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PREDICTORS OF DEATH, AND RESPONSE TO THERAPY IN PATIENTS WITH MULTI (THREE)-CLASS DRUG RESISTANT (MDR) HIV IN THE UK

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OBJECTIVE: To evaluate predictors of survival, and virological and immunological response in patients with multi-drug resistant (MDR) HIV in the UK.

METHODS: MDR resistance defined as at least one major mutation (IAS-USA) for each class, accumulated through multiple tests. Poisson and linear regression were used to determine factors associated with survival and HIV viral load (VL) response 24–48 weeks after MDR diagnosis. Change in regimen was defined as starting a regimen with one or more new drugs within 6 months after MDR diagnosis.

RESULTS: Six-hundred-and-twenty-eight patients with MDR HIV; 85.3% males; median age 43 years; median CD4 and VL at MDR diagnosis 238 cells/mm³ and 4.15 log₁₀ copies/ml; median number of ART drugs previously exposed to=8. There were 54 deaths after MDR diagnosis (median follow-up 23.9 months). Estimated probability of death was 3%, 8% and 13% by 12, 24 and 36 months respectively. After MDR diagnosis 280 patients changed regimen. In adjusted analysis, CD4 (incidence rate ratio (IRR); 0.75 per 100 cells/mm³ higher, 95% CI (0.54,0.99), *P*=0.05) and calendar year at MDR diagnosis (IRR 0.61 per 1 year increase (0.42,0.90), *P*=0.011) were significantly associated with a decreased risk of death. VL (IRR 2.06 per 1 log₁₀ copy higher (1.32,3.23), *P*=0.002) and number of ART drugs previously exposed to (IRR 1.25 per 1 drug higher (1.08,1.45), *P*=0.003) were also significantly associated with an increased risk of death. In patients changing therapy after MDR, genotypic sensitivity score of the new regimen was not significantly associated with a decreased risk of death (IRR 0.71 per 1 unit higher genotypic sensitivity score (IAS-USA), (0.39,1.29), *P*=0.26) but there was an association with decrease in VL after 24–48 weeks (*n*=262, -0.28 (-0.43, -0.13),

$P < 0.001$) and increased CD4 count at 24–48 weeks ($n=270$, 0.22 ($0.05-0.38$), $P < 0.001$). The three alternate strategies of a) continuing/changing therapy, b) undergoing an STI and re-starting therapy, or c) stopping therapy, after MDR diagnosis were associated with incremental increases in risk of death ($P < 0.001$).

CONCLUSION: Resistance test-guided treatment is associated with virological and immunological benefit in this group of advanced patients. Undertaking a treatment interruption after MDR diagnosis was associated with an increased risk of death compared to continued or change of therapy.

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