

ACTG 5211

Phase II Study of the Safety
and Efficacy of Vicriviroc (VCRV)
in HIV+ Treatment-Experienced
Subjects: 48-week Results

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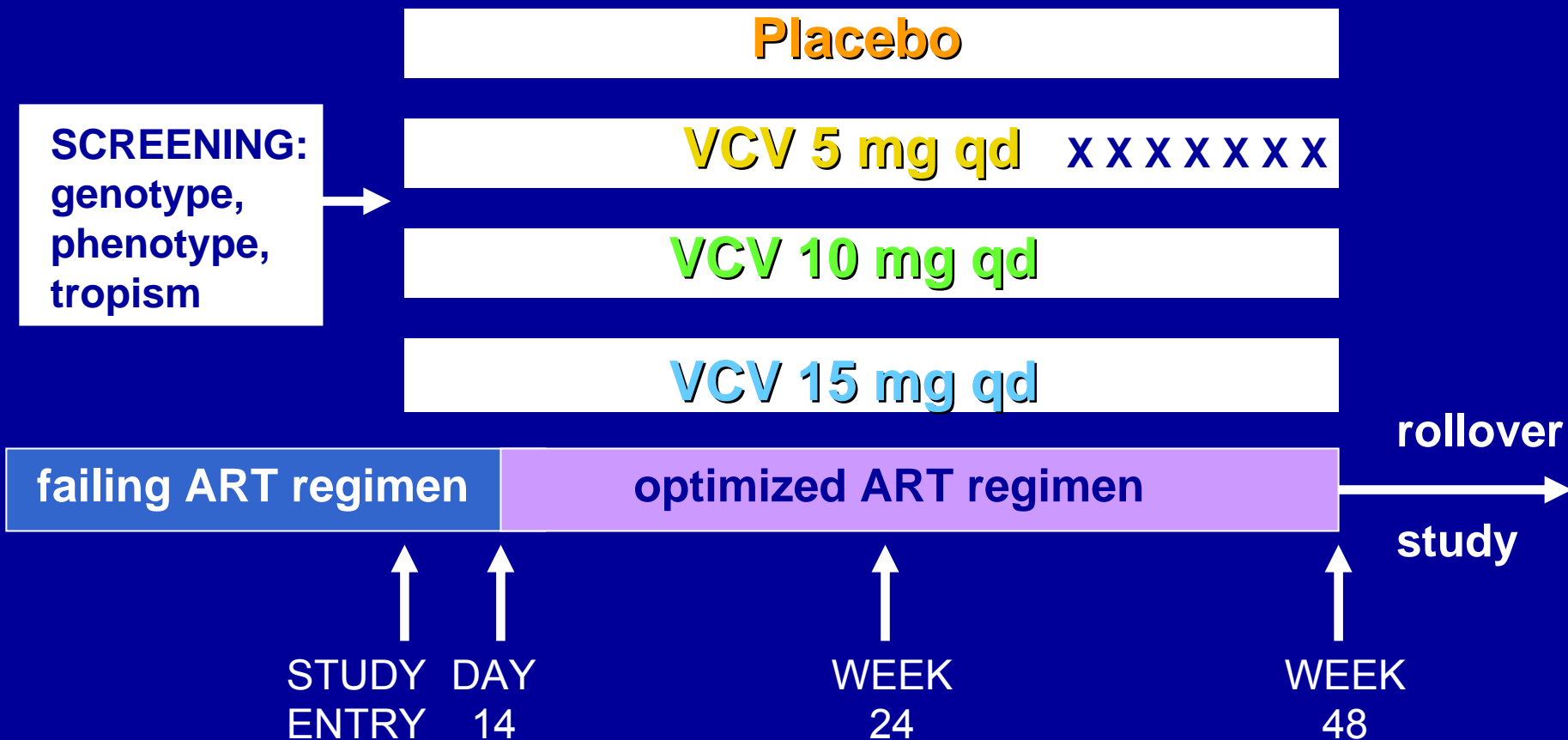
for the A5211 Protocol Team



A5211: Study Design (1)

- Study objective: To evaluate the safety, tolerability and antiretroviral activity of a VCV-containing regimen.
- Study population:
 - ART-experienced adults
 - HIV RNA ≥ 5000 copies/ml on a RTV-containing regimen
 - R5 phenotype (Trofile assay)
 - Stratified by:
 - enfuvirtide use; baseline CD4 $<$ or ≥ 50 cells/ μ L

A5211: Study Design (2)



All regimens included 100-800 mg RTV

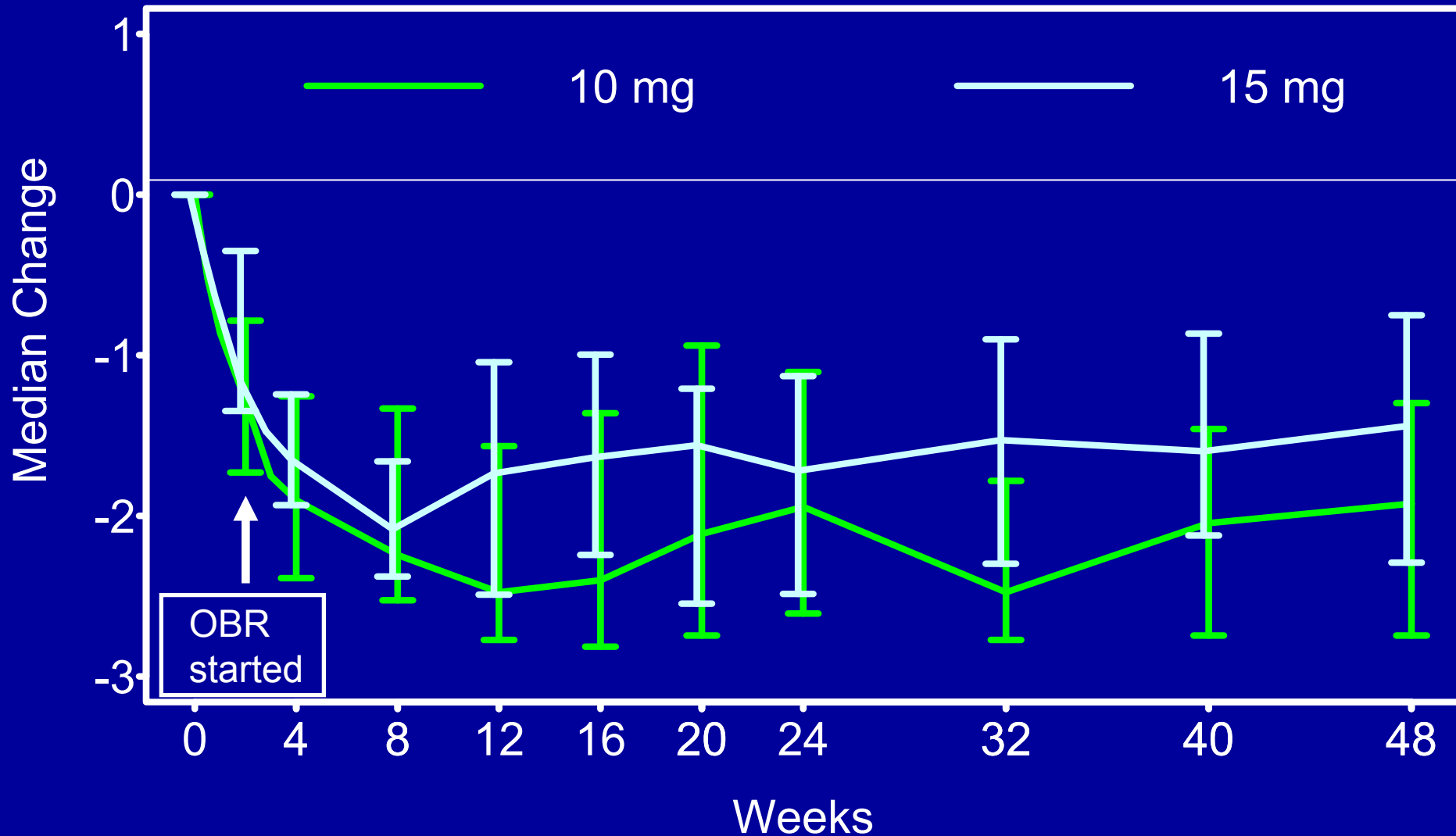
Virologic failure: confirmed $<1 \log_{10} \downarrow$ in HIV RNA at ≥ 16 wks

Cross-over option to VCV following virologic failure

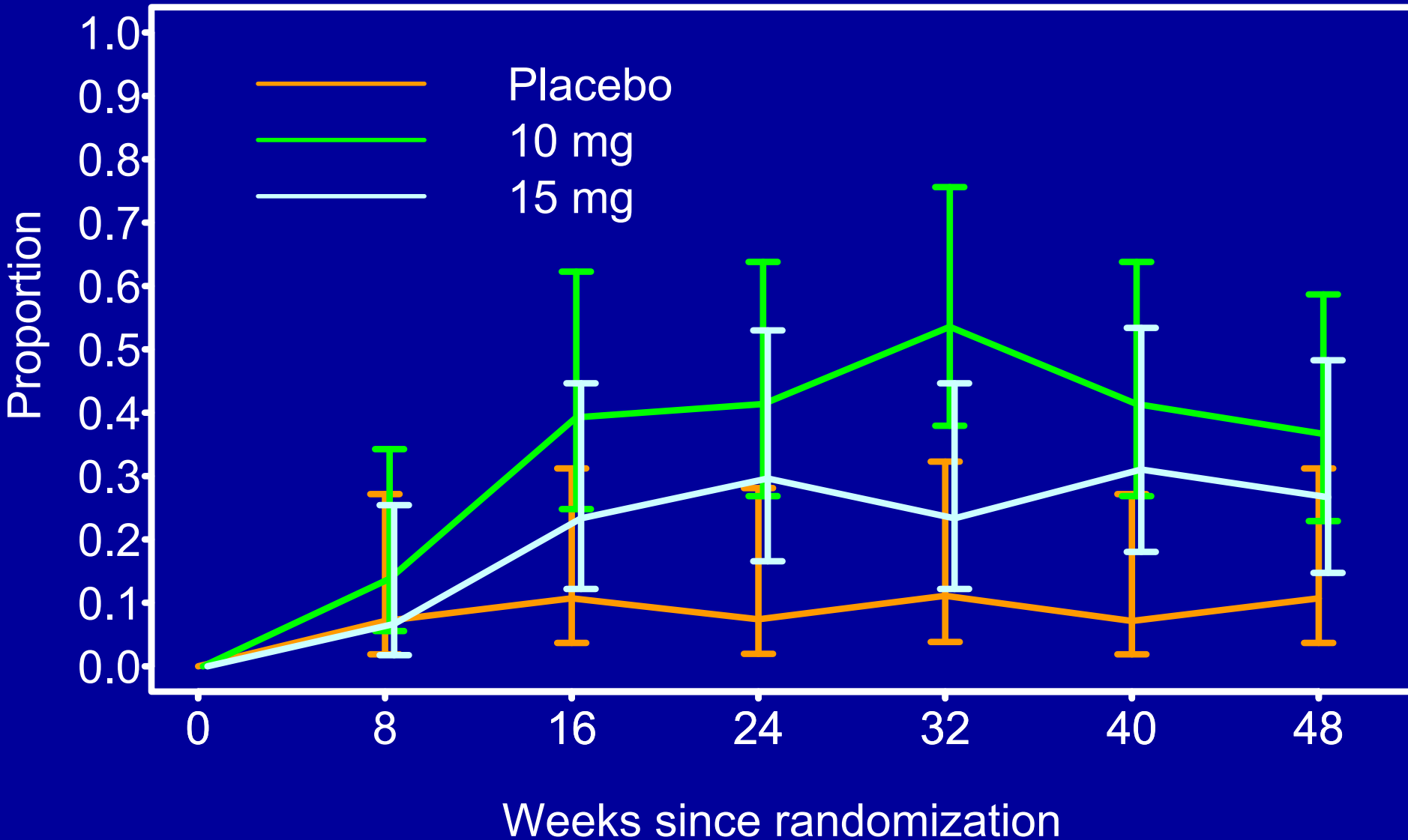
A5211: Baseline and Disposition

- Baseline characteristics:
 - N = 118 subjects
 - median age 46; 92% men, 8% women
 - 20% black, 12% Hispanic, 66% white, 2% other
 - 33% were ENF-experienced
 - Median HIV RNA 36380 cps/ml; CD4 146 cells/ μ L
 - 100% had R5 virus at screening
- Disposition (through 48 weeks):
 - Study treatment discontinued early:
82% (PBO), 30% (10 mg), 37% (15 mg)
 - Virologic failure:
86% (PBO), 27% (10 mg), 33% (15 mg)

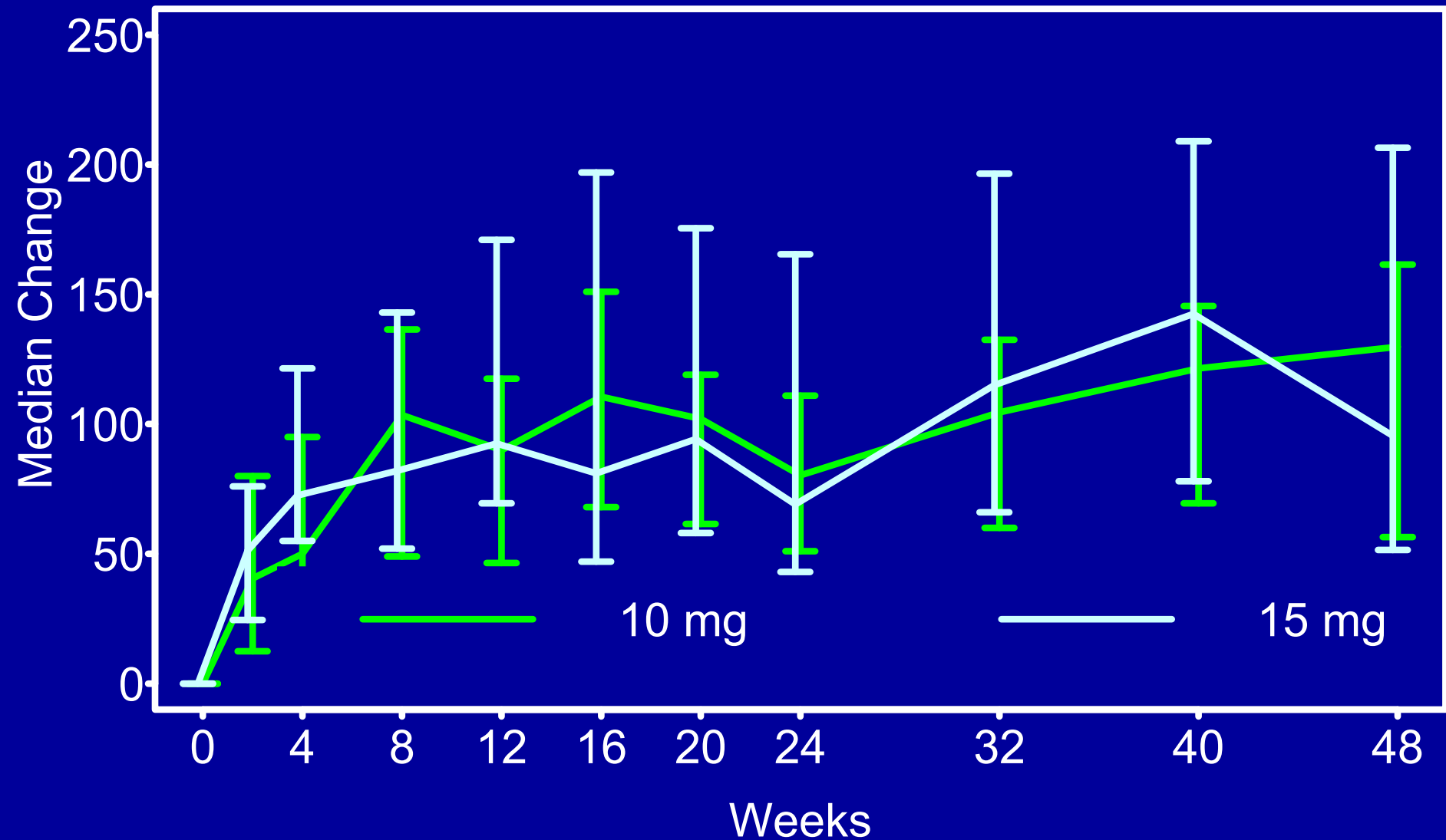
A5211: Median Change in HIV RNA (log₁₀ cps/ml; ITT)



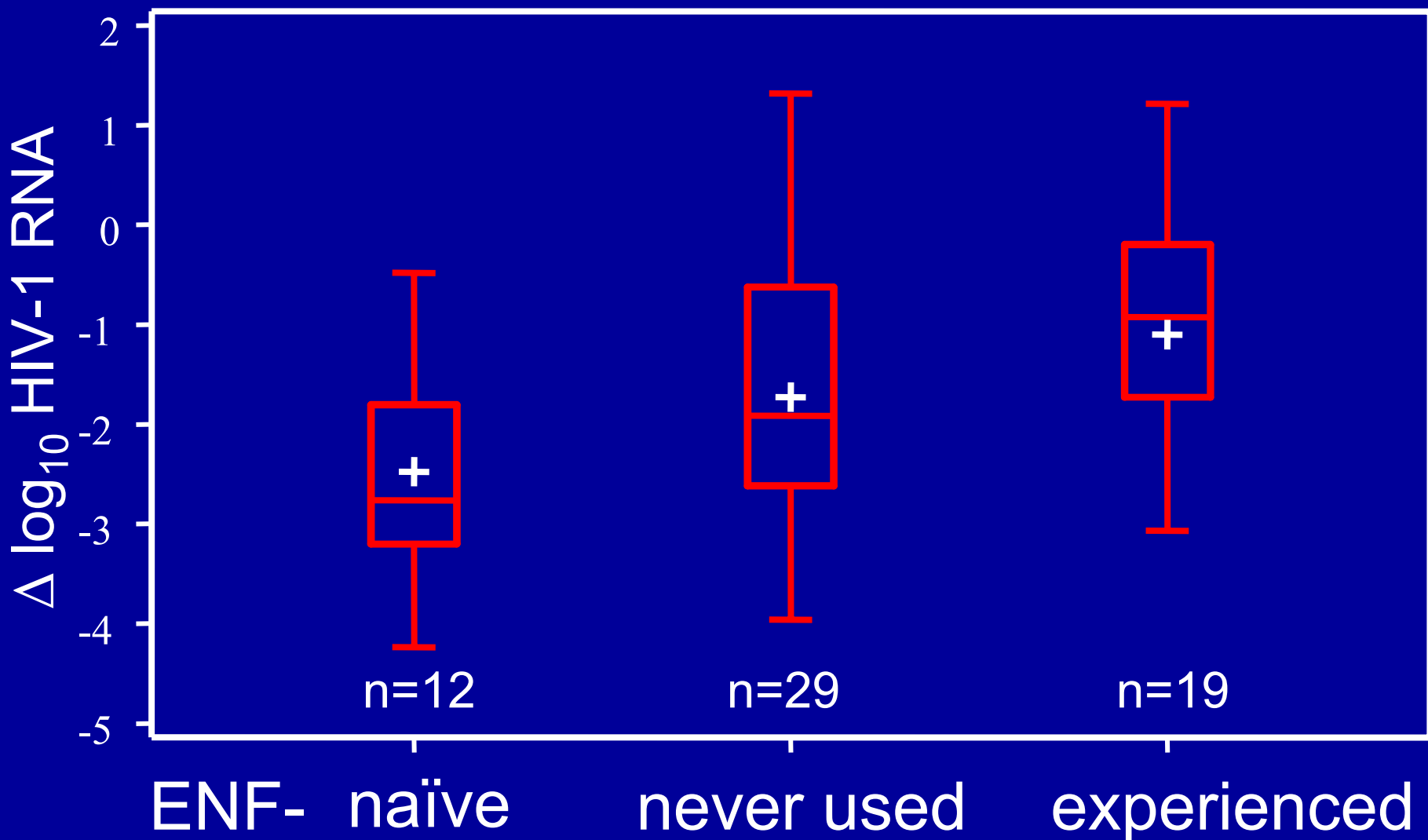
A5211: Proportion with HIV RNA <50 cps/ml



A5211: Median Change in CD4 Cell Count (ITT)



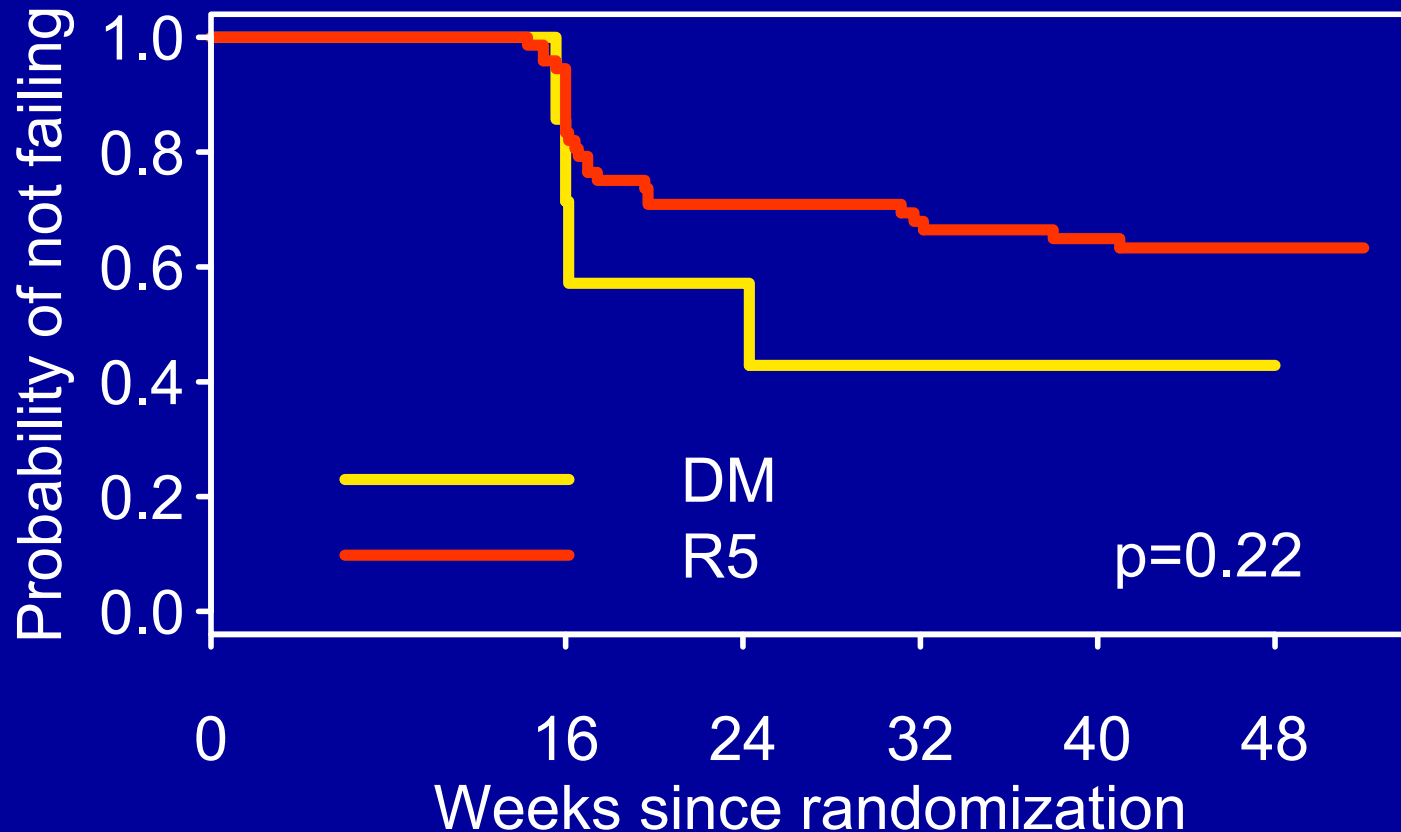
Week-48 Virologic Response for VCV (10 and 15 mg) by Enfuvirtide Use



A5211: Tropism

- Screening: 118 (100%) with R5 virus
- Study entry: 102 (86%) with R5 virus, 12 (10%) dual/mixed, 4 (4%) missing
- On study rx (n=106 with R5 or missing) 18 subjects changed tropism:
 - 3 on PBO (2 following crossover to VCV)
 - 15 on VCV: 8 (5 mg), 4 (10 mg), 3 (15 mg)
- Of 26 subjects with R5 virus on VCV who experienced virologic failure, 9 (35%) had D/M or X4 virus.

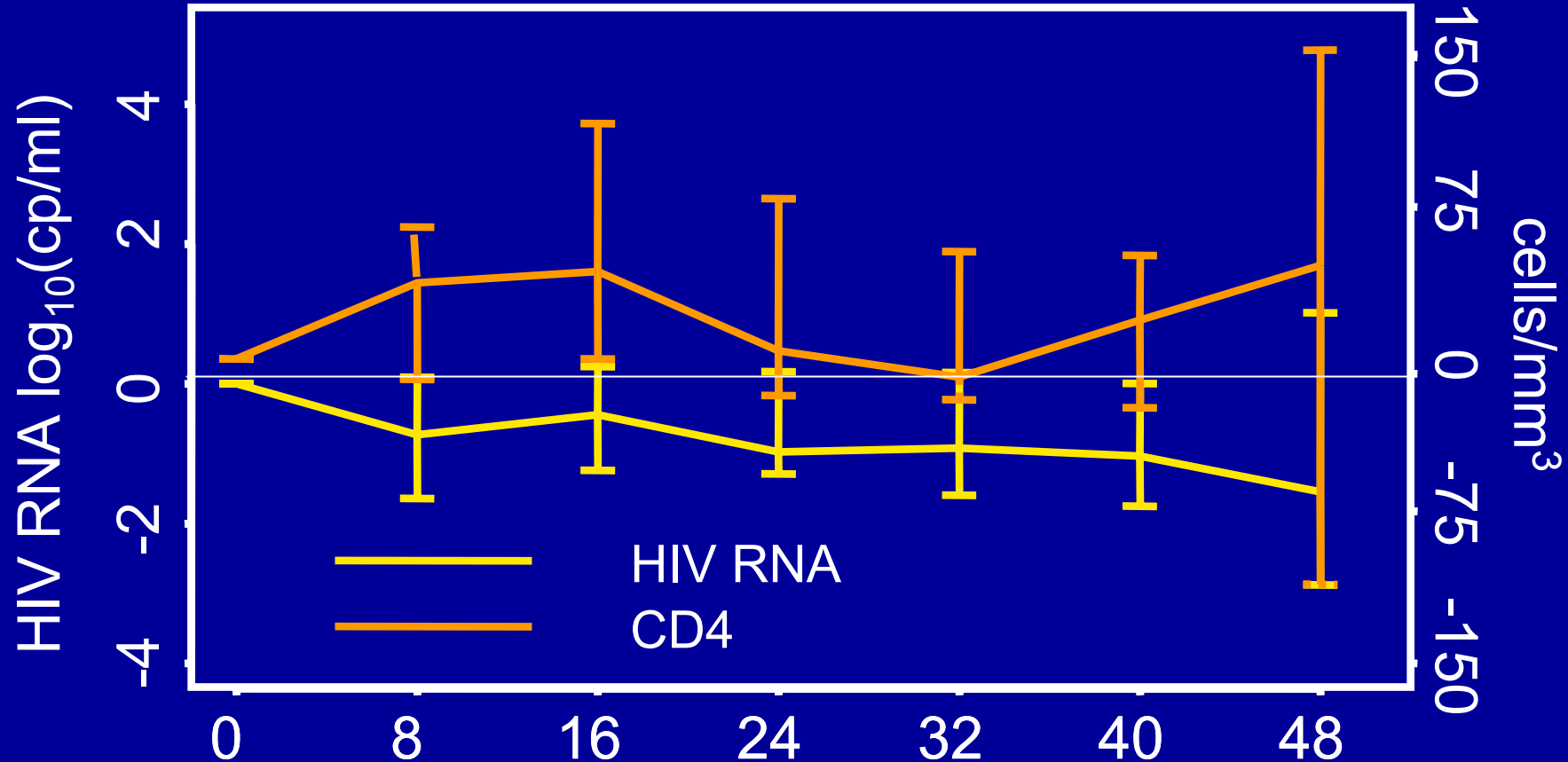
Time to Virologic Failure on VCV by Baseline Tropism



Number of subjects at risk:

DM	10	5	4	3	3	0
R5	80	60	51	46	41	28

Median Change in HIV RNA and CD4 after Tropism Change on VCV



Weeks since first DM or X4 co-receptor usage

Number of subjects contributing data:

CD4	23	20	16	17	17	12	7
HIV RNA	23	20	16	17	17	13	7

A5211: Adverse Events (1)

- No significant difference for grade 3 or 4 adverse events among 4 arms (pairwise comparisons, $p \geq 0.6$)
- No seizures reported

A5211: Adverse Events (2)

- Malignancies:
 - 8 subjects randomized to VCV (through 48 wks or on rollover study)
 - 6 previously reported at 24 weeks:
NHL X 2; Hodgkin's disease X 2;
gastric adenocarcinoma; SCC
 - Basal cell carcinoma (VCV 10 mg)
 - KS recurrence (VCV 5 mg)
 - 2 subjects randomized to PBO, both previously reported at 24 weeks:
 - SCC X 2 (one on VCV 10 mg X 3 months)

A5211: Conclusions

- In rx-experienced pts:
 - Following optimization of background ART, VCV (10 or 15 mg, with RTV) demonstrated sustained antiretroviral activity over 48 weeks.
 - Co-receptor change documented in ~1/3 of subjects on VCV at virologic failure.
- VCV was generally well tolerated.
- The relationship of VCV to malignancy remains uncertain.
- Longer-term follow-up continues.

A5211: Acknowledgments (1)

A5211 Protocol Team:

Co-chairs: Daniel Kuritzkes, MD

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A5211: Acknowledgments (2)

A5211 Protocol Team (continued):

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Laboratory Tech:	Antoine Simmons
Community Rep:	Jim Smith

A5211: Acknowledgments (3)

Pharmaceutical Supporters:

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A5211: Acknowledgments (4)

- ACTG study sites:

Harvard-BMC, Stanford, Rochester, Pitt-Georgetown, Cornell, NYU, Emory, U Washington, Vanderbilt, U Colorado, Case Western, UCLA, Wash U, Ohio State, Rush, Beth Israel, Miriam/RI, UNC, UCSF, U Iowa, U Texas/Galveston, UCSD, Wishard/Indiana, U Hawaii, Penn

- And the study participants!