Mallinckrodt Pharmaceuticals

American Association for the Study of Liver Diseases (AASLD) 2023 Liver Meeting Mallinckrodt-Sponsored Abstracts Summary

See here for the full list of AASLD 2023 Liver Meeting Abstracts

ORAL PRESENTATIONS

Abstract #211: Albumin Dosing with Terlipressin for the Treatment of HRS-AKI: A Double-Edged Sword[1]

Oral Presentation: Monday, November 13; 12:00 P.M. EST

Presenting Author: Florence Wong, Toronto General Hospital, Toronto, ON, Canada

A pooled analysis evaluated total albumin use in two of the largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies (REVERSE, CONFIRM) of terlipressin plus albumin versus placebo plus albumin in patients with hepatorenal syndrome-acute kidney injury (HRS-AKI), to further clarify optimal albumin levels before and during treatment.

Abstract #224: Improved Mean Arterial Pressure from Baseline to the End of Treatment with Terlipressin is Associated with Hepatorenal Syndrome Reversal: A Pooled Analysis of 3 Phase III Studies[2]

Oral Presentation: Monday, November 13; 9:45 A.M. EST

Presenting Author: Zachary Fricker, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

A pooled subgroup analysis from the three largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies (OT-0401, REVERSE, CONFIRM) of terlipressin plus albumin versus placebo plus albumin in patients with HRS, compared the change in mean arterial pressure (MAP) from baseline to the end of treatment based on HRS reversal status and treatment group.

Abstract #80: Decision-Analytic Model to Project the Benefit of Terlipressin Treatment Among Patients with Alcohol-Related Cirrhosis and HRS[3]

Oral Presentation: Monday, November 13; 5:45 P.M. EST

Presenting Author: Khalid Mumtaz, The Ohio State University, Wexner Medical Center, Columbus, OH

Health economics outcomes from a decision-analytic model evaluated the prevalence of an alcohol-related hepatorenal syndrome (HRS) diagnosis among hospitalized patients and the efficacy of terlipressin versus placebo. The model aimed to project potential additional responses (i.e., HRS reversal), reduction in intensive care unit stay duration, reduction in the need for renal replacement therapy, and increase in transplant-free survival.

INDICATION AND LIMITATION OF USE

TERLIVAZ® (terlipressin) for injection is indicated to improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function.

- Patients with a serum creatinine >5 mg/dL are unlikely to experience benefit.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS OR FATAL RESPIRATORY FAILURE

- **TERLIVAZ may cause serious or fatal respiratory failure. Patients with volume overload or with acute-on-chronic liver failure (ACLF) Grade 3 are at increased risk. Assess oxygenation saturation (e.g., SpO_2) before initiating TERLIVAZ.**

- **Do not initiate TERLIVAZ in patients experiencing hypoxia (e.g., SpO_2 <90%) until oxygenation levels improve. Monitor patients for hypoxia using continuous pulse oximetry during treatment and discontinue TERLIVAZ if SpO_2 decreases below 90%.**

Please see additional Important Safety Information below.

POSTER OF DISTINCTION

Abstract #3052-A: Understanding the Relationship Between Mean Arterial Pressure and Terlipressin in Hepatorenal Syndrome-Acute Kidney Injury Reversal: A Post Hoc Analysis of the CONFIRM, REVERSE, and OT-0401 Trials[4]

Poster of Distinction Presentation: Sunday, November 12; 5:00 P.M. EST

Presenting Author: Giuseppe Cullaro, University of California San Francisco Medical Center, San Francisco, CA

A post hoc analysis utilizing data from the three largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies of terlipressin plus albumin versus placebo plus albumin in patients with HRS aimed to determine the relationship between mean arterial pressure (MAP) and terlipressin in HRS-AKI reversal.

POSTER PRESENTATIONS

Abstract #3048-A: The Prevalence and Clinical Features of Acute Kidney Injury Across Various Stages of Ascites in Patients with Cirrhosis from a Single Quaternary Referral Academic Centre[5]

Poster Presentation: Sunday, November 12; 8:00 A.M. EST

Presenting Author: Florence Wong, Toronto General Hospital, Toronto, ON, Canada

A health economics, retrospective study evaluated patients with cirrhosis and ascites from a single quaternary referral academic center from April 2020 – March 2021 to collect demographics, clinical features, medications, ascites severity, AKI development, AKI and patient outcomes at six months to assess the prevalence of AKI amongst all patients with ascites.

Abstract #3013-A: Efficacy of Continuous Terlipressin Infusion in HRS-AKI in a Transplant-Enriched Population: A Comparative Prospective and Retrospective Cohort Study[6]

Poster Presentation: Sunday, November 12; 8:00 A.M. EST

Presenting Author: K. Rajender Reddy, University of Pennsylvania, Philadelphia, PA

An open-label study (INFUSE) of liver transplant candidates with cirrhosis, ascites, and HRS-AKI was conducted to determine the impact of continuous terlipressin infusion on HRS reversal and renal outcomes versus the standard of care.

Abstract #3019-A: Increased Baseline Indicators of Inflammation in Patients with Hepatorenal Syndrome Type 1 and Grade 3 Acute-on-Chronic Liver Failure: Implications for Terlipressin Therapy[7]

Poster Presentation: Sunday, November 12; 8:00 A.M. EST

Presenting Author: Florence Wong, Toronto General Hospital, Toronto, ON, Canada

A pooled analysis leveraged data from two of the largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies (CONFIRM, REVERSE) with terlipressin plus albumin versus placebo plus albumin in patients with HRS to explore inflammation as a possible contributor to the development of respiratory failure in HRS-1 patients with acute-on-chronic liver failure Grade 3 who were treated with terlipressin.

Abstract #3028-A: Patient Subset Analysis of the REVERSE Phase III Study: The Impact of Terlipressin Treatment on Rates of Transplant, Dialysis, and Survival in Patients with Hepatorenal Syndrome[8]

Poster Presentation: Sunday November 12; 8:00 A.M. EST

Presenting Author: Samuel H. Sigal, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY

A retrospective analysis of a subset of U.S. patients from one of the largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies (REVERSE) of terlipressin plus albumin versus placebo plus albumin for patients with HRS was conducted to determine the impact of terlipressin on liver transplantation incidence and survival by treatment group (terlipressin versus placebo) in patients with HRS.

Abstract #3043-A: Terlipressin Treatment and Time to Clinical Response: Characterization of Hepatorenal Syndrome Reversal Using a Pooled Database of 3 Placebo-Controlled Phase III Clinical Studies[9]

Poster Presentation: Sunday, November 12; 8:00 A.M. EST

Presenting Author: Brendan M. McGuire, University of Alabama at Birmingham, Birmingham, AL

A pooled analysis assessed the time to clinical response of HRS reversal in patients with HRS treated with terlipressin versus placebo, using data from the three largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies of terlipressin plus albumin versus placebo plus albumin in adults with HRS.

Abstract #3046-A: The Impact of MELD Score and ACLF Grade on Outcomes of Hepatorenal Syndrome Following Treatment with Terlipressin and Albumin in Patients with Alcohol-Associated Hepatitis[10]

Poster Presentation: Sunday, November 12; 8:00 A.M. EST

Presenting Author: Ethan M. Weinberg, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

A pooled, double-blind, retrospective analysis of patients with alcoholic-associated hepatitis (AH) and cirrhosis from the three largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies of terlipressin plus albumin versus placebo plus albumin in adults with HRS evaluated the relationship between renal and hepatic function in HRS reversal and survival among patients with AH.

Abstract #3054-A: Utility of Concurrent Administration of Albumin with Terlipressin for the Treatment of Hepatorenal Syndrome-Acute Kidney Injury: A Pooled Analysis of Two Randomized Controlled Trials[11]

Poster Presentation: Sunday, November 12; 8:00 A.M. EST

Presenting Author: Manhal Izzy, Vanderbilt University, Nashville, TN

A post hoc analysis of pooled data from two of the largest North American-centric, randomized, placebo-controlled, double-blind Phase III clinical studies (REVERSE, CONFIRM) of terlipressin plus albumin versus placebo plus albumin in patients with HRS aimed to evaluate clinical outcomes, including HRS-AKI reversal and respiratory adverse events, in patients with HRS-AKI who received terlipressin with albumin compared to those receiving terlipressin alone.

Please note that some of the information described in these materials may not be consistent with the FDA-approved labeling of TERLIVAZ® (terlipressin).

INDICATION AND LIMITATION OF USE

TERLIVAZ is indicated to improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function.

- Patients with a serum creatinine >5 mg/dL are unlikely to experience benefit.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS OR FATAL RESPIRATORY FAILURE

- **TERLIVAZ may cause serious or fatal respiratory failure. Patients with volume overload or with acute-on-chronic liver failure (ACLF) Grade 3 are at increased risk. Assess oxygenation saturation (e.g., SpO_2) before initiating TERLIVAZ.**
- **Do not initiate TERLIVAZ in patients experiencing hypoxia (e.g., SpO_2 <90%) until oxygenation levels improve. Monitor patients for hypoxia using continuous pulse oximetry during treatment and discontinue TERLIVAZ if SpO_2 decreases below 90%.**

Please see additional Important Safety Information on next page.

IMPORTANT SAFETY INFORMATION (cont'd)

Contraindications

TERLIVAZ is contraindicated:

- In patients experiencing hypoxia or worsening respiratory symptoms.
- In patients with ongoing coronary, peripheral, or mesenteric ischemia.

Warnings and Precautions

- **Serious or Fatal Respiratory Failure:** Obtain baseline oxygen saturation and do not initiate TERLIVAZ in hypoxic patients. Monitor patients for changes in respiratory status using continuous pulse oximetry and regular clinical assessments. Discontinue TERLIVAZ in patients experiencing hypoxia or increased respiratory symptoms.

  Manage intravascular volume overload by reducing or discontinuing the administration of albumin and/or other fluids and through judicious use of diuretics. Temporarily interrupt, reduce, or discontinue TERLIVAZ treatment until patient volume status improves. Avoid use in patients with ACLF Grade 3 because they are at significant risk for respiratory failure.

- **Ineligibility for Liver Transplant:** TERLIVAZ-related adverse reactions (respiratory failure, ischemia) may make a patient ineligible for liver transplantation, if listed. For patients with high prioritization for liver transplantation (e.g., MELD ≥35), the benefits of TERLIVAZ may not outweigh its risks.

- **Ischemic Events:** TERLIVAZ may cause cardiac, cerebrovascular, peripheral, or mesenteric ischemia. Avoid use of TERLIVAZ in patients with a history of severe cardiovascular conditions or cerebrovascular or ischemic disease. Discontinue TERLIVAZ in patients who experience signs or symptoms suggestive of ischemic adverse reactions.

- **Embryo-Fetal Toxicity:** TERLIVAZ may cause fetal harm when administered to a pregnant woman. If TERLIVAZ is used during pregnancy, the patient should be informed of the potential risk to the fetus.

Adverse Reactions

- The most common adverse reactions (≥10%) include abdominal pain, nausea, respiratory failure, diarrhea, and dyspnea

Please click here to see full Prescribing Information, including Boxed Warning.

References

[1] Wong F, et al. Albumin Dosing with Terlipressin for the Treatment of HRS-AKI: A Double-Edged Sword. Abstract to be presented in oral presentation at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[2] Fricker ZP, et al. Improved Mean Arterial Pressure from Baseline to the End of Treatment with Terlipressin is Associated with Hepatorenal Syndrome Reversal: A Pooled Analysis of 3 Phase III Studies. Abstract to be presented in oral presentation at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[3] Mumtaz K, et al. Decision-Analytic Model to Project the Benefit of Terlipressin Treatment Among Patients with Alcohol-Related Cirrhosis and HRS. Abstract to be presented in oral presentation at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[4] Cullaro G, et al. Understanding the Relationship Between Mean Arterial Pressure and Terlipressin in Hepatorenal Syndrome-Acute Kidney Injury Reversal: A Post Hoc Analysis of the CONFIRM, REVERSE, and OT-0401 Trials. Poster of Distinction to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[5] Wong F, et al. The Prevalence and Clinical Features of Acute Kidney Injury Across Various Stages of Ascites in Patients with Cirrhosis from a Single Quaternary Referral Academic Centre. Poster to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[6] Reddy KR, et al. Efficacy of Continuous Terlipressin Infusion in HRS-AKI in a Transplant-Enriched Population: A Comparative Prospective and Retrospective Cohort Study. Poster to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[7] Wong F, et al. Increased Baseline Indicators of Inflammation in Patients with Hepatorenal Syndrome Type 1 and Grade 3 Acute-on-Chronic Liver Failure: Implications for Terlipressin Therapy. Poster to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[8] Sigal S, et al. Patient Subset Analysis of the REVERSE Phase III Study: The Impact of Terlipressin Treatment on Rates of Transplant, Dialysis, and Survival in Patients with Hepatorenal Syndrome. Poster to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[9] McGuire BM, et al. Terlipressin Treatment and Time to Clinical Response: Characterization of Hepatorenal Syndrome Reversal Using a Pooled Database Of 3 Placebo-Controlled Phase III Clinical Studies. Poster to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[10] Weinberg EM, et al. The Impact of MELD Score and ACLF Grade on Outcomes of Hepatorenal Syndrome Following Treatment with Terlipressin and Albumin in Patients with Alcohol-Associated Hepatitis. Poster to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.
[11] Izzy M, et al. Utility of Concurrent Administration of Albumin with Terlipressin for the Treatment of Hepatorenal Syndrome-Acute Kidney Injury: A Pooled Analysis of Two Randomized Controlled Trials. Poster to be presented at the American Association for the Study of Liver Diseases (AASLD) 2023 The Liver Meeting. November 2023.