

Risk factors for hepatotoxicity of nevirapine-containing antiretroviral drug regimens in a large antiretroviral treatment program in Rwanda



Johan van Griensven[†], Edi F Atté[†], Freya Rasschaert[‡], Rony Zachariah[‡], Tony Reid[‡]

[†] Médecins Sans Frontières, 6089 Kigali, Rwanda, 08597623 ; jvgrie@yahoo.com; [‡] Médecins Sans Frontières, Operational Centre Brussels, Medical department, 1090 Brussels, Belgium; Tony.REID@brussels.msf.org

Objectives

Whereas studies from high-income countries have shown that female sex and a baseline CD4 cell count >250 cells/μL increase the risk of nevirapine-induced hepatotoxicity, data from low-income countries show conflicting results. However, given the tendency to start antiretroviral treatment (ART) at higher baseline CD4 cell counts, in particular within prevention-of-mother-to-child (PMTCT) programs, the safety of using nevirapine at CD4 counts > 250 cells/μL needs to be further assessed.

Analysis

Analysis of toxicity-related drug substitutions of 2367 adults starting nevirapine-containing ART regimens in two urban government health centers in Kigali, Rwanda. Risk factors for severe nevirapine-related hepatotoxicity (grade III/IV) were assessed using multivariate Cox regression analysis.

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Table 1: Baseline characteristics of adult patients started on NVP-containing antiretroviral treatment

Baseline characteristic	
Sex	
Male	643 (27%)
Female	1724 (73%)
Age at start of treatment (years)	35 (31-41)
Baseline WHO clinical stage	
Stage I	147 (6%)
Stage II	674 (28%)
Stage III	1378 (59%)
Stage IV	162 (7%)
Baseline CD4 count (cells/μL)	
Male	171 (106-232)
Female	140 (72-203)
Baseline body mass index (kg/m ²)	
Male	20.1 (18.5-21.8)
Female	21.8 (19.9-24.3)
Abnormal baseline liver test	
Male	77 (17%)
Female	133 (10%)

Table 2: Risk factors for NVP-related hepatotoxicity

	OR (95% CI)	P-value	aOR (95% CI)	P-value
Sex				
Male	1		1	0.71
Female	0.6 (0.3-1.3)	0.24	1.2 (0.4-3.6)	
Age (years)				
< 40	1	0.02	1	0.23
≥ 40	2.3 (1.2-4.8)		1.89 (0.7-5.1)	
WHO stage				
I	1	0.74	1	0.58
II/III/IV	1.1 (0.6-1.8)		1.4 (0.4-4.3)	
CD4 count				
< 250	1		1	0.78
≥ 250	0.6 (1.2-2.9)	0.36	1.2 (0.3-4.2)	
Baseline liver test				
Normal	1	<0.01	1	<0.01
Abnormal	4.1 (1.7-9.8)		5.4 (2.0-14.1)	
BMI (kg/m ²)				
≥ 20	1	0.02	1	0.04
< 20	2.8 (1.2-6.4)		2.3 (1.1-5.3)	

Results

Of a total of 2367 patients, 73% were female (n=1724). The median baseline CD4 count was 162 cells/μL and 22 % started ART with a baseline CD4 count > 250 cells/μL. Thirty patients (1.27%) developed severe hepatotoxicity (incidence rate 9/1000 patient-years). In multivariate analysis, abnormal baseline liver function tests (hazard ratio (HR): 5.37 (95% CI 2.04-14.14) P=0.001) and a body mass index (BMI) < 20 kg/m² (HR: 2.27 (95% CI 1.03-5.27.); P=0.037) were significantly associated with hepatotoxicity. There was no significant associated risk with baseline CD4 counts > 250 cells/μL (HR: 1.19 (95% CI 0.34-4.17.); P=0.778) or female sex (HR: 1.22 (95% CI 0.42-3.58.); P=0.711).

Conclusions

These data suggest that nevirapine administered to women with baseline CD4 counts > 250 cells/μL, as can occur in PMTCT programs, is not significantly associated with a higher risk of hepatotoxicity. Further evidence from other similar settings would be useful to compliment this finding.