

Appendix D: Participant Baseline Characteristics of included RCTs

Author, Year, Design	Mean Age \pm SD/ Median Age (Range)	Male (%)	Active Comparator	Baseline HBV DNA	Baseline ALT
HBeAg Positive					
Brouwer et al. 2015 Open-label	31 \pm 9 32 \pm 10	69 74	<ul style="list-style-type: none"> ETV 0.5mg daily ETV 0.5mg daily + Peg-IFN add-on (180 mg/week) from week 24 to 48 	7.8 \pm 1.1 7.8 \pm 1.3 (logIU/ml, mean \pm SD)	2.7 \pm 2.1 3.1 \pm 3.3 (mean \pm SD)
Cao et al. 2013	32.3 \pm 12 35.7 \pm 9.4	71 74	<ul style="list-style-type: none"> LAM 100mg daily + PEG IFNα-2a 135 mg weekly ADV 10mg daily + PEG IFNα-2a 135 mg weekly 	7.3 \pm 1.1 7.1 \pm 1.1 (log copies/mL, mean \pm SD)	144.2 \pm 64.5 149.8 \pm 62.7 (U/L, mean \pm SD)
Chan et al. 2007a Open-label	30 (19-47) 34 (18-60) 33 (18-53)	91 78 59	<ul style="list-style-type: none"> ADV 10mg daily TBV 600mg daily ADV 10mg daily for 24 weeks then switched to TBV 600mg daily 	9.98 \pm 0.23 9.57 \pm 0.26 9.47 \pm 0.29 (log ₁₀ copies/mL , mean \pm SE)	199 \pm 25.7 183 \pm 23.6 138 \pm 12.8 (U/L, mean \pm SE)
Chan et al. 2016 DB	38 \pm 11 38 \pm 12	64 65	<ul style="list-style-type: none"> TAF 25mg daily TDF 300mg daily 	7.6 \pm 1.34 7.6 \pm 1.41 (log ₁₀ IU/ml, mean \pm SD)	117 \pm 105.1 125 \pm 128.2 (U/L, mean \pm SD)
Chang et al. 2006 DB	35 \pm 13 35 \pm 13	74 77	<ul style="list-style-type: none"> LAM 100mg daily ETV 0.5mg daily 	9.69 \pm 1.99 9.62 \pm 2.01 (log copies/ml, mean \pm SD)	146.3 \pm 123.3 140.5 \pm 114.3 (U/L, mean \pm SD)
Dienstag et al. 1999 DB	38(20-67) 40(18-73)	80 86	<ul style="list-style-type: none"> PLA LAM 100mg daily 	56.5 (0.8-653) 102.2 (0.8-1753) pg/ml, median (range)	135 (33-592) 125 (46-401) U/L, median (range)
He at al. 2012	38.9 \pm 6.7 38.6 \pm 6.6 39.6 \pm 7.2	72 70 76	<ul style="list-style-type: none"> LAM 100mg daily ADV 10mg daily LAM 100 mg + ADV 10 mg daily for 12-24wks followed by ADV alone 	8.2 \pm 0.9 8.1 \pm 0.7 8.3 \pm 0.8 (log ₁₀ copies/ml, mean \pm SD)	4.5 \pm 2.1 5.3 \pm 2.2 5.2 \pm 2.2 (xULN, mean \pm SD)
Hou et al. 2015 DB	36.4(18-66) 36.1(18-66)	83.3 83.3	<ul style="list-style-type: none"> ADV 10mg daily TDF 300mg daily 	8.7 \pm 0.79 8.7 \pm 0.87 (log ₁₀ copies/ml, mean \pm SD)	189 \pm 121.5 199.1 \pm 132.8 (U/L, mean \pm SD)
Janssen et al. 2005 DB	36 \pm 14 34 \pm 12	79 75	<ul style="list-style-type: none"> PEGα-2b 100μg weekly (reduced to 50μg from wk 32) LAM 100mg daily + PEGα-2b 100μg weekly (reduced to 50μg from wk 32) 	9.1 \pm 0.8 9.1 \pm 1 (log copies/ml, mean \pm SD)	4.3 \pm 3.1 4.4 \pm 3.9 (xULN, mean \pm SD)
Jia et al. 2014 DB	29.9 (15-63) 29.3 (16-64)	76.4 80.8	<ul style="list-style-type: none"> LAM 100mg daily TBV 600mg daily 	9.4 \pm 0.14 9.2 \pm 0.12 (log ₁₀ copies/ml, mean \pm SE)	159.3 \pm 14.72 157 \pm 8.92 (IU/L, mean \pm SE)

Author, Year, Design	Mean Age \pm SD/ Median Age (Range)	Male (%)	Active Comparator	Baseline HBV DNA	Baseline ALT
Koike et al. 2017 DB	45 (22-69) 46.5 (30-67)	62 71	<ul style="list-style-type: none"> TDF 300mg daily ETV 0.5mg daily 	7 \pm 1.5 7.19 \pm 1.3 (log ₁₀ copies/ml, mean \pm SD)	90.4 \pm 99.1 76.7 \pm 80.7 (IU/L, mean \pm SD)
Lai et al. 1998 DB	29 (15-67) 31 (16-55)	72 74	<ul style="list-style-type: none"> PLA LAM 100mg daily 	99.4 (1-990) 74.2 (1-516) pg/ml, median (range)	1.5 (0-10) 1.5 (0-15) xULN, meaian (range)
Lai et al. 2005 DB	34 (18-61) 41 (19-68) 32 (19-53)	74 79.5 85	<ul style="list-style-type: none"> LAM 100mg daily TBV 400/600mg daily LAM100mg + TBV 400/600mg daily 	9.3 (6.6-12.9) 9.0 (6.3-13.3) 9.5 (5.9-13.2) log ₁₀ copies/ml, median (range)	122 (62-309) 130 (35-400) 142 (32-1657) U/L, median (range)
Lau et al. 2005 Partial DB	30 (17-65) 31 (18-77) 29 (18-66)	79 79 77	<ul style="list-style-type: none"> LAM 100mg daily PEGα-2a 180μg weekly + PLA LAM 100mg daily + PEGα-2a 180μg weekly 	10.1 \pm 2.0 9.9 \pm 2.1 10.1 \pm 1.9 (log copies/ml, mean \pm SD)	102.3 \pm 78.4 114.6 \pm 114.3 114.9 \pm 94.1 (IU/L, mean \pm SD)
Leung et al. 2009 Open-label	32 \pm 2 37 \pm 2.4	66 61	<ul style="list-style-type: none"> ADV 10mg daily ETV 0.5mg daily 	9.88 \pm 0.22 10.26 \pm 0.35 (log ₁₀ copies/ml, mean \pm SE)	172.3 \pm 37 110.6 \pm 14.6 (U/L, mean \pm SE)
Liang et al. 2015 Open-label	30(18-58) 28(18-59) 31(18-63)	78.3 77.5 75.4	<ul style="list-style-type: none"> LAM 100 mg + ADV 10 mg daily LAM 100 mg daily + ADV 10 mg daily to suboptimal responders from wk 30 LAM 100 mg 	8.6 \pm 0.9 8.6 \pm 0.9 8.6 \pm 0.9 (log ₁₀ copies/ml, mean \pm SD)	3.3 \pm 2.7 3.4 \pm 2.1 3.6 \pm 2.8 (xULN, mean \pm SD)
Liaw et al. 2009 DB	33 (16-67) 32 (16-63)	76 73	<ul style="list-style-type: none"> LAM 100mg daily TBV 600mg daily 	9.5 \pm 0.1 9.5 \pm 0.1 (log ₁₀ copies/ml, mean \pm SE)	158.9 \pm 6.3 146.4 \pm 5.37 (IU/L, mean \pm SE)
Liu et al. 2014 Open-label	24 (16-39) 27 (21-44)	68 63	<ul style="list-style-type: none"> PEGα-2b 1.5μg/kg weekly ADV 10mg daily + PEGα-2b 1.5μg/kg weekly 	7.51 (6.13-8.88) 7.37 (5.61-8.01) log U/ml, median (range)	4.1 (2.33-9.95) 3.83 (1.78-9.25) xULN, median (range)
Lok et al. 2012 Open-label	40 \pm 1.1 39 \pm 1	63.7 74.1	<ul style="list-style-type: none"> ETV 0.5mg daily ETV 0.5mg daily + TDF 300mg daily 	8.1 \pm 0.09 8.15 \pm 0.08 (log ₁₀ IU/ml, mean \pm SE)	127 \pm 7.3 158 \pm 13.1 (U/L, mean \pm SE)
Marcellin et al. 2003 DB	35 (16-66) 32 (16-65) 32 (17-68)	71 76 75	<ul style="list-style-type: none"> PLA ADV 10mg daily ADV 30mg daily 	8.12 \pm 0.89 8.25 \pm 0.90 8.22 \pm 0.84 (log copies/ml, mean \pm SD)	139 \pm 131 139 \pm 154 124 \pm 96 (U/L, mean \pm SD)
Marcellin et al. 2008 DB	34 \pm 12 34 \pm 11	71 68	<ul style="list-style-type: none"> ADV 10mg daily TDF 300mg daily 	8.88 \pm 0.93 8.64 \pm 1.076 (log ₁₀ copies/ml, mean \pm SD)	155 \pm 121.49 142 \pm 102.81 (IU/L, mean \pm SD)

Author, Year, Design	Mean Age \pm SD/ Median Age (Range)	Male (%)	Active Comparator	Baseline HBV DNA	Baseline ALT
Marcellin et al. 2016 Open-label	38 \pm 16.7 37 \pm 9 36 \pm 10.9 38 \pm 10.5	68 65 65 64	<ul style="list-style-type: none"> TDF 300mg daily + PEG α-2a 180μg weekly for 48 wks TDF 300mg daily + PEG α-2a 180μg weekly for 16 wks followed by TDF only for 32 wks TDF 300mg daily PEG α-2a 180μg weekly for 48 wks 	7.1 \pm 1.5 7.1 \pm 1.5 7.0 \pm 1.5 6.9 \pm 1.6 (log ₁₀ IU/ml, mean \pm SD)	121 \pm 181 112 \pm 94 101 \pm 68 107 \pm 92 (U/L, mean \pm SD)
Ren et al. 2007	31 \pm 12 33 \pm 10	52 57	<ul style="list-style-type: none"> LAM 100mg daily ETV 0.5mg daily 	8.49 \pm 1.10 8.52 \pm 1.02 (log copies/ml, mean \pm SD)	201.6 \pm 178.2 211.2 \pm 144.7 (IU/L, mean \pm SD)
Sriprayoon et al. 2017	41.6 \pm 11.5 41.2 \pm 11.6	60.5 56.5	<ul style="list-style-type: none"> ETV 0.5mg daily TDF 300mg daily 	7.1 \pm 1.5 7.0 \pm 1.3 (log ₁₀ IU/ml, mean \pm SD)	68.1 \pm 64.1 76.8 \pm 79.8 (U/L, mean \pm SD)
Sung et al. 2008 DB	36 (18-79) 33 (17-63)	74 83	<ul style="list-style-type: none"> LAM 100mg daily LAM 100 mg + ADV 10 mg daily 	9.17 (4.4-11.1) 8.87 (6.5-11.0) log ₁₀ copies/ml, median (range)	-
Tseng et al. 2014	45 \pm 10 42 \pm 12	59 55	<ul style="list-style-type: none"> ETV: 0.5mg daily PLA 	5.95 \pm 1.3 6.31 \pm 1.42 (log copies/ml, mean \pm SD)	0.6 \pm 0.2 0.6 \pm 0.2 (xULN, mean \pm SD)
Xie et al. 2014 Open-label	29.5 \pm 8.1 29.2 \pm 6.9 30 \pm 8.4	77.8 78.1 82.2	<ul style="list-style-type: none"> PEG α-2a 180μg weekly for 48 wks PEG α-2a 180μg weekly for 48 wks + 24 weeks of ETV add-on at week 13 ETV 0.5mg daily for 24 wks + PEG α-2a at week 21 for 48 wks 	7.1 \pm 0.8 7.1 \pm 1.2 7.1 \pm 1.1 (log copies/ml, mean \pm SD)	4.1 \pm 2.5 3.8 \pm 2.1 4.3 \pm 3.4 (xULN, mean \pm SD)
Yao et al. 2007 DB	30 \pm 9 30 \pm 9	83 82	<ul style="list-style-type: none"> LAM 100mg daily ETV 0.5mg daily 	8.65 \pm 1 8.77 \pm 0.86 (log copies/ml, mean \pm SD)	204 \pm 192 191 \pm 135 (U/L, mean \pm SD)
Zhang et al. 2016 Open-label	28.56 \pm 7.95 30.15 \pm 7.19 29.5 \pm 8.08 29.28 \pm 6.94	78.1 78.8 75 81.3	<ul style="list-style-type: none"> PEGα-2a 135 μg weekly for 48 wks PEGα-2a 135 μg weekly + ADV 10mg daily add-on at wk 0 PEGα-2a 135 μg weekly + ADV 10mg daily add-on at wk 12 PEGα-2a 135 μg weekly + ADV 10mg daily add-on at wk 24 	7.15 \pm 1.14 6.78 \pm 1.35 7.03 \pm 1.21 7.08 \pm 1.04 (log copies/ml, mean \pm SD)	4.3 \pm 2.6 3.9 \pm 2.4 4.1 \pm 2.7 3.7 \pm 2.4 (xULN, mean \pm SD)
HBeAg Negative					

Author, Year, Design	Mean Age \pm SD/ Median Age (Range)	Male (%)	Active Comparator	Baseline HBV DNA	Baseline ALT
Bozakaya et al. 2005	39.0 \pm 7.2 31.9 \pm 11.1	68 94	<ul style="list-style-type: none"> PLA (No treatment) LAM 100mg daily 	4.2 \times 10 ³ (1 \times 10 ² –3.6 \times 10 ⁵) 1.2 \times 10 ³ copies/ml, median (range)	48 (35–168) 63.5 (38–186) IU/L, median (range)
Buti et al. 2016 DB	45 \pm 12 48 \pm 10	61 61	<ul style="list-style-type: none"> TAF 25mg daily TDF 300mg daily 	5.7 \pm 1.3 5.8 \pm 1.3 (log ₁₀ IU/ml, mean \pm SD)	67(44-102) 67(47-102) U/L, median (IQR)
Chan et al. 2007b DB	39 \pm 11 39 \pm 10	83 84	<ul style="list-style-type: none"> PLA LAM 100mg daily 	5.6 \pm 1.5 5.7 \pm 1.6 (log copies/ml, mean \pm SD)	2.6 \pm 2.3 2.1 \pm 1.7 (\times ULN, mean \pm SD)
Hadziyannis et al. 2003 DB	45 \pm 10.4 46 \pm 9.8	82 83	<ul style="list-style-type: none"> PLA ADV 10mg daily 	6.9 \pm 1.0 6.9 \pm 0.9 (log copies/ml, mean \pm SD)	149.9 \pm 195.2 143.5 \pm 125.3 (U/L, mean \pm SD)
Hou et al. 2015 DB	36.4(18-66) 36.1(18-66)	83.3 83.3	<ul style="list-style-type: none"> ADV 10mg daily TDF 300mg daily 	7.0 \pm 1.13 6.9 \pm 1.18 (log ₁₀ copies/ml, mean \pm SD)	112.6 \pm 80.3 133.4 \pm 120.9 (U/L, mean \pm SD)
Jia et al. 2014 DB	36(19-58) 38(20-56)	86.4 85	<ul style="list-style-type: none"> LAM 100mg daily TBV 600mg daily 	7.5 \pm 0.3 7.8 \pm 0.4 (log ₁₀ copies/ml, mean \pm SE)	177 \pm 75.2 162 \pm 23.9 (IU/L, mean \pm SE)
Kaymakoglu et al. 2007 Open-label	42.6 \pm 10.9 43 \pm 7.8	68.4 69	<ul style="list-style-type: none"> PEGα-2b 1.5μg/kg weekly LAM 100mg daily + PEGα-2b 1.5μg/kg weekly 	182.3 \pm 175.4 209.6 \pm 207.8 (pg/ml, mean \pm SD)	130.4 \pm 45 161.5 \pm 127.4 (IU/L, mean \pm SD)
Lai et al. 2006 DB	44 \pm 11 44 \pm 11	75 76	<ul style="list-style-type: none"> LAM 100mg daily ETV 0.5mg daily 	7.6 \pm 1.7 7.6 \pm 1.8 (log copies/ml, mean \pm SD)	143 \pm 119.4 141 \pm 114.7 (IU/L, mean \pm SD)
Lampetico et al. 2013 Open-label	45 \pm 10.2 44 \pm 10.4 46 \pm 8.6	65 87 72	<ul style="list-style-type: none"> PEGα-2a 180μg weekly for 48 wks PEGα-2a 180μg weekly for 48 wks then 135μg weekly for 48 wks (LAM 100mg + PEGα-2a 180μg weekly) for 48 wks then PEG 135μg weekly for 48 wks 	6.1 (2.1->8.0) 6.0 (2.6->8.0) 6.2 (3.5->8.0) log ₁₀ IU/ml, median (range)	119 (34-897) 146 (51-897) 161 (34-897) IU/L, median (range)
Lee et al. 2017 DB for 96 wks then open-label	45.7 \pm 11.9 49.0 \pm 7.8	84 75	<ul style="list-style-type: none"> ETV 0.5mg daily LAM 100mg daily 	6.1 \pm 0.8 5.8 \pm 0.9 (log ₁₀ copies/ml, mean \pm SD)	110.5 \pm 82.0 93.9 \pm 58.5 (IU/L, mean \pm SD)
Liaw et al. 2009 DB	43 (18-68) 43 (17-68)	79 78	<ul style="list-style-type: none"> LAM 100mg daily TBV 600mg daily 	7.4 \pm 0.1 7.7 \pm 0.1 (log ₁₀ copies/ml, mean \pm SE)	143.7 \pm 8.7 137 \pm 6.94 (IU/L, mean \pm SE)

Author, Year, Design	Mean Age \pm SD/ Median Age (Range)	Male (%)	Active Comparator	Baseline HBV DNA	Baseline ALT
Lok et al. 2012 Open-label	40 \pm 1.1 39 \pm 1	63.7 74.1	<ul style="list-style-type: none"> • ETV: 0.5mg daily • ETV 0.5mg daily + TDF 300mg daily 	6.09 \pm 0.18 6.09 \pm 0.15 (log ₁₀ IU/ml, mean \pm SE)	127 \pm 7.3 158 \pm 13.1 (U/L, mean \pm SE)
Marcellin et al. 2004 Partial DB	40 \pm 11.1 40 \pm 11.7 41 \pm 10.8	86 85 82	<ul style="list-style-type: none"> • LAM 100mg daily • PEGα-2a 180μg weekly • LAM 100mg daily + PEGα-2a 180μg weekly 	7.24 \pm 1.78 7.14 \pm 1.84 7.35 \pm 2.00 (log copies/ml, mean \pm SD)	105.7 \pm 128.2 84.4 \pm 85.9 90.8 \pm 76.2 (IU/L, mean \pm SD)
Marcellin et al. 2008 DB	43 \pm 10.0 44 \pm 10.6	78 77	<ul style="list-style-type: none"> • ADV 10mg daily • TDF 300mg daily 	6.98 \pm 1.27 6.86 \pm 1.31 (log ₁₀ copies/ml, mean \pm SD)	163.6 \pm 146.02 127.5 \pm 101.21 (IU/ml, mean \pm SD)
Papadopoulos et al. 2009	46.3 46.7	86 74	<ul style="list-style-type: none"> • PEGα-2b 1.5μg/kg weekly • LAM 100mg daily + PEGα-2b 1.5μg/kg weekly 	6.16 5.78 (mean log ₁₀ copies/ml)	96.5 135.7 (mean IU/ml)
Piccolo et al. 2009 DB	45.9 \pm 10.2 48.3 \pm 10.7	60 73	<ul style="list-style-type: none"> • PEGα-2a 1.5μg/kg weekly • PEGα-2a 1.5μg/kg weekly + ADV 10mg/day 	5.7 \pm 0.9 5.9 \pm 1.0 (log ₁₀ IU/ml, mean \pm SD)	3.18 \pm 3.3 3.43 \pm 2.7 (xULN, mean \pm SD)
Tangkijvanich et al. 2016 Open-label	40.0 \pm 9.3 40.3 \pm 9.8	68.3 73	<ul style="list-style-type: none"> • PEGα-2b 1.5μg/kg weekly • ETV 0.5mg daily + PEGα-2b 1.5μg/kg weekly 	5.5 \pm 0.8 5.4 \pm 0.8 (log ₁₀ IU/ml, mean \pm SD)	75.5 \pm 32.2 72.5 \pm 40.0 (U/L, mean \pm SD)
Tassopoulos et al. 1999 DB	44 (17-63) 42 (24-65)	77 83	<ul style="list-style-type: none"> • PLA • LAM 100mg daily 	95.5 (1.3-3,900) 255 (1.3-18,000) pg/ml, median (range)	3.3 (0.7-12.5) 3.2 (0.6-16.4) xULN, median (range)
Yao et al. 2007 DB	30 \pm 9 30 \pm 9	83 82	<ul style="list-style-type: none"> • LAM 100mg daily • ETV 0.5mg daily 	7.59 \pm 1.33 7.7 \pm 1.28 (log copies/ml, mean \pm SD)	164 \pm 83 225 \pm 169 (U/L, mean \pm SD)

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