Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled " *FGFR2-TSC22D1*, a Novel *FGFR2* Fusion Gene Identified in a Patient with colorectal cancer: case report " (Manuscript NO: 65881). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The revised portion of manuscript are marked in red. The main corrections in the article and responds to the reviewer's comments are as following:

Reviewer #1

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The case report of Xiaoming Kao et al demonstrated a case a colorectal cancer patient with FGFR2-TSC22D1 fusion gene. It represents a novel FGFR2 fusion gene identified in colorectal cancer. The paper is well conceived, worthy of consideration, above all because it fulfills two of the criteria to be a case report: findings that shed new light on the possible pathogenesis and novel treatment. Also, the title reflects the main subject of the manuscript which is well summarize in the abstract. Minor revision: the case should be presented in more details. Importance may represent the personal medical history of the patient. Also, the authors should give more information on the further treatment of the patients. As, the manuscript does contain new and significant information according further consideration on the treatment development of the patients with colon cancer containing this gene, it justifies the publication.

Answer: Thank you for your recognition of our work. Dabrafenib /trametinib is known to be approved for cancer with *BRAF* mutations, and Larotrecinib for tumors with *NTRK* rearrangement. Given a specific inhibitor based on molecular diagnostic results, regardless of tumor histology, the patient's prognosis could be significantly improved (*Mol Cancer Ther*. 2016;15:533-47. *N Engl J Med*. 2018;378:731-9). In addition, the FDA recently accelerated approval of erdafitinib for urothelial cancer harboring *FGFR2/3* alterations (https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm635906.htm),

which brings new hopes for patients with *FGFR2/3* mutations. But no matter Colorectal Cancer, version 2. 2021 or the Chinese CSCO guidelines for colorectal cancer, neither of which provide specific treatment options for patients with *FGFR2/3* mutations. Therefore, although the patient was diagnosed with *FGFR2-TSC22D1* fusion, conventional treatment was ultimately chosen. We expect that as more *FGFR* fusion variants are found in colorectal cancer, the corresponding clinical trials can be carried out in colorectal cancer, bringing more treatment options and survival benefits to the corresponding patients.

Reviewer #2

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Colorectal cancer (CRC) affects millions people and is also one of the most common cancers in the world. Genetic alterations in Fibroblast growth factor receptor (FGFR) is commonly observed in many CRC cases. Common genetic alterations in FGFR includes simple mutations, as well as fusion of FGFR gene with another gene leading to abnormal expression of FGFR. Therefore, it is proposed that CRC patients could be treated with FGFR inhibitors to curtail cancer cell growth. In this case port, using the Next Generation Sequencing (NGS), , the authors identified a FGFR2-TSC22D1 fusion gene in a 59-year old individual. They observed that the fusion gene contained exons 1-17 of FGFR2 and exon 3 of TSC22D1, with the complete kinase domain of the FGFR2 gene. This was the first report showing the presence of a fusion gene between FGFR2 and TSC22D1 in CRC patient. The authors suggested that, FGFR2 inhibitors could be used in the treatment of CRC patients having a fused gene (FGFR2-TSC22D1). This is a novel study and demonstrated for the first time the existence of a fusion gene between FGFR2 and TSC22D1 and is of significant interest to the scientific community. Comments: This is a very interesting report, however, the authors can revise the manuscript as per the following suggestion. 1. Please explain the functions of TSC22D1 gene. The authors can include the following sentence in the text on page 3, line 66. TSC22D1 (TSC22 domain family protein 1) is a transcription factor belonging to the large family of early response genes. Dimers of TSC22D1 act as transcription factors and have tumor suppressor function. 2. Page 3, line 75, please change "…event mays represent… " to

"…event may represent….". 3. Page 3, line 70-71, the authors state that "FGFR2 positive was considered". Please rephrase the sentence to make it clear.

Answer: Thank you for your recognition of our work. We have made several revisions according to your comments. We hope that the revised manuscript will meet your requirement.

Science editor: 1 Scientific quality: The manuscript describes a Letter to the Editor of novel FGFR2 fusion in colorectal cancer. The topic is within the scope of the WJCC. (1) Classification: Grade A and Grade B; (2) Summary of the Peer-Review Report: Overall this is a highly interesting case report. Some sentences need to be rephrased. The authors should give more information on the further treatment of the patients. The questions raised by the reviewers should be answered; (3) Format: There are 2 figures; (4) References: A total of 10 references are cited, including 4 references published in the last 3 years; (5) Self-cited references: There is no self-cited reference; and (6) References recommendations (kindly remind): The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade A and Grade B. A language editing certificate issued by SNAS was provided. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: No financial support was obtained for the study. The topic has not previously been published in the WJCC. 5 Issues raised: (1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (2) 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; and (3) If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For

example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable. 6 Recommendation: Conditional acceptance.

Answer: Thank you for your suggest. We will provide the original figure documents using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. And we added the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references in the revised manuscript. In addition, we do not re-use a figure or figures published elsewhere, or that is copyrighted.

Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, the author(s) must provide the Signed Informed Consent Form(s) or Document(s). For example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Answer: Thank you for your suggest. We will upload the signed informed consent before its final acceptance.