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MULTIPLE DIDEOXYNUCLEOSIDE ANALOGUE-RESISTANT HIV-1 IN EUROPE

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Multiple dideoxynucleoside analogue-resistant HIV-1 strains have been isolated from 12 HIV-1-infected individuals from four different European countries and have been submitted to direct solid phase sequencing of the reverse transcriptase (RT) gene and to phenotypic drug resistance testing using the recombinant virus assay. Data on evolution and treatment were collected from the patients' hospital files. All virus isolates presented a mutation Q151M/L, mostly associated with several other mutations: V75I, F77L and F116Y. Phenotypically all the tested strains were highly resistant to zidovudine, didanosine, zalcitabine, stavudine and partially to lamivudine. Extensive replication studies on multiple dideoxynucleoside analogue-resistant virus strains from one patient showed no replication disadvantage for resistant compared to wild-type virus. Prior to the appearance of multi-dideoxynucleoside analogue resistance, patients had received different sequential or associative combinations of analogues. Once multi-dideoxynucleoside resistance was present, the patients failed to respond clinically or biologically (CD4⁺ cell count and viral load) to associations of dideoxynucleoside analogues. Thus, treatment options for multi-dideoxynucleoside-resistant virus are currently limited. Interestingly, a complete suppression of virus replication (*i.e.* undetectable plasma viral load) was achieved in two patients with a combination of two protease inhibitors (ritonavir/saquinavir and indinavir/saquinavir). In one of these patients we found a genotypic reversal of 151M to wild-type.

Multi-dideoxynucleoside analogue resistance under combination therapy is an emerging problem in European patients. Although treatment options are currently limited for patients harbouring multi-

dideoxynucleoside analogue-resistant strains, a combination of two protease inhibitors may be a promising alternative.

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