DR. CHINA AND COLLEAGUES REPLY: Elfeki and colleagues raise an interesting point regarding alcohol-induced cirrhotic cardiomyopathy, since 90% of the patients in the ATTIRE trial had alcohol-related cirrhosis. In the albumin group, serious adverse events included 15 that exclusively involved pulmonary edema and 23 that involved pulmonary edema or fluid overload. None of these events occurred in patients with disease that was not related to alcohol consumption. However, it is premature to draw conclusions from such small numbers.

Chauhan and colleagues state correctly that patients with extrahepatic organ dysfunction may have increased systemic inflammation. Figure S4 in the Supplementary Appendix of our article (available with the full text of the article at NEJM.org) shows no benefit of targeted albumin infusion in patients regardless of the number of organ dysfunctions they have at baseline (0 to 1 vs. 2 to 4). However, we acknowledge that only 3.1% of the patients in our trial fell into the latter category. This finding was consistent with our aim of preventing infection, organ dysfunction, and death, since multiorgan failure carries a very poor prognosis. Nevertheless, targeted albumin infusions had no apparent effect.

Table 3 in our article showed no between-group difference in gastrointestinal bleeding. However, additional analysis of data from patients with variceal bleeding at baseline showed a possible increase in the incidence of serious adverse events with subsequent gastrointestinal bleeding in the albumin group. Of the serious adverse events that included gastrointestinal bleeding, 7 of 11 in the albumin group occurred in patients who had variceal bleeding at baseline, as compared with 3 of 13 events in the placebo group.

In our trial, the protocol called for the infusion of a 20% human albumin solution until the serum albumin level reached 35 g per liter. If the serum albumin level subsequently fell below 35 g per liter, albumin was again infused (Table S2 in the Supplementary Appendix of the article). This stipulation suggests that the protocol was flexible, and if there was a risk of albumin administration (especially regarding fluid overload), the infusion could be withheld or adjusted.[1] In the albumin group, among the patients who had pulmonary edema or fluid overload, the median serum albumin level was 30.5 g per liter (interquartile range, 28.8 to 32.3) on the day of the serious adverse event, which does not suggest that infusions in patients with albumin levels of more than 30 g per liter contributed substantially to the increased incidence of pulmonary edema.

The requested beta-blocker data would ignore the confounding effects of albumin treatment. Also, it is more likely that beta-blockers would have been discontinued in patients with hypotension who had ascites and renal dysfunction than in those without these conditions, a factor that would have led to potential bias. The question of the value of the use of beta-blockers in hospitalized patients with cirrhosis would be best addressed in a prospective, randomized trial.

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Since publication of their article, the authors report no further potential conflict of interest.

1. China L, Skene SS, Bennett K, et al. ATTIRE: Albumin To prevenT Infection in chronic liveR failurE: study protocol for an interventional randomised controlled trial. BMJ Open 2018; 8(10):e023754.

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