

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53912

Title: Impact of primary tumour location on colorectal liver metastases: A systematic review

Reviewer's code: 02445638

Position: Peer Reviewer

Academic degree: PhD

Professional title: Academic Research, Research Scientist

Reviewer's Country/Territory: United States

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-31

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-02-14 14:13

Reviewer performed review: 2020-02-21 21:30

Review time: 7 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Bingham et al. have written a review evaluating the influence of primary tumor location in overall (OS)/disease free (DFS)/ progression free (PFS) survival of metastatic colorectal cancer. They have done a literature search and narrowed down appropriate studies to be examined, and present consensus results that indicate patients with l-CRCLM have better OS, with DFP AND PFS being less clear. Twenty-one out of thirty-eight (55%) of studies provided the positive OS correlation (this uncomfortably close to a 50:50 outcome for the studies examined). The review is carried out and written very well, and the clinical data is well presented and considered. Title, abstract, key words, background, methods, results, ok. Discussion could be augmented. Illustrations, biostatistics, units, references, organization ok. Because the authors do begin to approach a discussion about the molecular mechanisms that could be responsible for the results in the 21 positive studies, it seems appropriate to mention that this could be better developed. The major focus of the review isn't molecular, but there is a great deal known that could be applied to the major observations of the report. The authors do not mention that almost all tumors with MMR alteration are found on the right side. It is suggested that they go over the TCGA paper on colorectal cancer (Nature 2012 vol 487:330-337). What might the molecular mechanism be that would lead to holding off DFP in r-CRCLM with lower OS? For instance, is the implication that MMR types of mutation take longer to accumulate the mutations that would lead to extravasation but harbored more mTOR/AKT/Pik3CA mutation and either a different proliferation or growth rate. Maybe not so paradoxical? None of these studies have molecular analysis associated with them but there is a lot known that could be integrated into the review. What does the PTL outcome mean in terms of what is already known/thought about the molecular differences between MMR tumors and CIN? It

would make it a more interesting read.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53912

Title: Impact of primary tumour location on colorectal liver metastases: A systematic review

Reviewer's code: 03408355

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor, Research Scientist

Reviewer's Country/Territory: China

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-31

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-02-23 01:52

Reviewer performed review: 2020-02-23 01:55

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This paper overviewed the influence of primary tumor location on the oncological outcome of colorectal cancer liver metastasis, which is an interesting topic.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53912

Title: Impact of primary tumour location on colorectal liver metastases: A systematic review

Reviewer's code: 00722213

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Academic Fellow, Academic Research, Chief Doctor, Doctor, Full Professor

Reviewer's Country/Territory: Romania

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-31

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-02-24 14:02

Reviewer performed review: 2020-03-02 15:57

Review time: 7 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this review, Bingham et al. examined the role of primary tumor location in overall (OS)/disease free (DFS)/ progression free (PFS) survival of metastatic colorectal cancer. The paper is interesting but some aspects need to be modified, as follows: 1. To be more conclusive, Discussion should be fragmented in subchapters: Anatomic location, therapeutic options, molecular profile, etc. 2. It is necessary mentioning the role of TACE in evolution of these patients. In some papers, amazing evolution was reported after TACE (see papers such PMID: 26496332; DOI: 10.1097/MD.0000000000001848). There is a role of tumor location in these patients? 3. The molecular profile was examined but no data about NRAS were added. There is a role of these gene in evolution? In most of the laboratories, NRAS profile is also detected, together with KRAS and BRAF....Moreover, there is an utility of of NGS for daily diagnosis? What about MSI/MSS status? 4. Therapy - in the NCCN guideline, it is mentioned taht, in aptients with liver metastases, if carcinoamtosis is associated, HYPEC might be a therapeutic alternative. What about this method? In such review, taking into account onl location, without the other parameters is not enough...all of the data should be examined. 5. A histolglcal parameter which is recommend to be included in the histopathological reports is the budding degree. It is mandatory to mention data about this parameter (for definition see papers such PMID: 28780084; DOI: 10.1016/j.prp.2017.07.025) 6. No data bout antiangiogenic therapy was added, also ESMO guideline mention that therea are difference for answering in patients with right versus left-colon tumors. 7. The last data of literature search is October 2019. As it is March 2020, the paper should be updated and papers from 2020 should also be included.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53912

Title: Impact of primary tumour location on colorectal liver metastases: A systematic review

Reviewer's code: 00038617

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United Kingdom

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Reviewer chosen by: Le Zhang

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Reviewer performed review: 2020-03-08 16:26

Review time: 13 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

In this systematic review, the authors provided a summary of the available evidence on the impact of primary CRC location (PTL), right side versus left side, on oncological outcomes in patients with CRC liver metastases (CRCLM). The paper is well written overall. The methodology is reasonable, and the references are appropriate. This paper is worth publication. Minor comment 1) Page 7, Line 18; In addition, the authors reported enhanced 5-year OS (45.8% vs 44.5% $p=0.02$). Maybe this is the wrong number. Please correct.