



HIV-1 virological remission for more than 12 years after interruption of early initiated antiretroviral therapy in a perinatally-infected child

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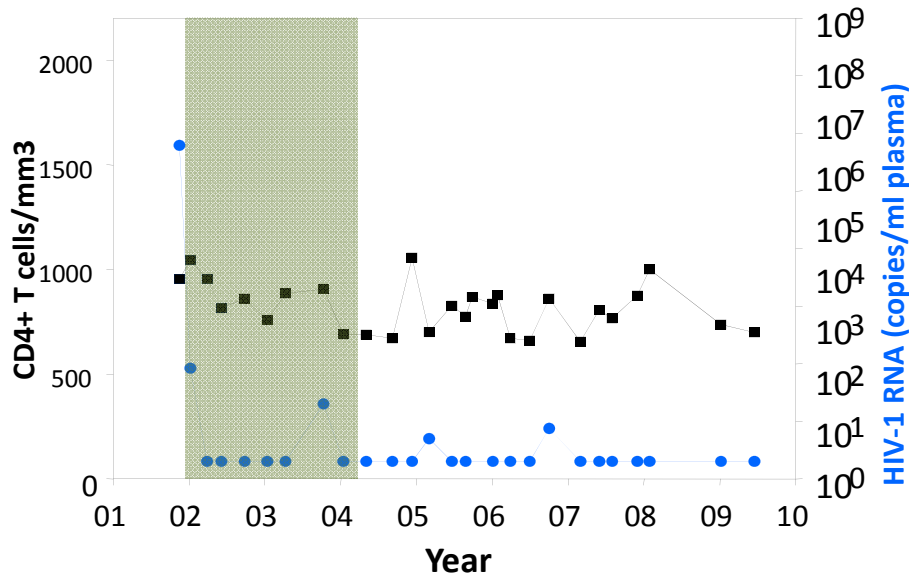
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HIV remission: examples are available



HIV remission should allow patients to durably discontinue therapeutic intervention, without (i) developing HIV-associated morbidities, (ii) showing decline of clinical parameters or progression to disease, (iii) while maintaining viremia at the lowest levels to avoid enhancing risk of transmission of infection.

Post-treatment controllers (PTC)

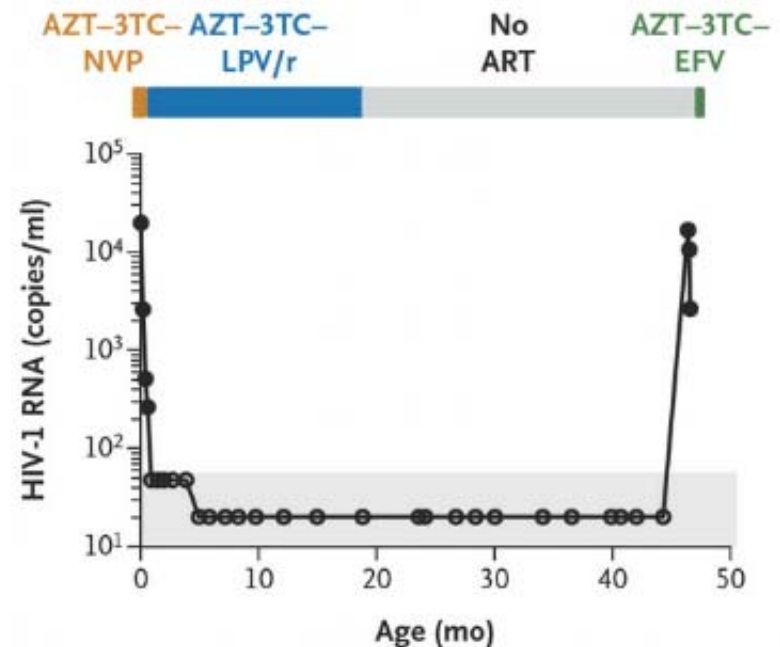


ANRS VISCONTI. 14 patients

Therapy started within 10 weeks following Primary Infection (median 39 days p.i.)

Saez-Cirion et al PLoS Path 2013

Mississippi Baby

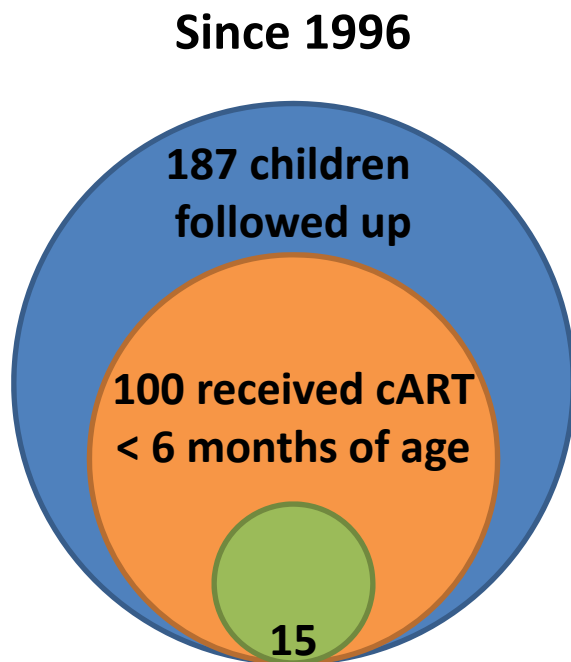


Therapy started within hours of birth

Persaud et al NEJM 2015

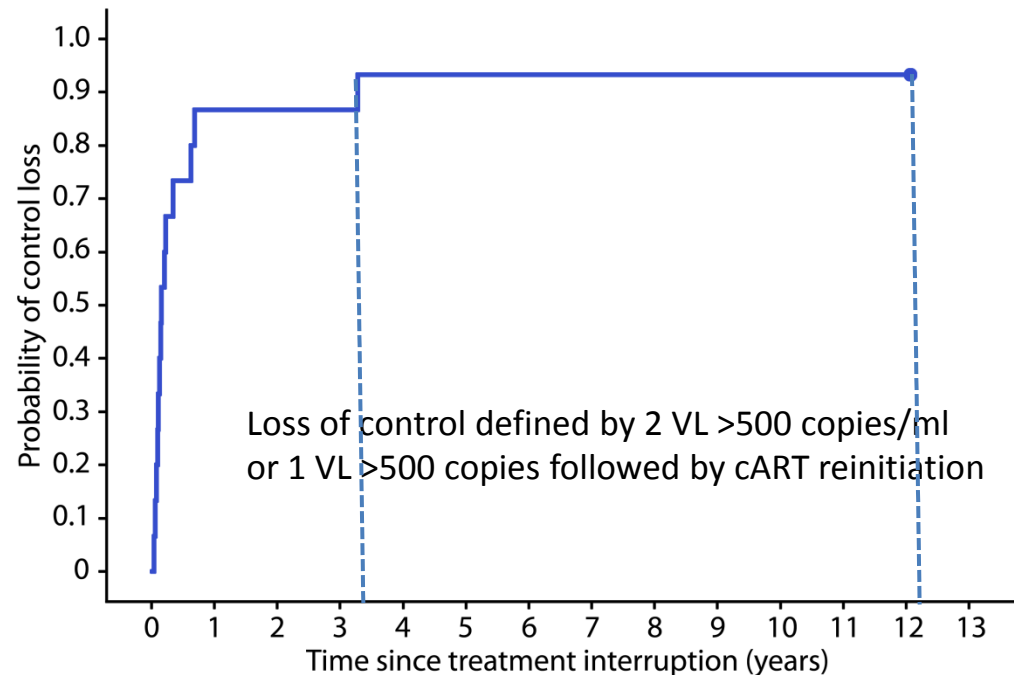
ANRS CO10 EPF paediatric cohort of HIV-1 infected children

One of the oldest ANRS cohorts. Monitoring over 10000 mother-infant couples
Since 1986: inclusion and follow up since birth of 579 HIV-1 infected children



15 interrupted treatment while their VL < 500 copies

Duration on cART before interruption:
33 months IQR [24-74]



Probability to still control infection 2 years after treatment interruption: 0.13 [0.02 - 0.35]

13 patients lost control before 12 months
1 patient controlled for >3 years
1 patient still controls infection (>12 years)

A paediatric case of durable remission of HIV-1 infection

Delivery at 37 weeks + 5 days of gestation

At delivery, the mother:

- treated with zalcitabine (ddC) (since 13 weeks of gestation)
- Plasma VL: 4.63×10^6 HIV-1 RNA copies/mL
- CD4+ T-cell count: $81/\text{mm}^3$
- CD4/CD8 ratio = 0.16

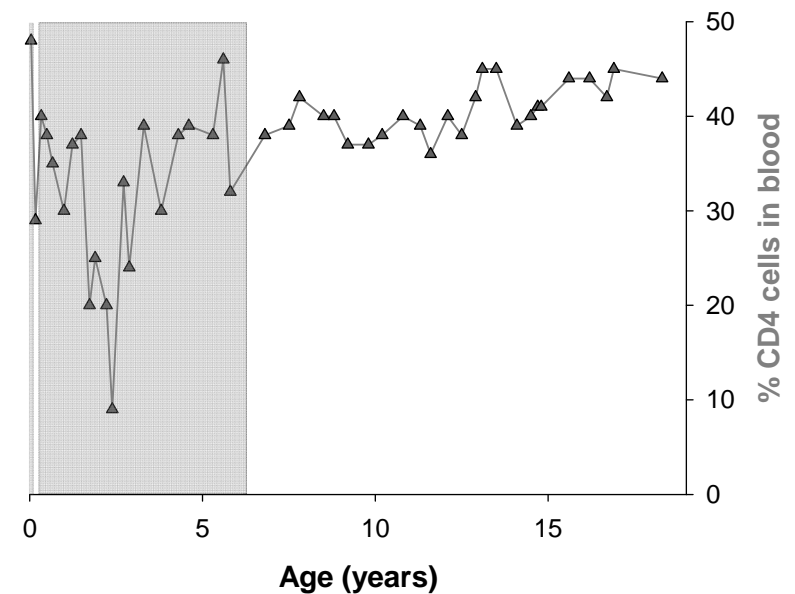
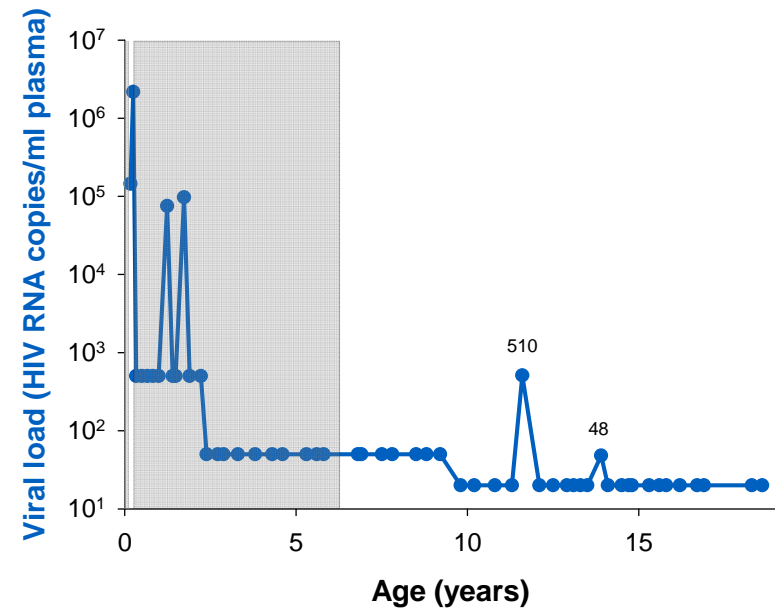
The baby:

- ZDV prophylactic treatment started at birth
- RNA viral load undetectable at day 3
- DNA viral load undetectable at days 3 and 14, detected at week 4.

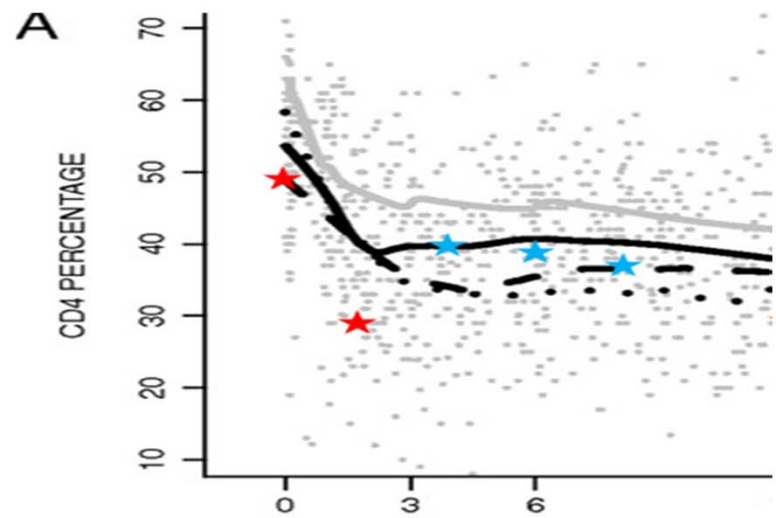
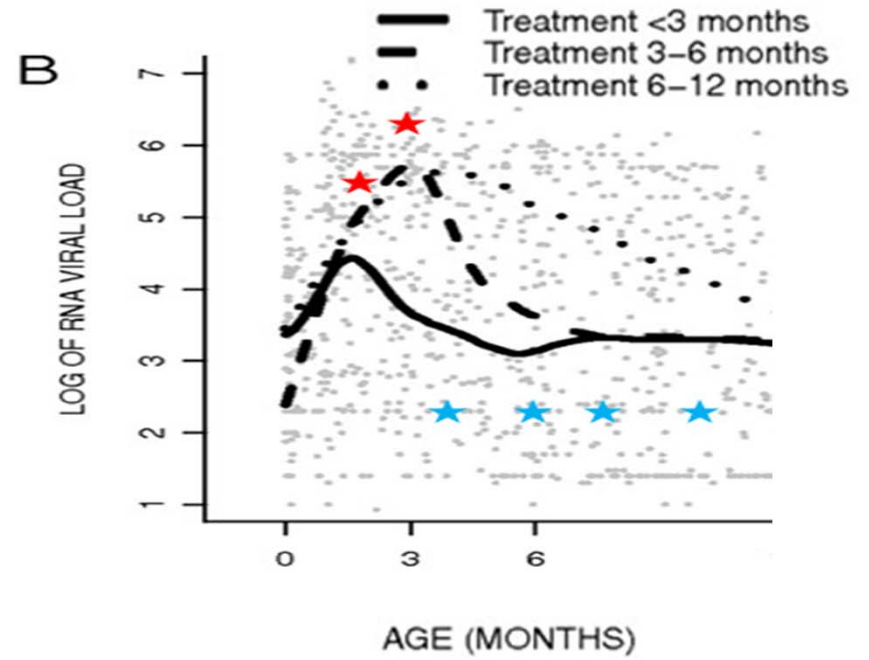
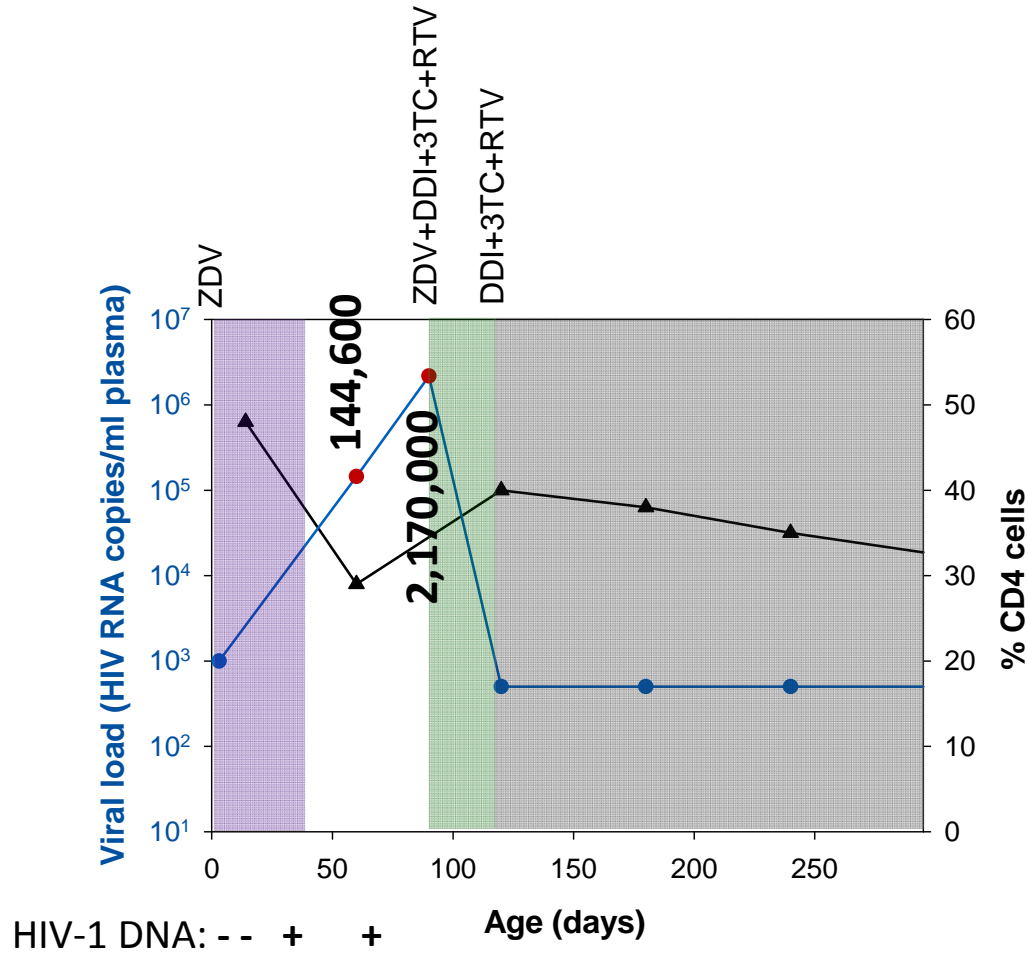
-ZDV interrupted at week 6.

-VL increased sharply : 2.17×10^6 HIV-1 RNA copies/mL at month 3 → initiation of cART (ZDV, ddi, 3TC, RTV)

-Loss for follow up between 5.8 and 6.8y, VL undetectable when she returns despite treatment interrupted a few months earlier

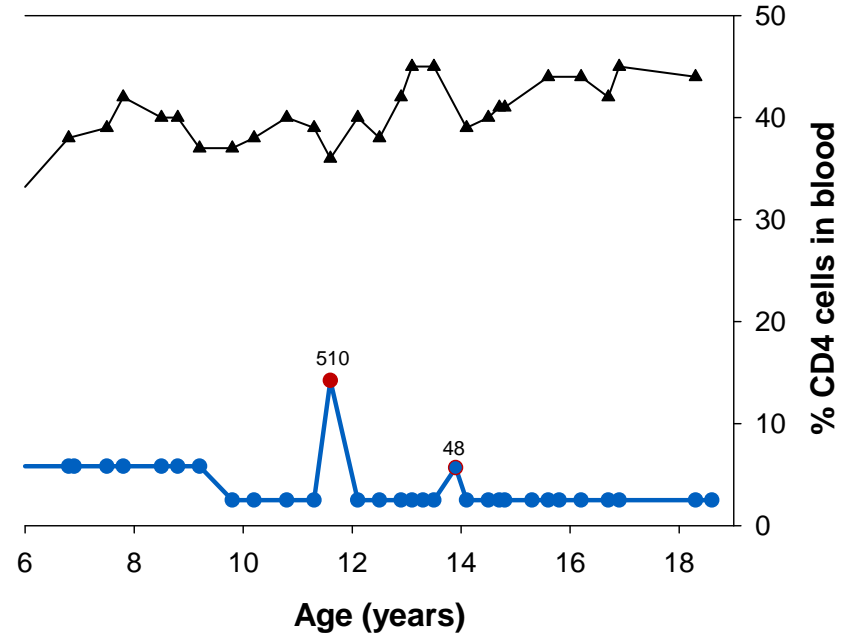
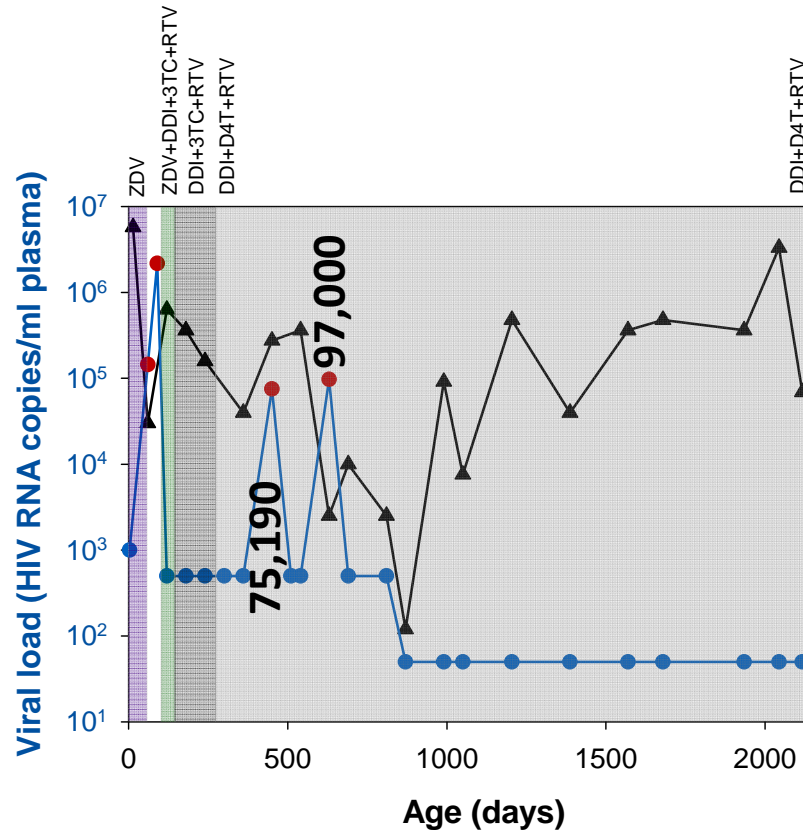


Focus on the Early phase of infection



Adapted from Dolfus et al CID 2010

Complete follow up

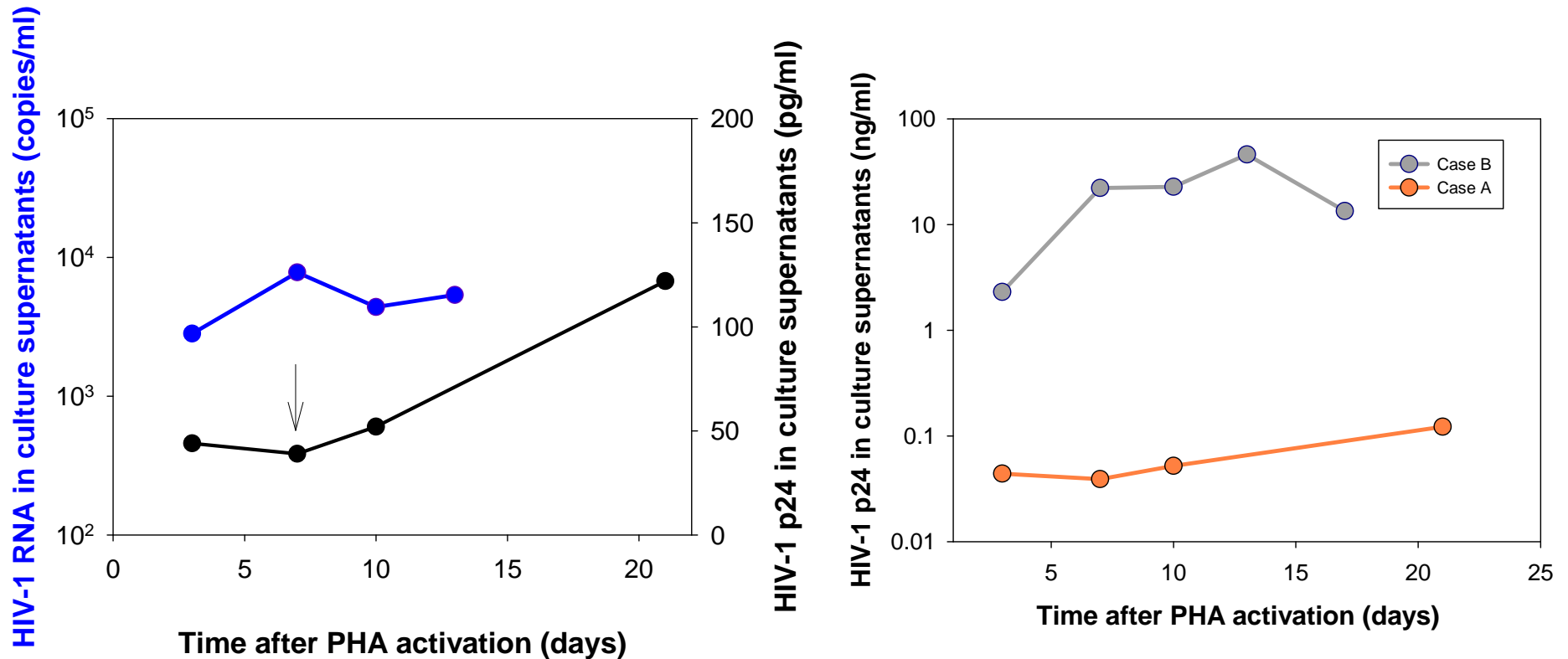


HIV-1 RNA: <9 copies/ml of plasma 2013
 <4 copies/ml of plasma 2014
 <7 copies/ml of plasma 2015

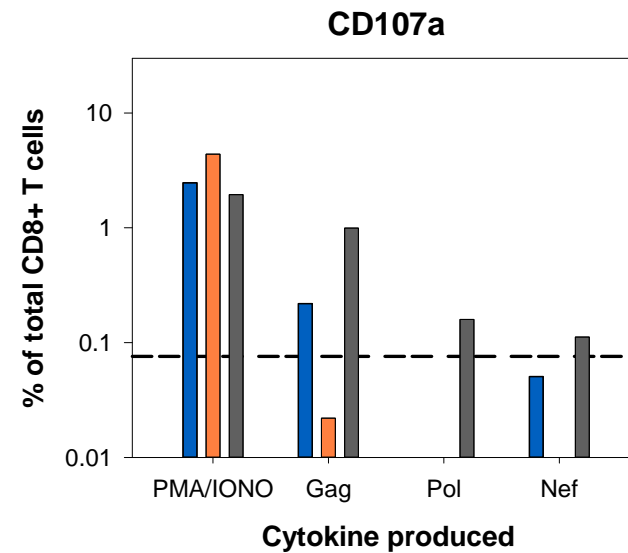
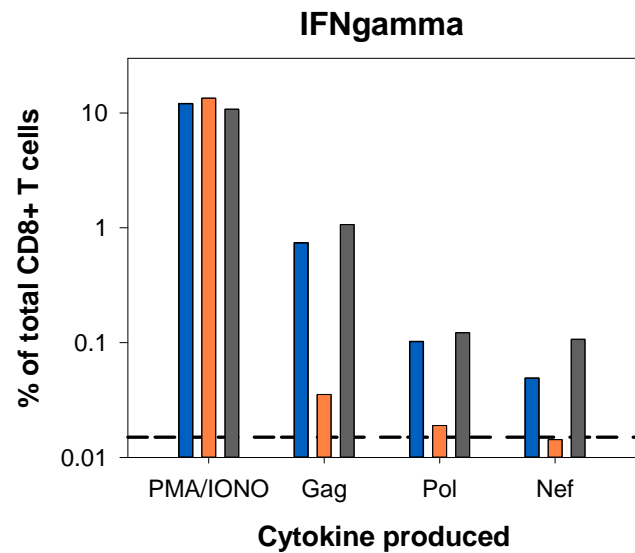
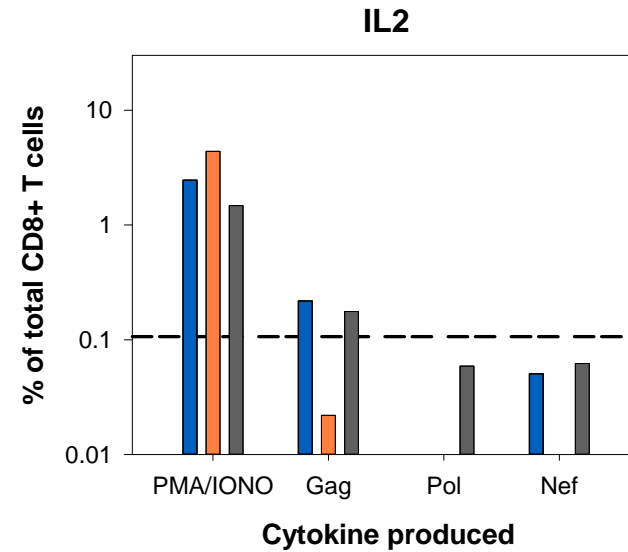
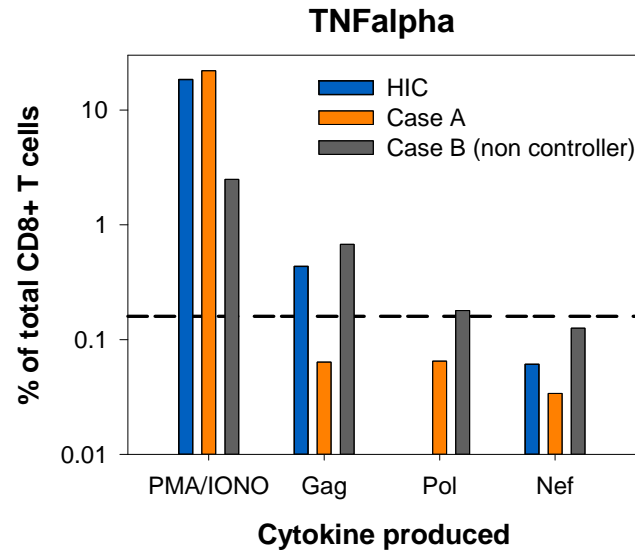
HIV-1 DNA: 2.1-2.5 log copies/ 10^6 PBMC between 2013-2015

2015 negative antiretrovirals in plasma
 (by liquid chromatography coupled with tandem mass spectrometry)

Detection of low levels of replicating virus after in vitro stimulation of purified CD4+ T cells

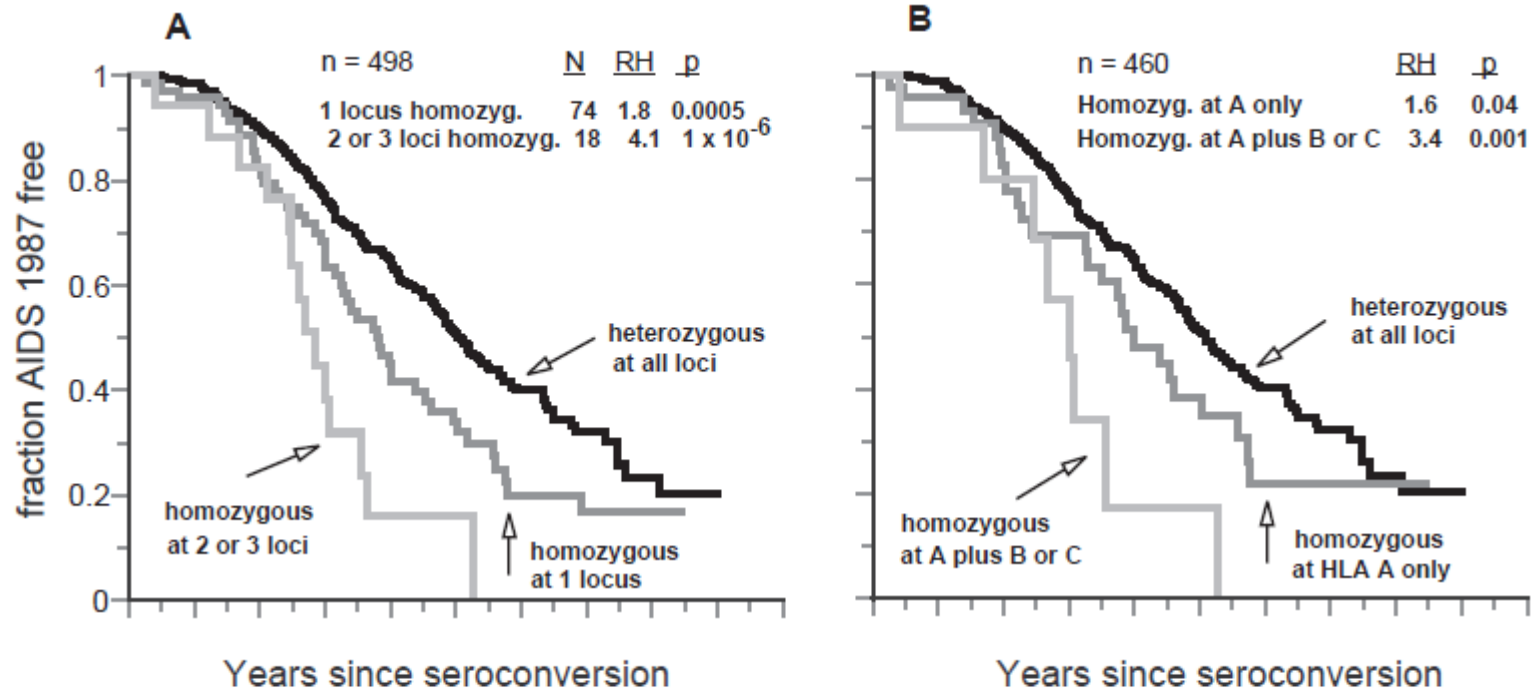


Weak HIV-specific T cell responses during period of control



HLA background not favourable for control of infection

HLA A	HLA B	HLA C	HLA DRB1	HLA DQB1
2301	1503	0201	1101	0602
-	4101	0802	-	-



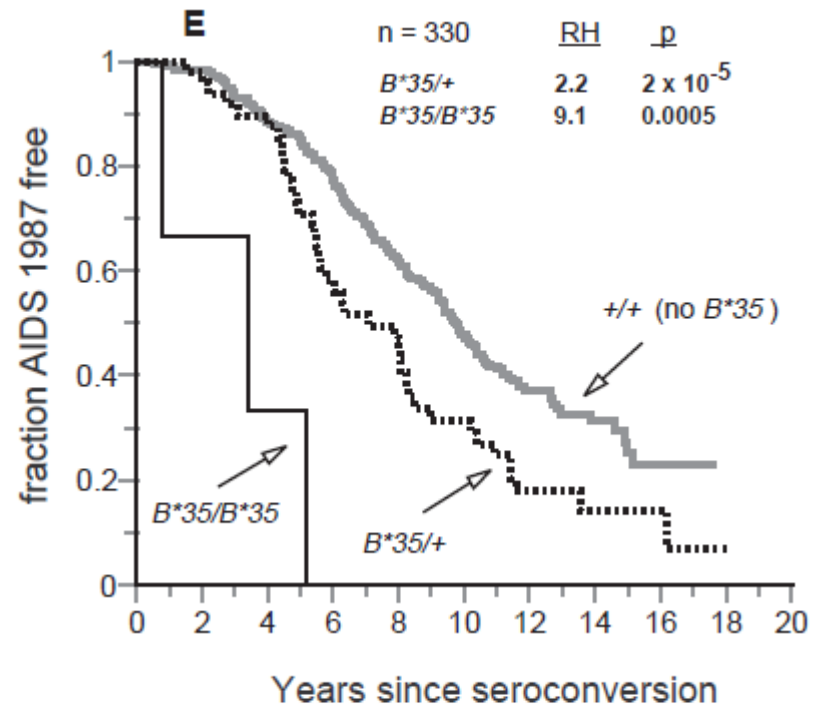
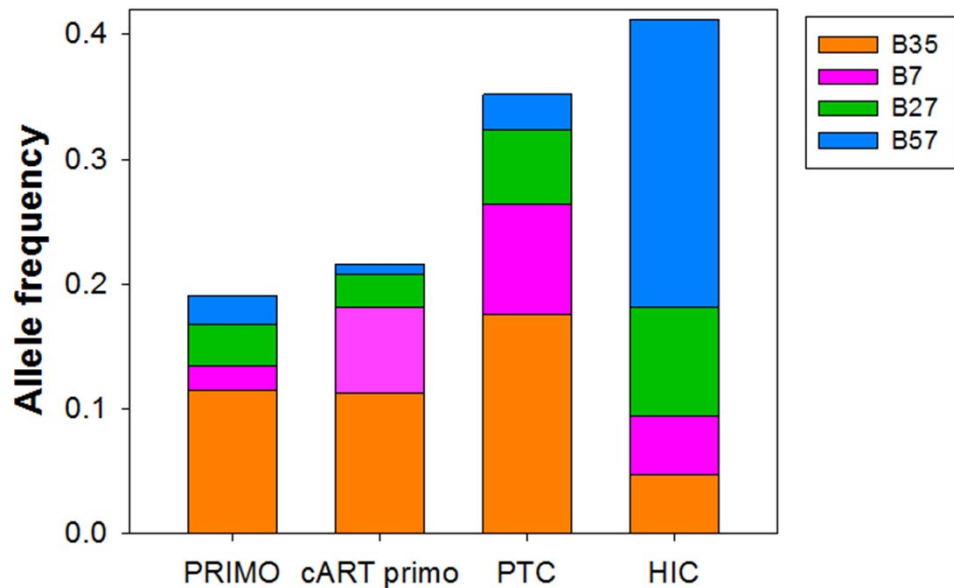
Carrington et al Science 1999

Non-favourable HLAs are also found in adults in remission of HIV-1 infection

Helene Mens, Hillerød Hospital, Denmark

C09 PHI 08-96 Rx [08-96 → 4-98]
 C21 PHI 01-99 Rx [01-99 → to 03-01]
 C25 PHI 05-00 Rx [08-00 → 08-04]

HLA*A	HLA*A	HLA*B	HLA*B	HLA*C	HLA*C
0201	-	4002	-	0202	-
0101	0201	3501	-	0401	-
02	-	07	27	01	07



Carrington et al Science 1999

Conclusions

Long-term (>12 years) virological remission of HIV-1 infection has been observed in a perinatally-infected girl

HIV-1 remission occurred after interruption of antiretroviral treatment initiated early after birth

During her early life the absence of efficient antiretroviral treatment was accompanied by rebound of viremia

HIV-1 DNA is consistently detected in circulating CD4+ T cells and some viral replication can be induced in vitro, however viremia is undetectable (<4 copies in some analysis)

Similarly to what has been observed in the adults in the ANRS VISCONTI study, this girl does not have favourable HLA background

Understanding the ability to durably contain HIV replication may guide new strategies towards HIV remission

Acknowledgements

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Institut Pasteur



HIPer
HIV, Inflammation
and Persistence

HIV inflammation and persistence
Michaela Müller-Trutwin

Mechanisms of control of HIV/SIV infection



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ANRS CO10

EPF Paediatric cohort



**ANRS
iVISCANTI**



**ANRS CO21
CODEX**



**ANRS CO6
"PRIMO"**