

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

ESPS manuscript NO: 26102

Title: Clinical impact of chemotherapy to improve tumor microenvironment of pancreatic cancer

Reviewer's code: 02446370

Reviewer's country: France

Science editor: Jing Yu

Date sent for review: 2016-04-01 13:07

Date reviewed: 2016-04-18 21:14

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This mini-review browses the latest data on chemotherapy regimens for pancreatic cancer associated with chemotherapeutic agents targeting cellular and acellular microenvironment. It is well written and of interest for the people working in the field. Minor points: - page 1 correct contractions for contributions - conclusion correct conclusion - correct immunotherapy for immunotherapy

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

ESPS manuscript NO: 26102

Title: Clinical impact of chemotherapy to improve tumor microenvironment of pancreatic cancer

Reviewer's code: 02677979

Reviewer's country: United States

Science editor: Jing Yu

Date sent for review: 2016-04-01 13:07

Date reviewed: 2016-04-26 23:52

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

GENERAL CRITIQUE: THE REVIEW LACKS INFORMATION ON THE MORE IMPORTANT ISSUES ON CHALLENGING CURRENT THERAPY STRATEGY BY SHOWING THE ADVANTAGES AND DISADVANTAGES OF CHEMOTHERAPY-IMMUNOTHERAPY MODALITY. ABSTRACT IS CONTRACTED AND DOES NOT REFLECT WHAT IS THE HOME TO-TAKE-MESSAGE. CONCLUSIONS ARE NOT COMPREHENSIVE AND LACK OF CLEAR FUTURE DIRECTIONS IN THE SUBJECT. THE MS SHOULD INCLUDE TABLES AND DIAGRAMS (FIG) ON THE MATTER DISCUSSED WITH ANNOTATED REFERENCES. DETAILED CRITIQUE: 1. page 3- introduction: " PC is the fifth leading cause of death worldwide". However, more recent papers (Siegel RL et al, Cancer Statistics 2015) describes PC as the 4th cause of cancer death and is expected to be the second cause of cancer death by 2030 in Western countries 2. Page 4- overview of standard chemotherapy for PC: what was the survival benefit of other chemotherapeutic regimens compared to gemcitabine alone? (for example: MPACT trial, consisting of Gem+Nab-paclitaxel had OS (overall survival) of 8.5 months compared to 6.7 months in

patients treated with gemcitabine alone). Mentioning this data allows to better understand the minimal improvement of survival by current chemotherapy regimens 3. Authors should describe treatment regimens for patients with PC based on stage (Locally advances vs metastatic) and patient performance status. Also, what is the benefit of radiation in combination with chemotherapy before surgery ? 4. It should be mentioned that the low 5 years survival rate is due also to chemoresistance ,relapse and metastasis even after surgical resection 5. Page 6- infiltrating T lymphocytes- it is worth mentioning that there is a study by Tewari N et al, BMC Cancer 2013) that demonstrated a positive correlation between prognosis and the presence of tumor infiltrating T cells 6. Page 6- regulatory T cells- a study by Yamamoto et al, Pancreas 2012) shows that low Treg percentage in circulation at 1 year after PC resection correlates with improved survival. Another paper by Keinan BP et al, Gastroenterology 2014) showed that immunization of mice with Listeria Monocytogenes engineered to express k-ras along with depletion of Treg cells reduces progression of early stages PAN INs. This could describe the role of Treg in cancer development. 7. Page 9- Myeloid derived suppressor cells (MDSCs). A paper worth mentioned in the review is by Markowitz et al, 2014, Cancer Immunology that describes MDSC in peripheral blood as a possible predictive biomarker of chemotherapy failure in PC patients 8. A few data regarding dendritic cells, another component of tumor microenvironment should be added- is has been showed that in PC, dendritic cells display maturation defects (Tjomsland V et al, PLoS One, 2010). Therapy aimed at improving DC function could be beneficial in PC treatment. 9. A subchapter regarding vaccine therapy against PC should be added 10. Throughout the paper, there are multiple words that are misspelled. For example: page 8- title "Myeloid derived suppressor cells" or page 11: " Conclusions"

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

ESPS manuscript NO: 26102

Title: Clinical impact of chemotherapy to improve tumor microenvironment of pancreatic cancer

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Reviewer's country: China

Science editor: Jing Yu

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In this Mini review manuscript, the authors reviewed the current status of chemotherapy in tumor microenvironment in pancreatic cancer. This review is informative and interesting. It summarized the potential roles of chemotherapy in immunomodulation. The authors mentioned that the effect of chemotherapeutic drugs on immune cells is controversial. It would be grateful to discuss in more detail on the mechanism underlying chemotherapeutic drugs modulation on immune cells.