

SUPPLEMENTARY TABLES

Table S1. Baseline characteristics after inverse probability weighting

Characteristic	LAM/ETV-R group (n=45)	LAM/ADV-R group (n=28)	LAM/ETV/ADV-R group (n=20)	<i>P</i> value*
Age (years)	53 (32–71)	50 (23–68)	47 (29–67)	0.433
Gender, male	32.2 (74.9)	14.8 (50.9)	10.4 (79.2)	0.063
Serum HBV DNA (log ₁₀ IU/mL) [†]	3.32 (0.87–7.37)	3.20 (1.88–6.71)	2.51 (2.02–8.23)	0.801
Serum ALT (IU/L) [†]	25 (9–275)	29 (11–843)	26 (14–57)	0.441
Serum creatinine (mg/dL) [†]	0.88 (0.53–1.26)	0.80 (0.53–1.31)	0.85 (0.54–1.14)	0.328
HBeAg, positive	31.8 (74.0)	22.2 (76.4)	11.1 (83.8)	0.763
Liver cirrhosis [‡]	12.0 (27.9)	7.5 (25.7)	2.5 (18.8)	0.805
Lines of prior antiviral treatment	3 (1–5)	3 (2–5)	4 (3–5)	0.065
Duration of previous treatment (months) [†]	16.9 (2.7–78.7)	15.4 (2.7–85.7)	18.2 (1.4–40.2)	0.507
Time point of rescue therapy				

Virologic breakthrough	18.4 (42.9)	8.3 (28.5)	2.3 (17.3)	0.170
Biochemical breakthrough	11.1 (25.8)	9.7 (33.6)	2.1 (15.6)	0.462

Note.—Unless otherwise indicated, data are number of patients and data in parentheses are percentages.

* Kruskal-Wallis test and χ^2 test (or the Fisher's exact test) were used to analyze the differences among the groups.

† Data are medians, and data in parentheses are ranges.

‡ Liver cirrhosis was diagnosed when the platelet count was below 100,000/mm³ and associated splenomegaly or esophageal-gastric varices were detected.

Abbreviations: LAM, lamivudine; ETV, entecavir; ADV, adefovir; HBV, hepatitis B virus; ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen

Table S2. Univariate and multivariate analysis of the clinical factors predictive of complete virologic suppression during rescue therapy after inverse probability weighting

Variable	Univariate analysis		Multivariate analysis	
	Hazard ratio	<i>P</i> value *	Adjusted hazard ratio	<i>P</i> value *
Age (per year)	1.016 (0.987–1.046)	0.271		
Baseline serum HBV DNA (per 1 log ₁₀ IU/mL)	0.667 (0.566–0.785)	<0.001	0.676 (0.557–0.820)	<0.001
Baseline serum ALT (per IU/L)	0.992 (0.983–1.000)	0.045	1.000 (0.995–1.006)	0.914
HBeAg (positive versus negative)	0.628 (0.369–1.068)	0.086		
Liver cirrhosis (positive versus negative) [†]	1.438 (0.852–2.427)	0.174		
Time point of rescue therapy				
Virologic breakthrough (yes versus no)	1.308 (0.800–2.138)	0.284		
Biochemical breakthrough (yes versus no)	0.437 (0.236–0.807)	0.008	0.874 (0.401–1.904)	0.735
Drug resistance				
LAM/ETV-R versus LAM/ADV-R	0.846 (0.496–1.445)	0.541		
LAM/ETV-R versus LAM/ETV/ADV-R	0.690 (0.364–1.308)	0.255		

LAM/ADV-R versus LAM/ETV/ADV-R	0.815 (0.415–1.598)	0.551
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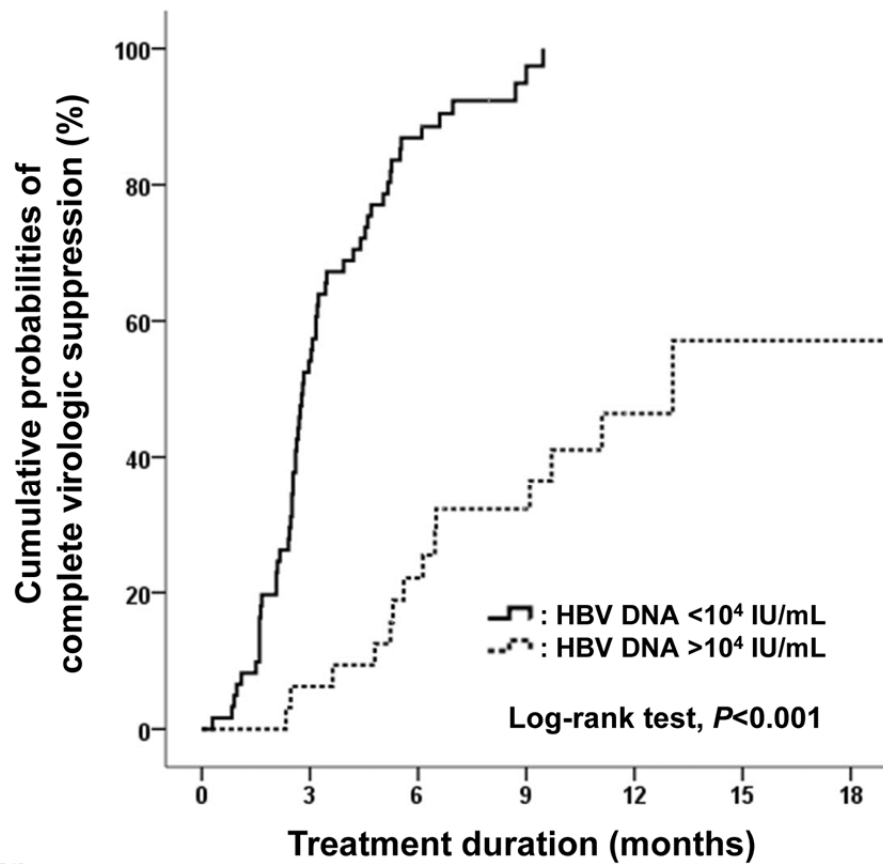
Note.—Data in parentheses are 95% CIs.

* *P* values were determined with Cox proportional hazards regression models. *P* < 0.05 indicated a significant difference.

† Liver cirrhosis was diagnosed when the platelet count was below 100,000/mm³ and associated splenomegaly or esophageal-gastric varices were detected.

Abbreviations: HBV, hepatitis B virus; ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen; LAM, lamivudine; ETV, entecavir; ADV, adefovir

SUPPLEMENTARY FIGURES



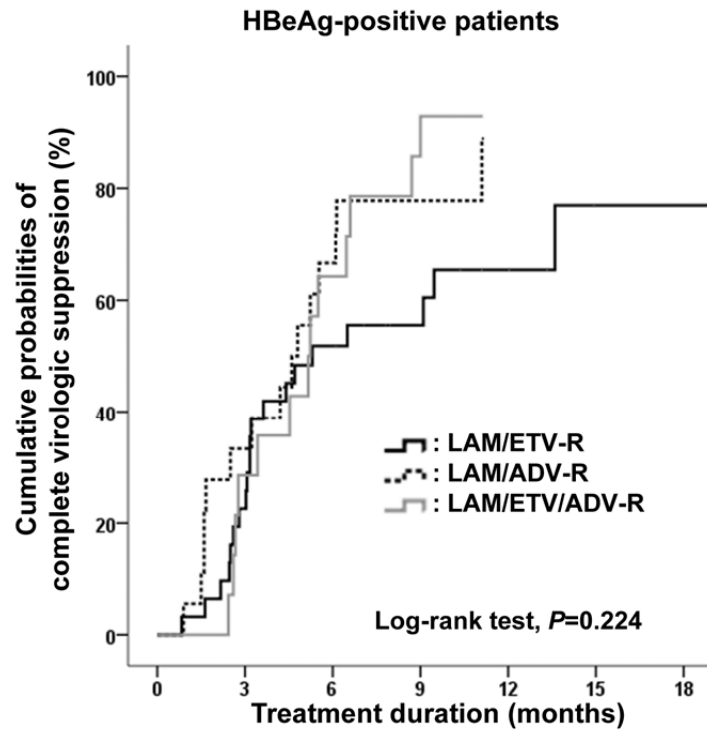
No. under observation

HBV DNA <10 ⁴ IU/mL at baseline	61	61	61	48	32	11	5
HBV DNA >10 ⁴ IU/mL at baseline	32	32	32	25	21	10	9

Fig. S1. Cumulative probability of complete virologic suppression during the rescue therapy.

Cumulative probabilities of complete virologic suppression, undetectable levels of HBV DNA according to PCR assays, during the treatment period, are plotted for those with low (<10⁴ IU/mL), and high HBV DNA levels (>10⁴ IU/mL) at baseline.

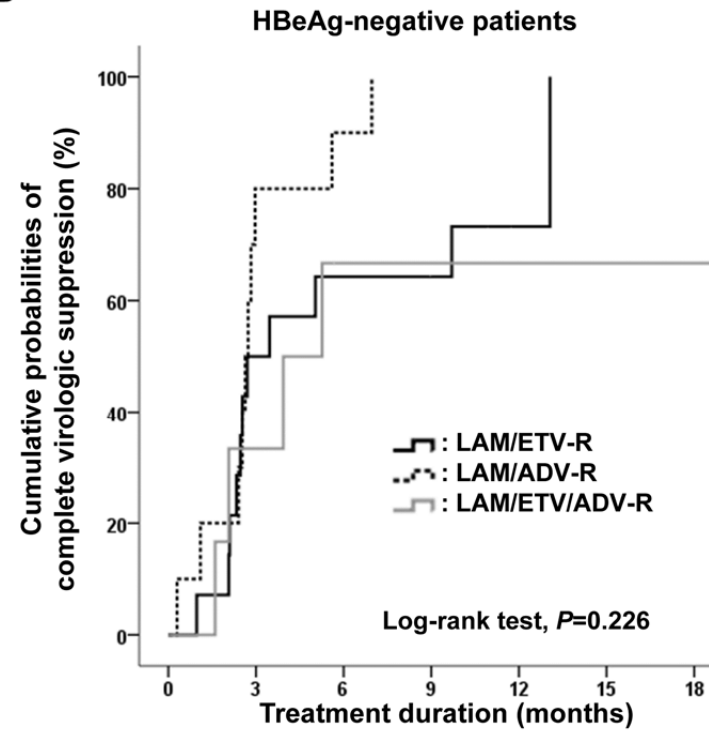
A



No. under observation

LAM/ETV-R	31	31	31	23	13	4	3
LAM/ADV-R	18	18	18	16	16	7	3
LAM/ETV/ADV-R	14	14	14	13	12	3	3

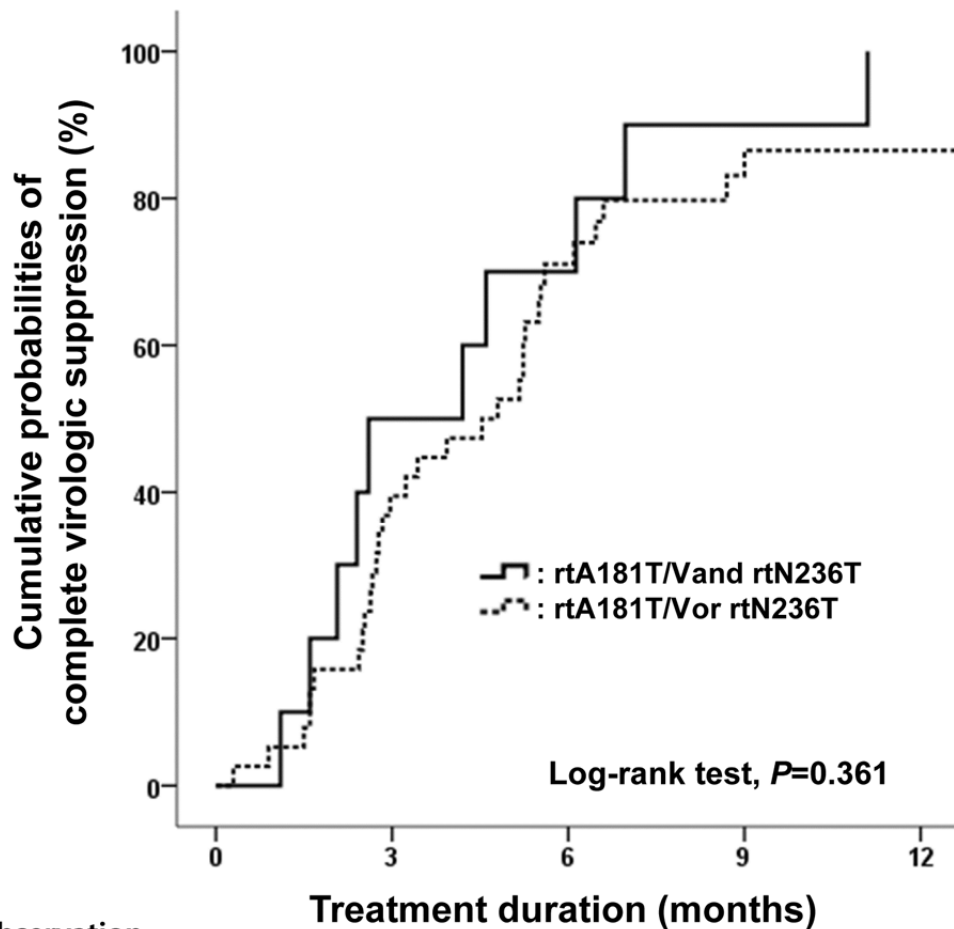
B



No. under observation

LAM/ETV-R	14	14	14	9	5	2	2
LAM/ADV-R	10	10	10	7	3	2	1
LAM/ETV/ADV-R	6	6	6	5	4	3	2

Fig. S2. Cumulative probability of complete virologic suppression during the rescue therapy. Cumulative probabilities of complete virologic suppression are shown for each group. (A) Data for patients who were positive for HBeAg at baseline. (B) Data for patients who were negative for HBeAg at baseline.



No. under observation

rtA181T/V and rtN236T	10	10	10	9	9
rtA181T/V or rtN236T	38	38	38	32	26

Fig. S3. Cumulative probability of complete virologic suppression in patients harboring substitutions associated with ADV-resistance at baseline. Cumulative probabilities of complete virologic suppression during the treatment period are shown according to amino acid substitution profiles.