Risk factors associated with HIV resuppression on 2nd line treatment following 1st line combination antiretroviral therapy (cART) virologic failure

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Background
- Increasing availability of new antiretrovirals has led guidelines to adopt suppression of HIV to levels below 50 copies/ml as the aim of treatment in all patients following 1st line failure.
- We performed an analysis within the ATHENA HIV observational cohort of factors associated with successful resuppression after starting 2nd line cART following 1st line cART virological failure

Methods
Patient selection
- Participants in the ATHENA national observational cohort
- ART-naive, and ≥16 years at start cART
- Start cART ≥1996
- With virological failure, (confirmed HIV-RNA >400 copies/mL after ≥24 weeks on cART)
- Starting a new cART regimen, HIV RNA subsequently measured with an assay with lower detection limit of ≤50 copies/ml

Outcome
- Virological success (confirmed HIV RNA >50 copies/ml on second line cART within one year after start 2nd line cART.

Statistical analysis
- Kaplan-Meier plots
- Unadjusted and adjusted Cox proportional hazard regression models
- Adjusted for gender, transmission risk group, region of origin, timing of 2nd line cART after 1st line failure, age, changing the NRT backbone (starting ≥1 new NRTI), CD4 cell count and HIV RNA at the start of 2nd line cART, HIV RNA assay type

Baseline

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<th>Initiation of 2nd line cART</th>
<th>Total</th>
<th>Male</th>
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<td></td>
<td>417</td>
<td>312 (75%)</td>
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Transmission risk group

| MSM | 190 (46%) |
| Heterosexual | 183 (44%) |
| other | 44 (10%) |

Region of origin

| Europe, N-America | 219 (53%) |
| Caribbean, S-America | 65 (16%) |
| Sub Saharan Africa | 118 (28%) |
| other | 15 (3%) |

Age

| Mean (16-68) |

Days till switch cART

| Mean | 210 (84-688) |

CD4 cells/mm³

| Median (IQR) | 478 (287-705) |

HIV RNA log10

| Median (IQR) | 3.9 (2.8-4.5) |

Table 1. Demographic and clinical characteristics at the start of 2nd cART

Results

- Within one year 70% (95% CI 65-74%) managed to resuppress <50 copies/ml
- However, this depended on CD4 cell count at the start of 2nd line cART (see Figure).
- In multivariate analyses (see Table 2), switching with a higher CD4 cell count (p=0.0003) and lower HIV-RNA (p<0.0001) and born in Sub Saharan Africa (p=0.009) was associated with a shorter time to resuppression
- 30% of those with resuppression on 2nd line cART experienced recurrent failure within 3 years

Conclusions

- A substantial proportion of patients virologically failing 1st line cART did not achieve resuppression of HIV
- A significant proportion experienced recurrent failure after resuppression
- Patients with lower CD4 cell count and higher HIV RNA at initiation of 2nd line cART were at increased risk of virological failure on 2nd line cART
- Patients born in Sub Saharan Africa also proved to have an increased risk of virological failure, possibly due to lesser adherence

Figure. Kaplan-Meier estimates of the percentage of patients with virological success after starting 2nd line cART according to CD4 cell counts at time of switch to 2nd cART

Table 2. Hazard ratio’s and 95% CI’s obtained with uni-, and multivariable Cox regression analysis