

ARTEMIS: Efficacy and Safety of Darunavir/ritonavir (DRV/r) 800/100 mg Once-daily vs Lopinavir/ritonavir (LPV/r) in Treatment-naïve, HIV-1–infected Patients at 96 Weeks

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ARTEMIS: Phase III Study Design and Key Objectives



LPV dosing		LPV formulation	
qd =	15%	Capsule only =	12%
bid =	75%	Tablet only =	2%
bid/qd =	11%	Capsule/tablet switch =	86%

- **Primary endpoint**
 - Proportion of patients with HIV-1 RNA <50 copies/mL
- **Primary objective**
 - Demonstrate non-inferiority of DRV/r qd versus LPV/r based on primary endpoint at Week 48
- **Secondary objectives**
 - Evaluate superiority of virologic response in the event that DRV/r was non-inferior
 - Evaluate long-term safety, tolerability and durability of virologic responses over 192 weeks

*qd or bid dosing was based on regulatory approval for naïve patients; switch from capsule to tablet (Meltrex) was made according to local regulatory approval and drug availability; TDF, tenofovir; FTC, emtricitabine

ARTEMIS: Baseline Characteristics

	DRV/r (n=343)	LPV/r (n=346)
Baseline demographics		
Female, n (%)	104 (30)	105 (30)
Mean age, years (\pm SD)	36 (9)	35 (9)
Caucasian, n (%)	137 (40)	153 (44)
Black, n (%)	80 (23)	71 (21)
Hispanic, n (%)	77 (22)	77 (22)
Asian, n (%)	44 (13)	38 (11)
Baseline disease characteristics		
Median HIV-1 RNA, copies/mL (range)	70,800 (835–5,580,000)	62,100 (667–4,580,000)
Median CD4 cell count, cells/mm ³ (range)	228 (4–750)	218 (2–714)
HBV/HCV co-infected, n (%)	43 (13)	48 (14)
Stratification factors		
CD4 cell count <200 cells/mm ³ , n (%)	141 (41)	148 (43)
HIV-1 RNA \geq 100,000 copies/mL, n (%)	117 (34)	120 (35)

SD, standard deviation; HBV, hepatitis B virus; HCV, hepatitis C virus

ARTEMIS: Patient Disposition at Week 96 Analysis

Incidence, n (%)	DRV/r (n=343)	LPV/r (n=346)
Discontinuation	59 (17)	81 (23)
AE ^a	13 (4)	32 (9)
Lost to follow-up	18 (5)	11 (3)
Withdrawal of consent	11 (3)	10 (3)
VF	3 (1)	8 (2)
Pregnancy	6 (2)	3 (1)
Non-compliance to study protocol	3 (1)	7 (2)
Other	5 (1)	10 (3)

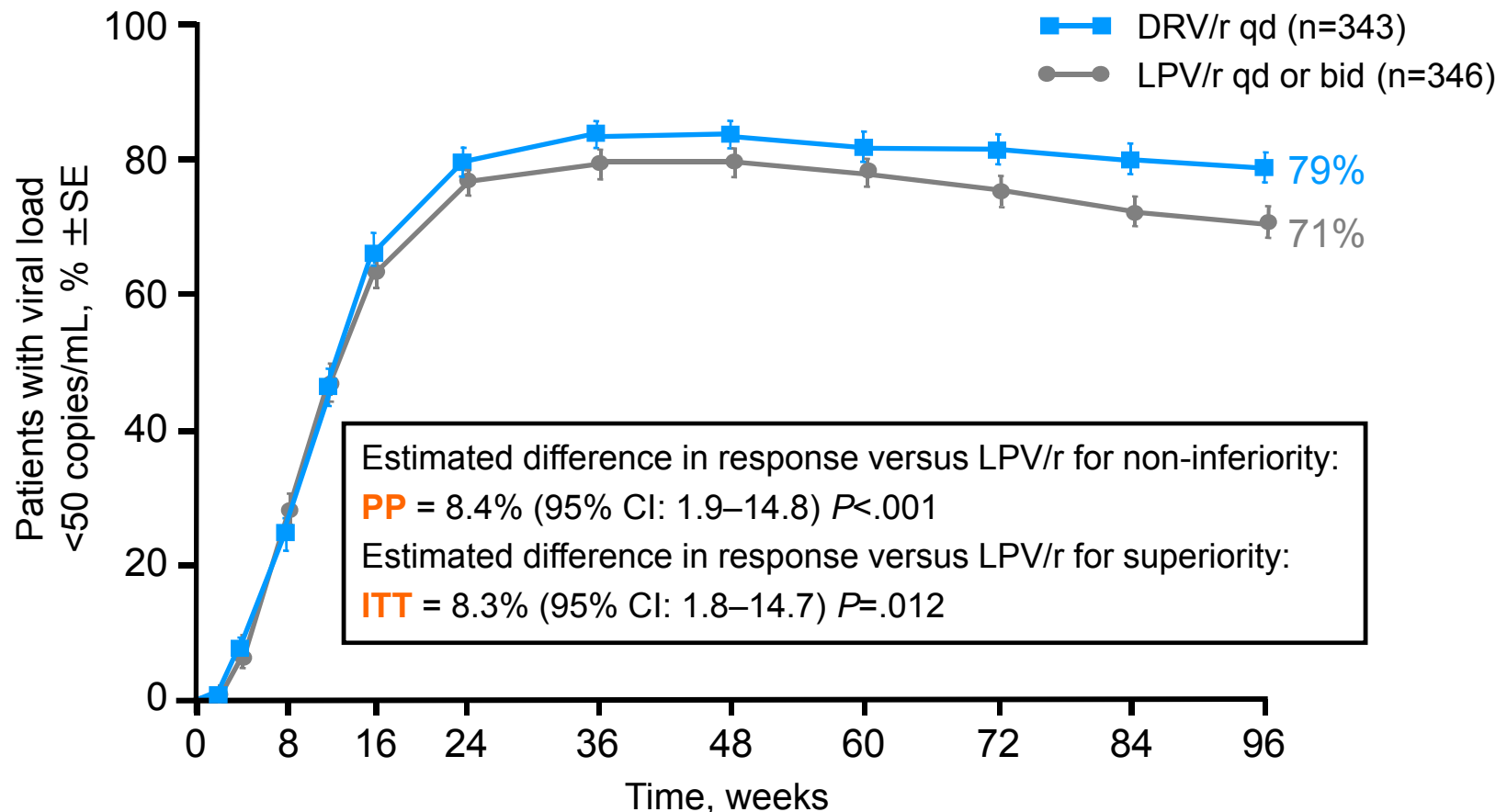
^aIncludes six deaths (one in DRV/r group; five in LPV/r group)

Table includes all data up to the point when the last patient reached Week 96

Mean exposure was 93 weeks (range 0–130 weeks)

SE, standard error

ARTEMIS: Viral Load <50 copies/mL to Week 96 (ITT-TLOVR)^a

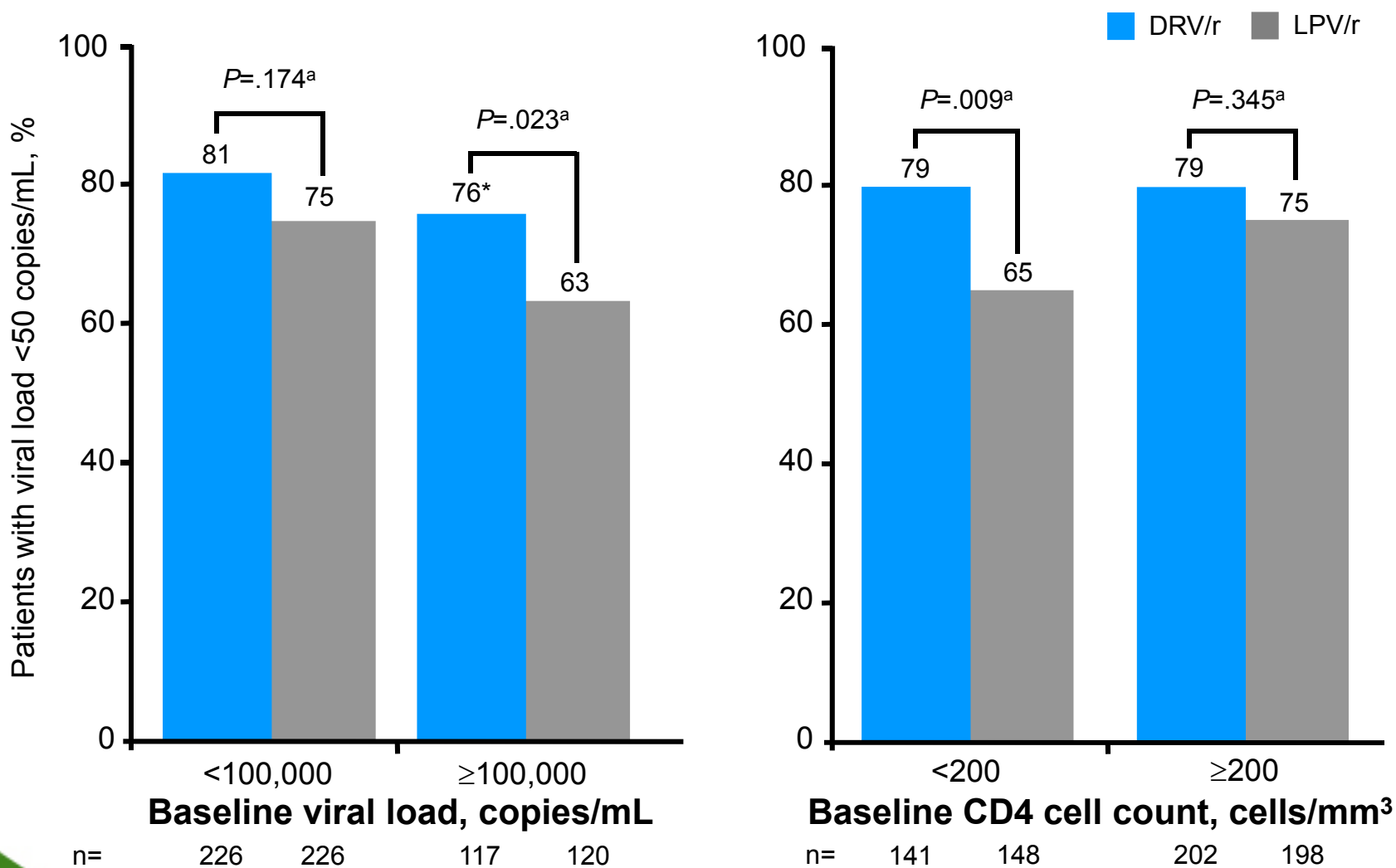


- **Median change in CD4 count from baseline to Week 96 in the DRV/r and LPV/r arms was +171 and +188 cells/mm³, respectively (ITT-NC=F)**

^aEstimated from a logistic regression model including treatment and stratification factors (baseline log₁₀ viral load and baseline CD4 cell count)

ITT, intention-to-treat; TLOVR, time to loss of virologic response; NC=F, non-completer = failure

ARTEMIS: Confirmed Response by Stratification Factor at Week 96 (ITT-TLOVR)



^aChi-square test

ITT, intention-to-treat; TLOVR, time to loss of virologic response

ARTEMIS: Analysis of Confirmed Virologic Failures (ITT Population)

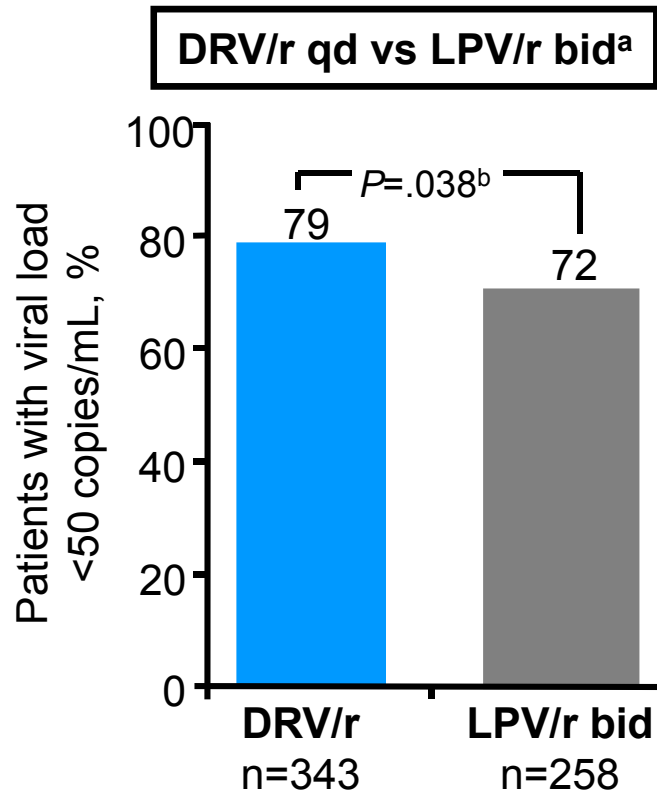
- The DRV/r arm had a lower rate of VF than the LPV/r arm at Week 96^a: 12% (40/343) vs. 17% (59/346)
 - This confirmed Week 48 findings: 10% (34/343) VF in DRV/r arm and 14% (49/346) VF in LPV/r arm
- All VFs (DRV/r and LPV/r) that had available matching baseline and endpoint phenotypes remained susceptible to all PIs^b

^aPatients with VF were defined as those with a confirmed viral load ≥ 50 copies/mL;

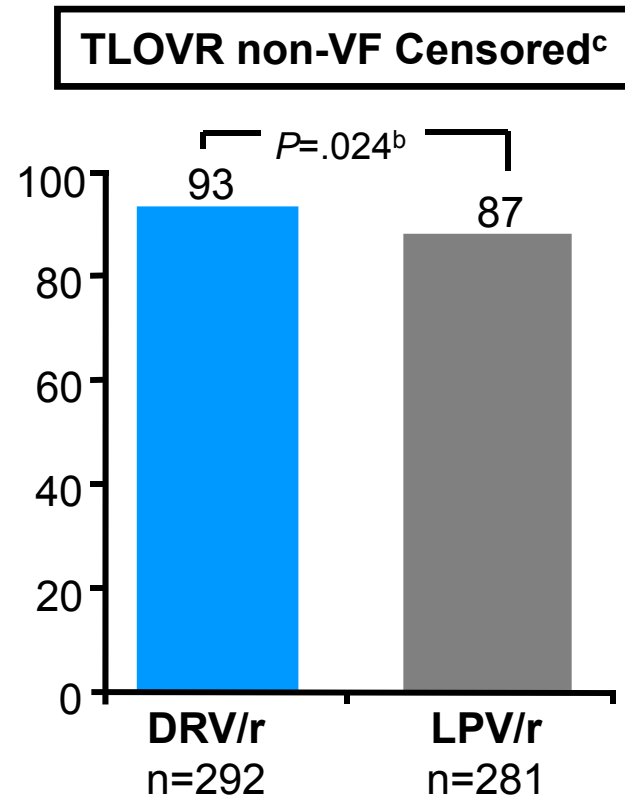
Patients who discontinued for reasons other than VF were censored at the time of discontinuation

^bResistance testing was performed on samples with viral load > 1000 copies/mL

ARTEMIS: Additional Analyses



- When patients receiving LPV/r qd were excluded, response rate was significantly higher in patients treated with DRV/r qd vs LPV/r bid



- Difference in response favoring DRV/r remained significant after censoring patients who discontinued for reasons other than VF

^aITT-TLOVR; ^bChi-square test; ^cPatients who discontinued treatment due to reasons other than VF were excluded
ITT, intention-to-treat; TLOVR, time to loss of virologic response; VF, virologic failure

ARTEMIS: Grade 2-4 Adverse Events and Serious AEs over 96 weeks

	DRV/r (n=343)	LPV/r (n=346)
<i>Mean exposure, weeks</i>	95.0	91.4
Any grade 2–4 AE at least possibly related^a	80 (23)	119 (34)
Gastrointestinal AEs (all types), n (%)	23 (7)	52 (15)
Diarrhea	14 (4) ^b	38 (11)
Nausea	6 (2)	10 (3)
Rash (all types), n (%)	9 (3)	5 (1)

^a≥2% incidence, laboratory abnormalities reported as AEs are not shown in the table; ^b*P*<.001 vs LPV/r

- Overall, 34 (10%) patients in the DRV/r arm and 55 (16%) patients in the LPV/r arm had a serious AE
- There was 1 death in the DRV/r arm and 5 deaths in the LPV/r arm; none were considered related to therapy

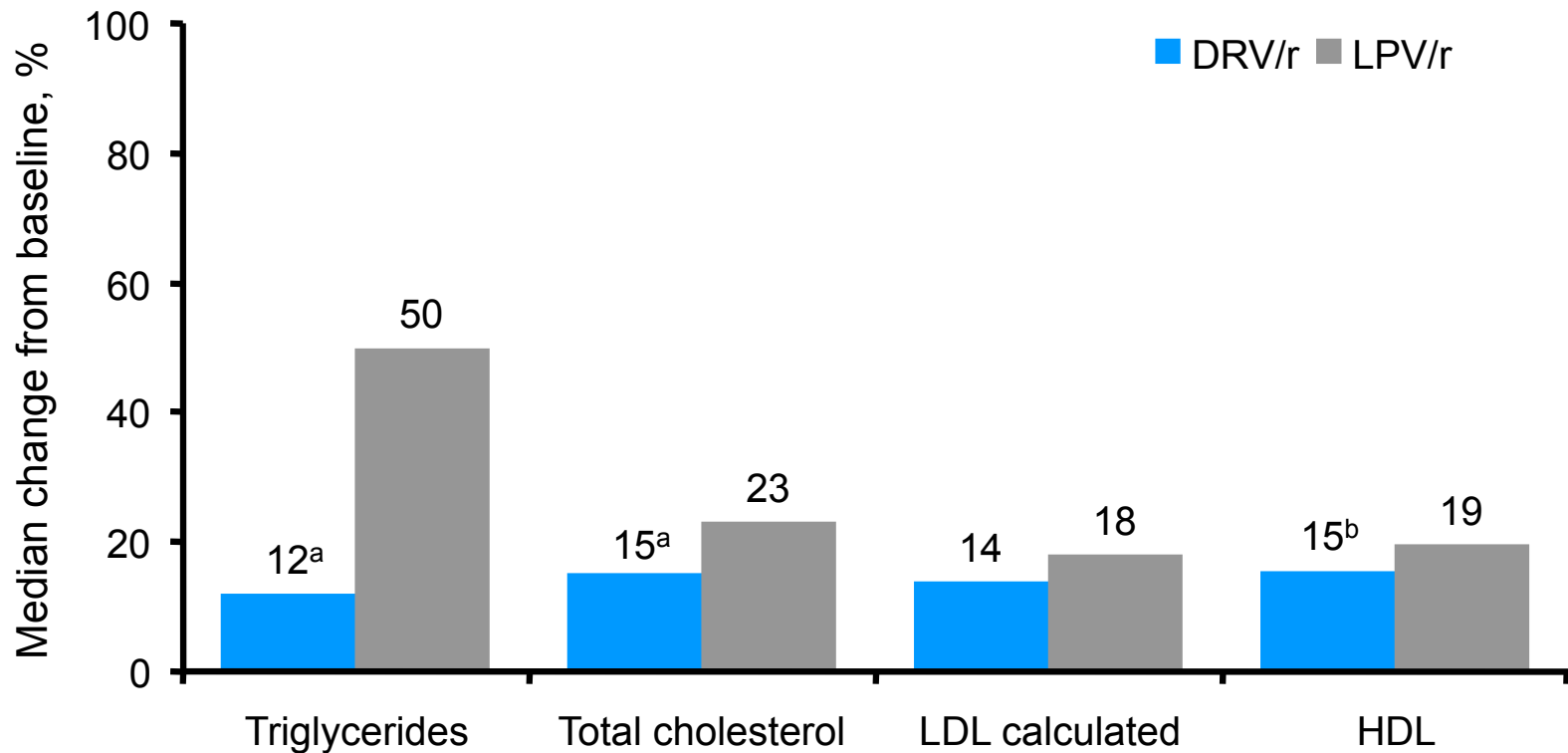
ARTEMIS: Grade 2–4 Laboratory Abnormalities over 96 weeks ($\geq 2\%$ Incidence)

n (%)	DRV/r (n=343)	LPV/r (n=346)
Alanine aminotransferase	38 (11)	40 (12)
Aspartate aminotransferase	39 (11)	35 (10)
Neutrophil count	30 (9)	11 (3)
Hyperglycemia	28 (8)	26 (8)
Pancreatic amylase	25 (7)	18 (5)
Alkaline phosphatase	5 (2)	5 (2)
Partial thromboplastin time	8 (2)	9 (3)
Pancreatic lipase	8 (1)	8 (2)
Hyperbilirubinemia	4 (1)	17 (5)
Prothrombin time	2 (1)	7 (2)
Total cholesterol	60 (18) ^a	95 (28)
Calculated low-density lipoprotein (LDL) ^b	62 (18)	50 (15)
Triglycerides	15 (4) ^c	46 (13)

^a $P=.0016$ vs LPV/r; ^bNot calculated where triglycerides were $>400\text{mg/dL}$; ^c $P<.0001$ vs LPV/r

- **No significant changes in calculated creatinine clearance between baseline and Week 96 visits**

ARTEMIS: Median Percent Change in Lipid Levels from Baseline at Week 96



- A similar proportion of patients used lipid-lowering agents in the DRV/r arm (7%) and in the LPV/r arm (8%)

^a $P < .001$; ^b $P = .0102$ vs LPV/r
Data analyzed by Wilcoxon rank test

ARTEMIS: Conclusions from 96-week Analysis

- This 96-week analysis of the ARTEMIS trial demonstrated that once-daily DRV/r 800/100mg is an effective and well-tolerated therapeutic option for treatment-naïve patients
- Virologic response to once-daily DRV/r was superior to that of LPV/r
 - DRV/r arm had a higher response rate and fewer discontinuations due to adverse events compared with the LPV/r arm; better efficacy and tolerability both contributed to superiority at Week 96
 - Statistical significance was maintained after excluding patients who discontinued for reasons other than virologic failure
- Virologic failure was infrequent in ARTEMIS
 - All patients who experienced virologic failure remained susceptible to all PIs, including the PI in their treatment regimen
- DRV/r had a lower incidence of grade 2–4 diarrhea and fewer grade 2–4 elevations in total cholesterol and triglycerides than LPV/r

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