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TRANSMITTED HIV DRUG RESISTANCE SURVEY IN TWO PROVINCES IN PAPUA NEW GUINEA

Evelyn Lavu¹, Nick Dala², Anup Gurung³, Ellan Kaye¹, Euodia Mosoro¹, Jessica Markby⁴, Eman Aleksic⁴, Janet Gare^{4,5}, Imogen Elsum², Gideon Nano⁶, Mark Myatt⁷, Petronia Kaima⁸, Suzanne Crowe⁴, Silvia Bertagnolio⁹, Anna Hearps^{4*}, Michael R. Jordan^{10*}

¹Central Public Health Laboratory, Port Moresby, Papua New Guinea (PNG), ²National Department of Health, Port Moresby, PNG, ³WHO, Port Moresby, PNG, ⁴Burnet Institute, Melbourne, Australia, ⁵Institute for Medical Research, Goroka, PNG, ⁶Port Moresby, PNG, ⁷Brixton Health, Wales, United Kingdom, ⁸Mt Hagen Hospital, PNG, ⁹HIV Department, WHO, Geneva, Switzerland, ¹⁰Tufts University School of Medicine, Boston, USA *Denotes co-senior authorship

BACKGROUND

- Papua New Guinea (PNG) is a Pacific island nation of 7.3 million people and has an estimated HIV prevalence of 0.65%
- The HIV epidemic in PNG is predominantly heterosexual, with females representing approximately 62% of HIV cases
 - Females are diagnosed with HIV at a younger age than males
 - 20% of HIV-infected women are aged 15-24 years
- Antiretroviral therapy (ART) became available in PNG in 2004; 80.3% of people in need were receiving it as of 2015
- Clinical monitoring of HIV-infected individuals is limited in PNG, with inconsistent availability of CD4+ T cell testing
 - Viral load and HIV drug resistance testing are not routinely available
- First-line ART in PNG consists of the nucleoside reverse transcriptase inhibitors (NRTIs) Zidovudine or Tenofovir + Lamivudine and one of the non-nucleoside reverse transcriptase inhibitors (NNRTIs) Efavirenz or Nevirapine
 - Protease inhibitors (PI) are used as second-line drugs
- The prevalence of transmitted HIV drug resistance (TDR) in recently infected antiretroviral drug naïve individuals in PNG has not been fully characterised

METHODS

Survey design:

- Surveillance of transmitted HIV drug resistance (TDR) in individuals recently infected with HIV was performed following WHO-suggested methods in two regions between May 2013-April 2014

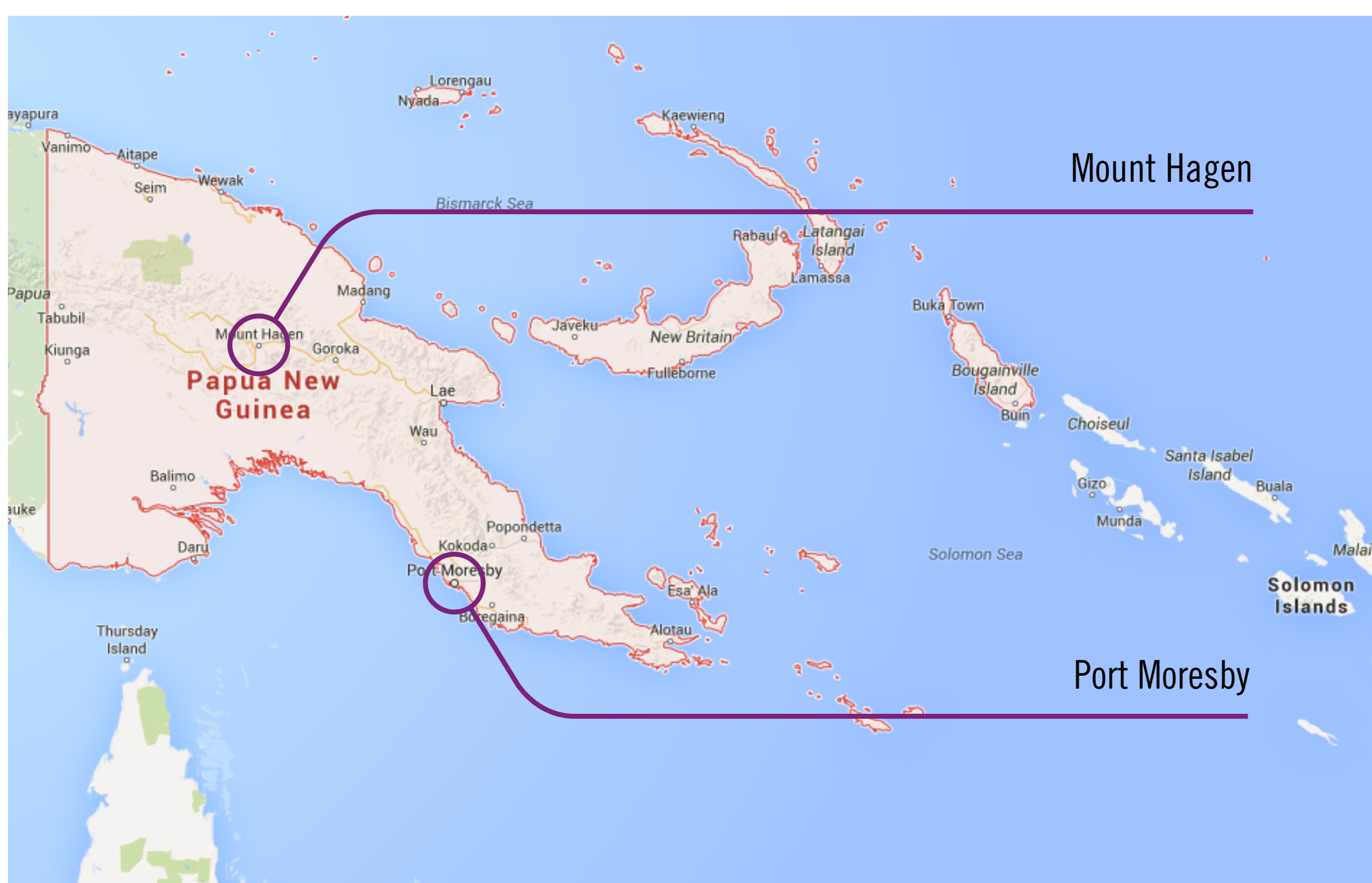


Figure 1: Map of PNG showing location of survey sites

Genotyping methods:

- Dried Blood Spots (DBS) prepared from venous blood
- Drug resistance detected using an in-house genotyping assay
 - Testing performed at the WHO-designated HIV Drug Resistance Laboratory at the Burnet Institute (Melbourne, Australia)

Recruitment areas:

- Port Moresby, National Capital District
 - Heduru HIV/STI clinic
 - Anglicare Clinic
- Mt Hagen, Western Highlands Province
 - Tininga Clinic, Mt Hagen Hospital
 - Rebiamul Hospital VCT centre

Recruitment criteria:

- HIV+, ART naïve, Aged ≤30
- First pregnancy or never pregnant, if female

Data analysis:

- Resistance mutations were defined using the WHO 2009 SDRM list
- Point prevalence with 95% CI were calculated
- Classification of TDR prevalence
 - To analyse all available specimens rather than N=47 per the WHO TDR survey method (Bennett and Myatt, AVT 2007); Lot Quality Assurance sampling with floor and ceiling decision rules modelled to return probabilities of classification similar to those of the original method were used (adapted from Myatt M, FHI 360/FANTA-III, 2012)

RESULTS

Survey population

- 70 individuals were recruited from each region
- The number of specimens successfully genotyped was:
 - 62/70 (88.6%) for Port Moresby
 - 61/70 (87.1%) for Mt Hagen
- Demographic details of participants with successfully genotyped specimens are shown in **Table 1**
- Consistent with previous publications, the median age of female participants was younger than males
 - 22.0 years for females vs. 27.0 years for males, (**Table 1**)

Table 1: Demographic details of survey population*

	Port Moresby	Mt Hagen	Combined cohort
Sample number	62	61	123
Female, n (%)	31 (50%)	41 (67%)	72 (58.5%)
Age, median (IQR)			
Entire cohort	25.0 (21.0-28.0)	25.0 (21.0-28.0)	25.0 (21.0-28.0)
Females	22.0 (20.0-28.0)	22.0 (20.0-27.5)	22.0 (20.0-26.0)
Males	27.5 (22.5-29.8)	27.5 (22.5-29.8)	27.0 (23.0-29.0)

*Only includes specimens which were successfully genotyped and passed quality assurance

Drug resistance levels - Port Moresby

- Drug resistance mutations were detected in 11/62 individuals (**Table 2 and Figure 2**)
 - NNRTI resistance mutations detected in 10 individuals
 - Point prevalence = 16.1% (95% CI 9.0%-27.2%)
 - NRTI resistance mutations detected in 2 individuals
 - Point prevalence = 3.2% (0.08%-11.0%)
 - No PI resistance mutations were detected
- Resistance classification:
 - NNRTI resistance: Moderate
 - NRTI resistance: Low
 - PI resistance: Low

Table 2: Drug resistance mutations detected - Port Moresby

	Port Moresby	Mt Hagen
1		K103N
2	M41L, T215Y	K103N
3		G190A
4		K103N, V106MV
5		Y181IV
6	K70E	
7		K103N
8		Y181C
9		Y181CY
10		K101E, G190A
11		V106IV, Y181CY, Y188CY

SDRM = Surveillance drug resistance mutations (2009 list)

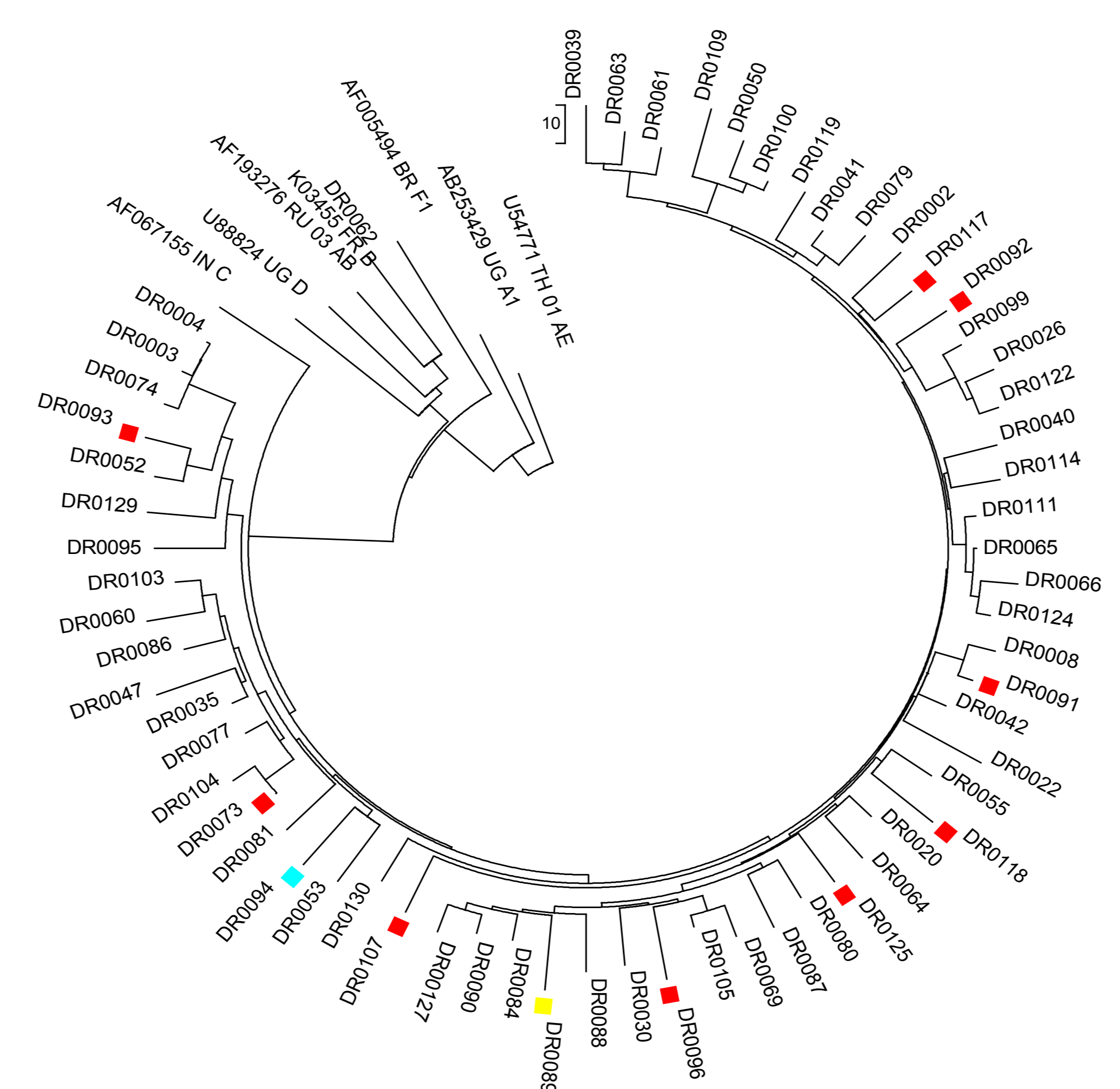


Figure 2: Neighbour-joining tree of sequences from Port Moresby. Sequences with one or more NNRTI SDRM denoted by red squares and sequences with one or more NNRTI and NRTI SDRM are denoted by yellow squares. WHO reference sequences also included

Drug resistance levels - Mt Hagen

- Drug resistance mutations detected in 5/61 individuals (**Table 3 and Figure 3**)
 - NNRTI resistance mutations detected in 5 individuals
 - Point prevalence = 8.2% (95% CI 3.5%-17.8%)
 - NRTI resistance mutations detected in 2 individuals
 - Point prevalence = 3.2% (0.09%-11.0%)
 - No PI resistance mutations were detected
- Resistance classification:
 - NNRTI resistance: Low
 - NRTI resistance: Low
 - PI resistance: Low

Table 3: Drug resistance mutations detected - Mt Hagen

Patient	NRTI SDRM	NNRTI SDRM
1	K219KN	Y181C, G190A
2		K103N
3		G190A
4	D67N, K70E, M184V	Y181C, G190A
5		Y181CY

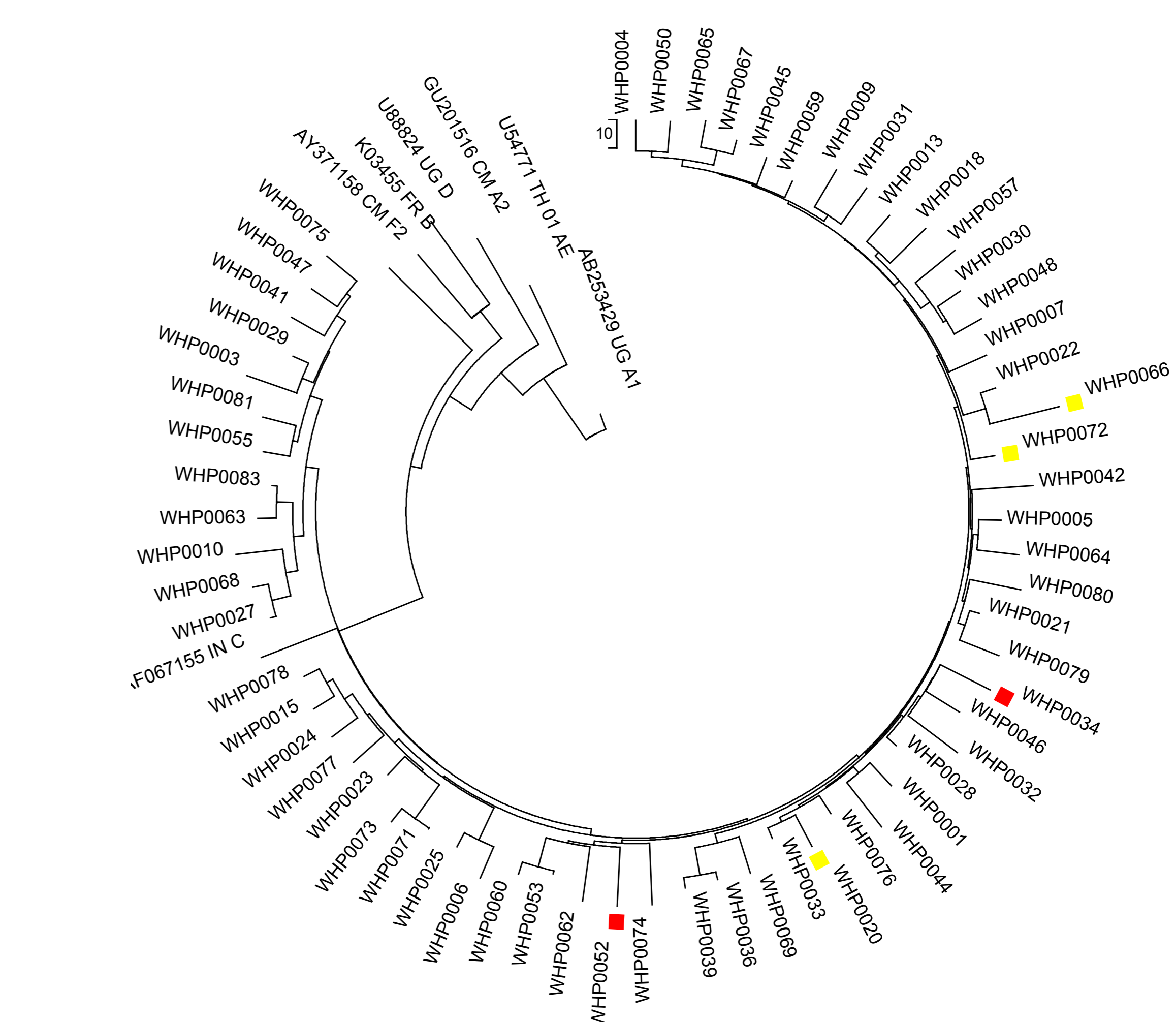


Figure 3: Neighbour-joining tree of sequences from Mt Hagen. Sequences with one or more NNRTI SDRM denoted by red squares and sequences with one or more NNRTI and NRTI SDRM are denoted by yellow squares. WHO reference sequences also include

CONCLUSIONS

- NNRTI drug resistance (16.1%) in ARV drug naïve individuals in Port Moresby is amongst the highest reported globally to date
- Observed levels of TDR threaten to limit the on-going effective use of NNRTIs as a component of first-line ART
- NNRTI resistance is less common in Mt Hagen but is detected with a point prevalence of 8.2%
- Improved monitoring and correction of ART programme factors associated with emergence and transmission of drug resistant HIV is essential
- Nationally representative surveillance of HIVDR among first-line ART initiators should be urgently implemented to support choice of nationally recommended first-line ART