

## LETTER TO THE EDITOR

# Genetic insight into COVID-19 related liver injury: A note on MBOAT7

Sir, with great interest we read the paper by Bianco et al,<sup>1</sup> presenting the association between genetic modifiers of liver injury and outcomes in patients with COVID-19. Whilst Bianco et al<sup>1</sup> showed that the PRS-HFC genetic score does not affect studied phenotypes, they also demonstrated that C3 and ABO genetic variants are associated with the severity of COVID-19. In this study, we would like to add to these interesting observations and present first data concerning the MBOAT7 polymorphism rs641738 (which is included among other variants in the PRS-HFC score), a known risk factor for liver steatosis and fibrosis.<sup>2</sup>

Prospectively, we analysed a cohort of 44 patients with COVID-19 (64% men; median age 62 years, range 21-91 years) hospitalized between March and October 2020 at our centre in Saarland, Germany. The MBOAT7 variant was genotyped using TaqMan<sup>®</sup> assays. The median length of stay in hospital was 14 days (range 1-227 days) and abnormal liver parameters (ie at least one of ALT, AST, ALP, GGT, bilirubin, albumin, or INR > ULN) were present in 66% of patients at admission and in 82% during the hospital stay. Among recruited patients, only eight carried the wild-type (WT) MBOAT7 allele in comparison to 36 patients carrying the variant allele (19 heterozygous and 17 homozygous carriers). We detected a significant ( $P = .013$ ) correlation between abnormal values of liver parameters at admission and the MBOAT7 polymorphism.

The presence of the MBOAT7 polymorphism was associated with more severe liver injury during hospitalization for COVID-19. Indeed, as compared to individuals with the WT MBOAT7 genotype, carriers of the risk allele showed significantly increased ALP ( $P = .002$ , Figure 1A), GGT ( $P = .009$ , Figure 1B), ALT ( $P = .003$ ) and bilirubin ( $P < .001$ ) and decreased albumin levels ( $P < .001$ ) during hospitalization as compared to admission. Panels A and B of Figure 1 illustrate the exemplary time courses of the ALP and GGT fluctuations in all hospitalized COVID-19 patients, respectively. A total of 739 values (ALP) and 758 values (GGT) from 44 patients during their stay were analysed, and the groups (WT vs variant) were graphically compared using local regression (Loess). Notably, 16/36 (44%) risk allele carriers and only 2/8 (25%) WT allele carriers presented ALP activities exceeding ULN ( $\delta > 129$  U/l;  $\varphi > 104$  U/l). In the exploratory analysis, we observed that 80% of the MBOAT7 risk allele carriers developed pneumonia in comparison to 50% of the non-risk allele carriers. Of note, 94% of patients hospitalized in the intensive care unit, 93% of patients requiring artificial ventilation and 100% of patients in need

of extracorporeal membrane oxygenation (ECMO) carried at least one copy of the MBOAT7 risk allele. Twenty-two percent and 25% of the patients with or without the MBOAT7 polymorphism died, respectively.

Individuals with metabolic-associated fatty liver disease (MAFLD) are at-risk of more severe COVID-19.<sup>3</sup> Here, by analysing trajectories of liver tests in hospitalized patients with COVID-19, we show that the MAFLD-predisposing MBOAT7 variant might also be linked to worsening of liver function during SARS-CoV2 infection. COVID-19 is a progressive disease characterized by dynamically changing clinical status and lab tests. Hence, it is obvious that analyses of liver tests coming from one single day strongly limit the chance to capture genetic modifiers of hepatic injury. For this reason, we analysed the cumulative laboratory data from the entire hospital stay and found that carriers of the MBOAT7 variant are at risk of severe liver injury. Still, we reckon that further studies are needed to confirm this association and its role in the course and treatment of COVID-19.

## CONFLICT OF INTEREST

None.

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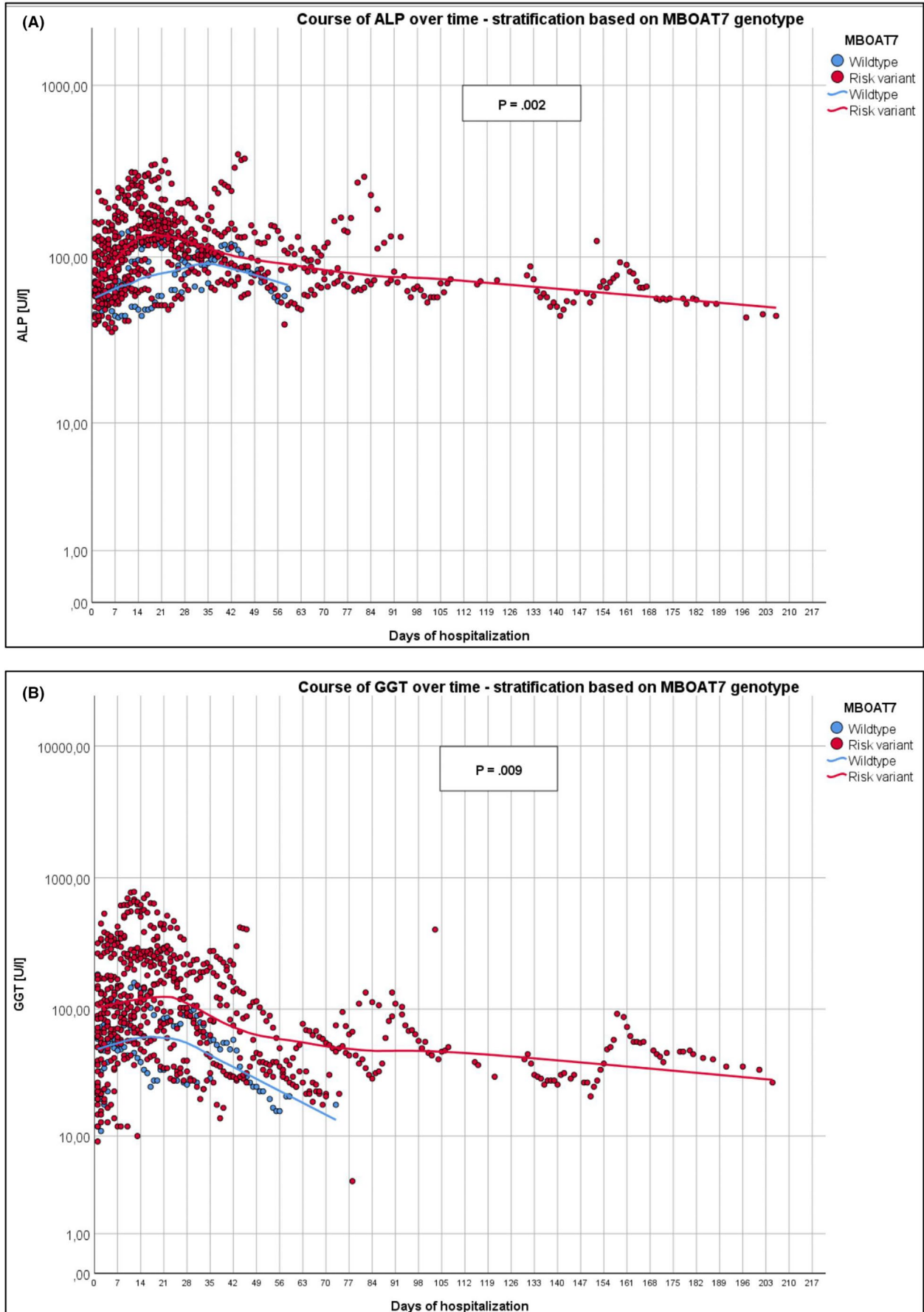
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**FIGURE 1** Course of ALP (A) and GGT activities (B) during patients' entire stay in the hospital, stratified based on MBOAT7 genotypes. Data are presented on a logarithmic scale

**REFERENCES**

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