Supplementary Table 1 Baseline characteristics by HCV status and baseline HIV RNA

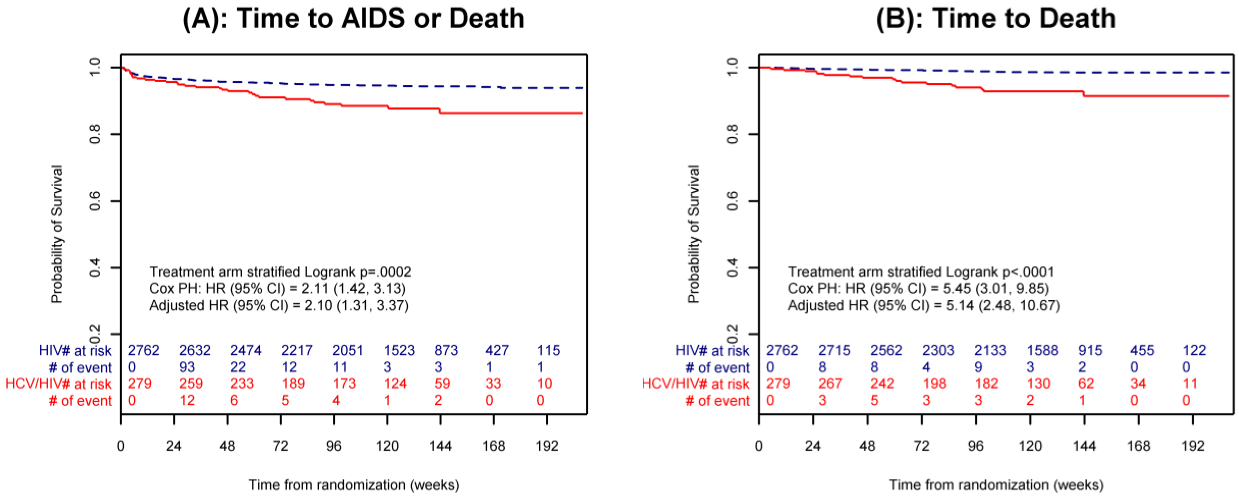
Characteristic		HCV/HIV		HIV		
		< 10,000 (N=27)	**≥ 10,000 (N=252)**	**< 10,000 (N=302)**	**≥ 10,000 (N=2460)**	**Total (N=3041)**
Age (years)	Mean (s.d.)	44.44 (7.46)	44.01 (7.67)	36.73 (9.73)	37.91 (9.97)	38.36 (9.92)
	Min, Max	28, 54	24, 62	18, 70	17, 73	17, 73
	Median (Q1, Q3)	46 (39, 51)	44 (39, 49)	36 (29, 43)	38 (30, 44)	38 (31, 45)
	<30	1 (4%)	14 (6%)	89 (29%)	621 (25%)	725 (24%)
	31-40	7 (26%)	61 (24%)	113 (37%)	895 (36%)	1,076 (35%)
	41-50	11 (41%)	132 (52%)	73 (24%)	684 (28%)	900 (30%)
	51-60	8 (30%)	44 (17%)	24 (8%)	214 (9%)	290 (10%)
	>60	0 (0%)	1 (0%)	3 (1%)	46 (2%)	50 (2%)
Race/Ethnicity	White Non-Hispanic	4 (15%)	86 (34%)	85 (28%)	1,022 (42%)	1,197 (39%)
	Black Non-Hispanic	19 (70%)	113 (45%)	155 (51%)	830 (34%)	1,117 (37%)
	Hispanic	4 (15%)	53 (21%)	62 (21%)	608 (25%)	727 (24%)
Sex	Male	21 (78%)	206 (82%)	204 (68%)	2,041 (83%)	2,472 (81%)
Prior history of AIDS	Yes	4 (15%)	44 (17%)	17 (6%)	506 (21%)	571 (19%)
Previous/current IV drug use	Yes	16 (60%)	128 (51%)	11 (3%)	131 (5%)	286 (9%)
HBsAg	N	26	242	301	2447	3016
	Positive	5 (19%)	7 (3%)	10 (3%)	76 (3%)	98 (3%)
Parent study	A5073	4 (15%)	34 (13%)	19 (6%)	239 (10%)	296 (10%)
	A5095	3 (11%)	37 (15%)	31 (10%)	225 (9%)	296 (10%)
	A5142	9 (33%)	72 (29%)	54 (18%)	569 (23%)	704 (23%)
	A5202	11 (41%)	109 (43%)	198 (66%)	1,427 (58%)	1,745 (57%)
Randomization year	2001	0 (0%)	7 (3%)	0 (0%)	1 (0%)	8 (0%)
	2002	3 (11%)	33 (13%)	31 (10%)	231 (9%)	298 (10%)
	2003	10 (37%)	64 (25%)	43 (14%)	481 (20%)	598 (20%)
	2004	3 (11%)	37 (15%)	29 (10%)	311 (13%)	380 (12%)
	2005	1 (4%)	19 (8%)	27 (9%)	167 (7%)	214 (7%)
	2006	7 (26%)	59 (23%)	120 (40%)	786 (32%)	972 (32%)
	2007	3 (11%)	33 (13%)	52 (17%)	483 (20%)	571 (19%)

HBsAg: HBV Surface Antigen

Supplementary Table 2 ARV Treatment Effect Modification for Virologic Failure

ART GROUP		HIV (N=2762)			HCV/HIV (N=279)			P-value *
		N (% of All)	VF (% of N)	HR (95% CI)	N (% of All)	VF (% of N)	HR (95% CI)	
PIs or EFV	EFV	1,277 (46%)	239 (19%)	1.00	126 (45%)	38 (30%)	1.00	0.658
	ATV/r included	809 (29%)	139 (17%)	1.08 (0.85, 1.37)	61 (22%)	18 (30%)	1.36(0.76, 2.42)	
	LPV/r included	467 (17%)	119 (25%)	1.41 (0.98, 2.04)	66 (24%)	20 (30%)	1.14 (0.61, 2.13)	
	LPV/r + EFV (A5142)	209 (8%)	50 (24%)	1.11 (0.75 1.64)	26 (9%)	8 (31%)	1.11 (0.50, 2.50)	
NRTI groups	FTC/TDF or 3TC/TDF included	1,043 (38%)	169 (16%)	1.00	100 (36%)	24 (24%)	1.00	0.746
	ABC/3TC	814 (29%)	156 (19%)	1.37(1.08, 1.74)	55 (20%)	13 (24%)	1.22 (0.61, 2.44)	
	3TC/ZDV or ABC/3TC/ZDV	428 (15%)	103 (24%)	0.92(0.61, 1.40)	62 (22%)	27 (44%)	1.28(0.68, 2.44)	
	FTC/d4T XR or 3TC/d4T XR	246 (9%)	60 (24%)	1.06(0.74, 1.54)	34 (12%)	12 (35%)	1.11 (0.54, 2.27)	
	No NRTI regimens	209 (8%)	50 (24%)	0.96 (0.64, 1.43)	26 (9%)	8 (31%)	1.03 (0.45, 2.38)	

VF: Virologic Failure; HR: Hazard Ratio; CI: Confidence Interval;
ART: antiretroviral therapy; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: nonnucleoside reverse transcriptase inhibitor; PI: protease inhibitor; FTC:emtricitabine; ABC:abacavir; 3TC:lamivudine; ZDV: zidovudine; d4T XR: stavudine extended release; TDF:tenofovir disoproxil fumerate; LPV/r:lopinavir/ritonavir; ATV/r:atazanavir/ritonavir; EFV:efavirenz;
**Testing for Interactions based on Cox PH model, stratified by study;*



Supplementary Figure 1 Distribution of (A) Time to AIDS/death; (B) Time to death only by HCV status (– HCV/HIV; - - - HIV)

Supplementary Table 3 Occurrence of AIDS or Death

	HIV (N=2762)	HCV/HIV (N=279)	Total (N=3041)	P-Value*
AIDS	112 (4%)	13 (5%)	125 (4%)	<.001
AIDS & Death	15 (1%)	4 (1%)	19 (1%)	
Death	19 (1%)	13 (5%)	32 (1%)	
No AIDS/Death	2,616 (95%)	249 (89%)	2,865 (94%)	

**Chi-Square Test*

Supplementary Table 4 Cause of Death by HCV co-infection status

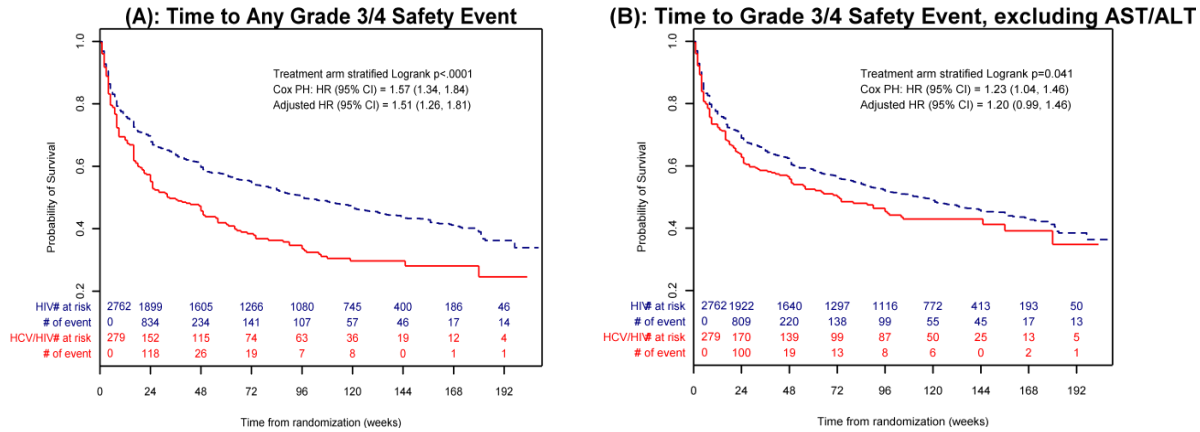
Outcome		**HIV (N=2762)**	**HCV/HIV (N=279)**	**Total (N=3041)**	**P-Value***
Death	**Overall**	**34 (1.2%)**	**17 (6.1%)**	**51 (1.7%)**	**<.001**
	Cause Unknown	4 (11.8%)	1 (5.9%)	5 (9.8%)	
	Accident, Suicide or Substance Abuse	7 (20.6%)	7 (41.2%)	14 (27.5%)	
	Treatment Toxicity	1 (2.9%)	0 (0%)	1 (2.0%)	
	Non-HIV/AIDS Diagnosis	11 (32.4%)	5 (29.4%)	16 (31.4%)	
	HIV/AIDS infection, HIV/AIDS-related Diagnosis	11 (32.4%)	4 (23.5%)	15 (29.4%)	

**Chi-Square Test;*

Supplementary Table 5 Summary of occurrence of first Grade 3/4 Events

Outcome		HIV (N=2762)	HCV/HIV (N=279)	Total (N=3041)	P-Value Chi-Square	P-Value PH model*
Grade 3/4 Events	**Overall**	**1,451 (53%)**	**180 (65%)**	**1,631 (54%)**	**<.001**	<.001
	G3/4 Events, excluding AST and ALT	1,397 (51%)	149 (53%)	1,546 (51%)	0.368	0.068
	G3/4 AST and ALT	77 (3%)	40 (14%)	117 (4%)	<.001	<.001

** Cox Proportional Hazard(PH) model, adjusted for baseline covariates;*



Supplementary Figure 2 Distribution of (A) Time to Any Grade 3/4 Safety Event; (B) Time to Grade 3/4 Safety Event, excluding AST/ALT, by HCV status (–HCV/HIV; - - - HIV)

Supplementary Table 6 ART Treatment Modification Effect for Grade 3/4 Safety Events

	ART GROUP	Grade 3/4 Events, excluding AST and ALT: HIV (N=2762) HR (95% CI)	Grade 3/4 Events, excluding AST and ALT: HCV/HIV (N=279) HR (95% CI)	P-value *	Increased AST and ALT only: HIV (N=2762) HR (95% CI)	Increased AST and ALT only: HCV/HIV (N=279) HR (95% CI)	P-value *
PI groups vs. EFV	EFV	1.00	1.00	0.483	1.00	1.00	0.832
	ATV/r included	2.31 (2.02, 2.64) †	1.81 (1.22, 2.69) †		0.77 (0.41, 1.42)	1.19(0.48, 2.97)	
	LPV/r included	0.98 (0.74, 1.30)	0.83 (0.51, 1.37)		1.02 (0.40, 2.56)	1.43 (0.50, 4.00)	
	LPV/r + EFV (A5142)	1.21 (0.93, 1.61)	0.79 (0.41, 1.54)		1.45 (0.59, 3.57)	1.96 (0.66, 5.88)	
NRTI groups	FTC/TDF or 3TC/TDF included	1.00	1.00	0.138	1.00	1.00	0.805
	ABC/3TC	1.28 (1.12, 1.46)	1.05 (0.66, 1.66)		1.01 (0.54, 1.88)	1.22 (0.49, 3.05)	
	3TC/ZDV or ABC/3TC/ZDV	0.90 (0.65, 1.25)	1.35 (0.82, 2.21)		1.16 (0.41, 3.26)	0.66(0.19, 2.34)	
	FTC/d4T XR or 3TC/d4T XR	1.41 (1.06, 1.85)	1.67 (0.96, 2.94)		1.43 (0.56, 3.70)	1.08 (0.34, 3.33)	
	No NRTI regimen	1.30 (0.97, 1.75)	1.01 (0.51, 2.00)		1.61 (0.62, 4.17)	1.69 (0.56, 5.00)	

VF: Virologic Failure; HR: Hazard Ratio; CI: Confidence Interval;
ART: antiretroviral therapy; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: nonnucleoside reverse transcriptase inhibitor; PI: protease inhibitor; FTC:emtricitabine; ABC:abacavir; 3TC:lamivudine; ZDV: zidovudine; d4T XR: stavudine extended release; TDF:tenofovir disoproxil fumerate; LPV/r:lopinavir/ritonavir; ATV/r:atazanavir/ritonavir; EFV:efavirenz;
**Testing for Interactions based on Cox PH model, stratified by study*
†due to expected increased creatinine kinase and total bilirubin with ATV/r

Supplementary Table 7 Summary of On-treatment Adherence

Week	HIV (N=2762)		HCV/HIV (N=279)		P- Value*
	N (on ART)	100% adherent	N (on ART)	100% adherent	
24	2437	2129 (87.4%)	238	216 (90.8%)	0.15
48	2307	1999 (86.7%)	312	181 (85.4%)	0.60
72	2004	1759 (87.8%)	155	131 (84.5%)	0.26
96	1891	1645 (87.0%)	147	126 (85.7%)	0.61

**Fisher's Exact Test;*

Supplementary Table 8 Selected Trial Eligibility Criteria

	A5073	A5095	A5142	A5202
HIV testing (confirmed ELISA)	Yes	Yes	Yes	Yes
HIV RNA (copies/mL) [1]	≥2000	>400 (>25% subjects >100,000)	>2000	> 1000
ART Naive	Yes	Yes	Yes	Yes
Lab				
Absolute Neutrophil Count (/mm^3)	≥ 500	≥ 500	≥ 750	≥ 500
Platelet (/mm^3)	≥ 50,000	≥ 40,000	≥ 50,000	≥ 40,000
Hemoglobin (gm/dL)	>9.1 (m), >8.9 (f)	≥ 8.0	≥ 8.0	≥ 8.0
AST/ALT[2] (x ULN[3])	< 5	≤ 5	≤ 5	≤ 5
Total Bilirubin (x ULN[3])	≤ 2.5		≤ 2.5	≤ 2.5
Total Serum Lipase (x ULN[3])	≤ 1.5	<2.0	≤ 1.5	
Creatinine (x ULN[3])		≤ 1.5		
CrCl[4] (mL/min)	≥ 50		≥ 50	≥ 60
Serum Phosphate (mg/dL)			≥ 2.0	
Karnofsky performance (within days)	≥ 70 (45)		≥ 70 (30)	
Age (years)	≥ 13	≥ 16	≥ 13	≥ 16
Weight (kg)	≥ 40			
Negative pregnancy test results	Yes	Yes	Yes	Yes

[1]All tested using the UltraSensitive Roche Amplicor HIV-1 Monitor assay at the Johns Hopkins University Laboratory
[2]AST: aspartate aminotransferase; ALT: alanine transaminase; [3]ULN: Upper Limit of Normal;
[4]Calcuated creatinine clearance estimated by the Cockcroft-Gault equation;