THE LANCET Infectious Diseases

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Eron JJ, Cooper DA, Steigbigel RT, et al, for the BENCHMRK Study Teams. Efficacy and safety of raltegravir for treatment of HIV for 5 years in the BENCHMRK studies: final results of two randomised, placebo-controlled trials. *Lancet Infect Dis* 2013; published online May 7. http://dx.doi.org/10.1016/S1473-3099(13)70093-8.

APPENDIX 1

Individual Study Results

1. BENCHMRK-1: Efficacy Analysis at Week 156 (Non-Completer=Failure)
2. BENCHMRK-2: Efficacy Analysis at Week 156 (Non-Completer=Failure)

BENCHMRK-1: Efficacy Analysis at Week 156
(Non-Completer=Failure Approach[†])

Parameter	Unadjusted Data Summary by Treatment Group[‡]		Treatment Effect (Raltegravir 400 mg b.i.d. vs. Placebo) Adjusted for Prognostic Factors[§]		
	Raltegravir.	Placebo	Relative Effect	95% CI	p-Value
	n/N(%)	n/N(%)		Odds Ratio	
Proportion of patients with HIV RNA <400 copies/mL	133/232 (57.3)	30/117 (25.6)	4.8	(2.82, 8.19)	<0.001
Proportion of patients with HIV RNA <50 copies/mL	124/232 (53.4)	30/117 (25.6)	4.1	(2.39, 6.90)	<0.001
Proportion of patients with >1 log_{10} drop from baseline in HIV RNA or HIV RNA level <400 copies/mL	136/232 (58.6)	32/117 (27.4)	4.6	(2.73, 7.78)	<0.001
	Mean (95% CI)	Mean (95% CI)		Mean Difference	
Change from Baseline in Log_{10} HIV RNA (Log_{10} copies/mL)	-1.44 (-1.60, -1.28)	-0.51 (-0.67, -0.34)	-1.42	(-1.82, -1.02)	<0.001
Change from Baseline in CD4 Cell Count (cells/mm^3)	170.9 (144.4, 197.4)	71.03 (46.28, 95.77)	99.04	(59.28, 138.8)	<0.001

[†] Approach to handling missing values: For binary endpoints (proportions), Non-Completer = Failure. For change from baseline in log_{10} HIV RNA and change from baseline in CD4 cell counts, Observed Failure (OF) approach assumes baseline value was carried forward for patients who discontinued assigned therapy due to lack of efficacy.

[‡] For binary endpoints (proportions), n/N (%) were reported for each treatment group, where n/N=(number of responders) / (number of patients). For continuous endpoints (changes from baseline in log_{10} HIV RNA level and CD4 cell count), mean changes with (95% CIs) were reported. Observed mean change from baseline in log_{10} HIV RNA level for each group was calculated using the conventional imputation (replace HIV RNA <400 copies/mL by 400 copies/mL if signal detected, or 200 copies/mL if signal not detected). Normal distributions were assumed for continuous endpoints.

[§] For binary endpoints (proportions), odds ratio (95% CI) and p-value was calculated using a logistic regression model adjusted for: baseline HIV RNA level (log_{10}), enfuvirtide use in OBT in enfuvirtide naïve patients, active PI in OBT determined by phenotypic resistance test, darunavir use in OBT in darunavir naïve patients, and treatment. An odds ratio of (<1, =1, >1) indicates that MK-0518 is (inferior, equivalent, superior) to Placebo. For change from baseline in log_{10} HIV RNA level, difference (95% CI) and p-value were calculated using a parametric regression model (normal assumption), which can handle censored observation and is adjusted for: baseline HIV RNA level(log_{10}), enfuvirtide use in OBT in enfuvirtide naïve patients, active PI in OBT determined by phenotypic resistance test, darunavir use in OBT in darunavir naïve patients, and treatment. For change from baseline in CD4 cell counts, difference (95% CI) and p-value were calculated using a mixed-effects model adjusted for: baseline CD4 cell count, stratum, treatment, visit, interactions between visit and previous variables.

BENCHMRK-2: Efficacy Analysis at Week 156
(Non-Completer=Failure Approach[†])

Parameter	Unadjusted Data Summary by Treatment Group[‡]		Treatment Effect (Raltegravir 400 mg b.i.d. vs. Placebo) Adjusted for Prognostic Factors[§]		
	Raltegravir	Placebo	Relative Effect	95% CI	p-Value
	n/N(%)	n/N(%)		Odds Ratio	
Proportion of patients with HIV RNA <400 copies/mL	115/229 (50.2)	25/119 (21.0)	4.2	(2.45, 7.20)	<0.001
Proportion of patients with HIV RNA <50 copies/mL	109/229 (47.6)	21/119 (17.6)	4.8	(2.71, 8.39)	<0.001
Proportion of patients with >1 $\log_{10}$ drop from baseline in HIV RNA or HIV RNA level <400 copies/mL	118/229 (51.5)	25/119 (21.0)	4.4	(2.55, 7.46)	<0.001
	Mean (95% CI)	Mean (95% CI)		Mean Difference	
Change from Baseline in Log_{10} HIV RNA (Log_{10} copies/mL)	-1.37 (-1.55, -1.20)	-0.52 (-0.71, -0.33)	-1.14	(-1.54, -0.75)	<0.001
Change from Baseline in CD4 Cell Count (cells/mm^3)	157.2 (130.7, 183.6)	54.17 (30.04, 78.30)	103.3	(63.33, 143.3)	<0.001

[†] Approach to handling missing values: For binary endpoints (proportions), Non-Completer = Failure. For change from baseline in $\log_{10}$ HIV RNA and change from baseline in CD4 cell counts, Observed Failure (OF) approach assumes baseline value was carried forward for patients who discontinued assigned therapy due to lack of efficacy.

[‡] For binary endpoints (proportions), n/N (%) were reported for each treatment group, where n/N=(number of responders) / (number of patients). For continuous endpoints (changes from baseline in $\log_{10}$ HIV RNA level and CD4 cell count), mean changes with (95% CIs) were reported. Observed mean change from baseline in $\log_{10}$ HIV RNA level for each group was calculated using the conventional imputation (replace HIV RNA <400 copies/mL by 400 copies/mL if signal detected, or 200 copies/mL if signal not detected). Normal distributions were assumed for continuous endpoints.

[§] For binary endpoints (proportions), odds ratio (95% CI) and p-value was calculated using a logistic regression model adjusted for: baseline HIV RNA level ($\log_{10}$), enfuvirtide use in OBT in enfuvirtide naïve patients, active PI in OBT determined by phenotypic resistance test, darunavir use in OBT in darunavir naïve patients, and treatment. An odds ratio of (<1, =1, >1) indicates that MK-0518 is (inferior, equivalent, superior) to Placebo. For change from baseline in $\log_{10}$ HIV RNA level, difference (95% CI) and p-value were calculated using a parametric regression model (normal assumption), which can handle censored observation and is adjusted for: baseline HIV RNA level($\log_{10}$), enfuvirtide use in OBT in enfuvirtide naïve patients, active PI in OBT determined by phenotypic resistance test, darunavir use in OBT in darunavir naïve patients, and treatment. For change from baseline in CD4 cell counts, difference (95% CI) and p-value were calculated using a mixed-effects model adjusted for: baseline CD4 cell count, stratum, treatment, visit, interactions between visit and previous variables.

APPENDIX 2

Week 156 Subgroup Analyses

1. Proportion of Patients With Plasma HIV RNA <50 Copies/mL by Prognostic Factors (Observed Failure Approach)
2. Proportion of Patients With Plasma HIV RNA <50 Copies/mL by Demographic Factors (Observed Failure Approach)
3. Change From Baseline in CD4 Cell Count (Cells/mm^3) by Prognostic Factors (Observed Failure Approach)
4. Change From Baseline in CD4 Cell Count (Cells/mm^3) by Demographic Factors (Observed Failure Approach)

Table 1

Proportion of Patients With Plasma HIV RNA <50 Copies/mL at Week 156 by Prognostic Factors (Observed Failure Approach)

Prognostic Factor	Response				Difference in Response
	Raltegravir + OBT		Placebo + OBT		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Total	233/396	58.8 (53.8, 63.7)	51/209	24.4 (18.7, 30.8)	34.4 (26.6, 41.7)
Baseline Plasma HIV RNA (copies/mL)					
≤ 50,000	128/181	70.7 (63.5, 77.2)	38/104	36.5 (27.3, 46.6)	34.2 (22.4, 45.0)
> 50,000	105/215	48.8 (42.0, 55.7)	13/105	12.4 (6.8, 20.2)	36.5 (26.6, 45.1)
Baseline Plasma HIV RNA (copies/mL)					
≤ 100,000	169/250	67.6 (61.4, 73.4)	44/137	32.1 (24.4, 40.6)	35.5 (25.4, 44.8)
> 100,000	64/146	43.8 (35.6, 52.3)	7/72	9.7 (4.0, 19.0)	34.1 (22.5, 44.0)
Baseline CD4 Cell Counts (cells/mm^3)					
≤ 50	55/126	43.7 (34.8, 52.8)	9/72	12.5 (5.9, 22.4)	31.2 (18.7, 42.1)
> 50 and ≤ 200	91/147	61.9 (53.5, 69.8)	17/71	23.9 (14.6, 35.5)	38.0 (24.4, 49.6)
> 200	87/123	70.7 (61.9, 78.6)	25/66	37.9 (26.2, 50.7)	32.9 (18.1, 46.2)
Enfuvirtide Use in OBT					
No	138/251	55.0 (48.6, 61.2)	29/136	21.3 (14.8, 29.2)	33.7 (24.0, 42.4)
Yes in enfuvirtide exp. pts	40/75	53.3 (41.4, 64.9)	5/36	13.9 (4.7, 29.5)	39.4 (21.3, 53.7)
Yes in enfuvirtide naïve pts	55/70	78.6 (67.1, 87.5)	17/37	45.9 (29.5, 63.1)	32.6 (13.6, 50.2)
Darunavir Use in OBT					
No	140/251	55.8 (49.4, 62.0)	23/132	17.4 (11.4, 25.0)	38.4 (28.9, 46.8)
Yes in Darunavir exp. pts	2/18	11.1 (1.4, 34.7)	0/9	0.0 (0.0, 33.6)	11.1 (-20.9, 33.3)
Yes in Darunavir naïve pts	91/127	71.7 (63.0, 79.3)	28/68	41.2 (29.4, 53.8)	30.5 (16.0, 43.9)
Number of Active PI in OBT by Phenotypic Resistance Test[†]					
0	68/152	44.7 (36.7, 53.0)	7/93	7.5 (3.1, 14.9)	37.2 (27.1, 46.4)
1 or more	156/226	69.0 (62.6, 75.0)	43/112	38.4 (29.4, 48.1)	30.6 (19.5, 41.0)
Missing	9/18	50.0 (26.0, 74.0)	1/4	25.0 (0.6, 80.6)	25.0 (-27.5, 58.6)
Phenotypic Sensitivity Score (PSS)[‡]					
0	26/61	42.6 (30.0, 55.9)	2/43	4.7 (0.6, 15.8)	38.0 (23.0, 51.5)
1	76/126	60.3 (51.2, 68.9)	13/64	20.3 (11.3, 32.2)	40.0 (25.9, 51.9)
2	81/123	65.9 (56.8, 74.2)	17/58	29.3 (18.1, 42.7)	36.5 (21.2, 49.8)
3 or more	39/64	60.9 (47.9, 72.9)	16/37	43.2 (27.1, 60.5)	17.7 (-2.5, 36.6)
Missing	11/22	50.0 (28.2, 71.8)	3/7	42.9 (9.9, 81.6)	7.1 (-32.6, 43.1)
Genotypic Sensitivity Score (GSS)[‡]					
0	41/110	37.3 (28.2, 47.0)	3/64	4.7 (1.0, 13.1)	32.6 (21.4, 42.8)
1	103/149	69.1 (61.0, 76.4)	19/84	22.6 (14.2, 33.0)	46.5 (34.0, 57.2)
2	62/91	68.1 (57.5, 77.5)	19/37	51.4 (34.4, 68.1)	16.8 (-1.6, 35.0)
3 or more	23/40	57.5 (40.9, 73.0)	9/20	45.0 (23.1, 68.5)	12.5 (-14.0, 37.4)
Missing	4/6	66.7 (22.3, 95.7)	1/4	25.0 (0.6, 80.6)	41.7 (-23.1, 80.2)

[†] Darunavir use in OBT in darunavir-naïve patients was counted as one active PI.

[‡] The Phenotypic Sensitivity Score (PSS) and the Genotypic Sensitivity Score (GSS) were defined as the total oral ARTs in OBT to which a patients viral isolate showed phenotypic sensitivity and genotypic sensitivity, respectively, based upon phenotypic and genotypic resistance tests. Enfuvirtide use in OBT in enfuvirtide-naïve patients was counted as one active drug in OBT and added to the GSS and PSS. Darunavir use in OBT in darunavir-naïve patients was counted as one active drug in OBT and added to the PSS and GSS.

Table 2

Proportion of Patients With Plasma HIV RNA <50 Copies/mL at Week 156 by Demographic Factors (Observed Failure Approach)

	Response				Difference in Percent Response [Group A Minus Group B]
	Raltegravir + OBT (Group A)		Placebo + OBT (Group B)		
OBT Factor	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Total	233/396	58.8 (53.8, 63.7)	51/209	24.4 (18.7, 30.8)	34.4 (26.6, 41.7)
Age (years)					
16-64	226/389	58.1 (53.0, 63.1)	51/208	24.5 (18.8, 30.9)	33.6 (25.7, 40.9)
≥65	7/7	100.0 (59.0, 100.0)	0/1	0.0 (0.0, 97.5)	100.0 (18.6, 100.0)
Age (years)					
≤median	114/208	54.8 (47.8, 61.7)	26/117	22.2 (15.1, 30.8)	32.6 (21.9, 42.2)
>median	119/188	63.3 (56.0, 70.2)	25/92	27.2 (18.4, 37.4)	36.1 (24.1, 46.8)
Gender					
Female	27/51	52.9 (38.5, 67.1)	7/27	25.9 (11.1, 46.3)	27.0 (3.8, 46.3)
Male	206/345	59.7 (54.3, 64.9)	44/182	24.2 (18.1, 31.1)	35.5 (27.1, 43.3)
Race					
White	145/250	58.0 (51.6, 64.2)	38/152	25.0 (18.3, 32.7)	33.0 (23.4, 41.8)
Black	31/57	54.4 (40.7, 67.6)	4/22	18.2 (5.2, 40.3)	36.2 (12.3, 53.8)
Asian	12/15	80.0 (51.9, 95.7)	2/6	33.3 (4.3, 77.7)	46.7 (0.9, 77.4)
Hispanic	27/48	56.3 (41.2, 70.5)	1/16	6.3 (0.2, 30.2)	50.0 (24.7, 65.4)
Native American	1/1	100.0 (2.5, 100.0)			100.0 (0.0, 100.0)
Others	17/25	68.0 (46.5, 85.1)	6/13	46.2 (19.2, 74.9)	21.8 (-10.7, 51.2)
Region					
North America	86/153	56.2 (48.0, 64.2)	17/83	20.5 (12.4, 30.8)	35.7 (23.2, 46.6)
South America	40/58	69.0 (55.5, 80.5)	10/30	33.3 (17.3, 52.8)	35.6 (13.7, 54.1)
Asia Pacific	26/34	76.5 (58.8, 89.3)	9/16	56.3 (29.9, 80.2)	20.2 (-6.8, 47.2)
Europe	81/151	53.6 (45.4, 61.8)	15/80	18.8 (10.9, 29.0)	34.9 (22.4, 45.8)
Viral Subtype					
Clade B	207/357	58.0 (52.7, 63.2)	45/193	23.3 (17.5, 29.9)	34.7 (26.5, 42.2)
non-Clade B	22/34	64.7 (46.5, 80.3)	5/14	35.7 (12.8, 64.9)	29.0 (-2.1, 54.6)
Hepatitis B and/or C co-infection[†]					
No	195/337	57.9 (52.4, 63.2)	46/175	26.3 (19.9, 33.5)	31.6 (22.9, 39.6)
Yes	38/61	62.3 (49.0, 74.4)	5/34	14.7 (5.0, 31.1)	47.6 (28.2, 62.5)

[†] Hepatitis B surface antigen positive or hepatitis C antibody positive.

Table 3

Change From Baseline in CD4 Cell Count (Cells/mm^3) at Week 156 by Prognostic Factors (Observed Failure Approach)

Prognostic Factor	Response						Difference in Response [Group A Minus Group B]
	Raltegravir + OBT (Group A)			Placebo + OBT (Group B)			
	N	Baseline Mean	Mean Change From Baseline (95% CI)	N	Baseline Mean	Mean Change From Baseline (95% CI)	
Total	396	150.8	164.3 (145.7, 183.0)	208	156.7	62.8 (45.6, 80.0)	101.5 (76.2, 126.8)
Baseline Plasma HIV RNA (copies/mL)							
≤ 50,000	181	226.5	160.3 (134.1, 186.5)	103	233.2	88.2 (61.4, 115.1)	72.1 (34.8, 109.5)
> 50,000	215	87.1	167.7 (141.2, 194.3)	105	81.7	38.0 (17.0, 58.9)	129.8 (96.1, 163.5)
Baseline Plasma HIV RNA (copies/mL)							
≤ 100,000	250	197.5	162.8 (140.2, 185.3)	136	201.2	78.4 (56.1, 100.7)	84.3 (52.7, 115.9)
> 100,000	146	70.9	167.1 (133.9, 200.2)	72	72.7	33.4 (7.8, 59.0)	133.7 (92.0, 175.3)
Baseline CD4 Cell Counts (cells/mm^3)							
≤ 50	127	17.3	161.2 (126.2, 196.3)	72	20.0	40.6 (13.1, 68.0)	120.7 (76.4, 164.9)
> 50 and ≤ 200	147	123.3	161.3 (132.4, 190.2)	71	123.8	66.7 (35.8, 97.5)	94.6 (52.6, 136.6)
> 200	122	323.1	171.3 (136.7, 205.8)	65	344.0	83.3 (51.6, 115.1)	87.9 (41.4, 134.5)
Enfuvirtide Use in OBT							
No	251	156.1	155.2 (132.1, 178.3)	135	164.2	59.9 (38.0, 81.7)	95.3 (63.6, 127.0)
Yes (enfuvirtide exp. pts)	75	121.5	167.2 (121.5, 212.8)	36	65.9	43.5 (1.9, 85.0)	123.7 (62.7, 184.6)
Yes (enfuvirtide naïve pts)	70	163.5	194.3 (149.1, 239.5)	37	217.8	92.5 (53.7, 131.4)	101.7 (42.9, 160.6)
Darunavir Use in OBT							
No	250	163.4	161.4 (137.8, 184.9)	132	169.2	46.3 (28.1, 64.6)	115.1 (85.4, 144.8)
Yes (Darunavir exp. pts)	18	72.1	33.9 (-5.2, 73.1)	9	117.1	0.0 (0.0, 0.0)	33.9 (-5.2, 73.1)
Yes (Darunavir naïve pts)	128	137.3	188.5 (154.8, 222.2)	67	137.4	103.8 (65.6, 142.0)	84.6 (34.1, 135.2)
Number of Active PI in OBT by Phenotypic Resistance Test[†]							
0	151	141.5	127.5 (98.4, 156.6)	93	157.1	23.7 (7.0, 40.4)	103.8 (70.4, 137.2)
1 or more	227	155.4	188.5 (163.6, 213.4)	111	156.1	96.8 (69.1, 124.5)	91.7 (54.6, 128.8)
Missing	18	171.4	169.0 (71.0, 267.0)	4	165.0	30.8 (-67.1, 128.6)	138.3 (20.6, 255.9)
Phenotypic Sensitivity Score(PSS)[‡]							
0	61	144.8	124.3 (79.1, 169.4)	43	152.9	18.0 (-8.7, 44.6)	106.3 (54.4, 158.2)
1	125	159.9	170.3 (135.0, 205.6)	64	151.8	61.2 (29.4, 93.1)	109.0 (61.9, 156.2)
2	123	127.0	193.5 (160.3, 226.7)	57	169.4	68.2 (34.8, 101.6)	125.3 (78.6, 172.0)
3 or more	65	177.8	135.5 (90.8, 180.2)	37	147.7	104.8 (54.8, 154.8)	30.7 (-35.5, 96.8)
Missing	22	170.3	164.1 (80.4, 247.8)	7	169.0	87.7 (-20.5, 195.9)	76.4 (-49.9, 202.7)
Genotypic Sensitivity Score(GSS)[‡]							
0	110	123.0	116.3 (83.2, 149.5)	64	150.9	14.1 (-4.1, 32.2)	102.2 (64.6, 139.9)
1	149	161.9	189.0 (158.5, 219.5)	83	158.0	56.2 (29.6, 82.8)	132.8 (92.6, 173.1)
2	91	143.3	210.4 (167.9, 252.8)	37	157.0	138.9 (87.5, 190.4)	71.4 (5.5, 137.4)
3 or more	40	202.9	90.0 (46.7, 133.2)	20	170.5	105.3 (36.7, 173.9)	-15.3 (-94.8, 64.1)
Missing	6	154.5	230.0 (-12.1, 472.1)	4	151.3	64.5 (-140.8, 269.8)	165.5 (-98.4, 429.4)

[†] Darunavir use in OBT in darunavir naïve patients was counted as one active PI.

[‡] The Phenotypic Sensitivity Score (PSS) and the Genotypic Sensitivity Score (GSS) were defined as the total oral ARTs in OBT to which a patients viral isolate showed phenotypic sensitivity and genotypic sensitivity, respectively, based upon phenotypic and genotypic resistance tests. Enfuvirtide use in OBT in enfuvirtide-naïve patients was counted as one active drug in OBT and added to the GSS and PSS. Darunavir use in OBT in darunavir-naïve patients was counted as one active drug in OBT and added to the PSS and GSS.

Table 4

Change From Baseline in CD4 Cell Count (Cells/mm^3) at Week 156 by Demographic Factors (Observed Failure Approach)

	Response						Difference in Response [Group A Minus Group B]
	Raltegravir + OBT (Group A)			Placebo + OBT (Group B)			
OBT Factor	N	Baseline Mean	Mean Change From Baseline (95% CI)	N	Baseline Mean	Mean Change From Baseline (95% CI)	(95% CI)
Total	396	150.8	164.3 (145.7, 183.0)	208	156.7	62.8 (45.6, 80.0)	101.5 (76.2, 126.8)
Age (years)							
16-64	389	149.4	165.9 (146.9, 184.8)	207	156.8	62.7 (45.4, 80.0)	103.2 (77.6, 128.8)
≥65	7	230.9	80.9 (16.3, 145.4)	1	130.0	94.0 (N/A)	-13.1 (N/A)
Age (years)							
≤median	209	144.8	162.7 (135.6, 189.7)	117	155.5	56.4 (34.4, 78.3)	106.3 (71.6, 141.0)
>median	187	157.6	166.2 (140.4, 192.0)	91	158.3	71.1 (43.4, 98.9)	95.1 (57.4, 132.8)
Gender							
Female	51	165.1	201.0 (140.2, 261.7)	26	134.7	76.0 (8.9, 143.1)	125.0 (36.2, 213.8)
Male	345	148.7	158.9 (139.4, 178.5)	182	159.8	61.0 (43.5, 78.4)	98.0 (71.8, 124.1)
Race							
White	250	153.2	151.2 (128.9, 173.6)	152	153.7	70.1 (48.2, 91.9)	81.2 (50.0, 112.3)
Black	57	118.1	184.3 (130.9, 237.8)	21	107.8	17.9 (-4.8, 40.5)	166.5 (109.0, 223.9)
Asian	15	79.5	252.5 (163.2, 341.9)	6	165.5	41.8 (-26.2, 109.9)	210.7 (107.4, 314.0)
Hispanic	48	174.5	159.3 (98.2, 220.4)	16	249.3	11.3 (-11.4, 34.0)	148.0 (83.6, 212.5)
Native American	1	97.0	483.0 (N/A)				(N/A)
Others	25	201.1	194.0 (106.6, 281.4)	13	153.2	124.2 (40.6, 207.8)	69.8 (-46.4, 185.9)
Region							
North America	153	130.0	164.2 (133.8, 194.7)	82	126.3	52.5 (26.9, 78.2)	111.7 (72.1, 151.3)
South America	58	212.8	180.0 (128.4, 231.7)	30	242.6	92.6 (37.3, 147.9)	87.4 (13.0, 161.9)
Asia Pacific	34	137.8	275.3 (198.2, 352.5)	16	202.6	140.8 (51.8, 229.7)	134.6 (20.5, 248.7)
Europe	151	151.1	133.4 (106.6, 160.3)	80	146.4	46.7 (22.0, 71.3)	86.8 (50.5, 123.0)
Viral Subtype							
Clade B	357	153.0	161.8 (142.0, 181.7)	192	157.9	62.4 (44.2, 80.6)	99.4 (72.6, 126.3)
non-Clade B	34	123.3	174.2 (115.2, 233.3)	14	153.1	59.4 (9.0, 109.7)	114.9 (39.8, 189.9)
Hepatitis B and/or C co-infection[†]							
No	337	145.3	168.2 (147.7, 188.6)	174	158.4	69.0 (49.2, 88.8)	99.2 (70.8, 127.5)
Yes	60	180.3	140.1 (94.0, 186.2)	34	148.1	30.8 (3.3, 58.2)	109.3 (56.2, 162.4)

[†] Hepatitis B surface antigen positive or hepatitis C antibody positive.