

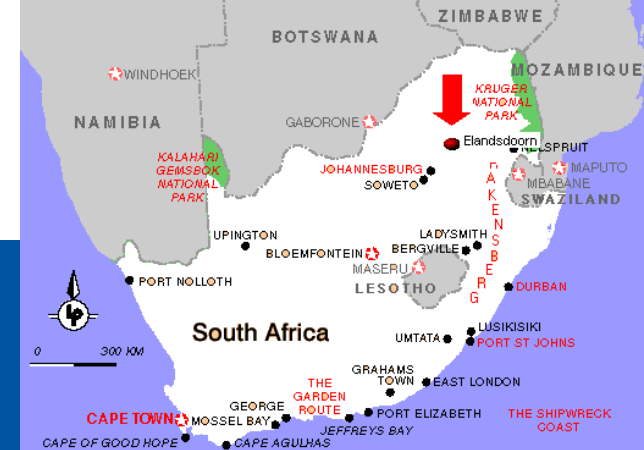
Rapid accumulation of drug resistance and loss of therapeutic options precede WHO-defined criteria for treatment failure

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- In resource limited settings systematic virological monitoring is not widely implemented
- Success of therapy is generally monitored by use of WHO defined criteria for failure
 - *Immunological failure* :
 - fall of CD4+ T-cell count to pre-therapy baseline
 - 50% drop from the on-treatment peak value
 - persistent CD4+ T-cell levels <100 cells/mm³
 - For children, a decline of five percentage points in CD4% at any age, or if > 5 years decline to the pre-therapy baseline
 - *Virological failure: HIV-RNA >10.000 copies/ml*

Ndlovu Cohort



- Ndlovu Medical Care Centre is located in a rural area of Limpopo in the northeast of South Africa.
- The ARV programme initiated in 2003.
- Free testing and treatment, with strong focus on adherence. Patients receive individual counselling at each clinic visit.
- First-line ART consists of
 - *NNRTI (efavirenz, nevirapine) +*
 - *3TC with either D4T or AZT*
- Clinical, immunological and virological monitoring every 6 months

Patient Characteristics of the Cohort



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	Adults	Children
Number of patients	735	101
Age, median	34 (29-41)	4.8 (2.9 – 7.0)
Female gender	72%	56%
Pre-therapy CD4, med, IQR	68 (20-140)	244 (130-666)
CD4%, med, IQR	-	11.0 (4.7 -13.5)
Log HIV-RNA, med, IQR	5.0 (4.5 – 5.4)	4.9 (4.6 - 5.5)
Therapy		
Efavirenz	58%	26%
Nevirapine	41%	73%
AZT + 3TC	21%	100%
d4T + 3TC	79%	
Follow – up, med, IQR	35 (29-45)	31 (22-48)

Treatment Response in the Cohort



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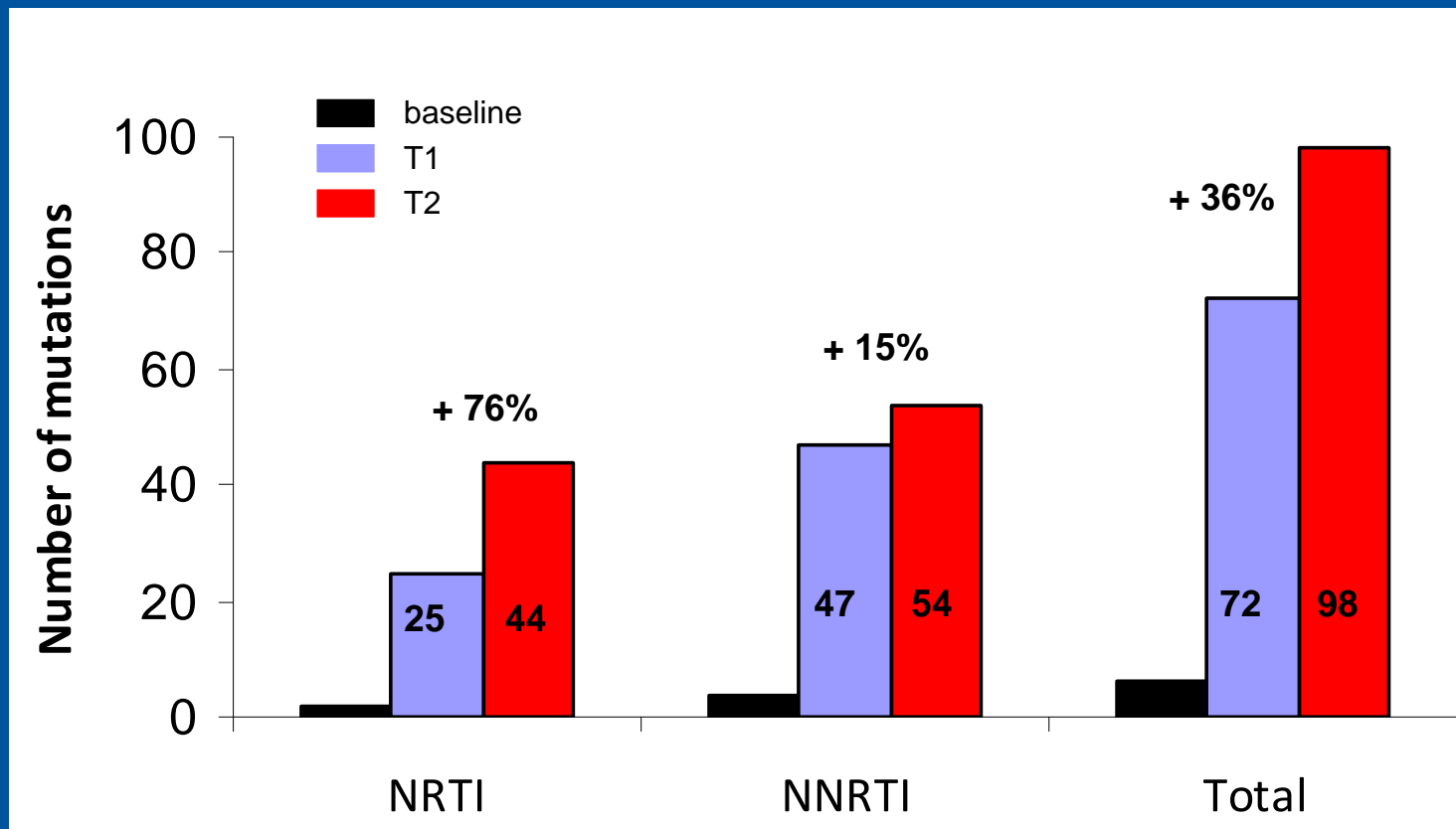
- Viral suppression (<50 copies/ml) was achieved in 77% (642/836) of individuals.
- The majority of those who did not reach virological suppression had died (60%) or were lost to follow up (21%) within 3 months.
- After initial virological suppression, 145 of 642 patients (23%) experienced a viral rebound (> 1000 copies/mL).
- Ongoing viraemia during first-line ART was documented in 58 patients (40%).

Genotypic Analysis

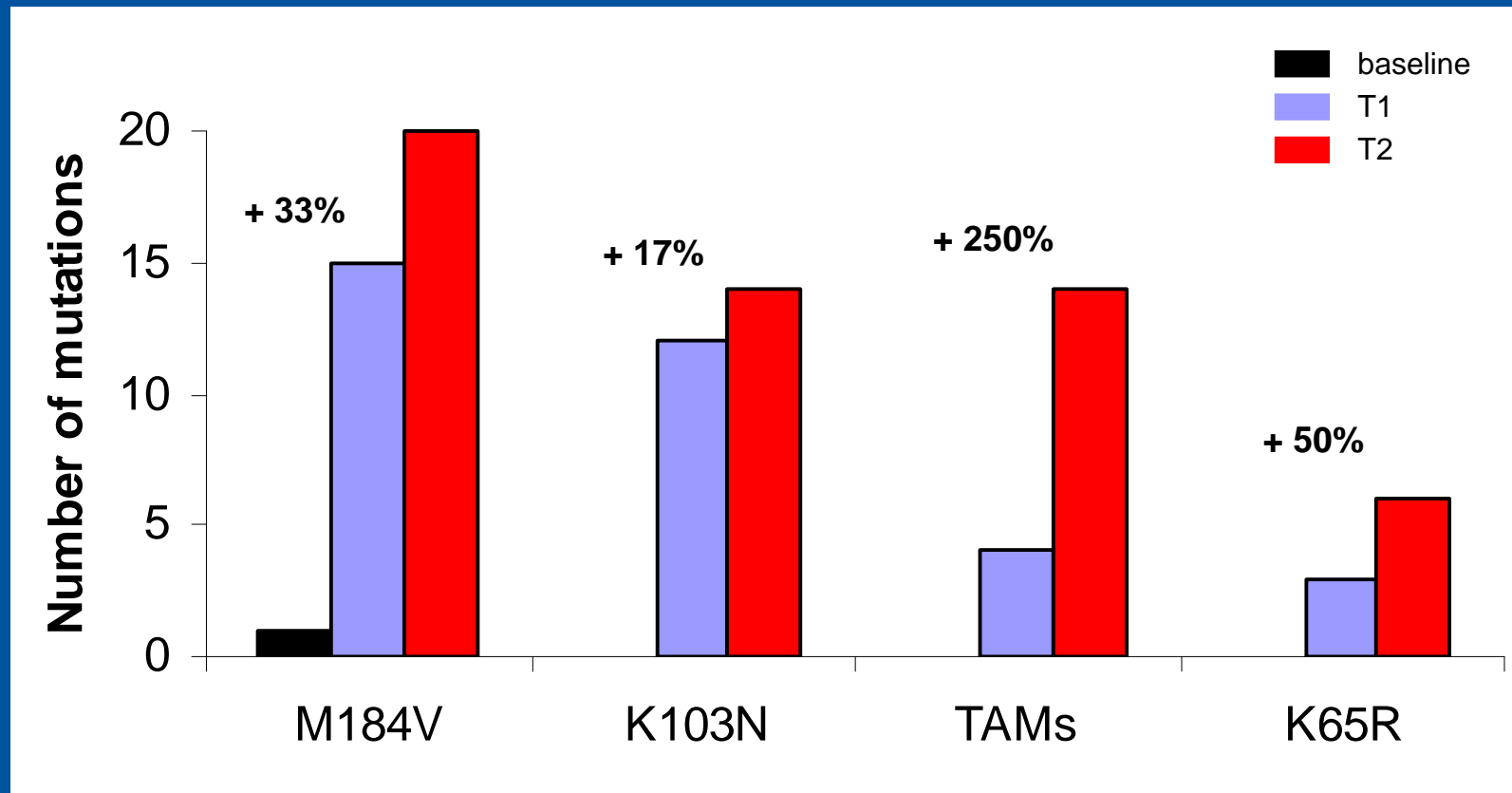


- Plasma samples were available for 40 of 58 patients with ongoing viraemia
- 26 patients with samples obtained at first moment of therapy failure (T1) and at 6 or 12 months (T2) were included in the analysis
- Population sequence analysis of *pol*
- Major IAS mutations were analysed
- All patients were infected with subtype C virus

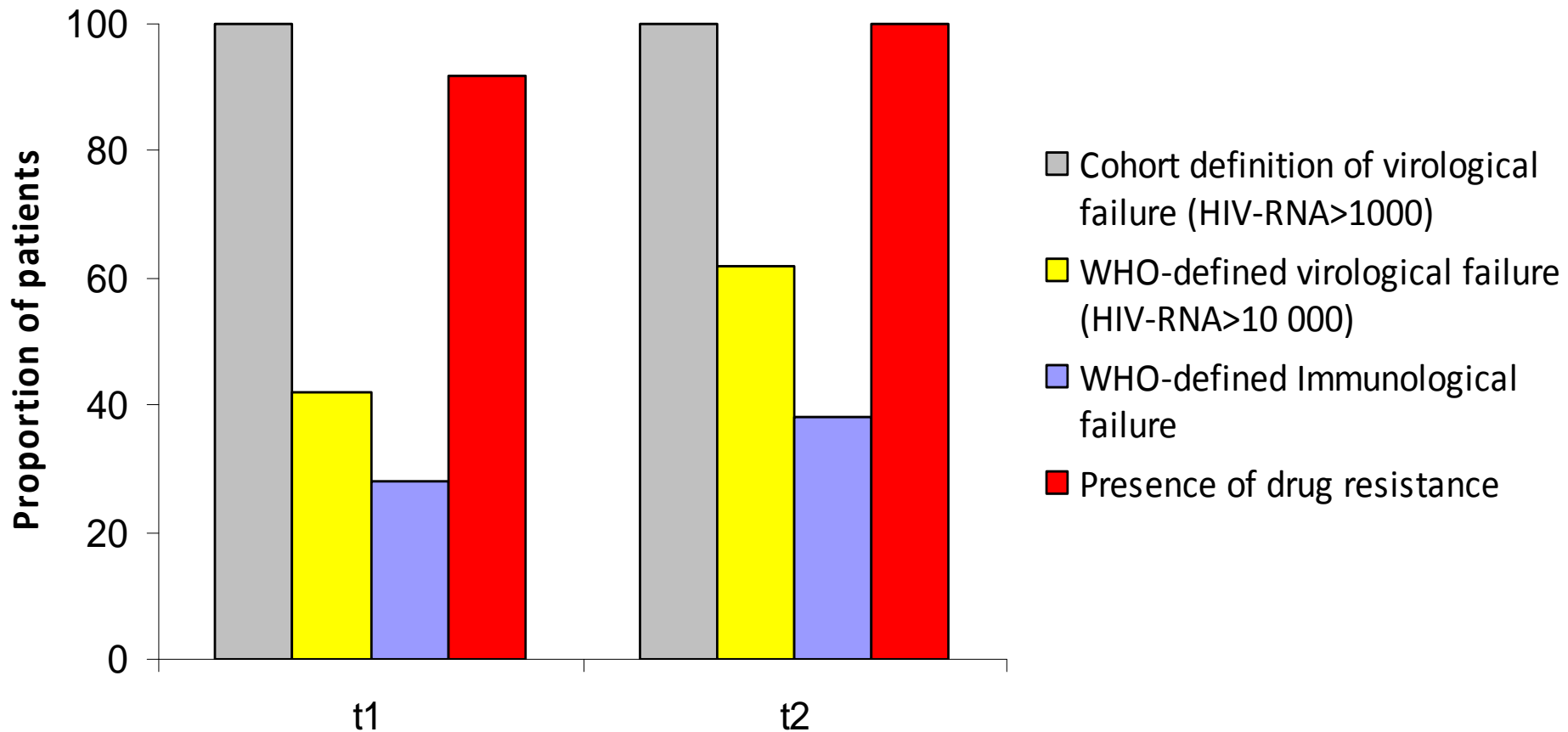
Drug resistance per class



specific drug resistance mutations



Drug resistance in relation to WHO defined failure criteria



Conclusions



- Accumulation of drug resistance was detected during continuation of failing ART, which may compromise future therapeutic options
- Although many patients did not meet WHO-defined failure criteria, considerable resistance was selected
- The results of this study supports wider access to virological monitoring in low-income countries

Acknowledgments



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Ndlovu Medical Centre

Hugo Tempelman

UMC Utrecht

Dept. Virology & Dept. Internal Medicine & Infectious Diseases

Roos Barth

Sue Aitken

Mei Ling Chu

Samira Lackbiach

Andy Hoepelman

Rob Schuurman

Arta-Project funded by NWO-Wotro