

Supplementary Table 1 Clinical staging criteria of American Association for the Study of Liver Diseases 2018 chronic hepatitis B guidance

Four-phases	Immune-Tolerant CHB	HBeAg-positive Active CHB	Immune Inactive CHB	HBeAg negative Active CHB	Immune
HBeAg	positive	positive	negative	negative	
ALT	< 1ULN	≥ 2*UNL	< 1ULN	≥ 2*UNL	
HBV-DNA	> 10 ⁶ IU/mL	≥ 2*10 ⁴ IU/mL	< 2*10 ³ IU/mL	≥ 2*10 ³ IU/mL	
Indeterminate-phase	A	B	C	D	
HBeAg	positive	positive	negative	negative	
ALT	< 1ULN	≥ 2*UNL	1-2 UNL	≥ 2*UNL	1-2 UNL
HBV-DNA	≤ 10 ⁶ IU/mL	< 2*10 ⁴ IU/mL	unlimited	≥ 2*10 ³ IU/mL	< 2*10 ³ IU/mL unlimited

Supplementary Table 2 Noninvasive model score in chronic hepatitis B patients of the different phases

Phase	Immune-Tolerant CHB	HBeAg-positive Immune Active CHB	Inactive CHB	HBeAg-negative		P-value
				Immune Active CHB	Indeterminate	
N, n(%)	118 (7.70%)	197 (12.86%)	317 (20.70)	86 (5.61%)	814 (53.13%)	
APRI						< 0.001
< 1	118 (100.00%)	101 (51.27%)	309 (97.48%)	57 (66.28%)	773 (94.96%)	
1- 2	0 (0.00%)	48 (24.37%)	6 (1.89%)	10 (11.63%)	20 (2.46%)	
> 2	0 (0.00%)	48 (24.37%)	2 (0.63%)	19 (22.09%)	21 (2.58%)	
FIB-4						< 0.001
< 1.45	114 (96.61%)	131 (66.50%)	264 (83.28%)	57 (66.28%)	662 (81.33%)	
1.45- 3.25	4 (3.39%)	52 (26.40%)	46 (14.51%)	16 (18.60%)	121 (14.86%)	
> 3.25	0 (0.00%)	14 (7.11%)	7 (2.21%)	13 (15.12%)	31 (3.81%)	
GPR						< 0.001
≤ 0.32	107 (90.68%)	47 (23.86%)	247 (77.92%)	22 (25.58%)	497 (61.06%)	
> 0.32	11 (9.32%)	150 (76.14%)	70 (22.08%)	64 (74.42%)	317 (38.94%)	

Supplementary Table 3 Noninvasive model score in the different indeterminate phase chronic hepatitis B

Phase	Indeterminate-A	Indeterminate-B	Indeterminate-C	Indeterminate-D	P-value
N, n(%)	62 (7.62%)	160 (19.66%)	304 (37.35%)	288 (35.38%)	
APRI stage, n(%)					< 0.001
< 1	59 (95.16%)	145 (90.62%)	301 (99.01%)	268 (93.06%)	
1- 2	2 (3.23%)	9 (5.62%)	3 (0.99%)	6 (2.08%)	
> 2	1 (1.61%)	6 (3.75%)	0 (0.00%)	14 (4.86%)	
FIB-4 stage, n(%)					0.136
< 1.45	49 (79.03%)	131 (81.88%)	257 (84.54%)	225 (78.12%)	
1.45- 3.25	10 (16.13%)	21 (13.12%)	43 (14.14%)	47 (16.32%)	
> 3.25	3 (4.84%)	8 (5.00%)	4 (1.32%)	16 (5.56%)	
GPR stage,n(%)					< 0.001
≤ 0.32	42 (67.74%)	75 (46.88%)	247 (81.25%)	133 (46.18%)	
> 0.32	20 (32.26%)	85 (53.12%)	57 (18.75%)	155 (53.82%)	

Supplementary Table 4 Predictors of liver histopathology changes in all chronic hepatitis B patients

	Univariable		Multivariable*	
	OR(95%CI)	P-value	Adjusted OR(95%CI)	P-value
Significant necroinflammation				
Age, y				
< 40	Referent		Referent	
≥ 40	0.96 (0.78, 1.19)	0.7335	1.57 (1.20, 2.05),	0.0011
Sex				
Male	Referent		Referent	
Female	0.81 (0.65, 1.02)	0.0774	0.81 (0.62, 1.06),	0.1241
HBeAg				
-	Referent		Referent	
+	3.38 (2.71, 4.21)	< 0.0001	2.53 (1.92, 3.34)	< 0.0001
HBV-DNA log10, IU/mL				
< 3	Referent		Referent	
≥ 3	3.22 (2.36, 4.41)	< 0.0001	1.95 (1.37, 2.77)	0.0002
PLT, 10 ⁹ /L				

>150	Referent		Referent	
≤ 150	2.78 (2.09, 3.70)	< 0.0001	2.64 (1.88, 3.71)	< 0.0001
ALT, U/L				
<ULN	Referent		Referent	
≥ ULN	5.17 (4.13, 6.48)	< 0.0001	4.00 (3.13, 5.13)	< 0.0001
Significant fibrosis				
Age, y				
< 40	Referent		Referent	
≥ 40	1.31 (1.03, 1.66)	0.026	1.36 (1.04, 1.77)	0.0258
Sex				
Male	Referent		Referent	
Female	0.73 (0.59, 0.91)	0.0059	0.81 (0.64, 1.03)	0.091
HBeAg				
-	Referent		Referent	
+	1.10 (0.89, 1.36)	0.3818	0.97 (0.75, 1.25)	0.808
HBV-DNA log10, IU/mL				
< 3	Referent		Referent	

≥ 3	1.31 (1.01, 1.70)	0.041	1.20 (0.90, 1.60)	0.2117
PLT, 10 ⁹ /L				
>150	Referent		Referent	
≤ 150	3.47 (2.55, 4.73)	< 0.0001	3.15 (2.26, 4.38)	< 0.0001
ALT, U/L				
<ULN	Referent		Referent	
≥ ULN	1.90 (1.55, 2.33)	< 0.0001	1.78 (1.42, 2.23)	< 0.0001
Significant liver histological changes				
Age, y				
< 40	Referent		Referent	
≥ 40	1.20 (0.94, 1.53)	0.1395	1.45 (1.10, 1.92)	0.0086
Sex				
Male	Referent		Referent	
Female	0.79 (0.63, 0.98)	0.036	0.86 (0.67, 1.10)	0.2278
HBeAg				
-	Referent		Referent	

+	1.73 (1.39, 2.15)	<0.0001	1.31 (1.01, 1.71)	0.0432
HBV-DNA log10, IU/mL				
< 3	Referent		Referent	
≥ 3	1.84 (1.42, 2.38)	< 0.0001	1.39 (1.04, 1.86)	0.0244
PLT, 10 ⁹ /L				
>150	Referent		Referent	
≤ 150	2.72 (1.97, 3.77)	< 0.0001	2.42 (1.70, 3.46)	< 0.0001
ALT, U/L				
<ULN	Referent		Referent	
≥ ULN	3.13 (2.53, 3.88)	< 0.0001	2.73 (2.16, 3.45)	< 0.0001

*Adjusted for age, sex, ALT level, HBeAg statue, PLT level, and HBV DNA level.

Supplementary Table 5 Predictors of liver histopathology changes in HBeAg positive indeterminate patients

Significant necroinflammation	Univariable		Multivariable*	
	OR, (95%CI)	P-value	Adjusted OR, (95%CI)	P-value
Age, y				
< 40	Referent		Referent	
≥ 40	2.43 (1.26, 4.67)	0.0078	2.31 (1.14, 4.67)	0.02
Sex				
Male	Referent		Referent	
Female	1.54 (0.86, 2.76)	0.1483	1.77 (0.94, 3.32)	0.0749
PLT, 10 ⁹ /L				
> 150	Referent		Referent	
≤ 150	4.56 (1.99, 10.49)	0.0003	4.22 (1.77, 10.06)	0.0011
ALT, U/L				
< ULN	Referent		Referent	
≥ ULN	0.73 (0.41, 1.32)	0.3039	0.66 (0.34, 1.27)	0.2116
HBV-DNA log ₁₀ , IU/mL				
< 3	Referent		Referent	

≥ 3	1.01 (0.36, 2.80)	0.9846	1.75 (0.56, 5.48)	0.3381
Significant fibrosis				
Age, y				
< 40	Referent		Referent	
≥ 40	2.37 (1.23, 4.56)	0.0096	2.05 (1.00, 4.20)	0.0513
Sex				
Male	Referent		Referent	
Female	1.15 (0.65, 2.06)	0.6324	1.28 (0.67, 2.42)	0.4538
PLT, 10 ⁹ /L				
> 150	Referent		Referent	
≤ 150	11.05 (3.77, 32.42)	< 0.0001	9.78 (3.27, 29.21)	< 0.0001
ALT, U/L				
< ULN	Referent		Referent	
≥ ULN	0.63 (0.35, 1.14)	0.1237	0.70 (0.36, 1.37)	0.2987
HBV-DNA log ₁₀ , IU/mL				
< 3	Referent		Referent	
≥ 3	0.32 (0.10, 1.02)	0.0533	0.45 (0.13, 1.59)	0.2154

Significant liver histological changes

Age, y

< 40

Referent

Referent

≥ 40

2.31 (1.11, 4.81)

0.0256

2.26 (1.01, 5.04)

0.0462

Sex

Male

Referent

Referent

Female

2.12 (1.09, 4.10)

0.0259

2.53 (1.25, 5.11)

0.0098

PLT, 10⁹/L

> 150

Referent

Referent

≤ 150

7.67 (2.28, 25.87)

0.0010

7.17 (2.08, 24.79)

0.0018

ALT, U/L

< ULN

Referent

Referent

≥ ULN

0.98 (0.53, 1.82)

0.9434

1.08 (0.54, 2.15)

0.8329

HBV-DNA log₁₀, IU/mL

< 3

Referent

Referent

≥ 3

0.41 (0.11, 1.48)

0.1715

0.54 (0.14, 2.14)

0.3779

*Adjusted for age,sex, ALT level, HBeAg statue, PLT level , and HBV DNA level.

Supplementary Table 6 Predictors of liver histopathology changes in HBeAg negative indeterminate patients

Significant necroinflammation	Univariable		Multivariable*	
	OR, (95%CI)	P-value	Adjusted OR, (95%CI)	P-value
Age, y				
< 40	Referent		Referent	
≥ 40	1.50 (1.05, 2.13)	0.0257	1.60 (1.09, 2.36)	0.0172
Sex				
Male	Referent		Referent	
Female	0.48 (0.30, 0.74)	0.0011	0.49 (0.30, 0.78)	0.0029
PLT, 10 ⁹ /L				
> 150	Referent		Referent	
≤ 150	2.76 (1.74, 4.37)	< 0.0001	2.37 (1.45, 3.88)	0.0006
ALT, U/L				

< ULN	Referent		Referent	
≥ ULN	2.17 (1.52, 3.10)	< 0.0001	2.30 (1.52, 3.48)	< 0.0001
HBV-DNA log ₁₀ , IU/mL				
< 3	Referent		Referent	
≥ 3	0.84 (0.51, 1.39)	0.504	1.42 (0.80, 2.51)	0.2254
Significant fibrosis				
Age, y				
< 40	Referent		Referent	
≥ 40	1.31 (0.95, 1.82)	0.0979	1.19 (0.85, 1.68)	0.3144
Sex				
Male	Referent		Referent	
Female	0.79 (0.54, 1.14)	0.2045	0.88 (0.60, 1.31)	0.5398
PLT, 10 ⁹ /L				
> 150	Referent		Referent	
≤ 150	3.27 (1.98, 5.39)	< 0.0001	2.99 (1.79, 4.99)	< 0.0001
ALT, U/L				
< ULN	Referent		Referent	

≥ ULN	1.56 (1.13, 2.16)	0.0069	1.56 (1.06, 2.29)	0.0227
HBV-DNA log ₁₀ , IU/mL				
< 3	Referent		Referent	
≥ 3	1.02 (0.64, 1.63)	0.9343	1.38 (0.80, 2.38)	0.2436
Significant liver histological changes				
Age, y				
< 40	Referent		Referent	
≥ 40	1.38 (0.99, 1.91)	0.0559	1.28 (0.91, 1.82)	0.1585
Sex				
Male	Referent		Referent	
Female	0.72 (0.49, 1.04)	0.0786	0.78 (0.53, 1.15)	0.21
PLT, 10 ⁹ /L				
> 150	Referent		Referent	
≤ 150	2.71 (1.61, 4.55)	0.0002	2.42 (1.42, 4.13)	0.0012
ALT, U/L				
< ULN	Referent		Referent	

≥ ULN	1.73 (1.24, 2.41)	0.0011	1.87 (1.26, 2.77)	0.0019
HBV-DNA log10, IU/mL				
< 3	Referent		Referent	
≥ 3	1.07 (0.67, 1.72)	0.7819	1.64 (0.95, 2.85)	0.0783

*Adjusted for age, sex, ALT level, HBeAg statue, PLT level, and HBV DNA level.