

THE DVD STUDY: Use of Twice Daily Darunavir to Replace Dual Boosted Protease Inhibitors in Virologically Suppressed Patients

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Background

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- **Despite few supportive data sets, there was considerable use of dual boosted PIs, esp. in triple class resistance**
 - **POWER study – 26% on the control arm were on dual boosted PIs**
- **The role of dual boosted PIs is challenged by the availability of newer PIs with greater activity despite pre-existing resistance**
 - **Some dual boosted PIs had worse lipid outcomes vs. single boosted PIs (Fontas et al, 2004)**
- ***In vitro* resistance data support preserved activity of darunavir in most pts with virologic suppression on any “first generation” PI**
 - **Supports the rationale to substitute a single PI for any active dual PI combination.**

Hypotheses: The Dual vs. Darunavir (DVD) Study

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- **Primary:**
- **Virologic suppression will be maintained when patients change two boosted “first generation” PIs to DRV/r 600/100 mg twice daily**
 - **Other meds in regimen continued**
- **Secondary:**
- **Patients will prefer boosted DRV/r 600/100 mg twice daily to dual boosted PI therapy**
- **Changing from dual-boosted PI therapy to DRV/r 600/100 mg twice daily will be associated with improvements in metabolic parameters**

Methods: Patients and Design

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- **Subjects: n=24 adults, HIV RNA < 400 for ≥ 12 weeks, On two first generation boosted PIs with ≥ 1 ARV from another drug class**
 - **Excluding non-nucleoside reverse transcriptase inhibitors**
- **Study Design: Randomized (1:1) pilot study, controlled, open-label, 48-week phase IV trial conducted at 6 centers in the United States.**
- **Treatment Arms: First 24 weeks**
 - **Continue baseline dual boosted PI regimen (control arm).**
 - **DRV/r 600/100 mg twice daily (experimental arm)**
 - **At week 24, Control arm could cross over to DRV/r if VL < 400 during the initial 24 weeks**
- **Primary Endpoint: Compare % with HIV RNA < 50c/mL at week 24**
 - **Virologic failure definition: Confirmed HIV RNA >400 c/mL**

Methods: Assessments

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- HIV-1 RNA, CD4 count and safety labs assessed at screening, baseline, and weeks 4, 12, 24, 36 and 48
- Fasting glucose and lipid profiles were assessed at baseline and at week 4, 24 and 48
- Treatment Satisfaction Questionnaires
 - ▣ English-speaking subjects completed the “change version” of the HIV Treatment Satisfaction Questionnaire* after 24 weeks on DRV

*Woodcock and Bradley, 2006

Baseline Characteristics

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	DRVr (N=12)	Control (N=12)	All
Male, n (%)	9 (75)	10 (83)	19 (79)
Median age, yrs (range)	46 (31-59)	51 (36-64)	50 (31-64)
White, n (%)	9 (75)	7 (58)	16 (67)
Black, n (%)	3 (25)	5 (42)	8 (33)
Median CD4, cells per ul (range)	532 (150-1207)	639(144-997)	553 (144-1207)
Baseline Regimen: PI component			
LPV/ATV/r, n (%)	4 (33)	3(25)	7(29)
LPV/SQV/r, n (%)	4(33)	3 (25)	7(29)
ATV/SQV/r, n (%)	2(17)	4 (33)	6 (25)
FPV/LPV/r, n (%)	1 (8)	2 (17)	3 (13)
NFV/SQV, n (%)	1(8)	0(0)	1(4)
Baseline Regimen: Non-PI component			
1 NRTI	10 (83)	4 (33)	14 (58)
2 NRTIs	2 (17)	7(58)	9 (38)
RAL		1 (8)	1 (4)

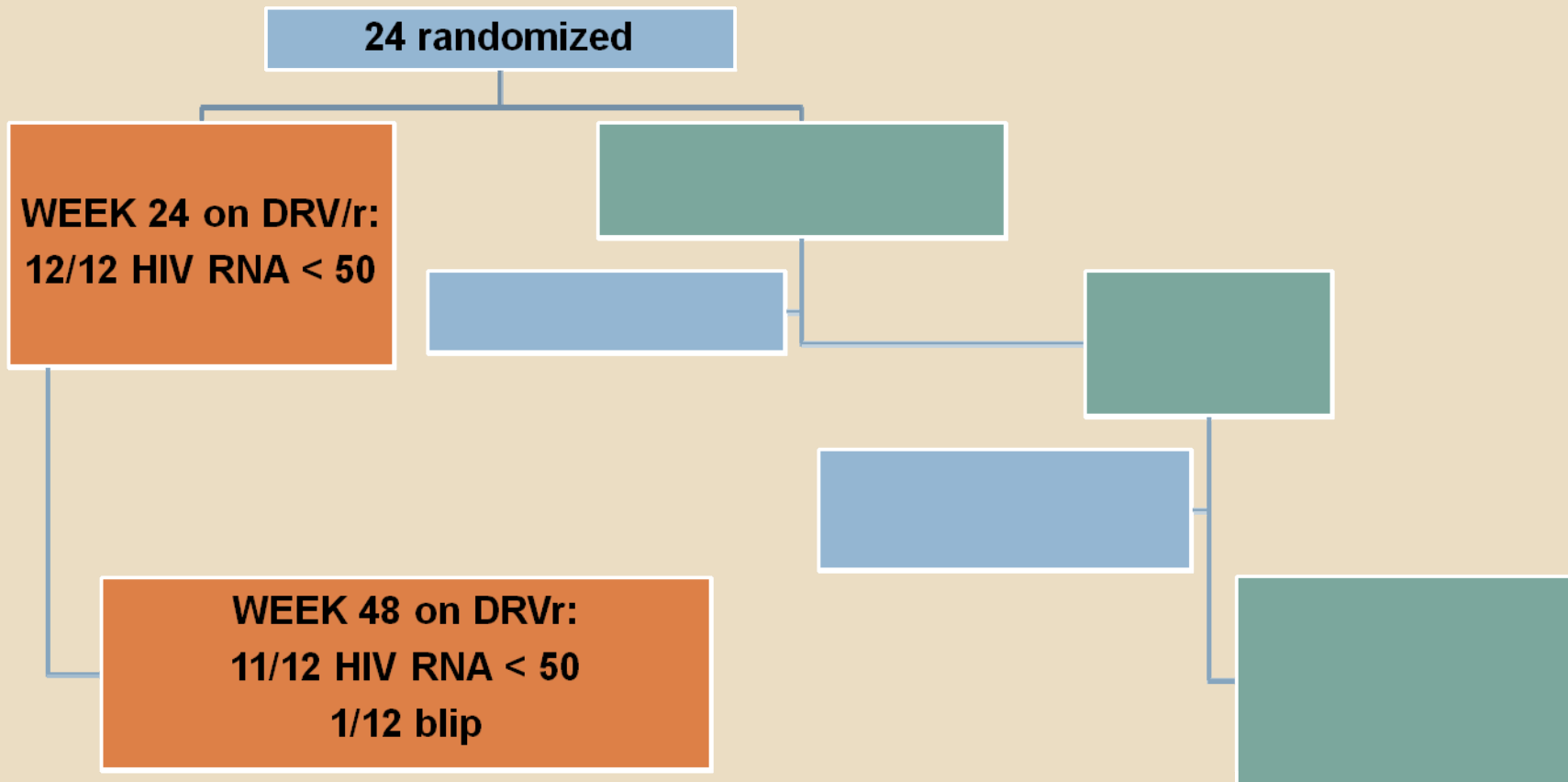
Concomitant ARVs

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Darunavir Arm		Control Arm	
One NRTI	N	One NRTI	N
TDF	3	TDF	2
3TC	2	FTC	1
Dual NRTIs		Dual NRTIs	
TDF/FTC	4	ABC/3TC	3
AZT/3TC	2	TDF/ABC	2
TDF/ABC	1	TDF/FTC	1
		TDF/DDI	1
		3TC/DDI	1

Disposition and Virologic Results

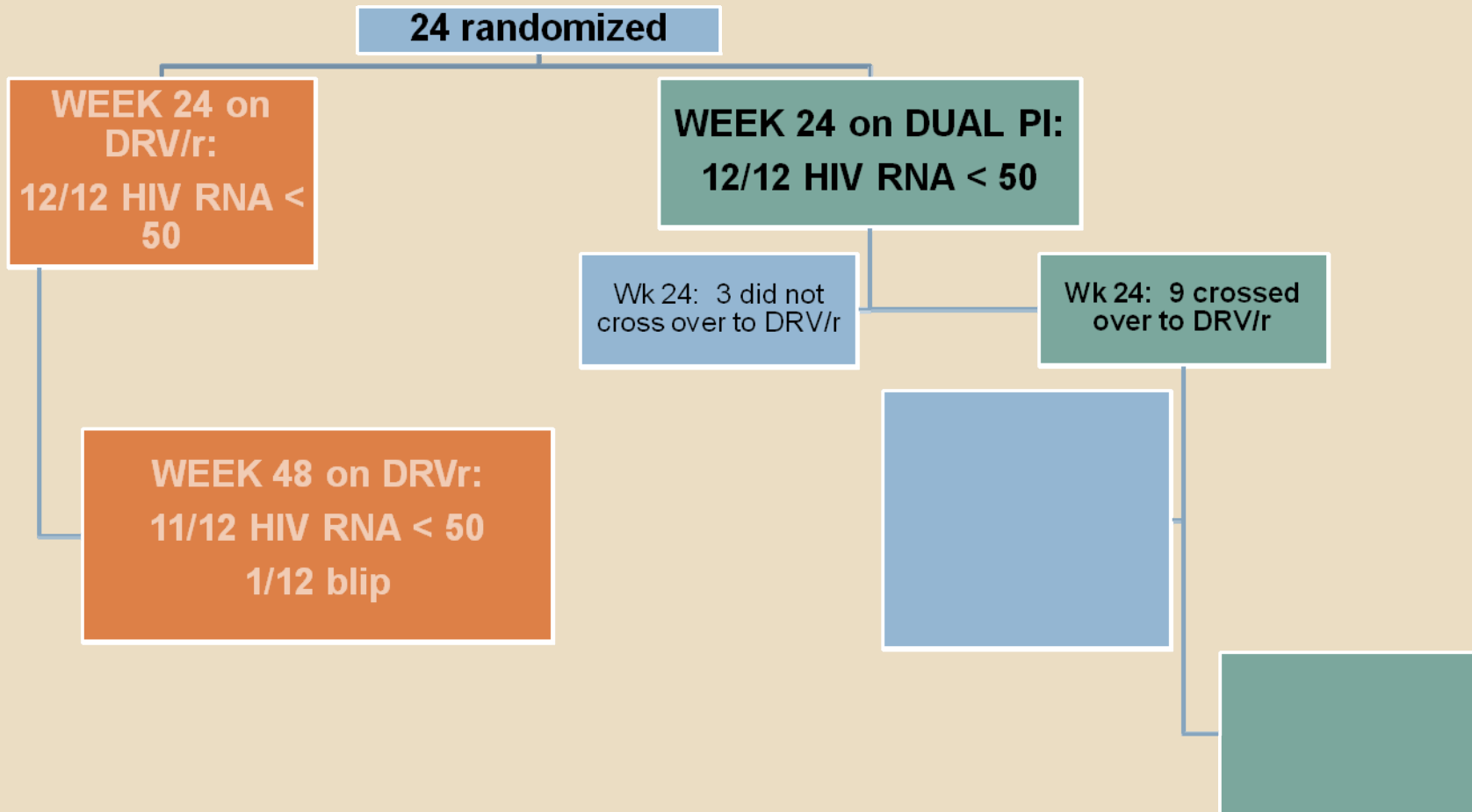
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•Blip: Week 48 VL = 151 c/mL;
repeat = 62 c/mL

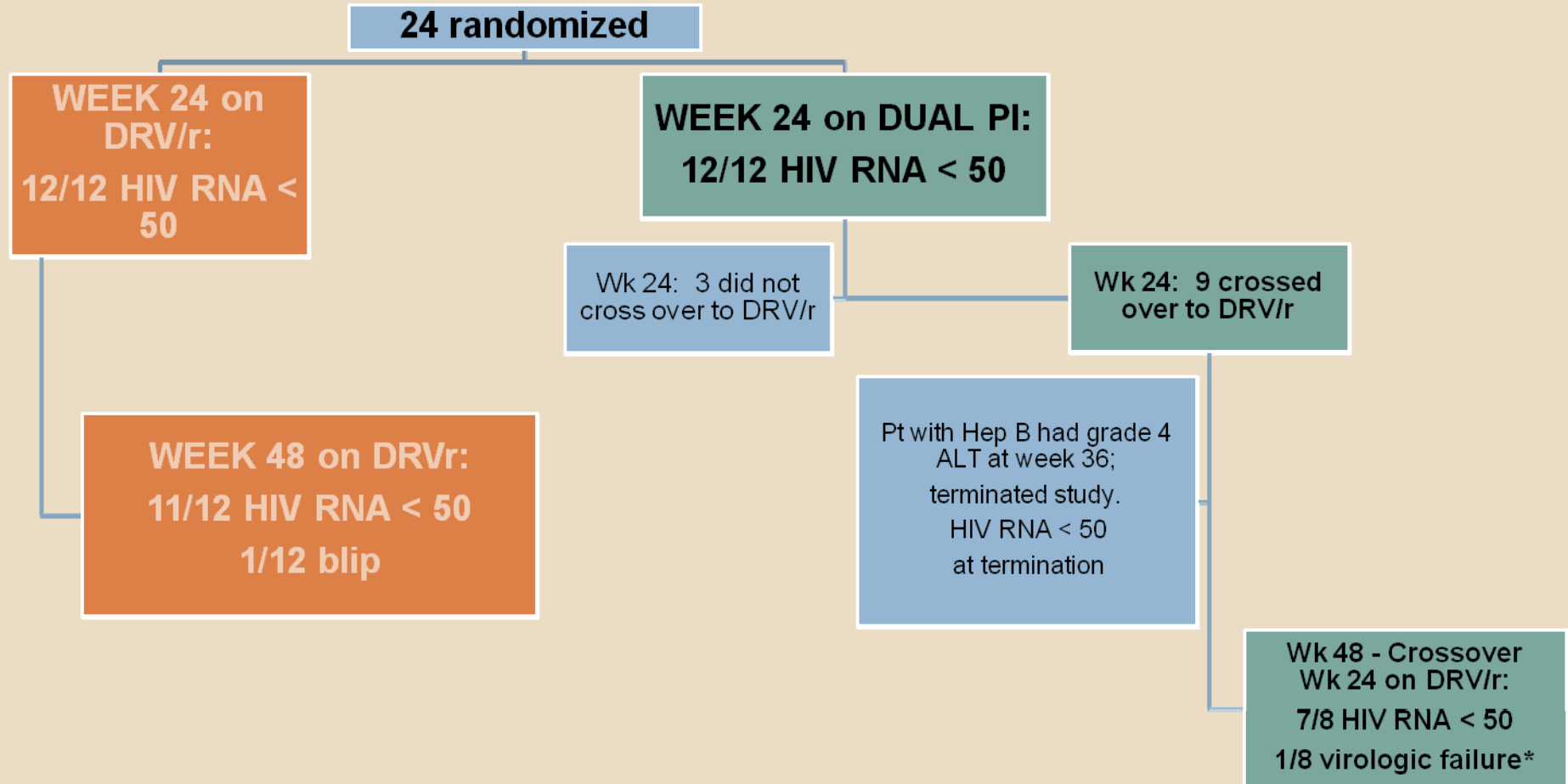
Disposition and Virologic Results

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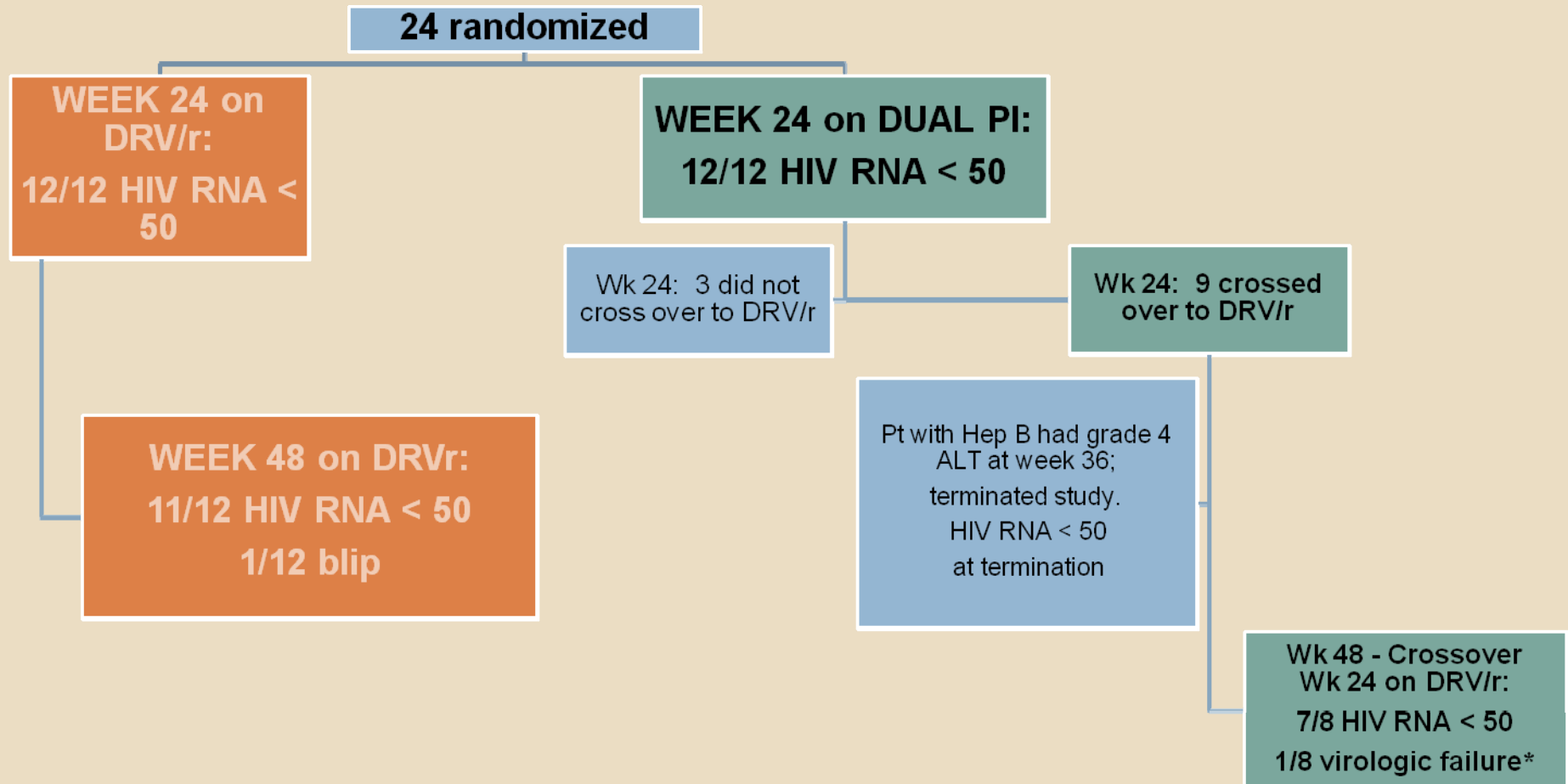
Disposition and Virologic Results

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Disposition and Virologic Results

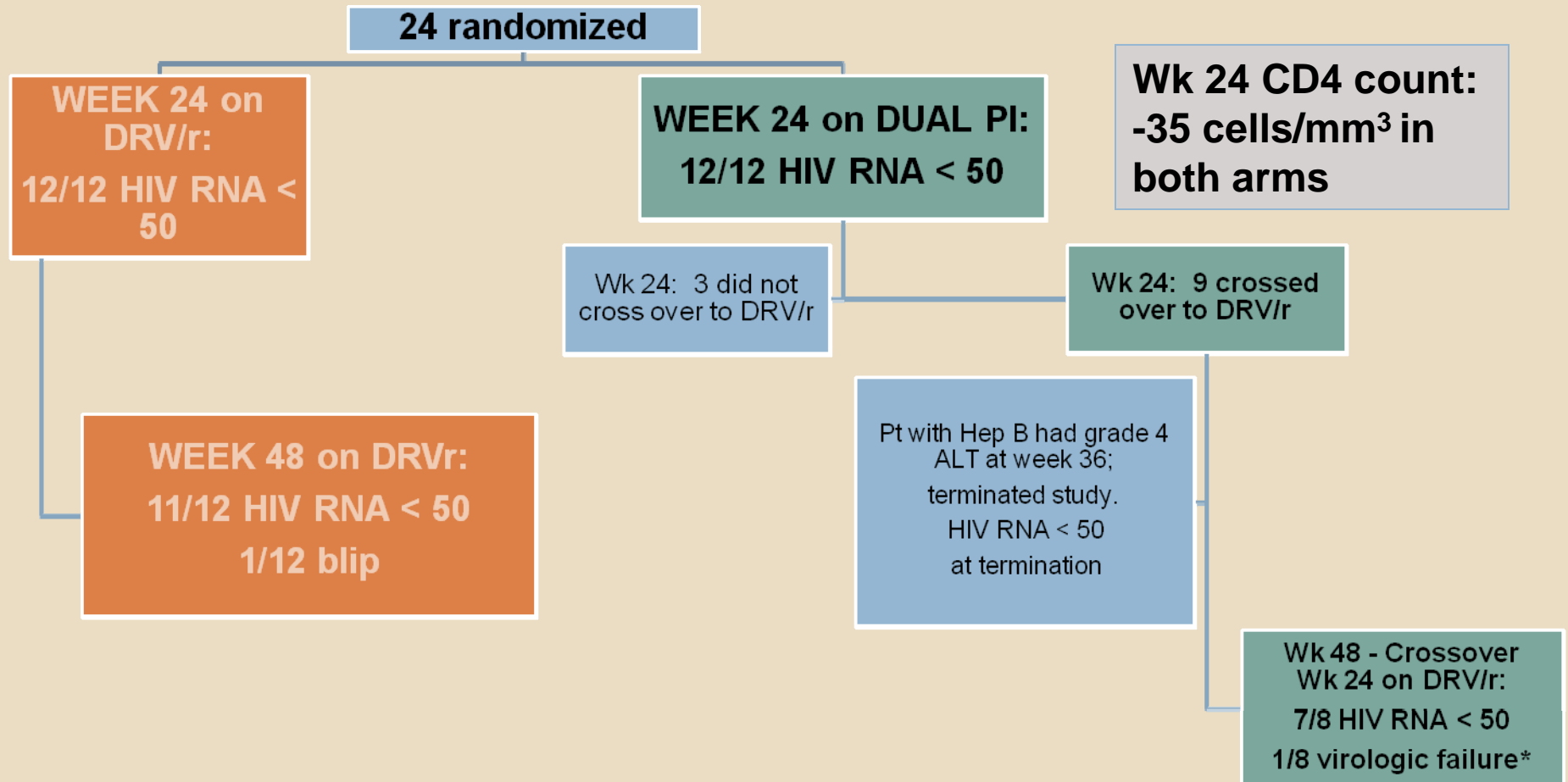
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* VF: HIV RNA = 446 c/mL; repeat VL = 10800 c/mL. Resistance test showed full susceptibility to all ARVs in regimen; repeat VL after resuming same regimen = 73 c/mL

Disposition and Virologic Results

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Week 24 Lipid Fraction Results (mmol/L)

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Lipid Fractions	Median (IQR) BL and Change from baseline	
	DRV/r Arm	Control Arm
Total Cholesterol	5.64 (1.6)	3.75 (0.8)
Total Cholesterol Change	-0.17	+0.06
LDL Cholesterol	3.28 (1.4)	2.8 (1.0)
LDL Cholesterol Change	-.11	+0.05
Fasting Triglycerides	1.26 (2.4)	2.6 (1.4)
Fasting Triglyceride Change	-0.34	0
HDL Cholesterol	1.07 (0.03)	0.57 (.4)
HDL-c	-0.04	+0.04

No significant differences by study arm were noted

Treatment Satisfaction: Data for 24 Weeks on DRV/r

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Response options +3 (much more satisfied now) to -3 (much less satisfied now)

	Week 24	Week 48 (crossover)
	median (range)	median (range)
How satisfied are you with your current treatment?	3 (0 to 3)	2.5 (2 to 3)
How satisfied are you with any side effects of your present treatment?	2 (0 to 3)	2.5 (2 to 3)
How convenient have you been finding your treatment to be recently?	3 (-1 to 3)	3 (2 to 3)
How satisfied are you with the extent to which the treatment fits in with your life-style?	3 (-1 to 3)	3 (2 to 3)
How likely would you be to recommend your present treatment to someone else with HIV?	3 (0 to 3)	2.5 (2 to 3)
How satisfied would you be to continue with your present form of treatment?	3 (0 to 3)	2.5 (1 to 3)

DVD: Study Conclusions

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- In patients with virologic suppression on dual boosted PIs, these data support the substitution of DRV/r 600/100 BID instead of dual boosted PI regimens
 - ▣ No case of true virologic failure noted
- Safety monitoring of LFTs as currently recommended is warranted if this substitution is undertaken
 - ▣ Study not powered to assess lipid differences, though no significant changes were observed
- Treatment satisfaction improved after the switch
- Cost differences of dual vs. single boosted PIs can be a consideration in this pt. population
 - ▣ On average, DRV/r is \$217 (US\$) less costly per pt per month than dual PI regimens