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CLINICAL VALIDATION OF ATAZANAVIR/RITONAVIR GENOTYPIC RESISTANCE SCORE IN PI-EXPERIENCED PATIENTS

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BACKGROUND: Virological response to ATV/RTV containing HAART in PI-experienced patients was used to develop a clinically relevant genotypic resistance score.

METHODS: We included 62 PI-experienced patients switched to ATV/RTV (300 mg ATV, 100 mg RTV, plus other ARVs) with HIV-1 RNA >1000 copies/ml at baseline and detectable ATV in plasma at month three (M3). The impact of baseline protease mutations on virological response (>1 log RNA decrease) at M3 was analysed using Fischer's exact test. Mutations with prevalence >8% and $P < 20\%$ were retained. Cochran-Armitage's test was used to select the combination of mutations most strongly associated with the virological response (lowest P value). Robustness of the score was investigated using bootstrap re-sampling.

RESULTS: Median baseline viraemia and CD4 count were 4.3 log₁₀ copies/ml and 226/mm³, respectively. Patients had been treated with a median of 7.5 ARV drugs including two PIs. At M3, 82% of patients had a virological response and 56% had RNA <50 copies/ml. The PI mutations associated with a reduced response were 10F/I/V, 16E, 33I/F/V, 46I/L, 54L/V/M/T, 60E, 62V, 71I/T/V/L, 82A/T, 84V, 85V, 90M and 93L. The strongest association with the virological response was found with the combination of 10F/I/V, 16E, 33I/F/V, 46I/L, 60E, 84V and 85V ($P = 8.0 \times 10^{-9}$). Using this ATV resistance score, virological response was observed in 100%, 100%, 80%, 42%, and 0% of patients with 0, 1, 2, 3, ≥ 4 mutations, respectively. The number of active drugs was also associated with virological response ($P = 0.001$). In patients with ATV resistance score ≥ 3 , virological response was observed in 0%, 29% and 60% of patients with 0, 1

and 2–3 active drugs ($P=0.024$). Addition of the 90M to the previous score provides also a strong association with the virological response ($P=8.7\times 10^{-9}$). The bootstrap analysis showed the robustness of both scores.

CONCLUSION: Most PI-experienced patients switched to ATV/RTV containing HAART had a virological response. The ATV/RTV resistance score predicts reduced response in patients with at least three mutations of a set of seven to eight mutations.

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