

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12127

**Title:** Prolonged survival in gastric cancer patients after adoptive immunotherapy

**Reviewer code:** 00503433

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-06-24 16:07

**Date reviewed:** 2014-07-12 13:18

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"/> Existing	<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"/> Existing	<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

he manuscript entitled: "Prolonged survival in gastric cancer patients after adoptive immunotherapy" is an interesting study which is missing the required details for a proper scientific review. For instance: -Patient descriptions, case and control matching, ethical guidelines, patient consent, duration of follow-up, description of "loss to follow-up", specific details of EAAL generation and biosafety measures, time of EAAL therapy in regards to conventional surgery (partial/total gastrectomy), radio and chemotherapy....are missing. -Tables and graphs are vague and lack description of the mentioned indices -Some units of the obtained values are missing. These are only some of the points that do not allow for a proper review of the manuscript findings. Therefore, a major revision (by which all the needed details become available for review) is required at this time.

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12127

**Title:** Prolonged survival in gastric cancer patients after adoptive immunotherapy

**Reviewer code:** 00181101

**Science editor:** Ya-Juan Ma

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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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<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

the novelty of the immunotherapy should be acknowledged, however major drawbacks are evident:

- EAAL should be absolutely spelled out at first appearance in the abstract - page 5: "...Activated lymphocytes were generated using anti-CD3 monoclonal antibody (OKT3) and IL-2 as described previously [24]....". Please, check whether reference is correct - page 5: "...human AB serum...", please spell out - page 6: "...The eighty-four patients (aged 40-85 years) enrolled in the present study...": these are already results and should be put in the appropriate section - page 6 "... (cellular immunotherapy time ranged from 2-24, total immunotherapy time was 242, median immunotherapy time was 5)....". It is not clear what 'cellular immunotherapy time' is: is it the number of cellular immunotherapy administrations per patient (number of treatment cycles)? is it the time elapsed (in months) since study inclusion? anyhow, they are results and should be put in the appropriate section
- overall survival is not defined: in particular what is the T0 (study entry)? the time of EAAL treatment? the time of surgery? time of histological diagnosis? - page 7 "...EAAL cell proliferation at different time points is summarized in Fig. 1...": 'summarized' is not correct. It seems actually a 'representative example of T cells proliferation from a patient of EAAL cohort' - page 7: "...After 13.55±1.25 d of culture, the total cell number went from about 7.65±1.52×10<sup>6</sup> to 8.76±1.82×10<sup>9</sup>...", please specify in the methods when the cells are counted before and after incubation - page 7: please specify in the methods what 'Proliferation multiplicity' is and how is calculated, as it is not just the percentage increase in number of cells, which is about +14% - page 7: "...The survival rate of

effector cells was  $97.57 \pm 0.94\%$  (Table 1)... "please specify in the methods how Survival rate is measured (trypan blue dye?) - page 7: "...After in vitro culture and proliferation, the percentages of CD3+, CD3+CD8+, CD8+CD27+, CD8+CD28+, and CD3+CD16+/CD56+ cells increased remarkably ( $P < 0.05$ ), while CD3+CD4+, CD4+CD25+, CD3-CD16+/CD56+ (natural killer cells, NK) were overtly decreased ( $P < 0.05$ ); no significant change was observed in CD4+CD25+CD127- cells ( $P = 0.448$ , Table 2)....": this is not what is said in the abstract (which is "...the percentages of CD3+, CD3+CD8+, CD3+CD4+, CD8+CD27+, CD8+CD28+, CD4+CD25+, CD4+CD25+CD127-, CD3-CD16+/CD56+ and CD3+CD16+/CD56+ cells increased sharply ( $P < 0.05$ )..." - page 7: "...Among the 58 pathologically confirmed stomach cancer patients...", please specify "...among 58 'screened' patients" - page 8: "Chemotherapeutic features": timing and setting of chemotherapy delivery is completely incomprehensible: authors should clarify 1) if overall survival is calculated since start of chemotherapy, 2) 2 patients received only EAAL: were they metastatic/locally advanced? or radically resected?, 3) in the EAAL group 33 patients received first or subsequent line chemotherapy meaning they were metastatic or inoperable locally advanced, how does this fit with 10 patients in the EAAL group being stage I or II? is this stage at diagnosis or at study entry? if it is at diagnosis and patients are included in the study later on when they develop inoperable recurrence, then using stage in multivariate analysis is meaningless! 4) it is first said that 7 patients in the EAAL group received adjuvant chemotherapy and then that EAAL was administered with adjuvant chemotherapy in 13 patients! 5) it is methodologically incorrect to perform a unique survival analysis for patients with radically resected cancer on adjuvant treatment and patients with metastatic/inoperable disease - finally: inclusion criteria for EAAL treatment is missing, how were they selected for EAAL+chemo or for chemo alone? was this trial registered in a clinical trial registry? what is the registration number? (i.e. clinicaltrial.gov)

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12127

**Title:** Prolonged survival in gastric cancer patients after adoptive immunotherapy

**Reviewer code:** 02731948

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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"/> Existing	<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"/> 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"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Interesting article. No information about the aprovation of the therapy regimen, which is not common clinical practice by the ethical committee have been given. Only for the retrospective evaluation of data. If author have the approvation of the ethical committee to perform the therapy they should give data about it, otherwise the article cannot be accepted for pubblication. The article cannot be evaluated for pubblication before to have these necessary data.