

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pharmacology and Therapeutics

ESPS manuscript NO: 28934

Title: How I treat my inflammatory bowel disease-patients with thiopurines?

Reviewer's code: 00055041

Reviewer's country: Italy

Science editor: Fang-Fang Ji

Date sent for review: 2016-07-26 08:47

Date reviewed: 2016-07-28 19:59

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input checked="" type="checkbox"/> Accept |
| <input checked="" 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 checked="" type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | [Y] No | <input type="checkbox"/> Major revision |
| | | BPG Search: | |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | [Y] No | |

COMMENTS TO AUTHORS

This is an interesting review. The results are clear and well described.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pharmacology and Therapeutics

ESPS manuscript NO: 28934

Title: How I treat my inflammatory bowel disease-patients with thiopurines?

Reviewer's code: 00012309

Reviewer's country: Italy

Science editor: Fang-Fang Ji

Date sent for review: 2016-07-26 08:47

Date reviewed: 2016-07-29 17:30

| 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 checked="" 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"/> Duplicate publication | |
| <input checked="" type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade E: Poor | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> No | <input checked="" type="checkbox"/> Minor revision |
| | | BPG Search: | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

The authors describe their own practical policies in treating IBD. I may have two main points. 1) The authors' pragmatic choice to skip genetic TPMT testing before prescribing thiopurines meets with this reviewer's agreement who admits that this testing still misses a number of toxicity instances. However, I myself reckon that things may not be that straightforward, because for example :a) in countries where health care is insurance-based TPMT testing may be found to be obligatory; b) 1:300 caucasian patients may be expected to develop deadly bone marrow aplasia if not tested (a figure that one can not easily neglect). Though my own practice is to skip TPMT testing (as the authors do) I believe that the non-specialist reader could be helped to reduce his/her confusion if the authors would expand a little more on this debated topic. 2) The authors could clearly define what they do intend for "deep remission".

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pharmacology and Therapeutics

ESPS manuscript NO: 28934

Title: How I treat my inflammatory bowel disease-patients with thiopurines?

Reviewer's code: 03478404

Reviewer's country: Romania

Science editor: Fang-Fang Ji

Date sent for review: 2016-07-26 08:47

Date reviewed: 2016-08-04 23:34

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | 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"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | | <input type="checkbox"/> Duplicate publication | |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade E: Poor | | <input checked="" type="checkbox"/> No | <input checked="" type="checkbox"/> Minor revision |
| | <input type="checkbox"/> Grade D: Rejected | BPG Search: | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

This is generally a very useful review concerning the use of thiopurines in clinical practice. The manuscript is concise and clear, has a pertinent structure and is written in a very elegant manner, easily to be followed, without too many references to studies and data, which is really good for a practical guide. References are correct. It was a pleasure to read it and I consider that this paper will benefit GIs (both experienced in the field of IBD and trainees) and, consecutively, their patients. Of course, those GIs who still want to use thiopurines and not to jump too quickly to biologics... Some minor comments/questions: 1. Adding 5ASA (mesalazine) in the abstract ("Extensive monitoring and the application of several treatment strategies, such as...") 2. "Indications of thiopurine therapy": maybe also include prevention of post-surgical recurrence in CD. 3. "Toxicity of thiopurine therapy": I agree with the authors regarding their strategy about measuring TPMT activity and their comments. However, given the fact that TPMT deficiency appears in 1 of 300 (0.3%) individuals (according to the data by Weinshilboum and Sladek) and this could lead to a significant risk of developing fatal leukopenia, I think this should be mentioned. 4. "Cancer risk": the authors mentioned correctly the risk of non-Hodgkin lymphoma; but maybe it would be useful to add a

sentence about HSTCL, especially in young men, on thiopurines or thiopurines associated with biologics. Other pearls for practice: use of thiopurines in EBV-naïve patients or during EBV infection? Testing for EBV before treatment with thiopurines? 4'. Regular dermatological screening required? 5. Obviously, this review does not include peculiarities of thiopurine therapy in children, being a practical guide written by adult GIs. However, maybe a phrase about pediatrics would not hurt. Like – for thiopurine use in pediatrics – see (e.g. reference – Pediatric CD guidelines. Ruemmele F, et al. JCC 2014) 6. “When to stop thiopurine therapy?” Maybe the authors could mention that recurrence after stopping thiopurines is high enough, especially in CD. Also, I would add histological remission to the sentence “An exception is the patient with deep prolonged (i.e. ≥ 2 -3 years) remission on thiopurine therapy with no signs of active disease on clinical, biochemical, endoscopic and radiologic evaluation”, especially based on new data in UC. 7. Table 2: Row 5: “<230, >>5700, Shunting...” “Hepatotoxicity” should be written instead of “myelotoxicity”.