

March 1, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8433-review.doc).



**Title:** HER-2 positive Breast Cancer Therapeutic Options - Perspectives and Future Directions.

**Author:** Gonzalo Recondo Jr.; Enrique Díaz-Cantón; Máximo de la Vega; Martin Greco; Gonzalo Recondo Sr. and Matias E. Valsecchi.

**Name of Journal:** *World Journal of Clinical Oncology*

**ESPS Manuscript NO:** 8433

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers

(1) **Reviewed by 02445418:** Comprehensive account of the HER2 literature It needs some grammatical and linguistic work. I am not aware of the word "neoadjuvance" I would have liked a more critical approach, rather than just a description of the published studies A comprehensive review should include some account of the biomarkers Other agents that may be worth mentioning are CD4-6, HDAC and HSP inhibitors, etc.

**Response:** We appreciate the reviewer's suggestions. The whole manuscript text was thoroughly assessed and changes were made in words, sentences and expressions to improve its linguistic and grammatical properties. We apologize for some obvious misspellings, such as the word "neoadjuvance". This should read "neoadjuvant" and it was corrected. We understand the reviewer's concern about a more "critical approach" in the description of the clinical trials included in this review. However, we respectfully disagree with this suggestion. One of the main objectives of this review was to present the available data that support the evidence-based practice of medicine in this particular field. It would be doubtfully useful to the reader to know our own, and perhaps biased, opinion regarding the clinical trials design, results or relevance. On the contrary, we indeed expressed our own opinions when we described the way that we personally approach some controversial issues. For example, on page 13-14 we extensively approached the arguable value of complete pathological response as a valid surrogate for clinical outcomes. Lastly, as per reviewer's request and with the objective to enhance this review, we have included new paragraphs describing some information on biomarkers, HDAC, HSP and CDK4-6 inhibitors.

(2) **Reviewed by 00105984:** The authors of this review have accomplished a complete and scientifically sound review on the topic of HER2-positive breast cancer treatment. I have neither major, nor minor comments.

**Response:** Thank you very much.

(3) **Reviewed by 02525711:** I would suggest only some minor revisions. Page 6, 3rd paragraph: the FEC regimen includes epirubicin, it does not include etoposide. Please correct it. Page 14, 3rd paragraph: You talk about three combination two of which are equal. Please clarify Table 1: the FinHER

trial included a regimen with vinorelbine, it did not include vincristine. Table 3: Please correct "anastrazole" in "anastrozole" In the text and tables: Please correct "adjuvance" and "neoadjuvance" in "adjuvant" and "neoadjuvant"

**Response:** We strongly appreciate the reviewer's suggestions. We once again apologize for these obvious errors and misspellings. We have made all the recommended changes. Thank you for picking up these errors and helping us to improve the quality of our work.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Clinical Oncology*.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'M. Valsecchi', written over a light blue horizontal line.

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