Peer Review File

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Reviewer A

This is an Editorial Commentary on an article PMID: 38170586, Clin Cancer Res, 2024, which concluded that transverse metastatic colorectal cancer (mCRC) has comparable prognostic and predictive features with right-sided mCRC. Transverse colon cancer is relatively rare, and the analysis of real-world data could prove crucial to understanding this disease. Transverse colon cancer represents an estimated 10% of all colon cancers. Embryologically, the proximal 2/3 of the transverse colon originates from the midgut, while the distal 1/3 derives from the hindgut. This variation in origin results in differences in disease presentation, histology, and mutational profile within the transverse colon. Due to the combined origins of transverse colon cancer, clear clinical and pathological features of these tumors have been difficult to define but known to be multifarious preceded by underlying mutational profiles found to have clusters that vary compared to other colon-sided locations. It is imperative for future clinical trials to not only include patients with transverse colon cancer but also have dedicated therapeutic trials for transverse colon cancer. Grouping transverse colon cancer solely within right-sided disease proves to be suboptimal, and judicious categorization based on embryologic origin, mutational profile, and tumor characteristics is imperative to attain ideal outcomes.

As commented herein, there is a significant need for clinical trials to include stratification based on tumor location within the colon, including the specific tumors within the transverse colon so that differences in therapeutic responses can be ascertained between primary tumor origins. Ultimately, to properly inform patients of optimal treatment regimen options and prognosis.

Reviewer B

1. It is suggested to add reference citation to the following sentence.

…Vasconcelos et al sought to examine the efficacity of anti-EGFR therapeutic agents in the treatment of transverse colon adenocarcinoma via a retrospective pooled population analysis of two prospective randomized Canadian Cancer Trials Group/Australian Gastro-Intestinal Trials Group (CTG/AGITG) trials.

Reply 2: Thank you for this suggested edit. The citation has been added.

Changes in the text: Citation 24 (highlighted in red). Page 6, Second paragraph

2. Table 1:

- Provide a header for the first column.
- it should be P <?
- Provide OR/HR etc. for DCR and ORR.
- Indicate if they are median PFS and OS?

	Transverse Colon (n = 32)	Left Sided Colon (n = 420)	Right Sided Colon (n = 101)
Cetuximab vs SC	DCR: 27.3% vs. 20.0% (CI 0.25–9.18; P= 0.66) PFS: 1.8 vs 1.3 months HR: 0.57 (CI 0.26-1.28, P= 0.16) OS: 5.9 months vs 2.1 months HR 0.63 (CI 0.28-1.42, P = 0.26)	DCR: 60.7% vs. 13.5% (CI, 4.91–19.90 P = < 0.0001) PFS: 3.8 vs 1.8 months HR: 0.37 (CI 0.28-0.48, P= < 0.0001) OS: 9.7 months vs 4.9 months HR 0.51 (CI 0.39-0.68, P = < 0.0001)	DCR: 33.7% vs. 16.7% (CI 0.52–12.3 P =0.25) PFS: 1.9 vs 1.9 months HR: 0.7 (CI 0.38-1.3, P= 0.25) OS: 5.6 months vs 4.7 months HR 0.68 (CI 0.35-1.32, P = 0.25)
ORR with Cetuximab	ORR: 0% (CI, 0–15.4)	ORR: 10.4% (CI 7.4–14.1)	ORR: 3.4% (CI, 0.7–9.5)
Sided Colon vs Transverse Colon: Cetuximab Alone	N/A	DCR: 60.7% vs. 27.3% (CI, 1.57–10.78 P = 0.004)	DCR: 33.7% vs. 27.3% (CI, 0.48–3.82 P = 0.58)

Reply 3: Thank you for these suggested edits. Our responses are as follows:

-First column header: Intervention

-Corrected to P <

-All DCR now have the appropriate OR associated. However, regarding ORR, as no response was observed in patients from the transverse colon group, a statistical comparison with right and left sided groups was not performed by the authors.

-"median" PFS and OS was added to the Table 1 caption

Changes in the text: An updated, editable table is provided separately with tracked changes.