

NASH and HBV

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Gastroenterologist

Region	Population studied	Prevalence of NAFLD in these populations (%)
USA	Pediatric population	13–14
	General population	27–34
	Morbid obesity	75–92
	European-Americans	33
	Hispanic-Americans	45
	African-Americans	24
Europe	Pediatric population	2.6–10
	General population	20–30
Western countries	General population	20–40
	Obesity or diabetes	75
	Morbid obesity	90–95
Worldwide	Obese population	40–90
Middle East	General population	20–30
Far East	General population	15
Pakistan	General population	18
Population with NAFLD studied		Prevalence of NASH in these populations (%)
Selected healthy liver donors		3–16%
No inflammation or fibrosis		5%
General population		10–20%
High-risk, severe obesity		37%
Patients at tertiary care centers		40–55%

Prevalence of NALFD in high risk groups

Population studied	Prevalence of NAFLD
Excessive BMI and visceral obesity Severe obesity undergoing bariatric surgery	90% NAFLD 5% of patients may have unsuspected cirrhosis
An ultrasonographic study of patients with T2DM	69% prevalence of NAFLD
Individuals with dyslipidemia attending lipid clinics	Prevalence of NAFLD 50%

Natural history of NAFLD/NASH

Study	Mean Follow-up (years)	Number of patients	% of NASH	Fibrosis, n (%)		
				Regression	Stabilization	Progression
Harrison , 2003	5.7 (1.4-15.7)	22	86	4 (18)	11 (50)	7 (32)
Fassio , 2004	4.3 (3-14.3)	22	100	3 (14)	14 (64)	5 (23)
Adams , 2005	3.2 (0.7-21.3)	103	93	30 (29)	35 (34)	38 (37)
Ekstedt , 2006	13.7 (10.3-16.3)	68	55	11 (16)	30 (43)	29 (41)
Wong, 2010	3	52	33	13 (25)	25 (48)	14 (27)

Adams, LA J Hepatol 2005
Ekstedt M, Hepatology 2006
Fassio, E Hepatology 2004
Harrison, SA Gastroenterol 2003

Independent predictors of fibrosis progression

- Age >45-50
- BMI >29-30kg/m²
- Degree of insulin resistance
- Diabetes
- Hypertension

NASH scoring system in pts with obesity

Factor	Points
Hypertension	1
Type II diabetes	1
AST ≥ 27 IU/L	1
ALT ≥ 27 IU/L	1
Sleep apnea	1
Nonblack	2
Point total	Risk of NASH
0–2	Low
3–4	Intermediate
5	High
6–7	Very high

NAFLD/NASH Progression

- Fibrosis and presence of steatohepatitis are biggest predictors of progression
- Fibrosis progression by 1 stage every 7 years in NASH
- Fibrosis progression 1 stage every 14 years in NAFLD
- Progression can be slowed with frequent visit/dietary counselling advice
- Meta-analysis of placebo arm patients in 35 NASH trials found minimal progression

NAFLD- Fibrosis staging

- Diagnosis of cirrhosis important
- 6 monthly USS for HCC surveillance
- Monitoring for signs and symptoms of decompensation or portal hypertension
- Risk of decompensation 3-20% per year for cirrhotic patients
- All cause mortality for F0-2 patients = 0.32 per 100 person years
- F3 = 0.89 per 100 person-years
- F4 = 1.76 per 100 person-years

FIBROSIS STAGE : INDEPENDENT FACTOR FOR LIVER MORTALITY

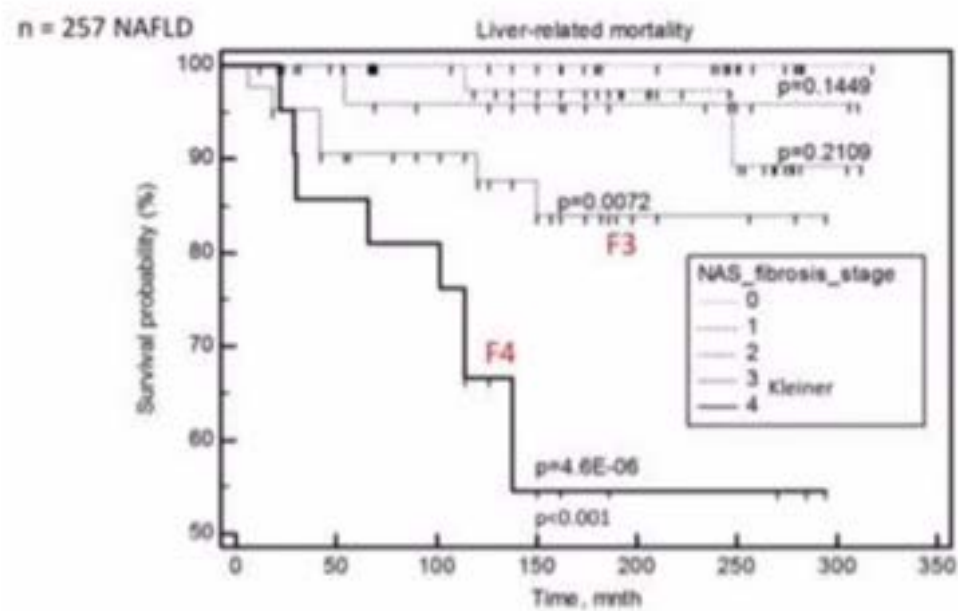


Table 1 Mortality in NAFLD/NASH

	Liver	Cardiac
General population	0.2%	7.5%
Simple Steatosis	0%	8.6%
NASH	1.6–6.8%	12.6–36%

Causes of mortality in cirrhotic NASH patients:

- Liver failure
- Sepsis
- Variceal hemorrhage
- HCC
- Cardiovascular disease

Clinical suspicion

- Obesity
- T2DM
- OSA
- Presence of insulin resistance
- Chronic elevation of AST/ALT
- Elevated ferritin

Blood tests

- AST/ALT ratio <1 (reverse of ETOH liver disease)
- Note the lab doesn't routinely do AST
- Please request FIB-4

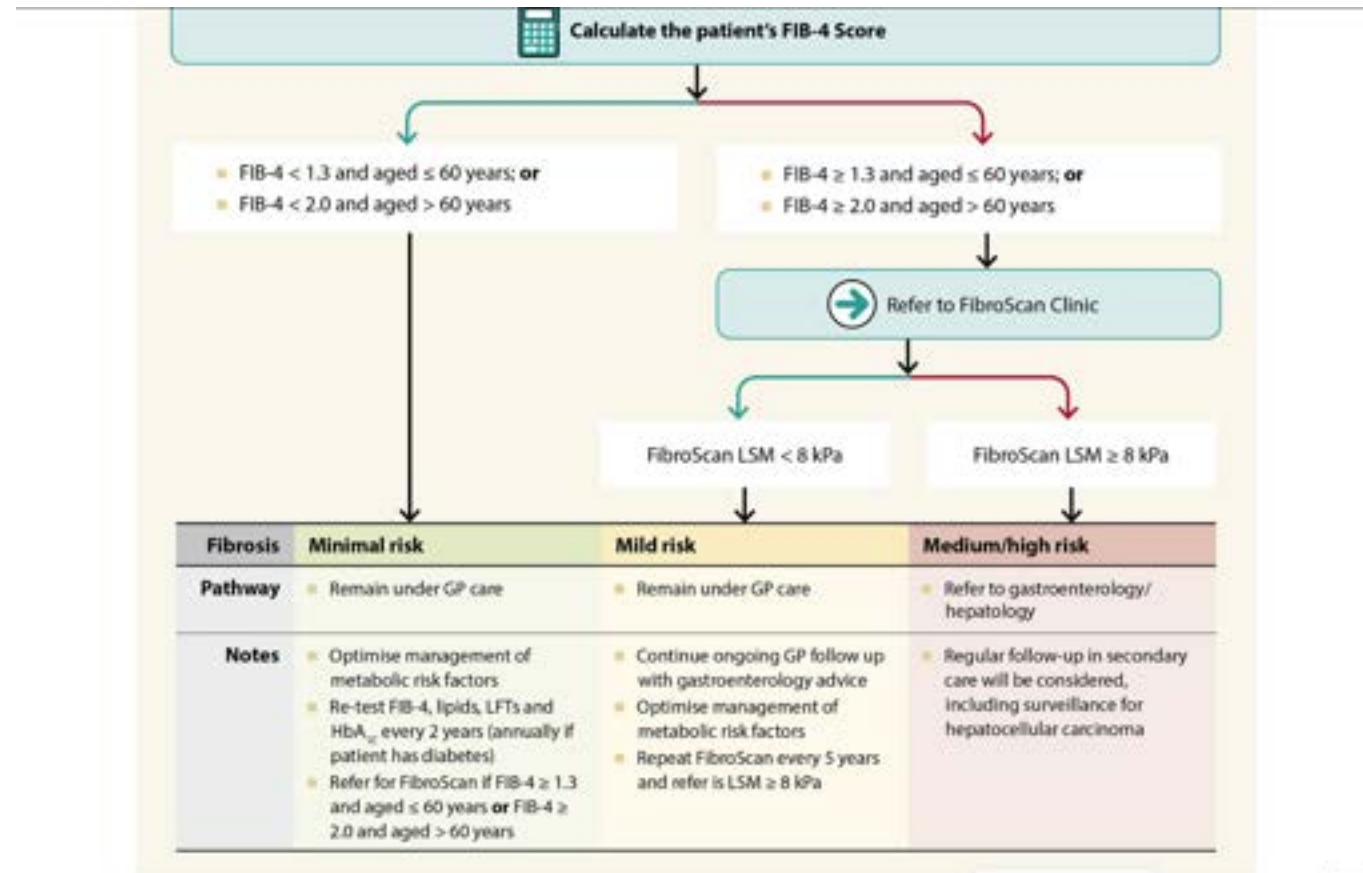
BPAC NZ guidelines

Table 1. Scoring tools for assessing the risk of fibrosis in patients with suspected MASLD.⁴

Scoring tool	Variables included	Interpretation of results	Notes
Fibrosis-4 (FIB-4) score* www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis	Age, ALT and AST levels, platelet count	• Thresholds separating fibrosis risk levels may differ depending on the calculator used, regional guidelines and by patient age • See Figure 1 for an example of risk/referral thresholds	May potentially overestimate fibrosis in patients with excessive alcohol intake. Seek gastroenterology advice if score is ≥ 1.3 for people aged ≤ 60 years or score is ≥ 2.0 for people aged ≤ 60 years (or refer for FibroScan, if available). [†]
NAFLD Fibrosis Score (NFS) https://www.mdcalc.com/calc/3081/nafl-non-alcoholic-fatty-liver-disease-fibrosis-score	Age, BMI, fasting glucose/diabetes status, AST:ALT ratio, platelet count and albumin	• < -1.455 suggests no significant fibrosis • -1.455 to 0.675 is an intermediate score • > 0.675 suggests fibrosis	The significance of BMI may differ between ethnic groups. Seek gastroenterology advice if score is ≥ -1.455 (or refer for FibroScan, if available). [†]

*An estimate of fibrosis stage (based on Ishak fibrosis staging) is usually given alongside the FIB-4 score.

BPAC NZ guidelines



Who should have a liver biopsy?

Liver biopsy should be considered in patients with NAFLD who are at increased risk to have steatohepatitis and advanced fibrosis. (Strength – 1, Evidence - B)

The presence of metabolic syndrome and the NAFLD Fibrosis Score may be used for identifying patients who are at risk for steatohepatitis and advanced fibrosis. (Strength – 1, Evidence - B)

Liver biopsy should be considered in patients with suspected NAFLD in whom competing etiologies for hepatic steatosis and co-existing chronic liver diseases cannot be excluded without a liver biopsy. (Strength – 1, Evidence - B)

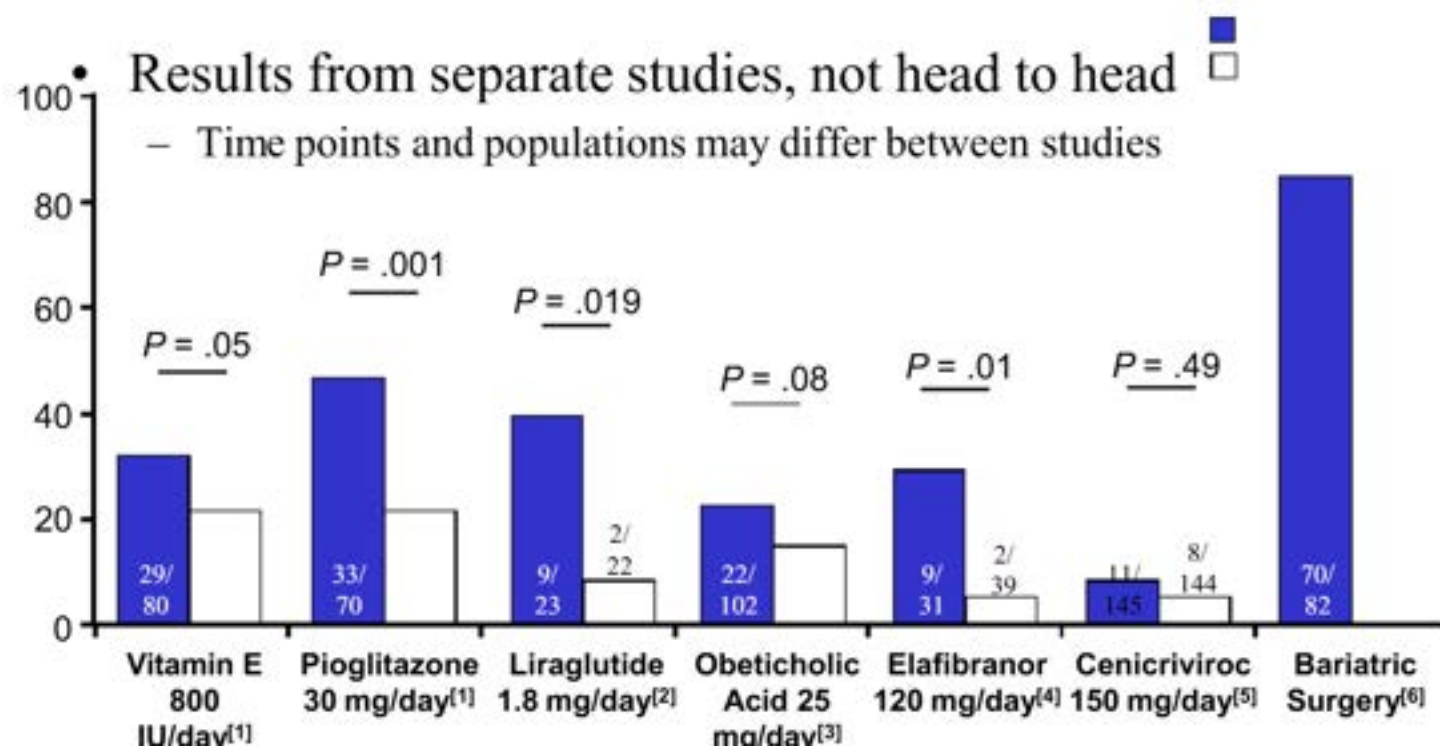
Treatment options for NASH

- Lifestyle interventions
- Weight loss of 3-5% can improve steatosis
- >10% weight loss to improve necroinflammation
- Pioglitazone –significantly improves liver enzymes, steatosis, ballooning and inflammation
- Vitamin E: Superior to placebo in adults with NASH but no DM

Treatment for NASH

- AASLD recommendations: Pioglitazone can be used to treat certain patients with NASH who do not have DM but long term safety and efficacy has not been established
- Vitamin E 800 IU/day improves liver histology in NASH patients BUT not recommended to treat NASH in those with other chronic liver diseases, diabetes, cirrhosis
- Why do we not empirically treat everyone with NASH with vitamin E?
- 50% of patients do not respond
- Risk of hemorrhagic stroke and prostate cancer

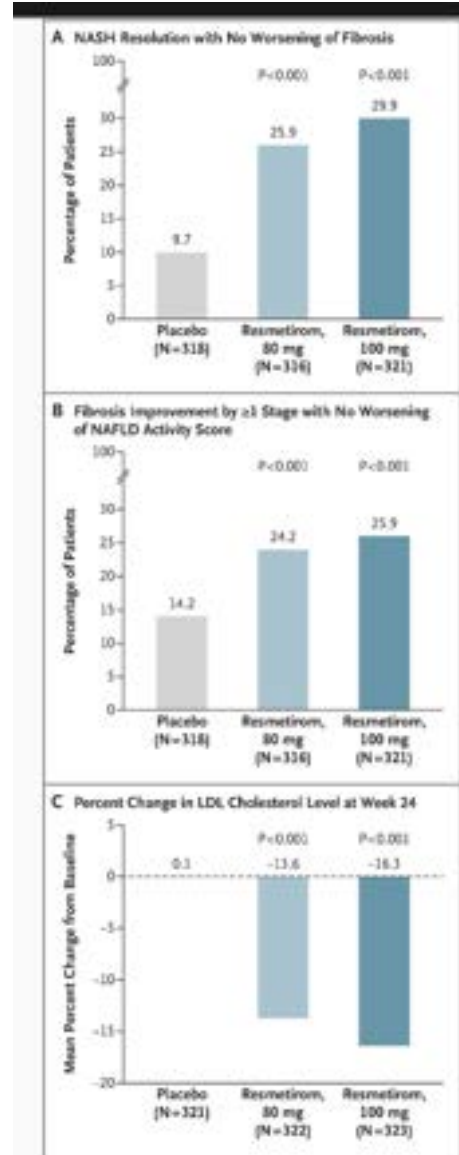
Key NASH Therapies: Resolution of NASH



Resmetirom

- Oral, liver directed thyroid hormone agonist
- First FDA approved medication for NASH F2-3 fibrosis in 2024
- Enters liver cells to enhance mitochondrial function, improve fat burning and reduce toxic fat accumulation
- 1:1:1 80mg: 100mg : placebo
- Common side effects- nausea, mild diarrhoea
- Cost: ~\$45,000 USD per year

Harrison S et al. NEJM 2024;390:497-509



Therapies for NASH

- Many agents have failed to improve NASH or reverse fibrosis in phase III studies, despite early promising results
- GLP agonists seem to be most promising but not funded for most in NZ
- Trulicity small effect
- Current clinical trials available for NASH:
- GLP agonist (sudorvutide) for F2-4 NASH- long term study
- Tirzepatide:Retatrutide:placebo study for F2-4 NASH
- Placebo arm 1:3

Clinical trials

- Fibroblast growth factor 21 (FGF21) – Efimosfermin for F2-4 NASH
- Once monthly subcut injections
- Phase II studies have shown improvement in fibrosis of 68% of patients after 6 months compared to placebo
- All patients would have fibroscan, MRI PDFF (fat %) and a liver biopsy
- Once monthly follow ups

NASH- take home messages

- High prevalence- be on the lookout for NAFLD/NASH in your patient population (>50% may have NAFLD)
- Order FIB-4 score (so automatically includes AST)
- Refer anyone with high FIB-4 or NAFLD fibrosis score for fibroscan
- Repeat fibroscan every 5 years if ongoing abnormal LFTs
- Newer treatment options becoming available
- Clinical trials a good option

HBV cases- Who would you start on treatment?

40 year old male, HBeAg negative

ALT 45

HBV DNA 20,000 IU/mL

Non cirrhotic

REACH-B HCC score

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Calculators, Specialty, Condition

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☰

Sex

Female

0

Male

+2

Age, years

30-34

0

35-39

+1

40-44

+2

45-49

+3

50-54

+4

55-59

+2

60-65

+3

ALT, U/L

<35

0

35-45

+1

46-55

+2

HBsAg

Negative

0

Positive

+2

Hepatitis B virus DNA level, copies/mL

<200 (undetectable)

0

200-5,999

0

10,000-99,999

+1

100,000-999,999

+3

>1M

+4

12 points

REACH-B Score

13.4 %

10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)

AAFLD Guideline

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Dr. Hwei-J Yang

Related Calculators

Liver Decompensation Risk

Predicts risk of liver decompensation after hepatorectomy for hepatocellular carcinoma (HCC).

BCIS Staging Classification

Determines progression of disease and proper treatment course for patients with HCC.

MELD Score

Calculates the pediatric version of the MELD score for liver transplant severity and transplant planning.

Guidelines

Treatment of Hepatocellular Carcinoma

Guideline from AASLD

40 year old female

HBeAg negative

ALT 25

HBV DNA 20,000 IU/mL

REACH B HCC score

Trending

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Specialties

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Calculator, Specialty, Condition

Log In

Dr. Hwai-I Yang

Related Calculators

Liver Decompensation Risk

Predicts risk of liver decompensation after hepatectomy for hepatocellular carcinoma (HCC).

BCLC Staging Classification

Determines prognosis of disease and proper treatment course for patients with HCC.

PELD Score

Calculates the pediatric version of the MELD score for liver cirrhosis severity and transplant planning.

Guidelines

Treatment of Hepatocellular Carcinoma

Guideline from AASLD

Sex

Female

0

Male

+2

Age, years

30-34

0

35-39

+1

40-44

+2

45-49

+3

50-54

+4

55-59

+5

60-64

+6

ALT, U/L

<35

0

35-44

+1

45-88

+2

HBsAg

Negative

0

Positive

+2

Hepatitis B virus DNA level, copies/mL

<300 (undetectable)

0

300-9,999

0

10,000-99,999

+2

100,000-999,999

+5

>1M

+4

8 points

REACH-B Score

2.0 %

50-year risk of HCC (See 3-year and 5-year risk in the Evidence section)

[AASLD guideline](#)

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Case 3

- 32 year old female
- ALT 25
- HBV DNA 2500 IU/mL

Sex	Female 0 Male +2
Age, years	30-34 0 35-39 +1 40-44 +2 45-49 +3 50-54 +4 55-59 +5 60-65 +6
ALT, U/L	<15 0 15-44 +1 ≥45 +2
HBsAg	Negative 0 Positive +2
Hepatitis B virus DNA level, copies/mL	<300 (undetectable) 0 300-9,999 0 10,000-99,999 +3 100,000-999,999 +5 ≥10⁶ +4

4 points

REACH-B Score

0.3 %

10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)

[AASLD guideline](#)

Copy Results

Next Steps

Case 4

- 50 year old male
- ALT 20
- HBV DNA 3000 IU/mL

Sex	Female 0	Male +2														
Age, years	<table><tr><td>30-34</td><td>0</td></tr><tr><td>35-39</td><td>+1</td></tr><tr><td>40-44</td><td>+2</td></tr><tr><td>45-49</td><td>+3</td></tr><tr><td>50-54</td><td>+4</td></tr><tr><td>55-59</td><td>+5</td></tr><tr><td>60-65</td><td>+6</td></tr></table>		30-34	0	35-39	+1	40-44	+2	45-49	+3	50-54	+4	55-59	+5	60-65	+6
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35-39	+1															
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55-59	+5															
60-65	+6															
ALT, U/L	<table><tr><td><15</td><td>0</td><td>15-44</td><td>+1</td><td>≥45</td><td>+2</td></tr></table>		<15	0	15-44	+1	≥45	+2								
<15	0	15-44	+1	≥45	+2											
HBeAg	<table><tr><td>Negative</td><td>0</td></tr><tr><td>Positive</td><td>+2</td></tr></table>		Negative	0	Positive	+2										
Negative	0															
Positive	+2															
Hepatitis B virus DNA level, copies/mL	<table><tr><td><300 (undetectable)</td><td>0</td></tr><tr><td>300-9,999</td><td>0</td></tr><tr><td>10,000-99,999</td><td>+3</td></tr><tr><td>100,000-999,999</td><td>+5</td></tr><tr><td>≥10⁶</td><td>+6</td></tr></table>		<300 (undetectable)	0	300-9,999	0	10,000-99,999	+3	100,000-999,999	+5	≥10 ⁶	+6				
<300 (undetectable)	0															
300-9,999	0															
10,000-99,999	+3															
100,000-999,999	+5															
≥10 ⁶	+6															

10 points
REACH-B Score

5.2 %
10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)
[AASLD guideline](#)

Copy Results  Next Steps 

Case 5

- 60 year old male
- ALT 50
- HBV DNA 600 Iu/mL

Sex	Female 0	Male +2														
Age, years	<table><tr><td>20-24</td><td>0</td></tr><tr><td>25-29</td><td>+1</td></tr><tr><td>40-44</td><td>+2</td></tr><tr><td>45-49</td><td>+3</td></tr><tr><td>50-54</td><td>+4</td></tr><tr><td>55-59</td><td>+5</td></tr><tr><td>60-65</td><td>+6</td></tr></table>		20-24	0	25-29	+1	40-44	+2	45-49	+3	50-54	+4	55-59	+5	60-65	+6
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25-29	+1															
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50-54	+4															
55-59	+5															
60-65	+6															
ALT, U/L	<table><tr><td><15</td><td>0</td><td>15-44</td><td>+1</td><td>≥45</td><td>+2</td></tr></table>		<15	0	15-44	+1	≥45	+2								
<15	0	15-44	+1	≥45	+2											
HBsAg	<table><tr><td>Negative</td><td>0</td></tr><tr><td>Positive</td><td>+2</td></tr></table>		Negative	0	Positive	+2										
Negative	0															
Positive	+2															
Hepatitis B virus DNA level, copies/mL	<table><tr><td><300 (undetectable)</td><td>0</td></tr><tr><td>300-9,999</td><td>0</td></tr><tr><td>10,000-99,999</td><td>+3</td></tr><tr><td>100,000-999,999</td><td>+5</td></tr><tr><td>≥10⁶</td><td>+4</td></tr></table>		<300 (undetectable)	0	300-9,999	0	10,000-99,999	+3	100,000-999,999	+5	≥10 ⁶	+4				
<300 (undetectable)	0															
300-9,999	0															
10,000-99,999	+3															
100,000-999,999	+5															
≥10 ⁶	+4															

10 points
REACH-B Score

5.2 %
10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)
[AASLD guideline](#)

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Case 6

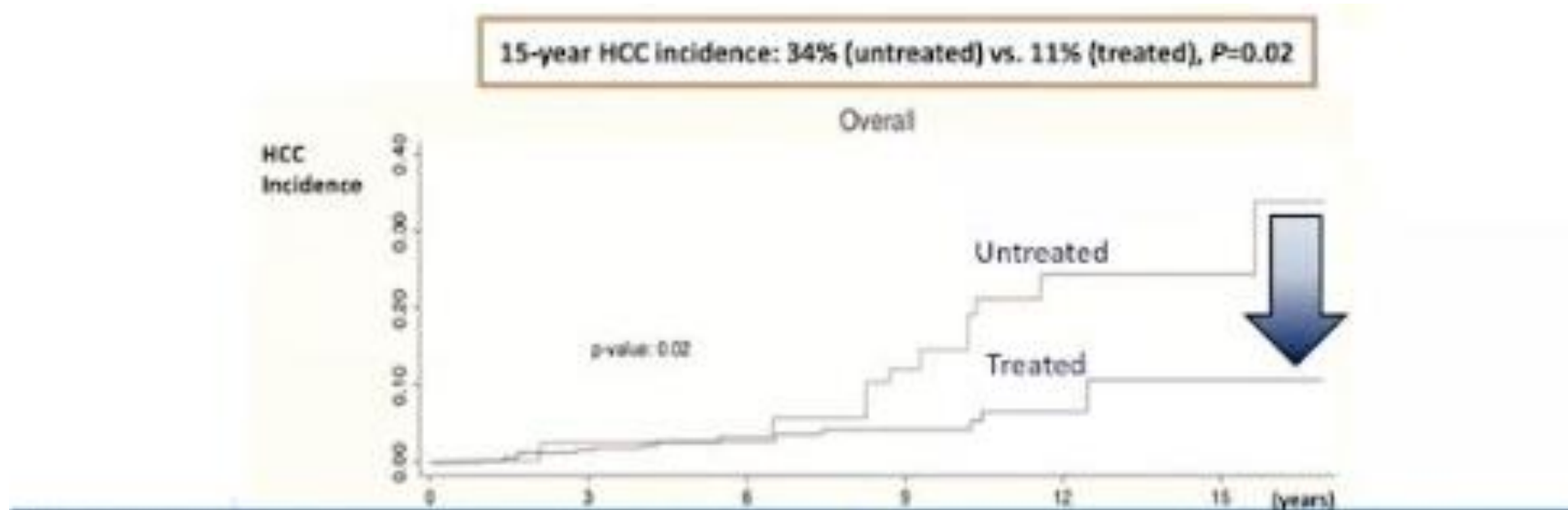
- 30 year old male
- HBeAg positive
- ALT 20
- HBV DNA 1,000,000 IU/mL

Sex	Female 0	Male +2														
Age, years	<table><tr><td>30-34</td><td>0</td></tr><tr><td>35-39</td><td>+1</td></tr><tr><td>40-44</td><td>+2</td></tr><tr><td>45-49</td><td>+3</td></tr><tr><td>50-54</td><td>+4</td></tr><tr><td>55-59</td><td>+5</td></tr><tr><td>60-65</td><td>+6</td></tr></table>		30-34	0	35-39	+1	40-44	+2	45-49	+3	50-54	+4	55-59	+5	60-65	+6
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35-39	+1															
40-44	+2															
45-49	+3															
50-54	+4															
55-59	+5															
60-65	+6															
ALT, IU/L	<table><tr><td><15</td><td>0</td><td>15-44</td><td>+1</td><td>≥45</td><td>+2</td></tr></table>		<15	0	15-44	+1	≥45	+2								
<15	0	15-44	+1	≥45	+2											
HBeAg	<table><tr><td>Negative</td><td>0</td></tr><tr><td>Positive</td><td>+2</td></tr></table>		Negative	0	Positive	+2										
Negative	0															
Positive	+2															
Hepatitis B virus DNA level, copies/mL	<table><tr><td><300 (undetectable)</td><td>0</td></tr><tr><td>300-9,999</td><td>0</td></tr><tr><td>10,000-99,999</td><td>+3</td></tr><tr><td>100,000-999,999</td><td>+5</td></tr><tr><td>≥10⁶</td><td>+4</td></tr></table>		<300 (undetectable)	0	300-9,999	0	10,000-99,999	+3	100,000-999,999	+5	≥10 ⁶	+4				
<300 (undetectable)	0															
300-9,999	0															
10,000-99,999	+3															
100,000-999,999	+5															
≥10 ⁶	+4															
<table><tr><td>9 points</td><td>3.2 %</td></tr><tr><td>REACH-B Score</td><td>10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)</td></tr><tr><td></td><td>AASLD guideline</td></tr><tr><td colspan="2"> Copy Results  Next Steps  </td></tr></table>			9 points	3.2 %	REACH-B Score	10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)		AASLD guideline	Copy Results  Next Steps 							
9 points	3.2 %															
REACH-B Score	10-year risk of HCC (See 3-year and 5-year risk in the Evidence section)															
	AASLD guideline															
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HBV

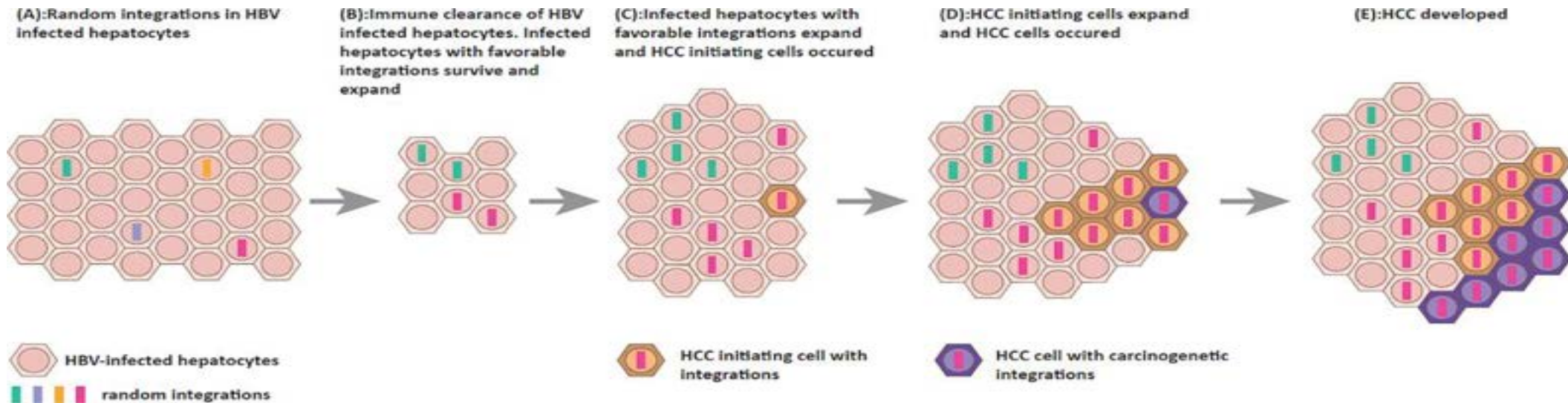
- In 2024, 1.1 million deaths were linked to HBV (HCC and cirrhosis)
- Incidence of HCC has been rising since 2015 despite availability of potent NRTIs (17% increase in HBV related deaths compared to 2015)
- 240 million people with HBV infection worldwide
- Only 65 million (27%) have been diagnosed
- 10 million (4.3%) receiving antiviral treatment

Treating CHB patients with detectable HBV DNA and normal ALT reduces the risk of liver cancer



Liver cancer rate reduced by 70% with oral NUC therapy

HBV integration into host genome



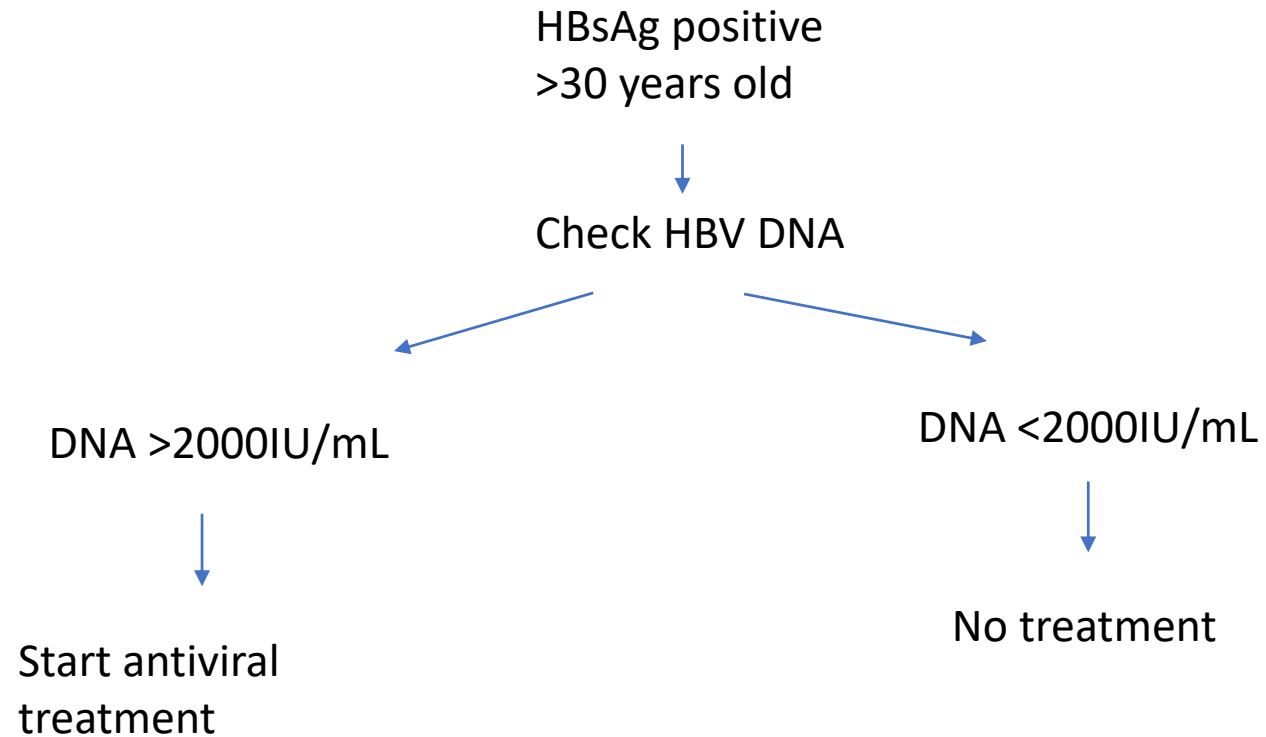
HBV is an oncogenic virus as it integrates into host genome

Can cause HCC even in absence of cirrhosis

Antivirals reduce HBV integration by 99.9% over 10 years

Start treatment based on HBV DNA levels and not ALT levels to reduce long term risk of HCC

Current NZSG guidelines for HBV treatment



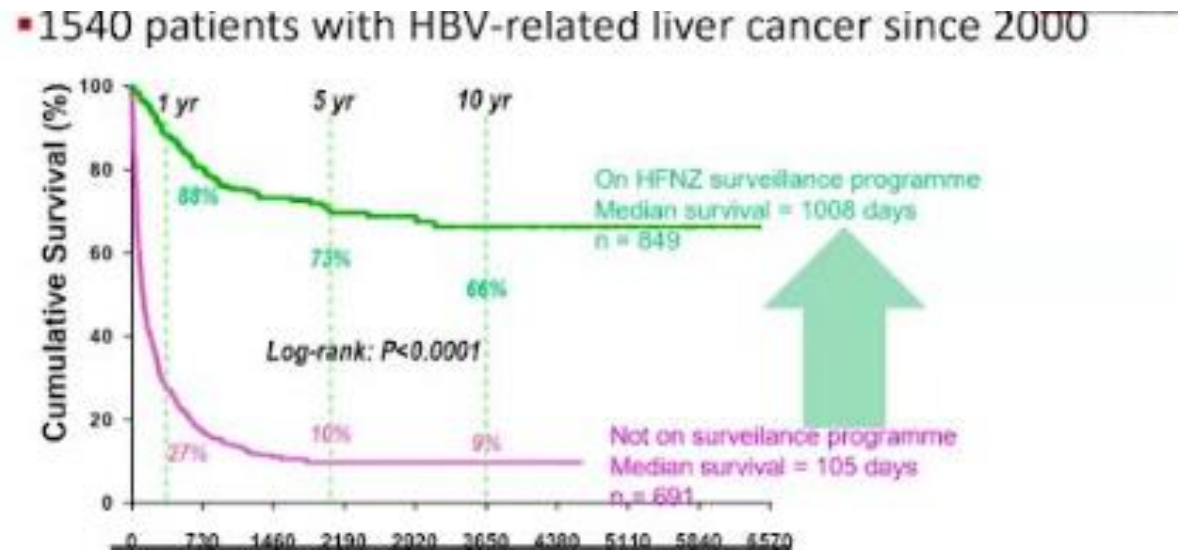
HBV treatment in NZ

- Entecavir or tenofovir
- Currently 94,000 infected
- 57,000 diagnosed (60%)
- 8800 treated (9%)
- Applying new guidelines, we would increase patients on antiviral treatment to 28,000

Importance of fibroscan

- Patients with severe fibrosis or cirrhosis needs HCC surveillance
- 6 monthly USS
- Facilitated by Hepatitis Foundation

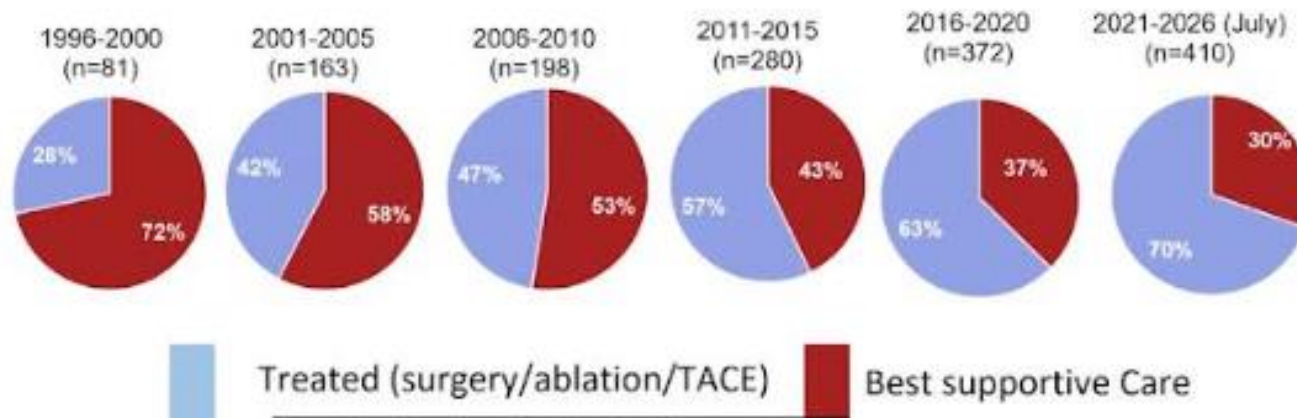
Monitoring for liver cancer improves survival



Surveillance improves survival by 10 fold

HCC surveillance improves treatment options and chances of survival

1540 patients with HBV related liver cancer since 2000 in NZ



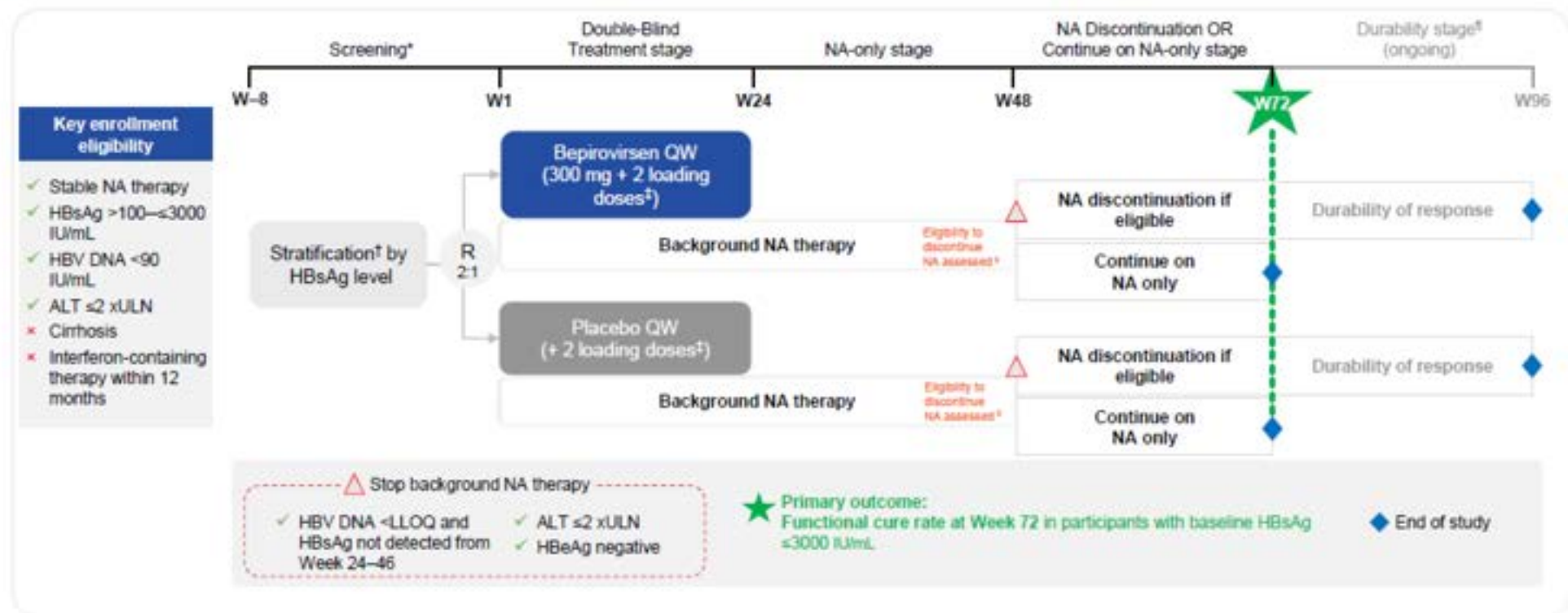
We need a cure for HBV (!)

Functional cure is the treatment goal in chronic HBV infection^{5,6}

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

Bepirovirsen, an antisense oligonucleotide, is the first HBV therapy in **global Phase 3** trials with **functional cure as the primary outcome**⁷⁻⁹

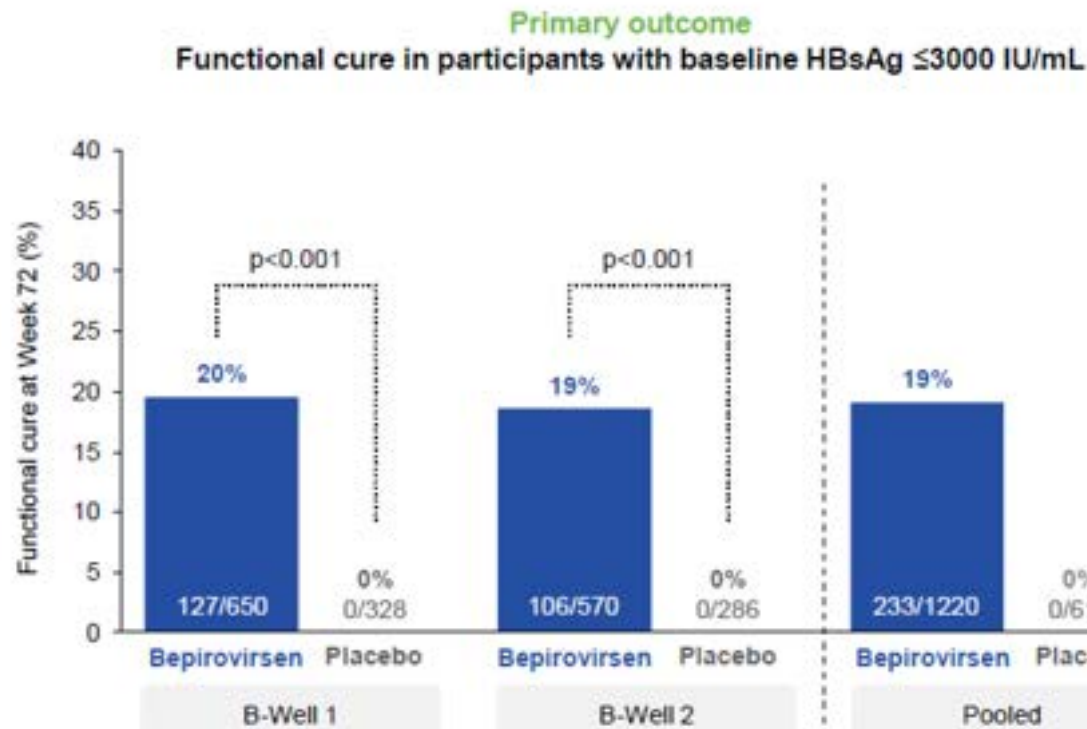
B-Well 1 and 2 were replicate studies, identical in design



*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. [†]Stratified by screening HBsAg level >100 to ≤1000 IU/mL or >1000 to ≤3000 IU/mL.

[‡]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. ^{††}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. ^{†††}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.

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

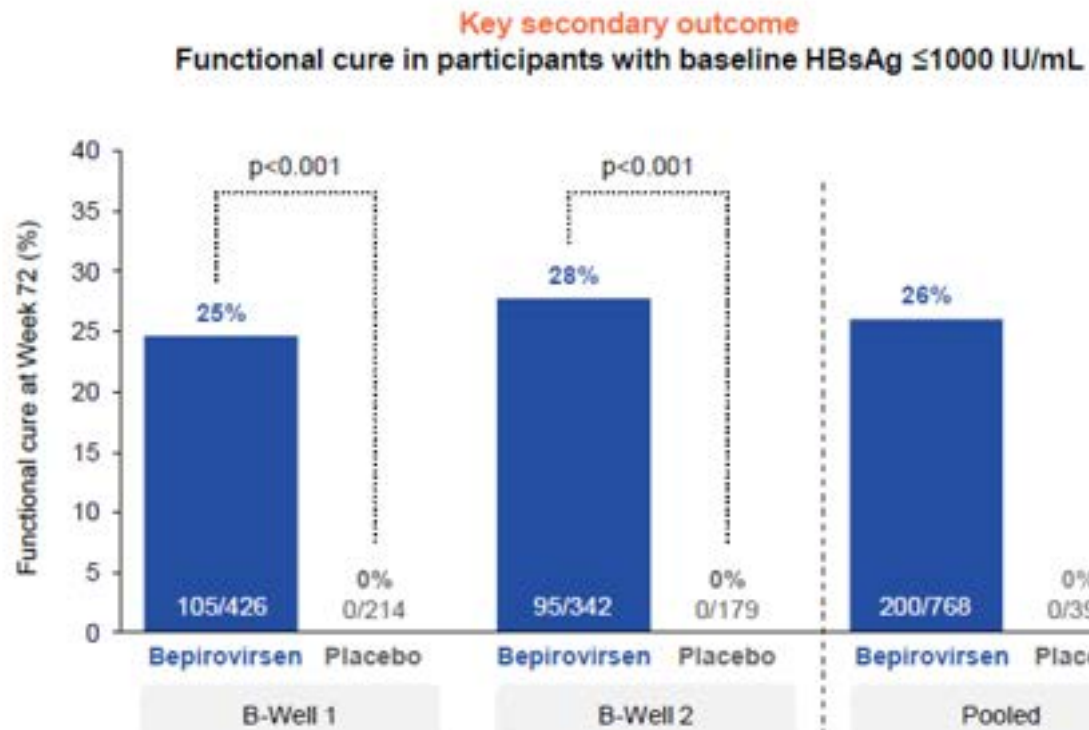


Pooled functional cure rate:

- Bepirovirsen 19%
- Placebo 0%

P-values presented are for common risk difference. 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). 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 $< \text{LLOQ}$ (< 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 ≤ 1000 IU/mL, and no placebo recipients



Pooled functional cure rate:

- Bepirovirsen 26%
- Placebo 0%

P-values are presented for risk difference. Risk differences in functional cure rate and 95% CIs using the Miettinen-Nurminen method: B-Well 1 = 24.6% (20.8, 29.0); B-Well 2 = 27.8% (23.3, 32.8). 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.
CI, confidence interval; HBsAg, hepatitis B surface antigen.

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

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)
ALT increased	269 (22)	18 (3)
Pyrexia	236 (19)	18 (3)
Injection site pruritus	219 (18)	9 (1)
AST increased	183 (15)	8 (1)
Platelet count decreased	180 (15)	5 (1)
Headache	168 (14)	70 (11)
Injection site bruising	176 (14)	28 (5)
Upper respiratory tract infection	147 (12)	72 (12)

On-treatment AEs Grade ≥ 3 [†] severity reported in $\geq 3\%$ [‡] of participants [Week 1–24]

n (%)	Pooled safety population	
	Bepirovirsen N=1223	Placebo N=611
ALT increase	77 (6)	0
AST increase	32 (3)	0

Laboratory monitoring

- Four participants (<1%) had 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

Regular monitoring for laboratory abnormalities and temporarily holding bepirovirsen were effective strategies to mitigate development of clinically significant AEs

* $\geq 10\%$ 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

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

Only for patients with HBsAg level <3000 IU/mL but more so in patients <1000 IU/mL

Is there a way to predict who is going to respond to treatment?

Response guided treatment

For participants with baseline HBsAg ≤ 1000 IU/mL, an HBsAg value < 1 IU/mL at Week 12 was identified as the optimal on-treatment predictor of FC response

	Stop bepirovirsen (Positive)	Continue bepirovirsen (Negative)
HBsAg at Visit 12	≥ 1 IU/mL	< 1 IU/mL
No FC at W72	273	247
FC at W72	7	179

- In the 280 participants recommended to stop treatment the probability of achieving FC was 2.5% (95% CI: 0.8%, 4.6%)
- In the 426 participants recommended to continue treatment:
 - 51.9% achieved NA cessation
 - 42.0% (95% CI: 37.2%, 47.0%) achieved FC
 - 50.2% achieved DNA suppression

Response guided treatment

For participants with baseline HBsAg >1000–≤3000 IU/mL, an HBsAg value <0.05 IU/mL at Week 12 was identified as the optimal on-treatment predictor of FC response

	Stop bepirovirsen (Positive)	Continue bepirovirsen (Negative)
HBsAg at Visit 12	≥ 0.05 IU/mL	< 0.05 IU/mL
No FC at W72	283	84
FC at W72	4	22

- In the 287 participants recommended to stop treatment the probability of achieving FC was 1.4% (95% CI: 0.3%, 3.1%)
- In the 106 participants recommended to continue treatment:
 - 32.1% achieved NA cessation
 - 20.8% (95% CI: 13.3%, 28.9%) achieved FC
 - 31.1% achieved DNA suppression

Application of the early treatment criteria to all participants in the B-Well study (HBsAg ≤ 3000) increased the FC rate from 19% to 38%

Baseline HBsAg level (IU/mL)	Observed FC rate in population	Week 12 HBsAg criteria	FC rate in population meeting Week 12 HBsAg criteria*	FC rate in population NOT meeting Week 12 HBsAg criteria*
>100– ≤ 1000	26.2% (200/768)	HBsAg <1 IU/mL	42.0% (79/426)	2.5% (7/280)
>1000– ≤ 3000	7.3% (33/452)	HBsAg <0.05 IU/mL	20.8% (22/106)	1.4% (4/287)
>100– ≤ 3000	19.1% (233/1220)	Combined	37.8% (201/532)	1.9% (11/567)

*Based on 1099/1220 participants with HBsAg data available at Week 12.
FC, functional cure; HBsAg, hepatitis B surface antigen.

What % of patients have HBsAg <1000 Iu/mL

Local HBsAg quantitation at MMH biochem lab from 2022-2026

Quantitative HBsAg (IU/mL)	Number	%
<0.05	17	4.9
0.06-100	96	27.5
100-1000	110	31.5
1000-3000	78	22.3
3000-10,000	35	10
10,000+	13	3.7
	349	100



ORIGINAL ARTICLE



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

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Abstract

BACKGROUND

Have questions about this content? Try AI Companion.



HBV take home messages

- Treatment of HBV has changed
- Majority of HBV patients >30 should be on antiviral treatment
- Aim to reduce long term risk of HCC
- New HBV cure treatments coming through
- We need to find the 40% still undiagnosed (!)