

Mallinckrodt Pharmaceuticals:

2017 Investor Briefing Presentation
Terlipressin Physician Guest Speaker

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Terlipressin for Hepatorenal Syndrome Type -1

Samuel H. Sigal, M.D.

Professor of Medicine and Chief of Liver Transplant
Montefiore Medical Center, New York



Hepatorenal Syndrome Type 1 (HRS type 1)



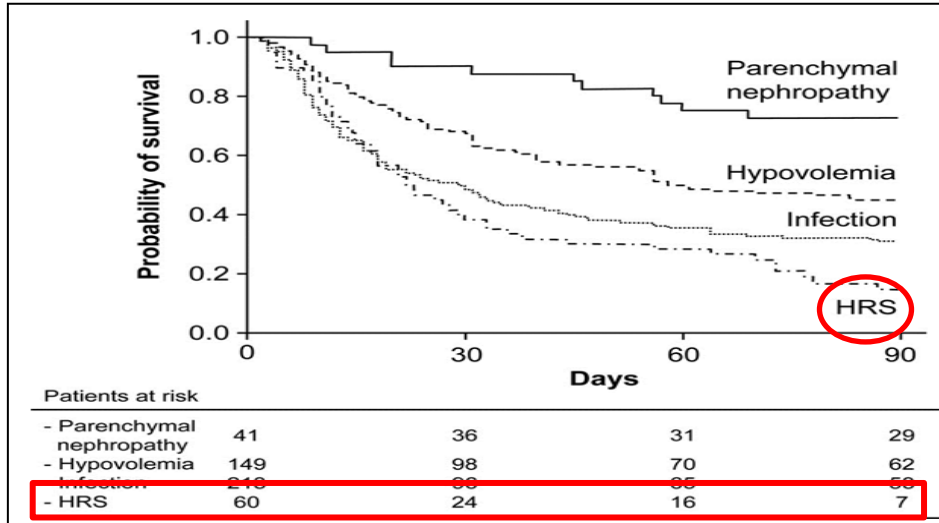
- HRS type 1 is a rare, life-threatening complication of cirrhosis that affects approx. 10-30 thousand patients in the U.S. (13% of patients with cirrhosis)¹⁻⁴
- Associated with acute functional renal failure due to reduced renal perfusion -- rapid increase in serum creatinine over two week period^{5,6}
- Kidneys appear structurally normal on diagnostic imaging^{5,6}
- Currently no approved pharmacological therapy in United States
- Survival improves with early diagnosis and treatment^{5,6}

1. Boyer TD et al. *Open Access Journal of Clinical Trials*. 2012;4:39-49.
2. Marrero J et al. *Am J Respir Crit Care Med*. 2003;168:1421-1426.
3. Muir AJ et al. *Liver Transpl*. 2002;8:957-961.
4. Gines A et al. *Gastroenterology*. 1993;105:229-236.
5. Barbano B et al. *Curr Vasc Pharmacol*. 2014;12:125-135.
6. Low G et al. *Gastroenterol Res Pract*. 2015;2015:207012.doi:10.1155/2015/207012. Epub 2015 Jan 12.

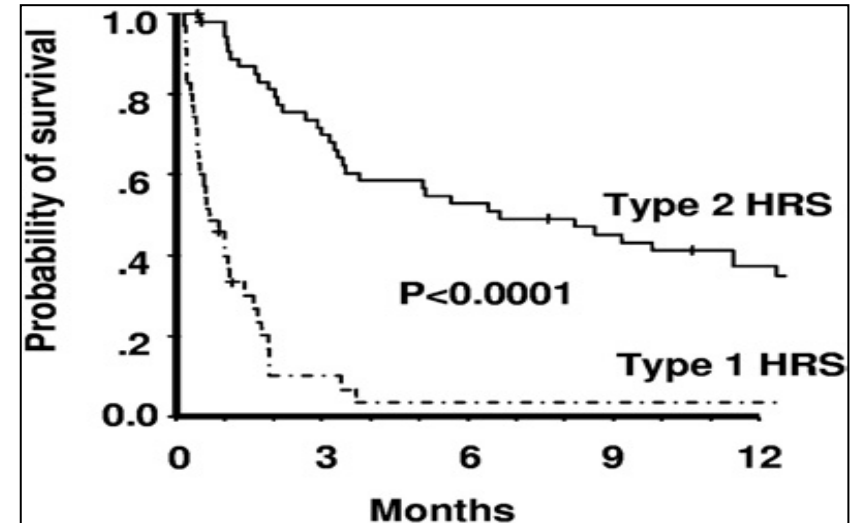
HRS has high rate of in-hospital mortality



- Median survival <2 weeks^{1,2}
 - Nearly fatal in all patients within 10 weeks of onset



Martin-Llahi et al, 2011



Salerno et al, 2011

1. Arroyo V et al. *Semin Liver Dis.* 2008;28:81-95.
2. Fagundes C et al. *AJKD.* 2012;59:874-885.
3. Martín-LLahí M et al. *Gastroenterology.* 2011;140:488-496.
4. Salerno F et al. *J Hepatol.* 2011;55:1241-1248.

Terlipressin for hepatorenal syndrome



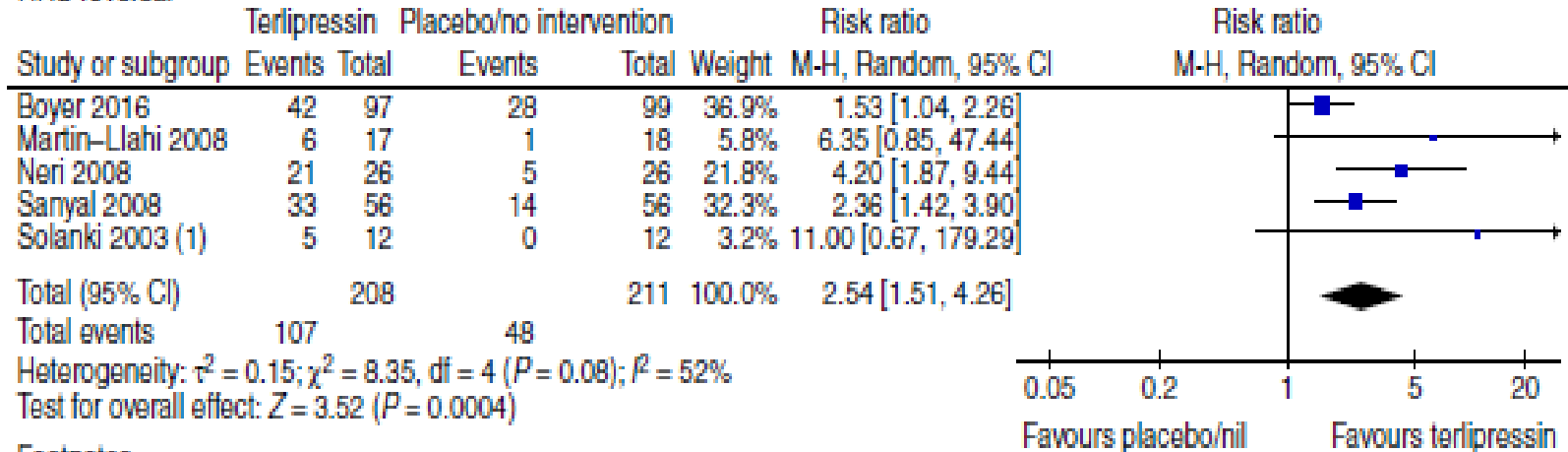
- Terlipressin has been approved for over 30 years; across 60 countries in EU, Asia, Latin America and Australia
- First line therapy for HRS Type 1 and Esophageal Variceal Hemorrhage per global treatment guidelines outside of the U.S.*
- Only potent vasopressor that can be administered outside ICU
- Terlipressin selectively acts via V1 receptors in splanchnic bed to restore renal blood flow
- Terlipressin is the most studied pharmacological agent in HRS with more than 44 published clinical studies to date

* EASL, AASLD, KDIGO guidelines; more than 40 published studies for each indication

Subjects treated with terlipressin plus albumin had greater incidence of HRS reversal than albumin alone



HRS reversal

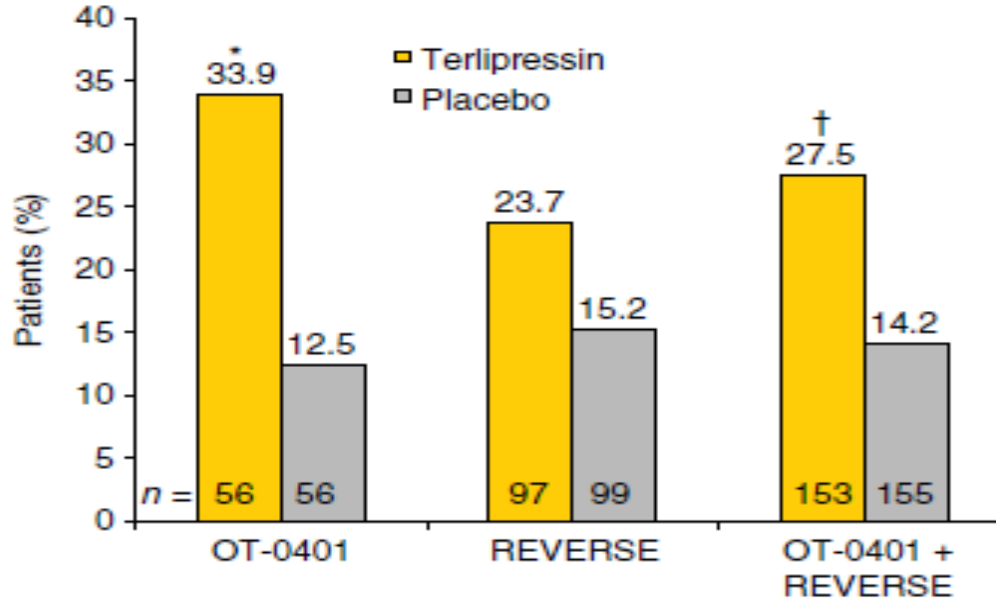


Footnotes

(1) Solanki – definition of HRS reversal not given

Improved sCr

Terlipressin use led to greater incidence of HRS reversal in previous U.S. clinical trials



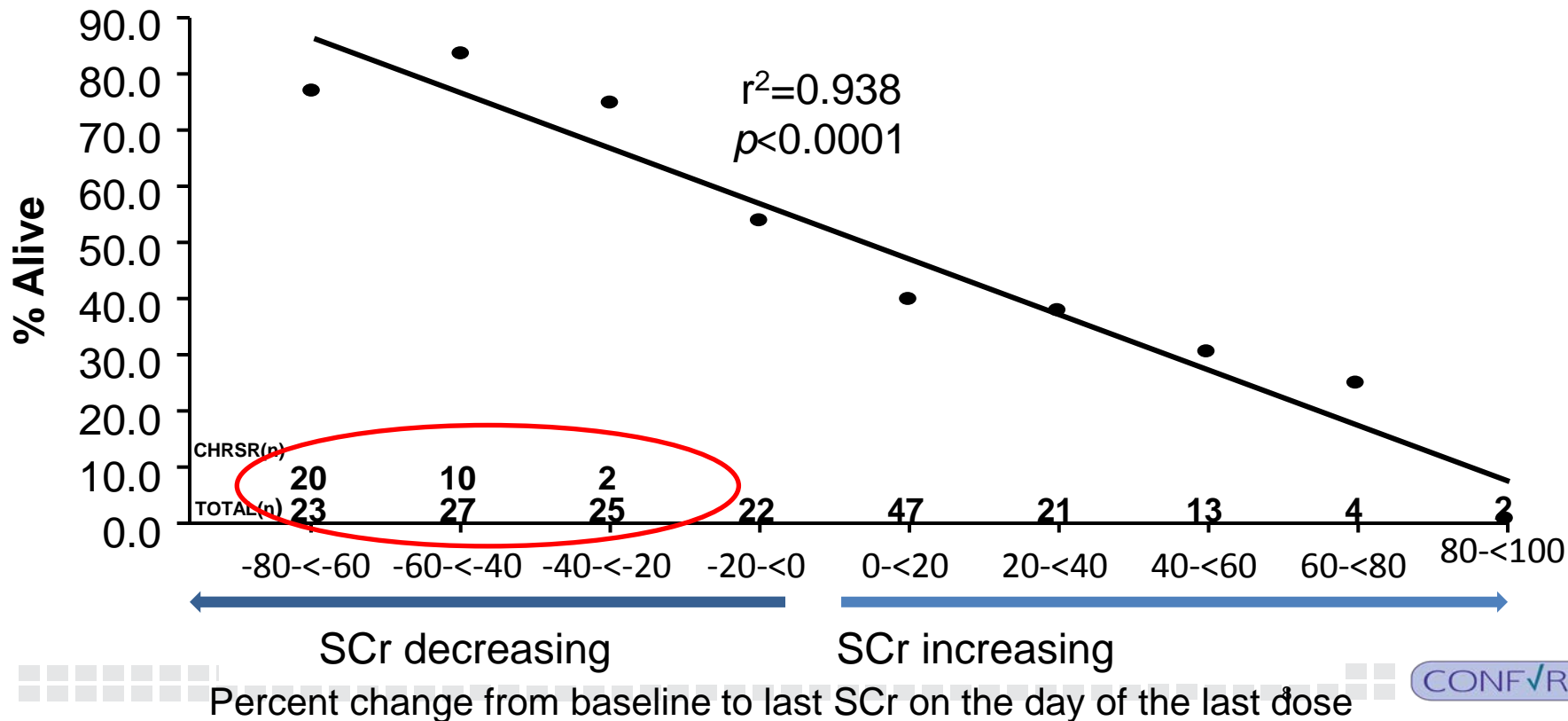
P: 0.008 vs. Placebo and †P: 0.004 vs. Placebo Sanyal A. J. et al Journal of APT 2017



European Liver Meeting (EASL 2015)



Improvement in renal function correlates with improved survival





Thank You

