Background

- Patients with decompensated liver disease may develop hepatorenal syndrome (HRS), a rapidly progressive form of acute kidney injury.
- The underlying liver disease is strongly associated with a hypotensive state. Thus, patients with HRS may present with a mean arterial pressure (MAP) below the optimal target MAP of 65 mm Hg, used in the management of septic shock.
- Terlipressin, a vasopressor analog, is used to treat adult patients with HRS to improve renal perfusion and kidney function.

Methods

- Patient data were collated from 3 Phase III placebo-controlled studies of terlipressin in patients with HRS and rapidly deteriorating kidney function (defined as a serum creatinine ≥ 2.5 mg/dL [OT-0401], REVERSE) or ≥ 2.25 mg/dL [CONFIRM])
- Patients with low baseline MAP (≤ 65 mm Hg) and baseline MAP ≥ 65 mm Hg were assessed for HRS reversal (defined as ≥ 24% increase in serum creatinine within a single treatment episode, up to 24 hours after the last dose of study drug) and overall survival (OS) at Day 90.

Aims

- This post hoc analysis of the largest database of patients who were treated with terlipressin in 3 prospective Phase III studies aimed to examine patient responses by MAP subgroup (MAP < 65 mm Hg; MAP ≥ 65 mm Hg).
- As treatment response appears to be tightly correlated with an increase in MAP, further understanding of the clinical response in patients who present with HRS and low MAP is of particular interest.

Results

- In the pooled intent-to-treat dataset (N = 608), most patients had a MAP ≥ 65 mm Hg (terlipressin, 86.1% [303/352]; placebo, 86.7% [221/255]).
- The proportion of patients with a low MAP (≤ 65 mm Hg) was 13%–14%, and was similar across treatment arms (terlipressin, 13.9% [49/352]; placebo, 13.3% [24/255]).
- While HRS reversal was higher among patients with MAP ≥ 65 mm Hg (compared with MAP < 65 mm Hg) for both terlipressin and placebo, significantly more patients achieved HRS reversal with terlipressin than with placebo in both the low MAP (22.4% [11/49] vs 9.9% [2/34]; P < .041) and MAP ≥ 45 mm Hg (35.0% [10/30] vs 18.1% [4/22]; P < .001) subgroups.

Conclusions

- Patients with HRS who presented with either MAP < 65 mm Hg or MAP ≥ 65 mm Hg at baseline derived a significant improvement in OS and HRS reversal in patients with low MAP.
- More than 50% of patients with a baseline MAP ≥ 65 mm Hg were alive at Day 90 (terlipressin, 50.5% [153/303]; placebo, 56.1% [124/221]), with no significant difference in survival estimates between the terlipressin and placebo treatment arms.
- Patients with low MAP (< 65 mm Hg) had a significantly improved survival in OS estimates up to 90 days in the terlipressin arm (P < .002), with 59.2% of patients alive at Day 90 (vs 26.5% in the placebo arm).
- The proportion of patients with low baseline MAP who received RRT was numerically higher in the placebo arm versus the terlipressin arm, at Days 30, 60, and 90 (terlipressin vs placebo: Day 30, 28.6% [14/49] vs 47.1% [16/34]; P = .038; Day 60, 30.6% [15/49] vs 47.1% [16/34]; P = .128; Day 90, 34.7% [17/49] vs 47.1% [16/34]; P = .258).

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