

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 54138

Title: Pharmacogenetics of immunosuppressant drugs: A new aspect for individualized therapy

Reviewer's code: 02887553

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor, Surgeon

Reviewer's Country/Territory: Turkey

Author's Country/Territory: Italy

Manuscript submission date: 2020-01-10

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-01-11 09:03

Reviewer performed review: 2020-01-12 22:41

Review time: 1 Day and 13 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No



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7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

Dear Authors, This is an invited review summarizing the pharmacogenetics of immunosuppressant drugs. The article was well written. I have no comments. This review adds new perspectives to the existing literature on the same subject and provides the reader with new summary information. So, the manuscript should be published in World Journal of Transplantation. No other comment. Best regards.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 54138

Title: Pharmacogenetics of immunosuppressant drugs: A new aspect for individualized therapy

Reviewer's code: 03291363

Position: Editorial Board

Academic degree: MBBS, MD

Professional title: Doctor, Full Professor, Professor

Reviewer's Country/Territory: Australia

Author's Country/Territory: Italy

Manuscript submission date: 2020-01-10

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-01-15 10:20

Reviewer performed review: 2020-01-21 05:08

Review time: 5 Days and 18 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

• Interesting paper and logically presented • Table listing all the established improved outcomes using pharmagenetics (done by authors) • Medical editing is needed • Several tables lack references and explanations of how LOR and QOE are defined • A greater explanation of the meaning of GWAS is required • A reference for tacrolimus delivering better outcomes than CsA is required • An explanation on page 8 as to why a higher rejection rate was found if the tacrolimus level was possibly higher

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- [] The same title
- [] Duplicate publication
- [] Plagiarism
- [Y] No

BPG Search:

- [] The same title
- [] Duplicate publication
- [] Plagiarism
- [Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 54138

Title: Pharmacogenetics of immunosuppressant drugs: A new aspect for individualized therapy

Reviewer's code: 02726701

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Chile

Author's Country/Territory: Italy

Manuscript submission date: 2020-01-10

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2020-01-20 14:48

Reviewer performed review: 2020-01-24 22:32

Review time: 4 Days and 7 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Comments on Pharmacogenetics of Immunosuppressant Drugs: A New Aspect for Individualized Therapy This a very welcome article related to how to prescribe narrow therapeutic windows drugs considering inter patient variability and factors that determine how those drugs are metabolized and eliminated from the organism. At the same time, it describes subtle differences in the enzymes involved in that metabolism because their DNA sequences and introduces several terms now in use in labs and in clinical practice. The information comes from studies retrieved from PubMed and are carefully analyzed by the authors. Nevertheless, the article omits what is/are its objectives: To summarize what is actually known about pharmacogenetics of immunosuppressant drugs? To serve as a reference paper for basic science investigators? To serve as a practical clinical tool for physicians involved in the care of transplanted patients? • Pharmacogenetics of Calcineurin inhibitors section Clinicians are familiarized with different pharmacokinetics in transplanted patients and the authors nicely review the subjacent causes, but, at the same time, they give us a lot names of cytochromes and genes involved in the metabolism that are difficult to “memorize/learn”. But, it does not matter very much because they give us a “Summary section” that clarifies how to handle the above information. From this point of view, the two clinical trials, from France and Netherland, are “strategic” to the clinical reader. Please, add a comment of how the authors interpret those two trials and how do they implement that information to care for their patients. It seems that the utility of study patients’ genotype is more an academic issue more than a clinical necessity. Is it true? What do authors think about the impact to genotype if after a not so long post transplantation follow up, there is no differences in the evolutions of patients genotyped versus those not genotyped? • Sirolimus and Mycophenolic acid sections Both are OK,

probably because there is less information about genetics in metabolism or pharmacodynamics in comparison with the CNI section. A short analogy: Several years ago, there were experts that thought that therapeutic drug monitoring of mycophenolic acid could improve post-transplant care of solid organ transplanted patients. Nevertheless, this hypothesis was not demonstrated to be real (Ams W, et al. Transplantation. 2006 Oct 27; 82(8):1004-12). Could this experience be extrapolated to pharmacogenetics of immunosuppressive drugs? • Conclusions Good section, but, do authors coincide (after their very good job) with the French National Network of Pharmacogenetics? Please, add a comment about this issue. • Tables and Figure They are good, but, at the same time, they are arid to read. • References, abstract and Core tip OK. In summary, this is a very well structured paper about a “hot theme” in clinical transplantation. It is well written, bit, I think, it merits an adaptation to the potential readers more interested in the clinical applications of pharmacogenetics than in the genes involved in immunosuppressive drug metabolism.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism



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[Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 54138

Title: Pharmacogenetics of immunosuppressant drugs: A new aspect for individualized therapy

Reviewer's code: 00505314

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: Italy

Manuscript submission date: 2020-01-10

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2020-01-19 01:25

Reviewer performed review: 2020-02-13 15:35

Review time: 25 Days and 14 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this review article, the others discuss the current literature on pharmaco-genetics of immunosuppressive agents in organ transplantation. They discuss in detail the existing data on calcinerine inhibitors, mTOR inhibitors and mycophenolate mofetil. This is a detailed review and the article is written well. Unfortunately the current data does not show a positive impact of pharmaco-genetic analysis based drug dosing on long-term outcomes. As the authors suggested, more research is needed in this area before wide adoption of the concept of pharmaco-genetics in clinical organ transplantation. I believe this review article is useful for clinicians to extend their knowledge in this field.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No