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

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**Introduction**Resistance to antiretrovirals (ARV), particularly protease inhibitors (PI), threatens to roll back progress towards expanding access to effective antiretroviral therapy in sub-Saharan Africa. Using routinely collected data from a MSF supported project in rural Malawi, we report ARV resistance and third-line treatment outcomes among patients failing second-line therapy.

**Methods**We analysed data from a retrospective cohort comprising patients failing second-line therapy, involving a PI-containing antiretroviral therapy (ART) regimen, who received genotyping between 2014-2018. Treatment failure was defined as two consecutive high viral loads (VL; >1,000 copies/mL). Third-line was defined as an ART regimen that changed at least two ARVs, and included one integrase inhibitor. Resistance was defined as scores of >=30 using the Stanford University HIV Drug Resistance Database. We used multivariable logistic models to assess the association between PI resistance and key risk factors.

**Ethics**
This research fulfilled the exemption criteria set by the MSF Ethics Review Board (ERB) for a posteriori analyses of routinely collected clinical data and thus did not require MSF ERB review. It was conducted with permission from Clair Mills, Operational Centre Paris, MSF.

**Results**Among 50,979 patients that were on ART from 2014-2018, 3,579 (7.0%) patients were started on second line. Among 177 patients failing second-line ART that received genotyping, 86 were receiving lopinavir/ritonavir and 91 atazanavir/ritonavir based regimens. Median age was 16.8 years (interquartile range (IQR) 11.8-40.4); 85 (48.0%) were female. Median time on second-line ART was 32.4 months (IQR 15.5-48.6), and 53 patients (29.9%) were resistant to at least one PI. 134 patients (75.7%) were resistant to at least one nucleoside reverse transcriptase inhibitor (NRTI), 29 (16.4%) were resistant to all available NRTIs, and 151 (85.3%) were resistant to at least one non-nucleoside reverse transcriptase inhibitor. PI resistance was more common amongst patients on second-line ART for more than two years (aOR 2.85; 95%CI 1.34-6.06). We did not observe an association between age or gender, and likelihood of PI resistance (age >= 20yr versus <20yr, aOR 1.07, 95%CI 0.55-2.11; male versus female, aOR 1.36, 95%CI 0.69-2.68). For 76 patients (42.9%) switched to third-line ART, retention in care at 12 months after third-line initiation was 97.2% (95%CI 89.4-99.3). VL suppression six and 12 months following third-line initiation was 87.0% (47/54) and 87.9% (29/33), respectively. Amongst 101 patients (57.1%) remaining on second-line ART, retention in care 12 months following genotyping was 89.0% (95%CI 78.9-94.4). VL suppression at six and 12 months following genotyping was 40.0% (24/60) and 45.0% (18/40), respectively.

**Conclusion**
Over 40% of patients failing second-line ART required third-line initiation, highlighting the need for genotyping to identify patients that require third-line therapies and the need for wider access to third-line drugs. We found that patients switched to third-line regimens can achieve good outcomes in a resource-limited setting. Those remaining on second-line treatment experienced poor outcomes, suggesting the need for simpler and better tolerated second-line regimens, and tailored adherence interventions.

**Conflicts of interest**None declared.

**David Maman**

David started to work for MSF in 2007, and has been medical coordinator in Malawi since February 2018, where MSF France has supported an HIV project since 1996. David is a medical doctor, also holding a Master’s, as well as a PhD, in epidemiology, which he started with Epicentre where he was based for 7 years, both in Paris and in Cape Town. In addition to his MSF work, David is also honorary senior lecturer at the University of Cape Town and co-supervises the PhD’s of two MSF staff.