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HIV-1 DNA levels after antiretroviral therapy in primary infection predict disease progression: the SPARTAC Trial.

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Background: The HIV-1 reservoir is the major barrier to HIV eradication. Measuring the reservoir using molecular qPCR techniques reveals associations with HIV-1 plasma viral load and the likelihood of 'post treatment control'. We investigated whether levels of 'total' and 'integrated' HIV-DNA measured by qPCR after 48 weeks of antiretroviral therapy (ART) were associated with surrogate disease markers and clinical progression in the SPARTAC trial, a large randomized RCT investigating short course ART in Primary HIV Infection (PHI).

Methods: 40 HIV+ve participants with PHI recruited to SPARTAC and randomized to receive 48 weeks of ART were investigated. All participants were recruited from the UK and were male. 38/40 (95%) were infected with subtype B HIV-1. Peripheral Blood Mononuclear Cell (PBMC) samples were taken at enrolment and on stopping 48 weeks of ART. Multi-clade compatible qPCR assays were performed on DNA from CD4 T cell enriched PBMCs to measure 'total' and 'integrated' HIV copies per CD4+ T cell. HIV-1 DNA levels were associated with baseline covariates and times to progression using logistic regression, Kaplan-Meier plots, and Cox models.

Results: Baseline plasma viral load levels and CD4 count were significantly associated with the total ($p=0.0003$ and $p=0.0135$, respectively) and integrated ($p=0.0007$ and $p=0.0161$, respectively) DNA levels after 48 weeks of therapy. There was no association between HIV-1 DNA levels and the estimated time since seroconversion at enrolment. Time to viral load rebound after stopping ART was associated with total ($p=0.027$) but not integrated HIV-1 DNA. Both total and integrated HIV-1 DNA levels were associated with the SPARTAC trial primary endpoint (HR 8.26; $p< 0.0001$ and HR 3.08; $p=0.014$; respectively) which was a composite of reaching either 350 CD4 cells/µl or starting long-term ART. In multivariate cox analyses, total HIV-1 DNA was more strongly associated with clinical progression than other covariates, including plasma viral load at enrolment.

Conclusion: The HIV-1 reservoir level after 48-weeks of treatment strongly predicted disease progression, with total HIV-1 DNA levels being more predictive than integrated HIV-1 DNA levels. These data confirm the significance of the HIV-1 reservoir in circulating CD4 cells and its importance in functional cure strategies.