

# ANTIRETROVIRAL TREATMENT INTERRUPTIONS IN HIV CLINICAL TRIALS: A SYSTEMATIC REVIEW

## Authors:

Lau JSY<sup>1</sup>, Smith MZ<sup>2</sup>, Lewin SR<sup>1,2</sup>, McMahon JH<sup>1</sup>

<sup>1</sup> Department of Infectious Diseases, Alfred Hospital and Monash University, Melbourne, Australia

<sup>2</sup> The Peter Doherty Institute for Infection and Immunity, University of Melbourne and Royal Melbourne Hospital, Melbourne, Australia

## Background:

Treatment interruptions (TI) of antiretroviral therapy (ART) were used to optimise clinical outcomes in the context of significant drug toxicities. More recently, HIV cure trials have used TI to assess strategies and interventions aimed at achieving virological control off ART. We describe the differences between TI in cure-focused (CF) research and non-cure focused (NCF) TI studies performed to minimise adverse effects of ART.

## Methods:

A systematic review was performed of clinical studies from 2000-2017 identified via Ovid MEDLINE, EMBASE and recent HIV conference abstracts. Extracted data included: demographics, frequency of CD4 and HIV viral load (VL) monitoring, criteria to restart ART, TI duration, and adverse outcomes of TI. A descriptive analysis of TI parameters was performed for CF and NCF studies.

## Results:

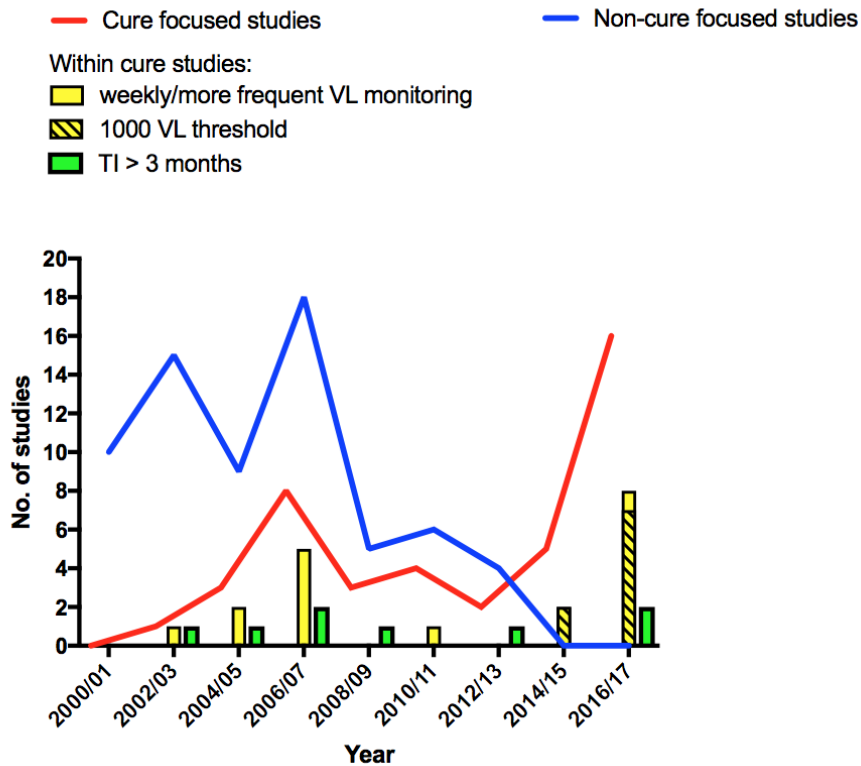
Data was extracted from 109 studies: 42 (39%) CF and 67 (61%) NCF (Figure). Most common monitoring strategies for VL and CD4 were: monthly for 18 NCF studies and weekly or more frequently for 19 CF studies. Commonest threshold to restart ART in all studies was CD4 <350 cells/mm<sup>3</sup>. In CF studies, the commonest VL threshold was >1000 copies/mL in 9 studies conducted since 2014, and >50,000 copies/mL in 6 pre-2014 studies. 22 NCF interrupted ART for >3 months, compared with 8 CF studies. TI-related adverse events were mostly related to immunological decline and reported in 25 (37%) NCF and 6 (14%) CF. One death from myocardial infarction during a CF study was reported in 2012, out of a total of 1597 participants in CF studies.

## Conclusion:

Marked heterogeneity was noted in study methodology and TI duration. ATI studies were more likely to re-initiate ART based on VL monitoring and the VL threshold for this has decreased over time. Summary data will assist the design of future trials involving ATI and potentially in standardising an approach to this intervention.

## Disclosure of Interest Statement:

SRL has participated in advisory roles and educational activities of Viiv and Merck Sharp & Dohme Corp. All honoraria were paid to the investigator's institutions.



**Figure: Summary of treatment interruption studies by year.**

The red line shows the number of cure studies, and the blue line shows non-cure focused studies published by year. The green bars (right y axis) show the total number of cure studies that interrupted ART for greater than 3 months. The yellow bars (right y axis) indicate the number of cure studies that check HIV viral load weekly or more frequently during TI, and the patterned yellow bars indicate how many of these studies had a viral load threshold to restart ART of 1000 copies/mL.