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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 11227
Title: Simeprevir with Peginterferon and Ribavirin induced interstitial pneumonitis : First case report
Reviewer code: 02729265
Science editor: Ya-Juan Ma
Date sent for review: 2014-05-10 21:39
Date reviewed: 2014-05-12 04:15

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[ ] 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:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
1) Good case report. Well written. 2) Simeprevir is unlikely to be the direct causative agent of the lung complication described and it would be wrong to attribute the complication to Simeprevir. It is most likely that IFN caused the interstitial pneumonitis in a patient who just happened to be on triple therapy. 3) Previously published similar case reports have better discussion section including literature review.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 11227
Title: Simeprevir with Peginterferon and Ribavirin induced interstitial pneumonitis : First case report
Reviewer code: 00012216
Science editor: Ya-Juan Ma
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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 the manuscript entitled "Simeprevir with Peginterferon and Ribavirin induced interstitial pneumonitis: First case report", author`s describe the first case report of interstitial pneumonitis in a patient treated with simeprevir plus peg-interferon and ribavirin. The case is well documented showing enough data to sustain the diagnosis of interstitial pneumonitis developed by the patient after 8 weeks of treatment (lung TC scan at pneumonitis onset and after treatment withdrawal, so that KL-6 level). Nevertheless, interstitial pneumonitis is a rare adverse event in Peg-interferon treatment. Therfore, all the anti-HCV regimens including interferon could develop this complication and it would not be different in simeprevir/IFN/RBV treatment. Authors suggest that the novelty of this case is that interstitial pneumonitis happens earlier than in cases treated with Peg-IFN+RBV alone. They comment that this could be due to the inhibition of OATPB1/3 and P-glycoprotein transporters by simeprevir, but they do not give any information about if IFN pharmacokinetic is involved in these pathways, so far. Moreover, authors should describe if there has been communicated any interstitial pneumonitis in simeprevir IFN-free regimens. To my knowledge, there is any case reported in PubMed in simeprevir IFN-free regimens; therefore in the reported case the development of this adverse event is probably due to the immune-modulatory properties of alpha-interferon and the only novelty of the case could be the earlier onset of the event because of the hypothetical simeprevir effect on IFN pharmacokinetics. These transporters constitute important determinants of drug hepatic clearance; therefore their inhibition could impact theoretically on IFN pharmacodynamics. For this reason, authors should comment deeper about the potential effect of OATPB1/3 and P-glycoprotein transporters inhibition on Peg-IFN action to make the case report

more interesting. If it were true, it should be expected that patients treated with simperevir and IFN had more IFN-related adverse events than patients treated with double therapy alone, such as either cytopenia or autoimmune disorders.