

***Phase II Dose Ranging  
Study of Vicriviroc in  
Tx-naive Patients (3802):  
A final analysis***

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# Study Objectives

To evaluate the safety, tolerability, and antiviral activity of vicriviroc in CCR5-only HIV-infected treatment-naïve individuals

- Safety monitored by clinical findings, laboratory parameters and adverse event reporting
- Plasma HIV RNA measured at screening, baseline, day-4, day-7, day-14, monthly to 6 months, then bimonthly
- Tropism tests at screening, baseline, day-14, wk-24, and at virologic failure or wk-48
- PK trough concentrations measured at virologic failure or wk-48
- 12-lead EKG at screening, day-14, wk-24, and wk-48

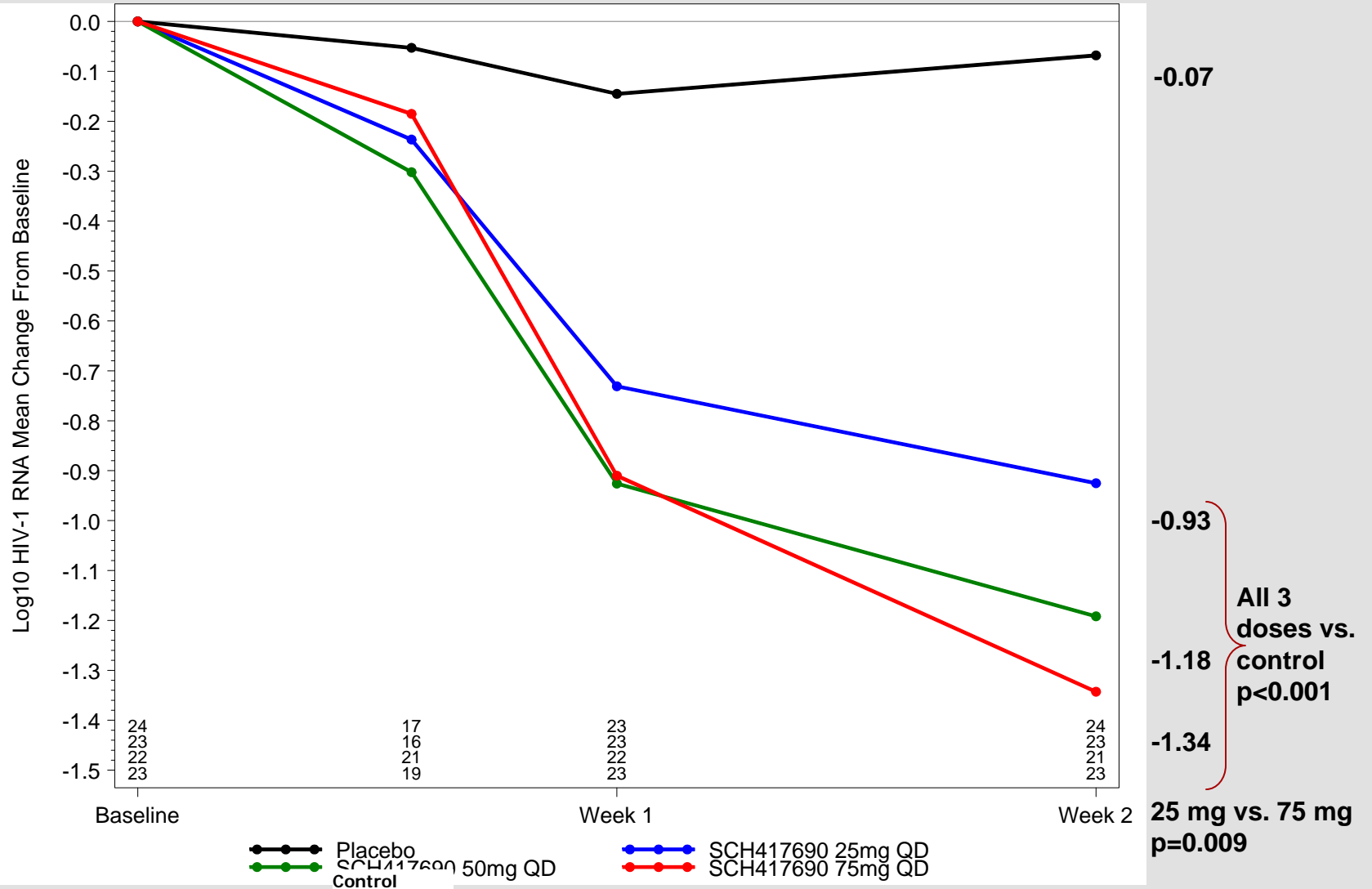
# Study Population

- HIV-infected ART-naïve individuals
- Only CCR5-tropic virus detected
- CD<sub>4</sub> count >150 cells/μL
- RNA ≥5000 copies/mL
- Baseline Characteristics
  - Age: median age 37 years (range 18-72); 80% male
  - CD4 count: median 289.5 cells/μL (range 103-687)
  - HIV subtype B: 72 (78%) of isolates
  - Log HIV RNA: mean 4.78 (3.55-6.02); 64% ≥100,000
  - Characteristics well balanced across dose groups

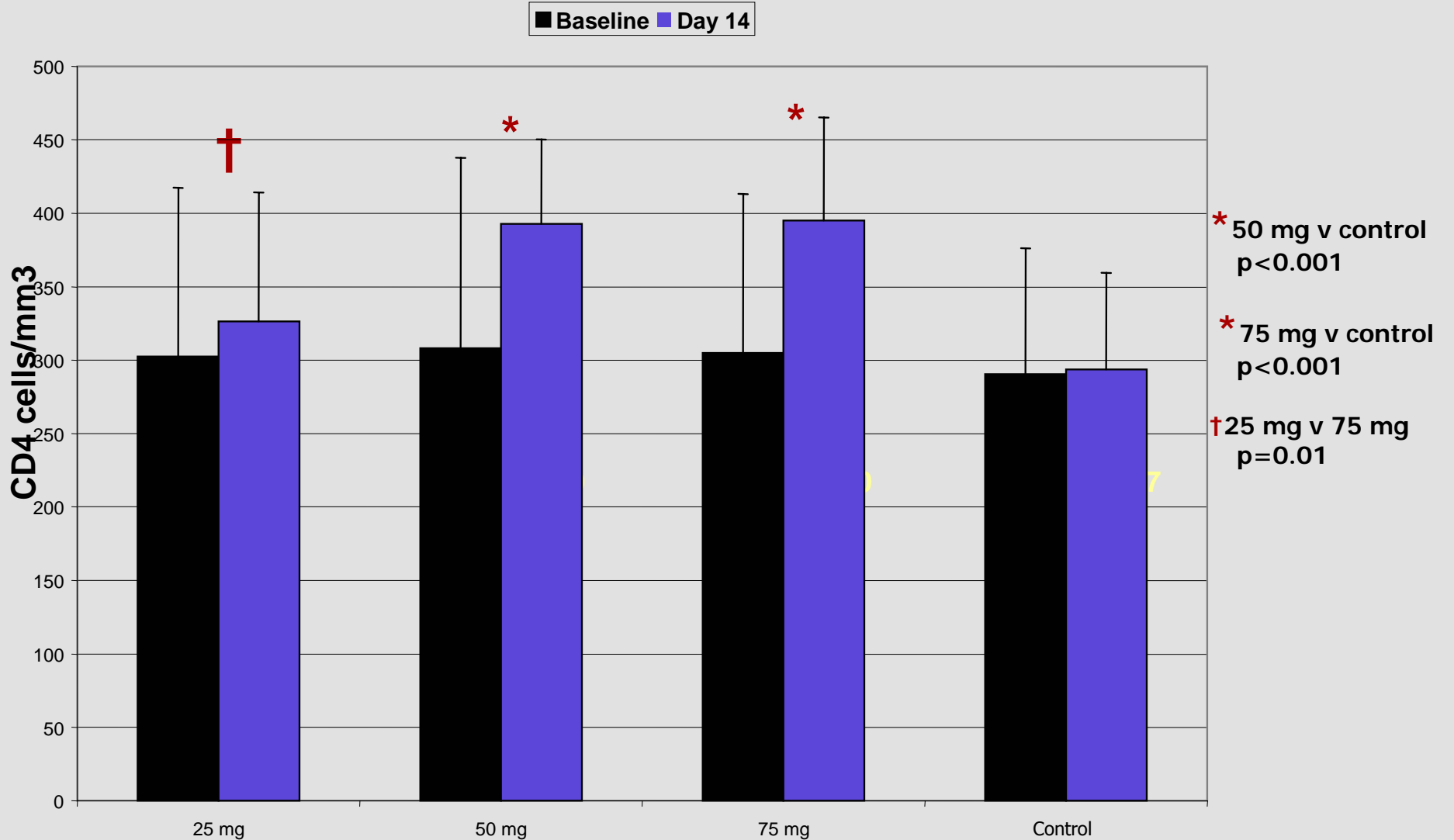
# Treatment Duration

Treatment Duration	Vicriviroc 25mg	Vicriviroc 50mg	Vicriviroc 75mg	Control
≥ 14 days	23	21	23	24
≥ 3 months	22	20	20	20
≥ 6 months	9	19	19	20
Mean (weeks)	27	34	35	33
Median (weeks)	24	33	36	36
Duration (weeks)	8 - 53	1 - 57	6 - 59	2 - 50

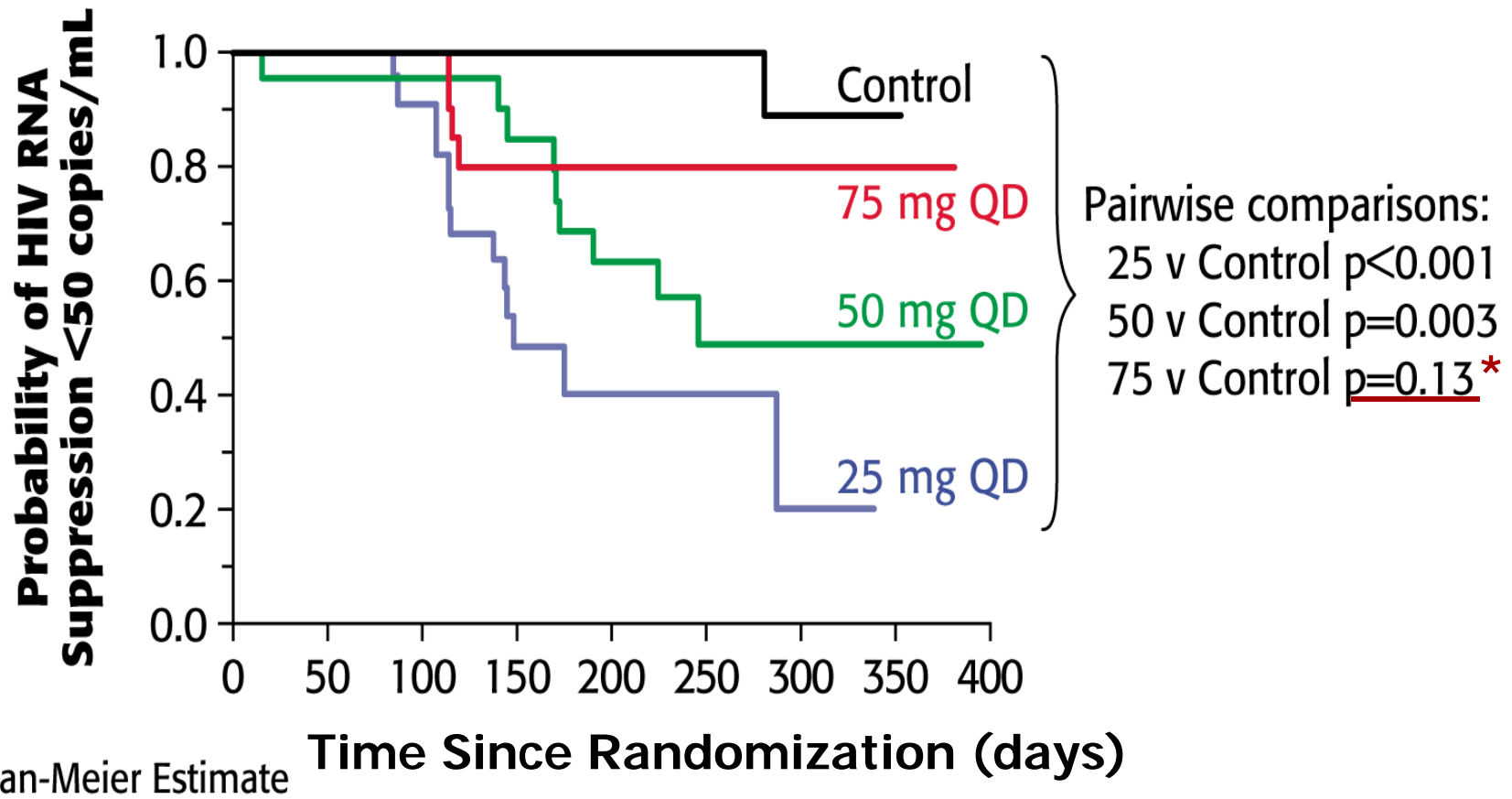
# Mean HIV RNA change Baseline to Day 14



# CD4 counts at baseline and Day 14



# Time to Viral Breakthrough



# Resistance

- At baseline, viral isolates from all patients were susceptible to vicriviroc (IC<sub>50</sub>, 0.4-27 nM; % maximal suppression 85-100%)
- At breakthrough, resistance to vicriviroc was not consistent
  - 22 of 26 patients with virologic breakthrough remained fully susceptible
  - 4 patients had reduced % maximal suppression <75%
- M184V/I mutation was present in 22/22 breakthrough isolates; M41L present in 1/22 isolates
- Numerous amino acid changes observed throughout gp160
  - no specific pattern of mutations associated with treatment doses, phenotypic susceptibility or viral tropism

# Tropism

- Eight subjects experienced tropism shifts from R5 to D/M or X4 phenotype during study, 3 on control arm
- Viral tropism shifts appeared unrelated to treatment assignment or vicriviroc dosage
  - Six of the 8 shifts were during monotherapy (3 control, one 25 mg, two 75 mg)
  - Tropism shifts were seen in the absence of vicriviroc exposure

# Tropism Shift vs. Viral Breakthrough

<50 copies/mL Threshold

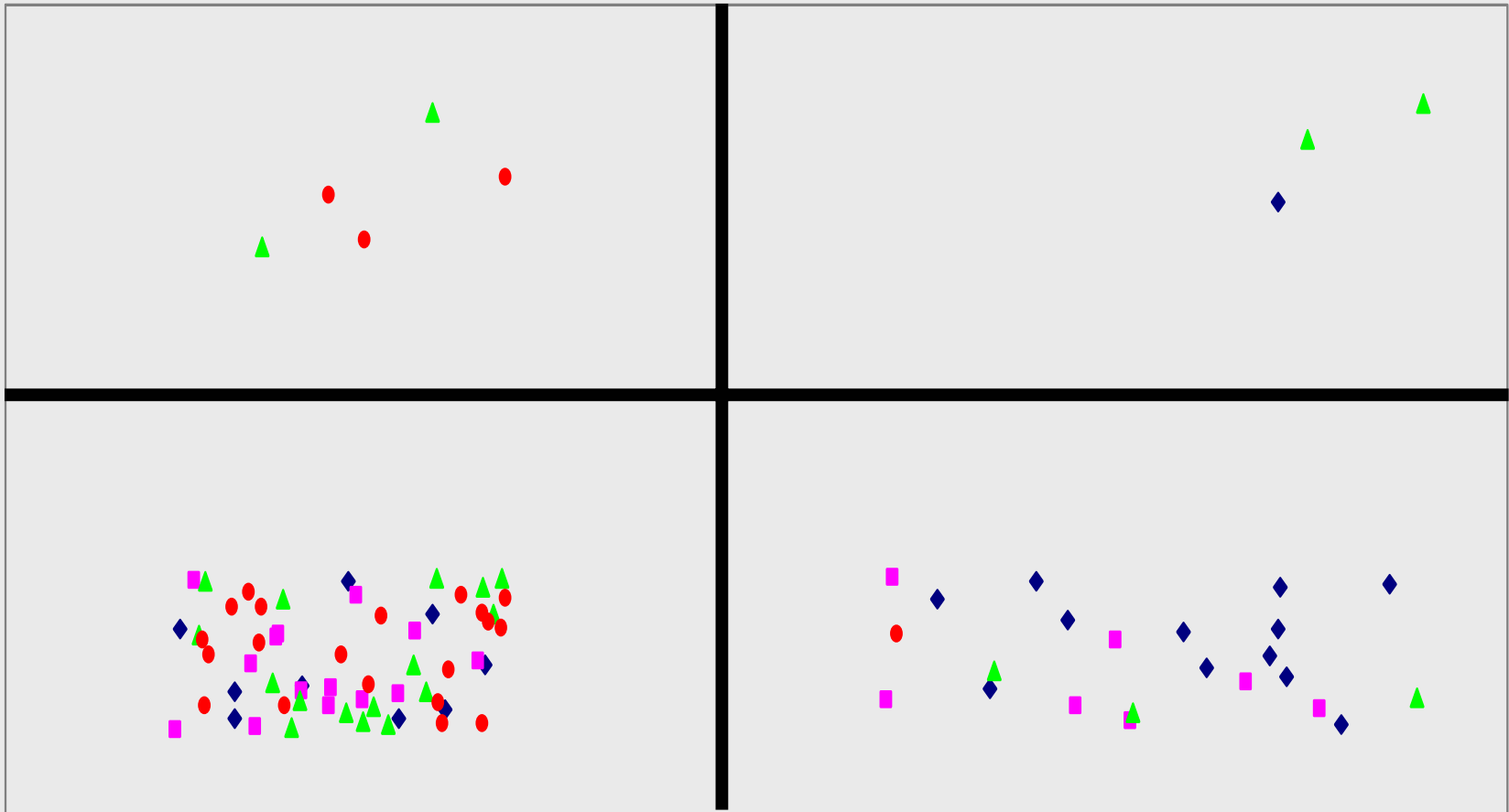
N=92

No Virologic Breakthrough

Virologic Breakthrough

Tropism Shift

No Tropism Shift



◆ 25 mg ■ 50 mg ▲ 75 mg ● Efavirenz

# Overall Safety Results

- Vicriviroc was well tolerated
- No evidence of seizures, cardiotoxicity, hepatotoxicity, lymphoma or adenocarcinoma
- No clinically significant changes in lab values
- No dose-related adverse events
- Nine treatment-emergent SAEs; none attributed to vicriviroc

# Conclusions

- Clear dose response in efficacy was observed
- Vicriviroc 75 mg was not statistically different from the control group in terms of virologic breakthrough at study termination
- Virologic breakthrough was not associated with a decline in CD4
- Tropism shift was infrequent and seen in all groups
- Vicriviroc was well tolerated with no evidence of seizures, cardiotoxicity, hepatotoxicity, lymphoma or adenocarcinoma
- Data indicate further study is warranted to elucidate the potential of this novel class in first-line therapy

# Acknowledgments

## The patients

### Investigators

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