Author’s response to reviews

Title: Umbrella and basket trials in oncology: ethical challenges

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Author’s response to reviews:

Dear Editor,

Thank you. Please find our responses below.

Rieke Van Der Graaf (Reviewer 1): The authors have appropriately addressed my comments, apart from the response to comment 3.

Although the title now reads "ethical issues" and no longer aims at presenting both risks and benefits (which were absent in the previous version), the issues that are presented still primarily consist of challenges. Let me explain: the first issue (scientific validity) mentions "major challenges" (pg 9 line 69). This is ok, but the reader would also expect whether and to what extent these designs meet scientific validity as a requirement. Accordingly, page 12, line 38 sets out "benefits". I would merge benefits with risks and turn it into a second ethical issue, among others because the content only focuses on the positive aspects and secondly because benefits should always be offset against the risks. Finally, as regards informed consent on page 21ff also mere challenges are addressed (line 47). In other words, please provide an overview of the issues presenting arguments for and against meeting the ethical requirements of validity, favorable risk-benefit and informed consent. Alternatively, put challenges in the title.

Response:

Thank you for these comments. We have changed the title as suggested. We have also merged the section “Benefits” with the section “Risks”.


Regarding arguments for and against meeting the ethical requirement of validity, favorable risk-benefit and informed consent: we believe that the assessment of meeting these ethical requirements should be performed by IRBs/RECs on the level of a particular umbrella or basket trial, rather than on the level of the entire class of trials.

The current version of our manuscript is to flag possible challenges (which we previously called “issues”) rather than to perform ethical evaluation. We hope that the Reviewer agree on our point.