

Sample Protocol

Combination Therapy after Nevirapine Exposure

Brief Summary: This is a Phase III study comprised of two trials. Both trials will compare the virologic response to NNRTI-based (Arm 1A) versus PI-based (Arm 1B) antiretroviral therapy (ART) in 640 HIV-infected, treatment-naïve women or women who have only received single dose nevirapine (NVP) as prevention of maternal to child transmission (MTCT).

Objectives:

1. To compare the time to virologic failure or death between participants initiating ART with a regimen including NVP versus a regimen including Lopinavir/ritonavir (LPV/RTV).
2. To evaluate the difference in the effect of NNRTI-based and PI-based ART on the time to virologic failure or death in participants with prior NVP prophylaxis (Trial 1) versus no prior NVP exposure (Trial 2).

Duration of Study: The study will last for 48 weeks after the last person enrolls. There are 9 visits the first year of the study and then visits are every 12 weeks.

Inclusion Criteria:

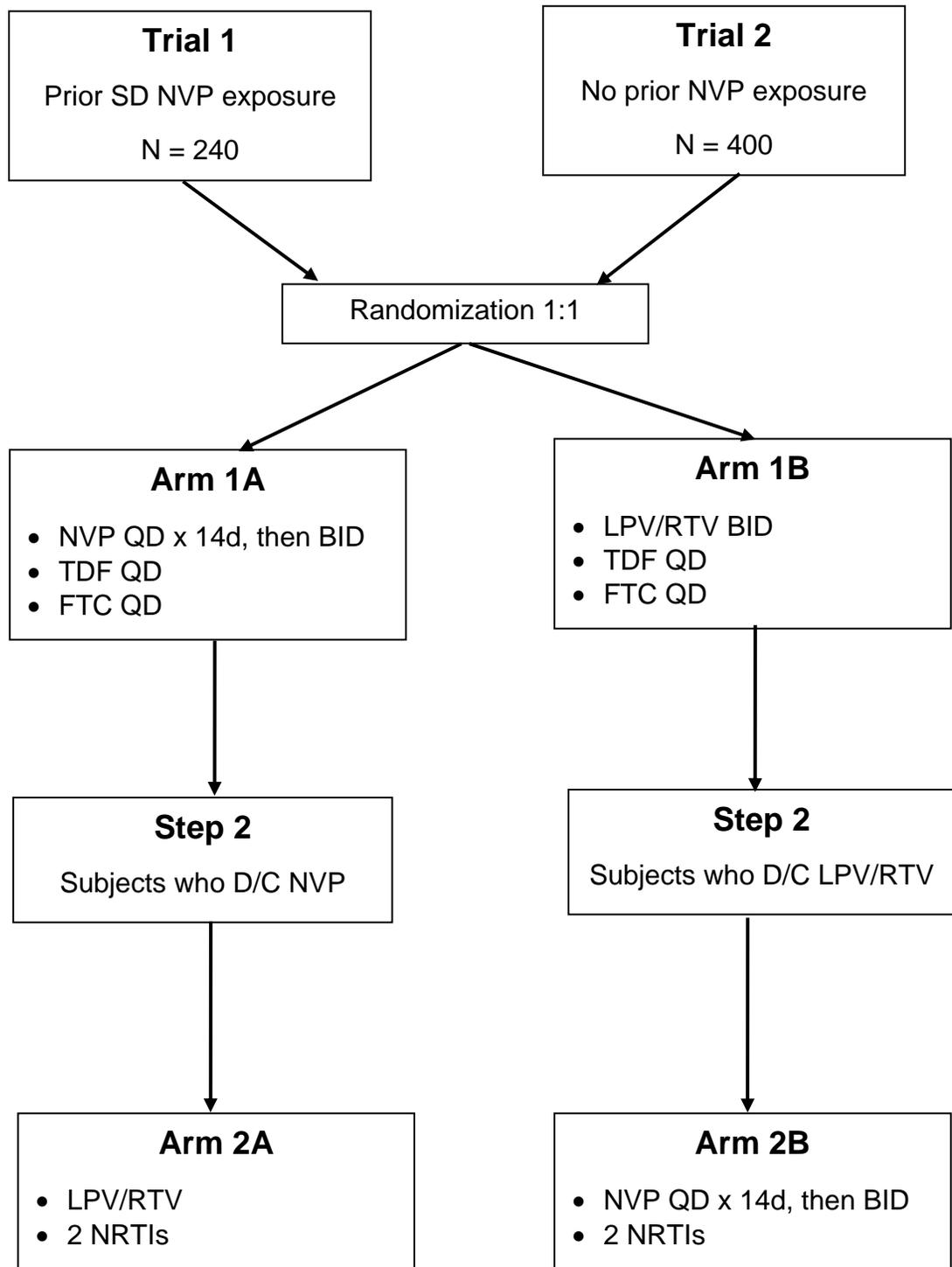
1. HIV infected
2. Women age 13 years or older
3. CD4+ cell count <200 cells within 90 days prior to study entry.
4. For participants in Trial 1:
 - Prior single dose (SD) NVP MTCT prophylaxis.
 - Receipt of SD NVP more than once for any given pregnancy or in >1 pregnancy is not exclusionary.
 - The last SD NVP MTCT prophylaxis must have been completed at least 6 months prior to study entry.
5. Viral Load within 45 days prior to study entry
6. Chemistry and CBC results as designated by the protocol.

Exclusion Criteria:

1. For participants in Trial 2, receipt of any antiretrovirals at any time prior to study entry.
2. For participants in Trial 1, receipt of any antiretrovirals, excepts as noted in item 4 above, at any time prior to study entry.
3. Breast feeding
4. Receipt of tuberculosis treatment within 30 days prior to study entry.

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Schema



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Schedule of Clinical and Laboratory Evaluations

Evaluation	Screening	Entry Week 0	Weeks after Entry								After 48 weeks	Virologic Failure	Step 2 Entry	D/C	
			2	4	8	12	16	24	36	48					
Documentation of HIV	X														
Medical/Medication History	X														
Concomitant Medications/ Treatment Modifications		X	X	X	X	X	X	X	X	X	X	q 12w		X	X
Clinical Assessments	X	X	X	X	X	X	X	X	X	X	X	q 12w		X	X
Hematology	X	X		X		X		X	X	X	X	q 12w		X	X
Blood Chemistries	X	X		X		X		X	X	X	X	q 12w		X	X
Lipid Levels		X						X		X	X	q 48w		X	X
Liver Function Tests	X	X	X	X	X	X	X	X	X	X	X	q 12w		X	X
Pregnancy Testing	X	X	Repeat if Indicated												
HbSAg		X	Repeat if Indicated												
Lipase			Perform for sx suggestive of pancreatitis												
CPK			Perform for sx suggestive of myositis												
Lactate			Perform for sx suggestive of lactic acidosis												
CD4+/CD8+	X	X				X		X	X	X	X	q 12w		X	X
HIV-1 RNA, real time	X	X				X		X	X	X	X	q 12w	X	X	X
HIV-1 RNA, batched				X			X								
Plasma for Resistance Testing		X											X	X	
Stored Plasma		X		X	X	X		X	X	X	X	q 12w	X	X	X
Stored PBMC		X						X		X	X	q 24w	X		
PK Sampling, Arm 1A only			X	X											
Adherence Assessments				X		X		X		X	X	q 24w			
QOL/RU Assessments								X		X	X	q 24w			