Clinical implementation of HIV-1 resistance testing on dried blood spots in a rural South African Setting

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Therapy failure in RLS

- Virological suppression reached in 76% of patients (OT) after 1 year of ART[1]
- Resistance mutations are present in the majority of patients experiencing virological failure
- Detection of resistance in individual patients currently not routinely implemented in RLS

[1]Barth RE et al. *Lancet infectious diseases* 2010

Therapy monitoring

Resource-limited settings

- Laboratory monitoring
- Immunological monitoring (yearly)
- Clinical monitoring

High-income countries

- Laboratory monitoring
- Immunological monitoring every 6 months
- Viral load testing every 3-4 months
- Drug resistance genotyping when viral load detectable
- Switch to alternative therapy guided by monitoring results

Genotyping in RLS

- Obstacles to genotyping
  - *High overall costs*
  - *Limited on-site laboratory facilities and interpretation expertise*
  - *Use of plasma, requiring cold-chain maintenance/transport*

- Dried blood spots (DBS) are an attractive sample alternative
  - *Easy to collect (venous blood, heel/finger prick)*
  - *Sufficiently stable at room temperature*[3]

- Genotyping on DBS has been shown to be accurate and cost-saving with high success rates[4]

[3]Johannessen, et al. IAS 2009
[4]Aitken SC, et al. JCV 2012

Study objectives

1. To study the feasibility of genotyping using DBS in RLS

2. To study resistance profiles in patients failing therapy in RLS

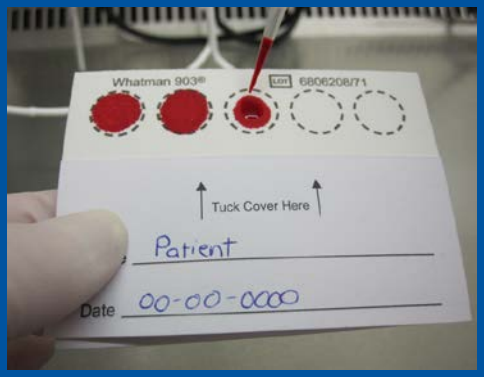
Methods – Study inclusion

- ✓ Age ≥ 18 years
- ✓ Received ART for ≥12 months
- ✓ HIV-RNA ≥ 10^3 copies/ml after previous response of <400 copies/ml
- ✓ No treatment interruption 30 days prior to sample

→ Inclusion between 2009 and 2013

Methods – procedures

- DBS
  - *Preparation at local site*
  - *Posted to reference lab*
- Sequencing
  - *Pol sequencing*[4]
  - *PR-RT or RT-only*
- Drug resistance interpretation
- Feedback to clinician

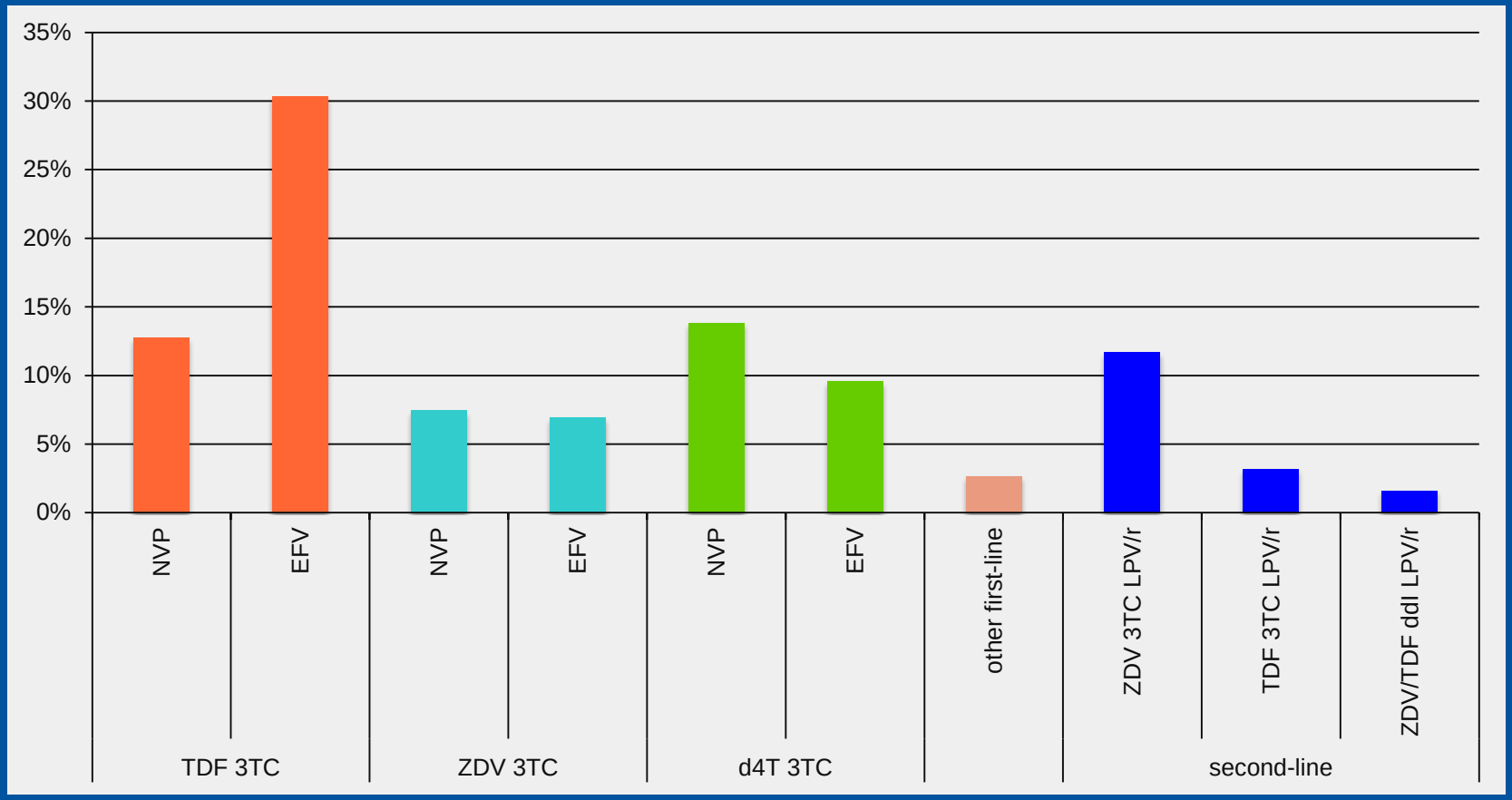


[4]Aitken SC, *et al*. JCV 2012

Results - Patient characteristics

Total samples (n)	n=191		
Sex			
	n = 190	Female	**118 (62%)**
Age			
	n = 179	median [IQR]	**35 [30 - 40] yrs**
Resistence			
	n = 191	resistant % (n)	**79% (150)**
disease status at baseline			
HIV-RNA	*n = 115*	Median [IQR] (copies/ml)	**4.9 [4.4-5.3]**
CD4-count	*n = 183*	(cells/mm3)	**68 [24-140]**
disease status at genotyping			
HIV-RNA	*n = 191*	Median [IQR] (copies/ml)	**4.2 [3.6-4.7]]**
CD4-count	*n = 159*	(cells/mm3)	**191 [78-346]**
Treatment status			
First-line therapy	*n = 189*	first line %	**83.6% (158)**
Time on treatment			
Time on current regimen	*n = 183*	median [IQR]	**450 [241-828] days**
Time since initiation of ART	*n = 180*		**844 [502-1445] days**

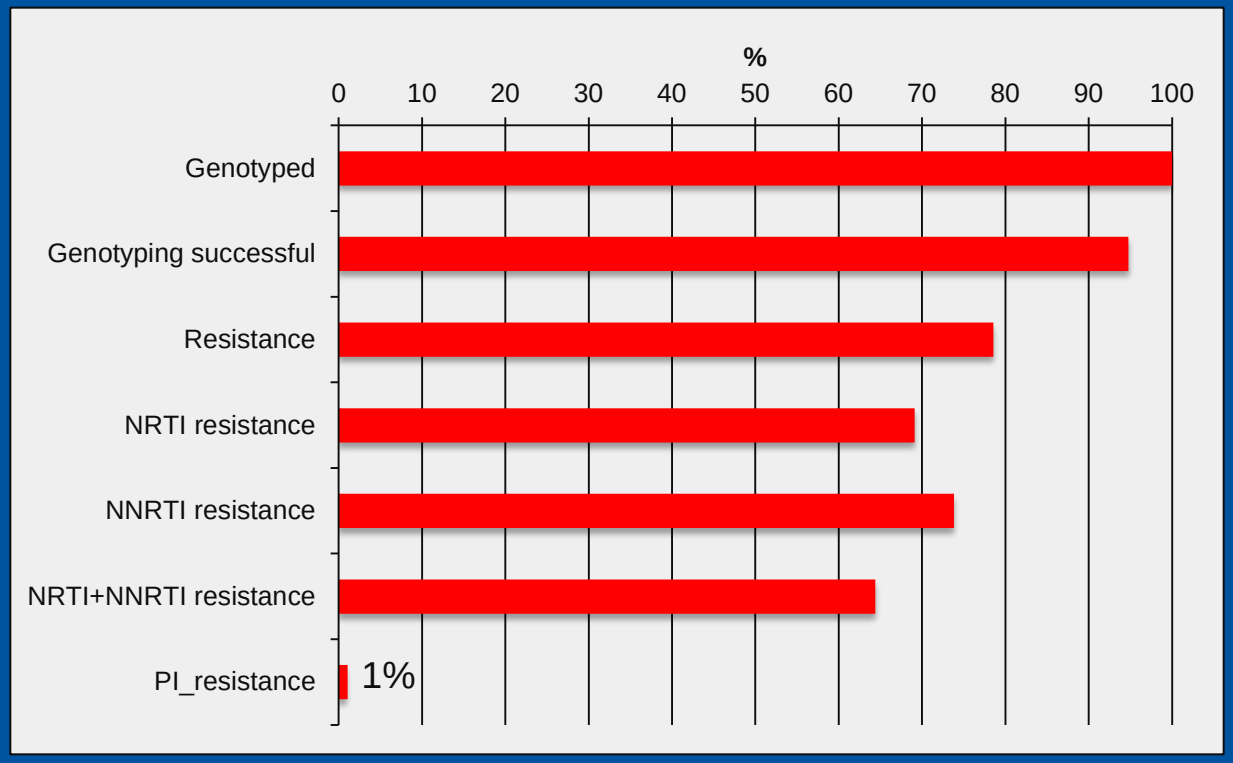
Results - ART regimes



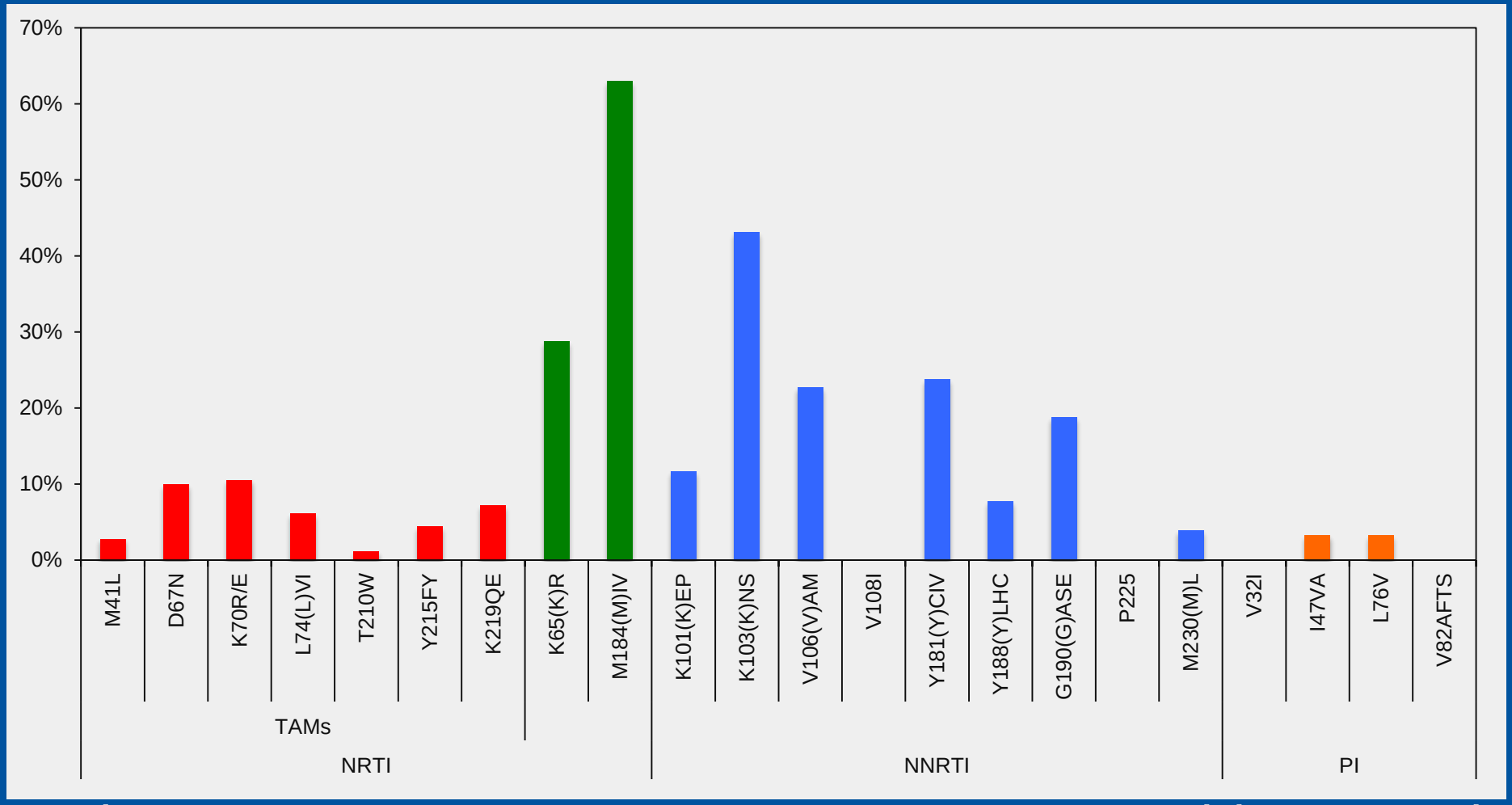
First-line: n = 157

Second-line: n = 31

Results - Mutations



Results - prevalence per mutation

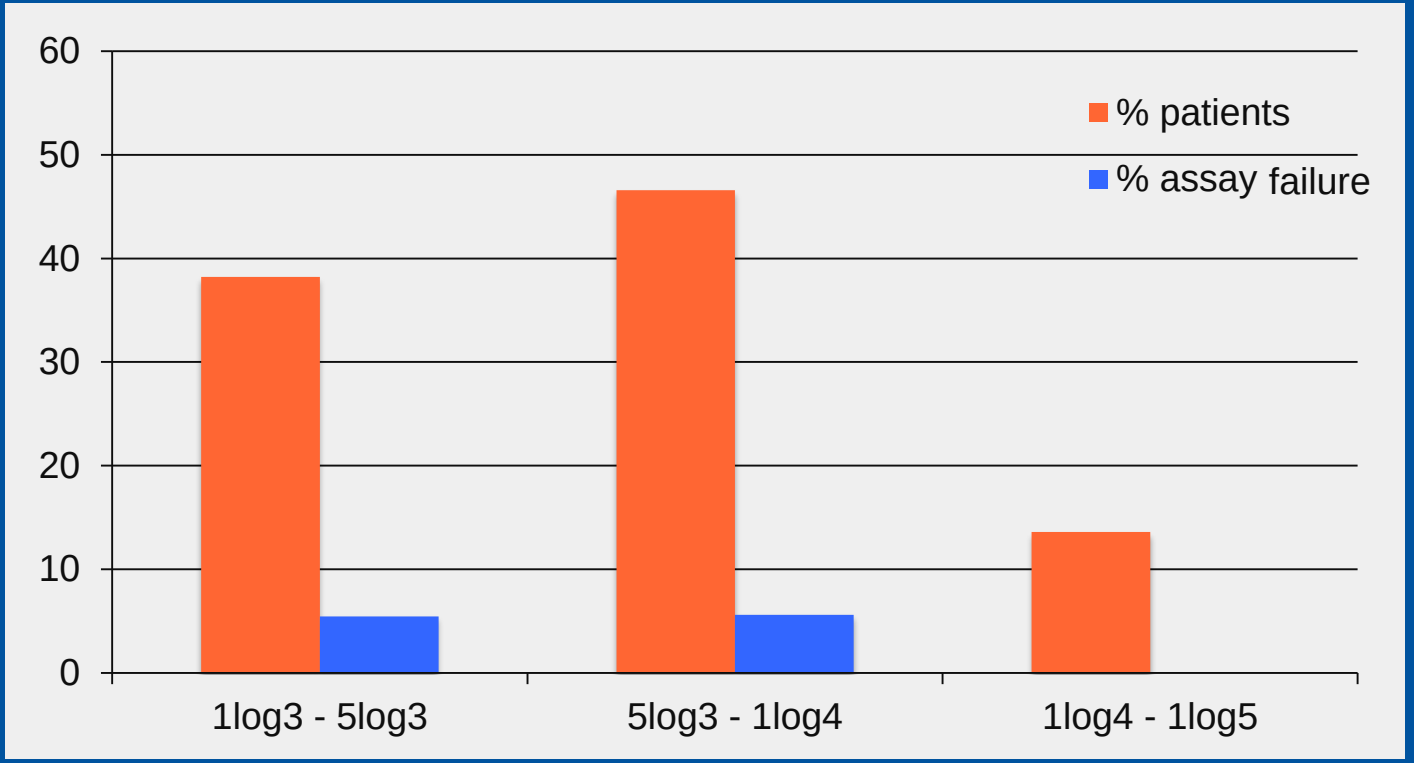


First-line + second-line: n = 148

Second-line: n = 30

Assay results

- Overall success rate: 181/191 (95%)
- Median turnaround time: 16 days [IQR: 8-33 days]
- High success rates also in lower VL range



Conclusions

- High prevalence of NRTI+NNRTI resistance mutations
- Low rate of PI-mutations does not warrant routine PI-resistance testing
- Routine DBS-based resistance genotyping for HIV-1 subtype C in RLS is feasible
- Optimization of laboratory logistics is required in order to achieve acceptable TAT
- Value of implementation (ie. clinician's response to genotyping result) needs to be assessed

Contributors

- UMC Utrecht (The Netherlands)
  - *Sue Aitken*
  - *Rob Schuurman*
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