



## ARV Therapies and Therapeutic Strategies

INDEPENDENT REPORTING ON CROI 2017

# Comprehensive Expert Review and Discussion of Key Presentations

An Independent CME Activity Jointly Provided by Postgraduate Institute for Medicine and ViralEd, Inc.  
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## ASSOCIATION BETWEEN CARDIOVASCULAR DISEASE & CONTEMPORARILY USED PROTEASE INHIBITORS

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On Behalf of the D:A:D Study Group

Abstract 128LB



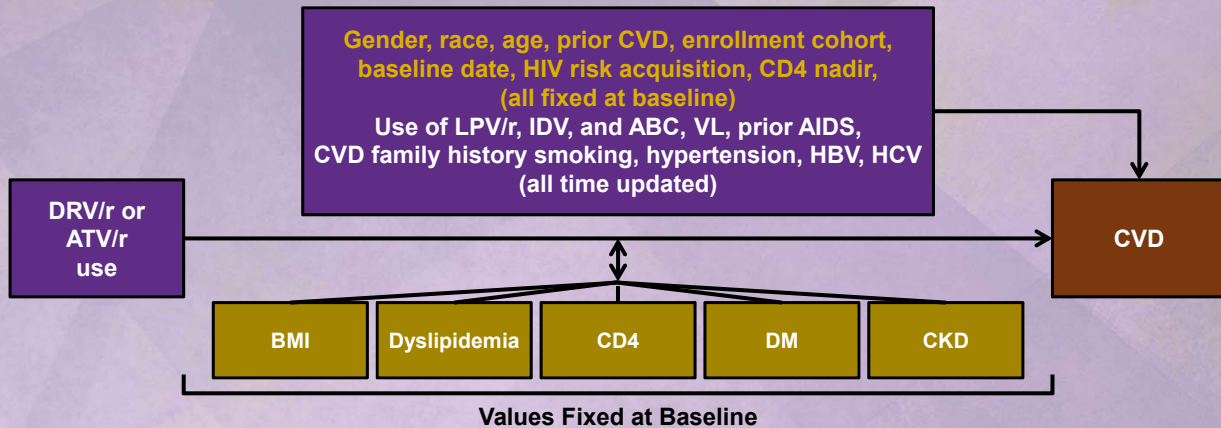
### D:A:D CVD & PIs: Methods

#### Definitions

- CVD was defined, as in previous D:A:D analyses, a composite endpoint including the following, centrally adjudicated, events:
  - Myocardial infarction
  - Stroke
  - Sudden cardiac death
  - Invasive cardiovascular procedures
    - Coronary bypass
    - Coronary angioplasty
    - Carotid endarterectomy

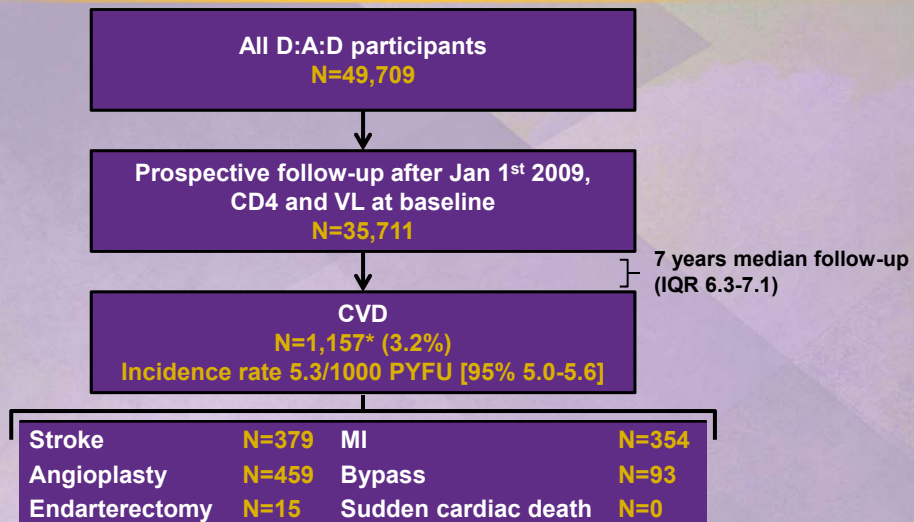
## D:A:D CVD & PIs: Methods (cont'd)

In the primary adjusted model, factors considered to potentially lie on the causal pathway between PI/r use and CVD were adjusted for using baseline values only



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## D:A:D CVD & PIs: Inclusion of D:A:D Participants into the Analysis



\*Persons could experience multiple events on the same day

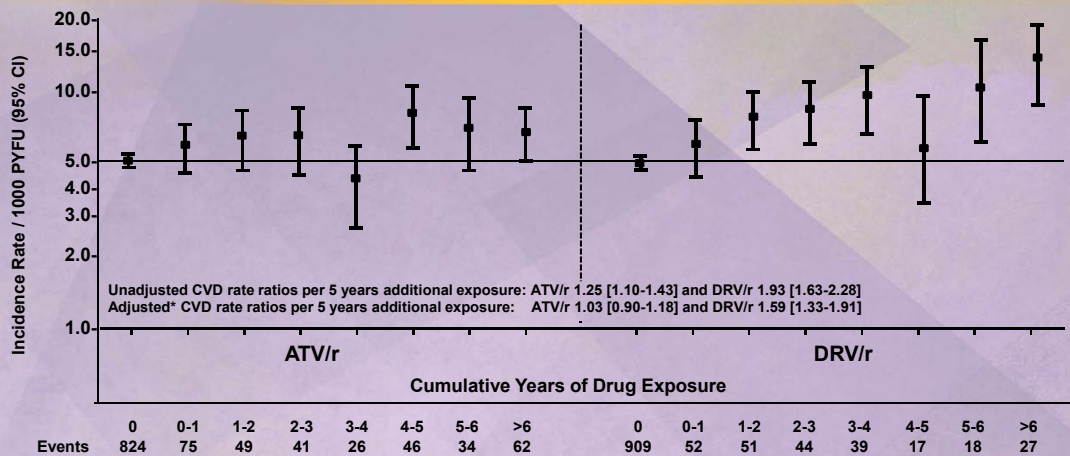
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## D:A:D CVD & PIs: Baseline Characteristics

		N	%
All		35711	100.0
Gender	Male	26288	73.6
Race	White	17085	47.8
HIV Exposure	MSM	16447	46.1
HCV	Positive	6864	19.2
HBV	Positive	1439	4.0
VL <400 copies/mL	Yes	27290	76.4
Smoking	Current	14014	39.2
Diabetes		1805	5.1
Hypertension		3471	9.7
Dyslipidemia		14347	40.2
Prior AIDS	Yes	9799	27.4
Prior CVD	Yes	8515	28.6
D:A:D CVD Risk	>10%	1753	5.3
D:A:D CKD Risk	High (≥5)	11952	38.4
		<b>Median</b>	<b>IQR</b>
Age	Years	44	38-44
CD4	Cells/mm <sup>3</sup>	501	360-689
Nadir CD4	Cells/mm <sup>3</sup>	210	100-322

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## D:A:D CVD & PIs: Cumulative Exposure to DRV/r Increase MI Risk



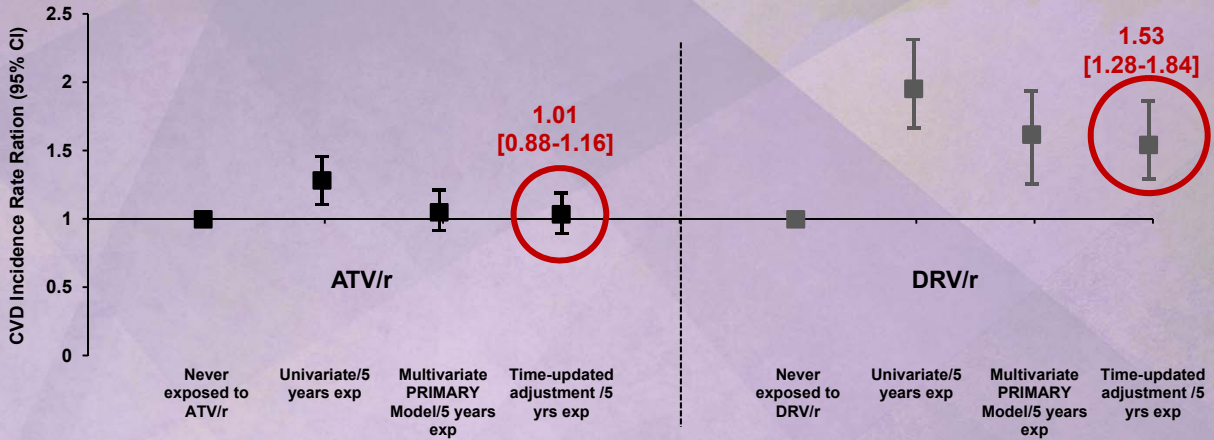
\*Adjusted for gender, race, HIV exposure group, enrollment cohort, baseline date, prior CVD, nadir CD4 count, current CD4 count\*\*, dyslipidaemia\*\*, BMI\*\*, diabetes\*\*, eGFR\*\*, age (all as fixed variates at baseline), HBV, HCV, smoking, family history of CVD, VL, hypertension, AIDS, cumulative exposure to darunavir, atazanavir, lopinavir & indinavir & recent exposure to abacavir (≤6 months) (all as time-updated variables).

\*\*Factors considered to potentially lie on the causal pathway between PI/r exposure and CVD and values hence fixed at baseline.

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## D:A:D CVD & PIs: Association Between CVD & Cumulative ATV/r and DRV/r Use

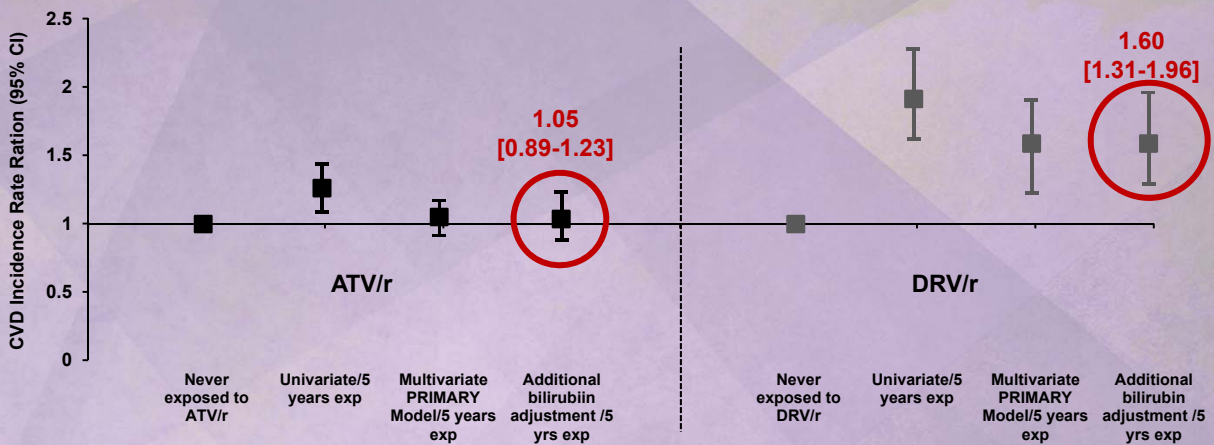
Additional Time-updated Adjustment for Factors Potentially on the Causal Pathway between PI/r use and CVD CD4, BMI, CKD, Dyslipidaemia, Diabetes



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## D:A:D CVD & PIs: Association Between CVD & Cumulative ATV/r and DRV/r Use (cont'd)

Additional Adjustment for Bilirubin Levels (Time-updated)



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## D:A:D CVD & PIs: Conclusions

- ◆ In this large heterogeneous cohort of HIV-positive persons, cumulative use of DRV/r, but not ATV/r was independently associated with a small, but gradually increasing risk of CVD of 59% per 5 years exposure
- ◆ The strength of the DRV/r association is of a similar size as found for the older PIs indinavir (IDV) and (ritonavir boosted lopinavir) LPV/r, but in contrast the DRV/r association does not seem to be modified by dyslipidemia
- ◆ Cautious interpretation is warranted due to the observational nature of the study and the risks of unmeasured confounding
- ◆ Finding call for further investigations of possible mechanisms