Reduction in Acute Kidney Injury (AKI) Stage is a Strong Predictor of Survival in Patients with Hepatorenal Syndrome Type-1 (HRS-1) Treated with Terlipressin plus Albumin or Albumin Alone

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Introduction and Aims: HRS-1 is a form of acute kidney injury (AKI) that occurs in patients with end-stage liver disease (ESLD). It is a serious complication that is often fatal if not treated. For AKI in general, it is well established that an increase in AKI stage (using the AKI Network classification), is associated with decreased survival. Conversely, data examining improvement of renal function (i.e. a decrease in AKI stage) and its correlation with survival is limited, particularly in HRS-1. The purpose of this study was to evaluate the impact of changes in AKI stage on survival in patients with HRS-1 in the REVERSE study, the largest, prospective, randomized trial of terlipressin plus albumin vs. albumin alone in cirrhotic patients with HRS-1.

Methods: 196 subjects with well documented HRS-1, based on International Ascites Club (IAC) criteria were enrolled; baseline AKI stage was determined using serial serum creatinine (SCr) values collected as part of the pre-enrollment assessment. Subjects were randomized to receive terlipressin (1 mg IV every 6 hours) or placebo, plus albumin. Change in AKI stage from baseline to end of study treatment (EOT) and overall survival at Day 90 were evaluated.

Results: AKI stage at baseline: stage 1 - 22.5%, stage 2 - 39.8%, stage 3 - 37.8%. Improvement in AKI stage from baseline to EOT occurred in 56/180 (31.1%) subjects; no change or an increase in AKI stage occurred in 91/180 (50.6%) and 33/180 (18.3%) subjects respectively. Of the 56 subjects with improvement in AKI stage, 32 (57.1%) improved by 1 stage; 24 (42.9%) improved by 2 or 3 stages. Linear regression analysis showed that survival was highly correlated with change in AKI stage from baseline to EOT (r² = 0.9536; p < 0.0007) (Figure).

Conclusions: These results show that in patients with HRS-1, a decrease in AKI stage from baseline to EOT is associated with improved survival. Down staging of AKI may be useful as a surrogate marker in the assessment of the efficacy of treatment for HRS-1.