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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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-enfant couples
Since 1986: inclusion and follow up since birth of 579 HIV-1 infected children

Since 1996

187 children followed up

100 received cART < 6 months of age

15 interrupted treatment while their VL<500 copies

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

Loss of control defined by 2 VL >500 copies/ml or 1 VL >500 copies followed by cART reinitiation

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: $4.63 \times 10^6$ HIV-1 RNA copies/mL
- CD4+ T-cell count: 81/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: $2.17 \times 10^6$ HIV-1 RNA copies/mL at month 3 $\Rightarrow$ 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

Time after PHA activation (days)

HIV-1 RNA in culture supernatants (copies/ml)

0 5 10 15 20

0 10 20 30 40 50

HIV-1 p24 in culture supernatants (pg/ml)

0 50 100 150 200

Time after PHA activation (days)

HIV-1 p24 in culture supernatants (ng/ml)

0.01 0.1 1 10 100

0 5 10 15 20 25

Case B

Case A
Weak HIV-specific T cell responses during period of control

**TNFalpha**

- Case A
- Case B (non controller)

**IL2**

- HIC

**IFN gamma**

**CD107a**
**HLA background not favourable for control of infection**

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<th>HLA A</th>
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<th>HLA C</th>
<th>HLA DRB1</th>
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*Graphs showing survival data for seroconversion*:

- **Graph A** (n = 498):
  - 1 locus homozygous: 74, RH 1.8, p = 0.0005
  - 2 or 3 loci homozygous: 18, RH 4.1, p = 1 x 10^-6

- **Graph B** (n = 460):
  - Homozygous at A only: 1.6, RH = 0.04
  - Homozygous at A plus B or C: 3.4, RH = 0.001

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Carrington et al. Science 1999
Non-favourable HLAs are also found in adults in remission of HIV-1 infection
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
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