



**Cell-associated HIV-1 unspliced RNA level predicts both time to virological suppression
and duration of post-treatment virological control in patients treated with
temporary early ART**

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Disclosure of speaker's interests

No conflict of interest

Potentially relevant company relationships in connection with event *[if there is a potential conflict of interest, please provide relevant details. See below for examples]*

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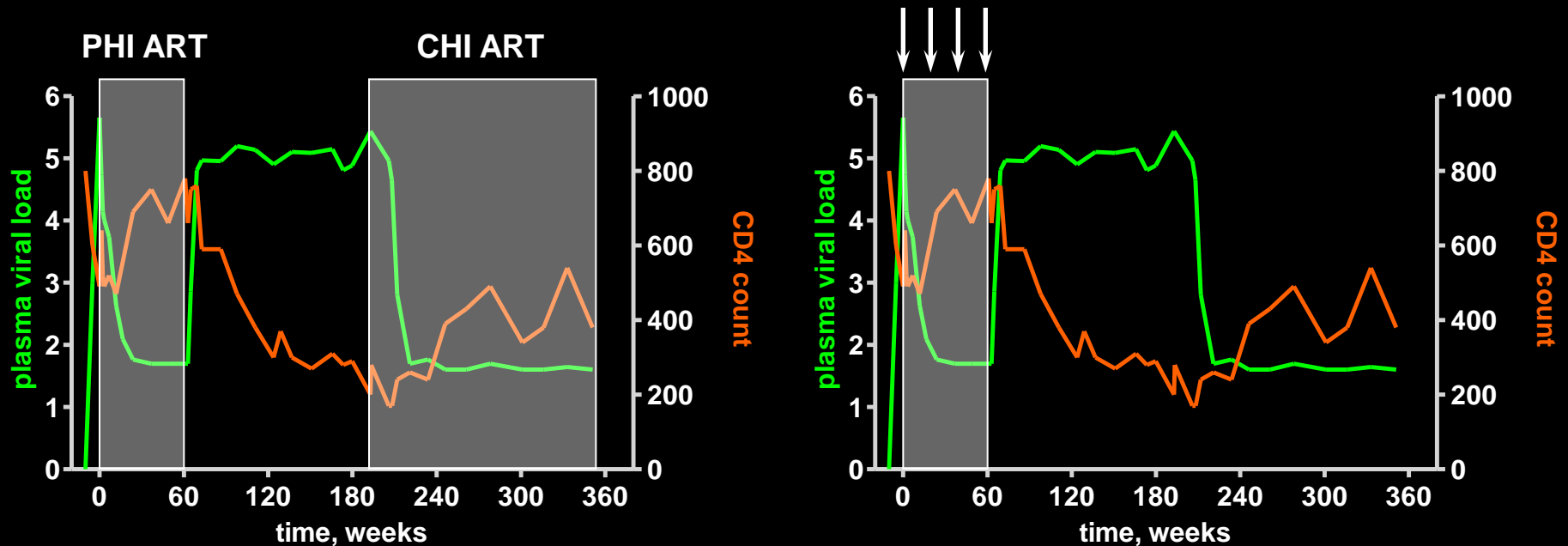
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No Treatment versus 24 or 60 Weeks of Antiretroviral Treatment during Primary HIV Infection: The Randomized Primo-SHM Trial

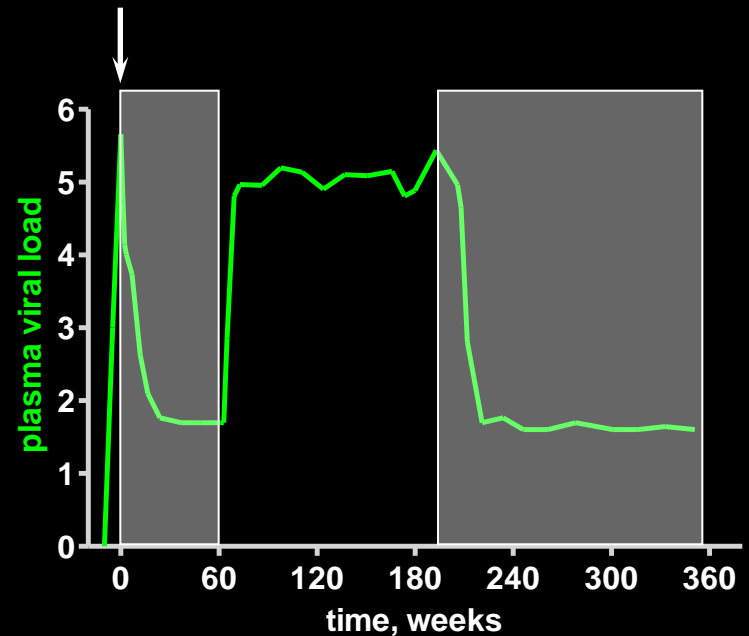
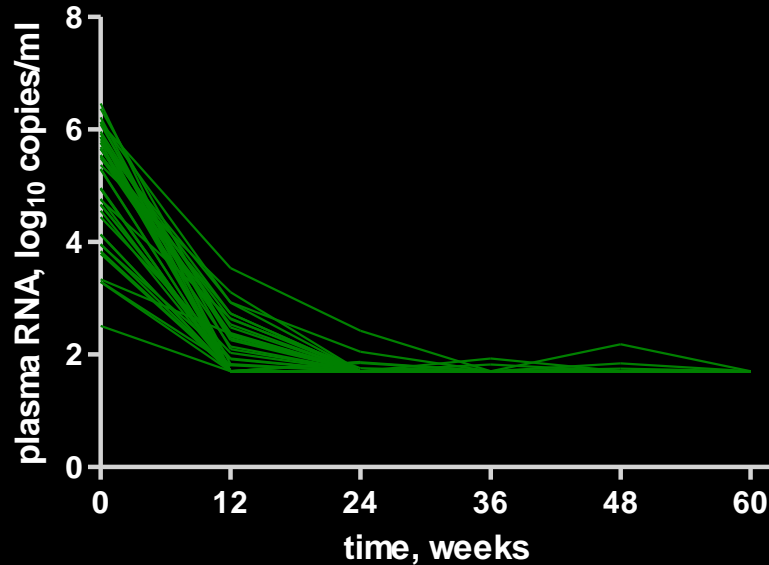
Marlous L. Grijzen^{1,9*}, Radjin Steingrover^{1,2,9}, Ferdinand W. N. M. Wit², Suzanne Jurriaans³, Annelies Verbon^{4,8}, Kees Brinkman⁵, Marchina E. van der Ende⁶, Robin Soetekouw⁷, Frank de Wolf⁸, Joep M. A. Lange², Hanneke Schuitemaker⁹, Jan M. Prins¹, on behalf of the Primo-SHM Study Group

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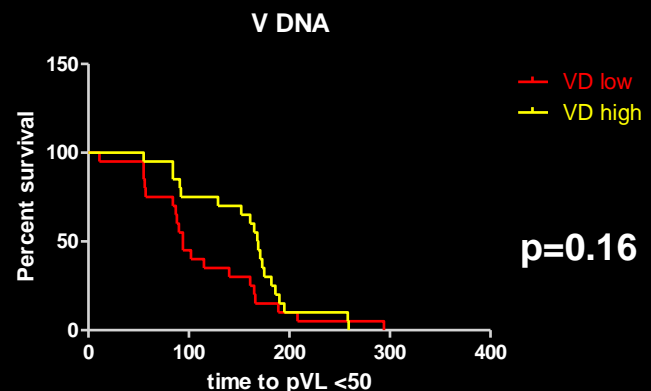
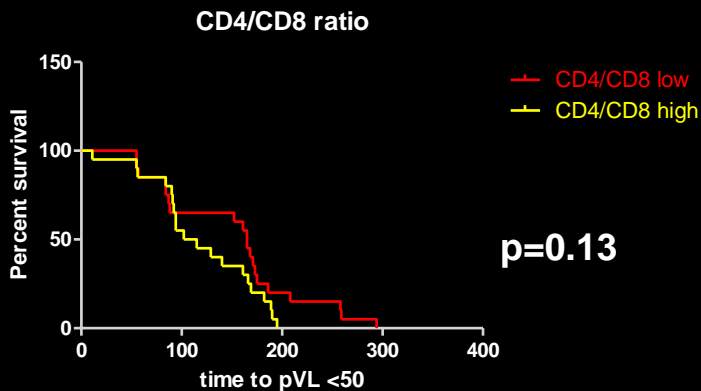
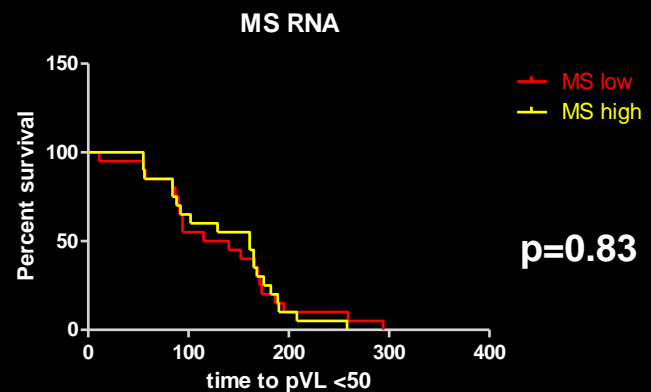
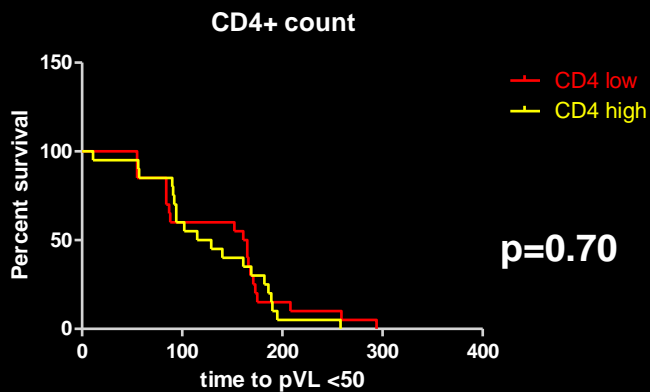
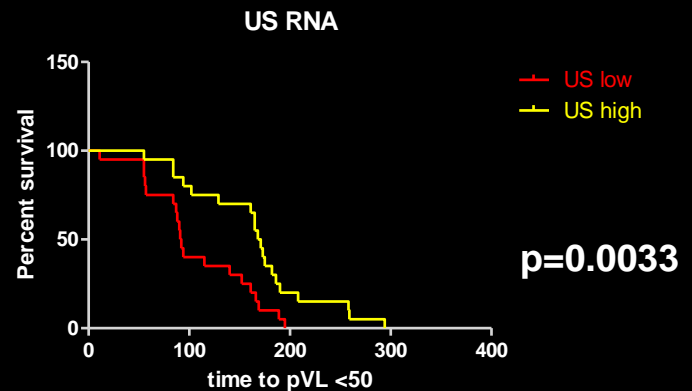
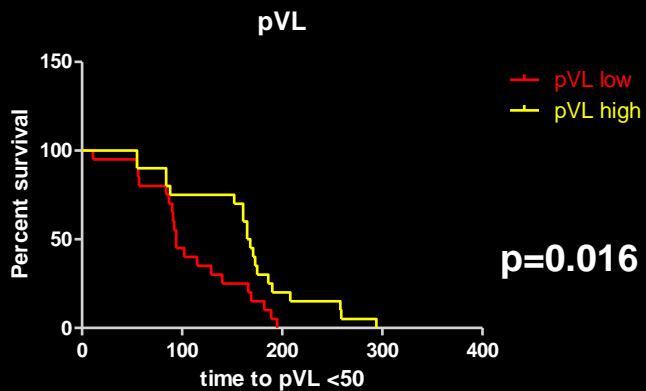
Cell-associated HIV nucleic acids were quantified in PBMC at PHI and every 12 weeks thereafter during early ART



What determines the rate of virological suppression after ART initiation?

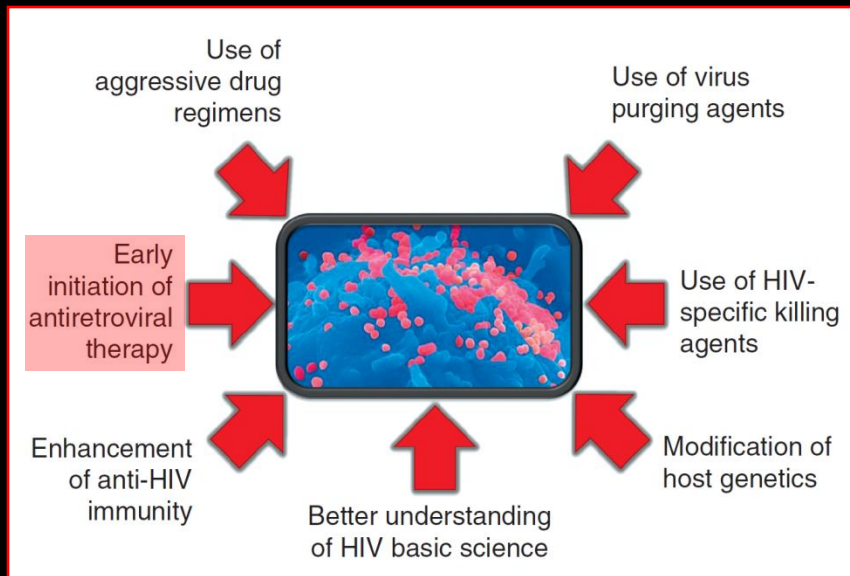


Plasma viral load, CD4+ count, CD4/CD8 ratio, unspliced RNA, multiply spliced RNA, and total viral DNA were measured at PHI



In the multivariate Cox regression, US RNA at PHI was the only significant predictor of the time to virological suppression (HR=0.65 per 1 log₁₀ increase in US RNA, 95% CI, 0.48-0.87, p=0.0043).

Early initiation of ART is one of the most promising strategies for HIV cure



Chun Fauci AIDS 2012

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PLOS PATHOGENS

Post-Treatment HIV-1 Controllers with a Long-Term Virological Remission after the Interruption of Early Initiated Antiretroviral Therapy ANRS VISCONTI Study

Asier Sáez-Cirión^{1*}, Charline Bacchus², Laurent Hocqueloux³, Véronique Avettand-Fenoel^{4,5}, Isabelle Girault⁶, Camille Lecroux⁶, Valerie Potard^{7,8}, Pierre Versmisse¹, Adeline Melard⁴, Thierry Prazuck³, Benjamin Descours², Julien Guernon², Jean-Paul Viard^{5,9}, Faroudy Boufassa¹⁰, Olivier Lambotte^{6,11}, Cécile Goujard^{10,11}, Laurence Meyer^{10,12}, Dominique Costagliola^{7,8,13}, Alain Venet⁶, Gianfranco Pancino¹, Brigitte Autran², Christine Rouzioux^{4,5*}, the ANRS VISCONTI Study Group^{*}

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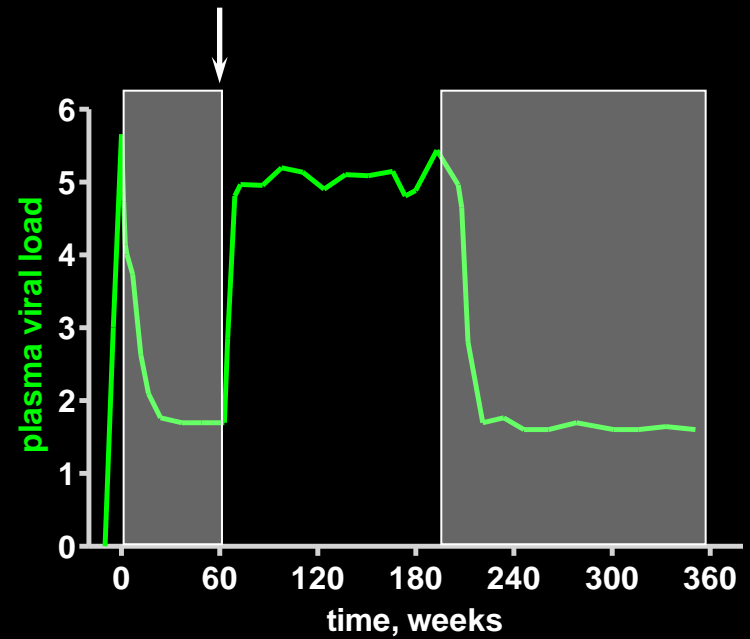
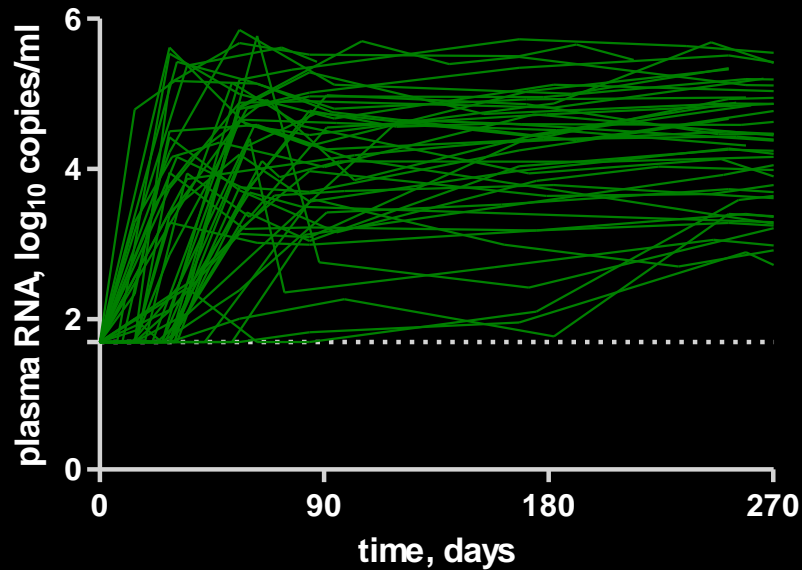
BRIEF REPORT

Absence of Detectable HIV-1 Viremia after Treatment Cessation in an Infant

Deborah Persaud, M.D., Hannah Gay, M.D., Carrie Ziemniak, M.S., Ya Hui Chen, B.A., Michael Piatak, Jr., Ph.D., Tae-Wook Chun, Ph.D., Matthew Strain, M.D., Ph.D., Douglas Richman, M.D., and Katherine Luzuriaga, M.D.

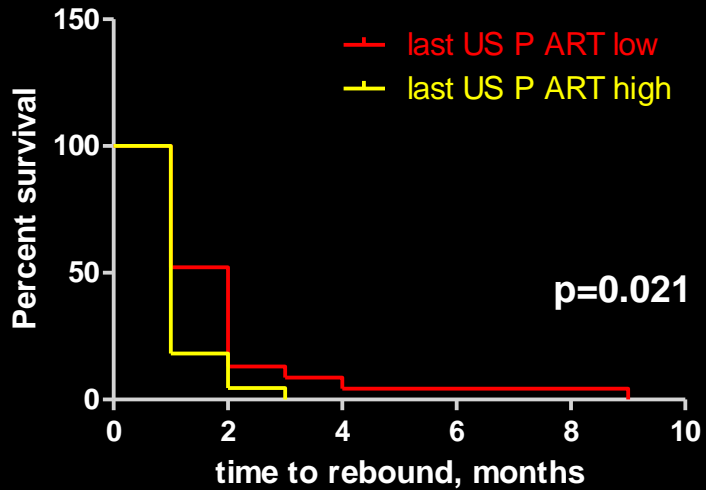
For the improved design of strategies towards HIV-1 functional cure, it is important to identify biomarkers that could predict the duration of post-treatment virological control (Visconti study, etc.)

What determines the rate of virological rebound after ART interruption?

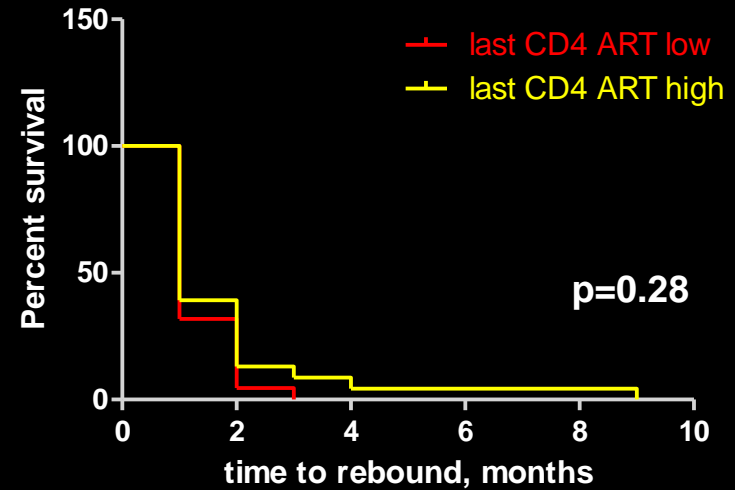


Unspliced RNA, total viral DNA, and CD4+ count were measured before interruption of early ART

US RNA

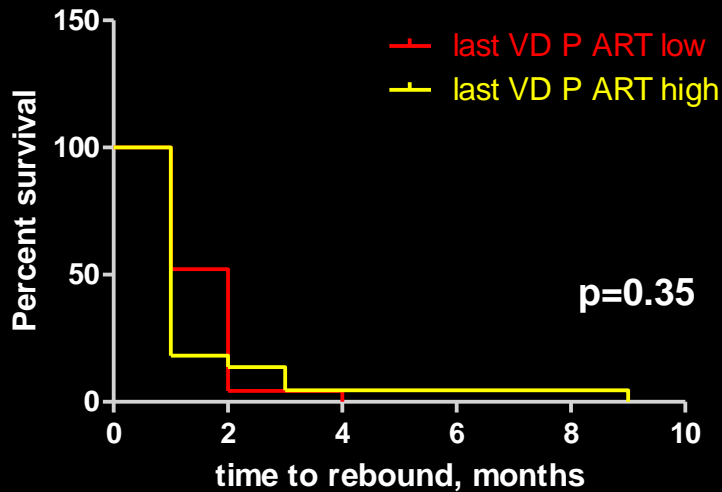


CD4+ count

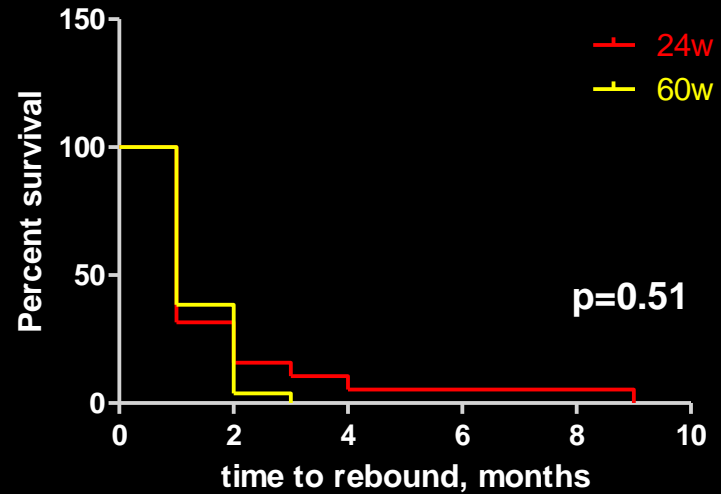


Further exploration of US RNA as a predictor of post-treatment control in large-scale clinical trials aimed at HIV functional cure is warranted

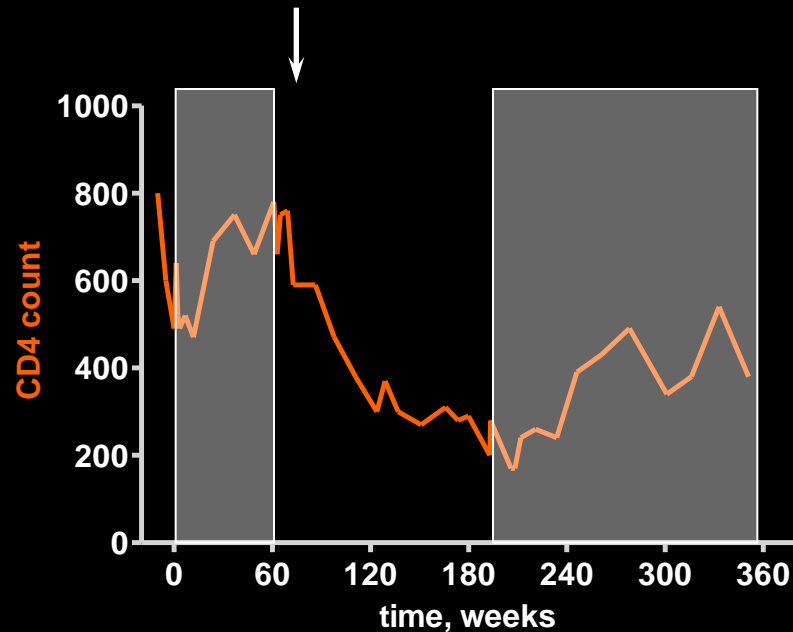
V DNA



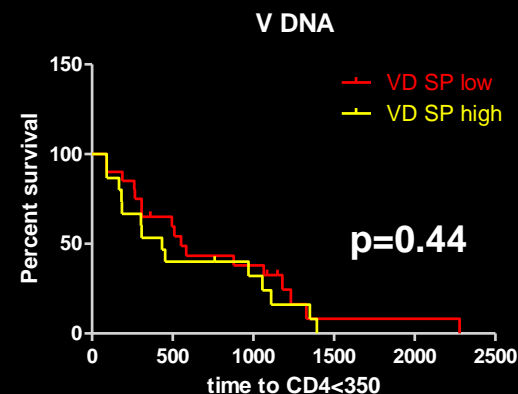
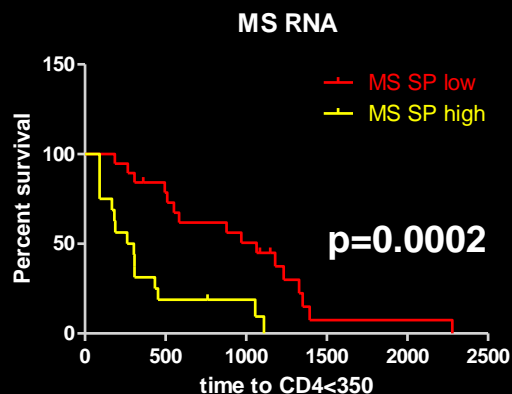
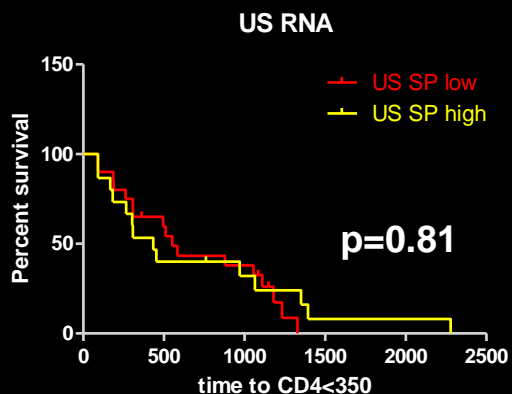
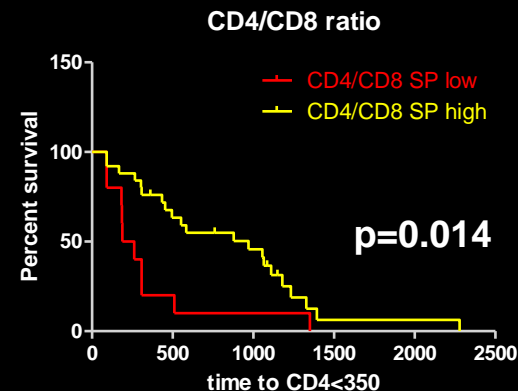
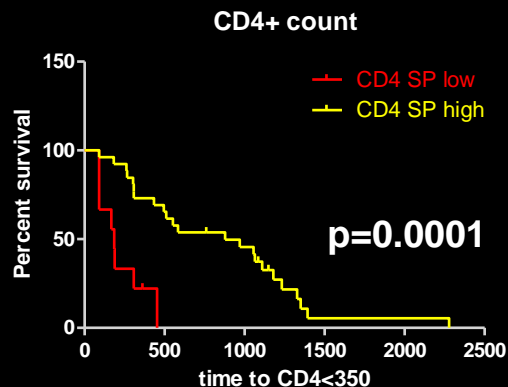
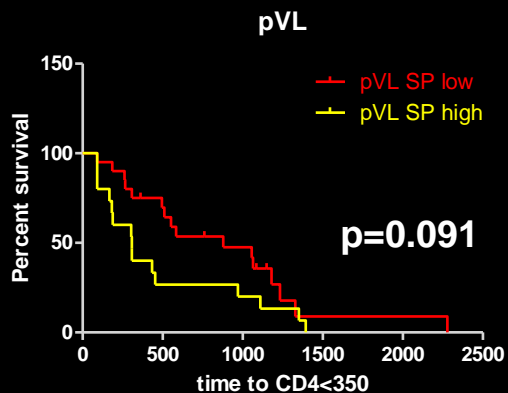
24 weeks vs 60 weeks ART



What determines the rate of disease progression (CD4+ T-cell loss) after interruption of early ART?



Plasma viral load, CD4+ count, CD4/CD8 ratio, unspliced RNA, multiply spliced RNA, and total viral DNA were measured at the virological setpoint (36 weeks after early ART interruption)



In the multivariate Cox regression analysis, CD4+ count ($p=0.0004$) and MS RNA level ($p=0.011$) were the only two significant predictors of disease progression.

Conclusions

Cell-associated HIV-1 unspliced RNA level independently predicted both time to virological suppression and time to virological rebound in patients treated with temporary early ART

Cell-associated HIV-1 multiply spliced RNA level independently predicted disease progression (CD4+ T-cell loss) after interruption of early ART, while unspliced RNA was not predictive

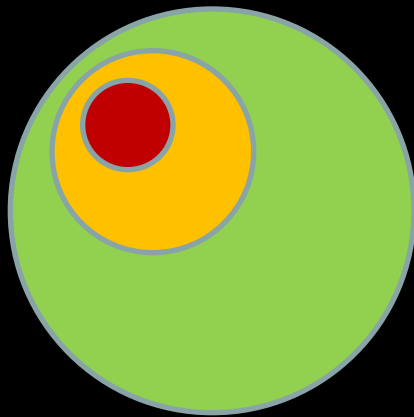
It looks like reactivation of HIV after therapy is interrupted and subsequent CD4+ T-cell loss are driven by different mechanisms

Reservoirs, reservoirs...

HIV DNA: a marker of total reservoir (mostly defective)

Unspliced RNA: a marker of active reservoir (cells transcribing viral RNA); overestimates but might correlate with functional reservoir (cells that produce virus or can become reactivated to do so upon latency reversal)

Multiply spliced RNA: a marker of “hyperactive reservoir” (cells with high MS RNA levels, a subset of active reservoir – the relative size of this “hyperactive reservoir” may drive HIV pathogenesis, determining the rate of CD4+ T-cell loss)



Total (DNA⁺)

Active (DNA⁺ US-RNA⁺)

Hyperactive (DNA⁺ US-RNA⁺ MS-RNA^{high})



Cell Host & Microbe

Previews

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HIV Reservoir: Finding the Right Needles in a Needlestack

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