Reviewer 1
This is a comprehensive and concise summary of biomarker aspects for colorectal cancer, highlighting current achievements but also indicating gaps in the area. Relevant Topics are adequately covered. It is suggested also to refer to the recent FDA-NIH biomarker guidance document (BEST): https://www.ncbi.nlm.nih.gov/books/NBK326791/ It is suggested to more critically discuss the clinical robustness and usability of miRNA Panels. The existing studies have Major limitations, e.g. small sample size, non-standardized sampling procedures, etc. Emerging Technologies like liquid biopsies, more current classification Systems (CSM), next Generation sequencing and esp the Need for biomarkers for immunotherapy approaches are missing and should be added. Minor Points: Please do not use "gender" when "sex" is meant Please discuss B-raf Status in Addition to K-ras The authors refer to MSI and Kras testing for the use of "monoclonal antibody-based adjuvant therapy". Please specify!

Thank you for your comments. Reference and definition from BEST have been added. A robust section on liquid biopsy and the clinical applicability and limitations has been added. Gender has been removed. BRAF mutation status has been added to the KRAS and NRAS mutation discussion, with the specific monoclonal antibody-based treatments impacted.

Reviewer 2
I wish to commend the authors for a clear review, extensive and concise of a subject relevant to clinicians, specifically surgeons and oncologists. This study is highly informative but lacks clear advices for using the described biomarkers in clinical practice. As most of the biomarkers (and radiological markers) are still in experimental phases and are not relevant currently in the ongoing treatment of patients suffering from CRC, the only thing i would advocate for is a paradigm or prehaps a illustrated figure of what is currently used by clinicians for decision making in patients suffering from CRC. I thank the authors for an enjoyable read.
Thank you for your review and comments. We have added some information on the clinical application of biomarkers and biomarker testing in clinical practice, with a figure, as per the author's suggestion.

Reviewer 3
This review described a current definition laid out by Cancer Research UK and the current status of those biomarkers in colorectal cancer, which is helpful to investigators to get out of traditional definition that a biomarker is a tumour characteristic.
Thank you for your review and comments

However, there are several minor mistakes. For example, in "MSI-high tumours have been shown to have a better outcome than patients with MSH-low tumours", MSH should be MSI.
This error has been corrected, thank you

Reviewer 4
An interesting albeit very technical paper. However, it brings together in one paper, many of the new advances and thinking regarding cancer biomarkers, which is helpful for clinicians in this field.
Thank you for your review and comments

Reviewer 5
The aim of this original review is to examine and critically appraise novel imaging and molecular-based approaches and highlight key findings for biomarker potential in the EMT pathway. The manuscript is of great clinical importance, well written, and well organized. Some points, however, need minor revision: - According to available data what do the authors think about the useof liquid biopsies as biomarkers? - Where do authors classify methylated SEPT9 as a CRC biomarker, and what is its significance? - Regarding EMT and MET what kind of other useful markers can be act as biomarkers? After major revision I suggest to accept is for publication.

A robust section on liquid biopsy, other biomarkers, and the clinical applicability and limitations has ben added. Per the author's recommendation, SEPT9 as a validated diagnostic biomarker has been added, with the current the current state that there is promise but current limitations.