

Appendix C: Characteristics of Included RCTs

Author, Year, Design	Treatment/ follow-up Duration (weeks)	Sample size	Active Comparators	Treatment codes used in network meta- analysis	Outcomes reported
HBeAg Positive					
Brouwer et al. 2015 Open-label	96	175	1. ETV 0.5mg daily 2. ETV 0.5mg daily + Peg-IFN add-on (180 mg/week) from week 24 to 48	ETV ETVPEG	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Cao et al. 2013	120	47	1. LAM 100mg daily + PEG IFN α -2a 135 mg weekly 2. ADV 10mg daily + PEG IFN α -2a 135 mg weekly	LAMPEG2 PEGADV1	HBV DNA, HBeAg sero, HBsAg loss
Chan et al. 2007a Open-label	52	131	1. ADV 10mg daily 2. TBV 600mg daily 3. ADV 10mg daily for 24 weeks then switched to TBV 600mg daily	ADV TBV ADV/TBV	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Chan et al. 2016 DB	48	873	1. TAF 25mg daily 2. TDF 300mg daily	TAF TDF	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Chang et al. 2006 DB	48	709	1. LAM 100mg daily 2. ETV 0.5mg daily	LAM ETV	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Dienstag et al. 1999 DB	68	137	1. PLA 2. LAM 100mg daily	PLA LAM	HBeAg loss, HBeAg sero, HBsAg loss
He at al. 2012	96	137	1. LAM 100mg daily 2. ADV 10mg daily 3. LAM 100 mg + ADV 10 mg daily for 12-24wks followed by ADV alone	LAM ADV LAMADV	HBV DNA, ALT norm, HBeAg sero
Hou et al. 2015 DB	48	202	1. ADV 10mg daily 2. TDF 300mg daily	ADV TDF	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Janssen et al. 2005 DB	78	266	1. PEG α -2b 100 μ g weekly (50 μ g weekly from wk 32) 2. LAM 100mg daily + PEG α -2b 100 μ g weekly (50 μ g weekly from wk 32)	PEG LAMPEG	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Jia et al. 2014 DB	104	290	1. LAM 100mg daily 2. TBV 600mg daily	LAM TBV	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Koike et al. 2017 DB	48	165	1. TDF 300mg daily 2. ETV 0.5mg daily	TDF ETV	HBV DNA, ALT norm, HBeAg sero
Lai et al. 1998 DB	52	215	1. PLA 2. LAM 100mg daily	PLA LAM	ALT norm, HBeAg sero, HBsAg loss

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Lai et al. 2005 DB	52	104	1. LAM 100mg daily 2. TBV 400/600mg daily 3. LAM100mg + TBV 400/600mg daily	LAM TBV LAMTBV	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Lau et al. 2005 Partial DB	72	814	1. LAM 100mg daily 2. PEG α -2a 180 μ g weekly + PLA 3. LAM 100mg daily + PEG α -2a 180 μ g weekly	LAM PEG LAMPEG1	HBV DNA, ALT norm, HBeAg loss, HBeAg sero
Leung et al. 2009 Open-label	48	65	1. ADV 10mg daily 2. ETV 0.5mg daily	ADV ETV	HBV DNA, ALT norm, HBeAg loss, HBeAg sero
Liang et al. 2015 Open-label	104	358	1. LAM 100 mg + ADV 10 mg daily 2. LAM 100 mg daily + add ADV 10 mg daily to suboptimal responders from wk 30 3. LAM 100 mg	LAMADV1 LAMADV2 LAM	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Liaw et al. 2009 DB	104	921	1. LAM 100mg daily 2. TBV 600mg daily	LAM TBV	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Liu et al. 2014 Open-label	52	61	1. PEG α -2b 1.5 μ g/kg weekly 2. PEG α -2b 1.5 μ g/kg weekly + ADV 10mg daily	PEG PEGADV	HBV DNA, ALT norm, HBsAg loss
Lok et al. 2012 Open-label	96	264	1. ETV 0.5mg daily 2. ETV 0.5mg daily + TDF 300mg daily	ETV ETVTDF	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Marcellin et al. 2003 DB	48	511	1. PLA 2. ADV 10mg daily 3. ADV 30mg daily	PLA ADV ADV2	HBV DNA, ALT norm, HBeAg loss, HBeAg sero
Marcellin et al. 2008 DB	48	266	1. ADV 10mg daily 2. TDF 300mg daily	ADV TDF	HBV DNA, ALT norm, HBeAg sero, HBsAg loss
Marcellin et al. 2016 Open-label	72	740	1. TDF 300mg daily + PEG α -2a 180 μ g weekly for 48 wks 2. TDF 300mg daily for 48 wks + PEG α -2a 180 μ g weekly for 1 st 16 wks 3. TDF 300mg daily for 72 wks 4. PEG α -2a 180 μ g weekly for 48 wks	TDFPEG1 TDFPEG2 TDF PEG	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Ren et al. 2007	48	42	1. LAM 100mg daily 2. ETV 0.5mg daily	LAM ETV	HBV DNA, ALT norm, HBeAg sero
Sriprayoon et al. 2017	144	400	1. ETV 0.5mg daily 2. TDF 300mg daily	ETV TDF	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Sung et al. 2008 DB	104	111	1. LAM 100mg daily 2. LAM 100 mg + ADV 10 mg daily	LAM LAMADV1	HBV DNA, ALT norm, HBeAg loss, HBeAg sero
Tseng et al. 2014	52	42	1. ETV: 0.5mg daily	ETV	HBeAg loss, HBeAg sero

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			2. PLA	PLA	
Xie et al. 2014 Open-label	72	218	1. PEG α -2a 180 μ g weekly for 48 wks 2. PEG α -2a 180 μ g weekly for 48 wks + ETV add-on at week 13 for 24 weeks 3. ETV 0.5mg daily for 24 wks + PEG α -2a from week 21 for 48 wks	PEG PEGETV ETVPEG1	HBV DNA, ALT norm, HBeAg loss, HBeAg sero, HBsAg loss
Yao et al. 2007 DB	48	446	1. LAM 100mg daily 2. ETV 0.5mg daily	LAM ETV	HBV DNA, ALT norm, HBeAg loss, HBeAg sero
Zhang et al. 2016 Open-label	96	129	1. PEG α -2a 135 μ g weekly for 48 wks 2. PEG α -2a 135 μ g weekly + ADV 10mg daily add-on at wk 0 3. PEG α -2a 135 μ g weekly + ADV 10mg daily add-on at wk 12 4. PEG α -2a 135 μ g weekly + ADV 10mg daily add-on at wk 24	PEG PEGADV1 PEGADV2 PEGADV3	HBV DNA, ALT norm, HBeAg sero, HBsAg loss

HBeAg Negative

Bozkaya et al. 2005	52	55	1. No treatment 2. LAM 100mg daily	PLA LAM	ALT norm
Buti et al. 2016 DB	48	425	1. TAF 25mg daily 2. TDF 300mg daily	TAF TDF	HBV DNA, ALT norm
Chan et al. 2007b DB	120	136	1. PLA 2. LAM 100mg daily	PLA LAM	HBV DNA, ALT norm
Hadziyannis et al. 2003 DB	48	184	1. PLA 2. ADV 10mg daily	PLA ADV	HBV DNA, ALT norm
Hou et al. 2015 DB	48	307	1. ADV 10mg daily 2. TDF 300mg daily	ADV TDF	HBV DNA, ALT norm
Jia et al. 2014 DB	104	42	1. LAM 100mg daily 2. TBV 600mg daily	LAM TBV	HBV DNA, ALT norm
Kaymakoglu et al. 2007 Open-label	72	48	1. PEG α -2b 1.5 μ g/kg weekly 2. LAM 100mg daily + PEG α -2b 1.5 μ g/kg weekly	PEG LAMPEG1	HBV DNA, ALT norm
Lai et al. 2006 DB	48	638	1. LAM 100mg daily 2. ETV 0.5mg daily	LAM ETV	HBV DNA, ALT norm

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Lampetico et al. 2013 Open-label	96	128	1. PEG α -2a 180 μ g weekly for 48 wks 2. PEG α -2a 180 μ g weekly for 48 wks then 135 μ g weekly for 48 wks 3. (LAM 100mg + PEG α -2a 180 μ g weekly) for 48 wks then PEG 135 μ g weekly for 48 wks	PEG PEGPEG LAMPEG	HBV DNA, ALT norm
Lee et al. 2017 Partial DB	240	120	1. ETV 0.5mg daily 2. LAM 100mg daily	ETV LAM	HBV DNA
Liaw et al. 2009 DB	104	446	1. LAM 100mg daily 2. TBV 600mg daily	LAM TBV	HBV DNA, ALT norm
Lok et al. 2012 Open-label	96	115	1. ETV: 0.5mg daily 2. ETV 0.5mg daily + TDF 300mg daily	ETV ETVTDF	HBV DNA, ALT norm
Marcellin et al. 2004 Partial DB	72	537	1. LAM 100mg daily 2. PEG α -2a 180 μ g weekly 3. LAM 100mg daily + PEG α -2a 180 μ g weekly	LAM PEG LAMPEG1	HBV DNA, ALT norm
Marcellin et al. 2008 DB	48	375	1. ADV 10mg daily 2. TDF 300mg daily	ADV TDF	HBV DNA, ALT norm
Papadopoulos et al. 2009	72	123	1. PEG α -2b 1.5 μ g/kg weekly 2. LAM 100mg daily + PEG α -2b 1.5 μ g/kg weekly	PEG LAMPEG1	HBV DNA, ALT norm
Piccolo et al. 2009 DB	72	60	1. PEG α -2a 1.5 μ g/kg weekly 2. PEG α -2a 1.5 μ g/kg weekly + ADV 10mg/day	PEG PEGADV	HBV DNA, ALT norm
Tangkijvanich et al. 2016 Open-label	96	126	1. PEG α -2b 1.5 μ g/kg weekly 2. ETV 0.5mg daily + PEG α -2b 1.5 μ g/kg weekly	PEG PEGETV	HBV DNA, ALT norm
Tassopoulos et al. 1999 DB	52	108	1. PLA 2. LAM 100mg daily	PLA LAM	HBV DNA, ALT norm
Yao et al. 2007 DB	48	73	1. LAM 100mg daily 2. ETV 0.5mg daily	LAM ETV	HBV DNA, ALT norm

Abbreviations: DB, double-blind; ADV, adefovir; ETV, entecavir; LAM, lamivudine; PEG, pegylated interferon; PLA, placebo; TAF, tenofovir alafenamide; TBV, telbivudine; TDF, tenofovir disoproxil fumarate; HBV DNA, undetectable HBV DNA levels; ALT norm, normalization of serum alanine aminotransferase levels; HBeAg sero, hepatitis B e antigen seroconversion; HBeAg loss, hepatitis B e antigen loss; HBsAg loss, hepatitis B surface antigen loss