## Contents

**REVIEW**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2403</td>
<td>Prehabilitation prior to intestinal resection in Crohn’s disease patients: An opinion review</td>
<td>Bak MTJ, Ruiterkamp MFE, van Ruler O, Campmans-Kuijpers MJE, Bongers BC, van Meeteren NLU, van der Woude CJ, Stassen LPS, de Vries AC</td>
</tr>
</tbody>
</table>

**MINIREVIEWS**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2429</td>
<td>Metabolic aspects of hepatitis C virus</td>
<td>El-Kassas M, Awad A</td>
</tr>
</tbody>
</table>

**ORIGINAL ARTICLE**

### Basic Study

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
</table>

### Retrospective Study

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2457</td>
<td>Application of endoscopic ultrasonography for detecting esophageal lesions based on convolutional neural network</td>
<td>Liu GS, Huang PY, Wen ML, Zhuang SS, Hua J, He XP</td>
</tr>
<tr>
<td>2468</td>
<td>Prognostic value of preoperative enhanced computed tomography as a quantitative imaging biomarker in pancreatic cancer</td>
<td>Gao JF, Pan Y, Lin XC, Lu FC, Qiu DS, Liu JJ, Huang HG</td>
</tr>
</tbody>
</table>

### Observational Study

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2494</td>
<td>Accurate and generalizable quantitative scoring of liver steatosis from ultrasound images via scalable deep learning</td>
<td>Li B, Tai DI, Yan K, Chen YC, Chen CJ, Huang SF, Hsu TH, Yu WT, Xiao J, Le L, Harrison AP</td>
</tr>
</tbody>
</table>

### Randomized Controlled Trial

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
</table>
LETTER TO THE EDITOR

2523 Future therapies for pancreatic carcinoma: Insights into cancer precision medicine

Jiang QY, Chen ZX, Zhang S, Xue RY
## ABOUT COVER

Editorial Board of *World Journal of Gastroenterology*, Conrado M Fernandez-Rodriguez, MD, PhD, Associate Professor, Unit of Gastroenterology, Hospital Universitario Fundacion Alcorcon, Av. Budapest-1, Alcorcón, Madrid 28922, Spain. cfernandez@fhalcorcon.es

## AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (WJG, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

## INDEXING/ABSTRACTING

The WJG is now indexed in Current Contents®, Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Report® cites the 2020 impact factor (IF) for WJG as 5.742; Journal Citation Indicator: 0.79; IF without journal self cites: 5.590; 5-year IF: 5.044; Ranking: 28 among 92 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG’s CiteScore for 2020 is 6.9 and Scopus CiteScore rank 2020: Gastroenterology is 19/136.

## RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Hua-Ge Yu; Production Department Director: Xu Guo; Editorial Office Director: Ze-Mao Gong.

## NAME OF JOURNAL

*World Journal of Gastroenterology*

## ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

## LAUNCH DATE

October 1, 1995

## FREQUENCY

Weekly

## EDITORS-IN-CHIEF

Andrzej S Tarnawski

## EDITORIAL BOARD MEMBERS

http://www.wjgnet.com/1007-9327/editorialboard.htm

## PUBLICATION DATE

June 14, 2022

## COPYRIGHT

© 2022 Baishideng Publishing Group Inc

## INSTRUCTIONS TO AUTHORS

https://www.wjgnet.com/bpg/gerinfo/204

## GUIDELINES FOR ETHICS DOCUMENTS

https://www.wjgnet.com/bpg/GerInfo/287

## GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

https://www.wjgnet.com/bpg/gerinfo/240

## PUBLICATION ETHICS

https://www.wjgnet.com/bpg/GerInfo/288

## PUBLICATION MISCONDUCT

https://www.wjgnet.com/bpg/gerinfo/208

## ARTICLE PROCESSING CHARGE

https://www.wjgnet.com/bpg/gerinfo/242

## STEPS FOR SUBMITTING MANUSCRIPTS

https://www.wjgnet.com/bpg/gerinfo/239

## ONLINE SUBMISSION

https://www.f6publishing.com

© 2022 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com
Future therapies for pancreatic carcinoma: Insights into cancer precision medicine

Qiu-Yu Jiang, Zhi-Xue Chen, Si Zhang, Ru-Yi Xue

Abstract
Pancreatic carcinoma (PC) has one of the highest rates of cancer-related death worldwide. Except for surgery, adjuvant chemotherapy, chemoradiotherapy, and immunotherapy have shown various efficacies depending on the stage of the patient. We read the review “Current and emerging therapeutic strategies in pancreatic cancer: Challenges and opportunities” and offer some opinions that may improve its precision and completeness. This review presents a map of appropriate therapies for PC at different stages. Based on the clinical trial outcomes mentioned in the review, we evaluated the potential therapeutic options for PC and helped explain the contradictory efficacy between different programmed cell death protein 1/programmed cell death ligand 1 clinical trials, which may have resulted from the unique features of PC. Although R0 resection and adjuvant chemotherapy are still the gold standards for PC, new modalities, with or without clinical validation, are needed to establish more specific and precise treatments for PC.

Key Words: Pancreatic carcinoma; Immunotherapy; Chemotherapy; Radiochemotherapy; Future therapies

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.
For the treatment of pancreatic carcinoma (PC), although surgery with adjuvant chemotherapy or chemoradiotherapy remains the gold standard for most patients, attention needs to be given to immunotherapy and other research hotspots. In addition to programmed cell death protein 1/programmed cell death ligand 1, we suggest that immunotherapies such as agonistic CD40, adoptive T cell therapy, myeloid-targeted therapies, stroma-targeted therapies, multiple immunomodulatory agents, and other treatments such as small-molecule inhibitors, antibodies, or viruses targeting tumors, as well as gene editing techniques, may help improve the prognosis of patients with PC in the future.

Citation: Jiang QY, Chen ZX, Zhang S, Xue RY. Future therapies for pancreatic carcinoma: Insights into cancer precision medicine. World J Gastroenterol 2022; 28(22): 2523-2526
URL: https://www.wjgnet.com/1007-9327/full/v28/i22/2523.htm

TO THE EDITOR
We read with interest the review “Current and emerging therapeutic strategies in pancreatic cancer: Challenges and opportunities” by Manrai et al[1], who summarized the current and emerging therapeutic strategies in pancreatic cancer (PC). We agree with the main thrust of this review and want to share some ideas after a careful review and further analysis of this article.

First, we consider this topic to be of practical significance. PC is a rare cancer (3.2% in the United States in 2020[2]), but with increasing incidence and mortality (5-year overall survival: 9% in the United States[2]), it remains a burden worldwide without promising effective therapies. In this review, the authors systematically summarized the mainstream clinical trial outcomes and focused on the challenges and available treatment modalities for PC at different stages, especially the standard management of resectable, borderline resectable, locally advanced, and advanced metastatic PC. The standard management for resectable or borderline resectable PC is surgery followed by adjuvant chemotherapy. The efficacy of adjuvant or neoadjuvant chemotherapy and chemoradiotherapy has been assessed in several clinical trials. The standard treatment for locally advanced and advanced metastatic PC is gemcitabine-based chemotherapy. In addition, newer potential modalities such as immunotherapy, targeted therapy, macrophage-targeted therapy, and cancer vaccines were also mentioned, providing researchers with guidelines for present clinical applications and future research work.

Second, the efficacy of the targeted agent erlotinib in combination with gemcitabine may depend on the different stages of PC, as confirmed by various clinical trials. In contrast to the efficacy shown in patients with metastatic PC, we found that two large clinical trials that focused on different stages of PC showed little benefit. The phase III LAP07 trial in 2016 investigated the clinical value of erlotinib combined with gemcitabine in patients with locally advanced PC. Unfortunately, the median overall survival of patients who received gemcitabine alone was 13.6 mo (95% confidence interval (CI): 12.3–15.3 mo) compared with 11.9 mo (95%CI: 10.4–13.5 mo) for patients receiving gemcitabine plus erlotinib[3]. The multicenter randomized phase III CONKO-005 Trial in 2017[4] assessed this combination therapy in patients with resectable PC after R0 resection and showed median disease-free survival of 11.4 mo vs 11.4 mo (gemcitabine alone) and median overall survival of 24.5 mo vs 26.5 mo. To date, such targeted agents combined with conventional chemotherapy may not show much of an advantage. We expect to see more advances in the future.

Thirdly, in the section “Immunotherapy for pancreatic cancer,” the authors stated that popular programmed cell death protein 1/programmed cell death ligand 1 (PD-1/PD-L1) suppressor pembrolizumab had limited performance in the phase II KEYNOTE-158 study, due to the rare metastatic microsatellite instability in PC. This type of poor reactivity has been explained by several unique factors in PC: The well-recognized suppressive elements in the tumor microenvironment; the functional and structural barrier imposed by stromal components; T-cell exhaustion; possible choice of the wrong immune targets; and microbial factors, including gut dysbiosis and the unexpected presence of tumor microbes[5]. We agree with this, but we want to add that the clinical feasibility of PD-1 inhibitors deserves to be recognized. Recently, several clinical trials have examined the efficacy of conventional chemotherapy in combination with PD-1 inhibitors and other antagonists that mobilize T-cell activation and have shown mild but promising success. The phase Ia COMBAT trial in 2020 utilized the CXC chemokine receptor 4 antagonist BL-8040 (motixafortide), which promoted T-cell tumor infiltration, combined with pembrolizumab and chemotherpay in metastatic pancreatic adenocarcinoma, showing that BL-8040 may increase the benefit of chemotherapy. It revealed an overall response rate of 32%, disease control rate of 77%, and median duration of response of 7.8 mo[6]. Another phase I ARC-8 trial in 2021 also preliminarily validated the feasibility of combining chemotherapy with the PD-1 inhibitor zimberelimab and AB680, which is an inhibitor of CD73, to reduce adenosine generation and thus proliferating T cells. Eleven of the 13 patients who received treatment for at least 16 wk experienced...
tumor shrinkage or stabilization[7,8]. Although the outcomes were not significant, they were encouraging, and future larger controlled studies are needed, and we are hopeful of good results. We believe that the abovementioned factors will be discussed in the future.

Importantly, except for the newer modalities mentioned in the review, we found that more therapies should be included. According to previous studies, other opportunities for PC immunotherapy, such as agonistic CD40, adoptive T cell therapy, myeloid-targeted therapies, stroma-targeted therapies, and multiple immunomodulatory agents are worthy of attention, and their efficacy in various PC stages has been proven by numerous clinical trials[9].

In conclusion, this review provides a valuable clinical reference for the management of PC, helping young clinicians to learn of appropriate clinical strategies for PC. It sheds light on different strategies for dealing with PC at different stages. In addition, it summarizes both the gold standard treatments and new therapeutic strategies such as immunotherapy and targeted therapy, which can guide clinicians and researchers to find a more promising combined treatment for PC. Recently, in different types of cancer, small molecule inhibitors, antibodies, or viruses targeting tumors, as well as gene editing techniques like CRISPR-Cas9 have shown antitumor potential, based on abundant research. We should always keep in mind that although early diagnosis and R0 resection are the first and best choice for PC patients, adequate basic research is still needed aimed at new targets or mechanisms that may provide patients with more specific and precise medical care to improve their prognosis.

FOOTNOTES

**Author contributions:** Jiang QY and Chen ZX wrote the original draft; Xue RY conceptualized and reviewed the manuscript; Zhang S edited and revised the manuscript.

**Conflict-of-interest statement:** The authors declare no conflict of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Country/Territory of origin:** China

**ORCID number:** Qiu-Yu Jiang 0000-0003-2874-8152; Zhi-Xue Chen 0000-0002-2534-0090; Si Zhang 0000-0002-5682-4995; Ru-Yi Xue 0000-0002-5710-0091.

S-Editor: Fan JR
L-Editor: Kerr C
P-Editor: Fan JR

REFERENCES


