SUPPLEMENTARY MATERIAL

Table S1. Demographic and disease characteristics of patients enrolled in the included studies.

Study	Country	Study duration/ period	Intervention / Comparator	*N*	Age (years), mean (SD)/ median (range)	eGFR equation	Baseline eGFR (mL/min), mean (SD)/median (range)
Izzedine 2004 [1]	International	64 weeks	Adefovir	171	34 (11.2)		
			Placebo	167	37 (11.8)		
Chan 2012 [2]	International	104 weeks	Telbivudine	114	49.6 (10.9)		
			Lamivudine	114	51.9 (10.0)		
Gane 2014 [3]	International	104 weeks	Telbivudine	680		MDRD	103.2 (1.2)
			Lamivudine	687			104.5 (1.1)
Ha 2009 [4]	USA	2002–2008	Adefovir	145	46.7 (11.8)	CG and MDRD	87.2 (19.3)
			Entecavir	145	46.2 (11.6)		89.3 (17.8)
Gish 2012 [5]	USA	2004–2010	Tenofovir	80	54.3 (13)	MDRD	84.41 (28.19–194.35)
			Entecavir	80	55.1 (12)		87.72 (26.07–241.65)
Tsai 2016 [6]	Taiwan	2006–2012	Tenofovir	170	51.8 (11.9)	MDRD	92.0
			Telbivudine	184	54.2 (14.6)		86.1
			Entecavir	233	52.8 (12.4)		81.1
Ha 2015 [7]	USA	2008–2012	Tenofovir	103	43.5 (10.4)		
			Entecavir	103	43.8 (10.7)		
Lee 2014 [8]	Korea	24 months	Adefovir + telbivudine	43	52.33 (11.22)	CKD-EPI	
			Adefovir + lamivudine	297	51.4 (11.88)		
			Adefovir + entecavir	59	53.66 (10.43)		
			Adefovir	140	50.61 (10.78)		
			Entecavir	292	52.76 (11.26)		
Tsai 2014 [9]	Taiwan	24 months	Telbivudine	115	52.9 (12.4)	MDRD	81.37
			Entecavir	115	53.6 (12.1)		77.20
Piratvisuth 2013 [10]	Argentina, Brazil, Germany, and Thailand	24 months	Telbivudine	55	37 (10.4)	MDRD	93.4 (15.1)
			Telbivudine + tenofovir	45	40 (15)		92.1 (18.5)
Koklu 2015 [11]	Turkey	24 months	Lamivudine	302	49.21 (13.17)	MDRD	
			Entecavir	282	49.86 (13.35)		
			Tenofovir	273	47.74 (12.45)		

Mauss 2011 [12]	Germany	48 months	Lamivudine	36	41 (18–68)	MDRD	107 (72–127)
			Adefovir	32	38 (18–63)		108 (77–134)
			Entecavir	32	43 (20–73)		108 (52–128)
			Tenofovir	37	43 (19–75)		103 (65–133)
			No treatment	60	39 (21–62)		108 (47–139)
Qi 2015 [13]	China	36 months	Lamivudine	50	53.5 (23–66)	MDRD and CKD-EPI	106.1 (67–172.5)
			Adefovir	60	49 (24–70)		102.8 (71.7–149.8)
			Telbivudine	68	33.5 (21–64)		105.1 (69.2–166.1)
			Entecavir	61	42 (19–64)		99.9 (6.1–163)
			No treatment	36	31 (21–59)		109.4 (68.7–131.5)
Tien 2015 [14]	USA	>18 months	Entecavir	44	51 (9)	CG and MDRD	102 (22)
			Tenofovir	42	49 (12)		103 (26)
			No treatment	60	46 (12)		118 (28)
Chen 2013 [15]	Taiwan	2 weeks	Telbivudine	9	48 (29–65)	MDRD and CKD-EPI	112 (77.8–148)
			Entecavir	12	47 (28–71)		110.6 (52.9–156.7)
Cholongitas 2015 [16]	Greece	25 months	Entecavir	21	58 (9)		
			Tenofovir	31	60 (10)		
Nguyen 2011 [17]	UK	12 months	Tenofovir	212			
			Entecavir	79			
Le 2012 [18]	Australia	24 months	Tenofovir	50			
			Entecavir	74			
Su 2013 [19]	Taiwan	2003–2011	Lamivudine	77	49.48	MDRD	86.58 (25.13)
			Entecavir	200	50.95		106.07 (36.91)
			Telbivudine	31	42.03		117.23 (42.7)
			Lamivudine + adefovir	57	54.63		86.96 (22.96)
Lee 2015 [20]	South Korea	18 months	Telbivudine	578	53.6 (10.9)	MDRD	89.1 (19.9)
			Entecavir	116	54.8 (11.3)		89 (18.6)
Hu 2015 [21]	Taiwan	44 months	Tenofovir	170			92.2
			Telbivudine	184			86.1
			Entecavir	233			80.5
Tsai 2014a [22]	Taiwan	12 months	Telbivudine	115		MDRD	78 (22.9)
			Tenofovir	162			93 (27.4)
Sriprayoon 2015 [23]	Not reported	144 weeks	Entecavir	200	41.6 (11.5)		
			Tenofovir	200	41.2 (11.6)		
Krastev 2014 [24]	Bulgaria and Turkey	104 weeks	Telbivudine	121	42.1 (11.5)		
			Tenofovir	120	43.3 (12.6)		

Hung 2014 [25]	Taiwan	24 weeks	Tenofovir	41			108
			Entecavir	148			92
Sun 2014 [26]	China	96 weeks	Telbivudine + adefovir				119.7
			Telbivudine				108.9
			Adefovir				121.2

CG Cockcroft–Gault, *CKD-EPI* Chronic Kidney Disease Epidemiology Collaboration, *eGFR* estimated glomerular filtration rate, *MDRD* Modification of Diet in Renal Disease, *N* number of patients, *SD* standard deviation.

Blank cells indicate that the study does not report corresponding information; 26 of the 40 included studies reported demographic and baseline characteristics. Age and baseline eGFR values without brackets are means.

Table S2. Sample size and mean eGFR change from baseline at 1 year as per treatment regimen.

Treatment regimen	Total number of studies	*N*	Mean eGFR change (mL/min) from baseline at 1 year
Adefovir	1	60	−6.92
Entecavir	7	1442	−1.14
Entecavir + adefovir	1	35	−3.58
Lamivudine	3	410	−2.56
Lamivudine + adefovir	3	243	−5.03
Telbivudine	8	708	8.11
Telbivudine + adefovir	2	115	2.45
Telbivudine + lamivudine	1	19	11.10
Telbivudine + tenofovir	2	64	13.15
Tenofovir	4	659	−7.98

eGFR estimated glomerular filtration rate, *N* number of patients.

Table S3. Renal function results from randomized controlled trials.

Study	Publication type	Intervention / Comparator	*N*	Renal function results
Krastev 2014 [24]	Conference abstract	Telbivudine	121	eGFR change from baseline at week 104 in telbivudine-treated patients was 6.14. Twice as many telbivudine-treated patients with an abnormal eGFR (60 to <90 mL/min/1.73m^2) at baseline reverted to normal eGFR compared to tenofovir-treated patients: 23/39 (60.5%) versus 11/41 (27.5%) patients, respectively.
		Tenofovir	120	eGFR change from baseline at week 104 in tenofovir-treated patients was -3.00.
Izzedine 2004 [1]	Journal article	Adefovir	171	There was no overall median change from baseline at week 48 in serum creatinine or serum phosphorus levels in the adefovir 10 mg group.
		Placebo	167	Serum creatinine increase and hypophosphatemia were more frequently observed in patients receiving adefovir 30 mg daily compared with adefovir 10 mg and placebo.
Chan 2012 [2]	Journal article	Telbivudine	114	eGFR steadily improved in telbivudine-treated patients with the greatest improvement seen during the second year of treatment.
		Lamivudine	114	Lamivudine-treated patients showed a steady decline in eGFR.
Gane 2014 [3]	Journal article	Telbivudine	680	In telbivudine-treated patients during the two-year GLOBE study, mean eGFR increased by 8.5% based on MDRD equation. Improved renal function was maintained for 4–6 years. Increased eGFR with telbivudine treatment was also observed in patients at increased risk for renal impairment: patients with baseline eGFRs of 60–89 mL/min/1.73 m^2 (+17.2%), older than 50 years (+11.4%), and with liver fibrosis/cirrhosis (+7.2% for patients with Ishak fibrosis score 5–6). In decompensated patients with high renal risk, eGFR was also improved on telbivudine (+2.0%).

		Lamivudine	687	Renal function declined over time in lamivudine-treated patients.
Sriprayoon 2015 [23]	Conference abstract	Entecavir	200	eGFR decrease ≥20% was observed in 28/200 (13.6%) patients.
		Tenofovir	200	eGFR decrease ≥20% was observed in 45/200 (22.5%) patients.
Park 2014 [27]	Conference abstract	Telbivudine + adefovir	NR	The proportion of patients with eGFR ≥90 mL/min/1.73 m^2 treated with telbivudine + adefovir increased from 49.1% (26/53) at baseline to 58.5% (31/53) at week 48.
		Lamivudine + adefovir	NR	The proportion of patients with eGFR ≥90 mL/min/1.73 m^2 treated with lamivudine + adefovir decreased from 37.7% (26/53) at baseline to 30.2% (16/53) at week 48.

eGFR estimated glomerular filtration rate, *N* number of patients, *NR* not reported.

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