Reviewer’s report

Title: Nal-IRI with 5-fluorouracil (5-FU) and leucovorin or gemcitabine plus cisplatin in advanced biliary tract cancer - The NIFE trial (AIO-YMO HEP-0315) an open label, non-comparative, randomized, multicenter phase II study

Version: 0  Date: 16 Jul 2019

Reviewer: Mairead Geraldine McNamara

Reviewer's report:

This is a well written protocol paper.

I am including some comments which may assist the authors in improving their manuscript.

Keywords:
Alter cholangiocellular carcinoma to "cholangiocarcinoma" which would be better recognised.

Background:
Within first sentence, please clarify what is meant by "ranks beyond 10th in Western World tumor statistics". Do you mean ranked 10th in world incidence?

Study objectives:
Provide Eisenhauer et al, Eur J Cancer reference following mention of RECIST 1.1.
Provide version number of CTCAE criteria that is being used within trial.
Within "Exploratory objectives section", please alter English to (cfDNA exome sequencing, transcriptome, miRNA-arrays prior to and after start of treatment, and on progression).

Treatment:
It is mentioned that "if one drug has to be discontinued permanently under therapy for a reason other than progressive disease, treatment should continue with the remaining drug in the trial...". What if the gemcitabine has to be discontinued in the Cis/Gem arm, would you continue with cisplatin alone? This would not be usual.

Figure 1:
How was cut-off for age stratification determined? A potential reference that could be used would be "McNamara MG et al 2017, BMC Cancer 17: 262."
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.

Yes

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

Yes

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:

Acceptable

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