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Treatment-Related Cost Analysis for Adults with Hepatorenal Syndrome with Rapid Reduction in Kidney Function

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BACKGROUND

- Hepatorenal syndrome (HRS), a special form of acute kidney failure is a rare, acute, life-threatening complication of cirrhosis and is associated with a very poor prognosis[1-4]
  - Estimated HRS incidence in the United States (US) is about 44,000 cases per year;[5-7] HRS was present in 3.2% of hospitalized patients with chronic liver disease (2012)[6]
  - If HRS is left untreated, median survival time is less than 2 weeks with 80% mortality within 3 months[8]
- From 2005 to 2011, annual costs for HRS increased from $1.4 billion to $3.5 billion[9]
  - HRS economic burden is primarily attributed to costly hospitalizations; key cost drivers in HRS from a hospital perspective include mortality, length of stay, dialysis administration, and discharge to skilled nursing (rather than home)[1,10]
- TERLIVAZ® (terlipressin) is the first and only Food and Drug Administration (FDA)-approved treatment (September 2022) to improve kidney function for adults with HRS with a rapid reduction in kidney function[11]
  - It is recommended as a preferred treatment for HRS by 2022 American College of Gastroenterology guidelines,[12] 2021 American Association for the Study of Liver Diseases guidance,[13] and 2018 international guidelines[14]
- Prior to the approval of terlipressin, midodrine and octreotide (M&O) or norepinephrine were used for HRS treatment, but are not FDA-approved treatments for patients with HRS;[15] therefore, the safety or effectiveness of these unapproved treatments have not been established
- There is a lack of economic evidence on the pharmacological treatments for the management of HRS
  - Health economic evaluations are needed to compare the cost and effectiveness of HRS treatments

OBJECTIVE

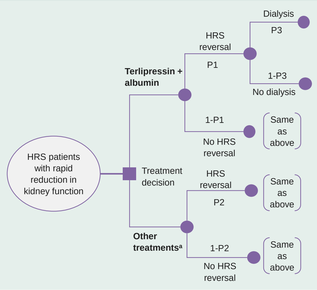
To estimate the cost per response of terlipressin + albumin versus other unapproved treatments, including M&O + albumin and norepinephrine + albumin, from the US hospital perspective

METHODS

Model Overview

- A decision-analytic model was developed to estimate the HRS treatment-related cost per response over an HRS hospitalization (assuming 14 days) [**Figure 1**] from the US hospital perspective
- Upon treatment, patients can experience HRS reversal (complete response; defined as a decrease in serum creatinine from baseline to ≤1.5 mg/dL on treatment [up to 24 hours after last treatment dose]) or no HRS reversal (partial/no response)
  - Patients may or may not undergo dialysis depending on HRS reversal/treatment response
  - The relationship between HRS reversal and likelihood for dialysis is based on analysis of pooled data of three North American randomized clinical trials (CONFIRM,[16] REVERSE,[2] and OT-0401[17])

Figure 1. Schematic of the decision-analytic model for cost-of-care analysis



Abbreviations: HRS, hepatorenal syndrome; P, probability

P1 = HRS reversal rate with terlipressin; P2 = HRS reversal rate with other treatments; P3 = Likelihood of the need for dialysis for patients with HRS reversal

[a]Other treatments: midodrine and octreotide + albumin or norepinephrine + albumin
HRS reversal or complete response is defined as a decrease in serum creatinine from baseline to ≤1.5 mg/dL on treatment (up to 24 hours after the last dose treatment)

Model Inputs

Treatment efficacy

- Efficacy, safety, and treatment duration were from published head-to-head randomized international trials
  - Response rate for terlipressin + albumin versus M&O + albumin comparison was sourced from a randomized controlled trial in patients with HRS[18]
  - Pooled analysis of four trials including patients with HRS based on International Club of Ascites 2015 (or similar) diagnosis criteria was used to estimate the response rate of terlipressin + albumin versus norepinephrine + albumin[19-22]

Healthcare resource utilization

- HRS-related utilization of healthcare resources (including the incremental cost of intensive care unit [ICU] bed, dialysis, and pulse oximetry monitoring) was estimated based on the level of response
  - 85% of patients receiving terlipressin + albumin or M&O + albumin were assumed to be treated on general floor (assumption based on the CONFIRM trial[16])
  - None of the patients receiving norepinephrine + albumin were assumed to be treated on general floor

Treatment costs

- Drug costs per package were obtained from the Red Book (Merative Micromedex® 2022) for each treatment using the wholesale acquisition cost price
- Treatment-related costs comprised ICU bed (including ICU cost for treatment to be administered in ICU and impact of HRS reversal on ICU stay), dialysis [intermittent or continuous], pulse oximetry monitoring for terlipressin, and adverse events were sourced from the published literature (estimated based on pooled analysis of CONFIRM,[16] REVERSE,[2] and OT-0401[17] trials)
- All costs were inflated to August 2022 US Dollars utilizing the historical Consumer Price Index for medical care from the US Bureau of Labor Statistics

Model Outcomes

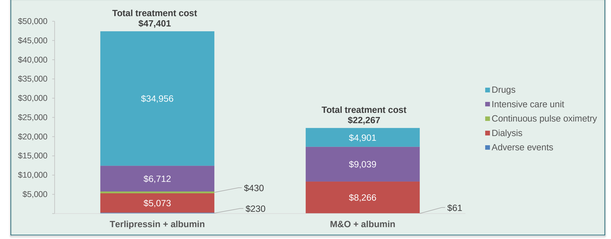
- **Cost per response**: Total treatment cost per HRS reversal was estimated for each treatment
  - **Total treatment costs**: Costs related to drug acquisition, ICU stay, continuous pulse oximetry, dialysis, and adverse events
- **Number needed to treat (NNT):** Number of patients treated to achieve one HRS reversal (inverse of treatment efficacy) was estimated for each treatment

RESULTS

Terlipressin + albumin versus M&O + albumin

- **HRS reversal rate** for terlipressin + albumin (55.56%) was higher than M&O + albumin (4.76%)
- **Total treatment cost** for terlipressin + albumin was $25,134 higher than M&O + albumin ($47,401 versus $22,267) (**Figure 2**).
  - M&O + albumin resulted in higher ICU- and dialysis-related costs
- **Cost per response** of terlipressin + albumin was lower than M&O + albumin ($85,315 versus $467,794)
- Two patients need to be treated with terlipressin + albumin to achieve one HRS reversal versus 21 patients who need to be treated with M&O + albumin

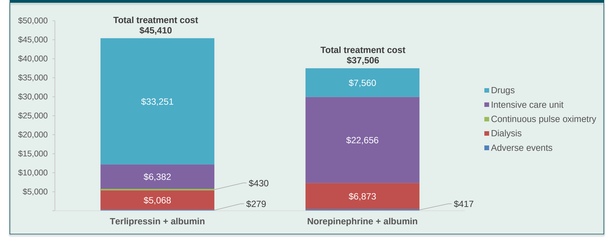
Figure 2. Total cost of terlipressin + albumin versus M&O + albumin



Terlipressin + albumin versus norepinephrine + albumin

- **HRS reversal rate** for terlipressin + albumin (55.64%) was higher than norepinephrine + albumin (26.92%)
- **Total treatment cost** for terlipressin + albumin was $7,904 higher than norepinephrine + albumin ($45,410 versus $37,506) (**Figure 3**).
  - Norepinephrine + albumin resulted in higher ICU- and dialysis-related costs
- **Cost per response** of terlipressin + albumin was lower than norepinephrine + albumin ($81,614 versus $139,324)
- Two patients need to be treated with terlipressin + albumin to achieve one HRS reversal versus four patients who need to be treated with norepinephrine + albumin

Figure 3. Total cost of terlipressin + albumin versus norepinephrine + albumin



LIMITATIONS

- Efficacy and treatment-related adverse event data are from published head-to-head randomized clinical trials, which may not be generalizable to the adult HRS population in the US
  - Further, verified HRS reversal, primary endpoint of the CONFIRM trial, was not used in this analysis
- The estimated cost for each adverse event (based on the IBM® MarketScan® database as well as drug acquisition and healthcare cost data from public sources (Micromedex, Medicare payment schedule, and published literature) may be different from a hospital/institution's experience
  - Drug costs do not reflect discounts and/or rebates offered by manufacturers
  - Analysis focuses on treatment-related cost of care, however, the cost of kidney or liver transplantation during the initial hospitalization (from hospital admission to discharge) is not considered
- Several assumptions were used in the analysis, including the proportion of patients treated on a general floor for each treatment
- Dialysis requirement by treatment response (HRS versus no HRS reversal) was estimated based on pooled data from three randomized clinical trials may be different from a hospital's/institution's experience
- The effect of HRS reversal on ICU-related costs, generated based on the CONFIRM trial may be different from a hospital's/institution's experience
- Due to a short time horizon, other mid-and long-term benefits of HRS reversal post-initial hospitalization, (reduced need for kidney transplantation and better outcomes post-liver transplantation) are not captured

CONCLUSIONS

- Based on the cost-of-care analysis, terlipressin + albumin was associated with a lower cost per HRS reversal than M&O + albumin and norepinephrine + albumin
- These findings suggest that terlipressin is a cost-effective treatment due to its higher efficacy and administration in the non-ICU setting
- The lower NNT with terlipressin + albumin (versus M&O + albumin or norepinephrine + albumin) suggested improved treatment efficacy of terlipressin + albumin
- Terlipressin is a value-based treatment option for appropriate adults with HRS with rapid reduction in kidney function

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DISCLOSURES

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