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Oral presentation

O133 HIV/TB: when is it safe to start HAART?

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Randomised controlled trials addressing the optimal timing of ART initiation in patients with tuberculosis are awaited but meanwhile, data from observational cohorts may inform policy. The decision of when to initiate HAART is complex, involving a number of variables including treatment tolerability, drug co-toxicities, pharmacokinetic drug interactions and impact of polypharmacy on adherence. However, of over-riding importance is mortality associated with delays in ART initiation versus mortality associated with immune reconstitution disease (IRD) when HAART is initiated early. Cross cohort comparisons are complicated by differing mortality in cohorts from high- and low-resourced settings and differing incidence of TB-associated IRD in TB patients initiating ART in different settings. While variable rates of IRD may represent differences between cohorts; analysis is complicated by variable ascertainment, and a lack of a standardised IRD definition. The proportion of patients reported to develop TB-associated IRD is higher and associated mortality lower in high- compared with low-income settings. Mortality in the first year of ART in sub-Saharan Africa (8–26%) greatly exceeds those in European and North American cohorts (approximately 2–3%), with most deaths occurring early after initiation of treatment. The mortality associated with delay in ART initiation is therefore likely to be much higher in Africa than in high-income countries. In South Africa, severe TB-associated IRD tends to develop in those patients who have high mortality risk, manifested by low CD4 cell counts and disseminated TB. Thus, although 10.5% of a South African cohort who developed TB-IRD died, 9.9% of TB patients who did not develop IRD also died. Thus, development of IRD in this study was not associated with significant excess mortality. In low-income settings the diagnosis of TB in HIV-infected patients is only diagnosed after prolonged delay and yet the mortality associated with even short delays in accessing HAART is unacceptably high. Variations in IRD frequency and associated mortality indicate that the optimum timing of ART initiation may differ between settings. In lower income countries, the risk of mortality associated with delays in ART initiation is likely to outweigh the excess mortality of TB-associated IRD. Therefore, the optimum timing of ART initiation may be earlier in the course of TB treatment for patients in resource-limited settings compared to those in high-income settings. Much interest has rightly focussed on the optimum timing of ART in relation to TB treatment. However, the potentially more important problem of delays in the care pathway has received little attention.