Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Violari A, Lindsey JC, Hughes MD, et al. Nevirapine versus ritonavir-boosted lopinavir for HIV-infected children. N Engl J Med 2012;366:2380-9.

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Members of the P1060 study team designed the study, patient data were collected at the sites and transmitted to Frontier Science (FSTRF, Albany, NY), and data analyses were performed by the Harvard Statistical Data Analysis Center statisticians (JCL, MDH). The manuscript was initially drafted by the study co-chairs (AV, PP) and revised with input from all manuscript authors, who vouch for the data. The P1060 team decided to publish the paper.

Figure S1: Time to death; solid line = NVP, dashed line = LPV/r

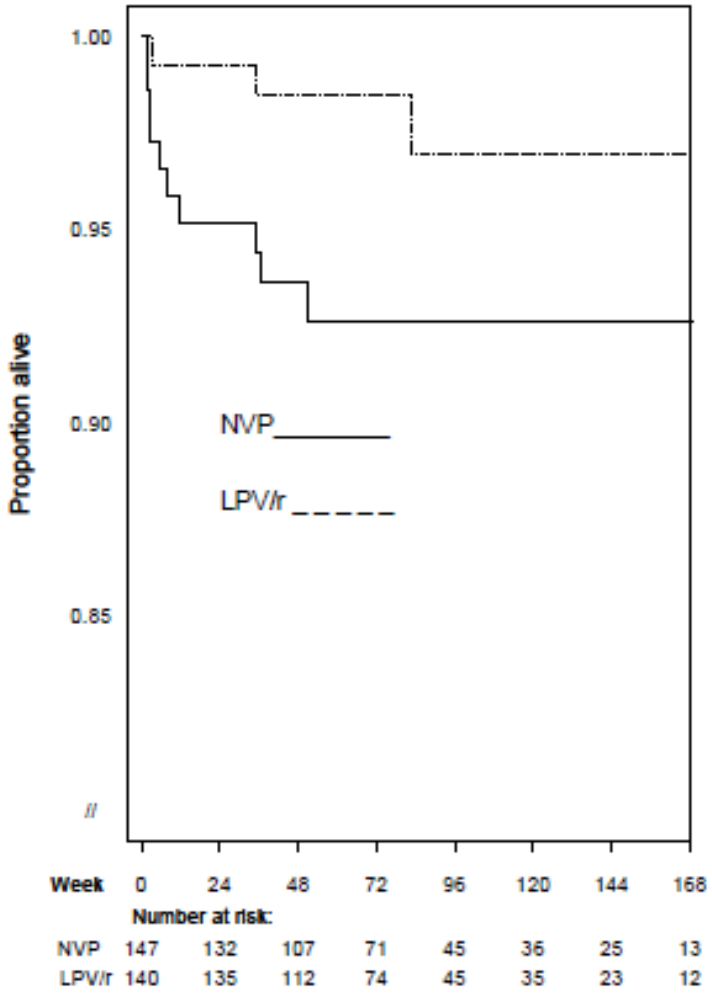

Table S1: Cohort Diagram

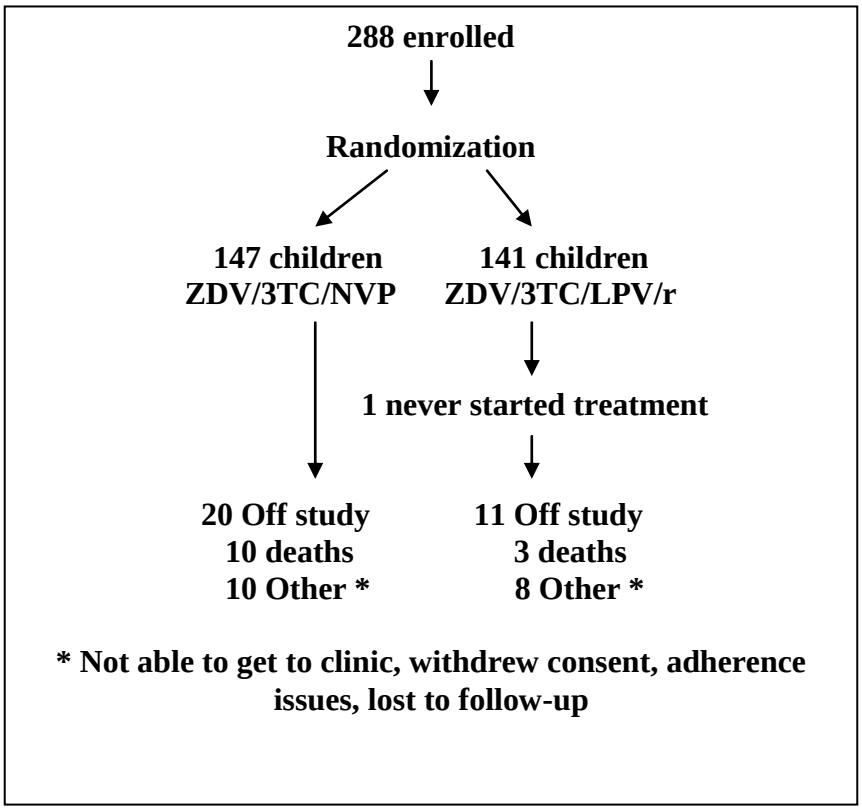

Table S2
Primary Endpoint: Off Study Treatment or Virologic Failure

					Type of endpoint met [1]		
			No endpnt	Primary endpnt	Off trt only	Virol Fail only	Both
Treatment	Age stratum	Total N	N	N	N	N	N
Total		287	200	87	42	43	2
LPV/r	2m - <12m	36	29	7	4	3	0
	≥12m	104	84	20	11	9	0
	Total	140	113	27	15	12	0
NVP	2m - <12m	41	24	17	9	8	0
	≥12m	106	63	43	18	23	2
	Total	147	87	60	27	31	2

[1] Counts indicate whether primary endpoint was from going off study treatment, experiencing virologic failure, or both at the same time

Table S3: Protocol-defined Toxicity Endpoints

	NVP	LPV/r
≥Grade 2B rash	**5**	
≥Grade 3 LFT	**2 (2)**	
Neutropenia	**2 (2)**	**2 (1)**
Anemia	**1**	**1**
Thrombocytopenia		**(1)**

Numbers depict events; Grade 3 events are numbers without parentheses;

Grade 4 events are numbers in parentheses.

Table S4: Numbers of deaths, new ≥ grade 3 signs, symptoms or laboratory abnormalities, new targeted diagnoses and changes in lipids occurring on study treatment. Note that counts within categories may not add up to totals in category as subjects could experience more than one event within the category.

Event	NVP (n=147)	LPV/r (n=140)	Total (n=287)
Death (on or off study treatment)	**10 (7%)**	**3 (2%)**	**13 (5%)**
Grade ≥ 3 laboratory abnormality	**66 (45%)**	**50 (36%)**	**116 (40%)**
Potassium	**4**	**0**	**4**
Sodium	**1**	**0**	**1**
Platelets	**2**	**4**	**6**
Hemoglobin	**13**	**8**	**21**
Absolute Neutrophil Count	**49**	**41**	**90**
White Blood Cells	**1**	**0**	**1**
SGOT	**7**	**2**	**9**
SGPT	**13**	**3**	**16**
Creatinine	**1**	**0**	**1**
Grade ≥ 3 sign/symptom	**31 (21%)**	**28 (20%)**	**59 (21%)**
General body (fever/weight loss)	**19**	**19**	**38**
Respiratory (cough, difficulty breathing, SOB, abnormal breath sounds, respiratory system dysfunction)	**8**	**4**	**12**
Circulatory/cardiac (cardiovascular dysfunction, swollen)	**2**	**1**	**3**
Gastrointestinal (diarrhea, vomiting, appetite loss)	**6**	**8**	**14**
Reproductive (discharge)	**1**	**0**	**1**

Skin (allergic rash, inflammation, papules, rash-non allergic)	**2**	**2**	**4**
Neurologic (convulsion/seizure, weakness)	**2**	**0**	**2**
Other (dehydration)	**1**	**0**	**1**
Targeted new diagnoses			
Immune reconstitution syndrome (IRIS)	**3**	**2**	**5**
AIDS encephalopathy	**0**	**2**	**2**
Malaria	**40**	**44**	**84**
Tuberculosis (disseminated, meningitis, pulmonary, peripheral lymph nodes)	**7**	**5**	**13**
Lipids: **mean (95% CI) change: week 48 minus baseline**			**Adjusted * p-value**
Total cholesterol (mg/dl)	**39.6** **(29.1, 50.1)** **(n=67)**	**32.9** **(23.3, 42.4)** **(n=95)**	**0.97**
Triglycerides (mg/dl)	**-48.1** **(-78.3, -17.8)** **(n=65)**	**-41.8** **(-64.6, -18.9)** **(n=95)**	**0.072**

* p-value for treatment difference from linear regression on change from baseline adjusted for entry value

Table S5: Change from Baseline to Weeks 24 and 48
Comparison of NVP versus LPV/r treatment

Outcome	Treatment	Week	N	Mean (95% CI)	Ttest p-value	Adjusted p-value*
CD4 count (cells/mm3)	NVP	24	132	477 (378, 576)	0.89	0.74
	LPV/r	24	135	468 (378, 557)		
	NVP	48	109	599 (479, 719)	0.52	0.24
	LPV/r	48	119	541 (411, 671)		
CD4%	NVP	24	132	12.4 (11.0, 13.8)	0.17	0.14
	LPV/r	24	135	11.1 (9.9, 12.3)		
	NVP	48	109	15.2 (13.6, 16.9)	0.41	0.34
	LPV/r	48	119	14.3 (13.0, 15.7)		
Height z-score	NVP	24	133	0.21 (0.09, 0.32)	0.30	0.24
	LPV/r	24	134	0.12 (0.00, 0.24)		
	NVP	48	110	0.43 (0.28, 0.57)	0.10	0.10
	LPV/r	48	119	0.25 (0.10, 0.40)		
Weight z-score #	NVP	24	133	1.03 (0.84, 1.23)	0.084	0.007
	LPV/r	24	134	0.78 (0.58, 0.99)		
	NVP	48	108	1.36 (1.12, 1.60)	0.064	0.009
	LPV/r	48	117	1.04 (0.80, 1.27)		
BMI #	NVP	24	133	1.1 (0.8, 1.4)	0.13	0.020
	LPV/r	24	134	0.8 (0.5, 1.1)		
	NVP	48	111	1.1 (0.7, 1.4)	0.23	0.031
	LPV/r	48	119	0.8 (0.4, 1.1)		

*** Adjusted for entry value and age stratum**
[#] Favoring the NVP treatment group

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