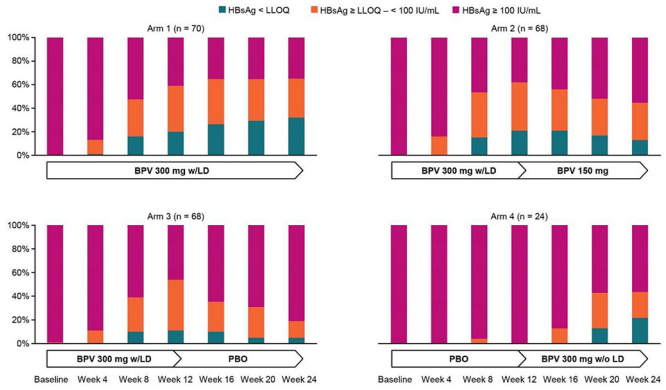
population (70, 68, 68 and 24 pts, respectively, in arms 1–4); 21 pts (9%) discontinued treatment. At EoT, 29%, 13%, 7% and 0% pts had HBsAg <LLOQ and HBV DNA <LLOQ in arms 1–4, respectively. HBsAg response data are shown in Figure. Overall, serious AEs (SAEs) were reported in 4% pts and treatment-related SAEs in 1% pts. No clinically meaningful differences in AEs across treatment arms.

Conclusion: 24 wks of 300 mg BPV resulted in HBsAg <LLOQ and HBV DNA <LLOQ in 29% of pts at EoT; the durability of this response is being assessed. There were no safety signals to preclude further development.

Funding: GSK (209668) [on behalf of the B-Clear study group].

Figure: Percentage of patients with HBsAg < LLOQ, ≥ LLOQ – < 100 IU/mL and ≥ 100 IU/mL over time by treatment arm.



BPV, bepirovirsen; LD, loading dose; LLOQ, lower limit of quantification; PBO, placebo; w/, with; w/o, without.

LB004B

Efficacy and safety of bepirovirsen in patients with chronic hepatitis B virus infection on stable nucleos (t)ide analogue therapy: interim results from the randomised phase 2b B-Clear study

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Background and aims: Bepirovirsen (BPV; GSK3228836) is an antisense oligonucleotide shown to induce a reduction in hepatitis B surface antigen (HBsAg), and in some cases transient HBsAg seroclearance, following 4 weeks (wks) treatment with a favourable safety profile in a phase 2a study in patients (pts) with chronic hepatitis B (CHB) infection. B-Clear is a phase 2b trial (NCT04449029) assessing the efficacy and safety of 12 or 24 wks BPV treatment in pts with CHB on-stable nucleos (t)ide analogue (NA) treatment or not on-NA therapy at study start. The study is ongoing; here we present interim results through the end of BPV treatment (EoT) for pts not on NA therapy.

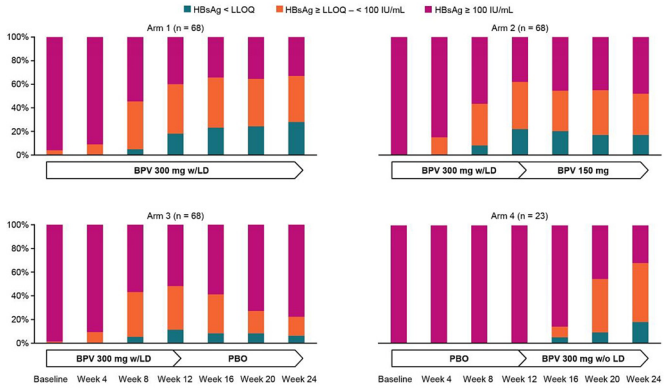
Method: Multicentre, randomised, partial-blind (investigator unblinded), parallel-cohort study in pts with CHB. Pts required HBsAg >100 IU/ml, HBV DNA <90 IU/ml and alanine aminotransferase ≤2× upper limit of normal. Pts were randomised (3:3:3:1) to 1 of 4 treatment arms, with treatment administered weekly with (w/) or without (w/o) loading doses (LD) on Days 4 and 11: 1. BPV 300 mg w/LD for 24 wks; 2. BPV 300 mg w/LD for 12 wks then 150 mg for 12 wks; 3. BPV 300 mg w/LD for 12 wks then placebo (PBO) for 12 wks; 4. PBO for 12 wks then BPV 300 mg w/o LD for 12 wks. Pts were stratified by baseline hepatitis B e antigen (HBeAg; positive/negative) and HBsAg level (≤3 or >3 log10 IU/ml). Primary end point: proportion of pts achieving HBsAg <lower limit of quantification (LLOQ) and HBV DNA <LLOQ sustained for 24 wks without rescue medication after planned BPV EoT. Secondary end points reported here: proportion of pts achieving HBsAg <LLOQ and HBV DNA <LLOQ by BPV EoT. Safety was assessed via adverse event (AE) monitoring.

Results: 227 pts (73% male, 52% Asian, 69% HBeAg negative, 28% HBsAg ≤3 log10 IU/ml) were included in the intent-to-treat population (68, 68, 68 and 23 pts, respectively, in arms 1–4); 12 pts (5%) discontinued treatment. At EoT, 28%, 17%, 9% and 14% pts had HBsAg <LLOQ and HBV DNA <LLOQ in arms 1–4, respectively. HBsAg response data are shown in Figure. Overall, serious AEs (SAEs) were reported in 3% pts and treatment-related SAEs in <1% pts. No clinically meaningful differences in AEs across treatment arms.

Conclusion: 24 wks of 300 mg BPV resulted in HBsAg <LLOQ and HBV DNA <LLOQ in 28% pts at EoT; the durability of this response is being assessed. There were no safety signals to preclude further development.

Funding: GSK (209668) [on behalf of the B-Clear study group].

Figure: Percentage of patients with HBsAg < LLOQ, ≥ LLOQ – < 100 IU/mL and ≥ 100 IU/mL over time by treatment arm.



BPV, bepirovirsen; LD, loading dose; LLOQ, lower limit of quantification; PBO, placebo; w/, with; w/o, without.