Supplementary Table 1. Comparison of Baseline Characteristics between Patients with and without AVT Initiation during the Study Period

Variable	AVT initiation during the study period (n=491, 41.0%)	No AVT during the study period (n=707, 59.0%)	p-value
Demographic			
Age, yr	48.1±11.3	49.5±12.1	0.055
Male sex	290 (59.1)	386 (54.6)	0.139
Diabetes mellitus	49 (10.0)	71 (10.0)	1.000
Cirrhosis	206 (42.0)	135 (19.1)	<0.001
Laboratory			
α-Fetoprotein, ng/mL	10.5±35.5	4.4±15.3	<0.001
HBeAg positivity	204 (41.5)	73 (10.3)	<0.001
HBV DNA, logIU/mL	4.2±2.5	2.9±1.9	<0.001
Aspartate aminotransferase, IU/L	62.0±100.6	28.4±20.5	<0.001
Alanine aminotransferase, IU/L	81.3±162.2	33.6±30.4	<0.001
Serum albumin, g/dL	4.3±0.4	4.4±0.3	<0.001
Total bilirubin, mg/dL	0.9±0.5	0.8±0.4	0.032
Platelet count, 10^9/L	162±59	192±60	<0.001

Data are presented as mean±SD or number (%).
AVT, antiviral therapy; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.

Supplementary Table 2. HRs of Hepatocellular Carcinoma Development by Ongoing Antiviral Therapy and Differently Adjusted Models at Each Institution

Model	HR	95% CI	p-value
Yonsei University			
Unadjusted	1.191	0.674–2.107	0.547
Adjusted			
Model 1	1.133	0.640–2.004	0.668
Model 2	1.140	0.644–2.017	0.653
Model 3	0.896	0.503–1.596	0.709
Model 4	1.012	0.516–1.987	0.972
CHA University			
Unadjusted	2.189	1.079–4.443	0.030
Adjusted			
Model 1	2.265	1.113–4.611	0.024
Model 2	2.217	1.089–4.514	0.028
Model 3	1.710	0.839–3.485	0.139
Model 4	1.586	0.700–3.594	0.270

HR, hazard ratio; CI, confidence interval; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus.
Model 1, age and gender; model 2, model 1 + diabetes mellitus; model 3, model 2 + cirrhosis; model 4, model 3 + α-fetoprotein, HBeAg positivity, HBV DNA, aspartate aminotransferase, alanine aminotransferase, serum albumin, total bilirubin, and platelet count.

Supplementary Table 3. HRs of Hepatocellular Carcinoma Development by Cirrhosis and Differently Adjusted Models

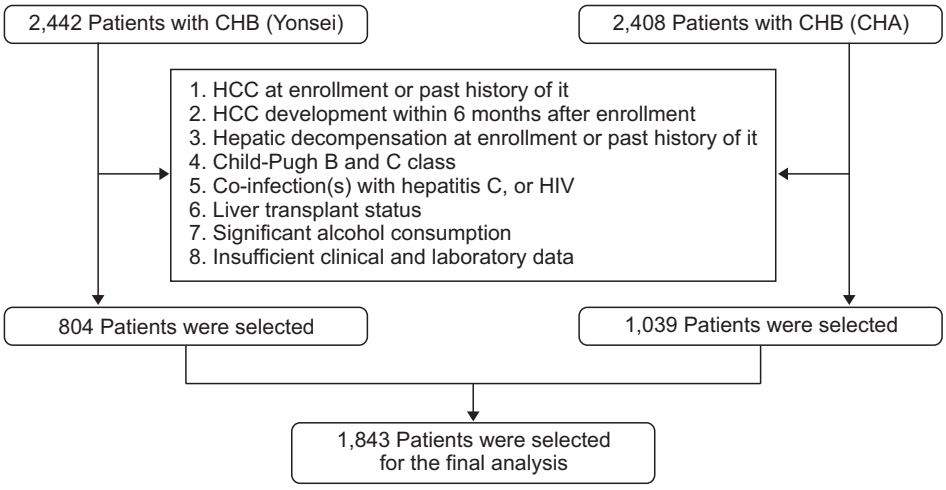
Model	With ongoing AVT at enrollment			Without ongoing AVT at enrollment		
	HR	95% CI	p-value	HR	95% CI	p-value
All study participants						
Unadjusted	7.810	3.272–18.642	<0.001	8.602	4.115–17.985	<0.001
Adjusted						
Model 1	6.060	2.511–14.624	<0.001	7.424	3.542–15.562	<0.001
Model 2	6.120	2.538–14.761	<0.001	7.451	3.552–15.628	<0.001
Model 3	5.322	2.049–13.822	0.001	5.008	2.166–11.581	<0.001
Model 4	5.391	2.051–14.173	0.001	4.184	1.771–9.883	0.001

HR, hazard ratio; AVT, antiviral therapy; CI, confidence interval; HBeAg, hepatitis B virus e antigen; HBV, hepatitis B virus.
Model 1, age and gender; model 2, model 1 + diabetes mellitus; model 3, model 2 + α-fetoprotein, HBeAg positivity, HBV DNA, aspartate aminotransferase, alanine aminotransferase, serum albumin, total bilirubin, and platelet count; model 4, model 3 + institution.

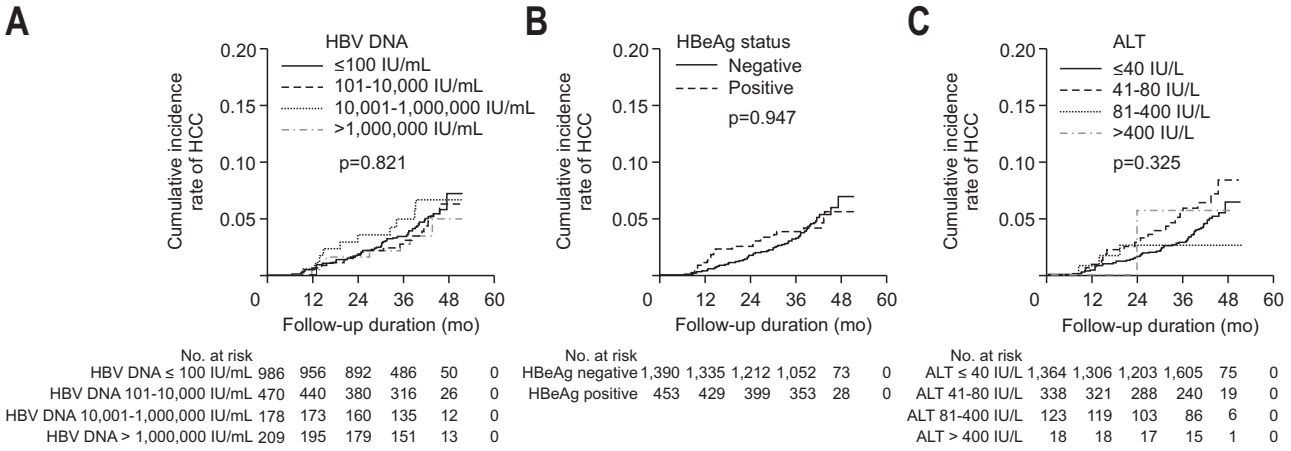
Supplementary Table 4. HRs of Hepatocellular Carcinoma Development by Cirrhosis and Differently Adjusted Models at Each Institution

Model	HR	95% CI	p-value
Yonsei University			
Unadjusted	4.795	2.327–9.883	<0.001
Adjusted			
Model 1	4.435	2.152–9.142	<0.001
Model 2	4.405	2.137–9.082	<0.001
Model 3	3.382	1.487–7.694	0.004
Model 4	3.380	1.485–7.694	0.004
Model 5	2.228	0.966–5.141	0.060
CHA University			
Unadjusted	14.021	5.770–34.070	<0.001
Adjusted			
Model 1	11.347	4.616–27.889	<0.001
Model 2	11.336	4.611–27.867	<0.001
Model 3	7.868	2.764–22.396	<0.001
Model 4	7.550	2.652–21.496	<0.001
Model 5	7.237	2.541–20.605	<0.001

HR, hazard ratio; CI, confidence interval; HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; AVT, antiviral therapy.
Model 1, age and gender; model 2, model 1 + diabetes mellitus; model 3, model 3 + α-fetoprotein, HBeAg positivity, HBV DNA, aspartate aminotransferase, alanine aminotransferase, serum albumin, total bilirubin, and platelet count; model 4, model 3 + AVT at enrollment; model 5, model 4 + AVT after enrollment.



Supplementary Fig. 1. Flow diagram of the study population selection. A total of 4,850 patients with chronic hepatitis B (CHB) were recruited. After excluding 3,007 patients according to our exclusion criteria, 1,843 patients were selected for statistical analysis.
HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus.



Supplementary Fig. 2. Cumulative incidence rates of hepatocellular carcinoma (HCC) based on stratified HBV DNA level (A), HBeAg (B), and stratified ALT level (C). (A) The cumulative HCC incidence rates were not significantly different based on the stratified HBV DNA level (p=0.821 by log-rank test; HBV DNA ≤100 IU/mL vs 101–10,000 IU/mL vs 10,001–1,000,000 IU/mL vs >1,000,000 IU/mL). (B) The cumulative HCC incidence rates were not significantly different based on the HBeAg status (p=0.947 by log-rank test). (C) The cumulative HCC incidence rates were not significantly different based on the stratified HBV DNA level (p=0.325 by log-rank test; ALT ≤40 IU/L vs 41–80 IU/L vs 81–400 IU/L vs >400 IU/L). HBV, hepatitis B virus; HBeAg, hepatitis B e antigen; ALT, alanine aminotransferase.