MOPEB071

Predicted susceptibility of etravirine in HIV patients experiencing virological failure secondary to nonnucleoside reverse transcriptase inhibitor resistance

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Background

Virological response to etravirine is dependent on the type and number of nonnucleoside reverse transcriptase inhibitor (NNRTI) resistance-associated mutations (RAMs). The aim of this work was to examine the predicted susceptibility of etravirine in patients experiencing virological failure secondary to NNRTI resistance attended at 'Franscico Muñiz' Hospital, Buenos Aires, Argentina (2001-2008).

Methods

Virological Data on NNRTI used in HAART at the time of failure and the number of NNRTI mutations were collected and retrospectively analyzed.

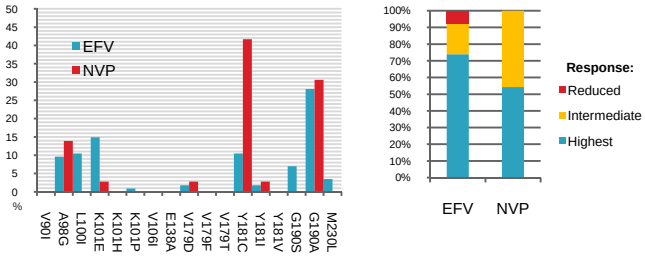
ETR-RAMs were defined and analyzed according to the weighted mutation score to predict susceptibility (Table 1): 0–2 (highest response), 2.5–3.5 (intermediate response), and 4 or more (reduced response)[1]. Data were analyzed by Fisher exact test.

Table 1. ETR-RAMs and the weighted mutation score

3	Y181I	Y181V					
2.5	K101P	L100I	Y181C	M230L			
1.5	E138A	V106I	G190S	V179F			
1	V90I	V179D	K101E	K101H	A98G	V179T	G190A

[1] Vingerhoets J. et. al. 2008

Figure 1. ETR-RAMs after virologic failure with NNRTI



Results

- N=150. Male=65.3%. Median age: 38 years (range 23-59). Efavirenz (EFV) containing regimen: 76.7%; nevirapine (NVP): 23.3%. Long-term virologic failure (>24-weeks): 81.3%.
- Most frequent NNRTI-RAMs after EFV exposure: K103N (70.2%), G190A (28.1%), P225H (22.8%) and after NVP exposure: K103N (44.4%), Y181C (41.7%), G190A (30.6%).
- Frequency of ETR-RAMs acquired after NNRTI failure: zero=38.7%, one=39.3%, two=17.3%, three=3.3%, four=1.3%.
- Most frequent ETR-RAMs after failure with EFV: G190A (28.1%), K101E (14.9%), L100I (10.5%); and with NVP: Y181C (41.7%), G190A (30.6%) and A98G (13.9%) (Figure 1).
- Global predicted susceptibility of ETR: highest response: 69.3%, intermediate response: 24.7%, reduced response: 6%.
- Comparing EFV with NVP: highest response: 73.9% vs. 54.3% (p=0.02), intermediate response: 18.3% vs. 45.7% (p=0.001), reduced response: 7.8% vs. 0% (p=0.08).
- Comparing highest response with duration of virological failure: EFV-containing regimen: 94.4% (<24-weeks) vs. 69.8% (>24-weeks) (p=0.02); NVP-containing regimen: 42.9% (<24-weeks) vs. 56.5% (>24-weeks) (p=0.41) (Figures 2-3).

Figure 2. Most frequent NNRTI-RAMs after short-term virologic failure

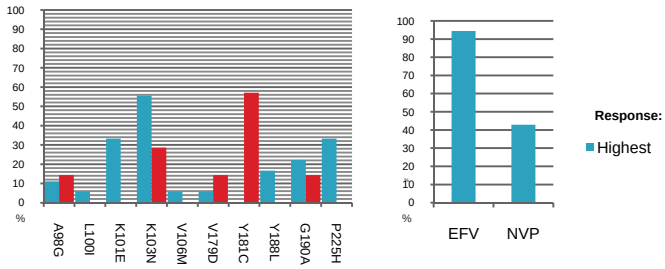
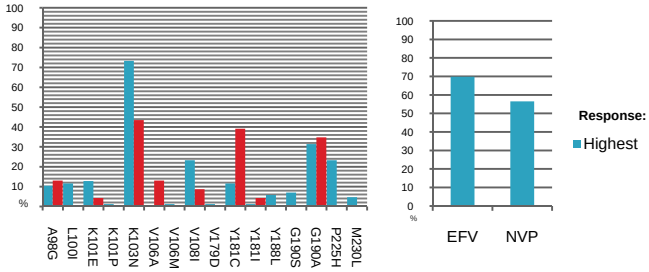


Figure 3. Most frequent NNRTI-RAMs after long-term virologic failure



Conclusions

- The majority of patients maintained susceptibility to ETR after the acquisition of NNRTI resistance.
- Failing with an EFV-containing regimen had a better predicted susceptibility to ETR than with NVP, especially after short-term virologic failure.