



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 35768

Title: Neoadjuvant hyperfractionated accelerated radiotherapy plus concomitant 5-FU infusion in locally advanced rectal cancer: A phase II study

Reviewer's code: 03262130

Reviewer's country: South Korea

Science editor: Jin-Xin Kong

Date sent for review: 2017-09-07

Date reviewed: 2017-09-15

Review time: 8 Days

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"/> 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 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

The authors explored preop HyperFx RT with conc. CTx for rectal cancer.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 35768

Title: Neoadjuvant hyperfractionated accelerated radiotherapy plus concomitant 5-FU infusion in locally advanced rectal cancer: A phase II study

Reviewer's code: 02411100

Reviewer's country: Israel

Science editor: Jin-Xin Kong

Date sent for review: 2017-09-07

Date reviewed: 2017-09-16

Review time: 8 Days

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
<input checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

This study was trying to evaluate the side effects and effectiveness of hyperfractionated accelerated radiotherapy with concomitant 5fu infusion in locally advanced rectal cancer patients. I have few major comments 1. This is a very small group of patients with limited follow up – this is a major limitation that should be discussed in the discussion section. 2. I suggest to change a part of the title from "concomitant chemotherapy" to concomitant 5fu infusion" 3. In the introduction, you state that " In randomized studies, local-regional recurrence despite mesorectal resection has been reported to occur in 15 to 30% of the patients undergoing surgery alone [3-8]." This statement is based on old data. Currently the rate of local recurrence without neoadjuvant radiotherapy for stage 2-3 rectal cancer averages 10%. (the Dutch trial and others) 4. There is a growing evidence that T3 rectal cancer with large circumferential margins (CRM) can be spared the



**Baishideng
Publishing
Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

preoperative treatment. Preoperative CRM is evaluated with MRI. It would be interesting to know how many patients in your group had T3N0 with a preoperative MRI evaluation of CRM > 2 mm and what was their long-term outcome. 5. In your very small series and limited follow up, one patient, (3.3%) had local recurrence. This rate is comparable to known data from larger studies with larger follow up time that evaluated preoperative radiotherapy without concomitant chemotherapy (5% local recurrence in the Dutch study). Thus, you cannot state, as you stated in your conclusions, that your protocol achieves better local control. 6. You have shown to achieve a 52% of complete or near-complete pathological response (which is a nice percentage). However, you did not report whether this was translated into a better disease-free and overall survival. Please report on the disease-free and over all survival of patients with complete or near-complete pathological response compared to patients with less favorable pathological response. If the 52% was not translated into better long-term outcome coupled with the fact that you did not show a better local control than standard preoperative radiotherapy (comment no. 5), It wouldn't be accurate to state that your results are "encouraging". 7. In the 3rd line of the discussion, I believe that the word "adjuvant" was a grammatical mistake and should be changed to "neoadjuvant"



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 35768

Title: Neoadjuvant hyperfractionated accelerated radiotherapy plus concomitant 5-FU infusion in locally advanced rectal cancer: A phase II study

Reviewer’s code: 03094792

Reviewer’s country: Spain

Science editor: Jin-Xin Kong

Date sent for review: 2017-09-07

Date reviewed: 2017-09-17

Review time: 10 Days

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
<input checked="" 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 checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

Congratulations on the initiative to do this phase II and to communicate the negative results. It is necessary for the advancement of radiation oncology. Observations: “Besides conventional radiotherapy (RT) consisting of 45-50 Gy/1.8-2 Gy/5-6 weeks, hypofractionated and hyperfractionated accelerated RT (HART - 42 Gy/1.5 Gy/18 days) are also used” The hypofractionated schemes are standard treatment in northern Europe. In addition its effectiveness has the level I of scientific evidence. In contrast, all hyperfractionated schemes are still experimental. They can not be grouped. In Table 1, you should include the estadio. And specify the T and N parameters together. For example, knowing the percentage of T2N0 and T3N0 gives great information about the characteristics of the analyzed series. “Positive margins have been found in two patients (6.6%).” You should include the number of cases in which the mesorectal



**Baishideng
Publishing
Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

fascia was involved in MR staging. And contrast this information with the state of the surgical margins. “In our study, radial surgical margin positivity was 7%” It would be a great contribution to the discussion if you included the relation of the appreciated local recurrences and the state of the resection margins. “Therefore, a biological effective dose (BED) formula was used for dose calculations instead of the given dose, according to a time-corrected linear quadratic model [30-31].” It would be interesting to specify in the text the BED of the scheme you used and compare it with the BED of the standard schemes. “The ongoing Stockholm III study is expected to shed some light on the effects of the timing of surgery [35]” This study is already published and you can refer to its results. “Surgical margin seems to be the most important factor for local recurrence [36].” For this reason you should provide the status of the mesorectal fascia in the staging MR.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 35768

Title: Neoadjuvant hyperfractionated accelerated radiotherapy plus concomitant 5-FU infusion in locally advanced rectal cancer: A phase II study

Reviewer's code: 00739752

Reviewer's country: Turkey

Science editor: Jin-Xin Kong

Date sent for review: 2017-09-07

Date reviewed: 2017-09-21

Review time: 14 Days

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"/> 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 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

In the abstract, in the conclusions word of the end of the first sentence (and) must be remove.