

## Clinical prediction guide

### A simple scoring system predicted clinical progression in HIV patients receiving highly active antiretroviral therapy

Lundgren JD, Mocroft A, Gatell JM, *et al*, for the EuroSIDA Study Group. A clinically prognostic scoring system for patients receiving highly active antiretroviral therapy: results from the EuroSIDA study. *J Infect Dis* 2002 Jan 15;185:178–87.

**QUESTION:** In patients with HIV who are receiving highly active antiretroviral therapy (HAART), does a scoring system predict clinical progression?

#### Design

Prognostic scoring system developed in 1 derivation cohort and validated in 2 cohorts of patients.

#### Setting

60 centres in Europe and Israel.

#### Patients

2027 patients (median age 37 y) formed the derivation set: inception cohort of participants in the EuroSIDA study who were  $\geq 16$  years of age and had started a protease inhibitor or non-nucleoside reverse-transcriptase inhibitor as part of a HAART antiretroviral regimen and had CD4 cell counts and viral loads measured within 6

months before starting HAART and  $\geq 1$  measurement after starting HAART. 2 cohorts of patients formed the validation set: 1946 patients in the EuroSIDA study who started HAART before recruitment to the study and 1442 patients from a clinic in Barcelona who had previously started HAART.

#### Description of prediction guide

Cox proportional hazards models were used to determine factors associated with clinical progression. The final prediction model comprised the latest CD4 cell count, viral load, haemoglobin concentration, and clinical status at the start of HAART (no AIDS, severe AIDS [progressive multifocal leucoencephalopathy and non-Hodgkin's lymphoma], or other AIDS diagnosis). For CD4 cell counts, the cut points were 50 and 200 cells/mm<sup>3</sup>; for viral loads, the cut points were 500 and 10 000 HIV-RNA copies/ml. The normal haemoglobin concentration was defined as  $> 14$  g/dl for men and 12 g/dl for women; severe anaemia was defined as  $< 8$  g/dl for men and women. Logarithms of the relative hazards were used to derive a score for the variables with independent association with the risk for clinical progression. The score ranged from 0 to 17 points.

#### Main outcome measure

Clinical progression (new diagnosis of an AIDS defining event or death).

#### Main results

Among patients in the derivation cohort, 200 patients (9.9%) clinically progressed (death 30%, first AIDS defining illness 47%, and new AIDS defining illness 24%). For a 1 unit increase in score, a mean increase of 38% (95% CI 33% to 43%) occurred in risk for clinical progression. The incidence of clinical progression was 3.9/100 person years. In the EuroSIDA and Barcelona validation cohorts, the incidence of clinical progression was 4.2 and 4.6 per 100 person years, respectively. A single point increase in score was associated with an increased risk for clinical progression of about 40% among the 3 cohorts.

#### Conclusions

In patients with HIV who are receiving highly active antiretroviral therapy, a scoring system based on the latest CD4 cell count, viral load, and haemoglobin concentration and a previous severe AIDS diagnosis was predictive of clinical progression. The risk for disease progression of a 1 unit increase in score was about 40%.

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#### COMMENTARY

Despite the success of HAART in reversing the immunosuppression seen in patients infected with HIV, some patients receiving HAART still have poor outcomes. To quantify the risk for a poor outcome, Lundgren *et al* developed a point system based on CD4 T cell numbers, viral load, haemoglobin concentration, and previous diagnosis of "severe" AIDS. (Readers should note that there is a typographic error in the description of the scoring system at the bottom of page 181; the cutoffs for the scoring of viral load are  $< 500$  copies/ml, 500 to 9999 copies/ml, and  $\geq 10\,000$  copies/ml.) The risk for progression varied from 1/100 person years with a score of 0, to about 11/100 person years with a score of 6, to  $> 100/100$  person years with a score of  $\geq 12$ . The strengths of this system are its simplicity, the fact that similar markers were used to predict progression in patients before use of HAART, the large numbers of patients used for both the derivation and validation sets, and the fact that intuitively the components of the prediction guide seem to be relatively important measures.

Despite these advantages, I suspect that most clinicians will not calculate a score but rather will use the individual variables to guide decision making because the study offers no insight into how a calculated score would change clinical practice. Furthermore, several recently recognised factors were not included in the derivation of the guide: co-infection with hepatitis viruses (especially hepatitis C and hepatitis G),<sup>1</sup> viral resistance, achieving a viral load  $< 50$  copies/ml,<sup>2</sup> and transient increases in viral load (referred to as "blips").<sup>3</sup>

This study will perhaps best be used as a starting point for a clinical trial in which patients with a high score are randomly allocated to 1 of several groups: continuing current treatment, switching to an alternative HAART regimen, using recombinant erythropoietin, or utilising a "drug holiday", usually referred to as a structured treatment interruption.

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- 1 Tillmann HL, Heiken H, Knapik-Botor A, *et al*. Infection with GB virus C and reduced mortality among HIV-infected patients. *N Engl J Med* 2001;345:715–24.
- 2 Durant J, Clevenbergh P, Halfon P, *et al*. Drug-resistance genotyping in HIV-1 therapy: the VIRADAPT randomised controlled trial. *Lancet* 1999;353:2195–9.
- 3 Havlir D, Bassett R, DeGruttola V, *et al*. Are episodes of transient viremia ("blips" in HIV RNA) predictive of virologic failure in heavily treatment-experienced patients? [Abstract]. 9th Conference on Retroviruses and Opportunistic Infections, Seattle, WA, 24–28 Feb 2002.