

Topic:

B9 Viral resistance testing in clinical trials and practice

Title:

Is there any potential for first line Etravirine use? Analysis from a large dataset of ART-naïve HIV infected patients undergoing resistance test.

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Text:

Background: drugs in the NNRTI class are widely used in first line therapy, but because of their low genetic barrier, resistance is frequent and transmitted NNRTI mutations are often found in ART-naïve patients. Thus, the potential for use of Etravirine (ETV), new NNRTI with high genetic barrier, as part of first line therapy was investigated, by estimating its predicted activity in ART-naïve patients by means of currently available interpretation scores.

Methods: Four scores were used. The score from DUET 1/2 trials included 17 mutations with different weights: a sequence was predicted to be fully resistant to ETV if the score is ≥ 4 and intermediate resistant if between 2.5-3.5. Monogram team identified 30 mutations with different weights: a score ≥ 4 defines resistance. The REGA (V17) and ANRS (V7.1.1) interpretation systems were also used.

Results: Overall, 1792 patients, tested between 1999-2008, were included, 51 of them (2.9%) harbored major mutations for Efavirenz/Nevirapine. The frequency of predicted ETV resistance according with scores used is reported in the table.

At multivariable assessment, detection of full/intermediate ETV resistance according to any score (59 patients) was associated with log HIV-RNA > 5 (OR:3.8; 95% CI:0.98-14.4, $p=0.05$), detection of ≥ 1 TAM (4.5; 1.2-11.7, $p < 0.001$) and ≥ 1 NNRTI-IAS mutation (38.5; 17.7-84.0, $p < 0.0001$), while CD4 count > 350 was inversely associated (0.4; 0.2-0.96, $p=0.04$).

Conclusions: the detection of mutations predictive of full or intermediate ETV resistance is infrequent in ART-naïve patients and therefore there may be potential for ETV use in first line therapy even in patients with primary resistance to previous NNRTI.

Predicted ETV susceptibility in the study population: a)
and in patients with concomitant detection of major IAS NNRTI mutations: b).

a) n=1792	Duet I/II	Monogram	ANRS V17	REGA V7.1.1
Susceptibile	1,771 (98.9%)	1,768 (99%)	1,790 (98.9%)	1,740 (96.9%)
Intermediate	19 (1%)	/	1 (0.05%)	51 (3%)
Resistant	2 (0.1%)	24 (1%)	1 (0.05%)	1 (0.1%)
b) n=51	Duet I/II	Monogram	ANRS V17	REGA V7.1.1
Susceptibile	37 (72%)	38 (75%)	49 (96%)	29 (57%)
Intermediate	12 (2%)	/	1 (2%)	21 (41%)
Resistant	2 (4%)	13 (25%)	1 (2%)	1 (2%)

[Table]

Country of research:

Italy

Ethical Research Declaration:

Yes