UNIVERSITY OF AMSTERDAM

UvA-DARE (Digital Academic Repository)

Drug-resistant HIV-1 in sub-Saharan Africa: clinical and public health studies

Hamers, R.L.

Publication date
2013

Link to publication

Citation for published version (APA):
Hamers, R. L. (2013). *Drug-resistant HIV-1 in sub-Saharan Africa: clinical and public health studies*. [Thesis, fully internal, Universiteit van Amsterdam].

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, P.O. Box 19185, 1000 GD Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (https://dare.uva.nl)

Download date:13 Nov 2026

Chapter 4

Cohort Profile: the PharmAccess African (PASER-M) and the TREAT Asia (TASER-M) Monitoring Studies to Evaluate Resistance – HIV drug resistance in sub-Saharan Africa and the Asia-Pacific

Raph L Hamers*, Rebecca Oyomopito*, Cissy Kityo, Praphan Phanuphak, Margaret Siwale, Somnuek Sungkanuparph, Francesca Conradie, Nagalingeswaran Kumarasamy, Mariette E Botes, Thira Sirisanthana, Saade Abdallah, Patrick CK Li, Nicoletta Ngorima, Pacharee Kantipong, Akin Osibogun, Christopher KC Lee, Wendy S Stevens, Adeeba Kamarulzaman, Inge Derdelinckx, Yi-Ming Arthur Chen, Rob Schuurman, Michèle van Vugt, Tobias F Rinke de Wit

International Journal of Epidemiology 2012;41(1):43-54

* These authors equally contributed to this manuscript and share first authorship.

HOW DID THE STUDY COME ABOUT?

According to World Health Organization (WHO) estimates, 33.4 million people were infected with the human immunodeficiency virus (HIV) type 1 globally at the end of 2008 [1]. Sub-Saharan Africa and Asia are the two regions having the highest HIV prevalence with 22.4 million and 4.7 million people infected, respectively [1]. During the 5 years prior, access to combination antiretroviral therapy (ART) in low- and middle-income countries increased 10-fold to reach 4 million people, providing coverage to 28% of those in need [2]. Several studies have reported significant reductions in HIV-related morbidity and mortality for individuals with access to treatment in these regions [3-5]. In resource-limited settings, to facilitate the rapid expansion of access to ART, WHO recommends a standardized, public health approach [6]. This is in contrast to the individualized patient-management strategies in developed countries, based on routinely available diagnostic monitoring [7]. Standardized first-line ART regimens consist of a non-nucleoside reverse transcriptase inhibitor (NNRTI) and a dual nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone, available in some countries as generic fixed-dose combinations [6]. Recommended second-line regimens combine a ritonavir-boosted protease inhibitor (PI) with two previously unused and/or recycled NRTIs [6].

Routine HIV viral load monitoring is not generally available in resource-limited countries and treatment failure is frequently identified based on immunological definitions and/or the occurrence of clinical events [6]. Virological breakthrough may be detected late while the failing regimen is continued, thus facilitating the acquisition and accumulation of drug resistance-associated mutations [8]. Drug-resistant HIV variants may compromise the effectiveness of subsequent lines of treatment and their transmission to newly infected individuals has severe public health consequences [9, 10]. To date, ART programmes have been implemented without accompanying HIV drug resistance (HIVDR) monitoring. Monitoring studies are hampered by the lack of a molecular laboratory infrastructure required for genotypic resistance testing, logistical challenges related to maintaining specimen integrity in remote settings and the high costs of testing [11]. Challenges to scaling up ART in resource-limited countries, such as absence of routine virological monitoring and limited choices of drug regimens, advocate for the development of a global public-health framework to monitor and prevent the emergence of HIVDR and thus maximize long-term ART effectiveness [12].

HIV-1 subtype B is the predominant viral subtype in North America, Western Europe and Australia, and antiretroviral (ARV) drugs have been developed on this subtype. However, in sub-Saharan Africa and Asia, the genetic diversity in HIV subtypes and circulating recombinant forms (CRFs), resulting from recombination between subtypes

within a dually infected person, is extensive [13]. Although current evidence is limited, some reports have suggested that the propensity to develop HIVDR and the spectrum of mutations that emerge during drug selective pressure, may differ across subtypes and CRFs [14-17]. Viral heterogeneity may, therefore, have implications for rates of disease progression and patient response to ART, warranting further study of inter-subtype differences in mutational pathways to resistance.

To help assess the extent of HIVDR in sub-Saharan Africa and Asia, a collaborative bi-regional programme was established, called LAASER [Linking African and Asian Societies for an Enhanced Response to HIV/AIDS; http://www.laaser-hivaids.org] with the primary aim of increasing regional capacities for the monitoring of HIVDR. PharmAccess Foundation, a non-profit organization dedicated to the strengthening of health systems and improving access to quality basic health care in sub-Saharan Africa, has developed the PharmAccess African Studies to Evaluate Resistance (PASER). TREAT Asia (Therapeutics, Research, Education and AIDS Training in Asia) is a network of clinics, hospitals and research institutions working to ensure safe and effective delivery of HIV/AIDS treatment throughout the Asia-Pacific and has developed the TREAT Asia Studies to Evaluate Resistance (TASER). Both PASER and TASER programmes incorporate a monitoring and evaluation (M) and a surveillance (S) protocol. Laboratories providing genotyping results for PASER and TASER are required to participate in the TREAT Asia Quality Assurance Scheme (TAQAS) which is an ongoing assessment program to build genotyping laboratory capacity, described elsewhere [18]. The focus of this cohort profile is the monitoring and evaluation protocols, PASER-M and TASER-M.

HOW ARE PASER AND TASER SET UP AND HOW ARE THEY FUNDED?

Through the LAASER program, PASER and TASER receive financial support from the Dutch Ministry of Foreign Affairs through a partnership with Stichting Aids Fonds, PharmAccess Foundation, TREAT Asia (a programme of amfAR, The Foundation for AIDS research) and International Civil Society Support. PASER-M is coordinated by PharmAccess Foundation, in collaboration with the Amsterdam Institute for Global Health and Development (AIGHD) and the Virology Department at the University Medical Center Utrecht, The Netherlands. TASER-M is coordinated by TREAT Asia and its statistical and data management centre is the National Centre in HIV Epidemiology and Clinical Research (NCHECR), The University of New South Wales in Sydney, Australia.

PASER constitutes a newly established collaboration between HIV treatment clinics, laboratories with the capacity to perform genotypic sequencing and research centers.

Thirteen clinical sites and two reference laboratories in six African countries (Kenya, Nigeria, South Africa, Uganda, Zambia and Zimbabwe) are collaborating on PASER-M (figure 1a). Details of the PASER-M collaborating clinical sites are summarized in table 1. Ethics approvals were obtained from the Academic Medical Center Institutional Review Board (IRB) and local IRBs. Sites are government, non-government, faith-based or private clinics and hospitals, situated in major cities or rural areas. ART was introduced at the sites at varying time points between 1992 and 2006 (median: 2004). Of the 13 sites, 11 provided drugs, consultations and routine lab testing free of charge. HIV viral load testing is available at 8 of 13 sites.

TASER collaborating sites are selected from within the existing TREAT Asia network based on their laboratory capacity to perform genotypic sequencing, described elsewhere [18, 19]. Sites that do not have internal laboratory genotyping capacity can participate through collaboration with a TAQAS-certified laboratory. Eleven clinical and laboratory sites in six Asian countries (China, Indonesia, Malaysia, Philippines, South Korea, Thailand) are collaborating on TASER-M (figure 1b). Ethics approvals were obtained from local IRBs having Federal wide Assurances (FWAs) in place from the United States Office for Human Research Protections. FWAs are required for TASER sites as they participate in the International Epidemiologic Databases to Evaluate AIDS (IeDEA) initiative, described elsewhere [20]. Sites are generally government or university-based clinics and hospitals or private clinics, situated in major cities and other urban areas. Those with ethics approvals prior to June 2010 are shown in figure 1b. ART has been available in Asia for more than 10 years, even in less-resourced countries in the region and all TASER-M clinical sites have on-site viral load testing.

Clinical sites follow their national guidelines to assess eligibility for ART initiation in accordance with the WHO recommendations [6]. Genotypic resistance testing on PASER and TASER clinical specimens are performed in TAQAS-certified genotyping laboratories [18]. Laboratories are encouraged to become accredited members of the WHO/HIVResNet HIV Drug Resistance Laboratory network [21]. Population-based nucleotide sequencing of the HIV protease (PR) and partial reverse transcriptase (RT) gene regions is performed on plasma specimens, which have HIV RNA of more than 1000 copies/ml. Plasma is obtained from blood collected in EDTA-tubes which is locally stored at -80°C and, if required, batch-shipped on dry ice to a genotyping laboratory.

PASER-M genotypic testing is concentrated in two central reference laboratories, and thus depends on a robust cold-chain and web-based specimen tracking system for managing specimen shipments. Approximately half of TASER-M clinical sites have an on-site or local genotyping laboratory. Most genotyping laboratories amplify viral

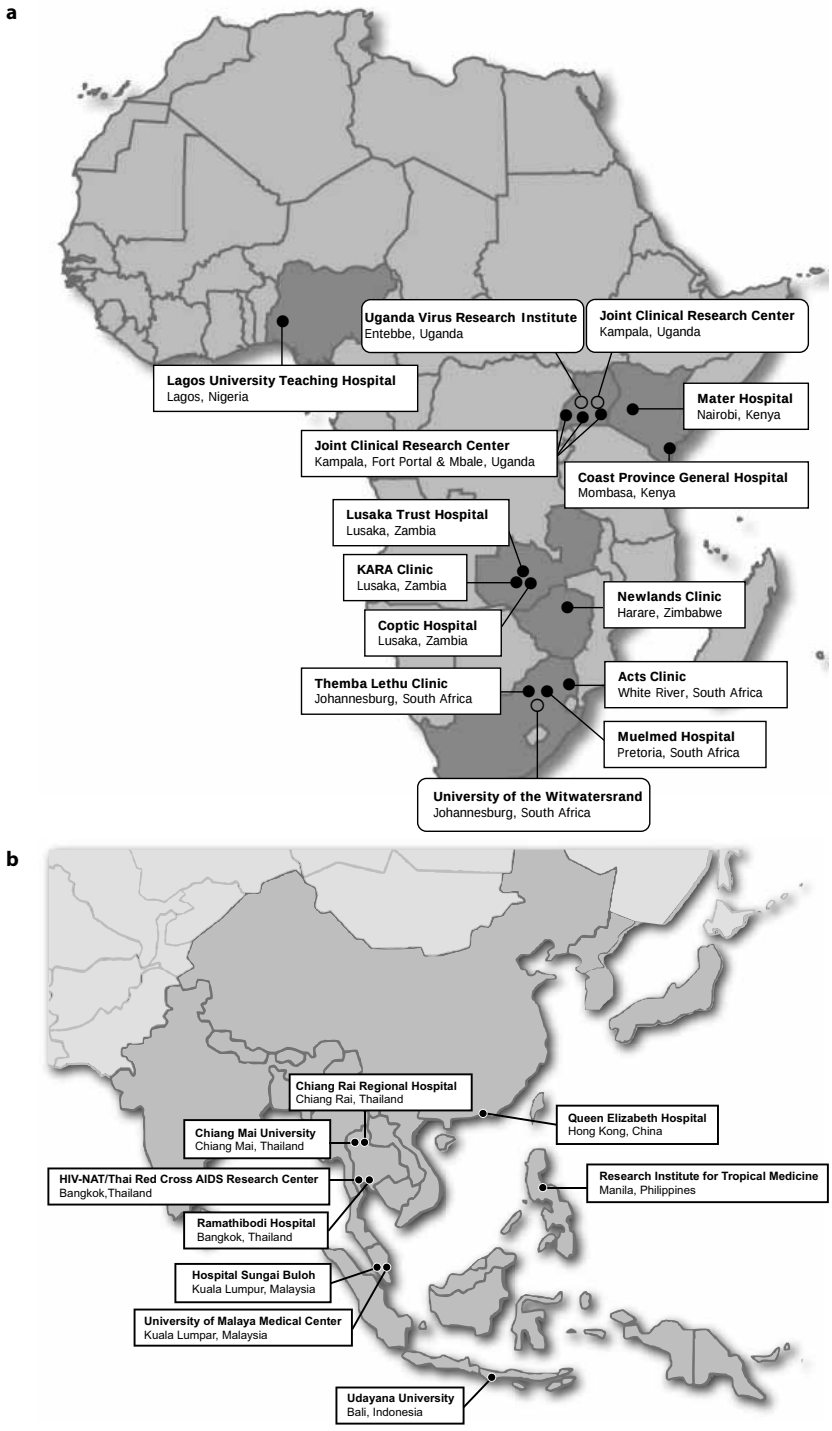

Figure 1. Geographical location of (a) PASER-M collaborating sites and (b) TASER-M collaborating sites

Table 1. Characteristics of the PASER-M collaborating clinical sites [a]

Country	Site	Sector	Site type	Setting	Year of ART introduction	Total adults HIV+	Total adults on ART	Research experienced	Number of staff [b]	Number of patients per staff [b]	Free care [c]	Patient tracing [e]	HIV viral load available	Main funding source	Month/ year of study initiation
Zambia	ZA/LTH	PFP	General hospital	Urban	1997	675	625	No	11	61	No [d]	No	Yes	Clients	03/07
	ZA/KAR	NGO	HIV clinic	Urban	2004	1540	870	No	7	220	Yes	Yes	No	CIDRZ/PEPFAR	03/07
	ZA/CHC	FBO	General hospital	Urban	2006	883	494	No	4.5	196	Yes	Yes	No	CHAZ/PEPFAR	05/07
S Africa	SA/MMH	PFP	HIV clinic	Urban	2000	2300	1150	Yes	3	767	No [d]	Yes	Yes	Clients	05/07
	SA/TLC	Public	HIV clinic	Urban	2004	14000	9500	Yes	15	933	Yes	Yes	Yes	MOH/USAID	09/07
	SA/ACC	NGO	HIV clinic	Rural	2004	4126	1201	No	5	825	Yes	Yes	Yes	USAID/PEPFAR	11/07
Zimbabwe	ZI/CON	NGO	HIV clinic	Urban	2004	1521	1292	Yes	14	109	Yes	Yes	No	SACI/SDC	09/08
Uganda	UG/JCR	Public	HIV clinic	Urban	1992	8308	4871	Yes	62	134	Yes	Yes	Yes	USAID/PEPFAR	01/08
	UG/JFP	Public	HIV clinic	Rural	2003	4849	2502	No	7	693	Yes	Yes	Yes	USAID/PEPFAR	01/08
	UG/MBA	Public	HIV clinic	Rural	2002	3615	2823	No	6	603	Yes	Yes	Yes	USAID/PEPFAR	02/08
Kenya	KE/CRH	Public	General hospital	Urban	2003	10653	4788	Yes	17	627	Yes	Yes	No	MOH/USAID	11/07
	KE/MAT	FBO	General hospital	Urban	2006	1402	839	No	7	200	Yes	Yes	No	PEPFAR	02/08
Nigeria	NI/LUT	Public	Teaching hospital	Urban	2002	5507	4237	Yes	16	344	Yes	Yes	Yes	MOH/PEPFAR	09/08

ART, combination antiretroviral therapy; NGO, non-governmental organization; FBO, faith-based organization; PFP, private for-profit; CIDRZ, Center for Infectious Diseases Research Zambia; PEPFAR, President's Emergency Plan for Aids Relief; CHAZ, Churches' Health Association Zambia; USAID, United States Agency for International Development; SACI, Swiss Aids Care International; SDC, Swiss Agency for Development and Cooperation; MOH, Ministry of Health;

[a] Data reflect situation at time of study initiation

[b] Medical doctors, clinical officers and nurses

[c] Includes consultations, medication and routine laboratory tests

[d] Approximation of cost (€) for consultation, ART/month, CD4 and HIV RNA test: SA/MMH 23, 28-46, 11, 59, respectively; ZA/LTH 10, 67-200, 27, 60, respectively

[e] Mostly by means of telephone calls to no-show patients

sequences using in-house methods, based on assembled commercially available assay components and laboratory-specific sequencing and amplification primers. One TASER laboratory uses the commercial kit TruGene (Bayer HealthCare, Tarrytown, NY, USA). The online Stanford interpretation system is used by most laboratories to identify drug resistance-associated mutations [22]. Resistance genotyping is generally performed retrospectively (i.e. not real-time) for all participants. Details of the genotyping laboratories are summarized in table 2. PASER and TASER sequences are submitted to the ViroScore database (Advanced Biological Laboratories SA, France) for data storage.

Table 2. PASER and TASER Genotyping Laboratories

Country	Genotyping laboratory	Sequencing Technology	Editing Software	Regions sequenced	Interpretation System
China	Hong Kong AIDS Trust Fund Molecular Laboratory, Dept of Microbiology, Queen Mary Hospital, Hong Kong [a]	In-house assay, BigDye Terminator, ABI	Staden Package version 1.6.0	PR: 1-99; RT: 1-400	Stanford
Malaysia	University of Malaya, HIV Research Laboratory, Medical Microbiology Department, University of Malaya, Kuala Lumpur [a]	In-house assay, PRISM® 3100-Avant Genetic Analyzer, ABI	BioEdit Version 7.0.9.0, Chromas Lite version 2.01	PR: 1-99; RT: 1-400	Stanford
South Africa	Department of Molecular Medicine and Haematology, University of the Witwatersrand, Johannesburg [b]	In-house assay, Prism 3100-*Avant* and 3730 Genetic Analyzer, ABI	Sequencher version 4.5	PR: 1-99; RT: 1-230	Stanford
Thailand	Vaccine and Cellular Immunology Laboratory (VCI lab), Division of Allergy and Clinical Immunology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok	In-house assay, BigDye Terminator, ABI	Sequence Navigator, ABI	PR: 1-99; RT: 20-270	Stanford
	Virology and Molecular Microbiology Unit, Ramathibodi Hospital, Mahidol University, Bangkok	TruGene, Bayer HealthCare	TruGene version 11	PR: 4-99; RT: 36-247	TruGene version 12
	HIV-1 Genotyping Laboratory, Chiang Mai University, Chiang Mai [a]	In-house assay, BigDye Terminator, ABI	SeqScape v2.0, ABI	PR: 1-99; RT: 1-250	Stanford
Uganda	Joint Clinical Research Center, Kampala [c]	In-house assay, CEQ 8000 Analyzer, BC	BioEdit version 7.0.9.0	PR:1-99; RT: 1-300	Stanford

[a] Laboratories serving 2 TASER-M clinical sites;

[b] Laboratory serving 7 PASER-M sites in southern Africa;

[c] Laboratory serving 6 PASER-M sites in east and west Africa

Manufacturer details: Applied Biosystems, Foster City, CA, USA; Bayer HealthCare, Tarrytown, NY, USA; Beckman Coulter Inc., Fullerton, CA, USA; BioEdit, www.mbio.ncsu.edu/BioEdit/bioedit.html; Chromas Lite, Technelysium, Queensland, Australia; Genecodes, Ann Arbor, MI, USA; Staden Package, http://staden.sourceforge.net/

WHAT DO PASER-M AND TASER-M COVER AND WHO IS INCLUDED IN THE SAMPLE?

The monitoring studies are multi-center prospective cohort designs with sequential patient enrolment. Patient eligibility criteria are listed in table 3. The main study objectives are to assess prevalence and incidence of HIVDR, mutational patterns and factors associated with HIVDR in persons initiating first-line ART or switching to a second-line regimen due to treatment failure under routine circumstances. Participants are required to sign informed consent prior to study enrolment and must initiate or switch ART within 30 days (PASER-M) or 181 days (TASER-M) following baseline specimen collection. Regimen switch due to treatment failure may be determined clinically, as assessed by disease progression, immunologically, by CD4 cell count, or virologically, by HIV viral load. A single drug substitution, due to toxicity or intolerance, is not considered a regimen switch. Each site aims to recruit a total of 240 participants. Second-line participants are recruited among first-line participants failing therapy and the clinical site patient population. The recommended maximum site-specific enrolment period is 18 months.

Table 3. Patient eligibility criteria for PASER-M and TASER-M

Inclusion criteria
Confirmed HIV-1 infection
≥18 years of age
Eligible [a] for initiation of a first-line ART regimen, or switch from a first-line ART regimen (containing at least three antiretroviral drugs and taken for at least six months) to a second-line ART regimen due to virological, immunological and/or clinical failure
Signed informed consent for study participation prior to enrolment
Exclusion criteria
Currently taking ART (minimum of 3 drug regimen), if initiating a first-line ART regimen [b]
Pregnancy at enrolment [c]
HIV-1/2 dual-infection (in endemic countries only) [c]

ART, combination antiretroviral therapy

[a] Eligibility for ART initiation defined in accordance with national ART guidelines (i.e. advanced immunodeficiency as defined by CD4 cell count <200 or <350 cells/µl, or advanced clinical disease according to WHO clinical stage/CDC classification).

[b] Specified PASER-M definition: re-initiation of a first-line ART regimen < 30 days after stopping previous first-line ART (previous use of antiretroviral prophylaxis or mono/dual therapy is not an exclusion criterion).

[c] Exclusion criteria applicable to PASER-M only

HOW OFTEN ARE PARTICIPANTS FOLLOWED-UP? WHAT DATA ARE BEING COLLECTED?

Participants are followed up as per local standard of care guidelines. The frequency of follow-up visits for patients varies by site (range: every 1 to 6 months). The studies make

use of clinical data collected during routine visits and recorded in medical records. HIV viral load measurement and, if HIV RNA value is more than 1000 copies/ml, genotypic resistance testing is performed on plasma specimens taken at baseline, prior to regimen switch due to treatment failure and at annual follow-up. For patients failing a first-line regimen, the treatment failure data collection becomes the new baseline for the second-line regimen. Annual follow-up is then calculated from this point. For patients failing a second-line ART, the treatment failure data collection is the final assessment prior to the patient going off study.

PASER-M clinical data are recorded on standardized hard-copy data forms which are completed at three-monthly intervals and entered in a web-based clinical data system, called the HAART Monitoring System. PharmAccess performs quality assurance measures which include (i) source data verification during 3 to 6-monthly site audits, (ii) checks to identify data entry inconsistencies or suspect data values and (iii) specimen tracking. TASER-M site personnel extract clinical data from site databases and medical records collected as part of usual care. From March 2008 to March 2009, TASER-M data were submitted electronically to NCHECR on a quarterly basis, as part of study start up, then at 6 monthly intervals. At each transfer, NCHECR performs quality assurance measures which include (i) checks to identify data entry inconsistencies or suspect data values, (ii) specimen tracking and (iii) ARV history completeness. Annually, a random 10% of TASER-M patients are selected for internal site audit where submitted data is compared to patient medical records.

The studies capture standardized virologic and genotypic data at protocol determined intervals. Genotyping data consists of HIV subtype and HIVDR mutations, including insertions and deletions. TASER-M also records discordant subtypes, i.e. when the PR and RT region subtypes differ. Laboratory specimen tracking information is recorded during specimen processing, allowing assessment of pre-analytical and assay validity. Genotyping laboratories complete an annual laboratory survey which includes the dynamic range of the virologic assay used, the regions of PR and RT genome routinely sequenced and the interpretation algorithm used. Observational patient data includes demographic parameters, physical measures, Centers for Disease Control and Prevention (CDC) class (TASER-M) or WHO clinical stage (PASER-M), serology of hepatitis and syphilis (TASER-M), opportunistic infections, current ART regimen, ARV history, concomitant medications, routine laboratory parameters (including CD4 counts) and assessment of drug adherence. Main analyses will include age, sex, ethnicity, HIV exposure category, WHO clinical stage (PASER-M) or CDC class (TASER-M), viral hepatitis co-infection status, CD4 count, HIV viral load, HIV subtype, drug adherence, ARV history and ART regimen as covariates. Predictors of drug resistance will be assessed using logistic regression models. Incidence

of drug resistance will be summarized using person-years methods and Kaplan-Meier plots. Cox proportional hazards models will be used to assess risk factors associated with developing drug resistance.

WHAT IS THE ANTICIPATED ATTRITION?

The actual attrition in PASER-M and TASER-M cannot currently be accurately estimated because the duration of follow-up in the databases is still limited. In sub-Saharan Africa patient retention in routine ART programmes has been estimated at 61.6% [23] to 66.8% [2] at 24 months on ART, attrition being mainly due to loss of follow-up and early death [23]. Therefore, in PASER-M the original site-specific sample size was calculated accounting for 20% loss to follow up and 25% mortality after 24 months. Attrition is expected to vary between sites, as a result of differences in patient populations, care provided and provisions for tracing lost to follow-up. TASER-M sites are generally sourced from the ongoing TREAT Asia HIV Observational Database (TAHOD) [19]. Loss to follow-up for TAHOD was 6.9/100 person-years for the 12-month period from September 2007 to September 2008. Since TASER-M monitors specified outcomes, we speculate that TASER-M follow-up will be similar to TAHOD or better.

WHAT HAS BEEN FOUND?

PASER-M

Patient recruitment commenced in March 2007 and was completed in September 2009. Of the 13 sites, 12 reached the site-specific target of 240 participants, enrolling a total of 3005 participants. Excluding patients with protocol violations (n=16) and key data missing (n=4), 2985 patients were included in the analysis. Of these, 2736 (91.6%) were eligible for a first-line ART regimen and 249 (8.3%) were eligible for second-line ART due to treatment failure. Patient characteristics are summarized in table 4. For first-line patients, the median age was 36.8 years (interquartile range, IQR 31.3-42.6) and 58% were women. HIV exposure was predominantly reported as heterosexual contact. More than 60% had advanced disease (classified as WHO stage III or IV) and 37% had pre-therapy CD4 counts of less than 100 cells/μL. Across all 13 sites, median baseline CD4 counts of first-line patients were less than 200 cells/μl (site median 135 cells/μL, range: 93 – 191). Median baseline HIV viral load was 4.9 $\log_{10}$ copies/ml (IQR 4.2-5.5). The most frequently prescribed first-line regimens were based on NNRTIs (99.7%), i.e. efavirenz (EFV) and nevirapine (NVP) at 60% and 40%, respectively. First-line dual NRTI backbones were predominantly lamivudine (3TC)/zidovudine (AZT) (37%), emtricitabine (FTC)/

Table 4. Baseline patient characteristics, by region and line of ART

	PASER-M (Africa)				TASER-M (Asia)		
	Total	Initiation of first-line ART [a]		Switch to second-line ART [b]	Initiation of first-line ART [a]		Switch to second-line ART [b]
		ARV-naive	ARV-experienced [c]		ARV-naive	ARV-experienced [c]	
Patients, no. (%)	3713	2598 (87.0)	138 (4.6)	249 (8.3)	693 (95.2)	10 (1.4)	25 (3.4)
Sex							
Female – no. (%)	1988 (53.5)	1494 (57.5)	105 (76.1)	124 (49.8)	239 (34.5)	10 (100.0)	16 (64.0)
Male – no. (%)	1725 (46.5)	1104 (42.5)	33 (23.9)	125 (50.2)	454 (65.5)	0 (0.0)	9 (36.0)
Age (years), median (IQR)	36.9 (31.7-43.3)	37.0 (31.2-42.8)	34.7 (29.2-40.2)	38.6 (32.9-44.2)	36.5 (31.1-43.2)	33.1 (27.4-38.4)	36.5 (32.4-41.9)
18-29	707 (19.0)	490 (18.9)	39 (28.3)	28 (11.2)	143 (20.6)	3 (30.0)	4 (16.0)
30-39	1668 (44.9)	1176 (45.3)	65 (47.1)	112 (45.0)	298 (43.0)	5 (50.0)	12 (48.0)
≥40	1338 (36.0)	932 (35.9)	34 (24.6)	109 (43.8)	252 (36.4)	2 (20.0)	9 (36.0)
HIV exposure, no. (%)							
Heterosexual contact	2583 (69.6)	1731 (66.6)	108 (78.3)	191 (76.7)	520 (75.0)	10 (100.0)	23 (92.0)
Homosexual contact	134 (3.6)	4 (0.2)	0 (0.0)	0 (0.0)	128 (18.5)	0 (0.0)	2 (8.0)
Other [d]	996 (26.8)	863 (33.2)	30 (21.7)	58 (23.3)	45 (6.5)	0 (0.0)	0 (0.0)
WHO clinical stage, no. (%)							
I	493 (16.5)	393 (15.1)	25 (18.1)	75 (30.1)	na	na	na
II	711 (23.8)	623 (24.0)	33 (23.9)	55 (22.1)	na	na	na
III	1281 (42.9)	1145 (44.1)	59 (42.8)	77 (30.9)	na	na	na
IV	500 (16.7)	437 (16.8)	21 (15.2)	42 (16.9)	na	na	na
CDC classification, no. (%)							
A	302 (41.5)	na	na	na	296 (42.7)	0 (0.0)	6 (24.0)
B	166 (22.8)	na	na	na	152 (21.9)	10 (100.0)	4 (16.0)

Table 4 (continued)

	PASER-M (Africa)				TASER-M (Asia)		
	Total	Initiation of first-line ART [a]		Switch to second-line ART [b]	Initiation of first-line ART [a]		Switch to second-line ART [b]
		ARV-naive	ARV-experienced [c]		ARV-naive	ARV-experienced [c]	
C	260 (35.7)	na	na	na	245 (35.4)	0 (0.0)	15 (60.0)
Ever pulmonary tuberculosis, no. (%)	741 (20.0)	569 (21.9)	25 (18.1)	74 (29.7)	69 (10.0)	na	4 (16.0)
Hepatitis B [f] – no. (%)	36 (4.9)	na	na	na	35 (5.1)	0 (0.0)	1 (4.0)
Hepatitis C [g] – no. (%)	56 (7.7)	na	na	na	55 (7.9)	0 (0.0)	1 (4.0)
History of ARV drug use, no. (%)	422 (11.4)	na	138 (100.0)	249 (100.0)	na	10 (100.0)	25 (100.0)
ART	334 (9.0)	na	60 (43.5)	249 (100.0)	na	0 (0.0)	25 (100.0)
Mono or dual therapy	10 (0.3)	na	6 (4.3)	4 (1.6)	na	0 (0.0)	0 (0.0)
Single-dose NVP for PMTCT	36 (1.0)	na	35 (25.4)	1 (0.4)	na	0 (0.0)	0 (0.0)
Combination therapy for PMTCT	31 (0.8)	na	19 (13.8)	2 (0.8)	na	10 (100.0)	0 (0.0)
Unspecified	22 (0.6)	na	22 (15.9)	0 (0.0)	na	0 (0.0)	0 (0.0)
CD4 cell count (cells/μL), median (IQR)	129 (56-205)	133 (62-204)	177 (92-262)	125 (46-196)	99 (33.5-201)	169 (151-222)	197 (109-299)
<100	1456 (39.2)	975 (37.5)	38 (27.5)	102 (41.0)	337 (48.6)	1 (10.0)	3 (12.0)
100-199	1215 (32.7)	914 (35.2)	42 (30.4)	81 (32.5)	164 (23.7)	6 (60.0)	8 (32.0)
≥200	1007 (27.1)	702 (27.0)	57 (41.3)	64 (25.7)	171 (24.7)	3 (30.0)	10 (40.0)
Unknown	25 (0.7)	7 (0.3)	1 (0.7)	2 (0.8)	21 (3.0)	0 (0.0)	4 (16.0)
HIV RNA (log_{10} c/ml), median (IQR)	4.9 (4.3-5.5)	4.9 (4.3-5.6)	4.8 (4.2-5.5)	4.1 (3.2-5.0)	5.0 (5.4-6.8)	4.8 (4.5-5.0)	4.0 (3.6-4.5)
ART regimen							
NNRTI-based triple regimen	3330 (89.7)	2590 (99.7)	135 (97.8)	2 (0.8)	593 (85.6)	10 (100.0)	0 (0.0)

Table 4 (continued)

	PASER-M (Africa)				TASER-M (Asia)		
	Total	Initiation of first-line ART [a]		Switch to second-line ART [b]	Initiation of first-line ART [a]		Switch to second-line ART [b]
		ARV-naive	ARV-experienced [c]		ARV-naive	ARV-experienced [c]	
AZT-containing	1302 (35.1)	964 (37.2)	51 (37.8)	1 (0.4)	170 (28.7)	10 (100.0)	0 (0.0)
TDF-containing	1088 (29.3)	868 (33.5)	49 (36.3)	1 (0.4)	110 (18.5)	0 (0.0)	0 (0.0)
d4T-containing	833 (22.4)	690 (26.6)	33 (24.4)	0 (0.0)	276 (46.5)	0 (0.0)	0 (0.0)
ABC-containing	106 (2.9)	68 (2.6)	2 (1.5)	0 (0.0)	37 (6.2)	0 (0.0)	0 (0.0)
3TC-containing	2387 (71.7)	1746 (67.4)	89 (65.9)	0 (0.0)	542 (91.4)	10 (100.0)	0 (0.0)
FTC-containing	942 (28.3)	843 (32.5)	48 (35.6)	0 (0.0)	49 (8.3)	0 (0.0)	0 (0.0)
PI-based triple regimen	351 (9.5)	6 (0.2)	0 (0.0)	247 (99.2)	73 (10.5)	0 (0.0)	25 (100.0)
Triple NRTI regimen	29 (0.8)	2 (0.1)	3 (2.2)	0 (0.0)	24 (3.5)	0 (0.0)	0 (0.0)
NNRTI+PI-based regimen	3 (0.1)	0 (0.0)	0 (0.0	0 (0.0)	3 (0.4)	0 (0.0)	0 (0.0)

Data are n (%) of patients, unless otherwise indicated. na, not available; ART, combination antiretroviral therapy; ARV, antiretroviral; CDC, US Center for Disease Control and Prevention; WHO, World Health Organization; PMTCT, prevention of mother-to-child transmission of HIV-1; IQR, interquartile range; NVP, nevirapine; d4T, stavudine; AZT, zidovudine; TDF, tenofovir; ABC, abacavir; 3TC, lamivudine; FTC, emtricitabine; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor

[a] Eligibility for ART initiation in accordance with national ART guidelines (i.e. advanced immunodeficiency as defined by CD4 cell count <200 or <350 cells/µl, or advanced clinical disease according to WHO clinical stages or CDC classification).

[b] Regimen switch due to treatment failure, defined by local standard of care guidelines as determined clinically, immunologically or virologically.

[c] ARV-experienced is defined as any previous use of ARVs, i.e. (first-line) ART, mono/dual therapy, and/or PMTCT

[d] Includes recipients of blood products, injecting drug users, perinatal transmission and unknown exposures

[f] Hepatitis B positive status was defined as being HBsAg positive

[g] Hepatitis C positive status was defined as being HCV antibody positive

tenofovir (TDF) (34%) and 3TC/stavudine (d4T) (26%). Overall, 67% of patients started a 3TC-containing first-line regimen. Among patients initiating first-line ART, 95% (n=2 598) reported to be ARV-naïve and 5% (n=138) had previous ARV experience, which included ART (n=60), mono/dual therapy (n=6), single-dose NVP for prevention of mother-to-child transmission of HIV (PMTCT) (n=35), combination therapy for PMTCT (n=19), and unspecified (n=22). Compared with ARV-naive first-line patients, ARV-experienced first-line patients had higher median CD4 counts (177 vs. 133 cells/μL, p<0.0001), were younger (median 34.7 vs. 37.0 years, p<0.0001) and were more likely to be female (76.1% vs. 57.5%; p<0.001). Other baseline characteristics did not differ between ARV-naïve and ARV-experienced patients.

For the 249 (8.3%) patients switching to second-line ART, the median age was 38.6 years (IQR: 32.9-44.2) and sex was equally distributed. HIV exposure was predominantly heterosexual contact and 48% of patients had advanced disease (classified as WHO stage III or IV). Median CD4 count was 125 cells/μL (IQR 46-196). Median pre-switch HIV viral load was 4.1 $\log_{10}$ copies/ml (IQR 3.2-5.0). Ritonavir-boosted lopinavir (LPV) was the PI used almost exclusively (98%).

As shown in table 5, analysis of the first available 1795 viral sequences demonstrated that the most common HIV subtypes in the cohort were C (1216, 68.7%), A (338, 18.7%) and D (179, 10.0%). The first PASER report published in 2008 reviewed the available data on HIVDR in sub-Saharan Africa [11]. Baseline HIVDR data from Lusaka, Zambia has recently been published [24]. International presentations have summarized preliminary baseline HIVDR mutations and subtype distributions [25, 26].

TASER-M

Patient recruitment commenced in March 2007 and for the March 2009 transfer, seven sites from Thailand, Hong Kong and Malaysia provided data. Of 773 patients, 755 (97.7%) commenced ART within 181 days of baseline specimen collection and 728 (96.4%) participants had genotypic data available. Of these, 693 (95.2%) ARV-naïve patients and 10 (1.4%) ARV-experienced patients, following prior PMTCT, were eligible for first-line regimens. A further 25 (3.5%) patients were eligible for second-line ART following first-line treatment failure. Patient characteristics are summarized in table 4. For ARV-naïve first-line patients, the median age was 36.5 years. Almost two-thirds of patients were male and HIV exposure was predominantly heterosexual contact. More than one third of patients were classified as CDC class C and almost half of patients had pre-therapy CD4 counts less than 100 cells/μL. Median baseline HIV viral load was 5.0 $\log_{10}$ copies/ml (IQR 5.4-6.8) and the most common first-line regimens were based on NNRTIs (85.6%). Excluding 14 (2.4%) patients on a randomized clinical trial with a blinded NNRTI com-

Table 5. HIV subtypes and circulating recombinant forms by region and country

	Total	PASER-M (Africa)						TASER-M (Asia) [a]		
		South Africa	Zambia	Uganda	Kenya	Nigeria	Zimbabwe	Thailand	Hong Kong	Malaysia
n (%)	2523 (100.0)	624 (24.7)	583 (23.1)	410 (16.3)	140 (5.5)	21(0.8)	17 (0.7)	542 (21.5)	111 (4.4)	75 (3.0)
A	340 (13.6)	2 (0.3)	4 (0.7)	235 (57.3)	97 (69.1)	1 (4.8)		1 (0.2)		
B	114 (4.5)	3 (0.5)						37 (7.0)	55 (49.5)	19 (25.3)
C	1236 (49.2)	617 (98.9)	571 (97.9)	9 (2.2)	19 (13.6)		17 (100.0)		2 (1.8)	1 (1.3)
D	179 (7.1)	1 (0.2)	1 (0.2)	160 (39.0)	17 (12.1)					
G	11 (0.4)		2 (0.3)	1 (0.2)	2 (1.4)	6 (28.6)				
CRF01_AE	585 (23.2)							485 (89.5)	52 (46.8)	48 (64.0)
CRF02_AG	20 (0.8)	1 (0.2)	3 (0.5)	1 (0.2)		14 (66.7)		1 (0.2)		
Other recombinants or discordant subtypes	32 (1.3)		2 (0.3)	1 (0.2)	2 (1.4)			18 (3.3)	2 (1.8)	7 (9.3)
Unclassified	6 (0.2)			3 (0.7)	3 (2.1)					

Data are n (%) of subtypes/CRFs, unless otherwise indicated. HIV subtypes were determined from the *pol* sequences, using the REGA HIV-1 subtyping algorithm version 2.0 (http://dbpartners.stanford.edu/RegaSubtyping) and/or Stanford HIV drug resistance database (http://hivdb.stanford.edu). CRF, circulating recombinant form. [a] The collaborating sites in Philippines, South Korea and Indonesia had not yet provided sequence data at time of the current analysis.

ponent, NVP was more commonly prescribed than EFV at 56% and 42%, respectively. First-line dual NRTI backbones were predominantly 3TC/d4T (47%), 3TC/AZT (29%) and 3TC/TDF (10%). For first-line PI regimens, the favored NRTI backbone was TDF/FTC (33%) compared to 3TC/d4T (30%) or 3TC/AZT (18%). For the ritonavir-boosted PI component, atazanavir (ATZ) was only slightly favored over LPV at 43% vs 41%, respectively. Overall, 542 (91.4%) of ARV naive patients started a 3TC-containing first-line regimen. The 10 PMTCT patients received perinatal prophylaxis of AZT/3TC/NVP (n=7), AZT (n=2) or AZT/NVP (n=1) for between 14 and 102 days and all were prescribed AZT/3TC/NVP as first-line regimens.

For the 25 (3.4%) second-line patients, 22 (88%) were of Thai ethnicity and the median age was 36.5 years (IQR 32.4 - 41.9). Females were in the majority (64%), HIV exposure was predominantly heterosexual (92%) and 60% of patients had experienced at least one CDC class C event. Of 21 patients with CD4 counts available within six months of starting a second-line therapy, the median CD4 count was 197 (IQR: 109-299). Median pre-switch HIV viral load was 4.0 $\log_{10}$ copies per/ml (IQR 3.6-4.5). All patients were on PI-based regimens, following failure on first-line NNRTI-based regimens (median duration 30.3 months). The most commonly prescribed PI was ritonavir-boosted LPV (88%).

As shown in table 5, from analysis of the 728 available viral sequences, the most common subtypes were CRF01_AE (584, 80.2%) and subtype B (111, 15.2%). Non-CRF01_AE recombinants were identified in 8 (1.1%) patient specimens. For 21 (2.9%) specimens, the subtype differed between PR and RT regions suggesting dual infection or recombination. International presentations have summarized 2009 baseline HIVDR mutations and subtype distributions [27, 28].

Complete baseline and prospective outcome data for PASER-M and TASER-M are anticipated to become available in 2010-2013.

WHAT ARE THE MAIN STRENGTHS AND WEAKNESSES?

Programmes that monitor national and regional levels of primary and secondary HIVDR contribute to evidence-based recommendations to inform treatment guidelines and provide feedback on the success of HIV treatment and prevention programmes. PASER and TASER, with TAQAS, are developing capacity in sub-Saharan Africa and the Asia-Pacific for coordinated HIVDR monitoring and genotypic laboratory testing. The study protocols are harmonized with the WHO HIV Drug Resistance Prevention Survey protocol [29]. An important strength is the large number of patients and sites participating, rep-

resenting a diverse spectrum of patient populations, clinic types, ART regimens and HIV subtypes. Opportunities exist to investigate the impact of drug resistance on HIV natural history, rates of disease progression and response to treatment in non-B subtypes. Data from genotypic resistance testing will also provide insight into the population genetics and dynamics of transmitted HIVDR in the region.

PASER-M and TASER-M have several limitations. First, patient samples at each site are not necessarily representative of the site, country or region. Second, data quality depends on the completeness of clinical information captured through routine patient care. In PASER-M, data may have been collected under varying conditions, since some sites had no or limited research experience at study initiation. Third, at some sites, study initiation was delayed by several months due to the time required for contract negotiation, IRB study approval and, in TASER-M, procurement of FWAs. After study initiation, recruiting the required number of patients within the recommended 18-month period proved difficult for some sites, due to asymptomatic patients not seeking care or treatment, cost of medication or low-prevalence in their setting. Fourth, HIVDR monitoring activities in resource-limited countries in sub-Saharan Africa are limited by high costs of laboratory testing. To address this challenge, PASER has initiated a public-private consortium, called Affordable Resistance Test for Africa (ART-A), which aims to evaluate affordable test algorithms for the detection and interpretation of HIVDR for use in laboratories and clinics (http://www.arta-africa.org).

HOW CAN I COLLABORATE? WHERE CAN I FIND OUT MORE?

Ownership of individual site data remains with the contributing site. Sites are represented by their principal investigators on the respective PASER and TASER Steering Committees. Research is to be the subject of peer-reviewed publications and analysis priorities are driven by a concept sheet process. Both studies accept concept proposals from external researchers for review, if submitted in collaboration with one or more of the site principal investigators. The PASER and TASER protocols contribute data under the LAASER partnership (http://www.laaser-hivaids.org) and TASER also contributes data to IeDEA [20]. Collaborating sites are also encouraged to make an appropriate subset of their data available to Ministry of Health in their respective country in order to contribute to local efforts in monitoring HIVDR. Questions regarding participation, research concepts or requests for data should be sent to Tobias Rinke de Wit, email: t.rinkedewit@pharmaccess.org (PASER), or Thida Singtoroj, email: thida.singtoroj@treatasia.org (TASER).

ACKNOWLEDGMENTS

The authors wish to thank the participants, site staff, and support staff at PharmAccess Foundation, Contract Laboratory Services, TREAT Asia and NCHECR. Special thanks to Donald Sutherland and Diane Bennett (World Health Organization) for encouraging the development of PASER and TASER.

Funding

The PharmAccess African Studies to Evaluate Resistance is an initiative of PharmAccess Foundation, supported by the Ministry of Foreign Affairs of The Netherlands through a partnership with Stichting AidsFonds (grant no. 12454). The TREAT Asia Studies to Evaluate Resistance is an initiative of TREAT Asia, a program of amfAR, The Foundation for AIDS Research, with major support provided by the Ministry of Foreign Affairs of The Netherlands through a partnership with Stichting Aids Fonds (grant no. 12454), and with additional support from amfAR and the National Institute of Allergy and Infectious Diseases (NIAID) of the U.S. National Institutes of Health (NIH) and the National Cancer Institute (NCI) as part of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) (grant no. U01AI069907). Queen Elizabeth Hospital and the Integrated Treatment Centre are supported by the Hong Kong Council for AIDS Trust Fund. The National Centre in HIV Epidemiology and Clinical Research is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, The University of New South Wales. The funders had no role in the study design, data collection, data analysis, data interpretation, decision to publish, or writing of the report. The content of this publication is solely the responsibility of the authors and does not necessarily represent the official views of any of the institutions mentioned above.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS and World Health Organization. AIDS epidemic update 2009. December 2009. Available at: http://data.unaids.org/pub/Report/2009/JC1700_Epi_Update_2009_en.pdf.
2. World Health Organization. Towards universal access: scaling up priority HIV/AIDS interventions in the health sector: progress report 2009. Available at: http://www.who.int/hiv/pub/tuapr_2009_en.pdf.
3. Braitstein P, Brinkhof MW, Dabis F, Schechter M, Boulle A, Miotti P, et al. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. Lancet 2006,367:817-824.
4. Ivers LC, Kendrick D, Doucette K. Efficacy of antiretroviral therapy programs in resource-poor settings: a meta-analysis of the published literature. Clin Infect Dis. 2005,41:217-224.
5. Jahn A, Floyd S, Crampin AC, Mwaungulu F, Mvula H, Munthali F, et al. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. Lancet 2008,371:1603-1611.
6. World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents: Recommendations for a public health approach, 2006 revision. Available at: http://www.who.int/hiv/pub/guidelines/artadultguidelines.pdf. Geneva, 2006.
7. Keiser O, Orrell C, Egger M, Wood R, Brinkhof MW, Furrer H, et al. Public-health and individual approaches to antiretroviral therapy: township South Africa and Switzerland compared. PLoS Med 2008,5:e148.
8. Gupta RK, Hill A, Sawyer AW, Cozzi-Lepri A, von Wyl V, Yerly S, et al. Virological monitoring and resistance to first-line highly active antiretroviral therapy in adults infected with HIV-1 treated under WHO guidelines: a systematic review and meta-analysis. Lancet Infect Dis 2009,9:409-417.
9. Rahim S, Fredrick LM, da Silva BA, Bernstein B, King MS. Geographic and temporal trends of transmitted HIV-1 drug resistance among antiretroviral-naive subjects screening for two clinical trials in North America and Western Europe. HIV Clin Trials 2009,10:94-103.
10. Wensing AM, van de Vijver DA, Angarano G, Asjo B, Balotta C, Boeri E, et al. Prevalence of drug-resistant HIV-1 variants in untreated individuals in Europe: implications for clinical management. J.Infect.Dis. 2005,192:958-966.
11. Hamers RL, Derdelinkx I, Van Vugt M, Stevens W, Rinke de Wit TF, Schuurman R. The status of HIV-1 resistance to antiretroviral drugs in sub-Saharan Africa. Antiviral Therapy 2008,13:625-639.
12. Bennett DE, Bertagnolio S, Sutherland D, Gilks CF. The World Health Organization's global strategy for prevention and assessment of HIV drug resistance. Antivir Ther 2008,13 Suppl 2:1-13.
13. Hemelaar J, Gouws E, Ghys PD, Osmanov S. Global and regional distribution of HIV-1 genetic subtypes and recombinants in 2004. AIDS 2006,20:W13-W23.
14. Dumans AT, Soares MA, Machado ES, Hue S, Brindeiro RM, Pillay D, Tanuri A. Synonymous genetic polymorphisms within Brazilian human immunodeficiency virus Type 1 subtypes may influence mutational routes to drug resistance. J Infect Dis. 2004,189:1232-1238.
15. Gonzalez LM, Brindeiro RM, Aguiar RS, Pereira HS, Abreu CM, Soares MA, Tanuri A. Impact of nelfinavir resistance mutations on in vitro phenotype, fitness, and replication capacity of human immunodeficiency virus type 1 with subtype B and C proteases. Antimicrob.Agents Chemother. 2004,48:3552-3555.

16. Kantor R, Katzenstein DA, Efron B, Carvalho AP, Wynhoven B, Cane P, et al. Impact of HIV-1 subtype and antiretroviral therapy on protease and reverse transcriptase genotype: results of a global collaboration. PLoS Med. 2005,2:e112.
17. Martinez-Cajas JL, Pant-Pai N, Klein MB, Wainberg MA. Role of genetic diversity amongst HIV-1 non-B subtypes in drug resistance: a systematic review of virologic and biochemical evidence. AIDS Rev 2008,10:212-223.
18. Land S, Cunningham P, Zhou J, Frost K, Katzenstein D, Kantor R, et al. TREAT Asia Quality Assessment Scheme (TAQAS) to standardize the outcome of HIV genotypic resistance testing in a group of Asian laboratories. J Virol Methods 2009,159:185-193.
19. Zhou J, Kumarasamy N, Ditangco R, Kamarulzaman A, Lee CK, Li PC, et al. The TREAT Asia HIV Observational Database: baseline and retrospective data. J Acquir Immune Defic Syndr 2005,38: 174-179.
20. McGowan CC, Cahn P, Gotuzzo E, Padgett D, Pape JW, Wolff M, et al. Cohort Profile: Caribbean, Central and South America Network for HIV research (CCASAnet) collaboration within the International Epidemiologic Databases to Evaluate AIDS (IeDEA) programme. Int J Epidemiol 2007,36: 969-976.
21. Bertagnolio S, Derdelinckx I, Parker M, Fitzgibbon J, Fleury H, Peeters M, et al. World Health Organization/HIVResNet Drug Resistance Laboratory Strategy. Antivir Ther 2008,13 Suppl 2:49-57.
22. Rhee SY, Gonzales MJ, Kantor R, Betts BJ, Ravela J, Shafer RW. Human immunodeficiency virus reverse transcriptase and protease sequence database. Nucleic Acids Res 2003,31:298-303.
23. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. PLoS Med 2007,4:e298.
24. Hamers R, Siwale M, Wallis C, Labib M, van Hasselt R, Stevens W, et al. HIV-1 drug resistance mutations are present in 6 percent of persons initiating antiretroviral therapy in Lusaka, Zambia. J Acquir Immune Defic Syndr 2010;55(1):95-101.
25. Hamers RL, Kityo C, Siwale M, Conradie F, Botes ME, Abdallah S, et al. Cohort Profile: The PharmAccess African Studies to Evaluate Resistance Monitoring Study (PASER-M) – HIV-1 Drug Resistance in sub-Saharan Africa. XVIII International AIDS Conference, July 18-23 2010, Vienna, Austria. Abstract no THPE0236.
26. Hamers RL, Wensing AM, Siwale M, Botes M, Conradie F, Abdallah S, et al. Prevalence of drug-resistant HIV-1 variants at initiation of standard first-line HAART in Africa. XVIII International HIV Drug Resistance Workshop. Fort Myers, Fl, USA. June 9-13, 2009. Abstract 155.
27. Sungkanuparph S, Oyomopito R, Sirivichayakul S, Sirisanthana T, Li P, Kantipong P, et al. HIV-1 drug resistance among antiretroviral-naive HIV-1-infected patients in Asia: results from the TREAT Asia Studies to Evaluate Resistance-Monitoring Study (TASER-M). European AIDS Conference. 11-14 November 2009. Cologne, Germany.
28. Oyomopito R, Phanuphak P, Sungkanuparph S, Kumarasamy N, Sirisanthana T, Li P, et al. Cohort profile: the TREAT Asia studies to evaluate resistance monitoring study (TASER-M) - HIV drug resistance in the Asia-Pacific. XVIII International AIDS Conference, July 18-23 2010, Vienna, Austria. Abstract no THPE0443. 2010.
29. Jordan MR, Bennett DE, Bertagnolio S, Gilks CF, Sutherland D. World Health Organization surveys to monitor HIV drug resistance prevention and associated factors in sentinel antiretroviral treatment sites. Antivir Ther 2008,13 Suppl 2:15-23.

APPENDIX

The PharmAccess African Studies to Evaluate Resistance

M Siwale* and C Njovu, Lusaka Trust Hospital, Lusaka, Zambia;
M Labib, Coptic Hospital, Lusaka, Zambia;
J Menke, KARA Clinic and Laboratory, Lusaka, Zambia;
ME Botes*, Muelmed Hospital, Pretoria, South Africa;
F Conradie* and I Sanne, Themba Lethu Clinic, Clinical HIV Research Unit, University of the Witwatersrand, Johannesburg, South Africa;
CL Wallis and WS Stevens†, Department of Molecular Medicine and Haematology, University of the Witwatersrand, and National Health Laboratory Services, Johannesburg, South Africa;
M Hardman, Acts Clinic, White River, South Africa;
N Ngorima*, M Wellington and R Luthy, Newlands Clinic, Harare, Zimbabwe;
K Mandaliya*, S Abdallah and I Jao, Coast Province General Hospital, International Center for Reproductive Health Kenya, Mombasa, Kenya;
M Dolan, Mater Misericordiae Hospital, Nairobi, Kenya;
C Kityo*, G Namayanja, L Nakatudde, M Kiconco, M Abwola and P Mugyenyi, Joint Clinical Research Center, Fort Portal, Mbale and Kampala, Uganda;
N Ndembi† and P Kaleebu*, Medical Research Council, Uganda Virus Research Institute, Entebbe, Uganda;
A Osibogun* and S Akanmu, Lagos University Teaching Hospital, Lagos, Nigeria;
AM Wensing, I Derdelinckx and R Schuurman†, Department of Virology, University Medical Center, Utrecht, The Netherlands;
RL Hamers*, K Sigaloff, E Straatsma, M van Vugt*, TF Rinke de Wit*§, PharmAccess Foundation, Center for Poverty-related Communicable Diseases, Amsterdam Institute for Global Health and Development, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.

* PASER Steering Committee member
§ Principal Investigator
† PASER Scientific Advisor

The TREAT Asia Studies to Evaluate Resistance

PCK Li*¶ and MP Lee, Queen Elizabeth Hospital and KH Wong, Integrated Treatment Centre, Hong Kong, China;
N Kumarasamy*§ and S Saghayam, YRG Centre for AIDS Research and Education, Chennai, India;
S Pujari* and K Joshi, Institute of Infectious Diseases, Pune, India;

TP Merati* and F Yuliana, Faculty of Medicine, Udayana University & Sanglah Hospital, Bali, Indonesia;
CKC Lee* and LL Low, Hospital Sungai Buloh, Kuala Lumpur, Malaysia;
A Kamarulzaman*¶ and LY Ong, University of Malaya, Kuala Lumpur, Malaysia;
M Mustafa and N Nordin, Hospital Raja Perempuan Zainab II, Kota Bharu, Malaysia;
R Ditangco† and RO Bantique, Research Institute for Tropical Medicine, Manila, Philippines;
YMA Chen*§, WW Wong and YW Yang, Taipei Veterans General Hospital and AIDS Prevention and Research Centre, National Yang-Ming University, Taipei, Taiwan;
P Phanuphak* and S Sirivichayakul, HIV-NAT/Thai Red Cross AIDS Research Centre, Bangkok, Thailand;
S Sungkanuparph* and B Piyavong, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand;
T Sirisanthana* and J Praparattanapan, Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand;
P Kantipong‡ and P Kambua, Chiang Rai Regional Hospital, Chiang Rai, Thailand;
JY Choi* and SH Han, Division of Infectious Diseases, Dept. of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea;
W Ratanasuwan and R Sriondee, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand;
R Kantor, Brown University, Rhode Island, U.S.;
AH Sohn, L Messerschmidt* and T Singtoroj, TREAT Asia, amfAR – The Foundation for AIDS Research, Bangkok, Thailand;
DA Cooper, MG Law*, A Jiamsakul, and J. Zhou, National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Sydney, Australia.

* TASER Steering Committee member
† Steering Committee Chair, ‡ Co-Chair
§ Protocol Chair
¶ Protocol Co-Chair