

## Difference between Enbrel and Benepali treatment groups in 'hepatobiliary disorders'

We read with interest the study from Emery *et al*<sup>1</sup> reporting the phase III trial comparing the biosimilar SB4 with originator etanercept, as well as the summary for the public that appeared in the European Public Assessment Report (EPAR)<sup>2</sup> issued by European Medicines Agency on 28 January 2016. In our reading of the documents, we were struck by the discrepancy of reporting safety between these two documents. The discussion on clinical safety Benepali EPAR notes, one can read the following, 'There was a difference between the treatment groups in the hepatobiliary disorders System Organ Class Adverse Events (SOC AES): 17 treatment-emergent adverse events (TEAEs) in 11 patients reported in the Benepali (SB4) compared with no AEs in the EU Enbrel group (four events of cholelithiasis in four subjects, three events of liver disease disorder in three subjects, three events of chronic cholecystitis in two subjects, two events of bile duct stone in one subject and one event of biliary colic, cholangitis, cholecystitis and associated gall bladder perforation and elevated transaminases each reported in one subject.

Could the authors comment on the decision to exclude this information from the primary manuscript and also help us understand the specific biliary risk factors in the Benepali arm that may have contributed to the hepatobiliary events. Given that the trials were very well balanced, this appears to be a rather significant difference between the two medicines.

We feel that this additional information once provided may help to understand the nature of these differences and if the missing data on the composite outcomes could have an impact on whether patients receiving Benepali should be previously screened for gallbladder disease.

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- 2 [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_Public\\_assessment\\_report/human/004007/WC500200380pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_Public_assessment_report/human/004007/WC500200380pdf)