



Letter to the Editor: Author Response

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Letter to the Editor: Author Response

Re: Rautenberg T, Siebert U, Arnold D, *et al.* Economic outcomes of sequences which include monoclonal antibodies against vascular endothelial growth factor and/or epidermal growth factor receptor for the treatment of unresectable metastatic colorectal cancer. *J Med Econ* 2014;17:99-110

Dear Editor,

We appreciate the reader's interest in our publication and welcome their feedback.

The letter to the editor states: "They suggest that the maximum PFS advantage would be achieved by using bevacizumab in first and second line and anti-EGFR only at third line." In Table 6 (and considering the published erratum) the top sequence includes anti-EGFR as 3L i.e. it has the highest combined PFS outcome of 19.2 months. Rather than a suggestion, this is the result of the analysis. For comprehensiveness and transparency, Table 6 also presents results of ALL the sequences evaluated with respect to health outcomes.

The letter goes on to say: "According to their original version 'the large difference in outcomes is driven by the favorable results of the 3rd line panitumumab studies'. In the erratum Rautenberg *et al.* admit that the PFS of their top three sequences were erroneously long. They provide technical calculations with the new figures, but do not find it necessary to change their conclusions." The two errors previously identified both relate to estimated median PFS of regimens and therefore only affect Table 6 – where health outcomes are approximated by summed median PFS. The conclusions of the study do not change because the main analysis uses standardized median PFS across all sequences (Table 7) and finds that 2L anti-EGFR sequences are least costly, 1L anti-EGFR strategies are most costly.

According to the letter: "The new erratum text stands: 'Two (not four) of the top five sequences include sequential bevacizumab-based regimens...' The appropriate observation should have been 'Five of the top seven sequences include anti-EGFR as first line treatment...'. The reported two of top five is not a sinister observation, and all results are transparently presented enabling the reader to interpret the results according to their own preference,

as indeed the reader has done. The manuscript simply uses the top five sequences as a reference point. Arbitrarily one of top three; five of top seven and six of top twelve sequences include anti-EGFRs as 1L, two of top three include 3L anti-EGFRs, etc.

The reader states: "Consequently, they should have proceeded comparing the first line anti-EGFR yielding the greatest health outcomes to other alternatives." I am not sure why this would be the case, when the top strategy with respect to health outcomes is sequential BEV and 3L cetuximab (therefore anti-EGFR 3L).

The reader states furthermore: "The current conclusion 'Clinical sequences consisting of 1L and 2L line bevacizumab followed by 3L anti-EGFR potentially yield the greatest health outcomes associated with a reasonable trade-off in additional cost when replacing 1L anti-EGFRs and are potentially cost-saving if replacing 2L anti-EGFRs, per patient per lifetime. To maximize health outcomes, optimal sequences include anti-EGFRs as 3L regimen, with an approximately equivalent trade-off in costs between the most costly (anti-EGFR 2L) and least costly (anti-EGFR 1L) sequences.' is not supported by the study observations and should be revised." This statement is supported by the study observations, but we thank the writer for identifying an error in the text – please see separate erratum.

Finally, in response to the sentence: "The superiority of 1st line anti-EGFRs is supported by two recently presented randomized trials (FIRE-3 and PEAK) demonstrating over 7 months' survival benefit compared to 1st line bevacizumab." As with all research, the manuscript does not claim to be timeless. New studies will continue to be published for each drug and the analysis can be updated to reflect these new results.

Yours sincerely,

Tamlyn Rautenberg

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Declaration of financial/other relationships:

T.R. has disclosed that she has acted as a consultant for F. Hoffmann-La Roche.