ONLINE EXPERT POSTER REVIEW AND DISCUSSION

ARV THERAPIES AND THERAPEUTIC STRATEGIES

Reporting From

THE ELEVENTH INTERNATIONAL CONGRESS ON DRUG THERAPY IN HIV INFECTION (HIV11)

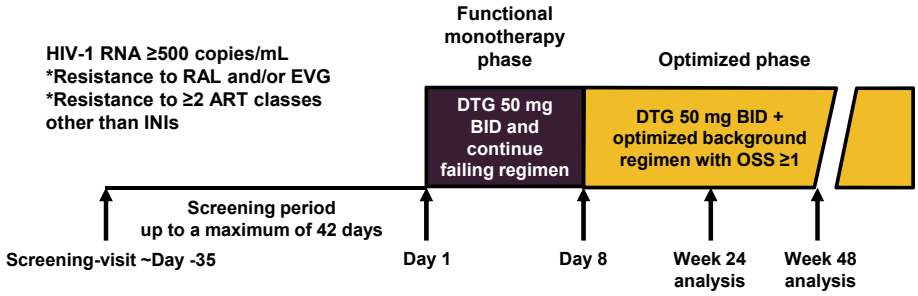
Jointly Sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC.

Antiviral Activity of Dolutegravir in Subjects With Failure on an Integrase Inhibitor-Based Regimen: Week 24 Phase 3 Results From VIKING-3

G Nichols, R Grossberg, A Lazzarin, F Maggiolo, A Mills, J-M Molina, G Pialoux, D Wright, M Ait-Khaled, J Huang, C Vavro, B Wynne, J Yeo

Abstract O232

Viking 3: Dolutegravir (50 mg BID) in Patients with Integrase Inhibitor Resistance



- Extensive ARV Resistance
  - 79% had ≥2 NRTIs, 75% had ≥1 NNRTI, and 70% had ≥2 PI resistance-associated mutations; 62% had non-R5 detected
  - All had INI (RAL and/or EVG) resistance*
    - 68% at screening, 32 documented resistance from prior INI failure

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

Viking 3: Integrase Genotypic and Phenotypic Resistance at Baseline

DTG 50 mg BID (N=183)						
	Q148 + ≥2	**Q148 + 1**	**N155**	**Y143**	**≥2 Primary**	**Primary Not Detected**
Subjects, n (%)	**21 (11)**	**31 (17)**	**30 (18)**	**28 (15)**	**7 (4)**	**59 (32)**
Median DTG FC	**10.00**	**4.60**	**1.49**	**1.10**	**4.57**	**0.89**
Q1	4.47	3.39	1.29	0.91	1.68	0.80
Q3	13.00	6.27	1.76	1.18	20.00	1.04
Min	**2.56**	**0.47**	0.82	0.78	**1.46**	0.45
Max	**37.00**	**12.00**	3.89	2.01	**27.00**	3.97

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

Viking 3: Day 8 Responses by Baseline Resistance

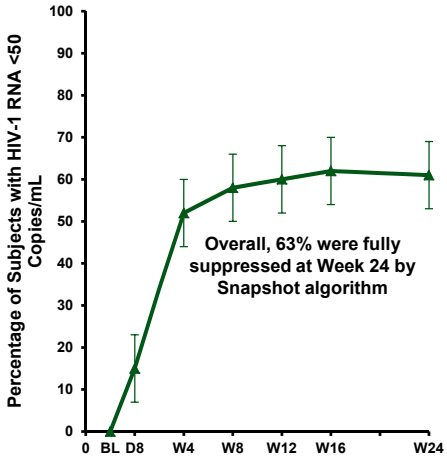
Primary INI-resistance Mutations at BL	N	Mean HIV-1 RNA (log_{10}) Change from BL (SD) at Day 8	% >1-log_{10} HIV-1 RNA Decline or <50 copies/mL at Day 8
Total	**183**	**-1.4 (0.61)**	**82%**
No primary mutations	60	-1.6 (0.55)	95%
T66	1	-1.9	100%
Y143	28	-1.7 (0.42)	96%
N155	33	-1.4 (0.51)	82%
≥2 Primary mutations	8	-1.4 (0.76)	75%
Q148 + ≤1 Secondary mutation*	32	-1.1 (0.51)	69%
Q148 + ≥2 Secondary mutations*	21	-1.0 (0.81)	48%

*Key secondary mutations were G140A/C/S, L74I, and E138A/K/T

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

Viking 3: Efficacy

- Day 8 change from BL: -1.43 log_{10} copies/mL, *P*<0.001
  - 95% CI, -1.52 to -1.34 (ITT-E, N=183)
- Week 24 by Snapshot (MSDF): 72/114 (63%) <50 copies/mL
  - 37/114 (32%) were virologic non-responders
  - 6/114 (5%) changed OBR
  - Only 5/114 (4%) were non-responders for discontinuation due to AEs



Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

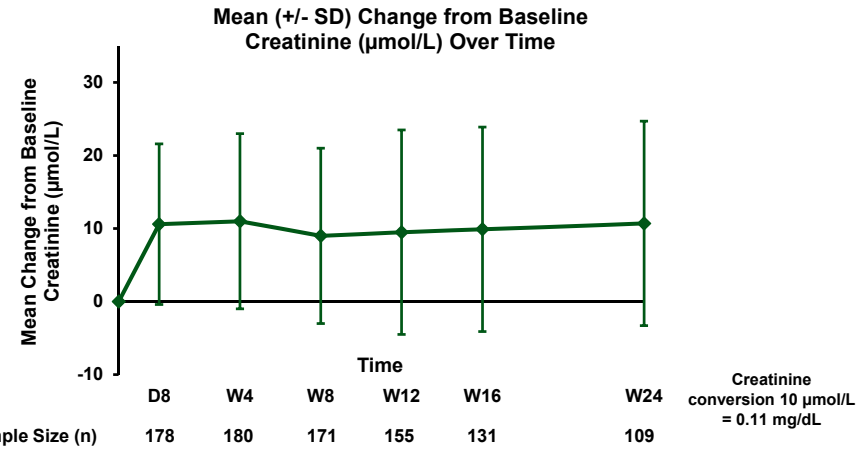
Viking 3: Week 24 Response by Mutation Category and OBR Overall Susceptibility Score (OSS)

	HIV-1 RNA <50 copies/mL at Week 24 (Snapshot) (N=101)			
Derived IN mutation group	OSS=0	OSS=1	OSS≥2	Total
No Q148, n (%)	2/2 (100)	24/29 (83)	31/41 (76)	57 (79)
Q148 + 1, n (%)	2/2 (100)	3/7 (43)	4/11 (36)	9 (45)
Q148 +≥2, n (%)	1/2 (50)	0/7(0)	0	1 (11)

- In multivariate analyses of baseline factors on Week 24 response rates, the presence of Q148 +≥2 mutations and increasing DTG FC were highly correlated with fewer subjects achieving <50 copies/mL (P≤0.001)
- Increasing OBR activity score did not impact response

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

Viking 3: Mean Change in Serum Creatinine



Expected non-progressive change in serum creatinine via OCT2 inhibition as previously described

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.