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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31948

Title: NONINVASIVE MOLECULAR ANALYSIS OF HELICOBACTER PYLORI: IS IT TIME FOR TAILORED FIRST-LINE THERAPY?

Reviewer's code: 03260131

Reviewer's country: Turkey

Science editor: Jing Yu

Date sent for review: 2016-12-19 17:12

Date reviewed:2017-01-10 17:57

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	GoogleSearch:	<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 checked="" 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

It would be better to give some knowledge if there is any about children.

Thank you for your suggestion to deal with this important aspect. Two references of our paper are referred to mutational analyses in stool samples performed in pediatric population: Vecsei et al (reference 38 of revised manuscript) and Booka et al (reference 35 of revised manuscript). Therefore, we underlined this aspect in the revised version of the manuscript and reported the main results of these studies, showing a good diagnostic accuracy for molecular stool investigations in pediatric populations.



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Reviewer’s code: 02993121

Reviewer’s country: Thailand

Science editor: Jing Yu

Date sent for review: 2016-12-19 17:12

Date reviewed:2017-01-11 14:55

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	GoogleSearch:	<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 checked="" 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

This review article tries to convince the good efficacy of tailored therapy as 1st line management for H. pylori infection. The authors provide some evidence based of this new methods but more information should be added.

1. More extensive reviews of tailored therapy as 1st line management for H. pylori infection. Recently, a Polish trial demonstrated that a culture guided triple therapy in first line may achieve the 95.5% and 96.6% of success rate, at per protocol and intention to treat analysis, respectively (reference 21 of revised manuscript). Additionally, Zhou et al (reference 22 of revised manuscript) demonstrated that a susceptibility based treatment in first line achieved a gain of about 10% in eradication rate over empiric concomitant or triple plus bismuth regimens. These results have been enclosed in revised manuscript.
2. Comments and discuss more on current standard guideline for H. pylori management such as Maastricht V, Asia-pacific guideline. We enclosed in the revised version some considerations about the most updated guidelines.



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Indeed, suggested first line schedules are those with an expected high overall eradication rate, i. e. bismuth containing quadruple therapy or non-bismuth concomitant quadruple therapy [references 10, 11] according to Maastricht V and Toronto guidelines. However, the 2009 Asia-Pacific guidelines suggest 14-day triple therapy or bismuth containing quadruple in first line, stating, moreover, that sequential therapy is not supported by convincing data in Asian countries [reference 12].

3. Make summary of previous studies

In table 1 of the manuscript, studies about molecular *H. pylori* investigation in stools for clarithromycin resistance are summarized. For each study, diagnostic accuracy parameter and reference standard are reported.



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ESPS manuscript NO: 31948

Title: NONINVASIVE MOLECULAR ANALYSIS OF HELICOBACTER PYLORI: IS IT TIME FOR TAILORED FIRST-LINE THERAPY?

Reviewer's code: 03261325

Reviewer's country: Romania

Science editor: Jing Yu

Date sent for review: 2016-12-19 17:12

Date reviewed:2017-01-12 08:17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	GoogleSearch:	<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"/> 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

It is an interesting review about the noninvasive investigations able to detect H. pylori resistances to antibiotics. However, I think that the message of the review is too optimist, because noninvasive molecular tests in stools need confirmation and there are few evidence in the literature to recommend them before first line therapy. The main conclusion "Noninvasive molecular tests may improve patient compliance, time/cost of infection management and therapeutic outcome" is only a supposition and need further confirmation. The article is well written, has a good English language, the references are relevant, and up-to-date (although there are some mistakes in tehnoedactation ex references no 15, 16).

Thank you for the kind comment. We agree that non invasive molecular test are currently at a very early phase of development; therefore cautions should be paid when discussing about their possible clinical applications. Only further studies aimed to evaluate sensitivity and specificity of



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molecular tests will afford novel data to make more solid considerations. These comment has been reported in Conclusive Remarks. The style of references was reviewed and modified according to the Journal style.



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Title: NONINVASIVE MOLECULAR ANALYSIS OF HELICOBACTER PYLORI: IS IT TIME FOR TAILORED FIRST-LINE THERAPY?

Reviewer’s code: 03008931

Reviewer’s country: China

Science editor: Jing Yu

Date sent for review: 2016-12-19 17:12

Date reviewed:2017-01-12 21:12

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	GoogleSearch:	<input type="checkbox"/> Accept
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		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This work by Drs. Ierardi et al, investigates noninvasive molecular analysis of H. pylori (Hp), and asks if it is time for tailored first-line therapy? Author summarized current treatment regimens used in clinical practice and briefly touched noninvasive test approaches for Hp antibiotic resistance detection. The opinion appears novel and interesting; however, after reading whole text, this reviewer noticed areas that require improvement from authors. It is clear that noninvasive assay to detect H. pylori antibiotic resistance are the directional approaches for future efforts, which could provide sensitive analysis and better eradication rate to guide Hp eradication. Therefore, it is hoped that authors could follow these principals to reorganize the text, and provide the field with a directional guild for future research and practice, these important points are missing from the current version. Minor points: Some sentences are very long and hard to understand, this reviewer recommend authors reorganize the manuscript and made it more concise and up-to-point.

We agree with the considerations expressed by the reviewer. Indeed, as already stated in



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Conclusive Remarks of revised manuscript, a non invasive test with an optimal sensitivity and specificity aimed to improve the eradication rate in comparison to first line empiric regimen is still ongoing. On these bases, we reorganized the text and, moreover, we rephrased some sentences that may appear hard to understand. In detail, we highlighted the most recent clinical trials clearly demonstrating the benefits of a tailored therapy as well as we analyzed point by point the main characteristics of each noninvasive molecular study performed until now.