

Cohort Profile: The PharmAccess African Studies to Evaluate Resistance Monitoring Study (PASER-M) HIV-1 drug resistance in sub-Saharan Africa

AIDS 2010 abstract number: THPE0236

RL Hamers¹, C Kityo², M Siwale³, F Conradie⁴, ME Botes⁵, S Abdallah⁶, N Ngorima⁷, A Osibogun⁸, WS Stevens⁴, KCE Sigaloff¹, I Derdelinckx⁹, R Schuurman⁹, M van Vugt¹, TF Rinke de Wit¹ on behalf of the PharmAccess African Studies to Evaluate Resistance (PASER)

PharmAccess
FOUNDATION

INTRODUCTION

With the expanding access to ART in sub-Saharan Africa, relatively little attention has been paid to implementing accompanying drug resistance monitoring. In the absence of viral load monitoring, late detection of treatment failure may result in accumulation of resistance-associated mutations. This may compromise treatment effectiveness and may also be transmitted to newly infected individuals. Additionally, the large genetic diversity of HIV-1 in Africa may effect mutational pathways of resistance.

OBJECTIVES

The PharmAccess African Studies to Evaluate Resistance Monitoring Study (PASER-M) aims to assess patterns and determinants of HIV-1 drug resistance in patients initiating first-line ART or switching to second-line after failure. ART effectiveness is evaluated at 12 and 24 months after initiation/switch.

METHODS

PASER-M is an ongoing multi-center prospective cohort study in >3,000 persons receiving first- or second-line ART in routine circumstances at 13 clinical sites in 6 African countries. Follow-up is at least 24 months. PASER is part of the bi-regional Africa-Asia LAASER collaboration. Protocols are harmonized with the WHO HIV Drug Resistance Prevention Survey.

LESSONS LEARNT

- PASER has developed regional capacity for the coordinated monitoring and surveillance of HIV-1 drug resistance.
- A new network of clinics, laboratories and research groups has been established.
- An observational database, a system for cross-border specimen shipments including specimen tracking have been developed.
- Improved regional laboratory capacity for quality-assured resistance genotyping.
- The large number and variation of patients and ART programs participating in PASER is an important strength.
- PASER will contribute to evidence-based recommendations to inform treatment guidelines and health policies.
- One of the limitations of the PASER program is the high cost of laboratory testing, which could not be sustained under the current country budgets.

AFFILIATIONS

¹PharmAccess Foundation, Amsterdam Institute for Global Health and Development, Academic Medical Centre, Amsterdam, The Netherlands; ²Joint Clinical Research Center, Kampala, Uganda; ³Lusaka Trust Hospital, Lusaka, Zambia; ⁴University of the Witwatersrand, Johannesburg, South Africa; ⁵Muelmed Hospital, Pretoria, South Africa; ⁶International Center for Reproductive Health, Mombasa, Kenya; ⁷Newlands Clinic, Harare, Zimbabwe; ⁸Lagos University Teaching Hospital, Lagos, Nigeria; ⁹University Medical Center, Utrecht, The Netherlands.

RESULTS

Table 1: Characteristics of the ART programs participating in PASER-M

Country	Clinic type	Sector	Setting	Year of first ART	Total adults on ART	Research experience	Number of staff	Patients per staff	Free care	Viral load available
Zambia	General hospital	Private	Urban	1997	625	No	11	61	No	Yes
	HIV clinic	NGO	Urban	2004	870	No	7	220	Yes	No
	General hospital	Church	Urban	2006	494	No	4.5	196	Yes	No
S Africa	HIV clinic	Private	Urban	2000	1 150	Yes	3	767	No	Yes
	HIV clinic	Public	Urban	2004	9 500	Yes	15	933	Yes	Yes
	HIV clinic	NGO	Rural	2004	1 201	No	5	825	Yes	Yes
Zimbabwe	HIV clinic	NGO	Urban	2004	1 292	Yes	14	109	Yes	No
Uganda	HIV clinic	Public	Urban	1992	4 871	Yes	62	134	Yes	Yes
	HIV clinic	Public	Rural	2003	2 502	No	7	693	Yes	Yes
	HIV clinic	Public	Rural	2002	2 823	No	6	603	Yes	Yes
Kenya	General hospital	Public	Urban	2003	4 788	Yes	17	627	Yes	No
	General hospital	Church	Urban	2006	839	No	7	200	Yes	No
Nigeria	Teaching hospital	Public	Urban	2002	4 237	Yes	16	344	Yes	Yes

Table 2: Baseline characteristics of PASER-M participants

	Total	First line ART (ARV-naive)	First line ART (ARV-experienced)	Switch to second-line ART
Patients – no. (%)	2987 (100%)	2598 (87%)	138 (5%)	251 (8%)
Female – no. (%)	1723 (58%)	1494 (58%)	105 (76%)	124 (50%)
Age (years) – mean (sd)	38.0 (9.0)	38.0 (9.0)	34.6 (7.9)	40.1 (9.0)
WHO clinical stage – no. (%)				
III	1281 (43%)	1145 (44%)	59 (43%)	77 (31%)
IV	500 (17%)	437 (17%)	21 (15%)	42 (17%)
History of ARV drug use – no. (%)	389 (13%)	-	138 (100%)	251 (100%)
ART	312 (10%)	-	60 (44%)	249 (99%)
Mono or dual therapy	10 (<0.5%)	-	6 (4%)	4 (2%)
Single-dose NVP for PMTCT	37 (1%)	-	35 (25%)	1 (<0.5%)
Combination therapy for PMTCT	21 (1%)	-	19 (14%)	2 (1%)
Ever pulmonary TB – no. (%)	668 (22%)	569 (22%)	25 (18%)	74 (30%)
CD4 cell count (cells/μL) – median (iqr)	135 (63-206)	133 (62-204)	177 (92-262)	124 (53.5-194.5)
HIV-1 RNA (log ₁₀ copies/ml) – median (iqr)	4.9 (4.2-5.5)	4.9 (4.3-5.6)	4.8 (4.2-5.5)	4.1 1.7 (3.3-5.0)
ART regimen – no. (%)				
NNRTI-based regimen	2727 (91%)	2590 (99%)	135 (98%)	2 (1%)
AZT-containing	1016 (34%)	964 (37%)	51 (38%)	1 (<0.5%)
TDF-containing	918 (31%)	868 (34%)	49 (36%)	1 (<0.5%)
d4T-containing	723 (24%)	690 (27%)	33 (24%)	-
PI-based regimen	253 (9%)	6 (<0.5%)	-	247 (99%)
Triple NRTI regimen	5 (<0.5%)	2 (<0.5%)	3 (2%)	-

Figure 1: Location of PASER-M collaborating sites

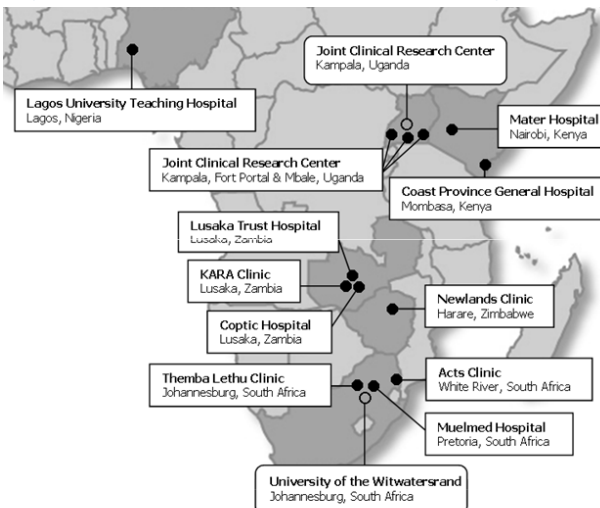
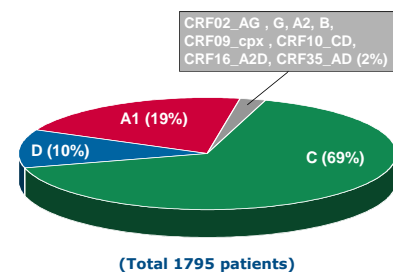


Figure 2: HIV-1 subtypes



NEXT STEPS

- Baseline and prospective HIV drug resistance data will become available in 2010-2012.
- A public-private consortium, entitled Affordable Resistance Test for Africa (ART-A), is developing affordable test algorithms for the detection and interpretation of HIV-1 drug resistance for use in laboratories and clinics.
- Resistance monitoring has been expanded to include HIV-1 infected children receiving ART
- **Correspondence: k.sigaloff@pharmaccess.org**