

**Supplementary Data** for Thompson et al. 2022 “Baseline Serum HBV RNA is Associated with Risk of Hepatitis Flare after Stopping Nucleoside Analog Therapy in HBeAg-negative Participants”

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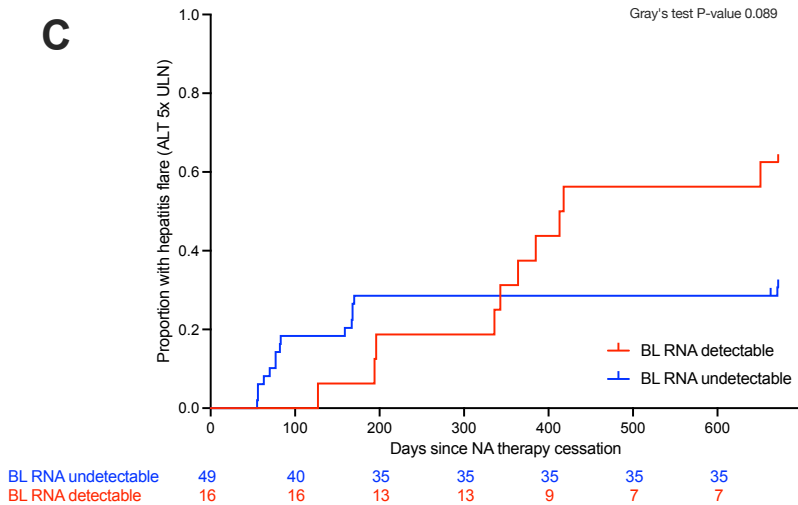
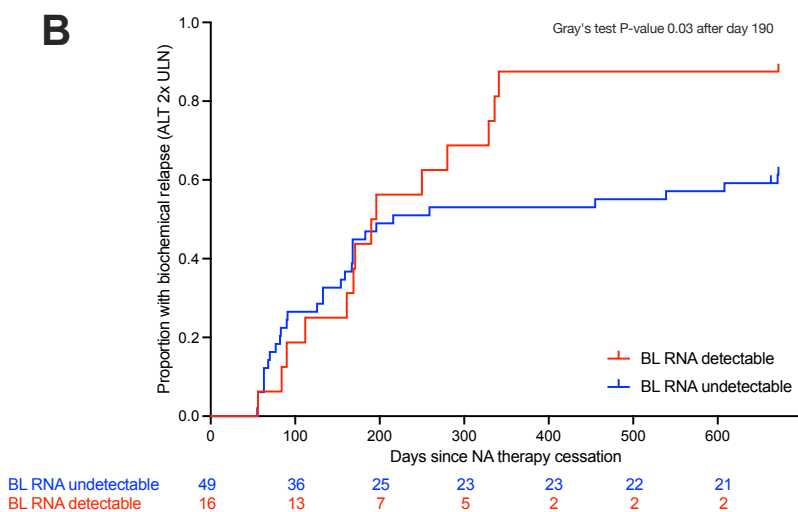
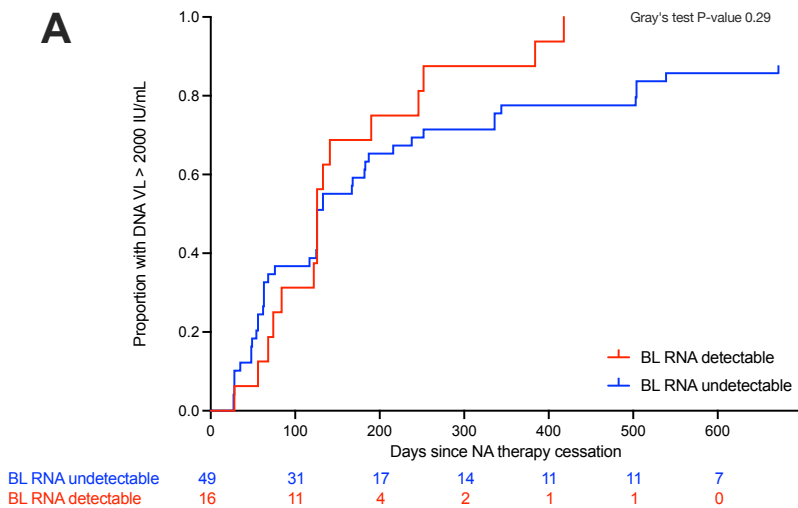
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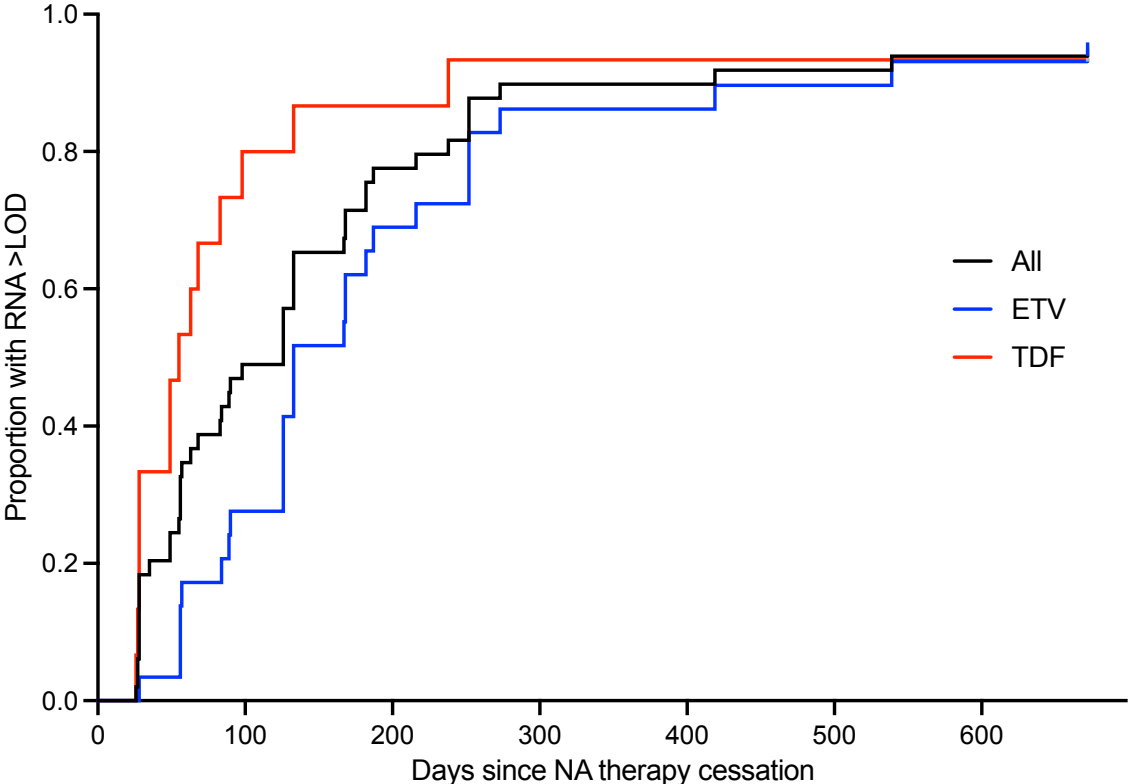
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**Figure S1. Cumulative incidence analysis for virological relapse (A), biochemical relapse (B), and hepatitis flare (C) in patients with detectable (red) or undetectable (blue) HBV RNA at baseline.**

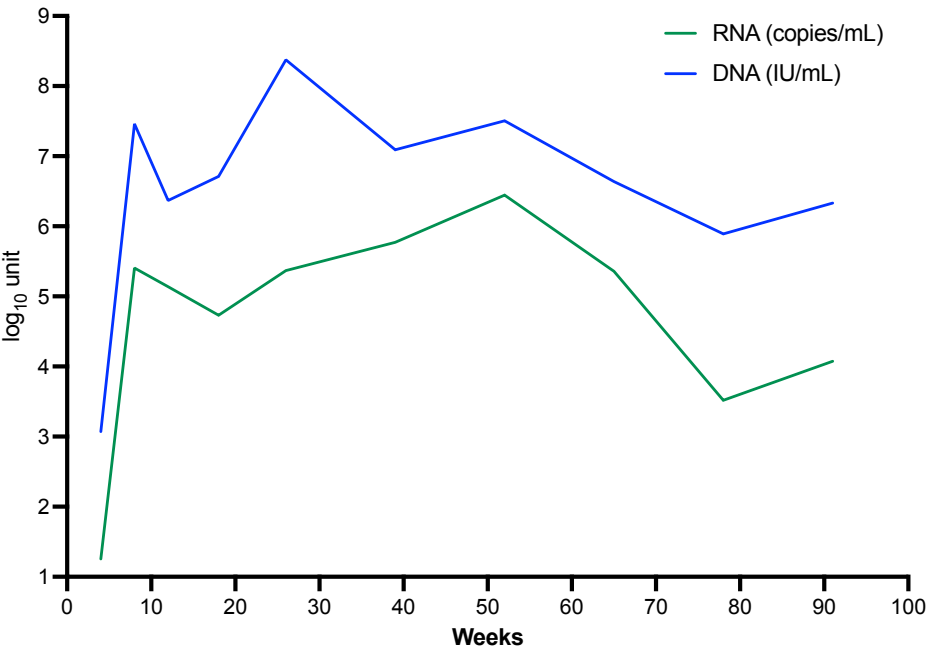


**Figure S2. Cumulative incidence analysis for HBV RNA detectability in all patients (black) or patients that had been treated with ETV (blue) vs TDF (red).**

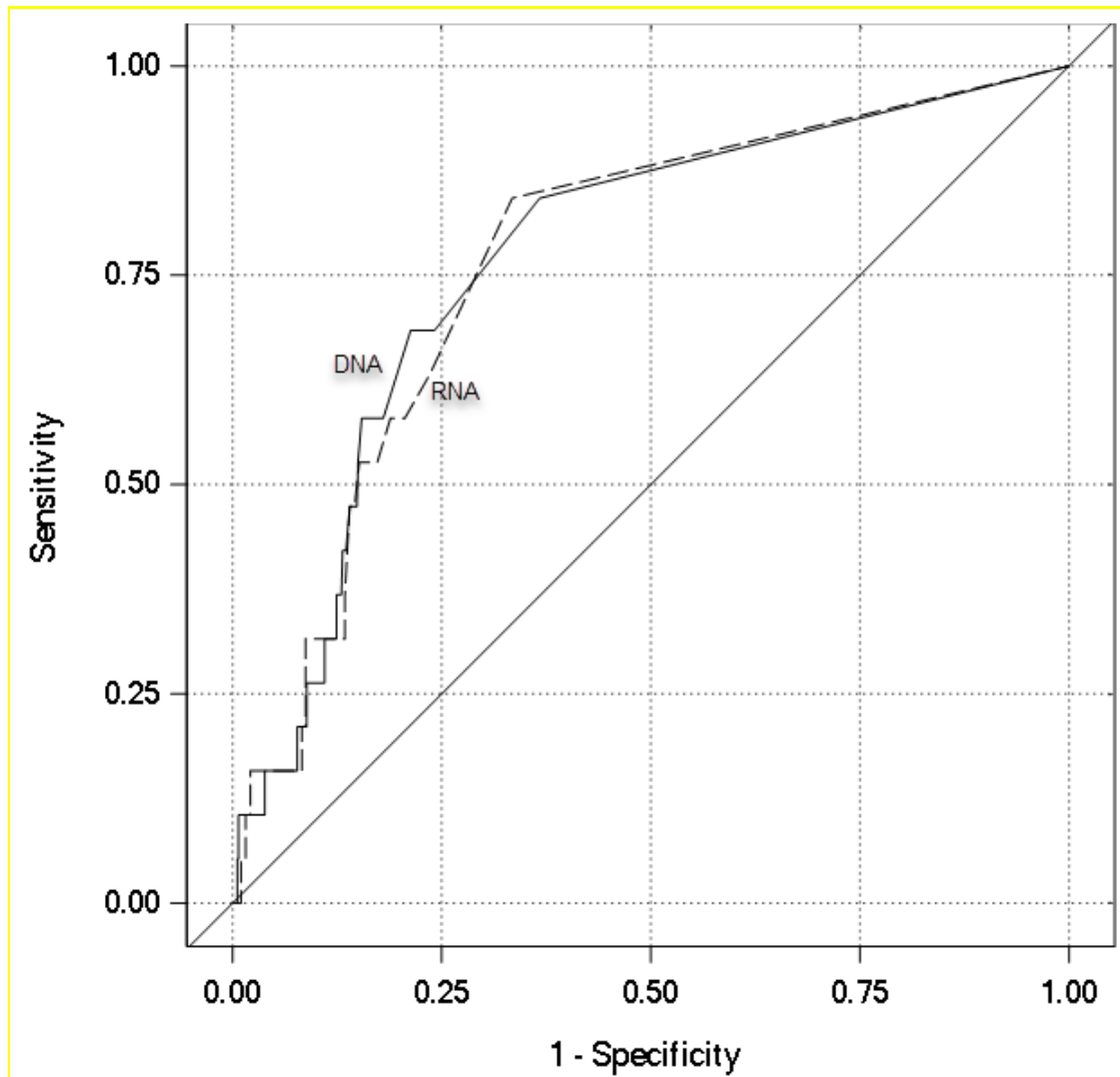


All:	49	25	11	5	5	4	3
ETV:	29	21	9	4	4	3	2
TDF:	15	3	2	1	1	1	1

**Figure S3. Mean HBV RNA (green) and DNA (blue) concentrations over time after stopping NA therapy.**



**Figure S4. Receiver-operator curves for RNA (dashes line) and DNA (solid line) as predictors of subsequent ALT flare.** Comparing the curves of the two independent markers shows they are not different statistically (DeLong's test  $p=0.97$ ).



**Figure S5. Individual profiles for RNA, DNA, ALT and HBsAg after cessation of NA therapy.**

















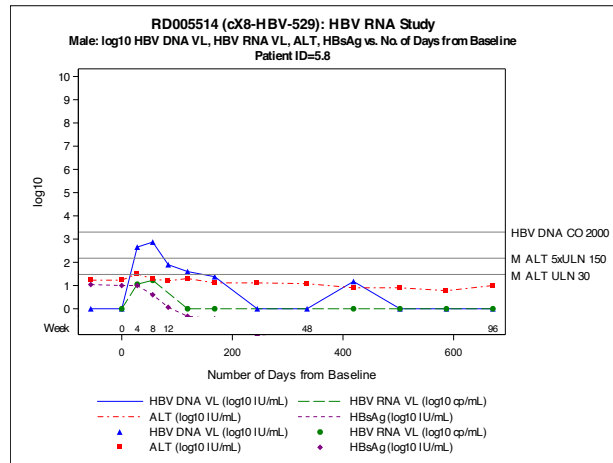
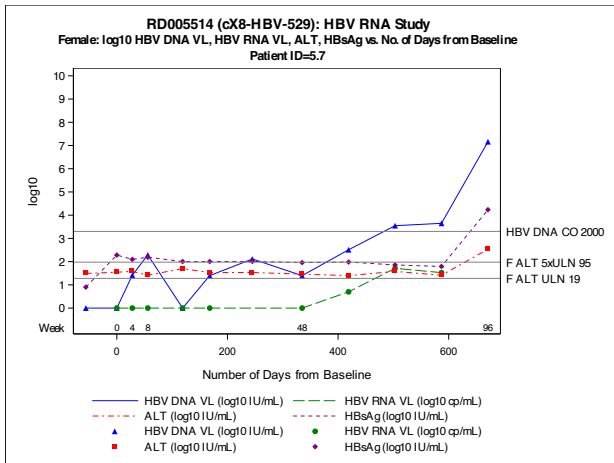


Figure S5

**Table S1. Rates of virological relapse, biochemical relapse, and hepatitis flare according to baseline HBV RNA detection and HBsAg level**

	<b>N (%) with virological relapse<sup>a</sup></b>	<b>P-value<sup>b</sup></b>	<b>N (%) with biochemical relapse<sup>c</sup></b>	<b>P-value</b>	<b>N (%) with hepatitis flare<sup>d</sup></b>	<b>P-value</b>
HBV RNA not detected	42/49 (86%)	0.18	25/49 (51%)	0.04	15/49 (31%)	0.04
HBV RNA detected	16/16 (100%)		13/16 (81%)		10/16 (63%)	
HBsAg ≤ 100 IU/mL	5/10 (50%)	0.0006	4/10 (40%)	0.30	2/10 (20%)	0.29
HBsAg > 100 IU/mL	53/55 (96%)		34/55 (62%)		23/55 (42%)	
HBsAg ≤ 1000 IU/mL	31/36 (86%)	0.45	18/36 (50%)	0.14	12/36 (33%)	0.44
HBsAg > 1000 IU/mL	27/29 (93%)		20/29 (69%)		13/29 (45%)	
HBsAg ≤ 100 IU/mL and HBV RNA not detected	4/9 (44%)	0.0009	3/9 (33%)	0.08	1/9 (11%)	0.04
HBsAg ≤ 100 IU/mL and HBV RNA detected	1/1 (100%)		1/1 (100%)		1/1 (100%)	
HBsAg > 100 IU/mL and HBV RNA not detected	38/40 (95%)		22/40 (55%)		14/40 (35%)	
HBsAg > 100 IU/mL and HBV RNA detected	15/15 (100%)		12/15 (80%)		9/15 (60%)	

	<b>N (%) with virological relapse<sup>a</sup></b>	<b>P-value<sup>b</sup></b>	<b>N (%) with biochemical relapse<sup>c</sup></b>	<b>P-value</b>	<b>N (%) with hepatitis flare<sup>d</sup></b>	<b>P-value</b>
HBsAg ≤ 1000 IU/mL and HBV RNA not detected	24/29 (83%)		12/29 (41%)		6/29 (21%)	
HBsAg ≤ 1000 IU/mL and HBV RNA detected	7/7 (100%)	0.58	6/7 (86%)	0.075	6/7 (86%)	0.01
HBsAg > 1000 IU/mL and HBV RNA not detected	18/20 (90%)		13/20 (65%)		9/20 (45%)	
HBsAg > 1000 IU/mL and HBV RNA detected	9/9 (100%)		7/9 (78%)		4/9 (44%)	

<sup>a</sup> HBV DNA > 2000 IU/mL at week 96

<sup>b</sup> P-values from Fisher's Exact Test for HBV RNA and HBsAg, or Freeman-Halton (27) for the combination

<sup>c</sup> ALT > 2x ULN and HBV DNA > 2000 IU/mL at week 96

<sup>d</sup> ALT > 5x ULN and HBV DNA > 2000 IU/mL at week 96



**Table S2. Agreement analysis for HBV RNA or DNA with ALT flares (>5x ULN)**

HBV RNA		ALT Flare 5x ULN			Measure <sup>1</sup>	Agreement	
		Yes	No	Total		% (n/N)	95% CI <sup>2</sup>
>128 cp/mL	<b>Yes</b>	11	168	179	PPA	57.9 (11/19)	36.3, 76.9
	<b>No</b>	8	557	565	NPA	76.8 (557/725)	73.6, 79.8
	<b>Total</b>	19	725	744	OPA	76.3 (568/744)	76.3, 73.2
<b>HBV DNA</b>							
>16,637 IU/mL	<b>Yes</b>	15	216	231	PPA	62.5 (15/24)	42.7, 78.8
	<b>No</b>	9	719	728	NPA	76.9 (719/935)	74.1, 79.5
	<b>Total</b>	24	935	959	OPA	76.5 (734/959)	73.8, 79.1

<sup>1</sup> PPA=Positive Percent Agreement, NPA=Negative Percent Agreement, OPA=Overall Percent Agreement.

<sup>2</sup> Wilson Score Confidence Interval.