

# Etravirine Resistance Mutations in Patients With Virologic Failure on Nevirapine or Efavirenz-based HAART



AIDS PREVENTION  
INITIATIVE NIGERIA

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## BACKGROUND

Etravirine, a potent diarylpyrimidine NNRTI, has clinical activity against nevirapine and efavirenz-resistant HIV-1 strains. The DUET studies showed that significant resistance to etravirine is predicted by the presence of  $\geq 3$  of 13 etravirine-resistance associated mutations (ETV-RAMs): V90I, A98G, L100I, K101E, K101P, V106I, V179D, V179F, Y181C, Y181I, Y181V, G190A, and G190S. Since September 2005, genotypic testing has been performed on patients in virologic failure as part of the APIN Plus/Harvard PEPFAR Program in Nigeria. ETV-RAMs has not been previously reported in a Nigerian population on HAART.

## STUDY OBJECTIVES

- Determine the prevalence of ETV-RAM in efavirenz or nevirapine virologic failures in the study cohort
- Determine the potential impact of the mutations on the efficacy of ETV

## INCLUSION CRITERIA

- Age > 18 years
- HIV-1 seropositive
- Virologic failure, defined as plasma HIV RNA > 1,000 copies/ml despite  $\geq 6$  months of NNRTI-based first line HAART
- Previous genotypic resistance testing as part of routine clinical care

## METHODS

Retrospective study using data previously collected for clinical care (N=210). Genotypes were analyzed by the Celeris ViroSeq HIV-1 Genotyping System and subtype determined by *pol*. Predicted ETV resistance was defined as presence of  $\geq 3$  of the 13 ETV-RAMs identified by International AIDS Society-USA 2007 resistance mutation update. The duration of prior NNRTI-based HAART was extracted from clinical databases. First line regimens included two NRTIs and either nevirapine or efavirenz, with only 12 of the 210 patients surveyed having received efavirenz.

## RESULTS

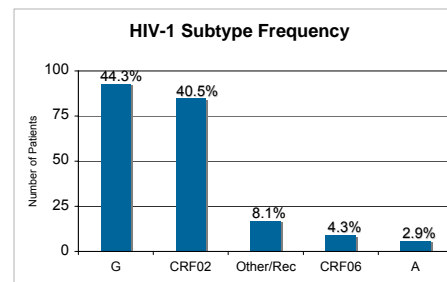


Fig. 1: HIV 1 subtype distribution: G and CRF02\_AG are responsible for 85% of HIV infections in this population, but CRF06 and other subtypes are also present.

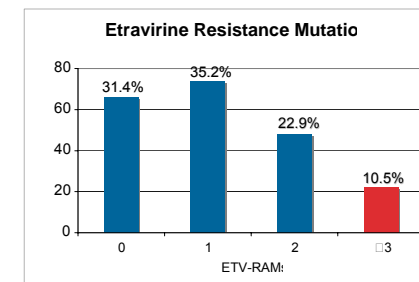


Fig. 2: Samples with 0, 1, 2 or  $\geq 3$  etravirine resistance associated mutations.

# of ETV-RAMs	0	$\geq 1$	$\leq 2$	$\geq 3$
Mean duration of ART (months)	18.9	25.4	22.8	27.8

Table 1: Duration of exposure to NNRTI-based ART and number of ETV-RAM (p=0.0001 for 0 vs  $\geq 1$ ; and p=0.0651 for  $\leq 2$  vs  $\geq 3$  ETV-RAM)

ETV-RAMs	Y 181 C	G 190 A	A 98 G	K 101 E	V 90 I	V 106 I	Y 181 V	Y 181 I	K 101 P	V 179 D	G 190 S	L 100 I	V 179 F
%	41.9	21.9	18.1	13.8	8.6	3.8	3.3	1.4	0.5	0.5	0.5	0	0

Table 2: Frequency of individual ETV-RAM

## CONCLUSION

Etravirine is likely to be effective in 90% of the patients in this cohort. Early discontinuation of a failing first-line NNRTI may prevent the accumulation of ETV-RAMs. The prevalence of A98G (18%) in our cohort is higher than reported from settings with different HIV-1 subtype distributions. Further studies are needed to fully characterize ETV-RAM, and determine if subtype-specific factors contribute to the high prevalence of A98G in our population