# Effect of Terlipressin on Patients With Hepatorenal Syndrome, Alcohol-Associated Hepatitis, and Acute-on-Chronic Liver Failure Grade 0–2

THU-074

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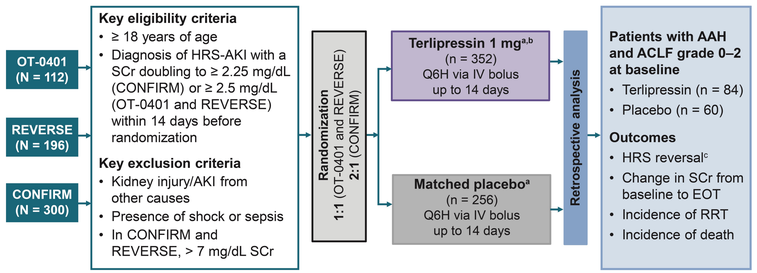
## Background and Aims

- Patients with severe alcohol-associated hepatitis (AAH) often have liver cirrhosis and, consequently, may develop acute kidney injury (AKI)[1]
- Hepatorenal syndrome (HRS) is a potentially reversible form of AKI[2]
- Terlipressin is the first and only treatment for adult patients with HRS-AKI approved by the United States Food and Drug Administration and is more likely to be of clinical benefit for those patients with acute-on-chronic liver failure (ACLF) grade 0–2[3]
- In this study, we determined the effect of terlipressin on renal function among patients with AAH and HRS-AKI who had ACLF grades 0–2

## Methods

- Data were pooled from a subpopulation from 3 Phase III studies (OT-0401[4], REVERSE[5], and CONFIRM[6]) of patients with AAH, HRS-AKI, and ACLF grades 0–2 who received terlipressin or placebo (**Figure 1**)

**Figure 1.** Study design



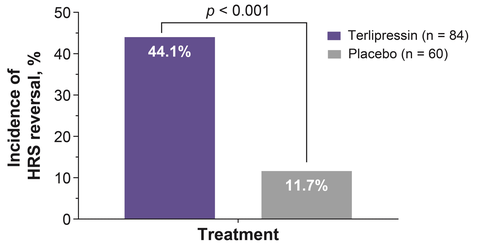

[a] **Concomitant albumin was strongly recommended** at a dose of 100 g on Day 1 and then 25 g daily until EOT in OT-0401; 20–40 g/day in REVERSE; and 1 g/kg to a maximum of 100 g on Day 1 and 20–40 g/day thereafter in CONFIRM.
[b] If, after Day 3, SCr levels had decreased—but by less than 30%—then the terlipressin dose could be increased to 2 mg Q6H.
[c] Defined as the percentage of subjects with 2 consecutive SCr values of no more than 1.5 mg/dL obtained at least 2 hours apart, while receiving treatment by Day 14 or discharge.
AAH, alcohol-associated hepatitis; ACLF, acute-on-chronic liver failure; AKI, acute kidney injury; EOT, end of treatment; HRS, hepatorenal syndrome; IV, intravenous; Q6H, every 6 hours; RRT, renal replacement therapy; SCr, serum creatinine.

- HRS reversal was defined as at least one SCr value of ≤ 1.5 mg/dL while on treatment by Day 14 or discharge
- Change in renal function was measured as least squares (LS) mean changes in serum creatinine (SCr) with and without interaction between treatment and day—from baseline through to the end of treatment (EOT)—and was evaluated within and between treatment arms
  - *P* values were calculated from repeated measures analysis of covariance with factors of study, treatment, and day for the analysis without interaction, and with the same factors plus treatment-by-day interaction for the analysis with interaction
- Incidence of death and renal replacement therapy (RRT) on Days 30, 60, and 90 were compared between treatment arms by Chi-square or Fisher's exact tests

## Results

- The study population with AAH, HRS-AKI, and ACLF grades 0–2 included 84 patients in the terlipressin arm and 60 patients in the placebo arm
- The incidence of HRS reversal was significantly higher in the terlipressin arm versus the placebo arm (44.1% vs 11.7%, $p < 0.001$ respectively, **Figure 2**)

**Figure 2.** Incidence of HRS reversal in patients with AAH and ACLF grade 0–2 at baseline; Pooled ITT population

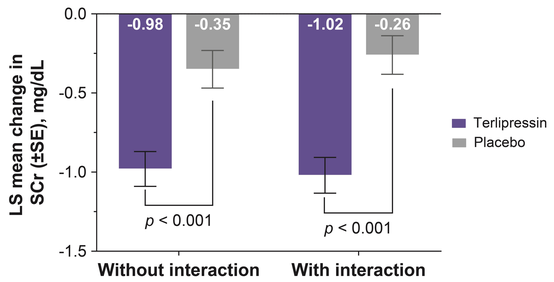



AAH, alcohol-associated hepatitis; ACLF, acute-on-chronic liver failure; EOT, end of treatment; HRS, hepatorenal syndrome; ITT, intent-to-treat.

***Change in renal function from baseline to the end of treatment***

- For the 141 patients evaluated, SCr decreased from baseline to the EOT in both treatment arms (**Figure 3**)
  - The decrease in SCr from baseline to EOT was significantly larger in the terlipressin vs placebo arms in the analyses with and without interaction between treatment and day
  - The difference in LS mean change in SCr between terlipressin and placebo was –0.64 mg/dL without interaction and –0.76 mg/dL with interaction (both $p < 0.001$)

**Figure 3.** Change in serum creatinine from baseline to the EOT[a] in patients with AAH and ACLF grade 0–2 at baseline; Pooled ITT population

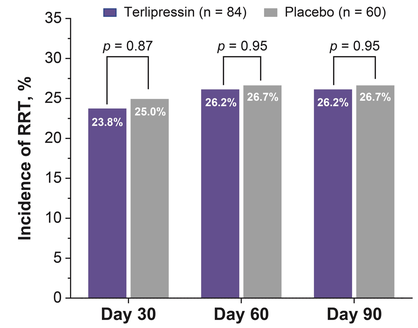



[a] Only SCr values collected after the treatment start date through 24 hours after the EOT were included; SCr values after RRT and liver transplant were excluded.
AAH, alcohol-associated hepatitis; ACLF, acute-on-chronic liver failure; EOT, end of treatment; ITT, intent-to-treat; LS, least squares; RRT, renal replacement therapy; SCr, serum creatinine; SE, standard error.

***Renal replacement therapy***

- Incidence of RRT on Days 30, 60, and 90 were similar between the terlipressin and placebo arms: 23.8% vs 25.0% on Day 30, and 26.2% vs 26.7% both on Days 60 and 90, respectively (all *p* values were not significant) (**Figure 4**)

**Figure 4.** Incidence of RRT in patients with AAH and ACLF grade 0–2 at baseline; Pooled ITT population

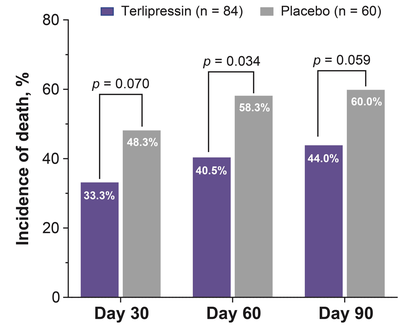



AAH, alcohol-associated hepatitis; ACLF, acute-on-chronic liver failure; ITT, intent-to-treat, RRT, renal replacement therapy.

***Death***

- Incidence of death was significantly smaller in the terlipressin arm versus placebo by Day 60 (40.5% vs 58.3% [$p = 0.034$]), and numerically smaller by Day 30 (33.3% vs 48.3% [$p = 0.070$]), and Day 90 (44.0% vs 60.0% [$p = 0.059$]) (**Figure 5**)

**Figure 5.** Incidence of death in patients with AAH and ACLF grade 0–2 at baseline; Pooled ITT population




AAH, alcohol-associated hepatitis; ACLF, acute-on-chronic liver failure; ITT, intent-to-treat.

## Conclusions

- Terlipressin significantly improved renal function and increased HRS reversal among patients with AAH and HRS-AKI who had ACLF grades 0–2, compared with placebo, and was associated with fewer deaths by Day 60
- Although SCr levels decreased significantly more in the terlipressin arm (versus placebo) from baseline to the EOT, the incidence of RRT in this population was similar in both treatment arms
- HRS reversal and improvement in renal function provide patients with AAH time to recover, receive other treatment, or achieve eligibility for liver transplantation[7]

## References

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