



# Failure of antiretroviral therapy (ART) in Australian adults is mainly due to ART toxicity

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# Background

- Lifelong antiretroviral therapy (ART) of HIV is recommended for all patients
- ART failure can comprise:
  - virological failure
  - ART regimen change for toxicity or pharmacodynamic (PD) interactions
  - loss to follow-up / non-adherence / not taking ART
  - death
- Aim:
  - To determine the reasons for ART failure in an Australian cohort

# Methods

## PAART study

- 522 participants at multiple Australian GP, sexual health and hospital sites
- **Eligibility**
  - HIV+ adult  $\geq 18$  years of age
  - on stable ART for previous 3 months (minimum)
  - plasma HIV-RNA  $< 50$  copies / mL
- **Assessments**
  - 90-item participant survey (including self-reported adherence)
  - neurocognitive function: Cogstate
  - pharmacy ART dispensing data
  - clinical and virological data (all results)

# ART Failure

Composite endpoint,  $\geq 1$  of the following:

Virological failure	<ul style="list-style-type: none"> <li>▪ viral load <math>&gt; 200</math> copies / mL</li> <li>▪ 2 consecutive viral loads <math>&gt; 50</math> copies / mL</li> <li>▪ 1 viral load <math>&gt; 50</math> copies / mL with an ART change</li> </ul>
ART toxicity	ART switch for toxicity <ul style="list-style-type: none"> <li>▪ renal</li> <li>▪ neuro</li> <li>▪ metabolic</li> <li>▪ CNS</li> <li>▪ hepatic</li> </ul>
Drug-to-drug / pharmacodynamic interaction eliciting ART change	
Non-adherence	Not taking ART and $\geq 1$ of: <ul style="list-style-type: none"> <li>▪ disengagement from care</li> <li>▪ virological failure</li> <li>▪ confirmation by pharmacy reports</li> </ul>
Loss to follow-up	<ul style="list-style-type: none"> <li>▪ Patient withdrawal from care, and</li> <li>▪ non-contactable and no evidence of continuing care at alternate site, and</li> <li>▪ no pathology results or pharmacy record of ART dispensing</li> </ul>

# Results

- **Participants**
  - 94% male
  - age = 51 years
  - HIV duration = 12 years
  - ART duration = 11 years
  - HIV RNA <50 copies/mL = 3.3 years
- **Data**
  - All data received at 6 months
  - 96.9% of data received at 12 months
  - Missing data:
    - no data from site
    - revocation of consent
    - transfer of care to a non-study site
    - incarceration
- 36% of source data verified

# ART failure

- **Failure rates**
  - 117 instances of ART failure over the first 12 months of follow-up
  - 101 participants experienced ART failure (19% of the cohort)
    - 87 (17%) had 1 episode
    - 12 (2%) had 2 episodes
    - 2 (0.4%) had 3 episodes

# ART failure

Causes of ART Failure	n (% of failures)
ART change for toxicity	68 (58.1%)
Confirmed virological failure	22 (18.8%)
ART change for drug-to-drug or pharmacodynamic interaction	11 (9.4%)
ART non-adherence	10 (8.5%)
Death	3 (2.6%)
Loss to follow-up	2 (1.7%)
Difficulty taking ART regimen	1 (0.85%)
Total	117 (100%)

# ART regimen changes

Reason for ART change	Changes n (%)	Changes n (%)
<i>Adverse effects / toxicity</i>	<i>68 (13.0%)</i>	
Nephrotoxicity		21 (4.0)
Side effects		14 (2.7)
Neurotoxicity		14 (2.7)
Hepatotoxicity		8 (1.5)
Metabolic		5 (1.0)
Neuropathy		2 (0.4)
Resistance		2 (0.4)
Virologic failure		1 (0.2)
Low CD4 T-cell count		1 (0.2)

# ART regimen changes

Reason for ART change	Changes n (%)	Changes n (%)
<b>ART-related</b>	<b>65 (12.5%)</b>	
Treatment simplification		48 (9.2)
Clinical trial start / completed, compassionate access		6 (1.1)
Drug-drug or PD interaction		11 (2.1)
<b>Patient-related</b>	<b>14 (2.7%)</b>	
Non-adherence		10 (1.7)
Patient self-request		3 (0.6)
Difficulty taking (e.g. swallowing)		1 (0.2)
<b>Other</b>	<b>5 (1.0%)</b>	
Unknown		4 (0.8)
Belief of superiority		1 (0.2)
<b>Total</b>	<b>152 changes</b>	<b>144 (27.6%)</b>

## Summary & Conclusions

- 19% of this sample experienced at least one episode of ART failure over 12 months of follow-up
- Primary reason for ART failure was toxicity
- Virological failure uncommon, loss to follow-up was rare

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