VH3810109 (N6LS) Reduces Viremia Across a Range of Doses in ART-Naive Adults Living With HIV: Proof of Concept Achieved in the Phase IIa BANNER (207959, NCT04871113) Study

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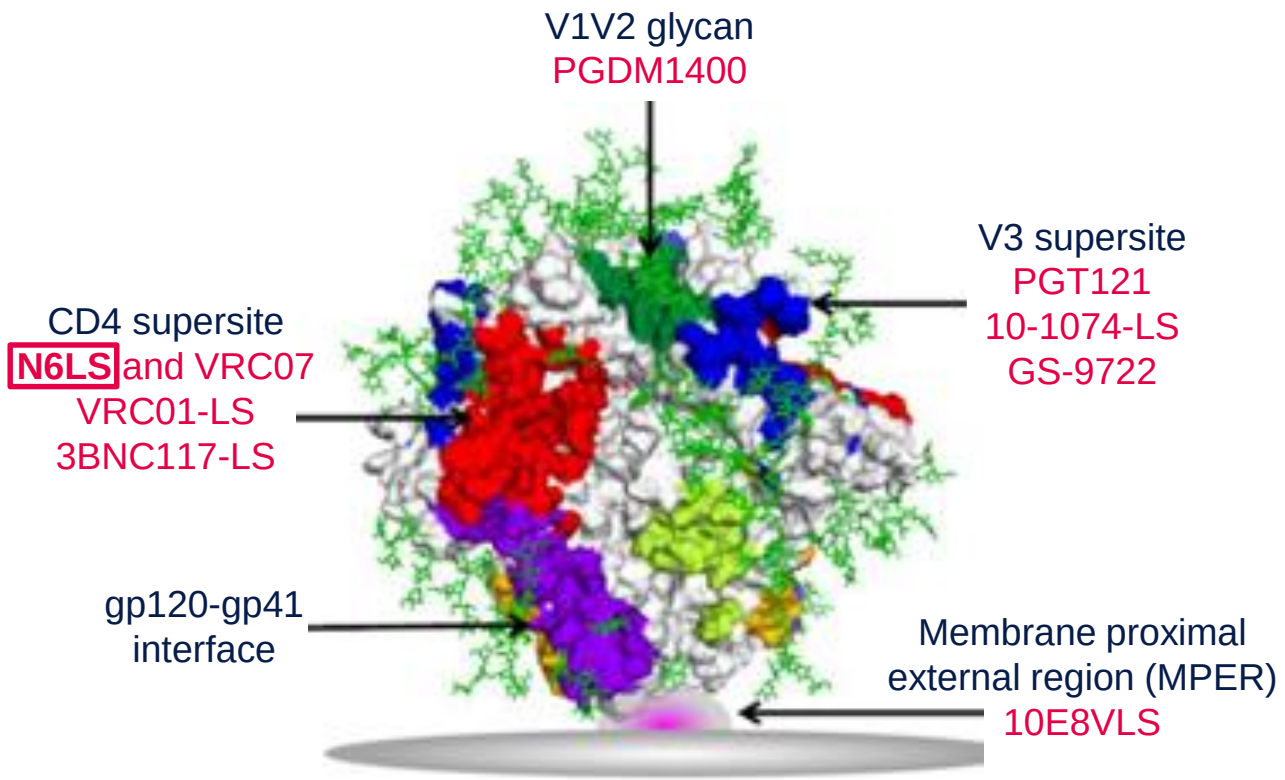
Disclosures

- Peter Leone is an employee of ViiV Healthcare and a shareholder of GSK

Introduction

- Broadly neutralizing antibodies (bNAbs) are under development for both the treatment and prevention of HIV-1
- VH3810109 (N6LS) is a novel bNAb with broad and potent neutralization activity in vitro targeting the CD4 binding site of the HIV-1 envelope protein
- Here we report first-time antiviral activity during monotherapy and cumulative ongoing safety of VH3810109 in treatment-naive people with HIV-1

bNAbs target 5 conserved regions on the envelope[1-8]



LS-containing bNAbs have been engineered to have long half-lives[9]

1. Bar et al. *N Engl J Med.* 2016;375:2037-2050. **2.** Kwon et al. *Retrovirology.* 2012;9(suppl 2):O34. **3.** Scheid et al. *Science.* 2011;333:1633-1637. **4.** Mouquet et al. *Proc Natl Acad Sci U S A.* 2012;109:E3268-E3277. **5.** Walker et al. *Nature.* 2011;477:466-470. **6.** Caskey. *Curr Opin HIV AIDS*. 2020;15:49-55. **7.** Doria-Rose et al. *J Virol.* 2015;90:76-91. **8.** Kwon et al. *J Virol.* 2016;90:5899-5914. **9.** Huang et al. *Immunity.* 2016;45:1108-1121.

BANNER Study Design: Randomized, Open-label, 2-Part, Multicenter, Single-Dose, Adaptive Study in ART-Naive Adults

Inclusion criteria
- Age 18-65 years
- HIV-1 RNA ≥5000 c/mL
- CD4+ cell count ≥250 cells/mm^3
- ART naive

Randomized 1:1

Single VH3810109 infusion

Part 1
- VH3810109 40 mg/kg IV (n=8)
- VH3810109 280 mg (~4 mg/kg[a]) IV (n=6)

Planned interim analysis[b]
- To determine whether to proceed to part 2 and to determine dose selection in part 2

Monotherapy endpoint criteria (Days 11-84)
- Virologic non-response (viral nadir decline <0.5 $\log_{10}$ c/mL at Day 11)
- Virologic rebound (VL rebound of ≥1.0 $\log_{10}$ c/mL increase from nadir or to <0.5 $\log_{10}$ c/mL from baseline)
- Missing/Delayed data from previous visits
- Reached Day 84

Participants receive INI-based SOC

- Primary endpoints were plasma HIV-1 RNA maximum change from baseline during monotherapy and safety parameters
- Secondary endpoints included VH3810109 PK parameters and incidence and titer of anti-VH3810109 antibodies
  - Antibody susceptibility was determined retrospectively using the PhenoSense monoclonal antibody assay

[a]For a 70-kg individual. [b]A planned interim analysis was performed to evaluate virologic response, safety, and PK from the monotherapy and ongoing SOC periods in part 1. [c]An SOC integrase inhibitor–based regimen (DTG/3TC) was provided at the end of the monotherapy periods in parts 1 and 2.

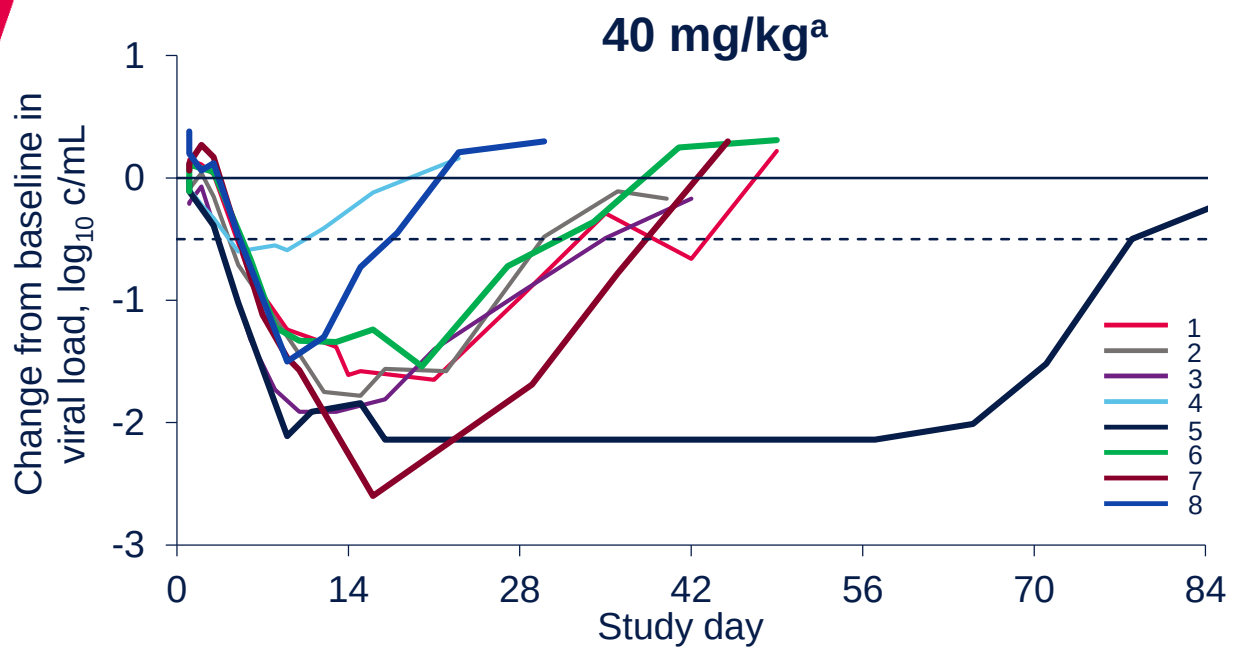
Demographics and Baseline Characteristics

Parameter	VH3810109 40 mg/kg IV (n=8)	VH3810109 280 mg IV (~4 mg/kg[a]) (n=6)
Age, median (range), years[b]	30.5 (24-51)	28.0 (18-54)
Sex, n		
Female	0	1
Male	8	5
Race, n		
Black/African American	2	1
White/Caucasian/European heritage	6	5
Ethnicity, n		
Latinx	6	4
Not Latinx	2	2
HIV-1 RNA, median (range), c/mL	12,259 (1351-173,710)	30,833 (5938-104,585)
HIV-1 RNA, median (range), $\log_{10}$ c/mL	4.1 (3.1-5.2)	4.5 (3.8-5.0)
CD4+ cell count, median (range), cells/mm^3	313.0 (190-700)	374.5 (265-601)
Body mass index, mean (SD), kg/m^2	27.0 (5.7)	27.5 (4.3)

- Participants were from the United States (n=6), Canada (n=1), and Argentina (n=7)

[a]For a 70-kg individual. [b]Age was imputed when full date of birth was not provided.

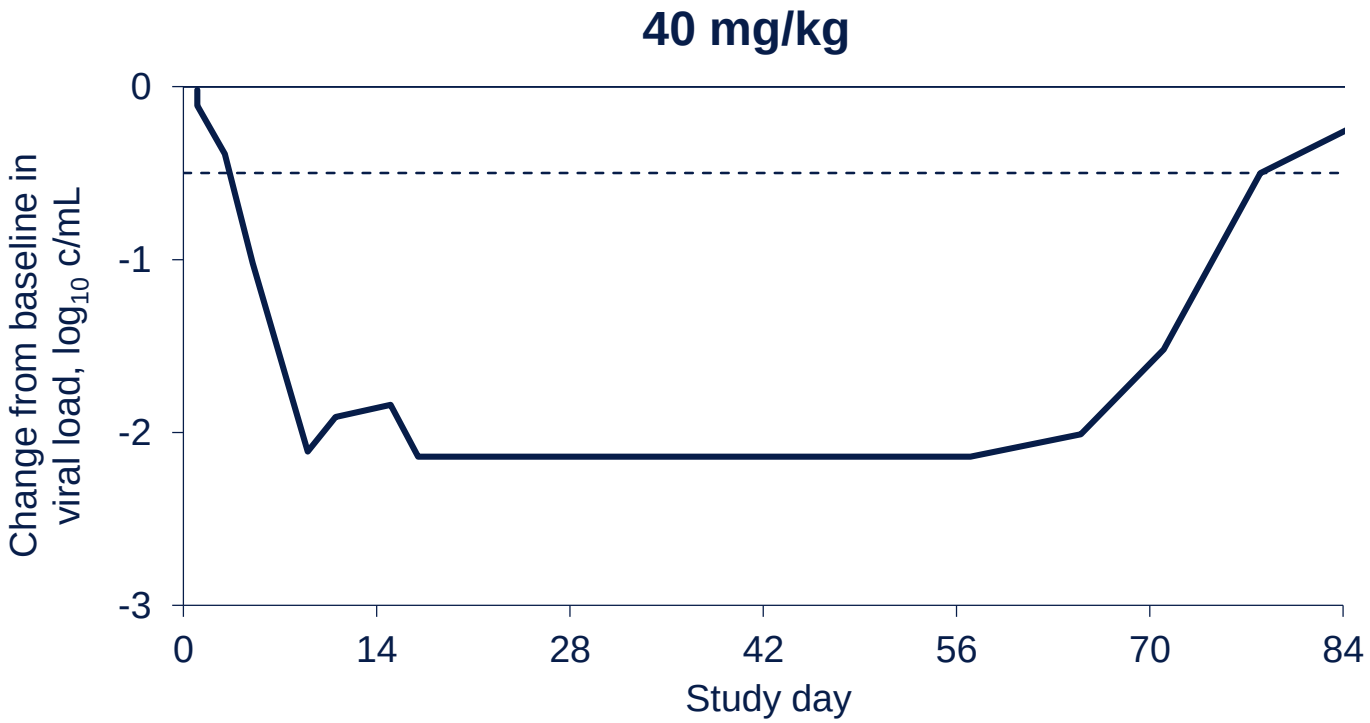
VH3810109 Led to Virologic Response in 13/14 Participants



Viral dynamic measures	VH3810109 40 mg/kg IV (n=8)
Median (range) viral nadir from baseline, log_{10} c/mL	−1.72 (−0.60, −2.60)
Median (range) time to viral nadir, days	16 (5-21)
Maximum viral nadir from baseline, log_{10} c/mL	−2.60
Median (range) time to viral rebound among responders, days	35 (12-78) [n=8]

Solid line represents no change from baseline and dashed line represents virologic non-response (viral nadir decline <0.5 log_{10} c/mL at Day 11).
[a]Each line represents an individual participant. [b]For a 70-kg individual. [c]Participant 14 is the only female participant in the study.

VH3810109 Virologic Response in Participant #5: Longest Suppression



Viral dynamic measures	Participant #5
Baseline viral load, c/mL	5309
Baseline CD4+ cell count, cells/mm^3	700
Time to rebound, days[a]	78
Maximum viral load decline, log_{10} c/mL	−2.14
Time to maximum viral load decline, days	17
Baseline IC_{80}, µg/mL	0.09

Solid line represents no change from baseline and dashed line represents virologic non-response (viral nadir decline <0.5 log_{10} c/mL at Day 11).
[a]Time to rebound is defined by time of VL ≥1.0 log_{10} c/mL increase from nadir or <0.5 log_{10} c/mL decrease from baseline.

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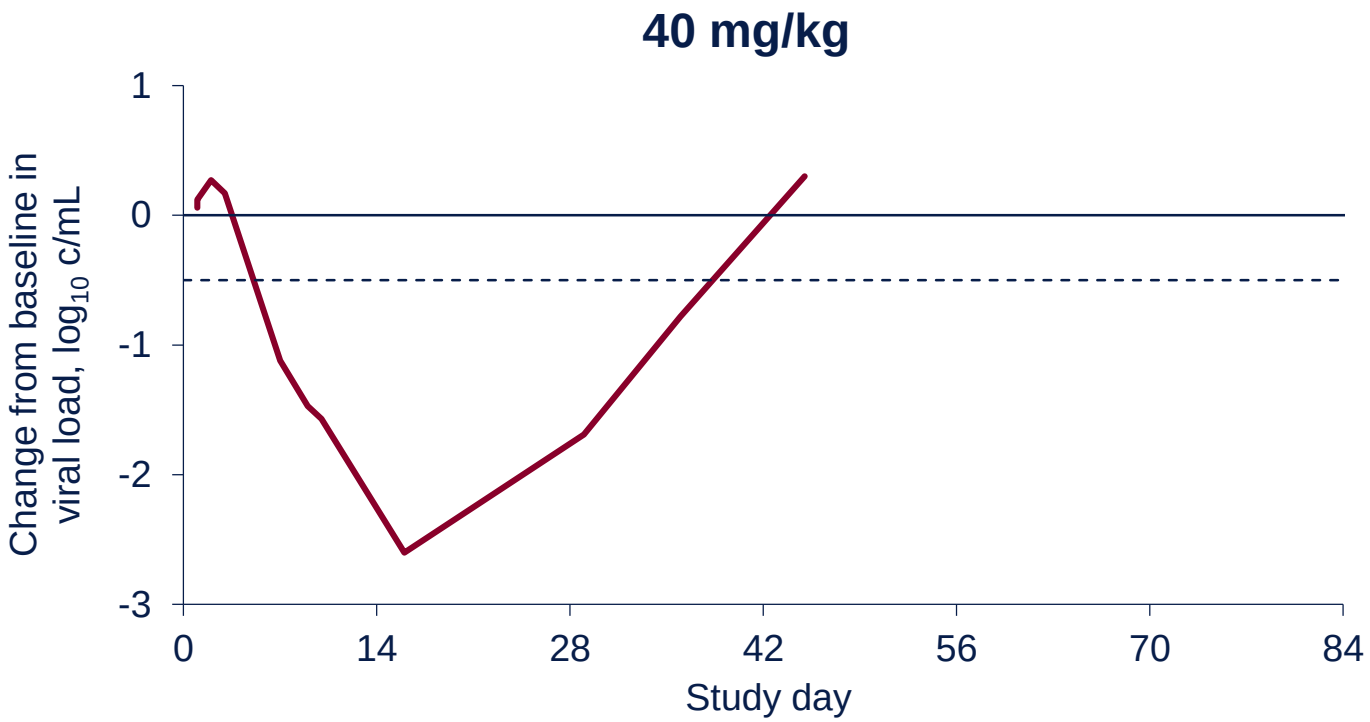
VH3810109 Virologic Response in Participant #7: Largest Viral Decline



Viral dynamic measures	Participant #7
Baseline viral load, c/mL	30,930
Baseline CD4+ cell count, cells/mm^3	482
Time to rebound, days[a]	36
Maximum viral load decline, log_{10} c/mL	−2.60
Time to maximum viral load decline, days	16
Baseline IC_{80}, µg/mL	0.52

Solid line represents no change from baseline and dashed line represents virologic non-response (viral nadir decline <0.5 log_{10} c/mL at Day 11).
[a]Time to rebound is defined by time of VL ≥1.0 log_{10} c/mL increase from nadir or <0.5 log_{10} c/mL decrease from baseline.

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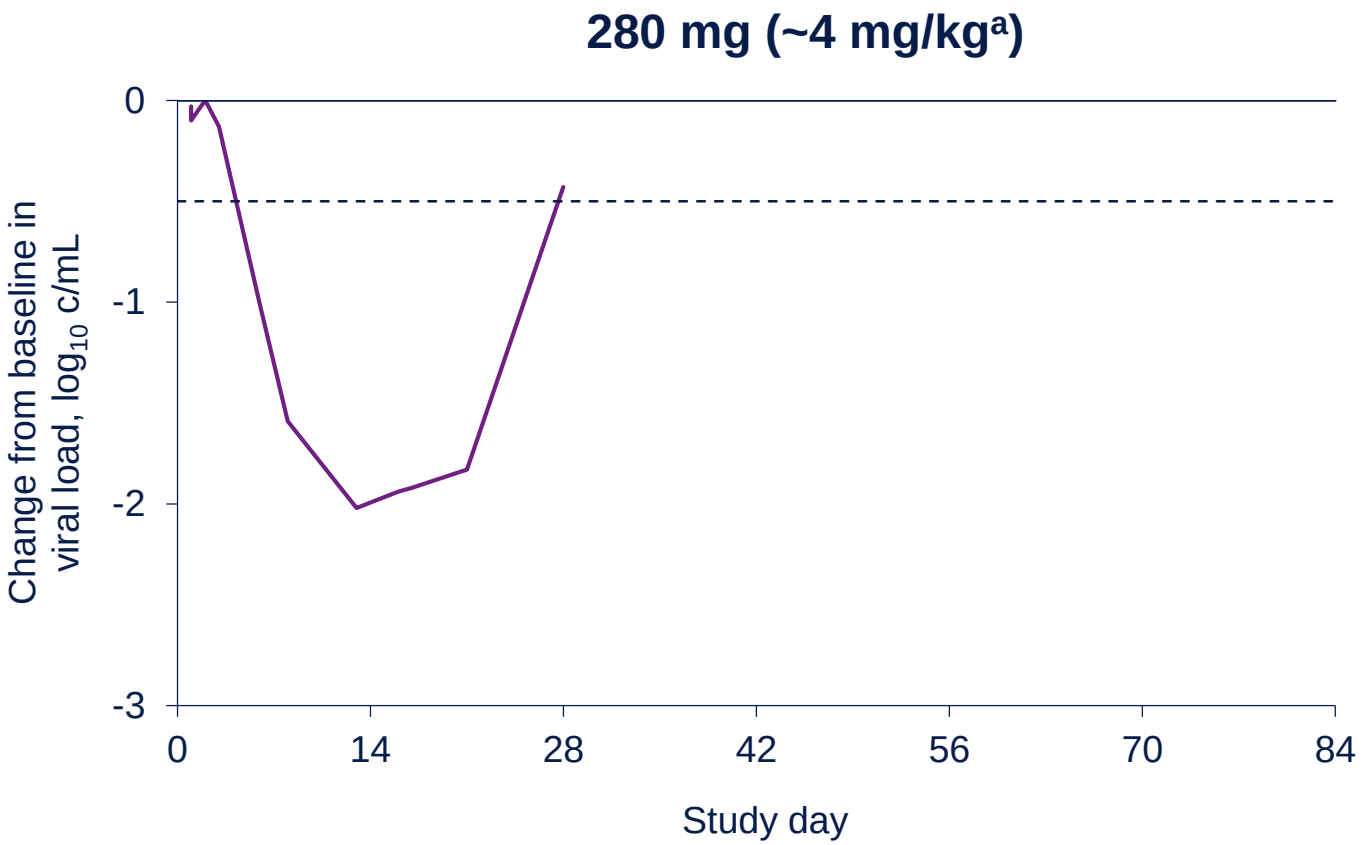
VH3810109 Virologic Response in Participant #11: High Baseline VL With High VL Decline



Viral dynamic measures	Participant #11
Baseline viral load, c/mL	104,585
Baseline CD4+ cell count, cells/mm^3	509
Time to rebound, days[b]	28
Maximum viral load decline, log_{10} c/mL	−2.02
Time to maximum viral load decline, days	13
Baseline IC_{80}, µg/mL	0.64

Solid line represents no change from baseline and dashed line represents virologic non-response (viral nadir decline <0.5 log_{10} c/mL at Day 11).
[a]For a 70-kg individual. [b]Time to rebound is defined by time of VL ≥1.0 log_{10} c/mL increase from nadir or <0.5 log_{10} c/mL decrease from baseline.

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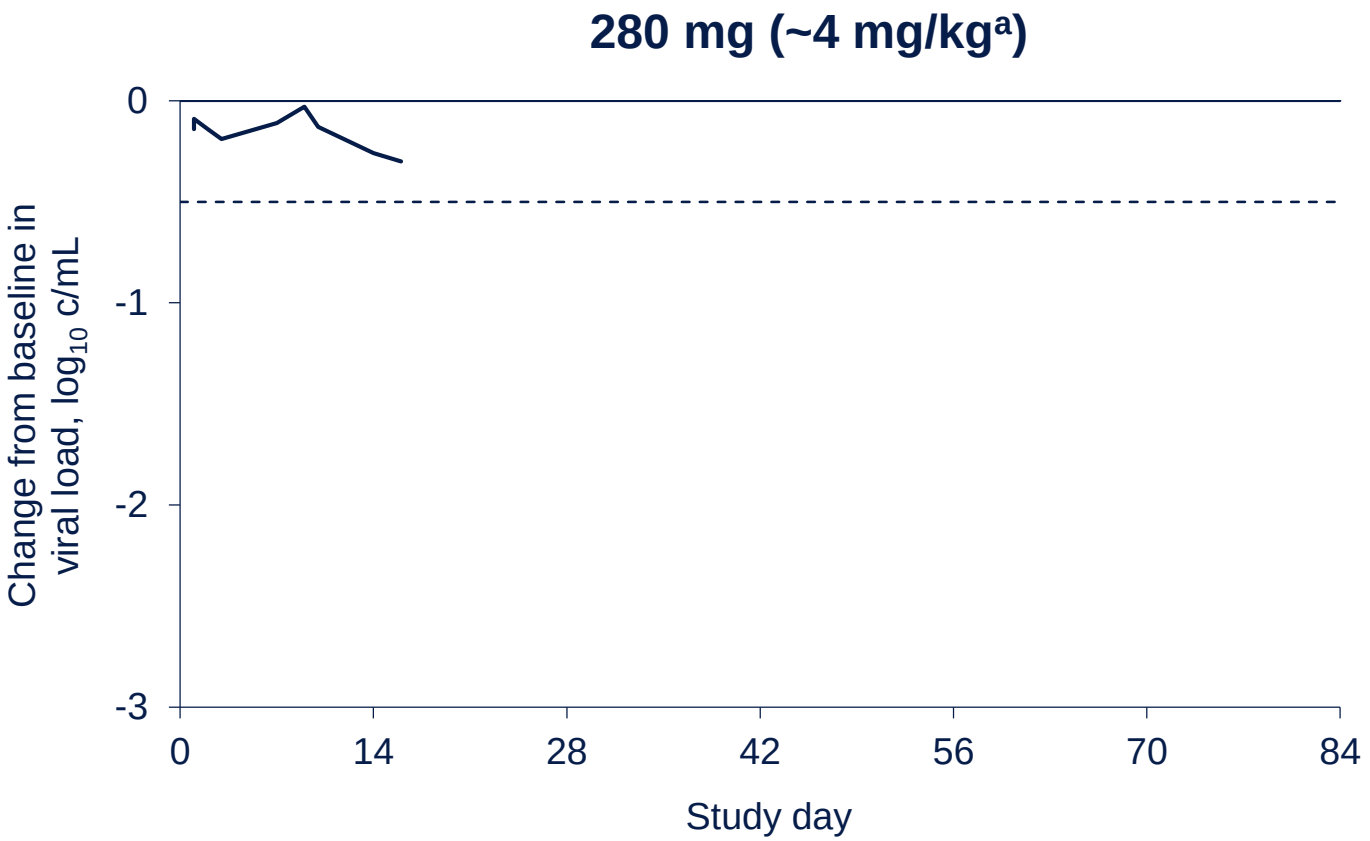
VH3810109 Virologic Response in Participant #10: Non-Responder



Viral dynamic measures	Participant #10
Baseline viral load, c/mL	100,299
Baseline CD4+ cell count, cells/mm^3	374
Time of observed non-response, days[b]	10
Maximum viral load decline, log_{10} c/mL	−0.30
Time to maximum viral load decline, days	16
Baseline IC_{80}, µg/mL	>50

Solid line represents no change from baseline and dashed line represents virologic non-response (viral nadir decline <0.5 log_{10} c/mL at Day 11).
[a]For a 70-kg individual. [b]For non-responders, time to rebound is imputed with Day 11 visit.

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Safety and Tolerability

Preferred term, n	VH3810109 40 mg/kg IV (n=8)	VH3810109 280 mg IV (~4 mg/kg[a]) (n=6)
Any AE	6	3
Grade 1	3	3
Grade 2	3	0
Grade ≥3	0	0
Any drug-related AE	1	2
Abdominal pain	1	1
Gastrointestinal pain	1	0
Pruritis	1	0
Asthenia	0	1
Myalgia	0	1
Any ISR	2	0
Infusion site erythema	1	0
Infusion site pain	1	0

- Overall, 35 AEs were reported by 9 of 14 participants (n=6 in the 40-mg/kg group and n=3 in the 280-mg group), with no grade ≥3 AEs or serious AEs reported
- All drug-related AEs and ISRs were grade 1

[a]For a 70-kg individual.

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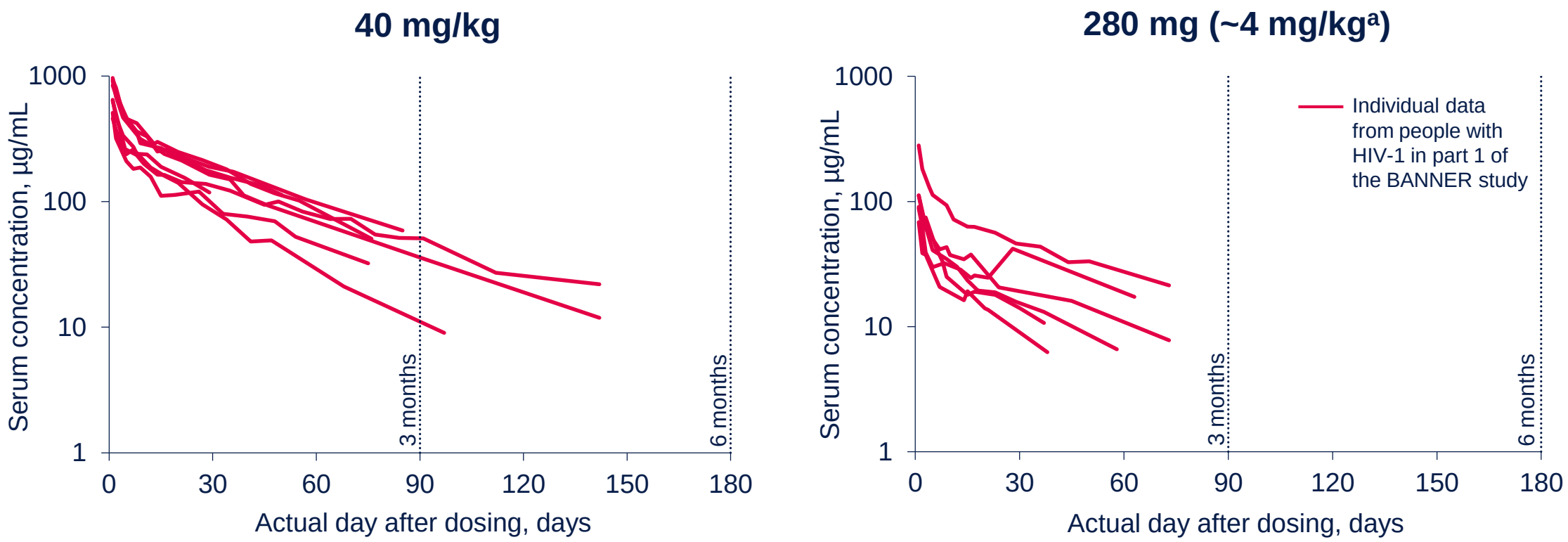
VH3810109 PK Results in People With HIV-1



- PK is consistent with other bNAbs and supports potential use as part of a long-acting regimen

[a]For a 70-kg individual.

Conclusions

- A single IV infusion of VH3810109 (N6LS) was well tolerated, with few drug-related AEs, no SAEs, and robust antiviral efficacy observed at both high and low doses
- When administered at 40 mg/kg, VH3810109 led to a median decline in viremia of 1.72 $\log_{10}$ c/mL and a maximum viral nadir from baseline of −2.60 $\log_{10}$ c/mL
- The 280-mg (~4 mg/kg) dose, which resulted in a median viral load decline of 1.18 $\log_{10}$ c/mL and a maximum viral nadir from baseline of −2.18 $\log_{10}$ c/mL, exceeded efficacy and duration of response reported for other bNAbs at similarly low doses[1]
- These data warrant further development, including exploring alternate dosing options and modalities, of VH3810109

1. Caskey et al. *Nature*. 2015;522:487-491.

Acknowledgments

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