

## PEER-REVIEW REPORT

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

**Manuscript NO:** 63449

**Title:** Pancreatic cancer in 2021: What you need to know to win

**Reviewer's code:** 05429162

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Academic Fellow, Doctor, Research Fellow

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

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-28

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-05-08 06:28

**Reviewer performed review:** 2021-05-12 21:06

**Review time:** 4 Days and 14 Hours

<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 Grade E: Do not publish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 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
<b>Conclusion</b>	<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
<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**

Summary Tonini et al. reviewed the current status and future perspectives of the pancreatic cancer treatment and diagnosis. Although the manuscript well reviewed almost all the aspects of pancreatic cancer, there are some major points to be revised. Major points [INTRODUCTION] 1) I agreed that the median age at diagnosis in pancreatic cancer is 60s-70s, however, there is no evidence that the median age at diagnosis is limited in 71 years old (GBD 2017 Pancreatic Cancer Collaborators. *Lancet Gastroenterol Hepatol.* 2019 Dec;4(12):934-947. doi: 10.1016/S2468-1253(19)30347-4.) Please reconsider the main text. [Hereditary risks factors and screening] 1) Indeed the IPMNs has certain genetic mutation profile, however the IPMNs does not a hereditary diseases. I would recommend that the surgical resection for IPMNs and other cystic lesions should be on another independent paragraph. 2) In table 1, the frequency of the mutated genes, such as BRCA1 should be described (Holter et al. *J Clin Oncol.* 2015 Oct 1;33(28):3124-9. doi: 10.1200/JCO.2014.59.7401). [Biomarkers and early detection] 1) In the clinical practice, SPAN-1 and DUPAN-2 are also used as a tumor marker. Please mention about the sensitivities and specificities of the SPAN-1 and DUPAN-2 (Satake et al. *Pancreas.* 1994 Nov;9(6):720-4. doi: 10.1097/00006676-199411000-00008) 2) Recently, several reports showed the usefulness of duodenal juice for detecting pancreatic cancer (Sunegawa et al. *pancreas.* 2018 Jan; 47(1): 35-39.doi: 10.1097/MPA.0000000000000956). Please describe the usefulness of not only the pancreatic juice and pancreatic cyst fluid, but also other liquid materials. [DIAGNOSIS] 1) Endoscopic retrograde cholangiopancreatography (ERCP) is one of the key modalities for diagnosis of the PDAC. Please describe the pros and cons of the ERCP (Ishii et al. *Diagnostics (Basel).* 2021 Feb 4;11(2):238. doi: 10.3390/diagnostics11020238.) 2) In the "Biopsy" section, the risk of needle-tract seeding when performint EUS-FNA should be described, although it doesn't affect to the patient's overall survival (Yane et al. *Dig Endosc.* 2020

Jul;32(5):801-811. doi: 10.1111/den.13615). [Surgery; Whipple's operation] 1) The Whipple's operation does not a common terminology except in the US. Please use the term of "pancreatoduodenectomy" or "pancreaticoduodenectomy". 2) Recently, the Blumgart anastomosis seems to reduce the risk of post-operative pancreatic fistula (Ricci et al. World J Surg. 2021 Jun;45(6):1929-1939. doi: 10.1007/s00268-021-06039-x.). Please describe comprehensive review of the complications of the pancreatoduodenectomy and describe the technique to reduce the risk of these complications. [Chemotherapy for resectable PDAC and BR-PDAC borderline resectable PDAC] [Immunotherapy] 1) Overall, these paragraphs contained several clinical trials with various evidence levels. We cannot discuss without mentioning the evidence levels of the trials. For example, therapeutic cancer vaccines don't have high-quality evidence compared with conventional chemotherapies and immune checkpoint inhibitors. I would recommend to show evidence level and clinical trial phase in each trial, and make a table to show these so that the readers easily understand. [Chemotherapy for resectable PDAC and BR-PDAC borderline resectable PDAC; Neoadjuvant chemotherapy (NACT)] 1) When discussion neoadjuvant chemotherapy for resectable/borderline-resectable PDAC, Gemcitabine+S-1 regimen should be described. Please mention about the result of the PREP-02/JSPS-05 study (Motoi et al. Jpn J Clin Oncol. 2019 Feb 1;49(2):190-194. doi: 10.1093/jjco/hyy190.) Minor points [Immunotherapy; Immune checkpoint blockade] 1) The term used in this section should be consistent. I would recommend to use immune checkpoint inhibitors instead of using immune checkpoint blockade.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<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

This paper is a significant contribution, and I think the current revision can be accepted



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