Supplementary table1 : Prominent studies of Rifaximin in Hepatic Encephalopathy

REFERENCE (location)	STUDY DESIGN	PATIENT POPULATION	MAIN OUTCOMES
Covert/Minimal HE therapy			
Bajaj et al 2011 (USA) https://pubmed.ncbi.nlm.nih.gov/20849805/	Double Blind RCT	-42 outpatients with cirrhosis with impaired performance on cognitive tests - 21 on placebo and 21 on rifaximin for 8 weeks -Cognitive testing and driving simulation	At end of 8 weeks in rifaximin compared to placebo - Improved cognitive performance (91% vs 61%, P=0.01) - Reduced driving errors (76% vs 31%; P = 0.01), speeding (81% vs 33%; P = 0.005)and illegal turns (62% vs 19%; P = .01) on the simulator - Improved quality of life on Sickness impact profile and increased anti-inflammatory molecule IL-10
Sidhu et al 2011 (India) https://pubmed.ncbi.nlm.nih.gov/21157444/	Double Blind RCT	-94 outpatients randomized to placebo or rifaximin for 8 weeks - Cognitive testing and quality of life tested	At end of 8 weeks in rifaximin compared to placebo -Lower mean abnormal cognitive tests (0.81 vs 1.97) -Improved quality of life using Sickness impact profile - Rifaximin had a good safety profile
Prevention of Recurrence			
Bass et al 2010 (North America, Russia, Ukraine) https://pubmed.ncbi.nlm.nih.gov/20335583/	Double Blind RCT	-299 patients with cirrhosis with ≥2 prior HE episodes of whom >90% were on lactulose -159 in placebo and 140 in rifaximin group and followed for 6 months	Rifaximin 550mg BID versus placebo was associated with - Reduced risk of breakthrough HE (HR 0.42), Number needed to treat=4 - Reduced risk of HE-related hospitalizations (HR 0.50), Number needed to treat=9 - Sensitivity analysis favored rifaximin in most subgroups - Acceptable safety profile of rifaximin
Mullen et al 2012 (open label part in USA) https://pubmed.ncbi.nlm.nih.gov/24365449/	Open-label extension and new initiation of rifaximin	-299 patients from Bass et al and 252 new patients with cirrhosis and HE included. -Safety assessed in 392 patients (140 RCT + 252 new) and efficacy compared to with 159 placebo-assigned patients -24 month follow-up	In the all-rifaximin group (n=392), - Rifaximin exposure was for a median of 427 days and 5105 per-years - Open-label extension and new patients on rifaximin exhibited favorable safety profile similar to the Bass et al RCT Hospitalization rate comparison - HE-related hospitalization rate remained low despite normalizing for exposure - 0.21 in n=392 all-rifaximin, 0.30 in those in original RCT on rifaximin compared to 0.72 in placebo
Bajaj et al 2015 (USA) https://pubmed.ncbi.nlm.nih.gov/25339518/	Cross-over analysis	-82 patients randomized to placebo in Bass et al who then received open-label rifaximin -Followed for 6 months on placebo and 6 months on rifaximin	Compared to when they were on placebo, patients crossed over on to rifaximin experienced - Lower HE episodes 39 vs 14 (p<0.0001) - Event rate reduced from 1.5 to 0.42 from placebo to rifaximin ; number needed to treat=3 - Numerically reduced HE-related hospitalization rate (0.57 placebo to 0.36 rifaximin)
Inpatients			
Sharma et al 2013 (India) https://pubmed.ncbi.nlm.nih.gov/23877348/	Double-blind RCT	-120 inpatients with cirrhosis and HE randomized into (a) rifaximin+lactulose (n=63) and (b) lactulose only (n=57)	Compared to lactulose, the lactulose+rifaximin group had - Higher HE reversal (76% vs 51%, p<0.004) - Lower mortality (24% vs 49%, p=0.05) - Shorter hospital stay (5.8 vs 4.6 days, p=0.001) - No change in gastrointestinal bleeding or hepatorenal syndrome

		-Inpatient mortality and stay were endpoints	
Health system changes			
Hudson et al 2017 (UK) https://pubmed.ncbi.nlm.nih.gov/29067149/	Observational study	-207 patients with rifaximin analyzed 6 months pre and post rifaximin -34% on 1100mg/day and 61% were on 1200mg/day	Compared to the 6 months pre-rifaximin to post-rifaximin - Reduced liver-related hospitalizations 1.3 to 0.5, p<0.001 - Reduced all-cause hospitalizations 1.9 to 0.9, p<0.001 - Also reduced hospital bed days/patient, readmissions and emergency room visits
Orr et al 2016 (UK) https://pubmed.ncbi.nlm.nih.gov/26950766/	Observational study	-326 patients on rifaximin followed over 12 months from seven hospitals in UK -Compared before rifaximin to after rifaximin	Compared to pre-rifaximin, rifaximin was associated with - Lower length of hospital stay (31-53%) - Reduced costs of hospitalization (4858-6607 pounds per year)