Reviewer's report

Title: Effect and safety of dual anti-HER2 therapy compared to monotherapy in patients with HER2-positive breast cancer: A Systematic Review and Meta-analysis

Version: 3
Date: 11 June 2014
Reviewer: Stefan Diem

Reviewer's report:

The authors were engaged with an interesting and important theme. The Title “Review and Meta-analysis” is misunderstanding. This manuscript is an overview about present published or unpublished studies. In this manuscript data is not consistent enough in the different groups and appear too inhomogeneous to call it a metaanalysis.

Overall methods are well described, but it is written too extensive. Figure 1 shows selection process very well, but it should be commented more clearly in the text.

Endpoints in the text included adverse events. It is not mentioned in the Abstract.

In line 75 anti-Her2-therapy is described as a standard therapy in the adjuvant setting. However I missed studies with anti-Her2-therapy in the adjuvant setting in your references.

Line 165 chapter pCR: A comment to the chemotherapy regimens in these 5 neoadjuvant trials would be meaningful.

Line 179 chapter PFS/OS: One study was with and one without chemotherapy. Please mention that in the text and describe different patient population. There are also 2 completely different settings (one first line, the other after progression after trastuzumab).

Line 193 Chapter subgroup analysis: The sentence “However, no significant difference of pCR was detected between the two groups in the case of chemotherapy-free therapy”.

It is not clear what you would like to say. Please rephrase.

Line 195 Chapter Subgroup analysis: There are only two studies (with or without chemotherapy). So subgroup analysis of one study is not possible.

Line 215 Chapter AEs: The second sentence is not clear. What does combination therapy means (dual anti-Her2-therapy or anti-Her2 with chemotherapy)?

Line 243 Chapter Discussion: What does the sentence “…56% improvement in

Line 278 Discussion: In your study you included neoadjuvant and metastatic patients. So it is not clear why you mentioned the APHINITY study, which analyzes patients in the adjuvant setting.

Figure 2 and 3 are the other way round than in the text and the legends.

The approach of this paper is interesting. The manuscript needs revision by a native English speaking person.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

No competing interests