

FAILURE OF ANTIRETROVIRAL THERAPY (ART) IN ADULTS IN AUSTRALIA IS MAINLY DUE TO ART TOXICITY

Authors:

Siefried KJ¹, Mao L², Riches S¹, Kerr S¹, Rule J^{3,4}, McAllister J¹, de Wit J^{2,5}, Carr A¹; on behalf of the PAART study investigators

¹ Centre for Applied Medical Research, St Vincent's Hospital, Sydney, Australia;

² Centre for Social Research in Health, UNSW, Sydney, Australia;

³ National Association of People with HIV Australia;

⁴ School of Public Health and Community Medicine, UNSW, Sydney, Australia;

⁵ Department of Interdisciplinary Social Science, Utrecht University, Utrecht, The Netherlands

Background

Lifelong antiretroviral therapy (ART) is recommended for all patients. Reasons for ART failure in virologically-suppressed patients are poorly understood.

Methods

We recruited 522 adults living with HIV on stable ART for ≥ 3 months with undetectable viral load into a nationwide cohort between September 2014 and November 2015. ART failure was defined by ART switch (for toxicity or interactions), virological failure, progression to AIDS, death, or loss to follow-up. Factors associated with ART failure through Month 12 were determined using Cox proportional hazards regression.

Results

115 episodes of ART failure occurred in 102 participants (19.5%), primarily for toxicity requiring an ART switch (n=64, 12.3%); mostly nephrotoxicity (n=21, 4.0%), central nervous system symptoms (n=14, 2.7%), side effects (e.g. nausea/vomiting) (n=16, 3.1%), hepatotoxicity (n=8, 1.5%), and metabolic toxicity (n=6, 1.1%). Other reasons for ART failure were: virological failure (n=26, 5.0%); drug interactions (n=13, 2.5%); death (n=3, 0.6%); AIDS (n=2, 0.4%); loss to follow-up (n=2, 0.4%); and difficulty taking ART (n=1, 0.2%). The median time to the first failure event was 187 days (IQR 106-282).

ART failure was independently associated with: interrupting concomitant medications in the year prior to baseline (adjusted hazard ratio [AHR] 2.3, 95% confidence interval [95% CI] 1.1-4.6, p=0.021); sexually transmitted infection in the year prior to baseline (AHR 0.4, 95% CI 0.2-0.9, p=0.044); diagnosed active psychiatric illness at baseline (AHR 1.9, 95% CI 1.2-3.0, p=0.005); developing a new comorbidity (AHR 2.9, 95% CI 1.6-5.3, p=<0.001), and developing a new estimated glomerular filtration rate (eGFR) <60mL/min/1.73m² (AHR 1.9, 95% CI 1.1-3.2, p=0.021). Suboptimal ART adherence was not predictive of ART failure.

Conclusions

Despite near universal ART availability and government-subsidised healthcare, nearly 20% of our sample experienced ART failure over 12 months, primarily for toxicity. Virological failure was less common.

Disclosure of interest statement

This work was supported by unrestricted educational grants from Gilead Sciences (IN-AU-264-0131); the Balnaves Foundation; the Victorian Department of Health and Human Services (Australia); the Government of Western Australia, Department of Health; the ACT Ministry of Health (Australia); and in-kind support from the Queensland Department of Health (Australia).

K.J.S. has received conference and travel sponsorships from Gilead Sciences. L.M. has no interests to declare. S.R. has no interests to declare. S.K. has no interests to declare. J.R. has no interests to declare. JM has received lecture fees from ViiV Healthcare, conference and travel sponsorships from ViiV Healthcare and MSD. J.d.W has received lecture sponsorship from BMS Australia. A.C. has received research funding from Bristol-Myers Squibb, Gilead Sciences, and ViiV Healthcare; lecture and travel sponsorships from Bristol-Myers Squibb, Gilead Sciences, and ViiV Healthcare; and has served on advisory boards for Gilead Sciences and ViiV Healthcare.