

**ESPS Peer-review Report**
**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 8325

**Title:** Long-term results of a “wait and see” strategy for rectal cancer achieving a pathological complete response after chemo-radiation and laparoscopic mesorectal excisio

**Reviewer code:** 00503612

**Science editor:** Su-Xin Gou

**Date sent for review:** 2013-12-26 09:57

**Date reviewed:** 2013-12-27 03:55

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

**COMMENTS TO AUTHORS**

I appreciate the opportunity to review this study. A few comments/questions: 1. You have performed surgery between 5-8 weeks. Prior studies have differences in outcomes based on this, did you? 2. More than anything, I disagree with your title. Wait and see with rectal cancer is traditionally used for patients who get a complete clinical response and then are not offered therapy. I think this confuses the population, the methodology and you need to change this by removing this from the title and in the manuscript. 3. Several errors in grammar and punctuation are present. Missing periods, misspellings. Please re-review. 4. Please clarify if the type of surgery (LAR vs APR) was in your multivariate analysis of DFS and OS. If note, it must be. 5. The discussion is not focused. Please have each section divided up by a thought (DFS, OS) then review in light of your findings and the literature.

# ESPS Peer-review Report

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

**ESPS Manuscript NO:** 8325

**Title:** Long-term results of a “wait and see” strategy for rectal cancer achieving a pathological complete response after chemo-radiation and laparoscopic mesorectal excision

**Reviewer code:** 00928913

**Science editor:** Su-Xin Gou

**Date sent for review:** 2013-12-26 09:57

**Date reviewed:** 2013-12-28 17:50

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

García-Albéniz et al. conducted a clinical study regarding long-term results of patients with ypT0N0 after conventional CRT and laparoscopic mesorectal excision without adjuvant therapy by analyzing 176 patients were treated with induction CRT and 170 underwent total mesorectal excision. They found that after a median follow-up of 58.3 months, patients with ypT0N0 have a 5-year disease-free survival and overall survival rate of 96% (95% CI 77 to 99%) and 100% (95% CI not estimable) respectively. The degree of pathological response is an important predictor of DFS and OS in both cohorts. Therefore, they concluded that withholding the adjuvant chemotherapy from those patients achieving a complete response after standard neoadjuvant CRT and laparoscopic mesorectal excision, if treated by an experienced multidisciplinary team, might be a reasonable option. Though this paper is relatively interesting and informative; however, there are a lot of criticisms and have the following comments that the authors need to address before the manuscript is suitable for publication. Major Compulsory Revisions: 1. The major flaw was the definition of the response as complete response, intermediate response and poor response by authors’ own standards, but not according to common used criteria such as based on a standardized tumor regression grading (TRG) as described by Dworak et al. (O. Dworak, L. Keilholz, A. Hoffmann, “Pathological features of rectal cancer after preoperative radiochemotherapy,” International Journal of Colorectal Disease, vol. 12, no. 1, pp. 19–23, 1997.). 2. In the Patients and Methods section, exclusion criteria for CRT treatment into the study were; (i) early stage (cT1-2N0), but in Table 1, 2 patients were classified into cT2N0? 3. Any patient develops distant metastasis after pre-operative CRT? It is estimated approximately 3-5% of

locally advanced rectal cancer patients would occur. 4. In table 2, baseline CEA level and days of admission following surgery were also predictive for DFS; in table 3, baseline CEA level was predictive for OS. But how to category studied patients into 2 groups of baseline CEA level and days of admission following surgery respectively should be addressed in more details in the text. 5. Regarding statistical analysis paragraph, multivariate analysis was built with those variables with a p-value < 0.10 in the univariate analysis. Why multivariate analysis was not built with those variables with a p-value < 0.05 in the univariate analysis as the common used criteria. 6. In Discussion section (page 16): However our study has a long follow-up and it is the first evaluating the natural history of patients after CRT without adjuvant therapy and included all patients with > cT3, mid and low rectal tumors younger than 85 years evaluated in this period, reflecting a non-selected population of patients. But in table 1, median distance from tumor to anal margin is up to 15 cm, upper rectal cancer patients were actually included in the current study. Minor Essential Revisions: 1. Histologic grade, lymphovascular invasion and perineural invasion are suggested to be analyzed simultaneously in the revised manuscript.

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**ESPS Manuscript NO:** 8325

**Title:** Long-term results of a “wait and see” strategy for rectal cancer achieving a pathological complete response after chemo-radiation and laparoscopic mesorectal excisio

**Reviewer code:** 00070140

**Science editor:** Su-Xin Gou

**Date sent for review:** 2013-12-26 09:57

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

None

# ESPS Peer-review Report

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

**ESPS Manuscript NO:** 8325

**Title:** Long-term results of a “wait and see” strategy for rectal cancer achieving a pathological complete response after chemo-radiation and laparoscopic mesorectal excision

**Reviewer code:** 00181023

**Science editor:** Su-Xin Gou

**Date sent for review:** 2013-12-26 09:57

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The manuscript entitled “Long-term results of a “wait and see” strategy for rectal cancer achieving a pathological complete response after chemo-radiation and laparoscopic mesorectal excision” which is presented by X. García-Albéniz and co-workers is a retrospective database analysis of rectal cancer patients who received neoadjuvant treatment. Those, who experienced complete remission, were not given adjuvant treatment and showed a very good outcome. A validation cohort is provided. In general, the study is well performed, the manuscript well written and easy to follow. Some comments have to be made. Major 1. Data how the pathological diagnosis was made are incomplete: Were routine diagnoses used? Was central pathology reading performed? The number of complete remissions is comparably high – how much effort was undertaken to find residual cancer foci (e.g. embedding of the whole tumor area, step sections, immunohistochemistry)? 2. You group the patients into the following groups: complete response, intermediate response, and poor response. In general, I believe this is feasible, but a rational and/or reference for this approach is mandatory. In addition, I deeply miss standard regression grading (e.g. according to Dworak) – why was it not performed? In my eyes this is necessary to enhance the comparability with other studies. 3. I feel, the validation cohort is not “ideal” as it is a cohort with rectal cancer patients who received neoadjuvant therapy, but not a cohort in which ypT0N0 patients did not receive adjuvant therapy. In this central aspect (please compare the title of your submission), you compare your 26 patients with just one single case, and this cannot, strictu sensu, be called “validation”. Minor 1. The identification number of the specific ethics committee vote is missing, please provide. 2. In the

material and methods section you refer to exclusion criteria, but inclusion criteria are not provided here (only in the introduction), please present the inclusion criteria where appropriate. 3. In the results section you refer to the median number of harvested and/or identified lymph nodes and give the range. We would also like to know about the percentage of cases in which you achieved a minimum of twelve nodes: in the entire cohort and in the three groups (table 2). 4. I like that you “mainly” have rounded the percentages to integers which is reasonable. But you have not done this consequently everywhere in the results section, please correct. 5. In the second paragraph of page 11, relapse is noted in 42 (43%) patients in the group with poor response, but percentages are not provided for the groups with intermediate response (this would be 6%, if I calculated it correctly) and complete response (4%). Looking at these so far missing percentages you see that the rate of relapse is also low in the group with intermediate response, how do you explain this? Should these patients receive adjuvant therapy – why? 6. The first sentence of the discussion appears to be a bit misleading. What you have done is a retrospective data analysis of a (in the best case) prospectively generated database, but not something like a “prospective study”. 7. Table 1: Please also provide the terms “complete response”, “intermediate response”, and “poor response” in the heading of this table to increase the readers’ understanding. 8. The DOI-numbers are missing in the reference list (journal requirement).