

SATuRN: Preliminary report 2011

Southern Africa Treatment and Resistance Network

HIV drug resistance in first and second line patients in South Africa: EC Free State and Pretoria cohorts.

Introduction:

There has been a lack of effective interaction between South Africa's research and prevention/treatment policies. To facilitate exchange of information between researchers and policy makers, SATuRN, in collaboration with researchers from the United States and Europe, has developed two HIV-1 drug-resistance databases (Stanford HIVdb and RegaDB) in southern Africa. These rapidly expanding databases (currently > 2,500 genotypes), which serve a resource for regional and global HIV-1 research, have the capacity to enhance the large scale systematic monitoring of antiretroviral rollout programs throughout southern Africa.

Results:

Free State 1st line: 116 of 131 (88.5%) patients experiencing virological failure an average of 874 days after the initiation of ART had resistance mutations. NRTI and NNRTI, the most prevalent mutations, were detected in 76.3% and 83.9% of patients, respectively. M184V/I, the most common NRTI mutation, was present in 71.7% of patients, followed by a range of NNRTI mutations (K013N, V106M, G190A, Y181C) present at levels ranging from 43.5% to 17.6%. Although 17.6% of sequences contained TAMs, only 7.6% had more than two TAMs, which limit the effectiveness of second line regimens.

Data source and Methods:

The databases are being populated with a large number of HIV-1 sequences from South Africa and neighbouring countries. Researchers in the University of the Free State (UFS) School of Medicine and the Departments of Family Medicine and Immunology at the University of Pretoria (UP) are instrumental in supplying data on patients failing therapy. The UFS and UP component of the database currently consists of two datasets that provide detailed information on the patients' treatment and clinical history, together with the patients' genotypic data.

Pretoria 1st line: Analysis of 111 patients (113 genotypes) failing first line (NRTI/NNRTI-based) ART indicated that 75.2% of sequences contained at least one NRTI or NNRTI mutation. M184V/I, the most prevalent resistance mutation, was detected in 71/113 genotypes (62.8%). This was followed, in order of decreasing prevalence, by mutations at K103N (40.7%), V106M (16.8%), G190A (16.8%) and Y181C (13.3%). At least one Thymidine Analog Mutation (TAM) was detected in 23/111 (20.7%) of patients.



SATuRN: Preliminary report 2011

Southern Africa Treatment and Resistance Network

Free State 2nd line: Resistance mutations were detected in 16/45 (35.5%) patients experiencing virological failure on average 714 (interquartile 245-955) days after initiation to second line ART containing at least one PI. Major PI mutations were identified in only 11.1% of patients. NRTI, NNRTI and TAMs mutations were more common and present at a frequency of 24.4%, 22.2% and 8.9%, respectively.

Pretoria 2nd line: 8/17 (52.9%) adults and 3/33 (9.1%) children had no detectable resistance, suggesting non-compliance. Major PI mutations (V32I, M46L, I47A, L90M) were detected in only of 1/17 (5.9%) adults compared to 7/33 (21.2%) pediatric patients. 5/33 (15.1%) pediatric sequences contained >3 PI mutations. The most prevalent, M46I and V82A, were detected in 18.2% of sequences, followed by I54V, L24I, I50V and L76V at a frequency of 3.0% each. Children also had more NNRTI and NRTI mutations (39.4% vs 29.4%), especially those related to NVP (K103) and 3TC (M184V/I) (27.3% vs 17.7% and 75.8% vs. 29.4%, respectively).

Results to be presented at SA AIDS Conference and IAS 2011:

Van Vuuren C, Goedhals D, Steyn D, Mamabolo MK, Monyane R, Murrell B, Cassol S, de Oliveira T, Seebregts C. Low Level of Protease Inhibitor (PI) Resistance in Patients Failing Second Line Drug Regimens in the Free State Province of South Africa. Poster IAS 2011, Rome, Italy.

Goedhals D, Van Vuuren C, Steyn D, Mamabolo MK, Monyane R, Murrell B, Cassol S, de Oliveira T, Seebregts C. HIV Drug resistance in adult patients failing first-line antiretroviral therapy (ART) in the Free State Province of South Africa. Poster IAS 2011, Rome, Italy.

Rossouw T, Mahasha P, Malherbe G, Manasa J, van Dyk G, Cassol S, Seebregts C, de Oliveira T SATuRN, the Southern African Treatment and Resistance Network: Application to the Management and Surveillance of HIV-1 Drug Resistance in a Public Health Setting in Pretoria. Oral presentation SA AIDS Conference (Session 4, Track , Hall 6, 4-6pm, abstract number 229).

Rossouw T, Malherbe G, van Dyk G, Seebregts C, Feucht U, Cassol S and de Oliveira T for the FIRST HIV-1 Drug Resistance Study Team and SATuRN. HIV-1 Drug Resistance in South Africans Failing Protease Inhibitor (PI)-Based Antiretroviral Therapy (ART): Comparative Analysis of Adult vs. Pediatric Patients. Poster SA AIDS Conference (PS1-26: 230).

