

Format for ANSWERING REVIEWERS

September 23, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 19264-Review.doc).

Title: Probable case of drug reaction with eosinophilia and systemic symptom syndrome due to combination therapy with daclatasvir and asunaprevir

Author: Takayoshi Suga, Ken Sato, Yuichi Yamazaki, Tatsuya Ohyama, Norio Horiguchi, Satoru Kakizaki, Motoyasu Kusano, Masanobu Yamada

Name of Journal: *World Journal of Clinical Cases*

ESPS Manuscript NO: 19264

The manuscript has been improved according to the suggestions of reviewers:

1. Re-check formatting, particularly indentation.

We have corrected the formatting, including the indentation.

Reviewed by 02645903

2. Dear Sir The paper entitled "A probable case of DRESS syndrome due to combination therapy with daclatasvir and asunaprevir" needs to be returned to the authors in order to clarify what they understand as eosinophilia. In "Case Report", line 21 they consider that the patients had eosinophilia "...total white cell count to 12,130 / μ L (eosinophils 121 / μ L),..." This count of eosinophils is not considered an eosinophilia. Later in the paper (Discussion, lines 37-38) they wrote: "He showed eosinophilia (more than $1.5 \times 10^9/L$)". It is important to unify the values and the units employed.

As the reviewer suggested, we agree that an eosinophil count of 121/ μ L at the onset of adverse events is not considered to be eosinophilia. However, on day 21 of the initiation of treatment, the eosinophil count increased up to 2673/ μ L (please see the "CASE REPORT" section in the main text). At this time, the prothrombin activity remained low compared with the baseline level, and a skin rash was persistent. Thus, in this case, eosinophilia was considered both a delayed symptom and a core symptom. We have unified the values and units used throughout the text.

Other seminal consideration is they are describing a "possible" DRESS syndrome. The hepatic compromise can be explained by the HCV hepatitis, and also the drugs used to treat HCV have as adverse events the lowering of the hepatic reserve and renal impairment. Our observations about DRESS syndrome include an important elevation of

transaminases (ALT and AST), always over 5 normal maximal values¹. In this patient transaminases were practically normal. A patient has a DRESS syndrome or not. The paper is not conclusive about this question. Sincerely yours, Dr. Domingo Palmero 1-Difficult clinical management of anti-tuberculosis DRESS syndrome. *Int J Tuberc Lung Dis* 2013 17(1):76-8.

*In terms of the clinical characteristics associated with DRESS syndrome, elevated liver function is reported as 84/142 (59%) [ref #9, Cacoub P, et al. *Am J Med* 2011; 124: 588-597]. Thus, DRESS syndrome does not always have elevated liver function, and the absence of elevated liver function does not preclude the diagnosis of DRESS syndrome. Hopefully, our response is a satisfactory reply to the reviewer's comment.*

Best regards,

Ken Sato, M.D., Ph.D.

Department of Medicine and Molecular Science

Gunma University Graduate School of Medicine

3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan

Tel: +81-272-20-8127

Fax: +81-272-20-8137

E-mail: satoken@showa.gunma-u.ac.jp