Adherence Predicts Failure on PI-Based Second-Line ART in Rural South Africa

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Introduction

Rollout of ART in sub-Saharan Africa has been accompanied by high prevalence of virological failure (VF) and resistance on NNRTI-based first-line ART, resulting in large numbers being switched to second-line ritonavir boosted protease inhibitor (PI) based ART.

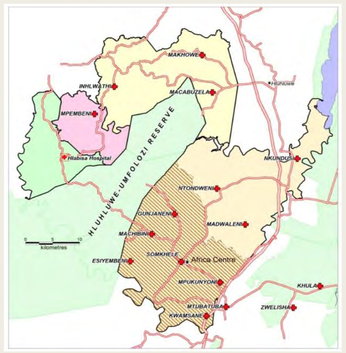
VF on PI-based ART is common and the reasons why are not well understood. Given the limited options for further lines of treatment in sub-Saharan Africa, it is important to understand the reasons and mechanisms of PI failure in order inform optimal use of second and third line regimens.

Aims

To determine the incidence and risk factors for VF amongst second line patients receiving routine HIV care and treatment in a government program in a poor and rural setting in Kwazulu-Natal.

Method

Setting: The study was based in the Hlabisa sub-district, Umkanyakude district of northern Kwazulu-Natal in South Africa.



Study Design: This is a retrospective analysis of a prospective cohort of HIV-1 positive patients initiating second line ART regimen between Mar 2006 and December 2012.

Primary Outcome: Virological failure (VF) defined as a viral load (VL) of > 1000 copies/mL at least 6 months after commencing second-line treatment.

Exposure: 1) Adherence was were measured using a modified medication prescription ratio (mMPR). This was calculated by taking the number of months for which a pharmacy refill prescription was submitted as a fraction of the number of months in any given treatment period and expressed as a percentage.

2) Other patients' clinical and demographic factors of interest were explored.

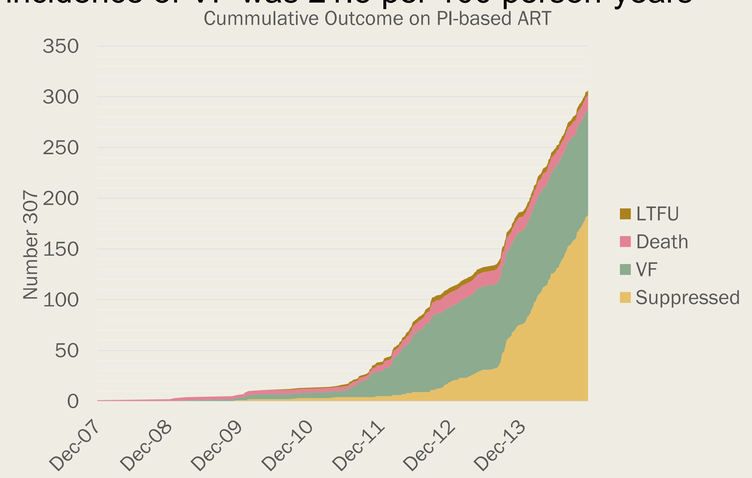
Analysis was done using competing risk regression, taking into account death and loss to follow up as competing risks.

Results

307 patients contributed a total of 539.08 person-years to follow up. Median age at PI initiations was 37 years (IQR 31.6 to 42.6 years) . 72.3% were female. The incidence of VF was 21.5 per 100 person-years (95% CI 17.9 to 25.8 per 100 person-years)

Factors	SHR(95% CI)	P value
Sex		
Male	-	0.05
Female	0.71 (0.50-1.00)	
Age at initiating PI *years*		
>15 -34	-	0.34
>35	0.86 (0.63-1.17)	
VL at switch (copies/ml)		0.041*
0-1000	-	
1001- 99 999	1.57 (1.00 to 2.47)	
100 000- 1 500 000	1.98 (1.14 to 3.45)	
CD4 at switch (cells/mm^3)		0.001*
0-200	-	
200-350	0.52 (0.33 to 0.79)	
350-500	0.74 (0.41 to 1.31)	
>500	0.27 (0.12 to 0.60)	
mMPR during second line regimen (%)		<0.001*
0-79	-	
80-89	0.69 (0.46 to 1.03)	
≥90	0.23 (0.10 to 0.49)	
mMPR during first line regimen (%)		0.026*
0-79	-	
80-89	0.61 (0.41 to 0.91)	
≥90	0.44 (0.16 to 1.18)	
Duration on failing regimen (months)		0.48
0-11	-	
12-23	0.75 (0.44 to 1.28)	
24-35	0.66 (0.37 to 1.18)	
36-72	0.89 (0.48 to 1.65)	

Results



Conclusion

There is a high incidence of VF on PI-based SLART in this rural setting with high unemployment. The level of adherence to treatment predicts VF. This has implications for the move to near universal, early ART in resource limited settings particularly as there are limited options for third line ART.