

Discordant responses to antiretroviral treatment: prevalence, risk factors and associated mortality in Rwanda



Johan van Griensven[†], Edi F Attét[†], Freya Rasschaert[‡], Anita Asiimwe[§], 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; [§] Treatment and Research AIDS Center, Kigali, Rwanda

Objective

Discordant (opposite virological and immunological) responses to antiretroviral treatment (ART) remain poorly understood in low-income countries. We aimed to identify the prevalence of and risk factors for discordant responses and the associated mortality.

Methods

Analysis of the outcomes of 962 adults within the ART program in two urban government health centers in Rwanda, where approximately 90% started a regimen containing stavudine/lamivudine/nevirapine. Viral load measurement was performed routinely after 1 year of treatment. Virological failure (VL-) was defined as a viral load >1000 copies/ml. Immunological success (CD4+) was defined as an increase in CD4 count >50 cells/ul from baseline. Multivariate analysis was done to identify risk factors for discordant responses and to assess the association of discordant responses with mortality, with complete responders as reference group.

Acknowledgements

We are grateful to all the staff of the Kimironko and Kinyinya health centres for their work on HIV/AIDS and the Ministry of Health of Rwanda for the excellent collaboration. We are particularly grateful to all patients who participated in this assessment. This project received funding from the European union, the Belgian Development Cooperation (DGCD) and the Global Fund to fight AIDS, Tuberculosis and Malaria.

Table 1. Logistic regression analysis to identify factors associated with discordant responses compared to complete responders

Risk factor	Virological-response only (VL+/CD4-) (n=188)			Immunological-response only (VL-/CD4+) (n =53)		
	OR ^a	Adjusted OR ^a	P	OR ^a	Adjusted OR ^a	P
Sex						
Male	1	1		1	1	
Female	0.61 (0.43-0.86)	0.59 (0.40-0.87)	0.007	0.63 (0.35-1.15)	0.74 (0.38-1.43)	0.367
Age (years)						
< 30	1	1		1	1	
30-40	1.49 (0.92-2.41)	1.50 (0.91-2.48)	0.113	0.72 (0.36-1.44)	0.73 (0.34-1.53)	0.402
>40	1.98 (1.20-3.27)	1.87 (1.09-3.20)	0.024	0.75 (0.35-1.60)	0.68 (0.29-1.57)	0.365
Baseline body weight (kg)						
≤ 65	1	1		1	1	
> 65	0.94 (0.60-1.46)	0.90 (0.57-1.43)	0.660	1.86 (0.97-3.56)	2.17 (1.08-4.36)	0.030
Baseline CD4 count (c/μL)						
< 50	1	1		1	1	
50-200	1.85 (1.03-3.31)	1.87 (1.02-3.45)	0.044	0.36 (0.19-0.70)	0.39 (0.20-0.80)	0.009
>200	1.85 (0.99-3.41)	1.93 (1.01-3.71)	0.048	0.27 (0.12-0.60)	0.26 (0.11-0.65)	0.004
Time on ART (years)						
≤ 1.5	1	1		1	1	
> 1.5	0.44 (0.30-0.64)	0.44 (0.29-0.66)	0.000	1.29 (0.73-2.26)	1.17 (0.63-2.17)	0.615
Baseline WHO stage						
I	1	1		1	1	
II/III/IV	0.56 (0.29-1.08)	0.57 (0.26-1.23)	0.152	1.12 (0.26-4.85)	0.80 (0.16-3.84)	0.772
NNRTI at start of ART						
EFV	1	1		1	1	
NVP	1.49 (0.74-2.99)	1.33 (0.62-2.88)	0.460	0.79 (0.30-2.06)	1.07 (0.34-3.33)	0.907
NRTI at start of ART						
AZT	1	1		1	1	
D4T	0.88 (0.49-1.58)	0.73 (0.36-1.44)	0.362	0.98 (0.34-2.83)	1.28 (0.36-4.84)	0.708
NNRTI toxicity						
No	1	1		1	1	
Yes	0.91 (0.45-1.86)	0.86 (0.41-1.81)	0.701	0.65 (0.15-2.78)	0.68 (0.15-2.97)	0.606
NRTI toxicity						
No	1	1		1	1	
Yes	0.89 (0.56-1.39)	1.01 (0.62-1.65)	0.955	0.92 (0.42-2.01)	0.90 (0.39-2.09)	0.814
TB on ART						
No	1	1		1	1	
Yes	1.92 (0.94-3.95)	2.75 (1.27-5.96)	0.010	1.13 (0.26-4.94)	0.95 (0.20-4.42)	0.944
Adherence ^b						
100 %	1	1		1	1	
95-99 %	0.66 (0.43-1.01)	0.76 (0.48-1.20)	0.242	1.48 (0.78-2.81)	1.13 (0.52-2.49)	0.755
<95 %	0.79 (0.55-1.15)	0.84 (0.57-1.26)	0.403	1.32 (0.53-3.27)	1.56 (0.78-3.09)	0.207

^a OR: odds ratio (95% confidence interval);

^b Based on clinical attendance as a measure of adherence to therapy

VL: viral load measurement; WHO: World Health Organisation; NNRTI: non-nucleoside reverse transcriptase; EFV: efavirenz; NVP: nevirapine; NRTI: nucleoside reverse transcriptase inhibitors; AZT: zidovudine; d4T: stavudine; ART: antiretroviral treatment; TB: tuberculosis

Results

In total, 691 (71.8%) subjects were complete responders, and 30 (3.1%) complete non-responders. Discordant responses were seen in 243 (25.1%) patients, with 188 (19.6%) virological-only responses (VL+/CD4-) and 53 (5.5%) immunological-only responses (VL-/CD4+). Patients with a virological-only response were significantly more likely to be > 40 years old, less likely to be of female sex and to be on ART for > 1.5 years. A baseline CD4 count >50 cells/μL and the development of tuberculosis while on ART were identified as additional risk factors. An immunological-only response was associated with a baseline body weight of >65 kg and with baseline CD4 counts <50 cells/μL. Virological-only responders had a higher short-term mortality (hazard ratio (HR) 7.16; P=0.006), no significant difference was observed for immunological-only responders (HR: 3.65; P=0.266).

Conclusions

This study confirms discordant responses to occur frequently in patients on ART in Rwanda, with different risk factors according to the type of discordance. Patients with virological-only responses are a population at risk and might require closer medical follow-up.