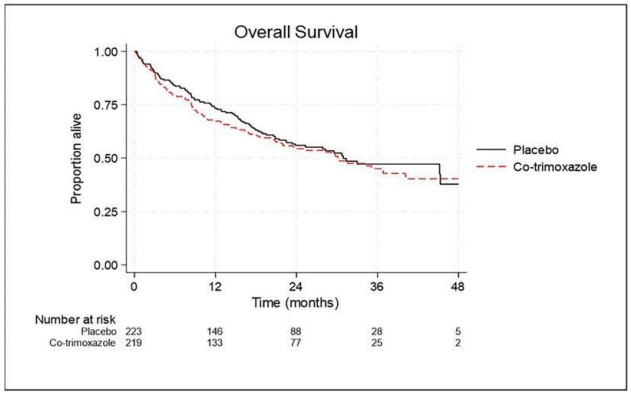
survival did not differ between groups with 101 (46.1%) deaths in Co-trimoxazole arm and 98 (43.9%) deaths in placebo, hazard ratio (HR) 1.10 (95% CI 0.83-1.45), p = 0.52. When adjusted for stratification factors at baseline (on transplant list, use of rifaximin, liver disease due to alcohol and active alcohol use), survival HR was 1.09 (95% CI 0.82-1.44). There was no difference in overall survival (HR 1.17, CI 0.85-1.6) nor unplanned hospital admissions (HR 1.07, CI 0.84-1.37) during trial treatment period and no difference in time to first incidence of spontaneous bacterial peritonitis (HR 1.58, CI 0.85-2.92). Predefined subgroup analyses of the 159 patients known to have an ascitic protein count ≤ 1.5g/L did not show a difference in survival between groups (HR 1.27, 95% CI 0.79-2.04). **Conclusion:** In the largest trial of primary antibiotic prophylaxis for patients with cirrhosis and ascites, use of Co-trimoxazole had no effect on overall survival. Given the increasing impact of antimicrobial resistance, our results strongly support abandoning primary prophylaxis.

Figure: Kaplan-Meier curve for overall survival. Log rank test P=0.52



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5007 | EFFICACY AND SAFETY OF LIBEVITUG (HH-003) IN PATIENTS WITH CHRONIC HEPATITIS D VIRUS INFECTION FROM AN INTERNATIONAL, MULTICENTRE, RANDOMIZED, CONTROLLED, OPEN-LABEL PHASE 2B STUDY

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Background: Libevitug (HH-003) is a human monoclonal antibody targeting the PreS1 domain of the large envelope protein of hepatitis B virus (HBV). By blocking HBV and HDV entry into hepatocytes, libevitug could lead to a profound reduction in HDV RNA and ALT levels in patients with chronic HBV/HDV infection. Libevitug is currently being evaluated in a pivotal Phase 2b study (HH003-204; NCT05861674) for treatment of chronic HDV infection. Here, we report the 48-week treatment outcomes from this ongoing study. **Methods**: Eligible patients with chronic HDV infection were stratified by cirrhosis status and country, and randomized in a 2:2:1 ratio into three groups: two libevitug dose groups receiving either 20 mg/kg or 10 mg/kg intravenously every two weeks, plus 25 mg oral tenofovir alafenamide fumarate (TAF) daily for 48 weeks followed by a 24-week follow-up period with TAF only, and a control group receiving only TAF for 48 weeks without follow-up. The primary endpoint, defined as a combined response, is the proportion of patients who, at week 24, achieve either HDV RNA below the lower limit of quantification (LLOQ) or a decrease of ≥ 2 $\log_{10}$ from baseline, together with ALT normalization. Other endpoints included the combined response at week 48, the rates of HDV RNA response and ALT normalization rates at weeks 24 and 48, changes in HDV RNA and ALT levels, and change in liver stiffness. **Results:** A total of 94 patients with abnormal baseline ALT were included in the main analysis set: 40 in libevitug 20 mg/kg group, 34 in the 10 mg/kg group, and 20 in the

control group. Baseline characteristics were generally balanced across groups with a mean age of 40.3 years, 68% males, 16% with compensated cirrhosis, mean HDV RNA 6.1 log_{10} IU/mL and mean ALT 103.8 U/L. The combined response rates at week 24 were 35.0% for the libevitug 20 mg/kg group and 32.4% for the 10 mg/kg group, increasing to 42.5% and 44.1% at week 48, respectively, which were significantly higher than that in the control group. Responses in HDV RNA, ALT and liver stiffness in the libevitug groups were also significantly greater than that in the control group. Additionally, libevitug was safe and well-tolerated, without serious adverse events (AEs) related to libevitug or AEs leading to discontinuation. **Conclusion:** Libevitug demonstrated good efficacy and safety profile in treating chronic HDV infection, with comparable results observed in both dose groups.

Table. Efficacy and safety results at weeks 24 and 48

Efficacy results at weeks 24 and 48						
n (%)	HH-003 20 mg/kg (N=40)		HH-003 10 mg/kg (N=34)		Control group (N=20)	
	Week 24	Week 48	Week 24	Week 48	Week 24	Week 48
Combined response 95% CI P Value [1]	14 (35.0%) 20.6%, 51.7% 0.0121	17 (42.5%) 27.0%, 59.7% 0.0026	11 (32.4%) 17.4%, 50.5% 0.0215	15 (44.1%) 27.2%, 62.1% 0.0022	1 (5.0%) 0.1%, 24.9% -	1 (5.0%) 0.1%, 24.9% -
HDV RNA response [2] 95% CI P Value	17 (42.5%) 27.0%, 59.1% 0.0026	24 (60.0%) 43.3%, 75.1% <0.0001	12 (35.3%) 19.8%, 53.5% 0.0188	17 (50.0%) 32.4%, 67.6% 0.0007	1(5.0%) 0.1%, 24.9% -	1(5.0%) 0.1%, 24.9% -
ALT normalization 95% CI P Value	31 (77.5%) 61.6%, 89.2% <0.0001	28 (70.0%) 53.5%, 83.4% <0.0001	20 (58.8%) 40.7%, 75.4% 0.0099	19 (55.9%) 37.9%, 72.8% 0.0012	4 (20.0%) 5.7%, 43.7% -	2 (10.0%) 1.2%, 31.7% -
Change from BL in HDV RNA levels (log_{10} IU/mL): Mean (SE) P Value	-2.00 (0.17) <0.0001	-2.53 (0.19) <0.0001	-1.70 (0.18) <0.0001	-1.95 (0.20) <0.0001	-0.38 (0.12) -	-0.49 (0.17) -
Change from BL in liver stiffness (Kpa): Mean (SE) P Value	-1.65 (0.57) 0.02	-2.3 (0.45) 0.01	-1.82 (0.37) 0.02	-1.52 (0.50) 0.23	0.17 (0.62) -	-0.45 (0.68) -
Overall safety# summary through week 48, n (%)						
TEAE	40 (95.2%)		37 (97.4%)		19 (95.0%)	
TEAE with Grade 3*	4 (9.5%)		3 (7.9%)		2 (10.0%)	
Grade 3 TEAE related to HH-003	1 (2.4%) &		0		0	
SAE related to HH-003	0		0		0	

BL=Baseline; TAF= Tenofovir alafenamide fumarate; LLOQ= Lower Limit of Quantification; CI= Confidence Interval
TEAE= Treatment Emergent Adverse Event; SE= Standard Error; SAE= Serious Adverse Event
Both HDV RNA and ALT samples were analysed in a central laboratory. HDV RNA was quantified using Robogene HDV RNA quantification kit version 2.0 (LLOQ=46.77 IU/mL), while the normal range for ALT is 0-33 U/L for female and 0-41 U/L for male.
1.Fisher's exact test was implemented in a hierarchical manner; Clopper-Pearson method was used to calculate the 95% CI.
2.HDV RNA response defined as plasma HDV RNA below the LLOQ or a decrease of ≥ 2 log_{10} from baseline.
Based on the safety set, 42 patients were in HH-003 20 mg/kg, 38 in HH-003 10 mg/kg and 20 in the control group.
& AE term: neutrophil count decreased, which was considered possibly related to HH-003; and it was transient, asymptomatic, and resolved spontaneously without intervention.
* No Grade 4 TEAEs were reported in this study.

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5008 | SAFETY AND EFFICACY OF INEBILIZUMAB IN IGG4 RELATED DISEASE IN PARTICIPANTS WITH HEPATIC, PANCREATIC, AND BILIARY INVOLVEMENT: RESULTS FROM THE PHASE 3 MITIGATE TRIAL

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Background: Pancreatic and hepatobiliary disease are frequent manifestations of IgG4 Related Disease (IgG4-RD), an immune-mediated, relapsing, fibroinflammatory disease that results in tissue damage and loss of organ function. Inebilizumab (INEB) is an anti-CD19 monoclonal antibody that results in rapid and durable B cell depletion. MITIGATE (NCT04540497) is a randomized, placebo (PBO)-controlled Phase 3 trial evaluating the safety and efficacy of INEB as a treatment for IgG4-RD. **Methods**: A post hoc subgroup analysis of MITIGATE trial results was conducted to evaluate safety and efficacy outcomes in subjects who had baseline disease activity in the pancreas, bile ducts, or liver. Eligible subjects had a history of at least 2 organs involved and had experienced an IgG4-RD flare that required glucocorticoid treatment during the screening period. Subjects were randomized 1:1 to INEB or PBO and were treated on day 1, day 15, and week 26 of the 1-year randomized controlled period (RCP). Steroids were tapered to discontinuation at the end of RCP week 8. Other immunosuppressive therapy for IgG4-RD was prohibited during the study. **Results:** Among 135 enrolled subjects, 52% had historic involvement of the pancreas, 32% of the bile ducts, and 7% liver. At study baseline, disease activity was seen in the pancreas, bile ducts, and liver in 51 (38%), 28 (21%), and 5 (4%) subjects, respectively. INEB reduced the risk of flare (primary endpoint of the study) relative to PBO in the pancreas group (HR = 0.03, nominal p = .0005). In the bile duct group, 0/13 INEB-treated and 12/15 PBO-treated subjects experienced a flare. In the liver group, 0/2 INEB-treated and 3/3 PBO-treated subjects experienced a flare. The proportion of subjects achieving flare-free, treatment-free complete remission were higher with INEB vs. PBO (odds ratios 10.8 and 35.8 for the pancreas and bile duct groups, respectively). Steroid use was substantially reduced with INEB vs. PBO in the pancreas and bile duct