When to Start

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Until recently HIV treatment guidelines suggested starting treatment in patients with symptomatic HIV disease or if asymptomatic when the CD4 count declined to between 200 and 350 cells/mm3. In reality many started with CD4 counts of approximately 200 cells/mm3 or lower mainly because of presenting late with advanced immunosuppression.

Recently guidelines have been recommending earlier treatment when the CD4 falls below 350 rather than allow patients to wait and let the CD4 approach the 200 level. In some patients it may be appropriate to start even earlier if risk factors for progression or non-HIV related morbidities are present. The recommendation for earlier treatment has evolved as several studies have shown a higher risk of clinical disease at higher CD4 counts than previously thought. In the SMART study of treatment interruption those individuals, all with CD4 counts greater than 350 cells/mm3, and including both not on treatment and those randomised to treatment interruption, had more disease events than those who remained on treatment throughout. Interestingly the excess of clinical disease was not only due to HIV related conditions but also non-HIV related such as cardiovascular, renal and hepatic disease.

The North American AIDS Cohort Collaboration identified 2620 patients who had started treatment at a CD4 count above 500 cells/mm^3, and compared their risk of death to those who started treatment later. They found a 60% higher risk of death for those who deferred treatment (relative hazard 1.60, $p<0.001$, after controlling for potential confounding factors such as age and baseline viral load.

After six years 10% of those who deferred treatment had died, and 15% by eight years, indicating that althoug the absolute risk of dead was small, it was not negligible. A second analysis, using data from 21,247 patients in seven cohorts, yielding 68,256 person-years of follow-up was carried out by the When to Start Consortium, They compared the effects of deferring treatment across a range of CD4 cell bands below 550 cells/mm^3, and found that there was no significant difference in the risk of AIDS or death between those who started in the range 451-550 cells/mm^3 and those who started in the range 351 to 450 cells/mm^3 (HR 0.99, 95% CI 0.76 – 1.29). As expected there was a significant difference in the range 351-450 cells/mm^3 when compared to 251-350 cells/mm^3 (HR 1.28, 95% CI 1.04 – 1.57).

A large study called START has commenced and is looking at this question of starting early or deferring treatment in a randomised fashion.

As a consequence of all this data from cohorts the European AIDS Clinical Society (EACS) recommend treating

all individuals with a CD4 between 200 and 350 but also to consider in those with CD4 counts between 350-500; if presence of a high viral load (greater than 100,000 copies/ml), a rapidly declining CD4, older age or hepatitis C co-infection. The Department of Health and Human Sciences (DHHS) guidelines state that if HIV related renal disease is present, early commencement of ARVs should be recommended. The IAS/USA guidelines suggest that therapy should be considered and decision individualized if an individuals CD4 count is above 350 cells/mm3, and there is the presence of, or high risk for, cardiovascular disease active HBV or HCV co-infection or HIV-associated nephropathy.