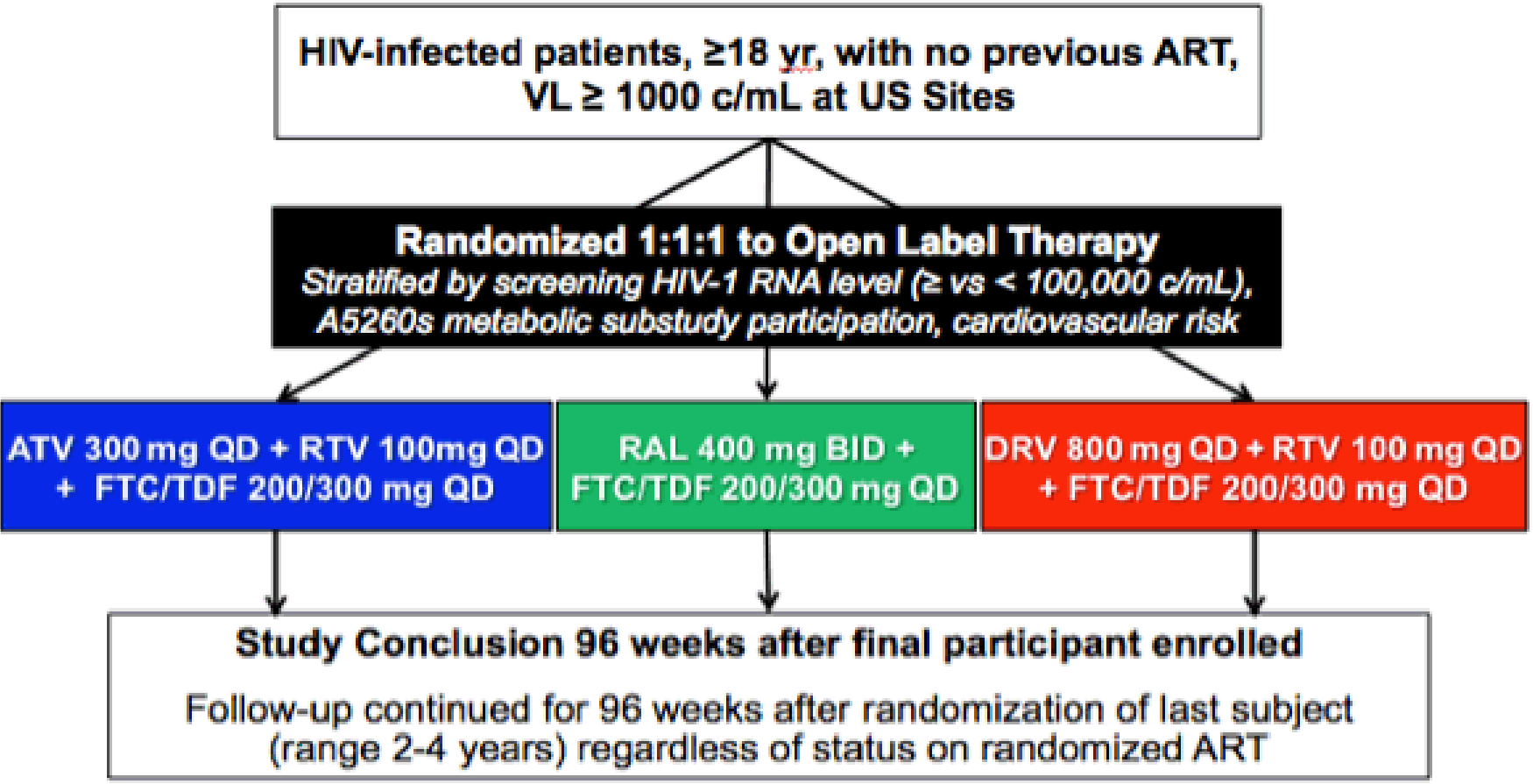
HIV-CUP CROI Boston, 3.-6. März 2014

HIV TTT
Bone and kidney

Hansjakob Furrer

A5257 Study Design*



*With the exception of RTV, all ART drugs were provided by the study

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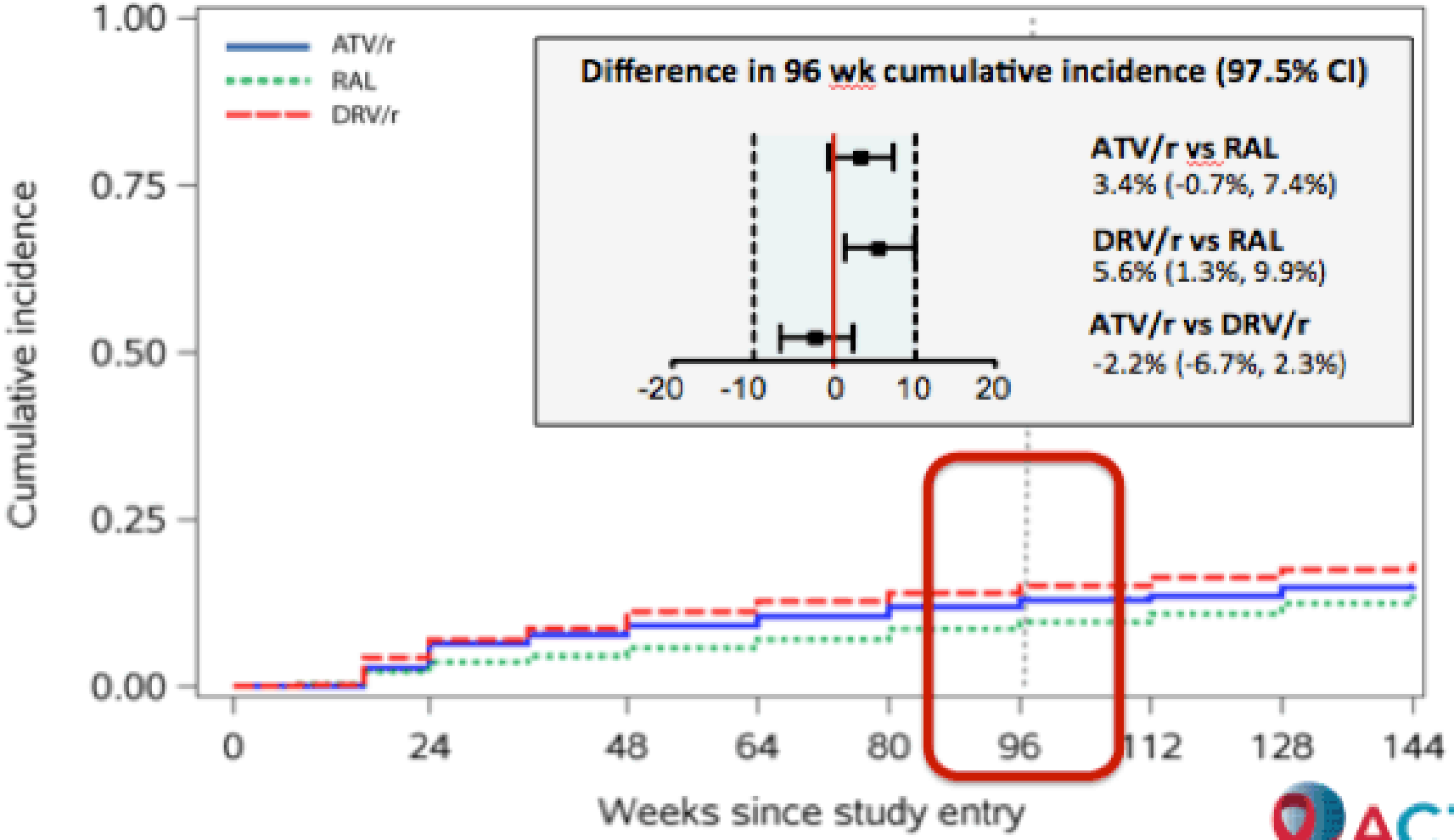
Cumulative Incidence of Virologic Failure



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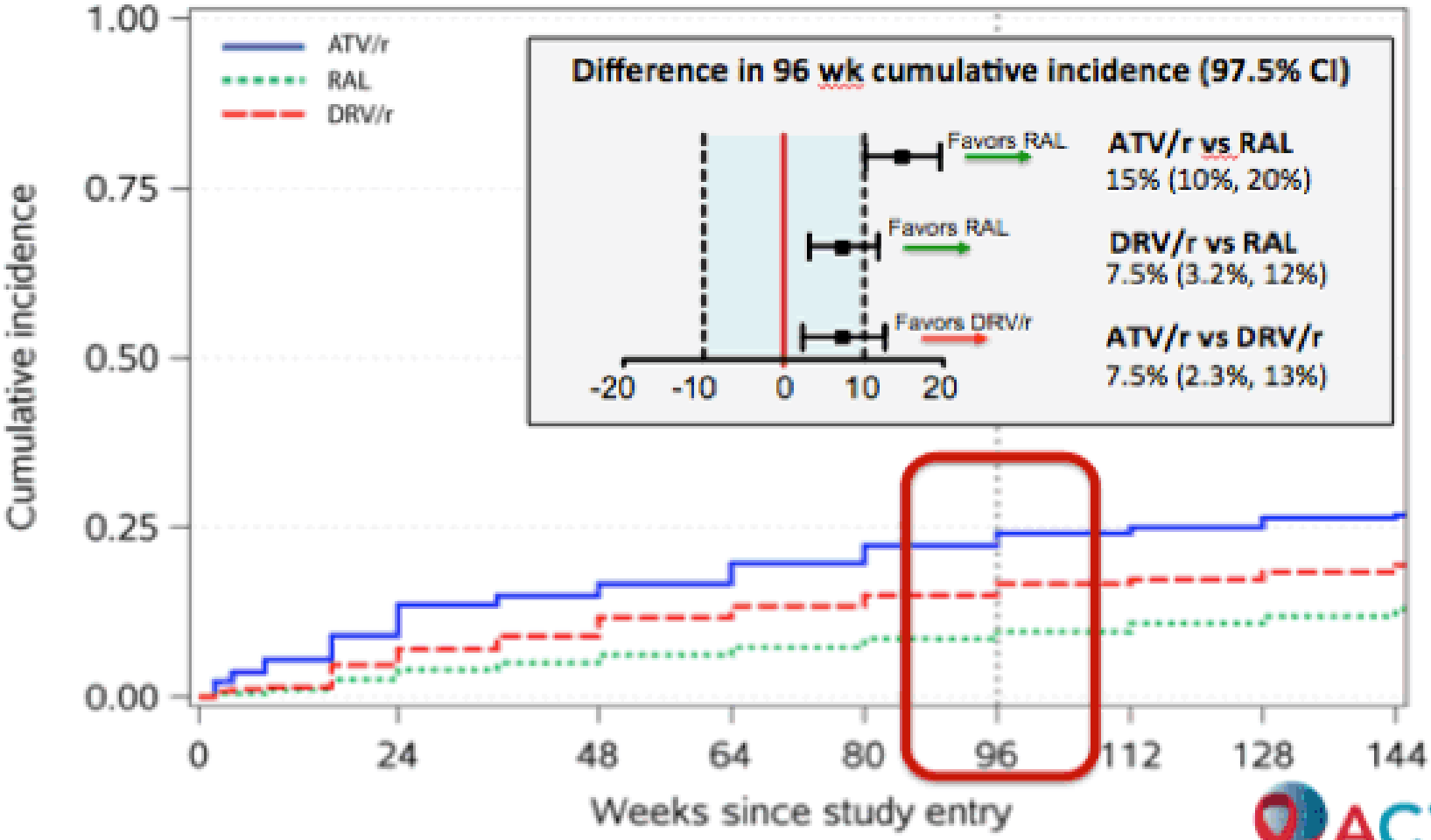
Cumulative Incidence of Virologic or Tolerability Failure



*Consistent results seen with TLOVR at a 200 copies/ml threshold

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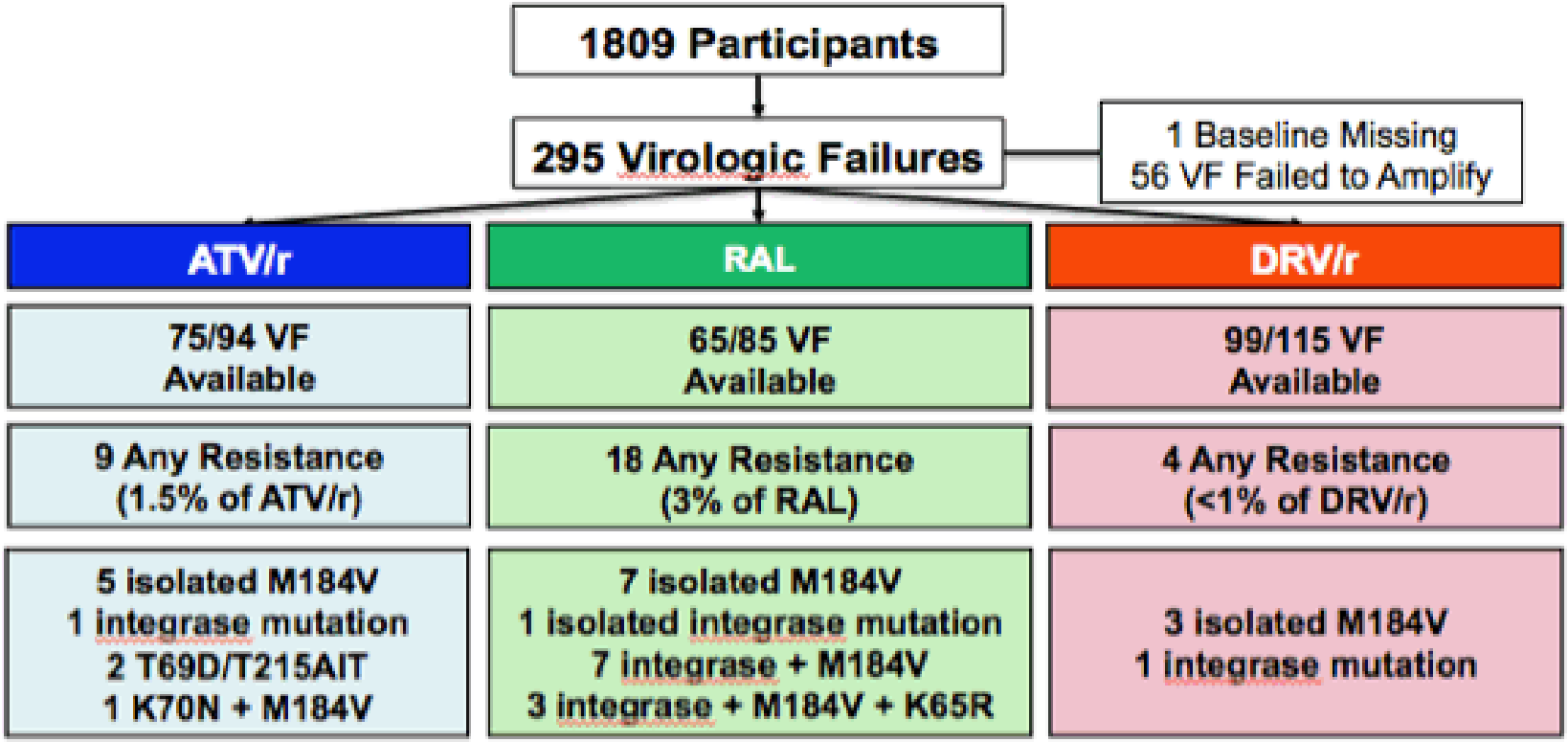
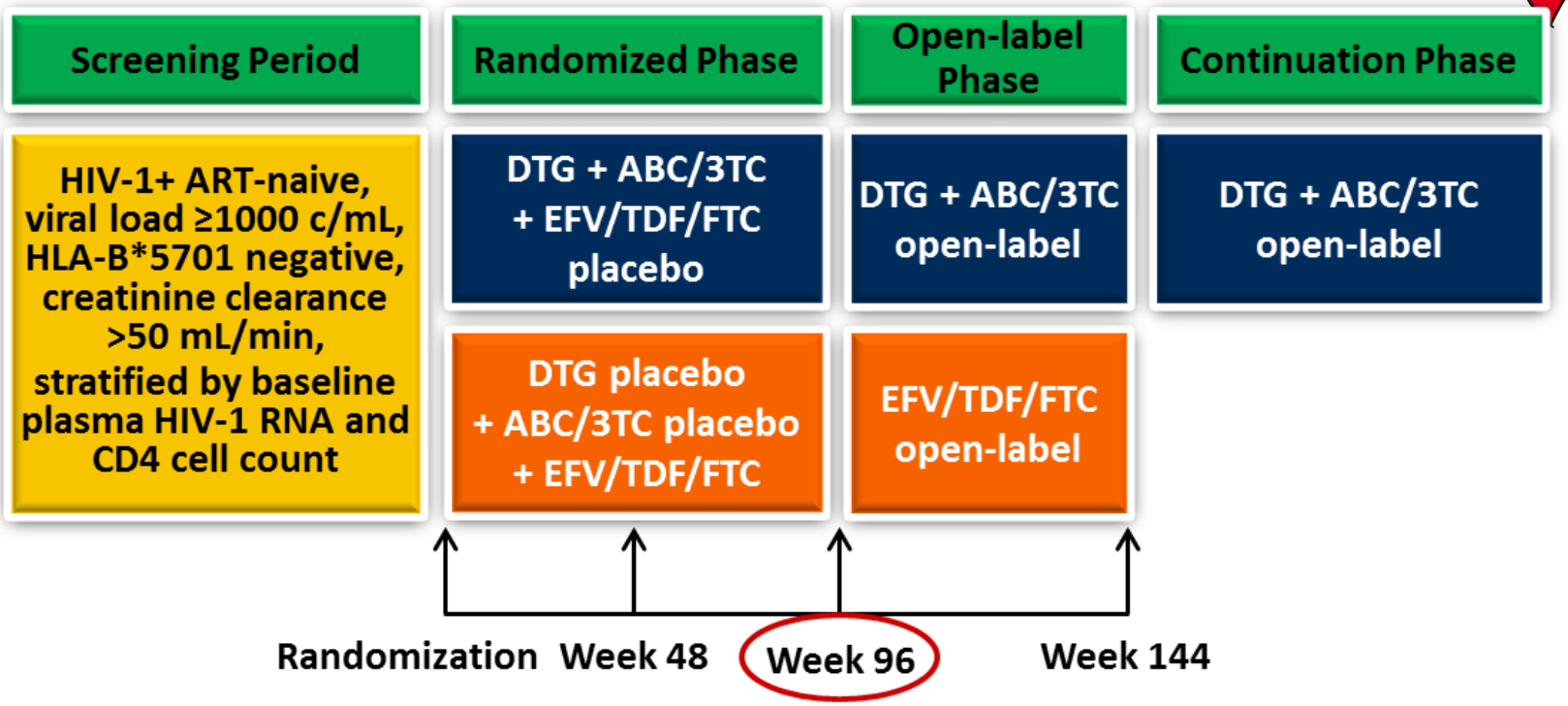
Resistance to Study Agents



ING11467 (SINGLE)



Walmsley et al. CROI 2014; Boston, MA. Poster 337.

ING11467 (SINGLE)

Protocol-Defined Virologic Failure

Time point	DTG + ABC/3TC QD (n=414)	EFV/TDF/FTC QD (n=419)
Up to Week 48	18 (4%)	17 (4%)
Week 60	1 (<1%)	3 (<1%)
Week 72	1 (<1%)	3 (<1%)
Week 84	5 (1%)	2 (<1%)
Up to Week 96	25 (6%)	25 (6%)

- PDVF was defined as confirmed HIV-1 RNA ≥50 c/mL at or after Week 24.
  - After 2 years of therapy, the majority of subjects who met PDVF at confirmed failure had low-level viremia (<200 c/mL HIV-1 RNA):
    - 20/25 (80%) subjects on DTG + ABC/3TC and 17/25 (68%) subjects on EFV/TDF/FTC

ING11467 (SINGLE)

Resistance Mutations in Individuals Who Met PDVF Criteria

Mutation	DTG + ABC/3TC QD (n=414)	EFV/TDF/FTC QD (n=419)
NRTI TE major mutations	0	1 (K65R)
NNRTI TE major mutations	0	6 (K101E, K103N, G190A)*
INI-r TE major substitution	0**	0

TE = treatment emergent

*n=1 with K101E, n=1 with K103N, n=2 with K103K/N, n=1 with G190A and n=1 with K103N + G190A

**E157Q/P polymorphism detected with no significant change in IN phenotypic susceptibility

Resistance Pattern EVG/C/FTC/TDF N=18/701 # 587, R Kulkarni et al.

Table 4. First Failure Analysis of Subjects with Emergent EVG/COBI/FTC/TDF Resistance (Integrated Analysis of Studies 102 and 103)

- Subjects with drug resistance at confirmation visit assessed for resistance at first failure

	EVG/COBI/FTC/TDF (n = 701) Confirmation Sample Resistance	EVG/COBI/FTC/TDF (n = 701) Resistance at First Failure
Resistance Analysis Population % (n)	6.0% (42)	2.6% (18)
Subjects with Data for RT and/or IN	6.0% (42)	2.4% (17)
Developed Any Primary Resistance to Study Drugs % (n)	2.6% (18)	2.1% (15)
Baseline to Week 48	1.9% (13)	1.4% (10)
>Week 48 to Week 96	0.4% (3)	0.4% (3)
>Week 96 to Week 144	0.3% (2)	0.3% (2)

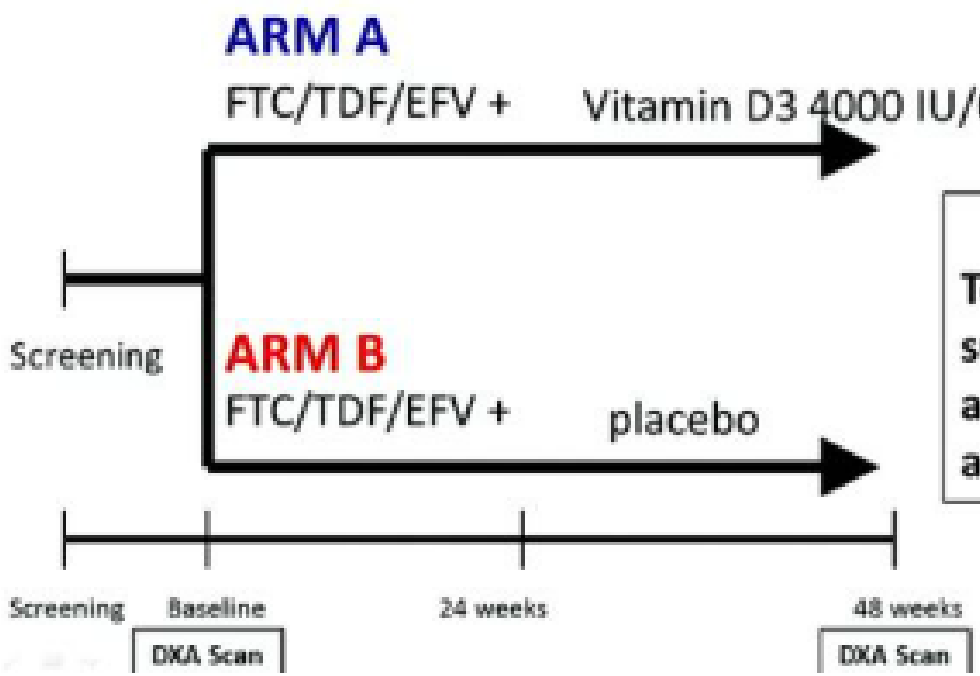
Resistance Pattern EVG/C/FTC/TDF N=18/701

Emergent Primary Resistance Mutations % (n)	NRTI-R	FTC/TDF **2.4% (17)**	FTC/TDF **2.0% (14)**
		M184V/I 2.4% (17) K65R 0.7% (5)	M184V/I 2.0% (14) K65R 0.4% (3)
	INSTI-R	EVG **2.1% (15)**	EVG **1.1% (8)**
		E92Q 1.3% (9) N155H 0.7% (5) Q148R 0.4% (3) T66I 0.3% (2) T97A 0.1% (1)	E92Q 0.4% (3) N155H 0.3% (2) Q148R 0.1% (1) T66I/A/V 0.1% (1) T97A 0.1% (1)

High-Dose Vitamin D and Calcium Attenuates Bone Loss with ART Initiation: Results from ACTG A5280

A Prospective, Randomized Pilot Trial of High-Dose Vitamin D and Calcium for Bone Health in HIV-Infected Individuals Initiating Highly Active Antiretroviral Therapy

Overton ET, Chan ES, Brown TT, Tebas P, McComsey GA, Melbourne K, Napoli A, Hardin R, Ribaudo HJ, Yin MT for the A5280 Study Team.



Primary Objective

To evaluate the impact of supplementation with vitamin D and calcium on bone loss associated with initiation of ART.

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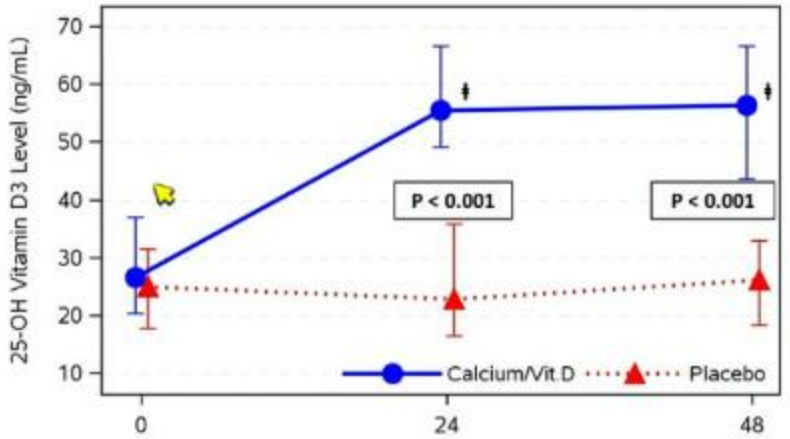
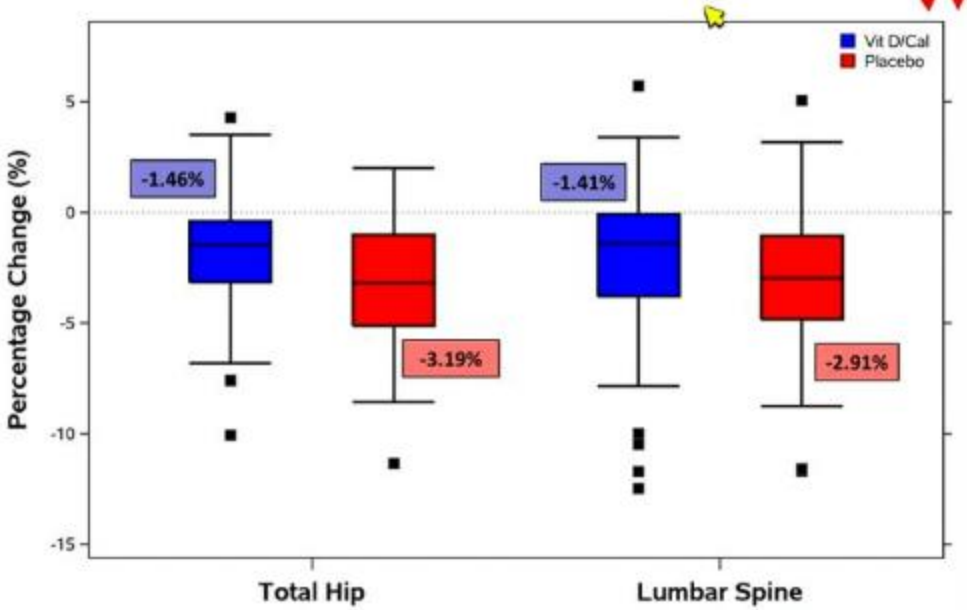
Changes in 25(OH) Vitamin D3



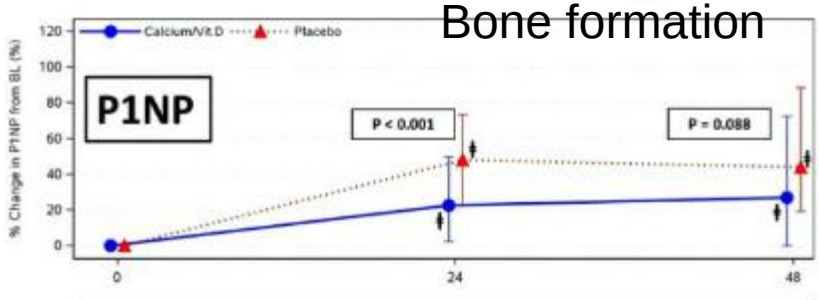
Median Values	Week 0	Week 24	Week 48
Calcium/VitD	26.7 ng/mL (67 nmol/L)	55.6 ng/mL (139 nmol/L)	56.4 ng/mL (141 nmol/L)
Placebo	25.1 ng/mL (63 nmol/L)	22.9 ng/mL (57 nmol/L)	26.2 ng/mL (66 nmol/L)
P value	-	<0.001	<0.001

Percent Decline in BMD from Baseline to 48 Weeks

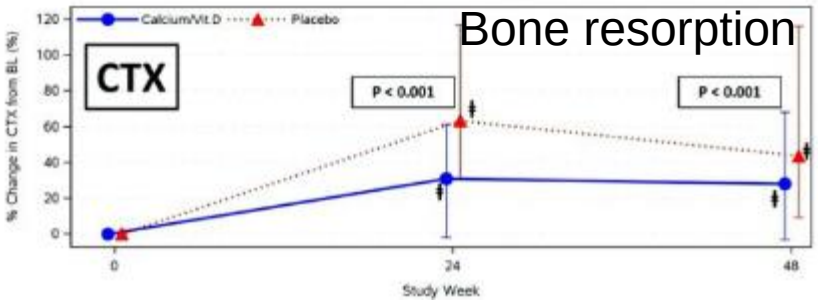


Percent Changes in Bone Turnover Markers

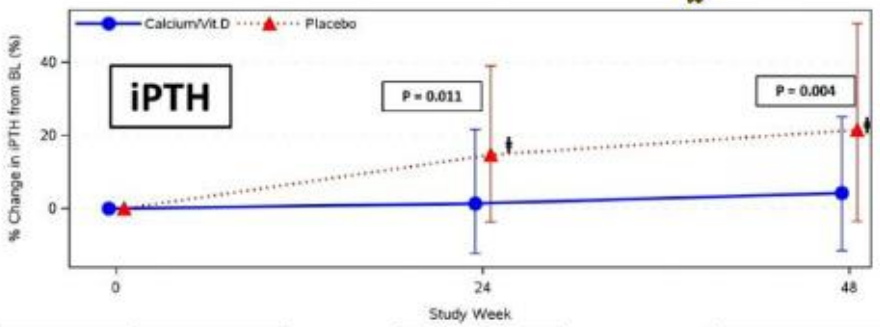
Bone formation



Bone resorption



Changes in iPTH & Phosphate Excretion

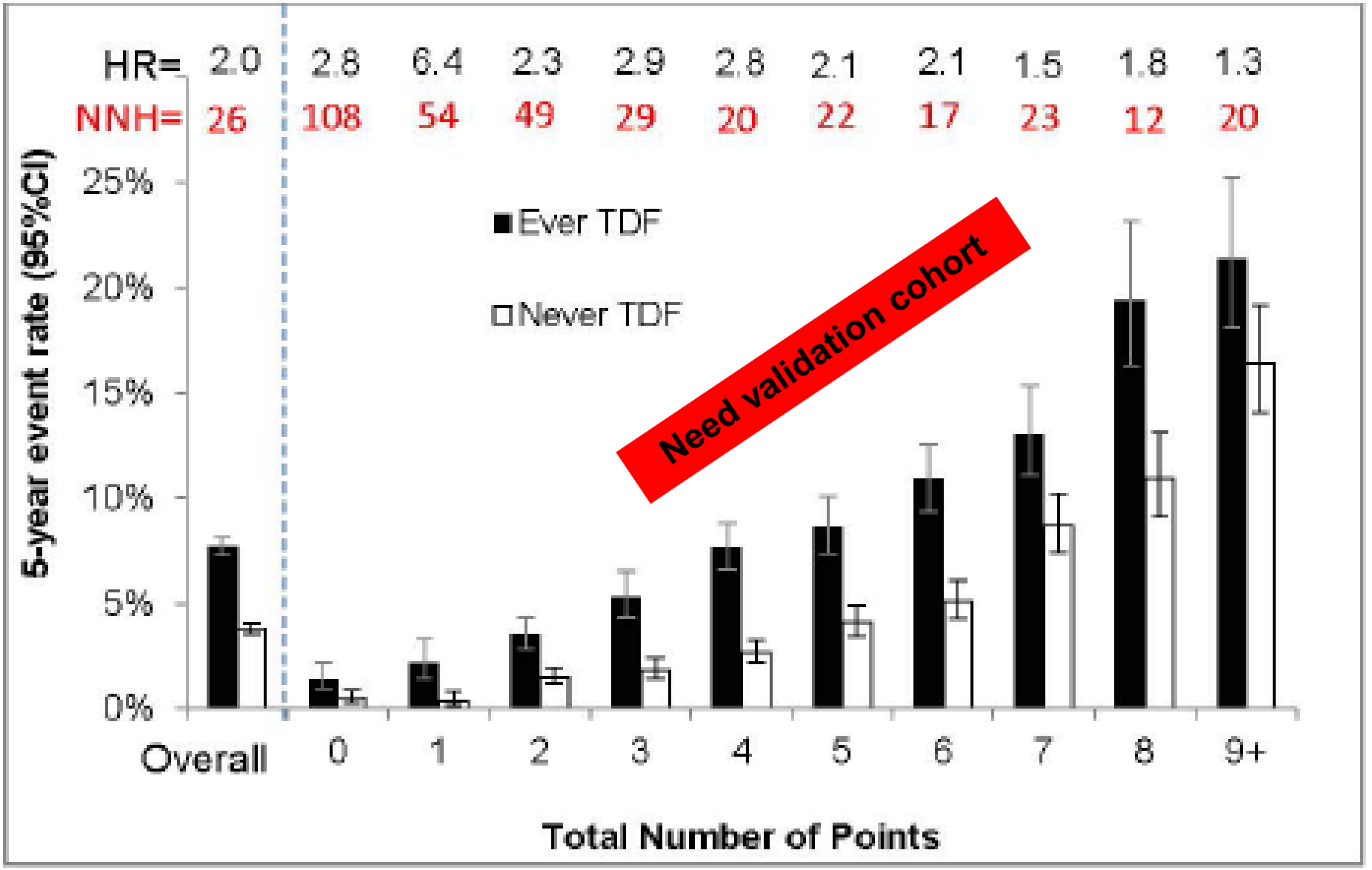


Median Values	Week 0	Week 24	Week 48
Calcium/VitD	28.3 pg/mL	29.2 pg/mL	30.0 pg/mL
Placebo	27.6 pg/mL	32.9 pg/mL	33.1 pg/mL
P value	-	0.011	0.004

798 **A Chronic Kidney Disease Risk Score To Determine Tenofovir Safety Among HIV+ Male Veterans**

Rebecca Scherzer[1], Monica Gandhi[1], Michelle Estrella[2], Phyllis Tien[1], Steven Deeks[1], Carl Grunfeld[1], Carmen Peralta[1], Michael Shlipak[1]

[1]University of California San Francisco, San Francisco, CA, United States, [2]Johns Hopkins University, Baltimore, MD, United States



Critical Issues in MTCT: Maternal Health, and HIV Treatment in Children

Lower Newborn Bone Mineral Content Associated With Maternal Use of Tenofovir Disoproxil Fumarate

George K. Siberry

- **Tenofovir SubStudy of SMARTT**
  - Gestational age ≥ 36 weeks
  - Classified by Maternal TDF use
    - No-TDF arm: no TDF during entire pregnancy
    - TDF arm: ≥ 8 weeks TDF use in 3rd trimester

Study Design - Primary Endpoint & Analysis

- **Endpoint: Whole-body bone mineral content (WB BMC)**
  - Obtained at age 2 weeks (window: 0-4 weeks)
  - Hologic dual-energy X-ray absorptiometry (DXA) scanner with software for infant whole-body DXA
  - Training: Single DXA technician-educator performed infant DXA training at each site
  - Standardization: Tufts Body Composition Center

Mean Whole-Body Bone Mineral Content (BMC) Significantly Lower in TDF Arm Infants

	No-TDF Arm	TDF Arm	P-Value
Mean Whole-Body BMC	63.8 g	56.0 g	0.002

Mean BMC was 7.8g lower in TDF arm, representing a significant difference of 12.2% or 0.5 SD.

Multivariable Model: Adjusted Mean BMC Lower in TDF Arm

	Adjusted* Mean Difference in BMC	P value
Whole-body BMC	**6.4g lower in TDF arm** (95%CI: 2.1, 10.7)	0.004
	Reminder: Unadjusted mean BMC diff: 7.8g	

***Adjusted for:**

- **site;**
- **infant gestational age, body length, race/ethnicity and age at DXA;**
- **maternal boosted PI use, age, and smoking.**