

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 17416

Title: Intensified intensity modulated radiotherapy in anal cancer with prevalent HPV p16 positivity

Reviewer's code: 02753679

Reviewer's country: Switzerland

Science editor: Jing Yu

Date sent for review: 2015-03-07 15:56

Date reviewed: 2015-03-25 04:38

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 checked="" type="checkbox"/> Grade C: Good	<input checked="" 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 paper reports on the 2-years outcome of 41 consecutive patients with anal cancer treated with HT using a simultaneous integrated boost technique. I have some comments: Material and methods: 1. The authors need to clarify if the study represents a retrospective series or data analyzed have been prospectively collected. 2. Dose constraints for OARs used for inverse planning are not mentioned in the text. The authors observed a relatively low rate of hematological toxicities compared to other studies: did they apply dose constraints for iliac crests to reduce hematological side effects? A table illustrating the OARs dose constraints and dosimetric results would be welcomed. 3. The authors should clarify if local failure concerned the relapse in the anal canal only or in the pelvic nodes too. This point is not clear (paragraph toxicity and follow-up). 4. Were the tumors located in the anal canal only or some lesions were found in the anal margin too? 5. The authors did not find in their cohort of patients any prognostic value of the HPV p16 positivity. However, recent literature showed a clear prognostic value of HPV infection with better prognosis in positive patients. As this point constitutes a major point of the paper (cfr title of the manuscript), the author should better comment

on that on the discussion section. 6. Why late toxicities were assessed only at the 6 month follow-up endpoint? 7. Kaplan-Meier curves: Please report on colostomy-free survival rates and KM estimates for stage I-II vs stages IIIA and IIIB. Minor comments: - Results: some data (age, gender) are repeated twice in the manuscript (result section and Table I). - - Tables II and III: please add Grade 0 toxicity and report on the total number of patients analyzed - - Figure 1. Please add numbers of patients at risk to the three figures.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 17416

Title: Intensified intensity modulated radiotherapy in anal cancer with prevalent HPV p16 positivity

Reviewer's code: 02962220

Reviewer's country: Australia

Science editor: Jing Yu

Date sent for review: 2015-03-07 15:56

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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 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

Thank you for the opportunity to review your paper. Overall this is a good article but I found it difficult to read because of grammatical errors - this will need to be proof read again please. Some other comments to help improve your paper. **MAJOR ESSENTIAL CHANGES** I found it difficult to follow the discussion. As it stands it is one big paragraph with no obvious structure. Can I suggest you please break this up into several paragraphs using topic sentences to introduce each paragraph. A good discussion will include the following points 1) Statement of principal findings 2) Strengths and weaknesses of the study 3) Strengths and weaknesses in relation to other studies, discussing particularly any differences in results 4) Meaning of the study: possible implications for clinicians and policymakers 5) Unanswered questions and future research **MINOR ESSENTIAL CHANGES** Abstract: Aim - could you define if you are looking at intracanal or perianal cancer? Introduction - has SIB been used for other cancers besides anal cancer? Can you please reference? materials and methods - population - could you please describe your Institute - is it a tertiary hospital? private? public? urban? regional? pg 6 under toxicity and follow up



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

- what sort of follow up investigations were done at 3 monthly intervals and then 6 monthly intervals?
pg 7 - can you please reference the Common Toxicity Criteria for Adverse Events and RTOG criteria?
Results - there seems to be an unusually large skew of anal cancer to women. Is this because the males did not want to participate in the research? Please clarify. pg 8 - under chemoradiotherapy - could you specify the hematological toxicity and cardiovascular disease you mention in the last line?

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 17416

Title: Intensified intensity modulated radiotherapy in anal cancer with prevalent HPV p16 positivity

Reviewer's code: 03002354

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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 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
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

It is an interesting paper about anal canal cancer treatment but it is not the first publication in this field. The follow-up is a little bit short. We need more informations about the population : histologic characteristics etc... How are defined low-risk and high-risk categories ? Is it important because, all the patients seem to be in the high-risk category ? Paragraph population : Is the last sentence is at the good place ? Toxicity : I don't understand the results, how more than 50% of patients need major anagesic therapy without garde 3 toxicity ? we need for more informations about pain. I don't agree with the authors when they state that the increase in radiotherapy dose is useful (page 10 and last sentence) (D Peiffert J Clin Oncol 2012). The authors must justify this opinion.