

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

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**Title:** Current Update on Molecular Cytogenetics, Diagnosis and Management of Gastrointestinal Stromal Tumors

**Reviewer's code:** 05212164

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Postdoc

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** United States

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<b>Scientific quality</b>	<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 Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

Overall, a great review that has the potential to serve as an excellent reference/resource for the readers. Although there are some revision requests, I do believe if this manuscript is revised according to the following requests, it will be very educational for the readers.

1. Although some of the following sentences are common sense to some readers, it is still essential to provide appropriate evidence: [Introduction] GISTs can arise anywhere in the GI tract, most commonly from the stomach and small intestine. [Introduction] The majority of GISTs occur as a result of activating mutations in two receptor protein tyrosine kinases: KIT and/or platelet-derived growth factor receptor- $\alpha$  (PDGFRA). [Introduction] Surgical resection is the preferred management for small GISTs, while tyrosine kinase inhibitors – imatinib mesylate and sunitinib malate – serve as crucial targeted therapies for locally advanced and metastatic GISTs. [Pathology and Molecular Cytogenetics] In the pediatric population, GISTs typically do not have KIT or PDGFRA mutations, and generally demonstrate the epithelioid subtype and express CD117.

2. The following sentences seem to contain contradictions with each other. Please revise them into appropriate expressions to avoid misunderstandings. [Clinical Features] Metastases are uncommon (10-20% of cases), but can occur via local or hematogenous spread [Computed tomography] Metastases are present in approximately 50% of patients and often involve the liver and mesentery

3. [Magnetic resonance imaging] “The presence of intratumoral cystic change with low apparent diffusion coefficient (ADC) values are predictors of high malignant potential.” As more specific evidence has been provided in the past regarding this statement (described below), it should be revised or added accordingly. - (PMID: 25341135) There was a negative linear correlation between the ADC values and the malignancy risk of GISTs ( $r = -0.670$ ,  $p < 0.05$ ).

4. [Positron emission tomography-computed tomography] Please clarify the

type of the radioactive tracer (I assume the authors are describing regarding 2-deoxy-2-[fluorine-18]fluoro-D-glucose (18F-FDG)) 5. [Management and Surveillance] With the recent advances in molecular targeted therapy, many drug-specific and characteristic adverse effects have become known. Please add a description of this point. The followings are some important examples: o imatinib-associated intratumoral hemorrhage (PMID: 16549611) o sunitinib- and sorafenib-associated pancreatitis (PMID: 32302358) o imatinib- and sunitinib-associated pancreatic volume changes may indicate a worse prognosis in patients with GIST (PMID: 33281059, 27643769) 6. [Table 2] for MRI findings of primary and metastatic GISTs, negative linear correlation between the mean ADC values and the malignancy risk should be noted (PMID: 25341135) 7. [Figure legend 2] A) Axial CT image -> Axial contrast-enhanced CT image 8. [Figure legend 2] B) Axial fused PET CT image -> Axial fused 18F-FDG PET CT image 9. [Figure legend 2] C) “marked FDG avid”: please provide the SUV max. 10. [Figure legend 3] E) “marked diffusion restriction”: please provide the ADC value.