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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37368

Title: High Tacrolimus intra-patient variability is associated with graft rejection, and de novo DSAs occurrence after liver transplantation

Reviewer's code: 00504591

Reviewer's country: Japan

Science editor: Xue-Jiao Wang

Date sent for review: 2017-12-05

Date reviewed: 2017-12-06

Review time: 19 Hours

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

Del Bello et al analyzed the risk factors of graft rejection, and de novo DSAs occurrence after liver transplantation and found that high tacrolimus intra-patient variability is one of the predictors. I have some comments. 1. What is the interval or indication to check the DSA after liver transplantation? 2. The authors described that "non-adherence to Tac seems to be the main cause of IPV in pediatric and adolescent liver transplantation". Is it also true in adults? Is the cause of high IPV related with non-adherence or non-compliance in the present study? Please discuss about it.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37368

Title: High Tacrolimus intra-patient variability is associated with graft rejection, and de novo DSAs occurrence after liver transplantation

Reviewer's code: 00051373

Reviewer's country: Taiwan

Science editor: Xue-Jiao Wang

Date sent for review: 2018-01-05

Date reviewed: 2018-01-06

Review time: 1 Day

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

Major comments This is a very interesting study design but lacking of the basic molecular data support such as genotype CYP3A4, CYP3A5 and multi-drug resistant 1 (MDR1). The author only used with the statistical method univariate and multi-variate analysis to explore the result. As we know, the HLA tapping is much difference from the donors between LDLT and DDLT. Tacrolimus concentration is closely related to the liver graft from the donors particularly when the recipients have difference genotypes in CYP3A4, CYP3A5 and MDR1. **Minor comments** Abstract: Un-structural present and lacking of conclusion at the end of abstract. Introduction: 1. In reference “ (1) (2) (3)” needs to be revise 2. In reference “(4) (5; 6)” it is not acceptable. Patients and Methods: 1. Donors’ age at transplantation is ranged from 9 to 85, the author needs to describe more detail 2. It is a LDLT or DDLT study needs to describe which should be impact the



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inter-individual and intra-individual variability 3. In reference “ (18) (19) (20)” needs to be revise Discussion: 1. In reference “ (14) (11) (22) (23)” it is a wrong list. 2. “The use of once-daily tacrolimus compared to a twice daily formulation has been found to improve adherence and IPV (11) (28). However, in our study, no significant difference between these Tac formulations was observed.” The author needs to describe and explain more detail. 3. The total number of patients receiving tacrolimus once daily is 164, but your study mentioned 116 cases were included. What’s it?



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37368

Title: High Tacrolimus intra-patient variability is associated with graft rejection, and de novo DSAs occurrence after liver transplantation

Reviewer's code: 02446483

Reviewer's country: Canada

Science editor: Xue-Jiao Wang

Date sent for review: 2018-01-05

Date reviewed: 2018-01-08

Review time: 3 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
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Figure 2 of the histograms should be implemented with the standard deviation. The section of the limitations should be expanded. Very interesting paper from a very good transplantation center!