

**Reviewer #1:**

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** Interesting case report of a successful treatment with lapatinib alone in a pretreated mCRC patient with RAS/BRAF WT, MSS mCRC and HER2 alteration. Interesting the ctDNA monitoring during treatment. Worthy of publication. Some minor comments: - Lapatinib was a third line (1st line xelox, 2nd line FOLFIRI+BEV and s1+BEV) and not 4th as reported - I would not stress the fact that 7 months PFS was longer than the one reported in clinical trials, because the comparison is not allowed (CT scan in clinical trials is performed every 6-8 week, for example). Moreover, We have not data about the efficacy and toxicity of lapatinib alone vs doublet therefore lapatinib alone is not recommended outside clinical trials; the discussion must be changed accordingly.

**Point-by-point Response to Reviwer #1**

1. “Lapatinib was a third line (1st line xelox, 2nd line FOLFIRI+BEV and s1+BEV) and not 4th as reported”

Response: Description of “fouth line therapy “has been replaced by “third line therapy” in the manuscript. ( **Line 65, 99, 115** )

2. “I would not stress the fact that 7 months PFS was longer than the one reported in clinical trials, because the comparison is not allowed (CT scan in clinical trials is performed every 6-8 week, for example)”

Response: Yes, We agree with this opinion. Comparison of PFS between lapatinib monotherapy and clinical trials (dual therapy) has been deleted in abstract, introduction and discussion section, accordingly.

3. “Moreover, We have not data about the efficacy and toxicity of lapatinib alone vs doublet therefore lapatinib alone is not recommended outside clinical trials; the discussion must be changed accordingly.”

Response: Discussion has been changed accordingly.

- (1) **Line 160-162** :“These studies indicated that lapatinib monotherapy might be effective for HER2-positive mCRC, which is consistent with our observations. Yet, further investigation is needed to confirm these findings.”

- (2) **Line 172-175**: “Whether adverse events of lapatinib monotherapy would be less than dual therapy, indeed, we need more clinical trials to further answer this question, and lapatinib

monotherapy is not recommended except clinical trials.

#### 4. Minor language polishing

Response: A native-English speaker had edited the manuscript for language issues.

#### **Science Editor:**

1 Scientific quality: The manuscript describes a case report about the serial circulating tumor DNA tests to monitor HER2-Positive colorectal cancer's response to off-label lapatinib monotherapy. The topic is within the scope of the WJGO. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The reviewer#03478726 thinks it is an interesting case report worthy for publication and suggests the authors not stressing the fact that 7 months PFS was longer than the one reported in clinical trials, because the comparison is not allowed. Moreover, there is no data about the efficacy and toxicity of lapatinib alone vs doublet, therefore lapatinib alone is not recommended outside clinical trials, the discussion must be changed accordingly. (3) Format: There are 4 figures and 1 supplementary figure. A total of 18 references are cited, including 7 references published in the last 3 years. There is no self-citation. 2 Language evaluation: Classification: Grade B. A language editing certificate issued by MedSci was provided. 3 Academic norms and rules: The Signed Informed Consent Form was not provided properly. The authors provided the CARE Checklist–2016. The authors signed the Conflict-of-Interest Disclosure Form and the Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was without financial support. The topic has not previously been published in the WJGO. 5 Issues raised: (1) The title is too long, and it should be no more than 12 words; (2) The “Case Presentation” section was not written according to the Guidelines for Manuscript Preparation. Please re-write the “Case Presentation” section according to the Guidelines and Requirements for Manuscript Revision; (3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout. 6 Re-review: Not required. 7 Recommendation: Conditional acceptance. (Han Zhang)

#### **Point-by-point Response to Science Editor:**

1. The title is too long, and it should be no more than 12 words;

Response: Title has been changed to “HER2-Positive Colorectal Cancer's Response to Lapatinib Monotherapy: A Case Report” (Line 1-2)

2. The “Case Presentation” section was not written according to the Guidelines for Manuscript Preparation. Please re-write the “Case Presentation” section according to the Guidelines and Requirements for Manuscript Revision;

Response: “Case Presentation” section has been modified according to the Guidelines ( **Line 67-134**).

3. PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references.

Response: All authors of the references are listed, and PMID and DOI numbers have been added to the references accordingly (**Line 225-310**).

4. The Signed Informed Consent Form was not provided properly

Response: The suitable Signed Informed Consent Form is provided.