



# EASL investor presentation

Bepirovirsen – B-Well 1 & 2 pivotal phase III studies

# Speakers



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All expectations, guidance and outlooks regarding future performance and the dividend should be read together with the section "Guidance and outlooks, assumptions and cautionary statements on pages 44 and 45 of our stock exchange announcement of the Group's Q1 2026 Results and the statements on page 328 of the Group's Annual Report for FY 2025.

Nina Mojas

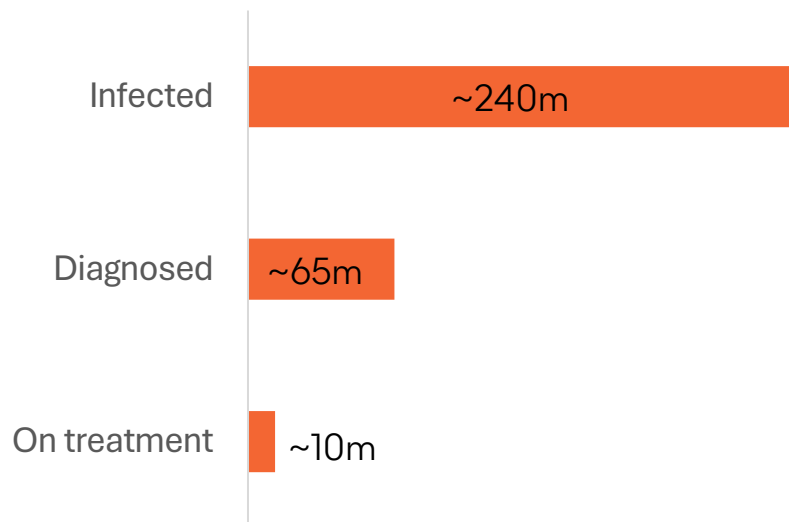
President, Global Product Strategy



# Chronic Hepatitis B (CHB) is a lifelong infection, globally undertreated

CHB puts people at high risk of death from cirrhosis and liver cancer

Diagnostic Gap globally: Only 27% diagnosed, less than 5% on treatment

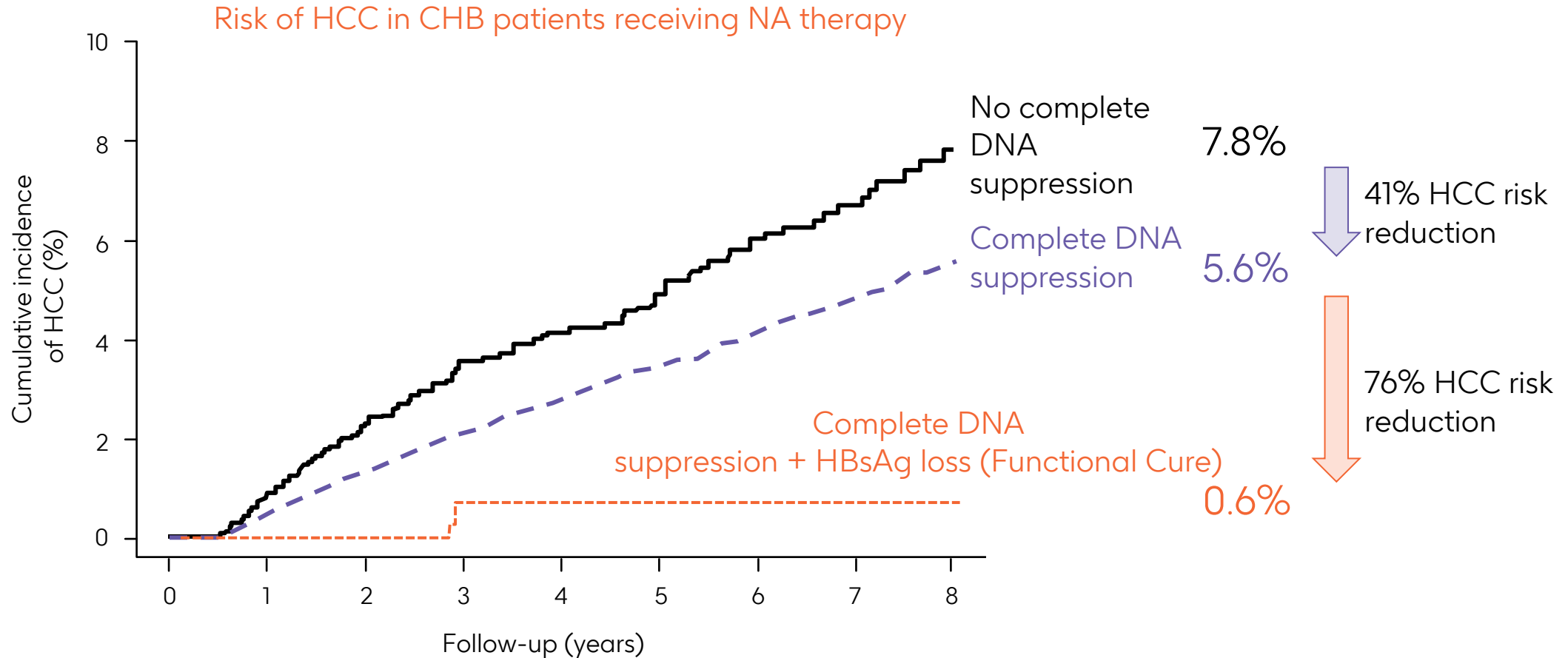


~800k deaths from liver cancer annually

- **Mostly spread** from mother-to-child
  - ~95% of these infections lead to CHB
- 
- **Standard of care (SoC):** Viral suppression only
  - Nucleos(t)ide analogues (NAs) suppress HBV DNA but rarely achieve functional cure
  - Lifelong therapy with no defined endpoint
- 
- **Unmet need:** Durable HBsAg (Hepatitis B surface antigen) loss
  - Functional cure would transform HBV into a finite treatment course

# Today's SoC is not sufficient to reduce Hepatocellular carcinoma (HCC) risk

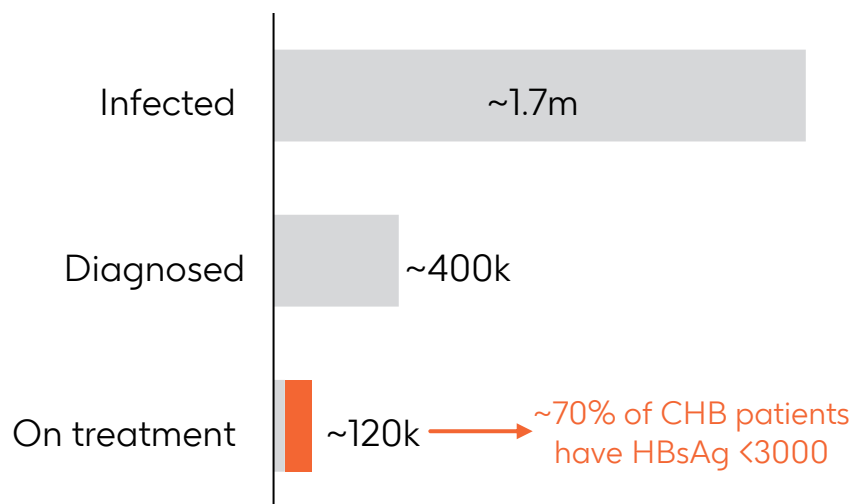
## HBsAg loss associated with significant reduction in risk of HCC



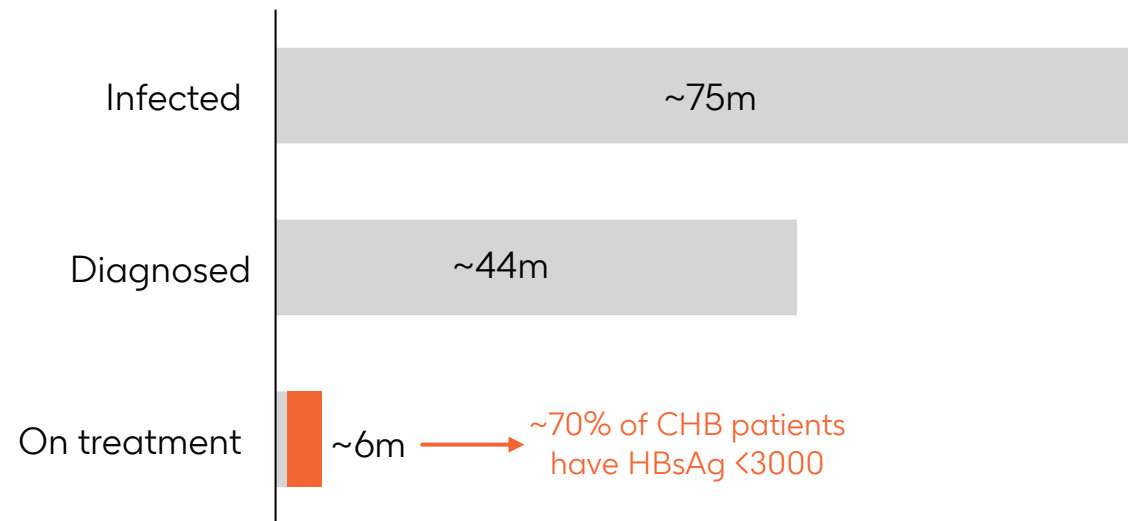
Functional cure will address unmet need in CHB and reduce HCC risk

# Significant diagnosed population waiting for better treatment options

## US patient opportunity



## China patient opportunity

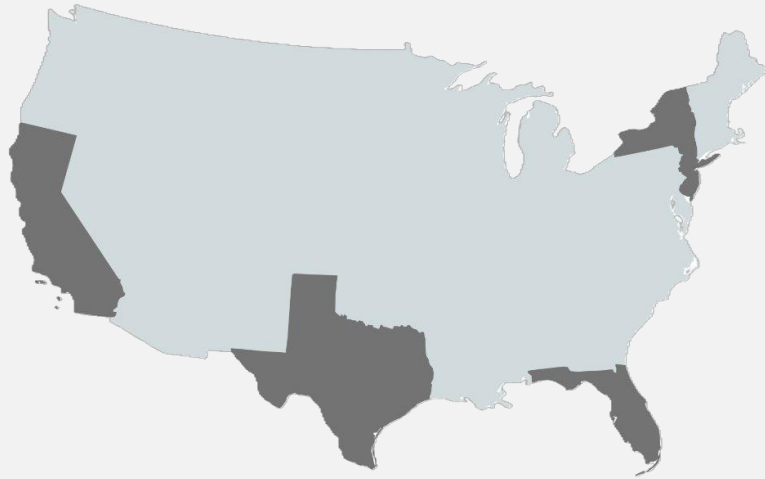


- Current SoC is NA
- Patients linked to populations originating from areas where prevalence typically higher (e.g. Africa and Asian sub-continent)

- 85% Chinese liver cancer cases associated with CHB
- CHB is a National Health Priority in China; Functional Cure is well understood

## 3 key markets represent ~80% global opportunity

### US



- **BTD** and **PDUFA 26 October**
- **>50%** of CHB population is concentrated in five US states
- **~50%** of CHB population with medical cover have commercial insurance, **~25%** have Medicaid and **~22%** have Medicare

### China

- **Priority Review** and collaboration with Sino Biopharmaceutical
- A market leader in hepatology
- Broad commercial footprint with access to **>5000** medical centres

### Japan

- **SENKU designation: 1<sup>st</sup> for GSK** accelerated 6-month review
- **Second largest treated population** with **~900k** CHB patients, **~140k** treated with NAs today

# B-Well 1 & 2

Prof Seng Gee Lim,  
Director of Hepatology  
National University Health System  
Singapore

**GSK**

# Clinically meaningful rates of functional cure in virologically suppressed patients with chronic hepatitis B infection treated with bepirovirsen: B-Well Phase 3 Trials

Professor Seng-Gee Lim, National University Health System, Singapore,  
on behalf of the B-Well Study Group

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# Therapies targeting functional cure are needed in chronic HBV infection

- Chronic HBV infection affects 240 million people worldwide<sup>1</sup>
- Causes over a million deaths annually<sup>1</sup> and increases patients' risk of HCC<sup>2-4</sup>

**Functional cure is the treatment goal** in chronic HBV infection<sup>5,6</sup>

- ≥24 weeks of sustained HBV DNA <LLOQ and HBsAg loss after finite therapy, with or without anti-HBs

## Bepirovirsen

- An antisense oligonucleotide that targets all HBV transcripts, reducing HBV DNA and HBsAg levels<sup>7,8</sup>
- First HBV therapy in **global Phase 3** trials with **functional cure as the primary outcome**<sup>9</sup>

**Here, we present the key efficacy and safety results of the B-Well 1 and B-Well 2 Phase 3 trials**

anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; LLOQ, lower limit of quantification.

1. World Health Organization. Global hepatitis report 2026. Available from: <https://www.who.int/publications/i/item/9789240122383> [Accessed May 2026]; 2. Fu MX, et al. *JHEP Rep* 2025;7(4):101312; 3. Toumi M, et al. *BMC Public Health* 2024;24(1):611; 4. Vitall A, et al. *Clin Liver Dis* 2019;23:417-32; 5. Ghany MG, et al. *Hepatology* 2023;78(5):1654-73; 6. Cornberg M, et al. *J Hepatol* 2025;83(2):502-83;

7. Yuen M-F, et al. *N Engl J Med* 2022;387(21):1957-68; 8. Yuen MF, et al. *Nat Med* 2021;27(10):1725-34; 9. Hou J, et al. *N Engl J Med* 2026; DOI: 10.1056/NEJMoa2515131.

## B-Well 1 and 2 objectives

### Primary outcome at Week 72

#### Functional cure rate in participants with baseline HBsAg $\leq 3000$ IU/mL

- 24 weeks after discontinuing all HBV treatments:
  - HBsAg loss (qualitative;  $<0.05$  IU/mL)
  - HBV DNA  $<$ LLOQ ( $<20$  IU/mL or target not detected)

### Key secondary outcomes at Week 72

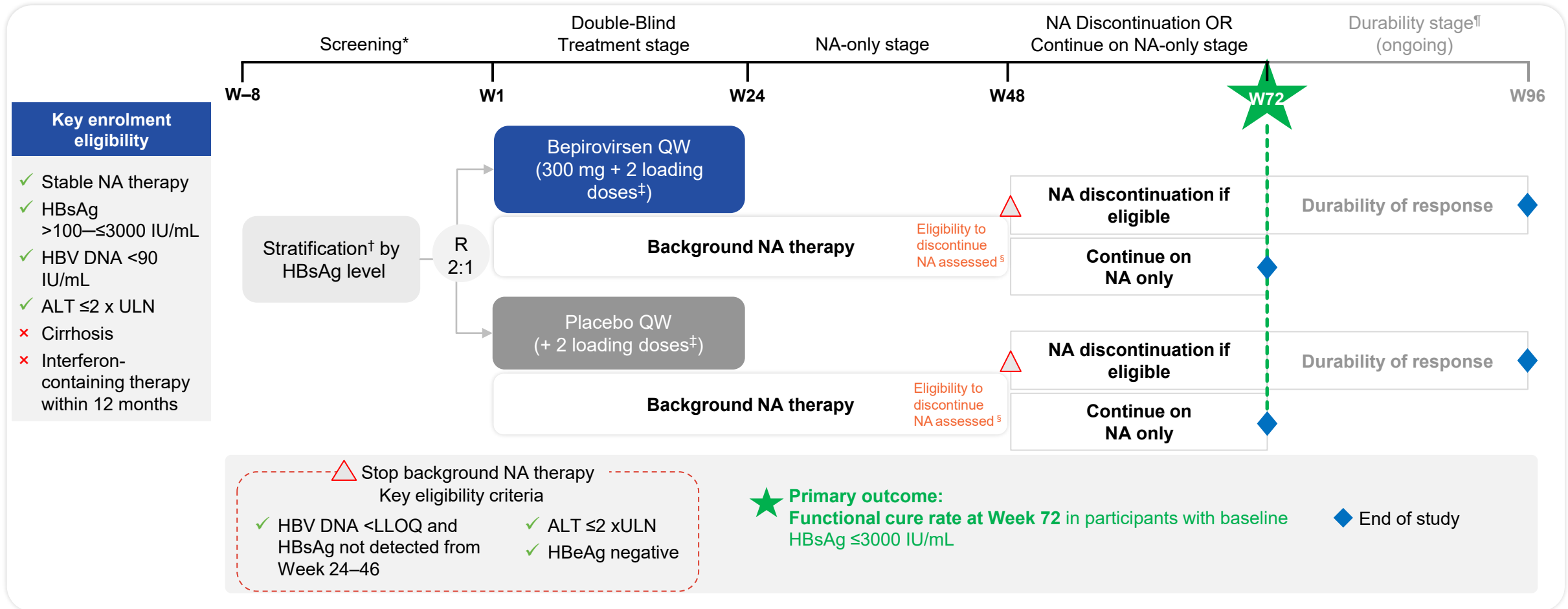
Functional cure rate among participants with baseline HBsAg  $\leq 1000$  IU/mL

Sustained HBV DNA  $<$ LLOQ\* off all HBV treatments among:

- i. Participants with baseline HBsAg  $\leq 3000$  IU/mL
- ii. Participants with baseline HBsAg  $\leq 1000$  IU/mL

\* $<$ LLOQ defined as  $<20$  IU/mL or target not detected  
HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; IU/mL, international units per milliliter; LLOQ, lower limit of quantification.

# B-Well 1 and 2 were replicate studies, identical in design



\*The screening window was 45 days; randomization could extend to 60 days with medical monitor agreement – for example, if waiting for re-test screening results. <sup>†</sup>Stratified by screening HBsAg level >100 to ≤1000 IU/mL or >1000 to ≤3000 IU/mL. <sup>‡</sup>Study treatments were administered as 2 subcutaneous injections once weekly, except in Week 1 and 2, which had additional loading doses on Days 4 and 11. <sup>§</sup>To be eligible for NA discontinuation, participants must have HBV DNA <LLOQ (<20 IU/mL or TND) and HBsAg not detected (qualitative assay <0.05 IU/mL) from Week 24 to Week 46, ALT values ≤2x ULN and HBeAg negative at Week 46. <sup>¶</sup>The durability stage is ongoing, and data after Week 72 will be reported separately. ALT, alanine aminotransferase; HBV, hepatitis B virus; HBeAg, hepatitis B e-antigen; HBsAg, hepatitis B surface antigen; LLOQ, lower limit of quantification; NA, nucleos(t)ide analogue; QW, once weekly; R, randomisation; TND, target not detected; ULN, upper limit of normal.

## Baseline characteristics were similar across treatment groups and studies

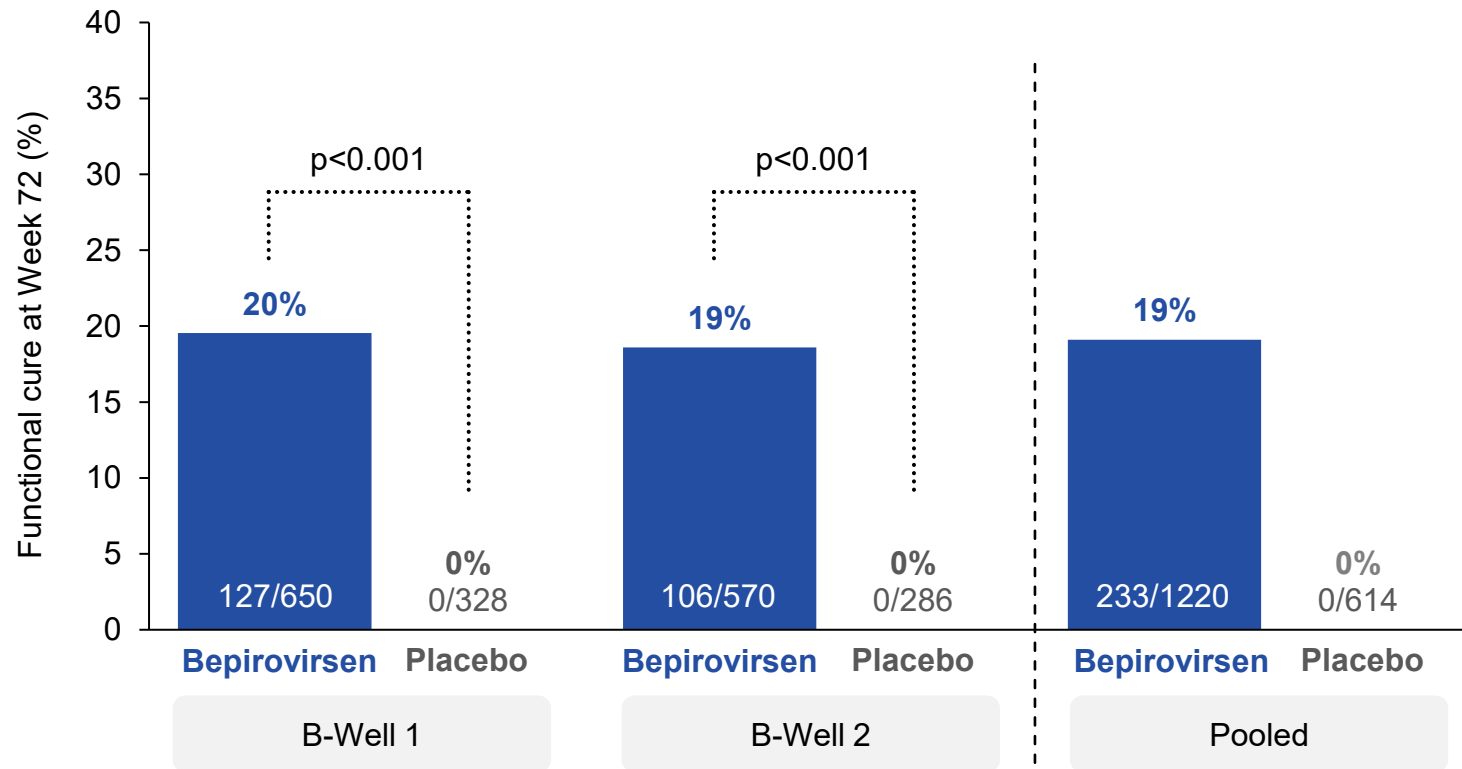
Characteristic	B-Well 1		B-Well 2	
	Bepirovirsen N=653	Placebo N=328	Bepirovirsen N=571	Placebo N=286
<b>Age, mean (SD) years</b>	50.2 (11.8)	49.2 (10.6)	48.7 (10.4)	49.2 (11.4)
<b>Male sex, n (%)</b>	461 (71)	227 (69)	414 (73)	202 (71)
<b>Race, n (%)</b>				
Asian	440 (67)	229 (70)	388 (68)	195 (68)
White	168 (26)	78 (24)	149 (26)	78 (27)
Other*	45 (7)	21 (6)	34 (6)	13 (5)
<b>HBsAg<sup>†</sup>, mean (SD) IU/mL</b>	952.4 (1046.6)	914.5 (760.3)	955.0 (740.5)	919.4 (691.0)
<b>HBsAg group, n (%)</b>				
≤1000 IU/mL	427 (65)	214 (65)	343 (60)	179 (63)
>1000 to ≤3000 IU/mL	226 (35)	114 (35)	228 (40)	107 (37)
<b>HBeAg positive status, n (%)</b>	55 (8)	28 (9)	43 (8)	26 (9)
<b>HBV DNA &lt;LLOQ<sup>‡§</sup>, n (%)</b>	641 (98)	322 (98)	564 (99)	283 (99)
<b>ALT ≤ULN, n (%)</b>	599 (92)	296 (90)	535 (94)	263 (92)
<b>Current NA<sup>†¶</sup>, n (%)</b>				
Entecavir	261 (40)	139 (42)	252 (44)	117 (41)
TAF/TDF/Tenofovir/TMF <sup>**</sup>	395 (60)	189 (58)	324 (57)	169 (59)
Other <sup>††</sup>	13 (2)	2 (1)	6 (1)	5 (2)

\*Other includes North American or Alaskan First Nations, Black or African American, Native Hawaiian or Other Pacific Islander, or multiple races selected. †B-Well 2 bepirovirsen N=570. ‡B-Well 1 bepirovirsen N=652. §<LLOQ defined as <20 IU/mL or target not detected. ¶Participants may be counted more than once for current NA at baseline. \*\*TAF includes tenofovir alafenamide and tenofovir alafenamide fumarate. TDF includes tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil orotate, and tenofovir disoproxil succinate. TMF includes tenofovir amibufenamide and tenofovir amibufenamide fumarate. Tenofovir includes tenofovir disoproxil maleate. ††Other includes emtricitabine, lamivudine, adefovir, besifovir dipivoxil maleate, alafenamide emtricitabine + tenofovir, emtricitabine + tenofovir disoproxil fumarate and telbivudine.  
HBeAg, hepatitis B e-antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus. NA, nucleos(t)ide analogue; SD, standard deviation; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TMF, tenofovir amibufenamide; ULN, upper limit of normal.

# Functional cure was achieved in 19% of bepirovirsen recipients and no placebo recipients

## Primary outcome

### Functional cure in participants with baseline HBsAg $\leq 3000$ IU/mL



Pooled functional cure rate:

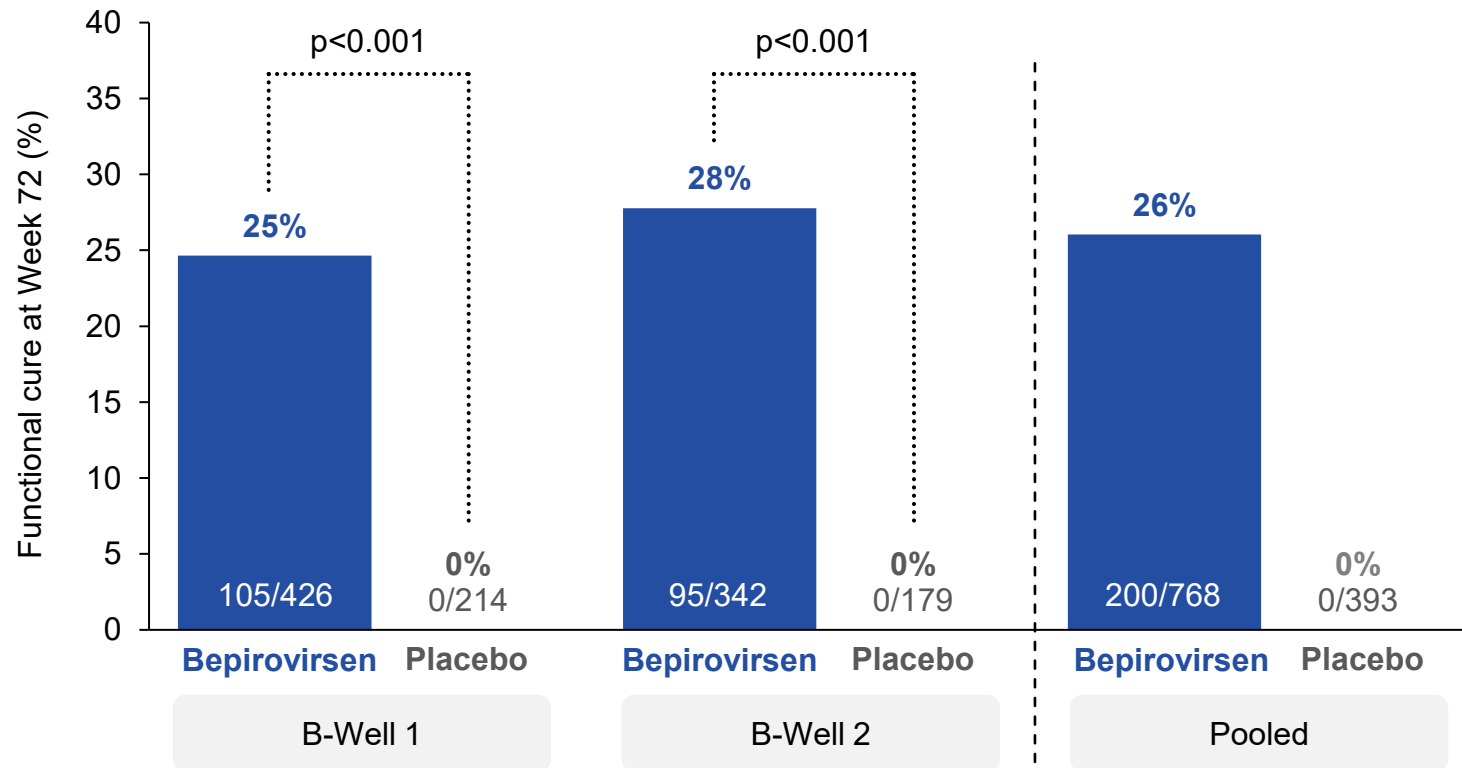
- Bepirovirsen 19%
- Placebo 0%

Common risk differences in functional cure rate and 95% CIs using the summary Miettinen-Nurminen (score) method: B-Well 1 = 17.5% (14.6, 20.3); B-Well 2 = 13.3% (10.4, 16.1). Two-sided p-value for exact Cochran-Mantel-Haenszel test are presented. The pooled population reports the functional cure rate at Week 72 for the full analysis sets of B-Well 1 and B-Well 2 combined. Functional cure defined as: HBsAg not detected (qualitative; < 0.05 IU/mL) and HBV DNA < LLOQ (< 20 IU/mL or target not detected) 24 weeks after discontinuing all HBV treatment. CI, confidence interval; HBsAg, hepatitis B surface antigen.

# Functional cure was achieved in 26% of bepirovirsen recipients with baseline HBsAg $\leq 1000$ IU/mL, and no placebo recipients

## Key secondary outcome

### Functional cure in participants with baseline HBsAg $\leq 1000$ IU/mL

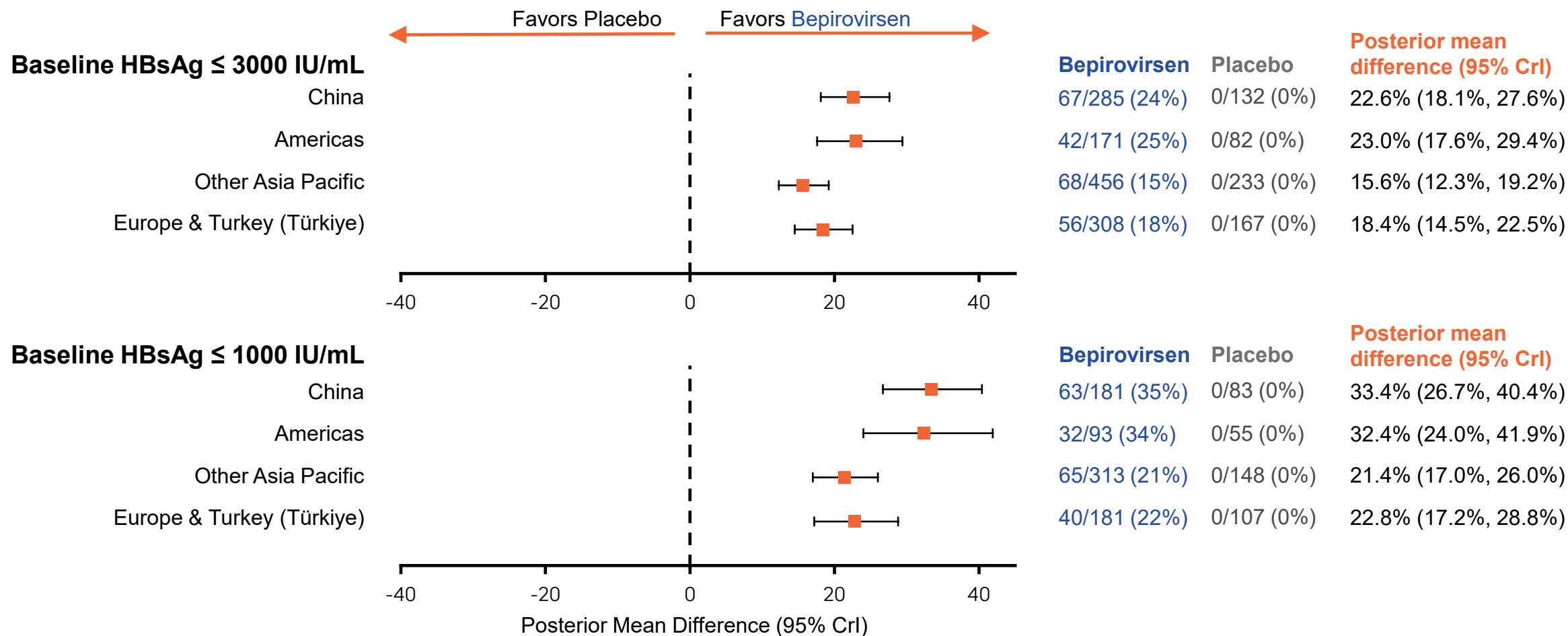


Pooled functional cure rate:

- Bepirovirsen 26%
- Placebo 0%

# A treatment effect favouring bepirovirsen was seen across all regions

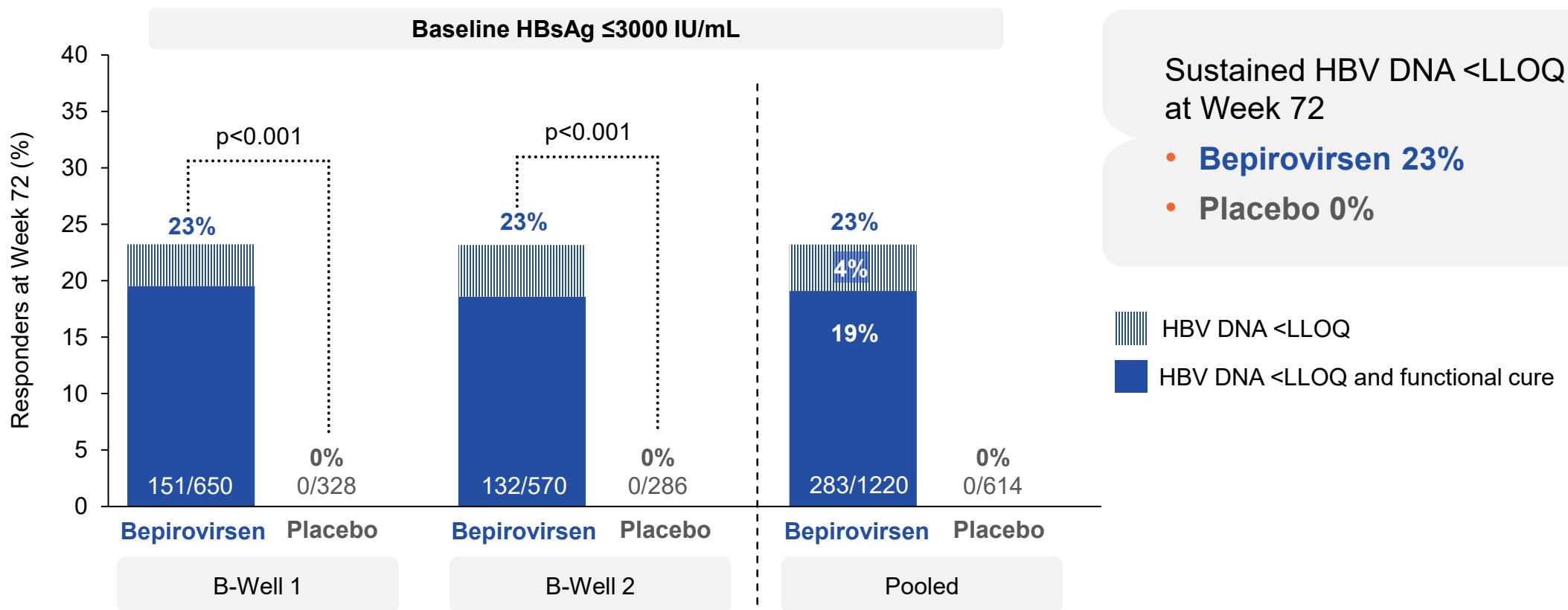
## Functional cure rate at Week 72 by country group (pooled data)



A Bayesian Hierarchical Model (BHM) has been used for shrinkage estimation. Only subgroup levels with 5 or more participants within each treatment arm are included in the analyses. Posterior mean differences are estimated if at least two sublevels in a subgroup have 5 or more participants within each treatment arm. CrI, credible interval; HBsAg, hepatitis B surface antigen.

# Sustained HBV DNA <LLOQ off all HBV treatments was achieved in 23% of bepirovirsen recipients, and no placebo recipients

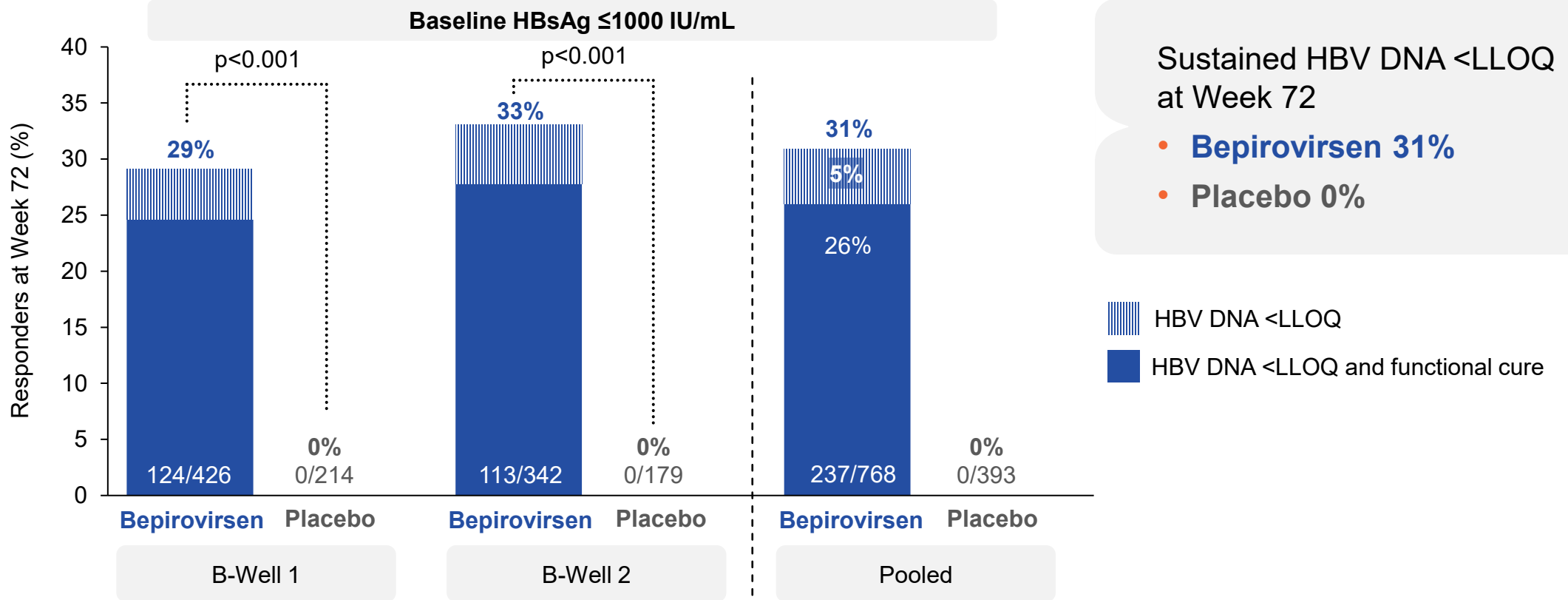
## Key secondary outcome HBV DNA <LLOQ at Week 72 off all HBV treatments



Common risk differences and 95% CIs using the summary Miettinen-Nurminen (score) method: B-Well 1 = 21.0% (17.9, 24.0); B-Well 2 = 18.2% (15.1, 21.3). Two-sided p-value for exact Cochran-Mantel-Haenszel test are presented. The pooled population reports the proportion of participants who stopped NA and had HBV DNA <LLOQ at Week 72 for the full analysis sets of B-Well 1 and B-Well 2 combined. <LLOQ defined as <20 IU/mL or target not detected. CI, confidence interval; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; LLOQ, lower limit of quantification; NA, nucleos(t)ide analogue.

# Sustained HBV DNA <LLOQ off all HBV treatments was achieved in 31% of bepirovirsen recipients with baseline HBsAg ≤1000 IU/mL, and no placebo recipients

## Key secondary outcome HBV DNA <LLOQ at Week 72 off all HBV treatments



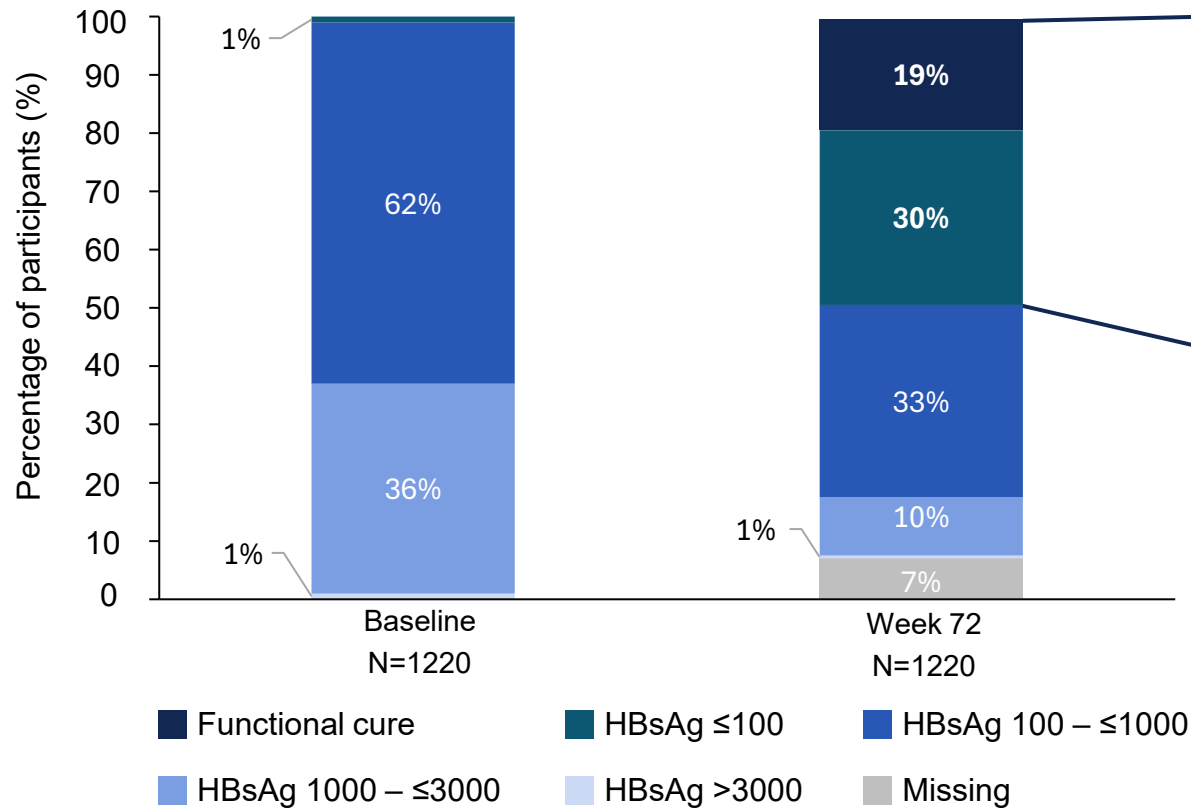
Sustained HBV DNA <LLOQ at Week 72

- Bepirovirsen 31%
- Placebo 0%

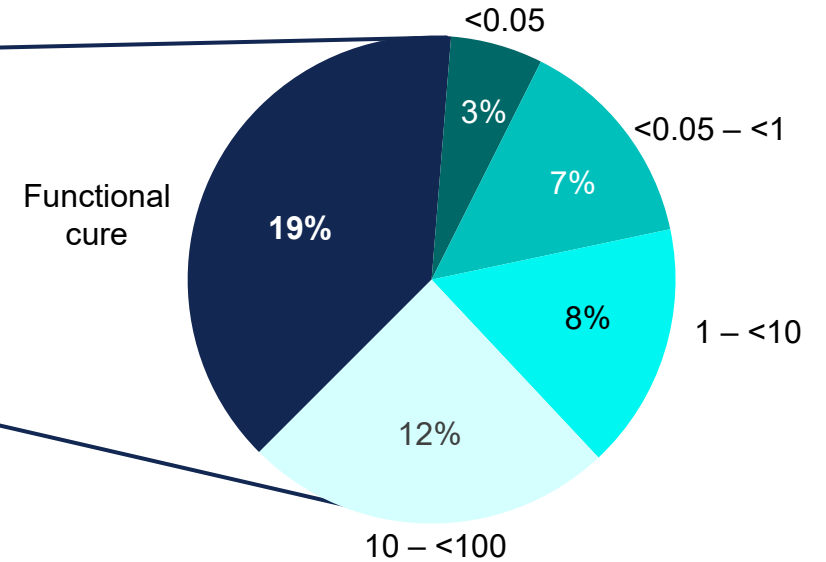
Risk differences and 95% CIs using the Miettinen-Nurminen method: B-Well 1 = 29.1% (25.0, 33.6); B-Well 2 = 33.0% (28.3, 38.2). Two-sided p-values for Boschloo's test are presented. The pooled population reports the proportion of participants who stopped NA and had HBV DNA <LLOQ at Week 72 for the full analysis sets of B-Well 1 and B-Well 2 combined. <LLOQ defined as <20 IU/mL or target not detected. CI, confidence interval; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; LLOQ, lower limit of quantification; NA, nucleos(t)ide analogue.

# In addition to 19% achieving functional cure, 30% of bepirovirsen recipients had qHBsAg $\leq 100$ IU/mL ~1 year after end of treatment

HBsAg at baseline and at Week 72 with bepirovirsen treatment



Functional cure or HBsAg  $\leq 100$  IU/mL breakdown



At Week 72

- 19% functional cure
- 30% had qHBsAg  $\leq 100$  IU/mL without FC

## The on-treatment safety profile was consistent across B-Well 1 and 2

- AEs leading to permanent treatment discontinuation were low in frequency (3% of bepirovirsen recipients)
- Few participants (2%) had serious adverse events related to bepirovirsen

	B-Well 1		B-Well 2		Pooled data	
	Bepirovirsen N=652	Placebo N=326	Bepirovirsen N=571	Placebo N=285	Bepirovirsen N=1223	Placebo N=611
<b>Any on-treatment AEs [Week 1-24], n (%)</b>	575 (88)	210 (64)	512 (90)	189 (66)	1087 (89)	399 (65)
AEs leading to permanent discontinuation of study treatment	26 (4)	0	15 (3)	2 (<1)	41 (3)	2 (<1)
AEs leading to dose reduction	13 (2)	0	11 (2)	0	24 (2)	0
AEs leading to dose interruption/delay	100 (15)	10 (3)	93 (16)	3 (1)	193 (16)	13 (2)
AEs of Grade ≥3 severity*	96 (15)	8 (2)	101 (18)	8 (3)	197 (16)	16 (3)
AEs related to study treatment	512 (79)	111 (34)	469 (82)	104 (36)	981 (80)	215 (35)
<b>Any on-treatment SAE [Week 1-24], n (%)</b>	25 (4)	5 (2)	23 (4)	3 (1)	48 (4)	8 (1)
SAEs related to study treatment	12 (2)	0	11 (2)	0	23 (2)	0
<b>Fatal SAEs [Week 1-72]<sup>†</sup>, n (%)</b>	1 (<1)	0	1 (<1)	0	2 (<1)	0
Fatal SAEs related to study treatment [Week 1-72]	0	0	0	0	0	0

\*Adverse events were graded according to the Division of AIDS (DAIDs) Table for Grading the Severity of Adult and Pediatric Adverse Events, corrected version 2.1. Grade 1 indicates a mild event, Grade 2 a moderate event, Grade 3 a severe event, Grade 4 a potentially life-threatening event, and Grade 5 death. Investigator's judgement may be used in assigning clinical severity and may not always align with DAIDs grading.

<sup>†</sup>A death in B-Well 1 occurred following a reported "near drowning" event during Weeks 37–48, 10 months after the last dose of study treatment. The death in B-Well 2 was aortic dissection 25 days after study treatment initiation, with autopsy findings indicative of cardiovascular disease. An additional death, not recorded on study, occurred after participant withdrawal due to an SAE of pancreatic neoplasm.

AE, adverse event; AESI, adverse event of special interest; SAE, serious adverse event.

# On-treatment AEs were consistent with the known safety profile of bepirovirsen

The most common AEs on treatment were injection site reactions; none of which were serious

## On-treatment AEs reported in $\geq 10\%^*$ of participants [Week 1–24]

n (%)	Pooled safety population	
	Bepirovirsen N=1223	Placebo N=611
Injection site erythema	384 (31)	12 (2)
Injection site pain	277 (23)	31 (5)
Injection site pruritus	219 (18)	9 (1)
Injection site bruising	176 (14)	28 (5)
ALT increased	269 (22)	18 (3)
AST increased	183 (15)	8 (1)
Pyrexia	236 (19)	18 (3)
Platelet count decreased	180 (15)	5 (1)
Headache	168 (14)	70 (11)
Upper respiratory tract infection	147 (12)	72 (12)

## Laboratory monitoring

- Four participants (<1%) had permanent treatment discontinuation for a liver event
- Transient ALT increases after bepirovirsen initiation were associated with HBsAg reduction
- Platelet and eGFR declines resolved once treatment was completed or paused
  - No clinically significant bleeding events attributed to bepirovirsen
  - Clinically significant eGFR reduction was not associated with other markers of renal injury

\* $\geq 10\%$  of participants in either treatment arm for the pooled safety population; †adverse events were graded according to the Division of AIDS (DAIDs) Table for Grading the Severity of Adult and Pediatric Adverse Events, corrected version 2.1. Grade 1 indicates a mild event, Grade 2 a moderate event, Grade 3 a severe event, Grade 4 a potentially life-threatening event, and Grade 5 death. Investigator's judgement may be used in assigning clinical severity and may not always align with DAIDs grading; ‡ $\geq 3\%$  of participants in either treatment arm for the pooled safety population.  
 AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; HBsAg, hepatitis B surface antigen.

# Bepirovirsen induces superior, clinically significant functional cure rates

At Week 72, B-Well 1 and 2 Phase 3 trials demonstrated:

## Functional cure rates of:

- **19% with bepirovirsen** among those with baseline HBsAg  $\leq 3000$  IU/mL
- **26% with bepirovirsen** among those with baseline HBsAg  $\leq 1000$  IU/mL
- 0% with placebo

## Sustained HBV DNA $< \text{LLOQ}$ off all HBV treatments:

- **23% with bepirovirsen** among those with baseline HBsAg  $\leq 3000$  IU/mL
- **31% with bepirovirsen** among those with baseline HBsAg  $\leq 1000$  IU/mL
- 0% with placebo

Bepirovirsen is a **first-in-class, 24-week finite therapy, achieving functional cure** in virologically suppressed patients with chronic HBV infection, with an acceptable safety profile



## Further reading

The New England Journal of Medicine primary publication



The NEW ENGLAND  
JOURNAL of MEDICINE



Access the B-Well  
primary paper  
in NEJM at the  
QR code

ORIGINAL ARTICLE

### Phase 3 Results of Bepirovirsen Treatment for Chronic Hepatitis B Virus Infection

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for the B-Well Study Group\*

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SVP, R&D Head of RI&I, Head of Translational  
Development and Sciences

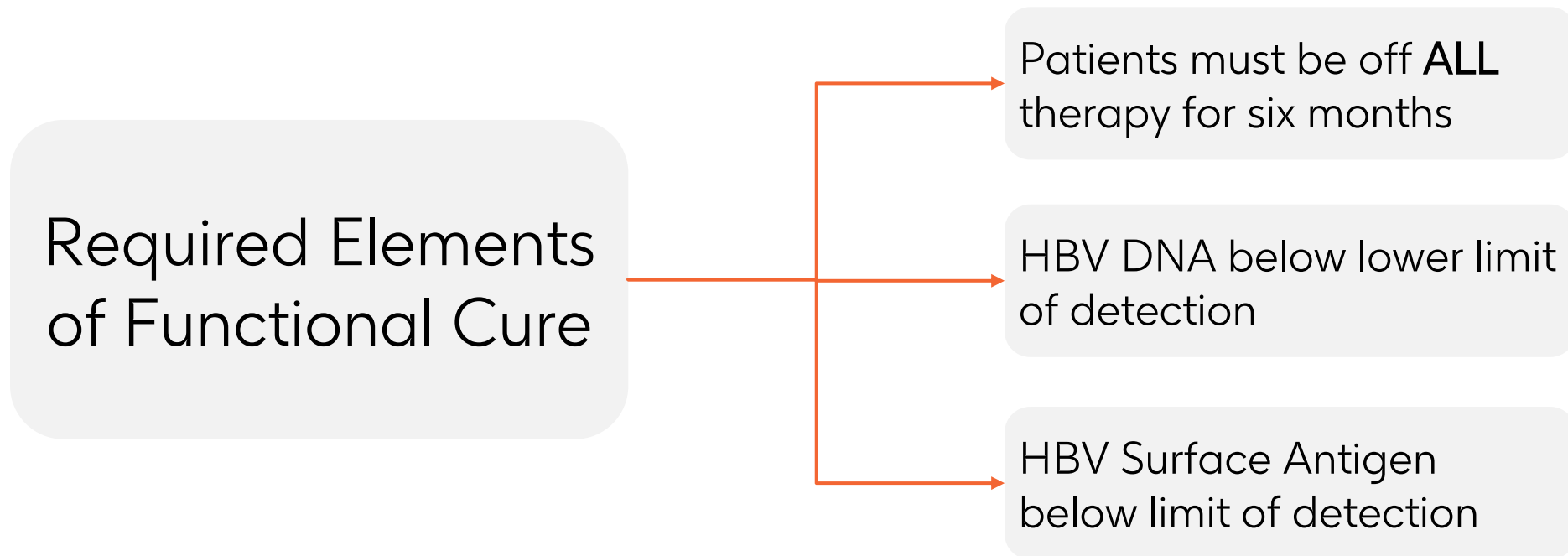
**Melanie Paff**

VP, MDL for HBV

**GSK**

# Functional cure is the gold standard for treatment

Functional cure is a regulatory defined end point



# Bepirovirsen addresses key three requirements for functional cure

1. **Suppresses** viral surface antigen (HBsAg)
2. **Suppresses** CHB viral replication
3. **Innate stimulation** of the immune system

# Established SoC with low functional cure rates and/or poor tolerability

Functional cure (FC) will reduce risk of HCC and ACM

## SoC today

### Nucleoside analogues

- Established SoC
  - Daily oral dosing
  - Viral suppression
  - Favourable safety
  - Low cost
- Not a cure (FC rate <1% annually\*)
  - Life-long therapy
  - Risk of HCC remains
  - Stigma retained

### Peg-interferon

- SoC in China
  - Treatment for HBsAg loss
- Low FC rate (~2-8%\*)
  - Unfavourable safety profile / limited tolerability
  - High drop-out rate

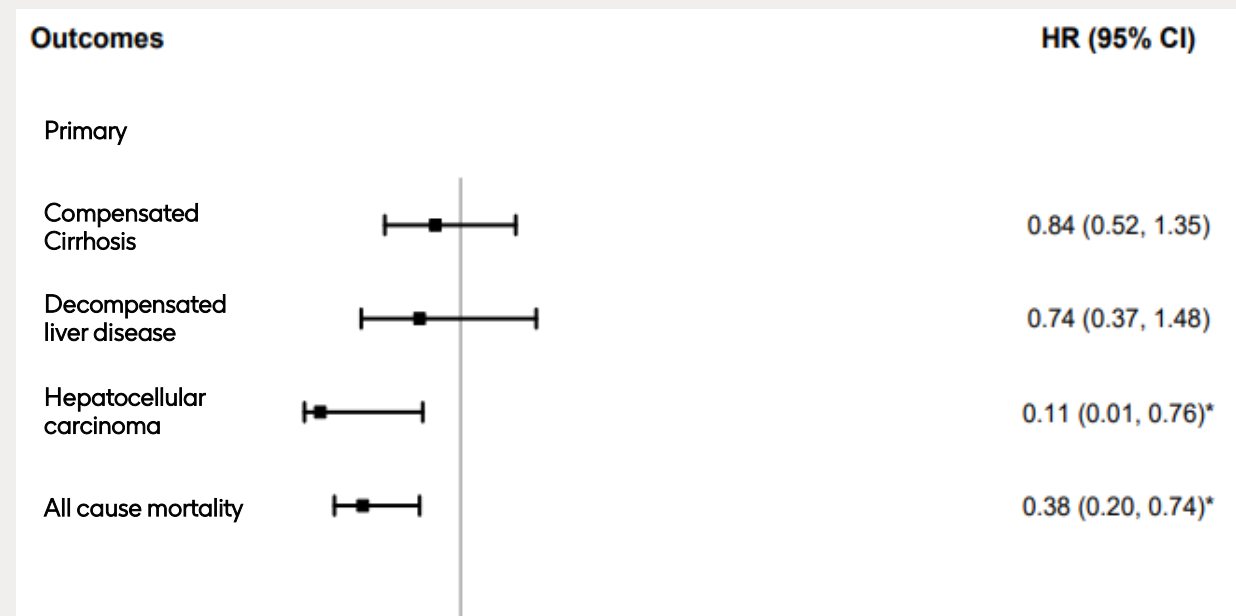
## SoC tomorrow

- Higher functional cure
- Finite duration of therapy
- Lower risk of cirrhosis and HCC with associated reduction in morbidity, mortality and cost
- Larger eligible patient population
- Freedom from the psychological burden of chronic infection and life-long medication

# Clinical benefit of functional cure

Surface antigen loss is associated with better clinical outcomes

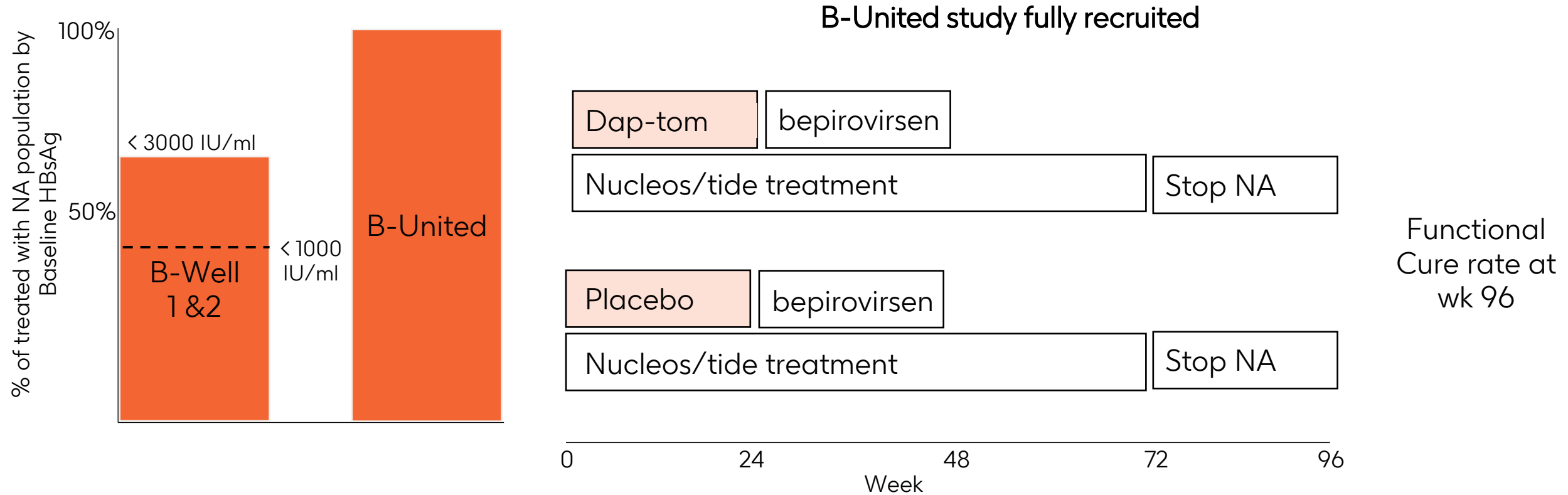
## Association of HBsAg loss and clinical outcomes



- Loss of surface antigen** associated with
- **89%** reduced risk of hepatocellular carcinoma
  - **62%** reduced risk of all cause mortality

# Ongoing development plan in HBV

Expanding further eligible population of patients who may benefit from bepi therapy



B-United is a phase II, sequential trial investigating daplusran/tomligisran followed by bepirovirsen in 283 CHB patients regardless of baseline HBsAg

# Summary

- Bepirovirsen induces superior, clinically significant functional cure rates
- FC is achievable and durable
- An additional 30% of patients had very low surface antigen ( $\leq 100$  IU/ml) at week 72 (vs placebo 4%)<sup>1</sup>
- Recognition of innovation by regulators - granting review acceleration pathways in key markets:
  - **US** – Fast Track, Priority Review, Breakthrough Therapy Designation and PDUFA 26 October '26
  - **China** – Breakthrough Therapy Designation, Accepted for regulatory review and awarded Priority Review in April '26
  - **Japan** – SENKU designation and accepted for regulatory review in February '26

1. This is a post-hoc analysis



# Q & A