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***IN VITRO* PHENOTYPIC SUSCEPTIBILITY TO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS OF HIV-2 ISOLATES WITH Q151M MUTATION IN THE REVERSE TRANSCRIPTASE GENE**

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BACKGROUND: The Q151M mutation confers resistance to almost all the nucleoside reverse transcriptase inhibitors (NRTIs) in HIV-1 infected patients. In HIV-2 infection, many studies have reported a high frequency of selection of this mutation but its impact on phenotypic susceptibility of HIV-2 isolates remains unclear.

METHODS: Four HIV-2 infected patients from the French ANRS HIV-2 cohort, with evidence of Q151 mutation in both plasma and available PBMCs co-cultivated supernatants were selected. *In vitro* phenotypic susceptibilities to different NRTIs: zidovudine (AZT), didanosine (ddI), stavudine (d4T), abacavir (ABC), lamivudine (3TC), and tenofovir (TDF) were evaluated using the ANRS PBMC method. IC₅₀s values were compared either before (T0) and after the selection of the Q151M (T1) or to wild type reference isolates when NRTIs mutations were present at T0.

RESULTS: At T0, mean IC₅₀ of the 2 HIV-2 wild-type isolates were: 0.01 µM for AZT, 0.07 µM for 3TC, 0.04 µM for d4T, 0.70 µM for ddI, 0.10 µM for ABC and 0.30 µM for TDF. The two other isolates had M184V mutation at T0 and showed a >60-fold increase in IC₅₀ for 3TC, fourfold for ddI and >sevenfold for ABC as compared to wild-type reference strains. At T1, RT bulk sequencing showed the selection of Q151M alone (*n*=1) or associated with other mutations (*n*=3). When Q151M mutation was alone there was no decrease in susceptibility to AZT, 3TC, ddI and TDF but an increase in IC₅₀ for d4T and ABC (22- and 37- fold respectively) was observed. When Q151M was selected with M184V (*n*=1), an increase in IC₅₀ (>10-fold) was observed for all NRTIs except TDF.

When Q151M was selected with V111I ($n=2$) an increase in IC_{50} ($4 \rightarrow 10$) was observed for all NRTIs, except for ddI when K65R/N69S/V111I/Q151M ($n=1$) were co-selected.

CONCLUSION: In HIV-2 isolates, Q151M mutation alone impacts only the phenotypic susceptibility to d4T and ABC. A decrease in susceptibility to all NRTIs was observed when Q151M was selected with V111I, mutation of unknown impact on HIV-1 resistance. Clinical relevance of these phenotypic susceptibility results needs to be evaluated in HIV-2 treated patients.

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