

Mutant HIV minority variants detected by ultradeep sequencing do not condition virological failure in patients starting ARV therapy including low genetic barrier drugs.

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Background: Clinical impact of mutant HIV minority variants has not been fully established. This study evaluates the participation of mutant-HIV minority variants in response to initial ARV therapy with low genetic barrier drugs (LGBD).

Methods: Fifteen patients (baseline wild-type standard genotype) initiating ARV therapy with LGBD were selected. A PCR fragment comprising K103N/Y181C/M184V was designed. Primers were tagged per patient allowing ultradeep sequencing in one PicoTiterPlate (454 LifeSciences-Roche).

Results: All patients presented mutant minority variants to some extent. The mean proportion in which mutations were present was 3.63, 0.00 and 3.63% for K103N, Y181C and M184V, respectively. Undetectable VL was achieved in all cases but one.

| Initial ARV therapy | Baseline VL (log) | K103N | Y181C | M184V | Months to VL <1,7 log |
|---------------------|-------------------|-------|-------|-------|-----------------------|
| RTV/EFV | 4.6 | 4.96 | 0.05 | 5.49 | 7.0 |
| AZT/3TC/EFV | 5.5 | 0.91 | 0.00 | 1.25 | 11.0 |
| ddl/3TC/EFV | 5.1 | 1.45 | 0.00 | 1.50 | 11.0 |
| ddl/3TC/EFV | 5.4 | 2.82 | 0.00 | 3.19 | 11.0 |
| AZT/3TC/EFV | 3.8 | 1.14 | 0.00 | 0.86 | 9.0 |
| 3TC/TDF/EFV | 5.0 | 2.38 | 0.00 | 2.46 | 11.0 |
| AZT/3TC/EFV | 5.4 | 7.37 | 0.00 | 5.74 | 12.0 |
| 3TC/D4T/EFV | 4.9 | 5.97 | 0.11 | 5.44 | 8.0 |
| ddl/3TC/EFV | 5.0 | 4.43 | 0.05 | 4.18 | 9.0 |
| AZT/3TC/EFV | 5.0 | 6.41 | 0.10 | 6.89 | 8.0 |
| ddl/3TC/EFV | 3.8 | 1.64 | 0.04 | 2.35 | Not achieved |
| ddl/3TC/EFV | 4.9 | 0.05 | 0.00 | 0.96 | 4.0 |
| 3TC/ABC/ATV | 5.3 | 2.00 | 0.00 | 1.79 | 6.0 |
| 3TC/TDF/EFV | 5.7 | 0.17 | 0.00 | 0.45 | 10.0 |
| AZT/3TC/NVP | 5.2 | 12.70 | 0.04 | 11.93 | 10.0 |

Conclusions: Although mutant HIV minority variants associated with resistance to LGBD in the initial regimen were detected, virologic failure occurred in only one case. Achievement of undetectable VL was observed in the rest, but with certain delay.