Reply to: “Prognostic value of histologic parameters in alcoholic hepatitis: A word of caution”

To the Editor:
We thank Deltenre & Marot for their interest in our study on the novel SALVE grading and staging system for alcohol-related liver disease (ALD). While their discussion is related to the prognostic value of histologic parameters in alcoholic hepatitis (AH) in the clinical context of sepsis and/or corticosteroid treatment, this was not the focus of our study. The primary goal of our study was to establish a grading and staging system for AH which has been hitherto lacking. Most AH studies to date have used the Clinical Research Network (CRN) grading and staging system which has been designed and validated for non-alcoholic fatty liver disease (NAFLD). However, ALD may show striking features such as canicular/ductular cholestasis, broad septa and/or marked pericellular fibrosis which are rarely observed in NAFLD and not included in the CRN grading and staging system.

In addition, we aimed to determine the prognostic value of the SALVE grading and staging system in patients with compensated or decompensated ALD in a large cohort of 445 patients from 4 European centers which provided liver biopsy slides as well as clinical and outcome data. Collaboration of several centers within the EASL–SALVE consortium enabled us to test the prognostic value of the SALVE grading and staging system across the whole spectrum of ALD. On multivariable analysis of clinical, biochemical and histological parameters, the presence of histological steatohepatitis due to ALD (hASH) and/or severe cirrhosis (SALVE fibrosis stage 4C/CP) emerged as independent predictors of survival. We also performed multivariable analyses in subgroups of patients with compensated ALD, decompensated ALD, and the presence of hASH. However, we did not aim to determine the prognostic value of the SALVE grading and staging system within the clinical setting of severe AH nor to compare it with other prognostic tools such as the Alcoholic Hepatitis Histologic Score (AHHS).

A recent study by Dubois et al. evaluated 107 patients with severe biopsy-proven AH (89% receiving steroid treatment) and identified prognostic trends for AHHS and Laennec stage 4B/4C for short-term survival, but failed to demonstrate the independent prognostic value of these histologic parameters when adjusted for age and model for end-stage liver disease score. Their results are consistent with our finding of the prognostic impact of severe cirrhosis (SFS 4C/CP).

While most of our patients with severe AH (Maddrey’s discriminant function >32) and biopsy-proven hASH received steroid treatment, our subgroup of decompensated patients with hASH also included ‘non-severe’ patients with AH not treated with steroids. Therefore, steroid treatment was not included in multivariable analysis. The impact of histological parameters on response to steroid treatment is the subject of an ongoing study, which was published in abstract form at this year’s ILC. Preliminary analyses revealed steatosis grade and ductular cholestasis as predictors of steroid response, however, a larger number of patients is needed to draw robust conclusions.

We are well aware of the impact of abstinence in studies evaluating outcome in patients with ALD and included this parameter in multivariable Cox regression of compensated ALD where it remained as an independent predictor of decompensation-free survival. Unfortunately, data on abstinence were only partly available in patients with decompensated ALD and therefore not included in multivariable analyses.

Finally, we fully agree with the need for external validation of any novel diagnostic tool and thus look forward to application of the SALVE grading and staging system in future studies evaluating liver histology in independent prospective ALD cohorts.

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Conflicts of interest
All authors declare that they have no conflicts of interest related to the study.
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Authors’ contributions
RES: drafting of the manuscript; all authors: critical revision for important intellectual content and final review.

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Letter to the Editor

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