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Using the latest resistance score to predict etravirine (ETV) resistance in naïve and NNRTI-failing patients

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Purpose of the study

To assess the feasibility of a rescue ETV-containing cART regimen in naïve patients with primary NNRTI resistance mutations or after first NNRTI failure, using the latest resistance score presented.

Methods

A set of 17 mutations (V90I, A98G, L100I, K101E/H/P, V106I, E138A, V179D/F/T, Y181C/I/V, G190A/S, M230L) were found associated with ETV resistance in the Phase III DUET-1 and DUET-2 trials. Recently, a different score was assigned to each mutation (i.e. Y181C/I have the highest score: 3). An overall score of ≤4 was associated with reduced response and a score between 2.5–3.5 with intermediate response (reference). ETV resistance was calculated from a large database of patients undergoing genotypic resistance test.

Results

Overall, 241 ARV-naïve patients and 311 failing a first NNRTI regimen (EFV = 189, NVP = 122) were analyzed. Among naïve patients, 14 (5.8%) harbored ≤1 major NNRTI resistance mutation but only in one patient (0.4%) a ≤4 score, and in five patients (2.1%) a score between 2.5–3.5 were detected.

Among failing patients, two-thirds harbored major NNRTI mutations (about half had K103N). In contrast, a ≤4 score was found in 5.8% of patients, with similar proportion in EFV- and NVP-treated patients (5.8% vs. 5.7%), though among NVP patients a score between 2.5–3.5 was more frequently found (28.7% vs. 20.1%).

The probability of developing a ≤4 score was 0.0% during the first 3 months of NNRTI failure and 3.1% between 3–6 months (2.6% in EFV vs. 3.9% in NVP failure). Subsequently, during EFV failure, the probability of developing a ≤4 score increased between 6–12 months to 20.0% (particularly between 9–12 months: 23.5%) and during NVP failure, between 9–12 months to 9.1%.

At adjusted logistic regression, remaining in NNRTI failure between 6–12 months was the only factor associated to developing a ≤4 ETV score (OR: 22.0, 95& CI: 2.65–182.89, p = 0.004).

Conclusion

The presence of mutations predictive of full or intermediate ETV resistance is uncommon among naïve patients, thus, in almost all cases, ETV use may be allowed. The detection of ETV-resistance is also infrequent in patients failing a NNRTI regimen because usually they develop the K103N mutation, that alone or in combination does not affect ETV sensitivity. Our data also suggest that a quick withdrawal of a failing NNRTI regimen, possibly in the first 3 months of failure, can maintain ETV sensitivity, thus preserving a treatment option.

References

1. Vingerhoets J, *et al.*: **An update of the list of NNRTI mutations associated with decreased virological response to etravirine: multivariate analysis of the pooled DUET-1 and DUET-2 clinical trial data. [XVII International Drug Resistance Workshop, June 10–14, Sitges, Spain; Abstract 24].** *Antivir Therapy* 2008, **13(Suppl 3):**A26.

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