BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: editorialoffice@wjgnet.com http://www.wjgnet.com

ESPS Peer-review Report
Name of Journal: World Journal of Orthopedics
ESPS Manuscript NO: 8580
Title: Tofacitinib for treatment of rheumatoid arthritis
Reviewer code: 02527882
Science editor: Huan-Huan Zhai
Date sent for review: 2013-12-31 09:38
Date reviewed: 2014-01-14 14:20

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

In this article, the mechanism of action and adverse event/safety profile of Tofacitinib are well described. I would suggest changing the title to "A Review of Pharmacology of Tofacitinib in the treatment of RA" and editing the manuscript to focus on the pharmacology aspect. The description under "Efficacy studies" is rather repetitive and has already been included in Table 1. I would suggest deleting major portion of this part of manuscript. This would also help reduce the length of manuscript and make it more focussed and readable. Please see the attached word document which has my comments in bubbles (Tracked changes).

BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: editorialoffice@wjgnet.com http://www.wjgnet.com

ESPS Peer-review Report
Name of Journal: World Journal of Orthopedics
ESPS Manuscript NO: 8580
Title: Tofacitinib for treatment of rheumatoid arthritis
Reviewer code: 00505024
Science editor: Huan-Huan Zhai
Date sent for review: 2013-12-31 09:38
Date reviewed: 2014-02-13 09:13

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[Y] Grade D (Fair)	[Y] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The subject matter is interesting. However, I have the following major concerns: 1, Abstract should summarize what is described in the paper, which is the pharmacology, safety and efficacy of tofacitinib. That should then be followed by approval status, not about guideline recommendations. Information, such as tofacitinib is a pan JAK inhibitor and RA synovium has increased expression of JAK-STAT pathway, etc, should included in the abstract. 2, The efficacy data should not be symply described as in original publications. The unique feature of each study should be mainly discussed, for example, the study durations were different, were there any different results with different terms of observations? The p value should be inserted in the table 2. The numbers alone do not mean anything to readers. 3, Incidence rate for each adverse event should be described. It is better to do intergrated analysis of all study data. 4. what are the authors position about the therapeutic agent? what is the advantage comparing with other agents?

BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: editorialoffice@wjgnet.com http://www.wjgnet.com

ESPS Peer-review Report
Name of Journal: World Journal of Orthopedics
ESPS Manuscript NO: 8580
Title: Tofacitinib for treatment of rheumatoid arthritis
Reviewer code: 02523327
Science editor: Huan-Huan Zhai
Date sent for review: 2013-12-31 09:38
Date reviewed: 2014-02-17 23:30

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
Well-written review about the role of tofacitinib in managing rheumatoid arthritis. Some minor revisions are needed to make the manuscript suitable for publication. -In the abstract the authors should give more details about the mechanism of action of tofacitinib -Specify that the manuscript is not a systematic review -In the section "efficacy studies" several data are repetitive, since their presence in table 1. I suggest to reduce this part in the text; -P values are needed in table 2

BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: editorialoffice@wjgnet.com http://www.wjgnet.com

ESPS Peer-review Report
Name of Journal: World Journal of Orthopedics
ESPS Manuscript NO: 8580
Title: Tofacitinib for treatment of rheumatoid arthritis
Reviewer code: 02570690
Science editor: Huan-Huan Zhai
Date sent for review: 2013-12-31 09:38
Date reviewed: 2014-02-27 15:54

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[Y] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

Comments to the Author Thank you for your paper. It provides a reasonable general overview of the studies on this drug in rheumatoid arthritis. General comments: It is probably incorrect to label tofacitinib as a 'non-biologic' DMARD. There has been considerable controversy with regards to this drug which is synthetic but acts like a biologic and a suggested terminology as adopted by EULAR is 'targeted synthetic DMARD' The authors have explained the pharmacology of the drug well. In the paper the authors should mention that though approved by USA FDA, approval has been rejected (twice) by EMA (European Medicines Agency) The authors should clarify, for the non-rheumatologist, what DAS28-4ESR (i.e. disease activity score using a 28 joint count, ESR and patient global assessment) is References should be written in full as they appear on PubMed. As an example, reference 15 "Tofacitinib (CP-690,550) in patients with rheumatoid arthritis receiving methotrexate." is actually "Tofacitinib (CP-690,550) in patients with rheumatoid arthritis receiving methotrexate: twelve-month data from a twenty-four-month phase III randomized radiographic study." Efficacy studies: Even though this is not a formal systematic literature review or meta-analysis, the authors should mention their search strategy Only a study description and a comment that "results were statistically significant" should be further qualified in each instance by the magnitude of benefit so as to be of use to the reader. for e.g. for the Oral Solo trial, instead of writing "All patients who received tofacitinib had statistically significant improvement in ACR20, ACR50, and ACR70 response criteria and HAQ-DI scores at month 3", the authors should mention, for e.g. ACR20 response was 59.8% in the 5 mg tofacitinib group, 65.7% in the 10mg group and 26.7% in the placebo group, etc. If possible odds ratios with CIs, numbers need to treat/ harm etc. should be provided. The authors should also

comment on study results rather than just stating them. As an example, in the above study, there were no differences in the DAS28 in the placebo and tofacitinib groups and it will be of interest to the reader as to why this robust index of disease activity was no different for an apparently effective drug? Following on from the above comment, rather than only stating study findings, the authors should try to – at least briefly- critique studies to make it more worth while for the reader (e.g. radiographic score at 6 months as the primary outcome- why not at 12 months?) Either in the table or elsewhere the authors should mention secondary outcomes. Again, from my previous comment, there is little point in only providing the 6 month radiographic score, as especially the 12 and to a slightly lesser extent the 24 month scores are important. Indeed on looking at the full length papers, these scores have been analysed but have not been mentioned in the paper The authors should give either plots with odds ratio/ figures of efficacy (and safety) data to enhance readability Safety and tolerability studies I am not sure what the authors intend to say when they write "only two deaths" for a chronic illness like RA where there should be no medication related deaths The general impression is the authors have undercalled adverse events. As an example, the authors mention "Although infections were reported in patients receiving tofacitinib, the reports were mainly mild to moderate in severity" and "no opportunistic infections were reported"- but both the Oral Solo and Tof. vs. adalimumab studies have mentioned events that seem opportunistic, for e.g. herpes zoster, liver abscess, pyelonephritis, etc The authors should also preferably give numbers (e.g. risk ratios with CIs) for adverse events in the main text

BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: editorialoffice@wjgnet.com http://www.wjgnet.com

ESPS Peer-review Report
Name of Journal: World Journal of Orthopedics
ESPS Manuscript NO: 8580
Title: Tofacitinib for treatment of rheumatoid arthritis
Reviewer code: 02705576
Science editor: Huan-Huan Zhai
Date sent for review: 2013-12-31 09:38
Date reviewed: 2014-03-01 06:16

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This is a concise review of the clinical program for the drug. Please consider if the trial names are well-known enough to cite (as in easily found on clinicaltrials.gov and in the literature) or if you wish to also use the lead author's name. Also, be consistent with NSAIDs as a term, rather than splitting out "NSAIDs and cox-inhibitors". In the US there is no separate therapeutic category dividing the two.