly.

1) So, it would be more appropriate to conclude in the abstract
"When comparing oxaliplatin with capecitabine or 5-FU/FA, we have not observed significant differences within this trial, but differences cannot be excluded with the number or patients enrolled in the trial."

The inclusion of stage II patients makes it not to a trial in an high risk population.

2) The discussion (line 355 ff) should be rephrased as well.

It remains a difference whether trial will unlikely show a statistically significant difference if completed (this is the question of a futility analysis) or whether a significant difference is excluded (would require an equality of at least non-inferiority design with markedly higher patient number). Furthermore, the inclusion of stage II patients potentially decreases the probability that a difference can be demonstrated as the effect in this stage is very limited.

At least, it should be reflected, that a difference cannot be excluded due to the large confidence intervals / patient number that therefore, the formal prove was NOT demonstrated (line 358).

An acceptable formulation would be “… to compare these two standard regimens did not demonstrate a significant difference. Although the trial was not designed to demonstrate non-inferiority, his study contributes to the knowledge drawn from other trials that capecitabine/oxaliplatin is an acceptable regimen for adjuvant treatment of colon cancer.”

The AVANT Trial (de Gramont) has given a direct comparison in the adjuvant setting (but in combination with bevacizumab) and might be added to the studies supporting this hypothesis.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

none