

Antiretroviral drug resistance and third-line treatment amongst HIV patients failing second-line therapy in Malawi

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Introduction: ARV Resistance

- Rising resistance to 1st line drugs
- More patients on 2nd line
 - Higher level of treatment failure
 - Genotype to confirm treatment failure not routinely available
 - Limited information on outcomes of patients on 3rd line

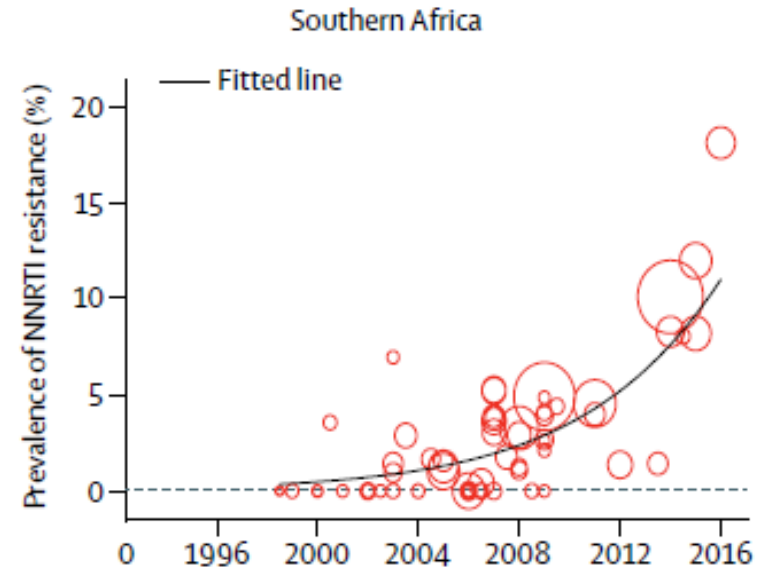


Image Source: Gupta RK, Lancet Infect Dis 2017;18: 346–55

NRTI: Nucleoside Reverse Transcriptase Inhibitors
NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitors
PI: Protease Inhibitor
INSTI: Integrase Strand Transfer Inhibitor

Study Objectives

- 2nd line resistance profile
- Virological Outcomes following genotypes



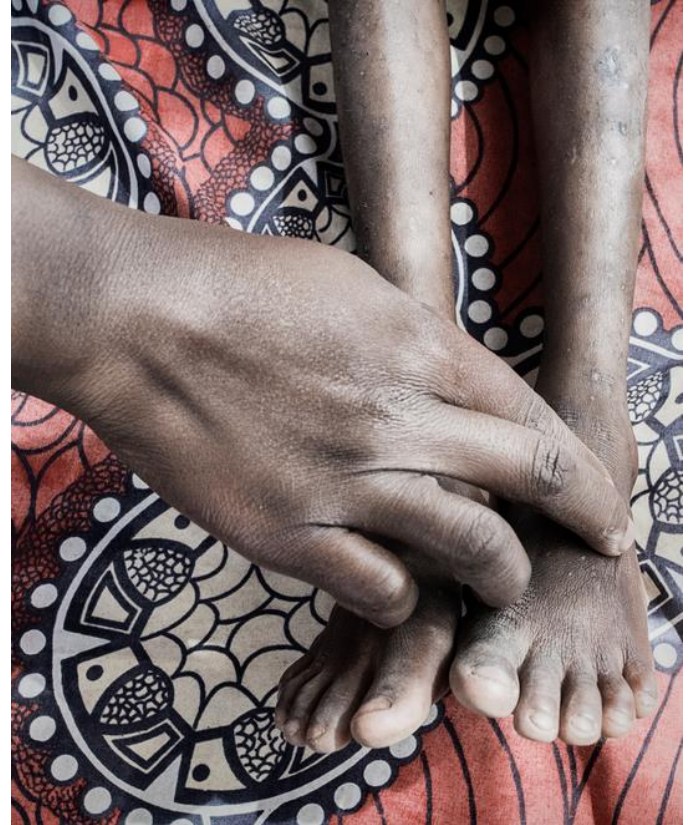
Methods: Settings

- **MSF History in Chiradzulu**
 - **2001:** ARVs Started
 - **2003:** Decentralisation/Scale-up
 - **2007:** Nurse initiation ARV
 - **2013:** Point of Care Viral Load
 - **2017:** Hand-over stable cohort
- **Chiradzulu in 2019**
 - Pop: 336,000
 - 34,000 patients on ART
 - 10% on 2nd line (45% <20yo)
 - Virological Failure on 2nd line
 - **Adults:** 8% (15% in 2016)
 - **Children/Adolescents:** 16% (25% in 2016)



Methods (II)

- **Retrospective cohort analysis**
 - Inclusion criteria: 2nd line patients failing treatment that received a genotype
- **Data Sources**
 - Routinely collected data (FUCHIA, M+, and Baobab databases)
 - > 2,000,000 consultations



Methods (III)

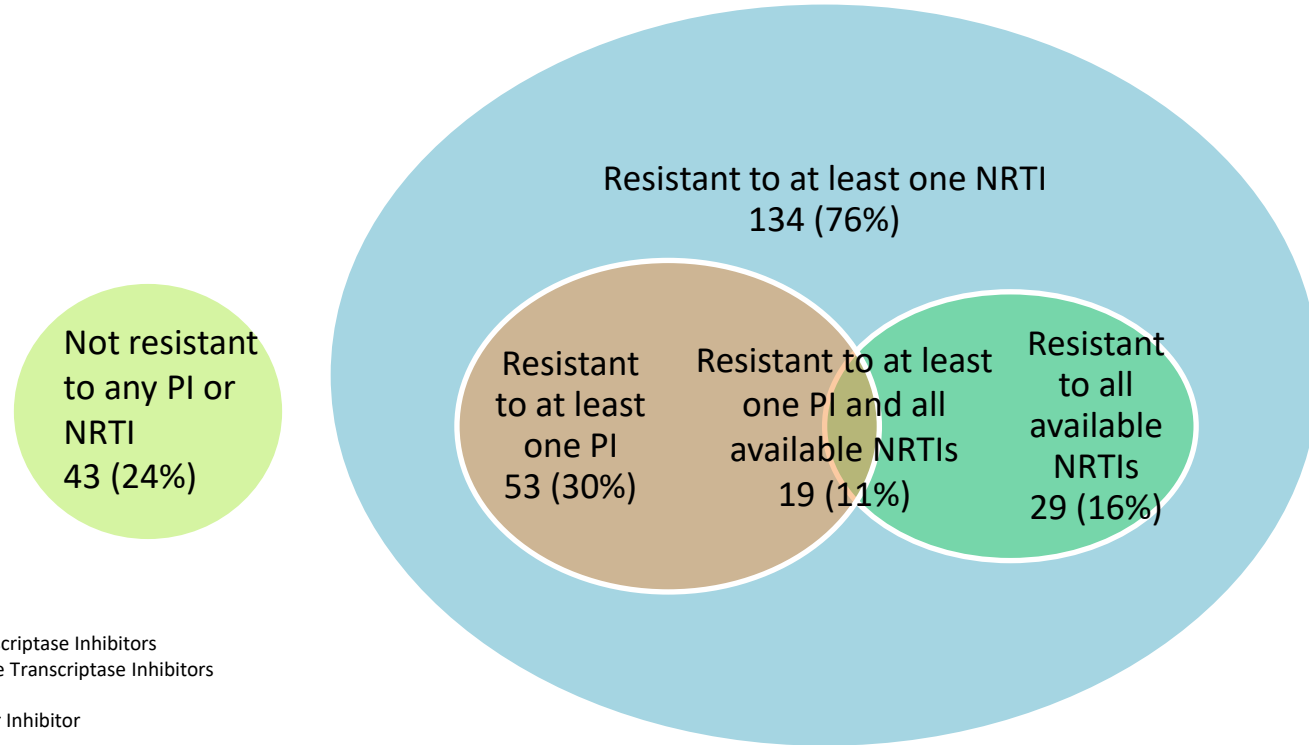
- **Laboratory**
 - **Viral Load:** point-of-care Samba then GeneXpert
 - **ARV Resistance:**
 - Genotype: UVRI Uganda - DBS
 - Scores of ≥ 30 using the Stanford University HIV Drug Resistance Database
- **Definitions**
 - **Treatment failure:** Two consecutive VL $>1,000$ cp/mL
 - **3rd line:** ART regimen that changed at least two ARVs, and included one integrase inhibitor.
- Met the criteria of the MSF Ethics Review Board for exemption from ethics review



Results: Participant Characteristics

N (%)	
Female Gender	85(48%)
Median Age (Years)	17
Time on 2nd line (Years)	
< 2	67 (38%)
≥2	110 (62%)
Protease Inhibitor in 2nd line	
Atazanavir (ATV/r)	91 (51%)
Lopinavir (LPV/r)	86 (49%)
Total	177

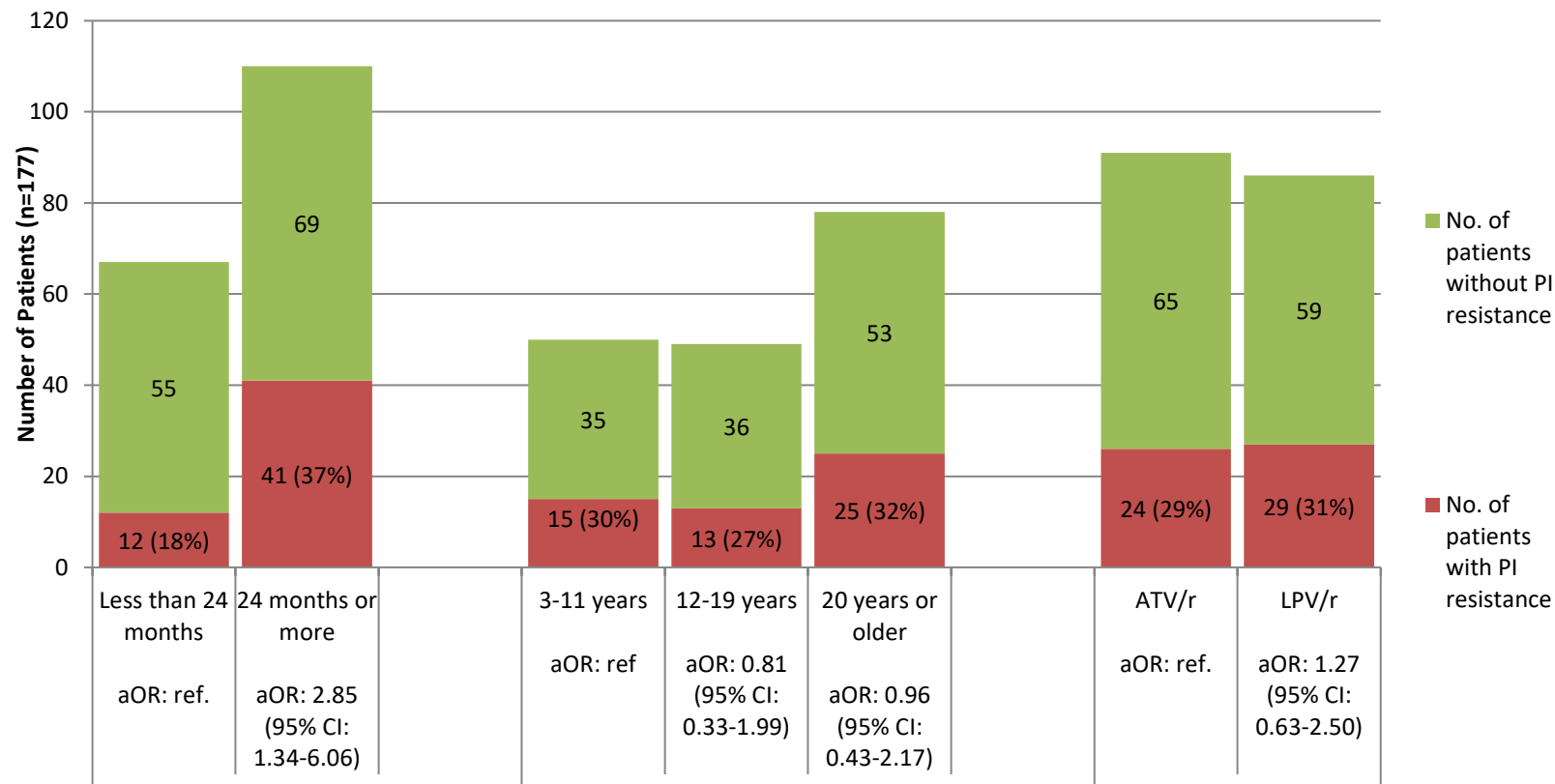
Results: ARV Resistance Profiles



NRTI: Nucleoside Reverse Transcriptase Inhibitors
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Overall, 76 patients (43%) were switched to 3rd line

Results: Protease Inhibitor Resistance

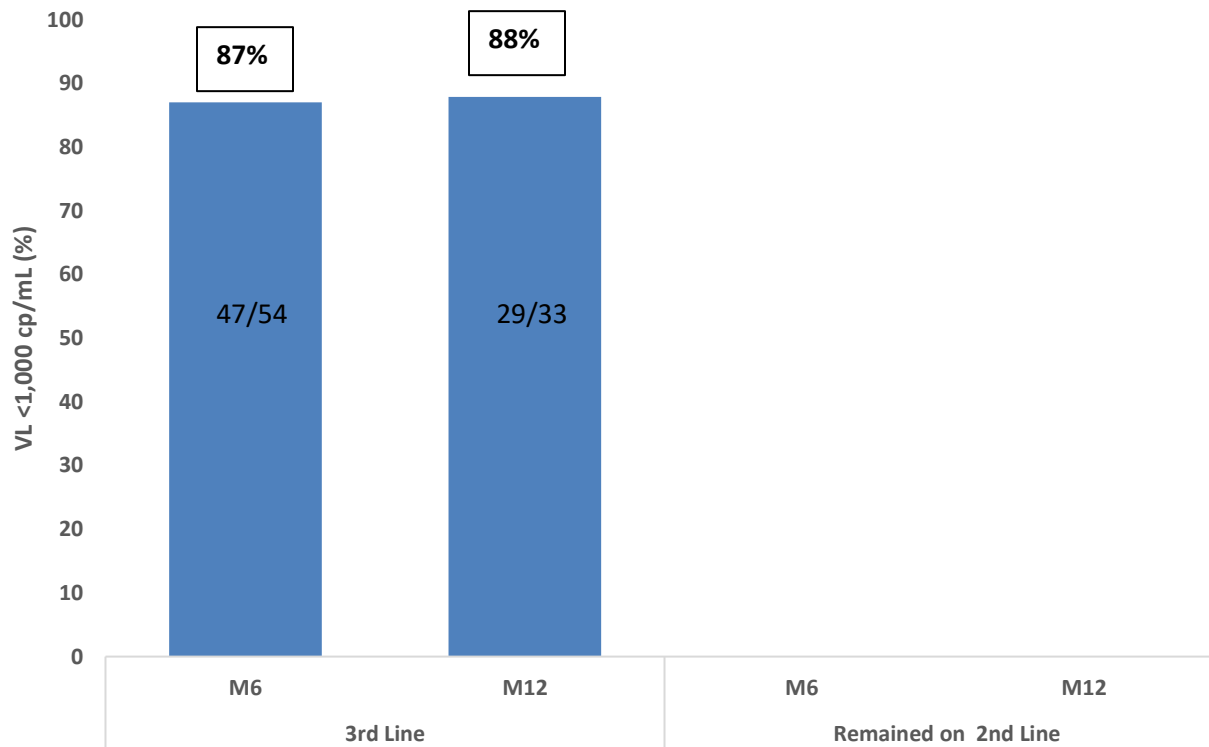


Results: Type of 3rd line

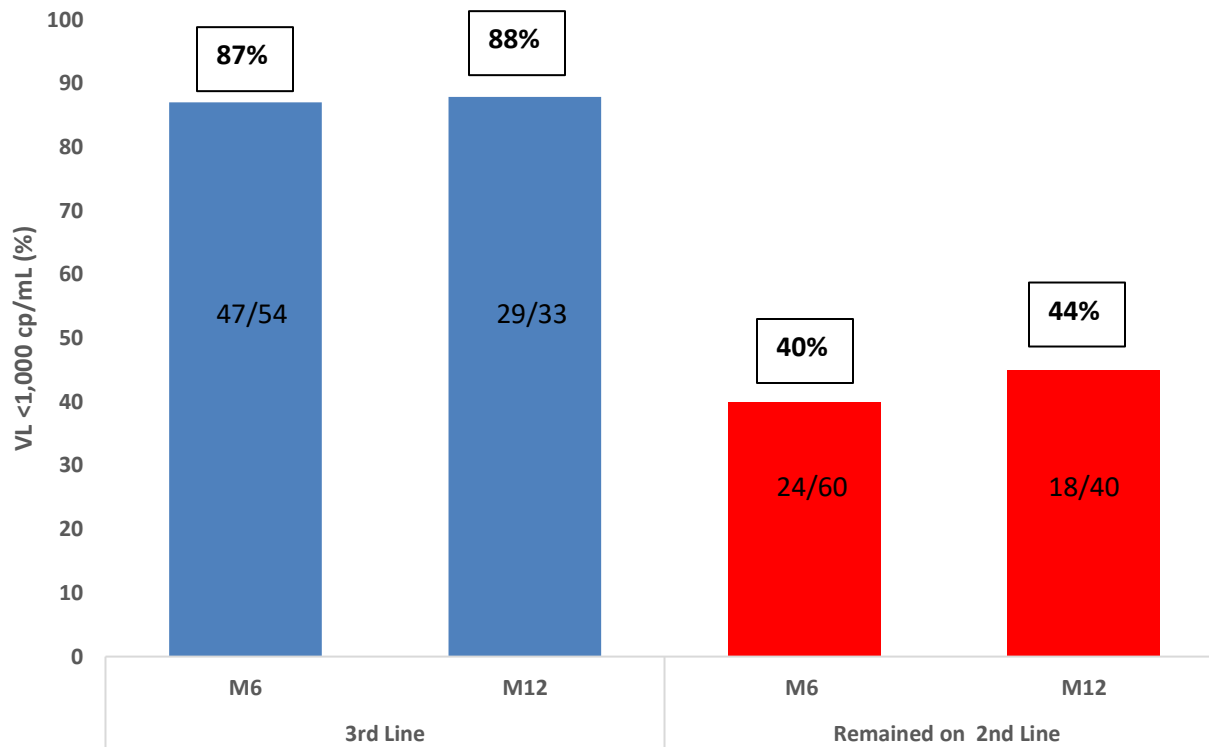
- **INSTI (DTG or RAL) + DRV/r based regimens: 58%**
- **DTG+NRTI: 25%**
- **INSTI+PI (other than DRV) based regimen: 14%**

- **DTG: Dolutegravir**
- **RAL: Raltegravir**
- **DRV: Darunavir**
- **R: Ritonavir**

Results: Viral Load Outcomes



Results: Viral Load Outcomes



Discussion

1. Over 40% of patients required 3rd line initiation

- Genotyping needed to identify ARV resistance

2. High level of VL suppression on 3rd line

- Similar outcomes to a recently reported multi-country trial (ACTG 5288)
- Access to 3rd line drugs, especially for children, difficult and expensive

3. Poor outcomes among those who remain on 2nd line

Discussion: Future of ART in Africa

- **Complete change of 1st and 2nd regimens:**
 - All adults and children >20kg on 1st and 2nd line: transition to DTG
 - All children put on Lopinavir/r until 20kg.
- **How to monitor those patients?**
- **Enhanced DTG monitoring study: Epicentre**

Conclusion: Limitations

- Genotyping only done for patients with confirmed treatment failure
 - Some died or lost to follow-up before genotype
- Non-experimental study design
- Small numbers

Acknowledgments

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