

# Effects of Treatment During Acute HIV Infection on HIV Persistence

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*On behalf of the RV254/SEARCH010 Study Group*



*The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.*



# Outline

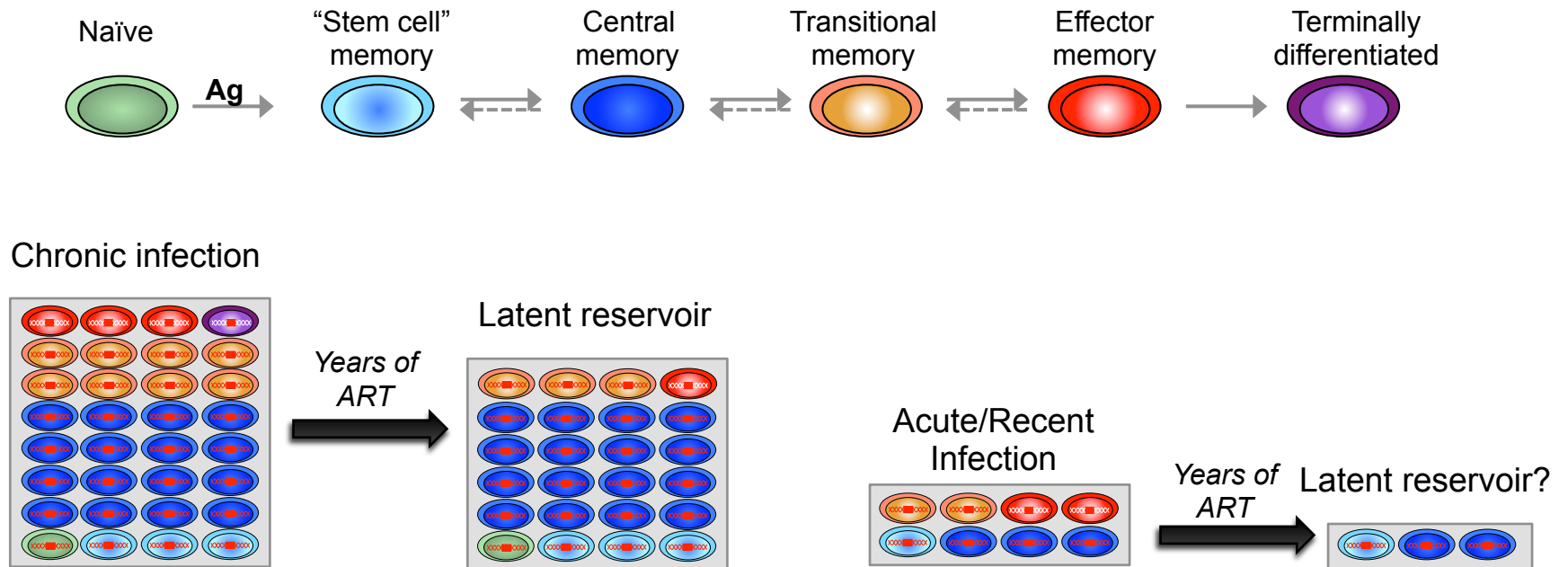
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- Recent published studies and the RV254/SEARCH 010 study
  - How does early ART affect HIV persistence?
  - Are there preferred regimens for early ART?
  - How does early ART affect viremic control after treatment interruption?
  
- Research gaps
  - Finding acutes
  - Finding biomarkers for HIV remission

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How does early ART affect  
HIV persistence?

# Early ART affects the size and composition of the latent HIV reservoir



## Lower levels of cell-associated HIV DNA with early ART

| Studies               | N   | ART onset   | ART duration  | Outcomes  |
|-----------------------|-----|-------------|---------------|---|
| Laanani M, CID 2015   | 327 | Median 41 d | Median 2.3 yr | <ul style="list-style-type: none"> <li>Continued decay of DNA with early ART</li> <li>Faster initial decay when ART started by 3 mo post infection</li> </ul> |
| Jain V, JID 2013      | 34  | < 6 mo      | Unk           | <ul style="list-style-type: none"> <li>5-times lower DNA in early vs. late ART</li> </ul>   |
| Gianella S, AVT 2011  | 32  | < 2 mo      | Median 18 mo  | <ul style="list-style-type: none"> <li>0.4 log lower DNA in early vs. late ART</li> </ul>   |
| Koelsch KK, AIDS 2011 | 8   | < 4-6 wk    | 1 yr          | <ul style="list-style-type: none"> <li>Lower DNA in PBMCs and colon with early ART</li> </ul>   |

## Early ART restricts frequency of replication competent virus in resting CD<sub>4</sub>

| Studies              | N  | ART onset | ART time | Outcomes  |
|----------------------|----|-----------|----------|---|
| Archin NM, PNAS 2014 | 27 | <45 d     | > 6 mo   | <ul style="list-style-type: none"> <li>• Early ART restricts RCV</li> <li>• Little RCV is generated after ART initiation</li> </ul> |
| Buzon MJ, JV 2014    | 9  | <6 mo     | > 10 yr  | <ul style="list-style-type: none"> <li>• Lower RCV in early vs. late ART</li> </ul>   |
| Strain MC, JID 2005  | 27 | < 6 mo    | > 1 yr   | <ul style="list-style-type: none"> <li>• Lower RCV in early vs. late ART</li> </ul>   |

RCV: replication competent virus

# Early ART in Thai Adults: RV254/SEARCH010 Study

Real time screening of ~ 130,000 samples at  
Thai Red Cross Anonymous Clinic

2 days



Enrollment (n= 260)

1 day



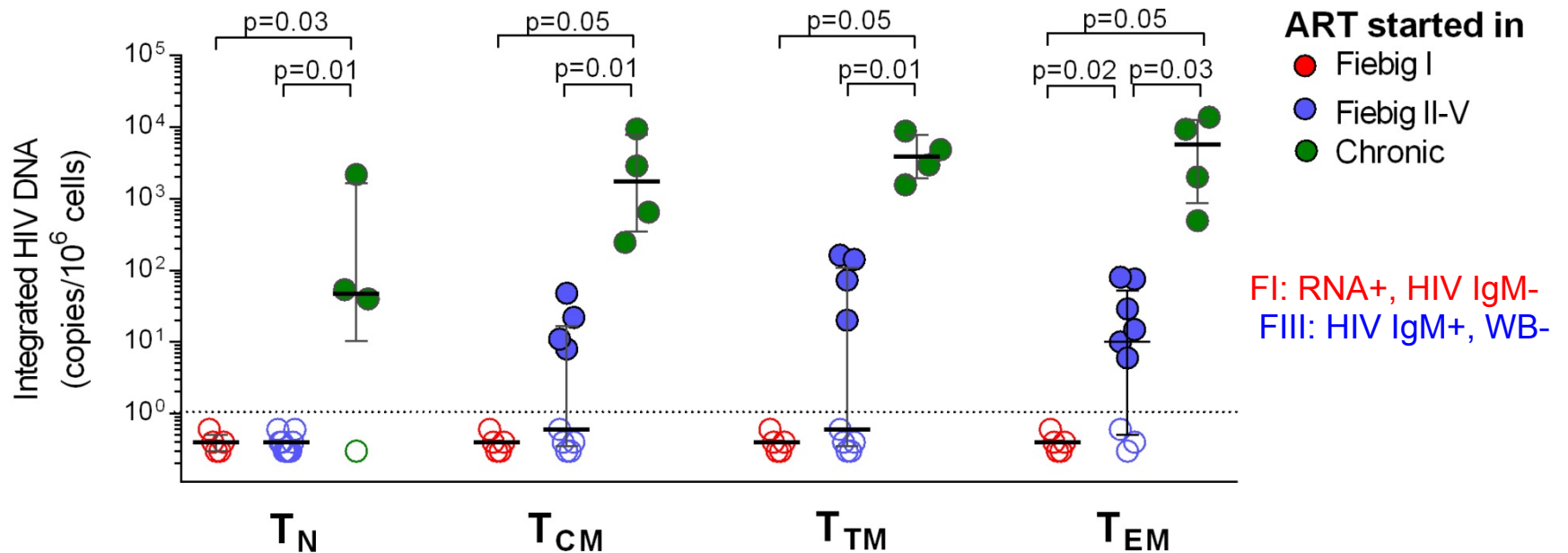
Early ART

## Optional procedures

Sigmoid biopsy  
Lymph node biopsy  
Lumbar puncture  
MRI/MRS  
Genital secretion collection

| Characteristics              | Values  |
|------------------------------|---------|
| Median duration of infection | 18 days |
| Fiebig I/II (< 2-3 weeks)    | 51%     |

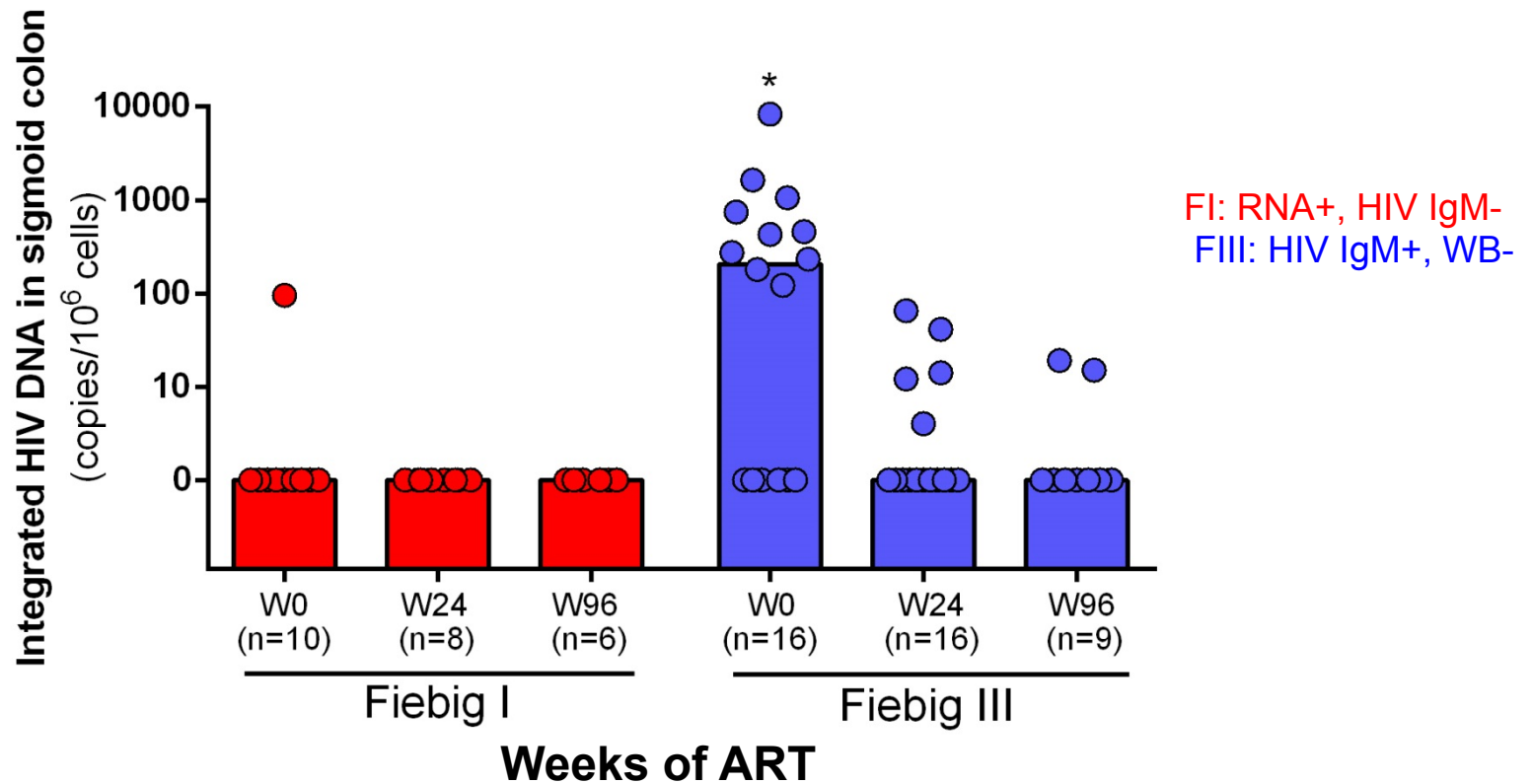
# Early ART limits persistence of HIV reservoir in all CD4+ T cell subsets



After 2 years of ART, integrated HIV DNA is undetectable in all subsets of Fiebig I individuals.



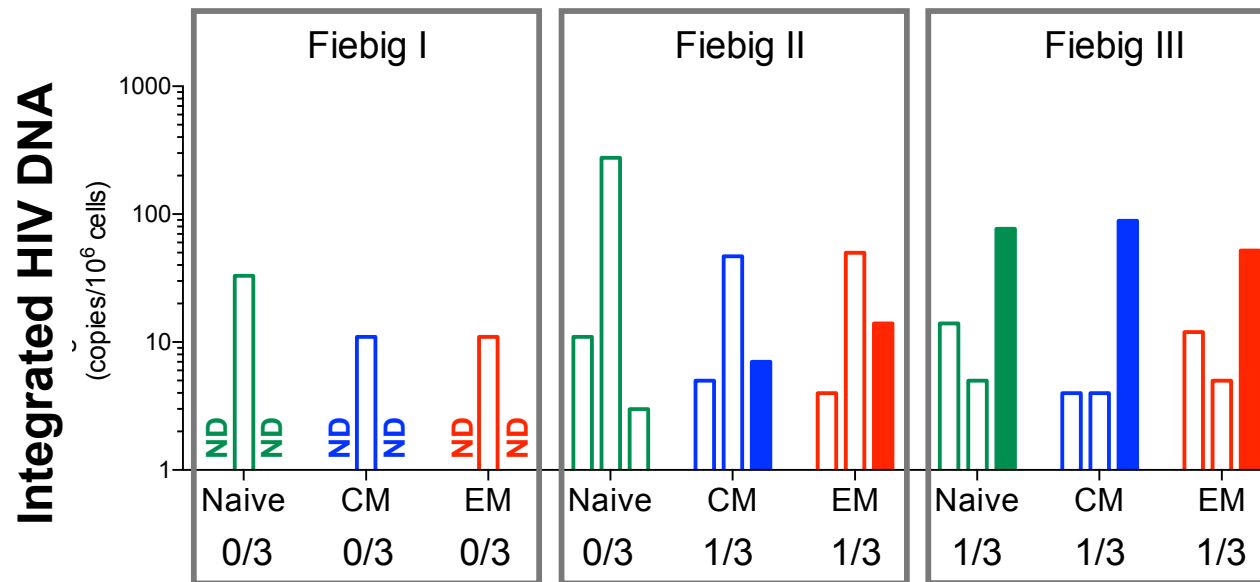
# Decay in integrated HIV DNA in the sigmoid colon after ART



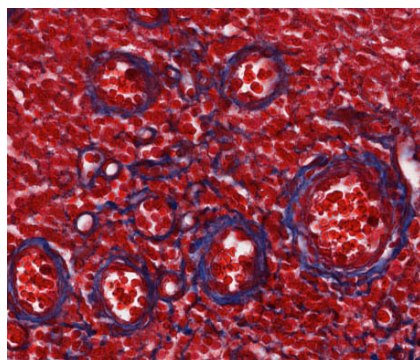
Integrated HIV DNA vanishes quickly in the sigmoid colon of both Fiebig I- and III-treated subjects.

# Low integrated HIV DNA in lymph node after 6-24 months of ART

All on ART



ND = not done; total HIV DNA not detected



Fiebig I  
13%

Collagen deposition

Fiebig III  
25%

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Are there preferred regimens  
for early ART?

# Randomized study of 3 vs. 5 drugs for acute/recent HIV infection

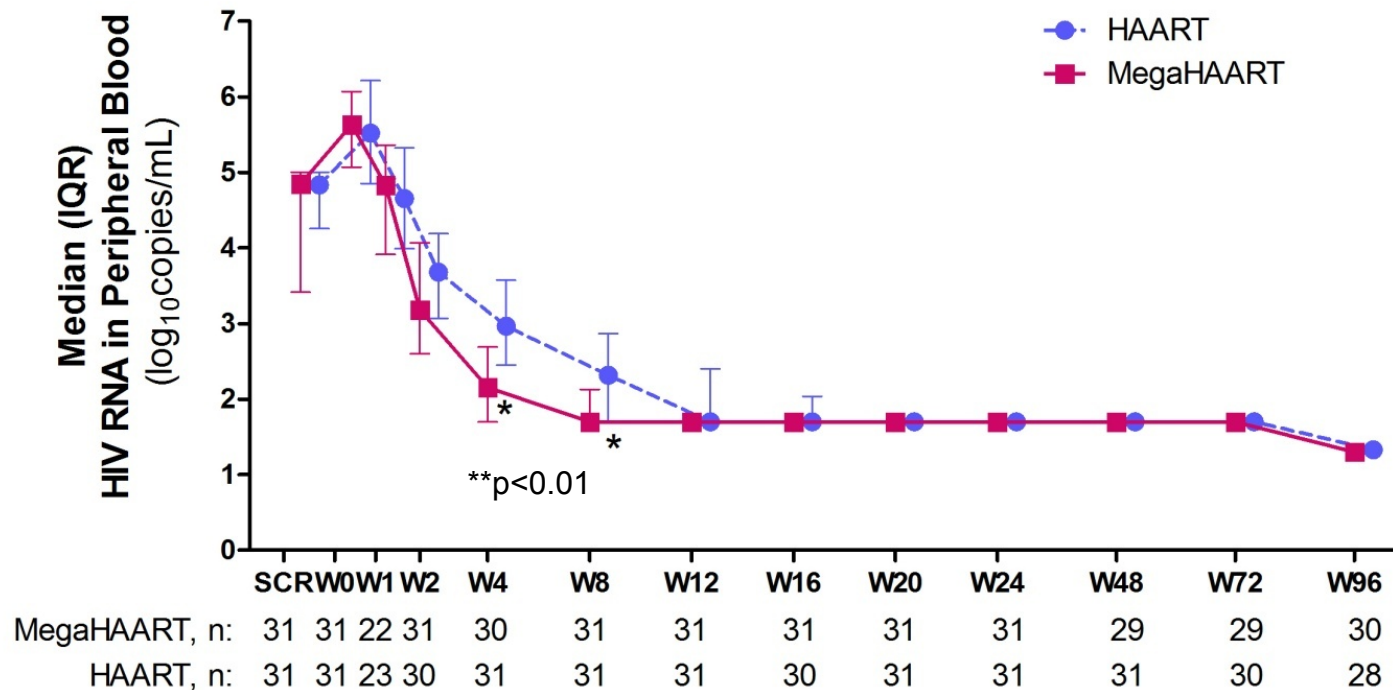
3-drug: TDF + FTC + DRV/r  
5-drug: TDF + FTC + DRV/r + RAL + MVC

- **Markowitz M**  
(JAIDS 2014)
  - 40 enrolled
  - < 4 week HIV onset in most
  - 96-week follow up
  - No differences for
    - HIV RNA (3 copies/ml)
      - 3 VF in 5-drug arm
    - Cell-associated HIV DNA (2.9 log/10<sup>6</sup> CD4)
    - Change in cell-associated HIV RNA
    - Infectious virus in resting CD4+ T cells
    - CD4 and subsets
    - sCD14
- **OPTIPRIM-ANRS147**  
(Cheret A, Lancet ID 2015)
  - 90 enrolled
  - Median 35 days from HIV onset
  - 96-week follow up
  - No differences for
    - HIV RNA
      - But poorer adherence and more VF with 5-drug
    - Cell-associated HIV DNA (2.8 log/10<sup>6</sup> CD4)
    - CD4
      - But lower CD4/CD8 ratio with 5-drug (1.06 vs. 1.24, p=0.04)

# HIV RNA decline faster with MegaHAART

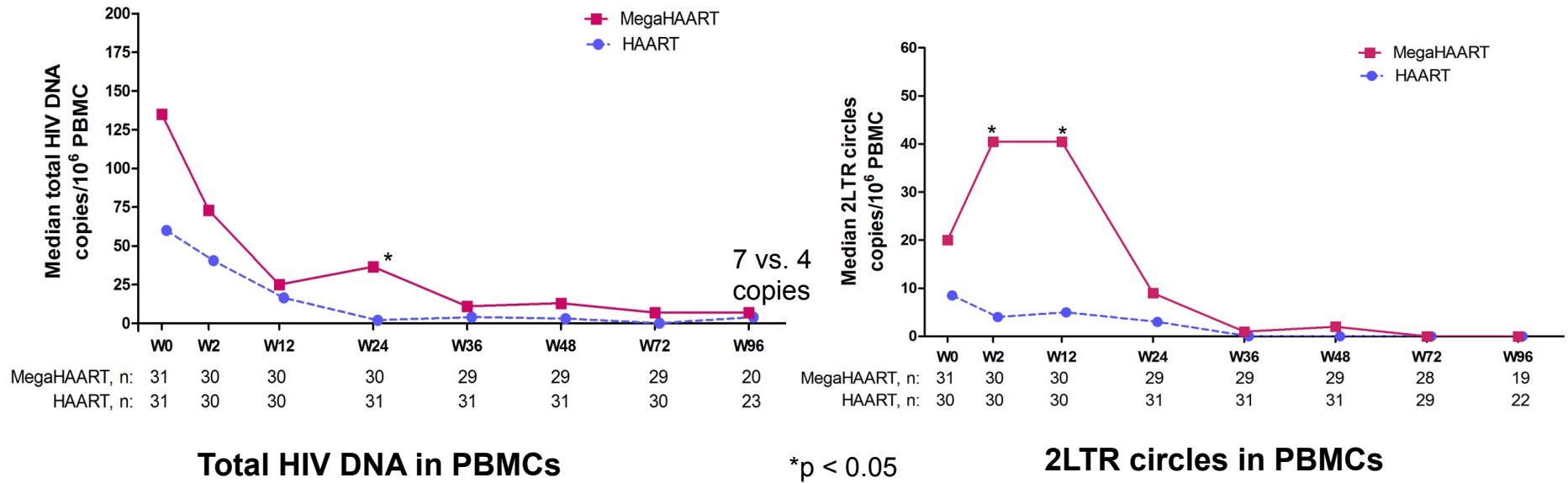
HAART: TDF + FTC + EFV

MegaHAART: Intensified with RAL and MVC for the first 24 weeks



Median time to HIV RNA < 50 copies/ml  
HAART **83** days vs. megaHAART **55** days (p = 0.04)

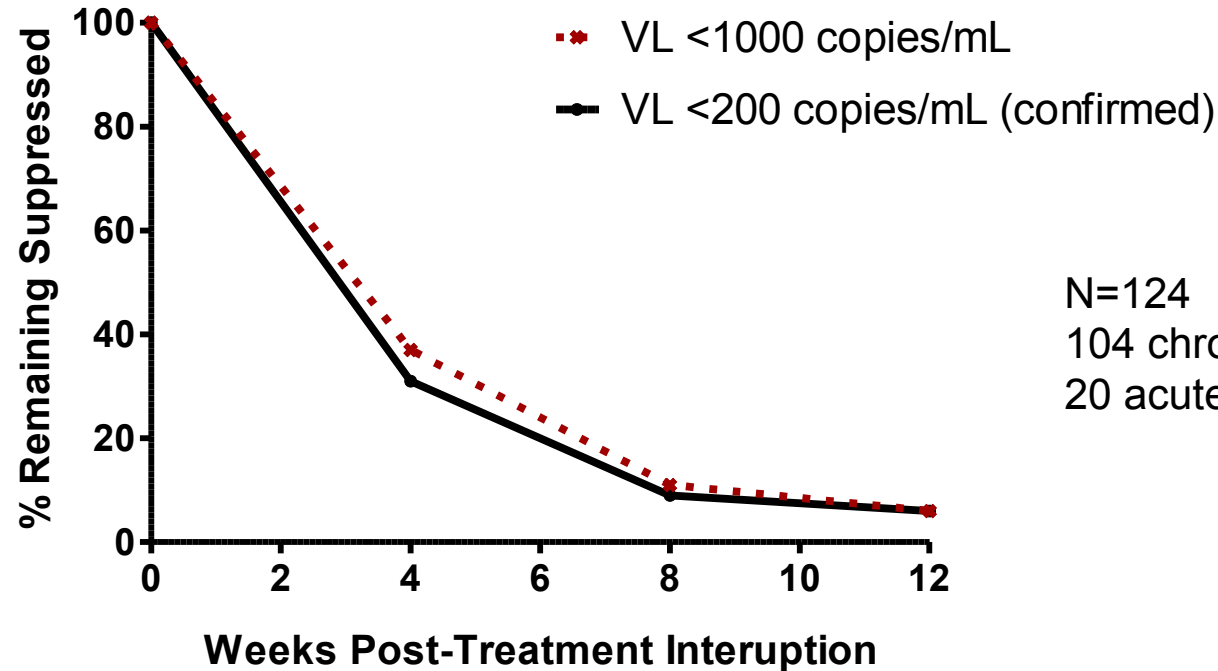
# No differences in total HIV DNA but higher 2LTR circles with MegaHAART



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How does early ART affect viremic control after treatment interruption?

# Loss of HIV Suppression post-ATI (ACTG)



N=124  
 104 chronic HIV  
 20 acute HIV

% Virologically suppressed to

|                  |     |     |    |
|------------------|-----|-----|----|
| <1000 copies/mL: | 37% | 11% | 6% |
| <200 copies/mL:  | 31% | 9%  | 6% |

VL < 200 at week 12  
 13% in acute  
 3% in chronic



## SPARTAC

About 1 in 10 early treated individuals remained virally suppressed at 1 year after interruption

| <b>VL &lt; 400 after interruption</b> | <b>3 months</b> | <b>12 months</b> | <b>24 months</b> |
|---------------------------------------|-----------------|------------------|------------------|
| Total                                 | 26%             | 9%               | 4%               |
| ART 48 wks                            | 32%             | 14%              | 5%               |
| ART 12 wks                            | 21%             | 4%               | 4%               |

## Post Treatment Controllers after early ART

| Published Studies  | Viremic control  |
|--|--|
| <b>Optiprim</b> (n=90)<br>(Cheret A, Lancet ID 2015)                         | 2 of 90 ( <b>2%</b> ) had VL < 50 at 2 years             |
| <b>Spartac</b> (n=165)<br>(Stohr W, Plos One 2013)                           | 4 of 165 ( <b>2%</b> ) had VL < 400 at 3 years           |
| <b>VISCONTI</b> (n=14)<br>Saez-Cirion A, Plos Pathogens 2013)                | <b>15%</b> had VL < 50 for > 6 years                     |
| <b>Swiss HIV Cohort Study</b> (n=32)<br>(Gianella S, Antiviral Therapy 2011) | 3 of 32 ( <b>9%</b> ) had VL < 50 at 1 year              |
| <b>Primo-SHM</b> (n=173)<br>(Grijzen ML, PLoS Medicine 2012)                 | 4 of 79 ( <b>5%</b> ) had VL < 100 at wk 24              |
| <b>ANRS CO6 PRIMO</b> (n=164)<br>(Goujard C, Antiviral Ther 2012)            | VL < 50 in <b>11%</b> at 1 year, <b>8.5%</b> at 2 years  |
| <b>CASCADE</b> (n=259)<br>(Lodi S, Arch Intern Med 2012)                     | VL < 50 in <b>8.2%</b> at 1 year, <b>5.5%</b> at 2 years |

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# Research Gaps

“Finding Acutes”

# Edutainment online/offline platform for engaging young MSM into HIV testing and care

[Become a Member SIGN UP HERE](#)

[www.adamslove.org](http://www.adamslove.org)

**ADAM'S LOVE**  
 for Men who love Men

**Thailand's Official MSM Health Website**  
 มีคำขอความช่วยเหลือ (Need Support) | ต้องการคำปรึกษา สุขภาพ... (Need to Talk?) | E-mail Subscription  Google

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 จุดตรวจใกล้บ้านคุณ  
 HIV/STI Testing Site Near You

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- **AdamsLove Webboard**  
Adams Love webboard offers online assistance and support for all your HIV and STI related
- **The Making of We Deserve It Campaign**  
The Making of Adams Love We Deserve It Campaign featuring

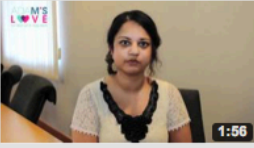
‘เราอยากรู้จักคุณมากขึ้น’  
 Click here

# Comprehensive HIV/AIDS & STI Awareness

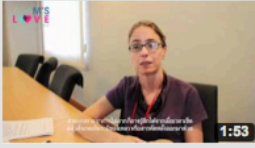
HIV/STI transmission, prevention, treatment, and MSM sexual health advise videos

AdamsLoveThailand's channel Subscribed 162 162 subscribers 251,588 video views

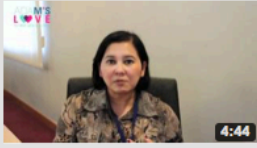
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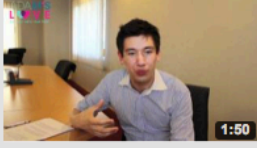
**"My Name is Ery"**  
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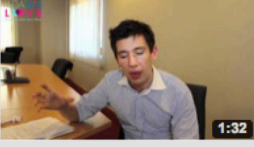
**Interview with Prof Dr Tuti Parwati Me**  
185 views | 11 months ago



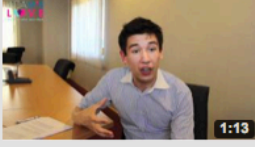
**NAT Test at Anonymous Clinic**  
1,616 views | 11 months ago



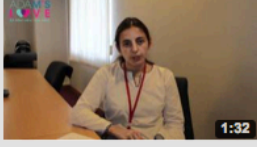
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## Web board

### NAT Testing during the Course of PEP

After reading the webboard message, <http://www.adamslove.org/gallery.php?mid=86> I am wondering whether the test results of a NAT test can be false negative if tested while taking a course of "emergency anti-viral medication (PEP)". I was tested 16 days after taking PEP and was informed that I could be 100% confident in the results. How confident can I be that PEP will work? Please explain this to me again. I am stressed out.

by



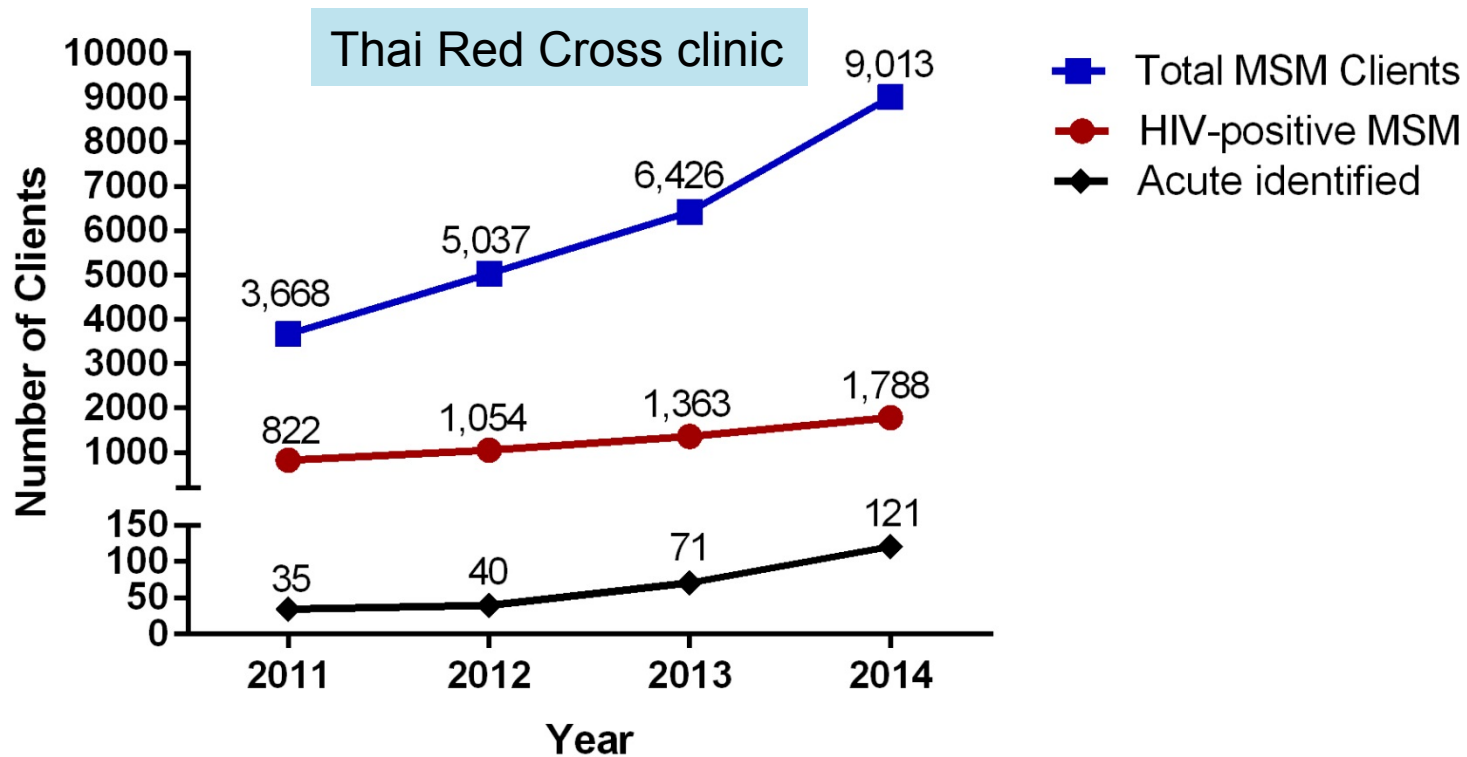
Celebrity gets HIV testing



Club card member and partner for couple HIV testing

# AdamsLove Impact

- 1.7 million visitors with 8 million page views
  - Thailand, USA, UK are top visiting countries



Temannya.org in Indonesia and Malaysia  
Adamslove.org in Taiwan and South Korea

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## Research Gaps

“Finding biomarkers for HIV remission”

# Biomarkers for longer time to viral load rebound after treatment interruption

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- Clinical parameters
  - Earlier ART initiation and longer duration of ART
  - High CD4 nadir
  
- Low markers of peripheral blood HIV reservoir size
  - Active reservoirs (Etemad B, CROI 2015, Abs 110LB)
    - Cell-associated HIV RNA and single copy HIV RNA
  - Cell-associated total HIV DNA (Williams JP, Elife 2014, Saez-Cirion A, Plos Pathogens 2013)
  
- Strong HIV-specific immune responses
  - Strong HIV-specific CD4+ T cell response (Frater J, AIDS 2014)
  - Low expression of PD-1, Lag-3 and Tim-3 on CD4 and CD8 T cells (Hurst J, CROI 2015, Abs 111LB)
  - Unique NK phenotype and function (Scott-Algara D, CROI 2015, Abs 52)



Low markers of  
HIV reservoir size  
in RV254

Intervention/Treatment  
Interruption

HIV  
Remission

**RV409**

Latency reversing agent+ anti-  
inflammatory + entry inhibitor

**RV411**

Treatment in Fiebig I

**RV397**

Broadly neutralizing antibody

**RV405**

Therapeutic HIV Vaccine

**RV438**

Latency reversing agent +  
broadly neutralizing antibody

Behavioral  
Research

Participants'  
decision making  
and expectation

# RV254 Acknowledgements

## Volunteers

### AFRIMS

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- Thai GPO (TDF, 3TC, EFV, LPV/r)
- Gilead (TDF, FTC, Atripla)
- Merck (EEV, RAL)
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