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POSTER
491

Response to First-line ART in Adults With Drug Resistant HIV, ANRS 12249 TasP Trial

AFRICA HEALTH RESEARCH INSTITUTE

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1. Background

Mathematical models suggest that high levels of pre-treatment drug resistance could compromise ART programmes

In the context of universal test and treat, the number of people initiating ART will increase, as well as the number of individuals failing ART with drug resistance

It is plausible that an increasing proportion of recent infections will be from drug resistant HIV

Studies of pretreatment drug (PDR) resistance with virologic outcomes on ART are rare in low income countries

We examined the prevalence of PDR and the response to first-line ART in individuals enrolled in the ANRS cluster-randomized HIV Treatment as Prevention (TasP) trial

2. Methods

Participants were enrolled in a two arm cluster-randomised trial aimed at investigating the impact of population ART on HIV incidence over the period 9 March 2012 to 30 June 2016.

Individuals in the intervention arm were offered ART regardless of CD4 count while those in the control arm were offered ART based on South African guidelines

Individuals were eligible for enrolment if they were aged ≥ 16 years and resident members. Participants were visited every six months in their homes and offered rapid HIV testing and given results within 20 minutes. Individuals testing HIV-positive were referred to trial clinics for clinical care. In addition, they were asked to give dried blood spots (DBS) on filter paper six monthly This was used in establishing HIV seroconversion.

Baseline plasma samples of participants who linked to trial clinics and were ART naïve at enrolment as well as DBS of participants who seroconverted but did not link to care was used for assessment of PDR

For DBS samples from recently infected individuals, Sanger sequencing was performed on the POL gene with a detection threshold of 20%. On plasma samples from chronically infected and the few recently infected individuals in which this was available, deep sequencing was performed on full-genome or partial full-genome. The reads were aligned against a subtype C reference with the Geneious software, and low-level variants were called at a 2% level according to the 2009 WHO surveillance list

We used cox regression models to estimate hazard ratios and their 95% confidence intervals of the association between PDR and virologic suppression. Adherence was measured using the visual analogue scale

3. Results

1148 (1060 chronic infection & 88 recent infections) plasma and 189 DBS from recently-infected individuals were sequenced (Fig 1)

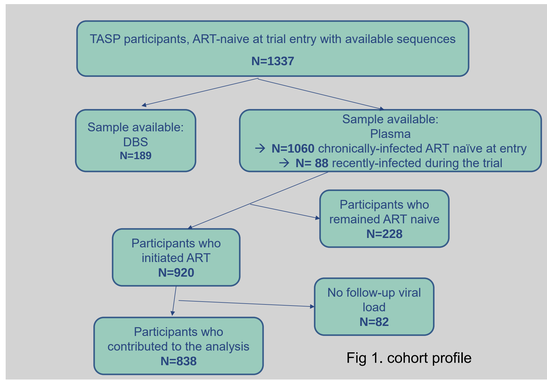


Fig 1. cohort profile

4. Prevalence of PDR in minority and majority virus

The overall prevalence for any PDR in majority virus for all participants was 8.7% (95% CI 7.3-10.3)-Fig 2

Any PDR prevalence in chronic infection at >2% threshold was 16.7% (Fig 3)

Any PDR prevalence in recent infection at >2% was 21.6% (Fig 4)

Predominantly NNRTI drug class; K103N/S

Low levels of K65R mutation in both recently and chronically infected individuals

Two individuals with chronic infection and one individual with recent infection had triple class resistance in minority virus (<2%) but none in majority virus

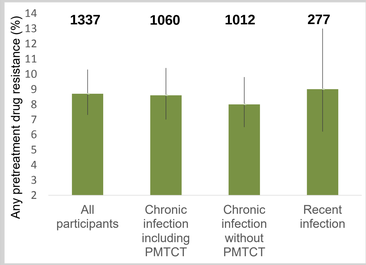


Fig 2. PDR in majority virus in different groups

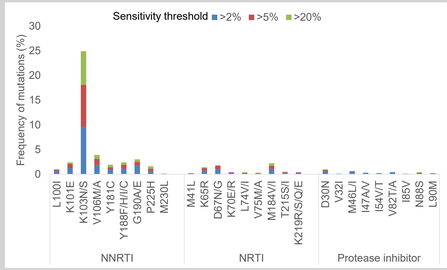


Fig 3. Prevalence of PDR in those with chronic infection

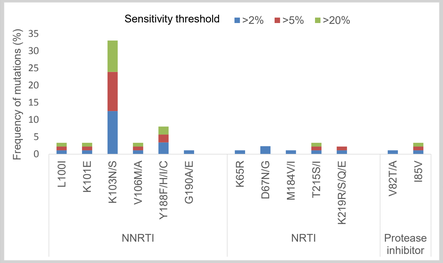


Fig 4. Prevalence of PDR in those with recent infection

5. Impact of drug resistant mutation on virologic suppression

Included Participants

Of the 1337 individuals sequenced, 1148 received care from the trial clinics; of whom 920 initiated ART. 838 individuals had at least one follow up viral load available and contributed to the analysis

The median age of included participants was 34 years (27, 46) and the majority were female (72%) and on fixed dose combination of TDF/FTC/EFV (

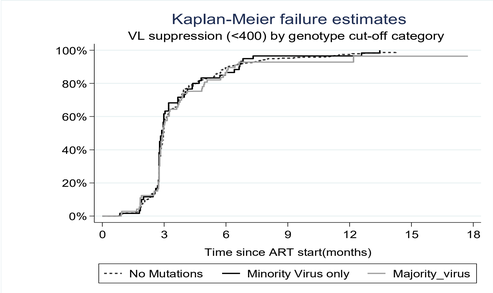
Virologic suppression

Virologic suppression: Viral load <400 copies/mL

Cumulative probability of suppression at 12 months was 97% (95% CI 96, 98)

Median time to suppression: 2.96 months (IQR 2.76, 3.88)

Median duration on ART: 1.36 years (IQR 0.91, 2.13)



6. Factors associated with virologic suppression

	Rate/100 person-months	Crude OR (95% CI)	P Value	*Adjusted OR (95% CI)	P Value
Pre-treatment Drug resistance			0.754		0.885
No mutation	25.7 (23.8-27.7)	1		1	
Minority Mutation only	26.7 (20.7-34.4)	1.05 (0.81-1.37)		1.04 (0.79-1.37)	
Majority mutation	23.9 (18.9-30.3)	0.93 (0.72-1.19)		0.96 (0.74-1.23)	
Sequence Viral load			**0.0006**		**0.006**
≤10,000	28.7 (24.9-33.0)	1		1	
10,000-100,000	26.6 (23.9-29.6)	0.92 (0.77-1.10)		0.91 (0.76-1.09)	
>100,000	22.7 (20.1-25.6)	0.72 (0.59-0.86)		0.74 (0.60-0.90)	
Adherence			**0.0001**		**0.002**
<95%	20.4 (17.1-24.4)	1		1	
≥95%	27.0 (25.0-29.1)	1.47 (1.21-1.78)		1.37 (1.12-1.67)	

*Adjusted for age, sex, CD4 count at ART initiation & factors in table

7. Conclusion

PDR prevalence of 9% in majority virus, doubling of prevalence when minority variants are taken into account

Mutations belonging to NNRTI drug class predominate, mainly K103N/S

No impact of PDR on virologic suppression in the short-term

Optimal adherence independent predictor of virologic suppression

Interventions to optimise adherence such as use of fixed dose combination ART may be key to successful ART programmes

Further studies on long-term outcomes are needed to confirm findings

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