9. TÜRKİYE EKMUD
ULUSLARARASI BİLİMSEL PLATFORMU
20-23 Mayıs 2021 - Online Kongre -

Düşük Düzey Viremi: Anlamı, Yönetimi

9. EKMUD Kongresi 2021- HIV/AIDS kursu
-İzlemde Sorunlar-

DOÇ. DR. ULUHAN SİLİ

MARMARA ÜNİVERSİTESİ TIP FAKÜLTESİ

ENFEKSİYON HASTALIKLARI VE KLİNİK MİKROBİYOLOJİ AD

20 MAYIS 2021 14:45 – 15:15

MARMARA ÜNİVERSİTESİ 1883 | Tıp Fakültesi

ANTİRETROVİRAL TEDAVİ (ART) HEDEFİ

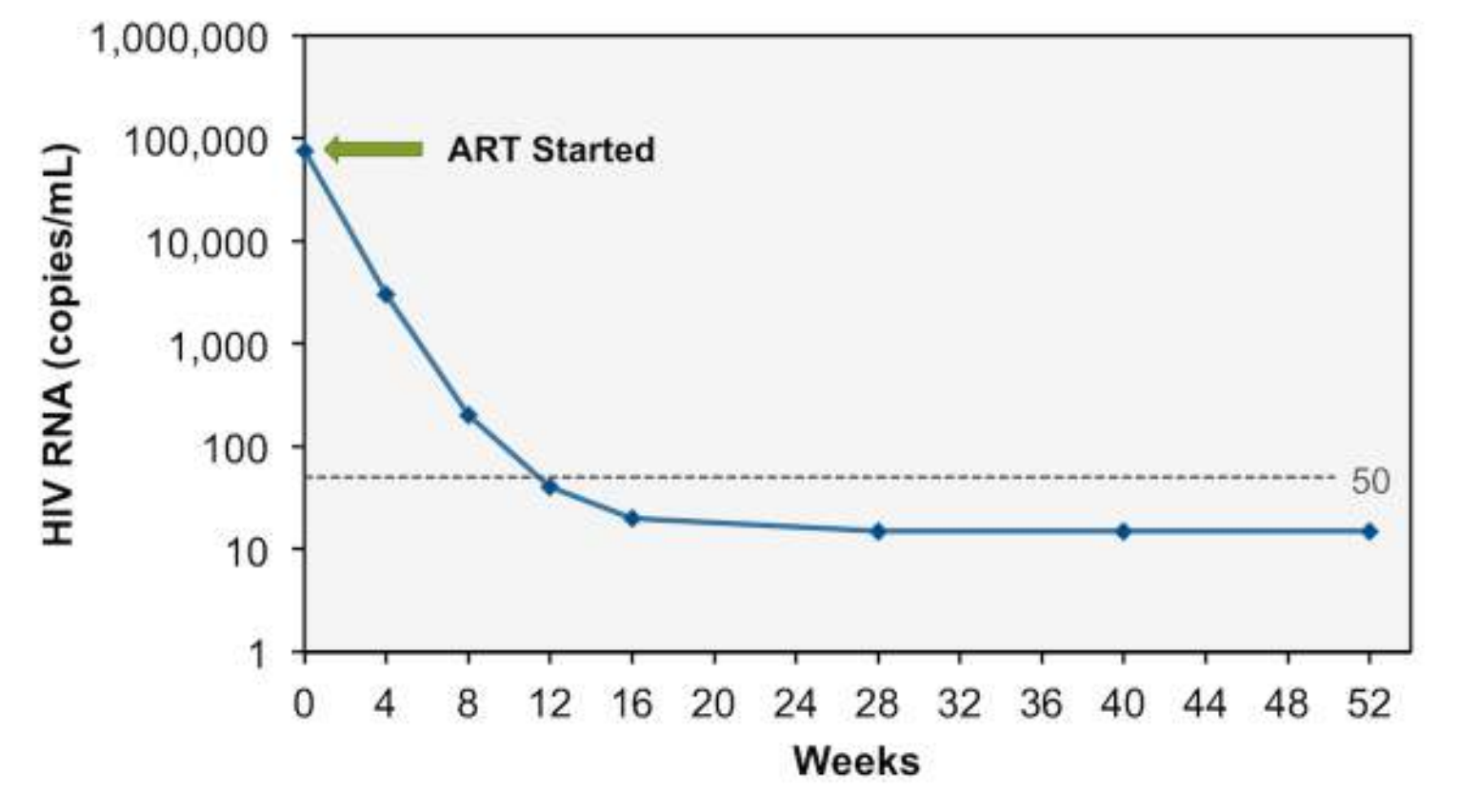
- HIV tedavisinde primer hedef azami ve kalıcı viral **baskılamayı** sağlayıp immunolojik derlenmeyi başarmak

- Virolojik hedef ➔ viral yükü saptama eşiğinin altına **indirip** orada **tutmak**
  - alt saptama eşiği (lower limit of detection)= 20 – 75 kopya/mL
  - "kesinleşmiş (conclusive)" olmasa da bu düzeyde tutulduğunda ilaca dirençli mutant **seçilmesi** beklenmiyor_*Kieffer TL et al. 2004*

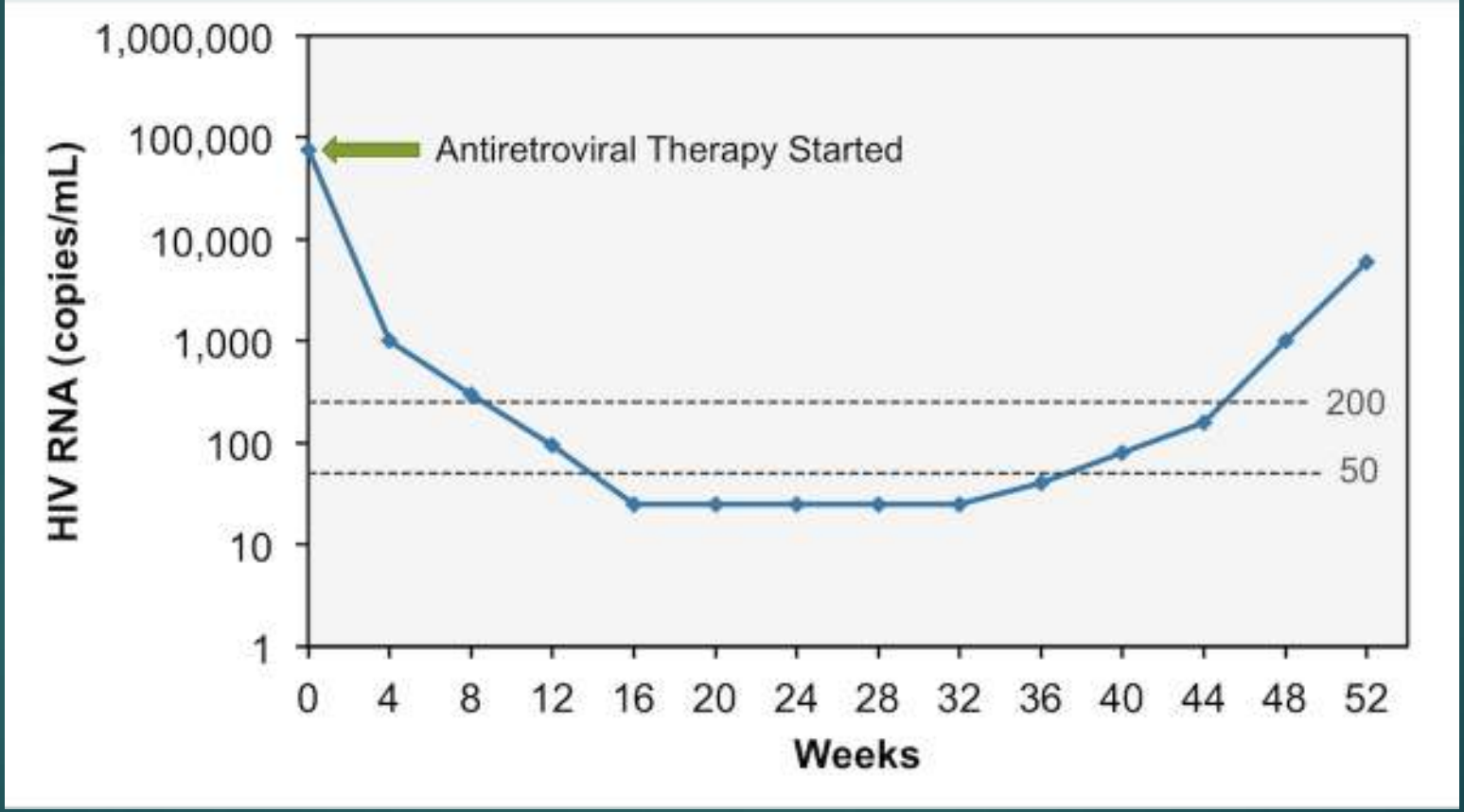
- ≥2 anti-retroviral ilaç sınıfından ≥2, tercihen 3 tam aktif ilaçla
  - (ABC/3TC veya TAF/FTC veya TDF/FTC) + (INSTI veya NNRTI veya güçlendirilmiş PI)
  - 3TC + DTG

Clinical INFO HIV.gov, 12-2019

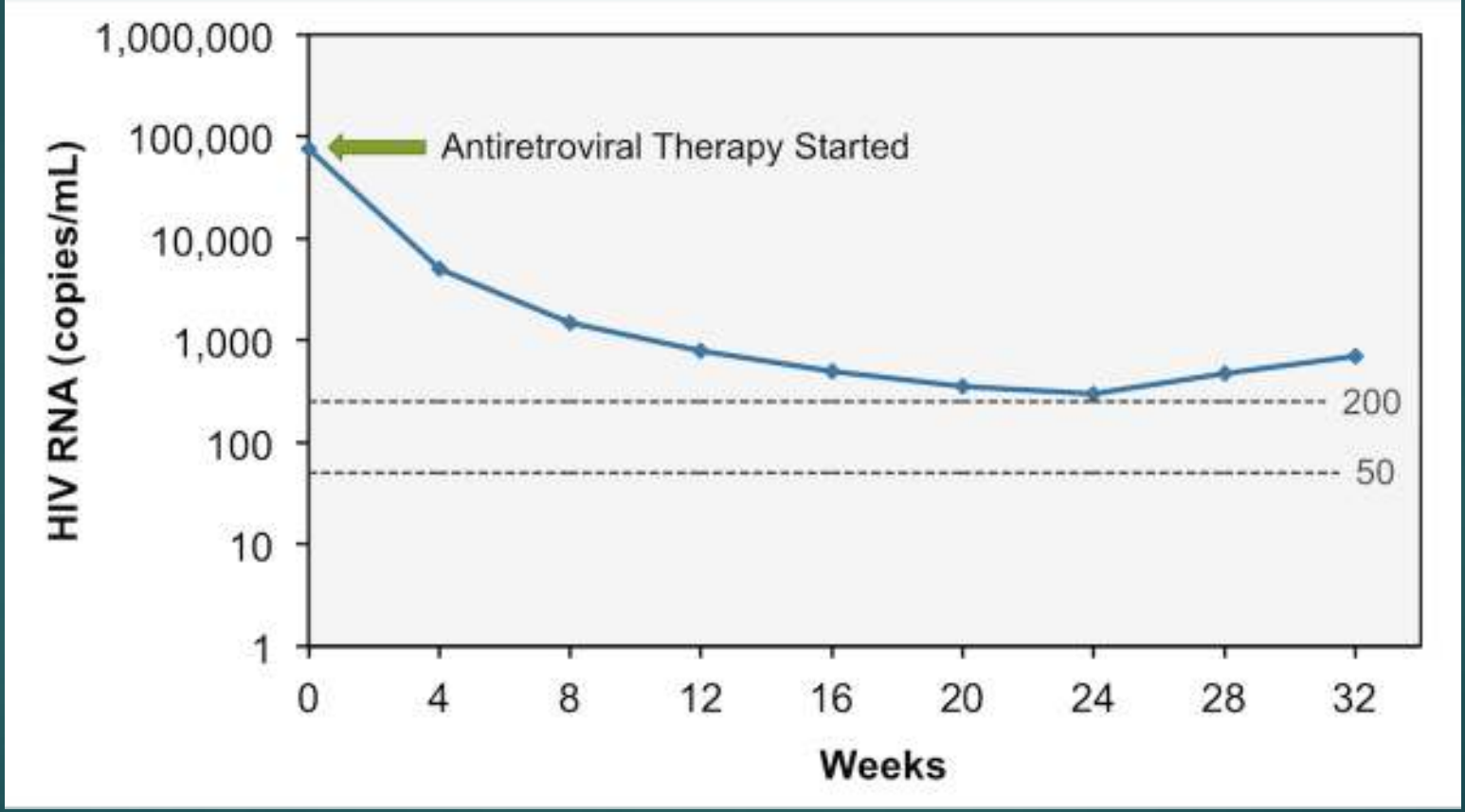
Virolojik baskılama (suppression)



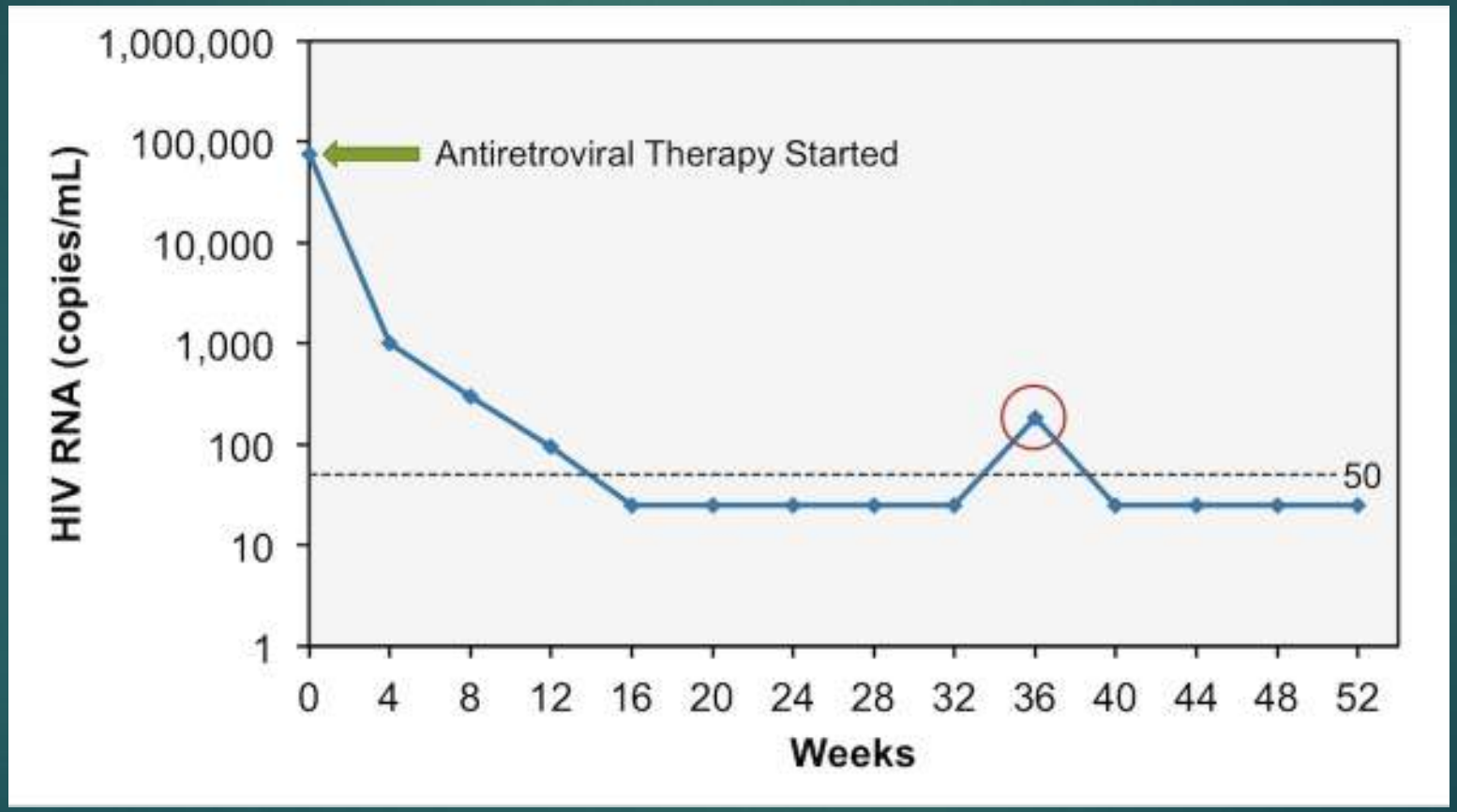
Virolojik kaçış (rebound)



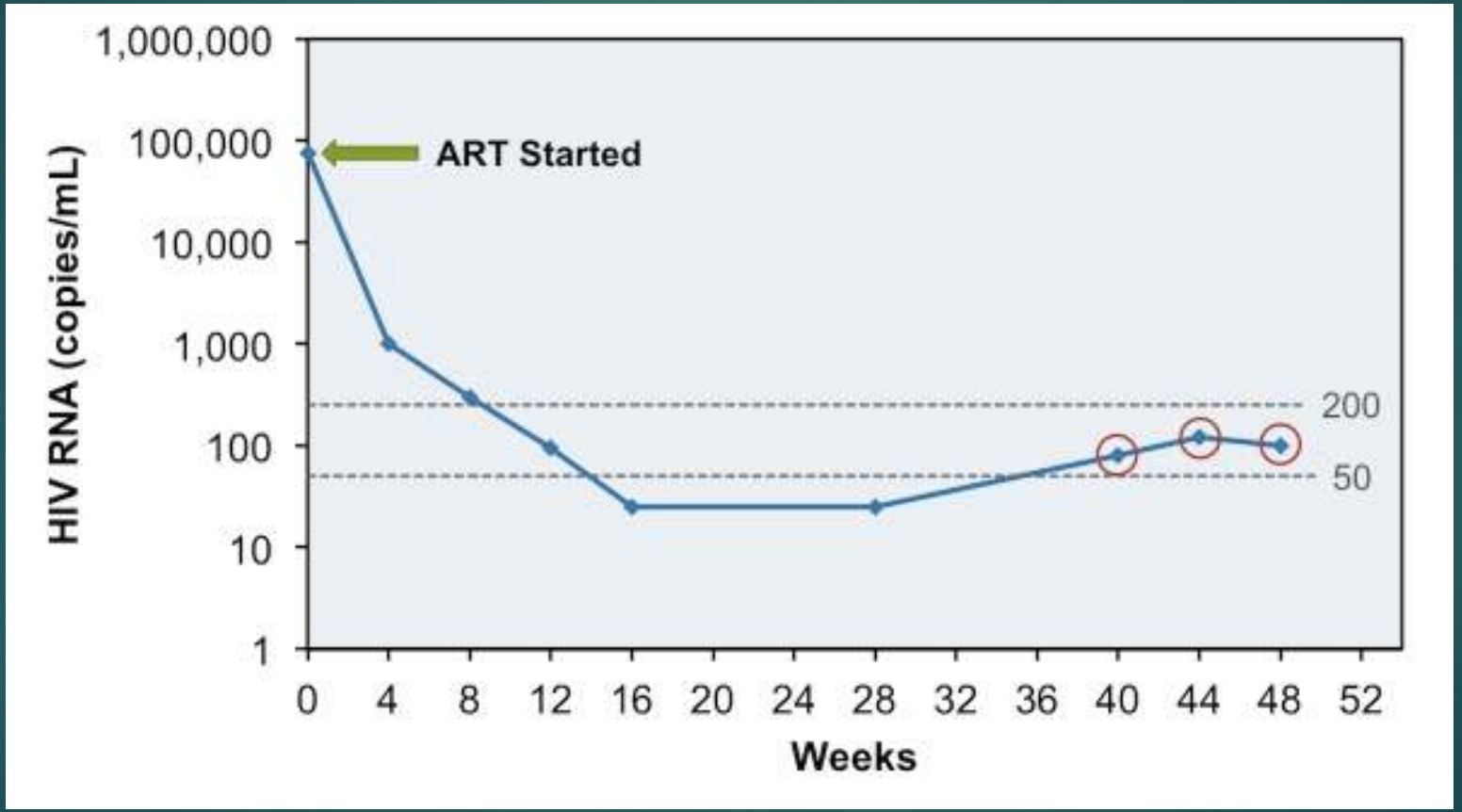
Eksik virolojik yanıt (Incomplete virologic response)



Virolojik sıçrama (blip)



Düşük düzey viremi (low-level viremia)



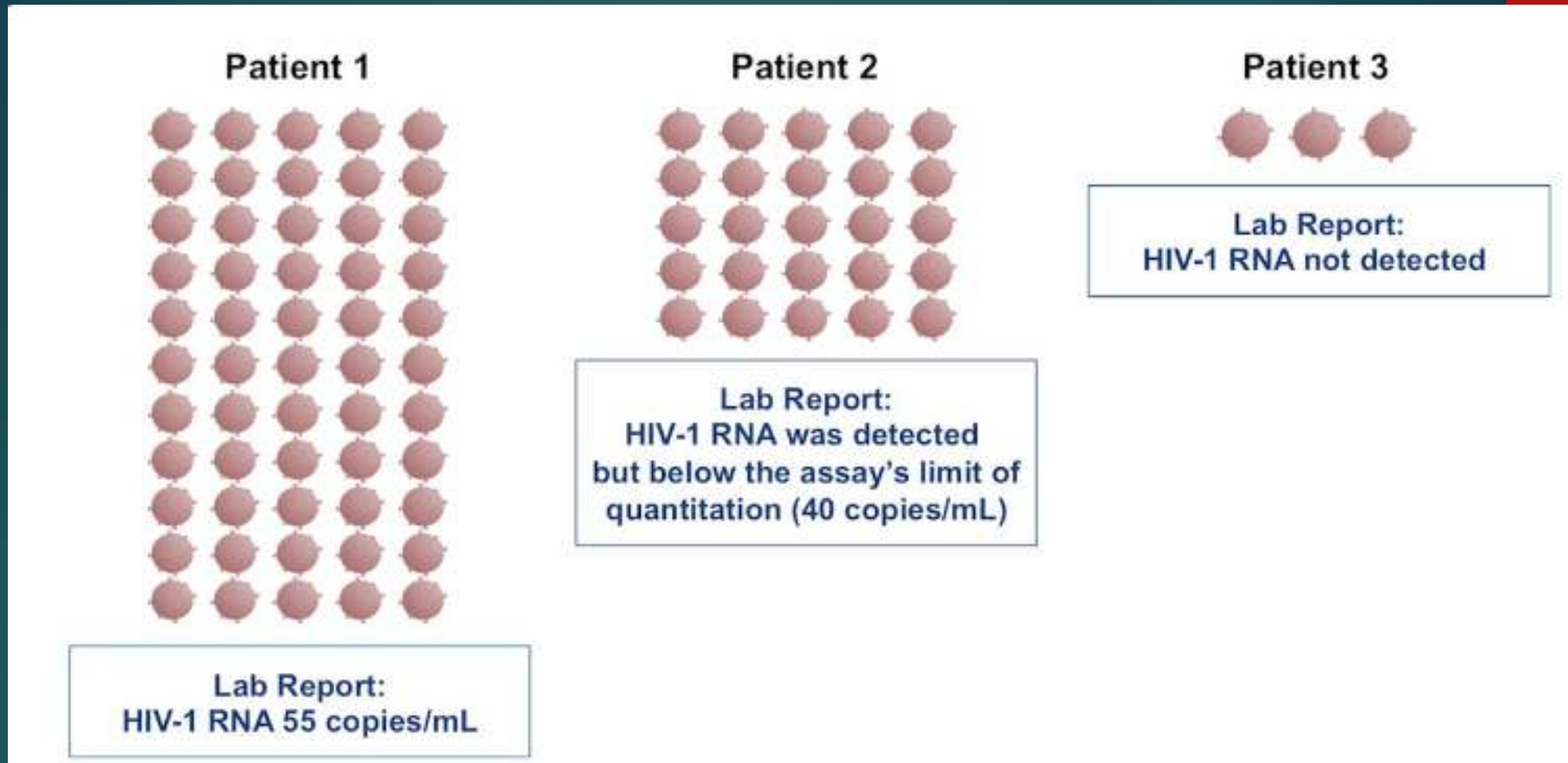
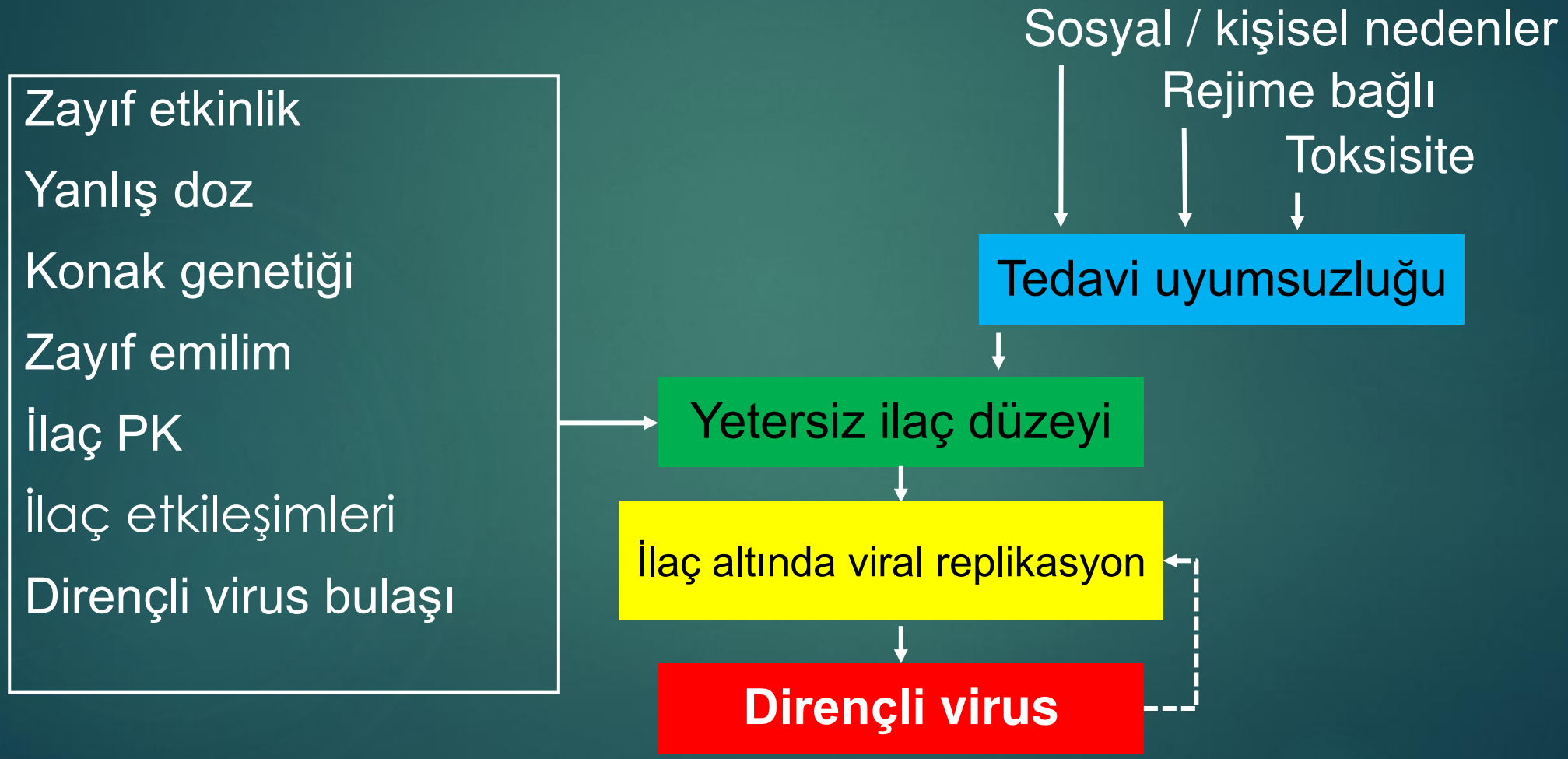
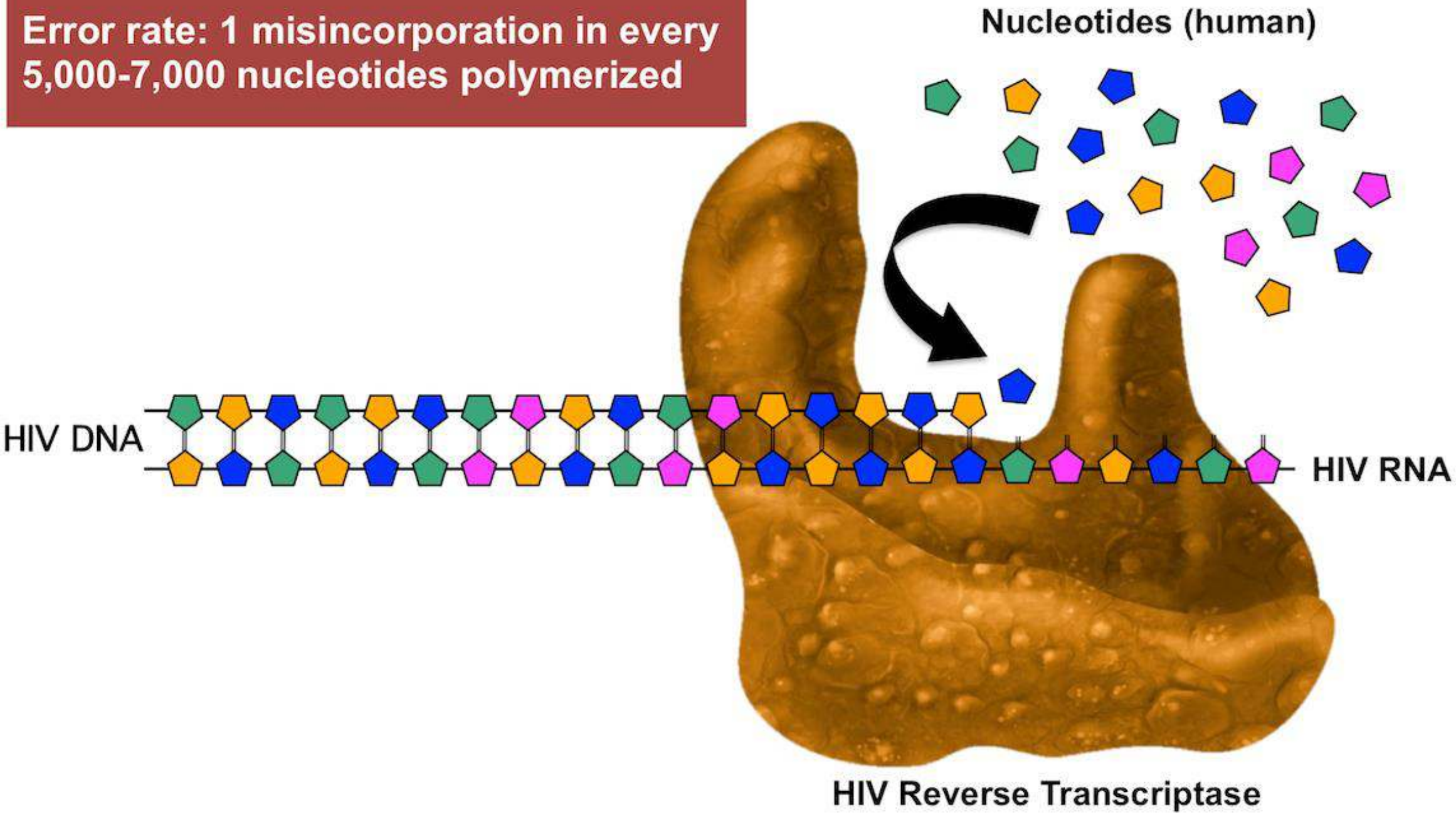


Figure 8 - Detectable HIV RNA Below the Limit of Quantification
As shown in the sample from patient 2, in some individuals with HIV infection, HIV RNA is detectable in a plasma sample but the amount of HIV RNA is so low (less than 40 copies/mL) that the laboratory assay cannot accurately quantitate the HIV RNA level. In this situation, the laboratory report typically states HIV-1 RNA was detected in this sample but below the assay's limit of quantitation. This contrasts with the sample from patient 1 that corresponds with a quantitative HIV-1 RNA level since it is above 40 copies/mL. For the sample from patient 3, the HIV RNA level is extremely low and would not be detected on most standard commercial assays.

ART başarısızlık nedenleri



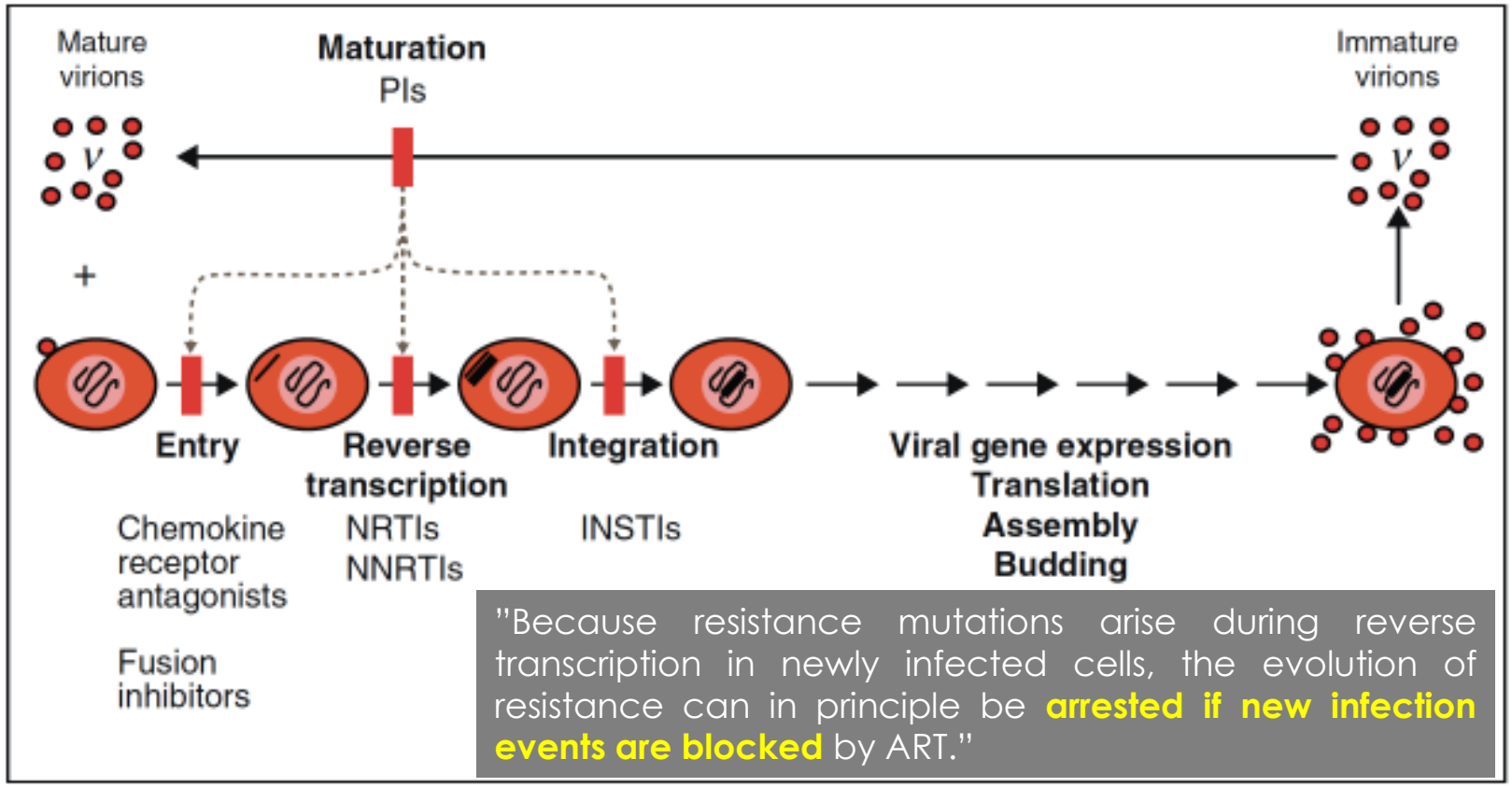
Error rate: 1 misincorporation in every 5,000-7,000 nucleotides polymerized



Recent trends in HIV-1 drug resistance

Janet D Siliciano[1] and Robert F Siliciano[1,2]

Current Opinion in Virology 2013, **3**:487–494



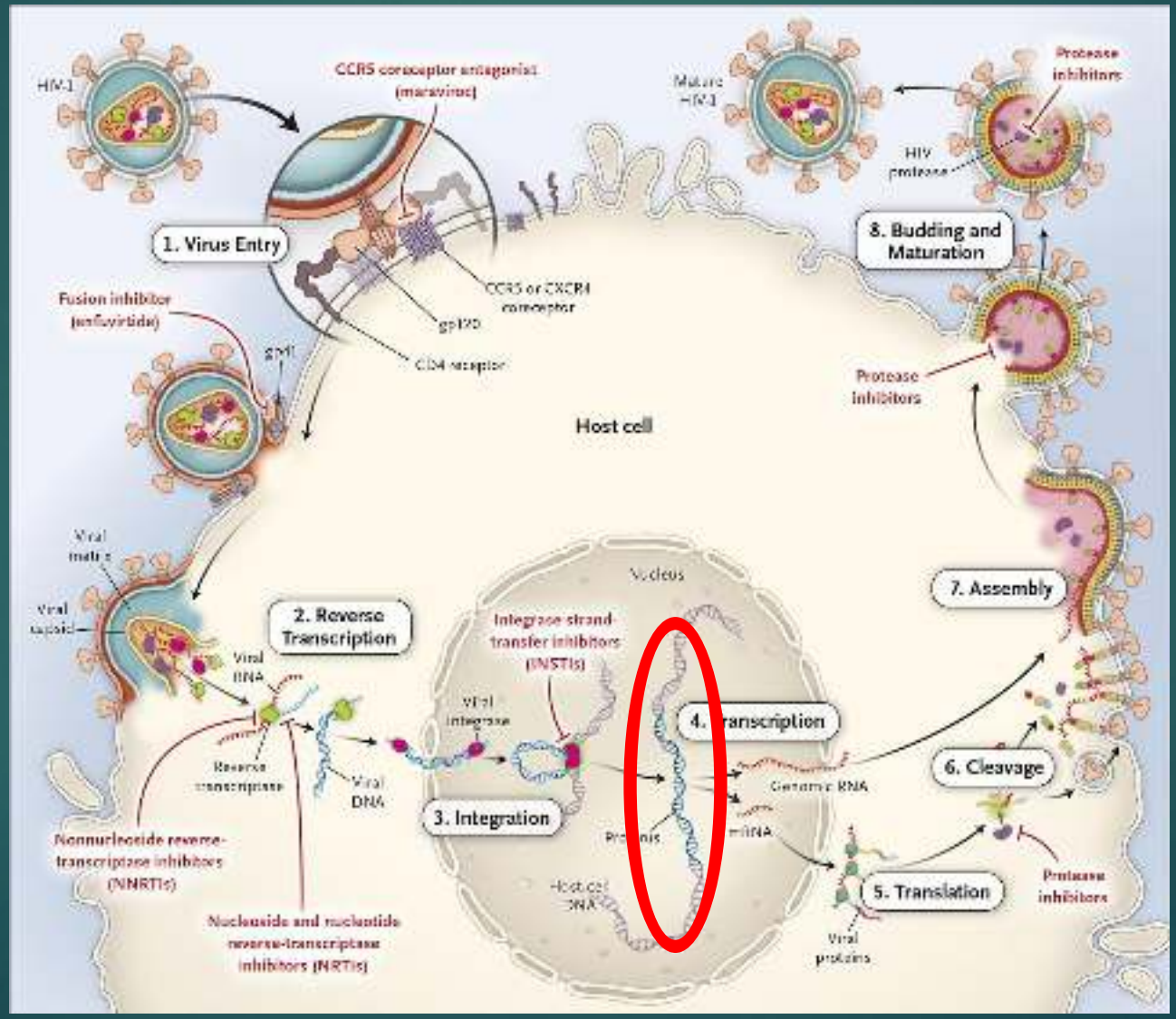
Antiretroviral therapy for HIV-1 infection. The steps in the life cycle blocked by different classes of antiretroviral drugs are indicated. Current ART regimens consist of two NRTIs and either an NNRTI, a PI, or an InSTI. Inhibitors of HIV-1 entry, chemokine receptor antagonists and fusion inhibitors, can also be used. Note that all current antiretroviral drugs act to prevent new cells from becoming infected. They do not block the production of virus particles by a cell that already carries an integrated provirus. The PIs prevent virus particles from maturing to an infectious form. Immature virus particles show defects at multiple downstream steps in the virus life cycle (dotted lines), including entry, reverse transcription, and integration. See text for references.

Düşük düzey viremi neye bağlı?

Viral replikasyon mu, proviral ekspresyon mu ya da ikisi de mi?

Viral replikasyon

- yeni enfekte hücre
- yeni proviral genom içeren hücre oluşumu
- RT çalışıyor mu?
- RT çalışıyorsa ilaca dirençli mutant geliştirme olasılığı var



Proviral ekspresyon

- mevcut rezervden üretilen virüs
- proviral genomu hücrenin RNA polimerazı eksprese ettiğinden mutasyon olasılığı çok düşük

Virolojik Başarısızlık (VF)

Clinical Info HIV.gov (12-2019)

- Sıçramalar (blip) genelde VF'yi **öngördürmez**_*Nettles RE et al. 2005*
- Alt saptama eşiği ile <200 c/mL arası değerlerin öngördürücülüğü **tartışmalı**
  - <200 c/mL ile <50 c/mL arasında öngördürücülük açısından fark yok_*Ribaudo H et al. CROI 2009*
  - >200 c/mL 50-199 c/mL'ye göre VF'yi öngördürür_*ATCC et al. 2015, Boillat-Blanco N et al. 2014*
  - <200 c/mL ilaç direncinin seçilmesine zemin sağlar ve VF'yi öngördürür_*Eron JJ et al. 2013, Laprise C et al. 2013, Taiwo B et al. 2010*
- ≥200 c/mL'de sebat eden değerler sıklıkla viral evrim ve ilaç direnci ile ilişkili mutasyonların birikmesi ile ilişkilidir_*Aleman S et al. 2002*
  - özellikle >500 c/mL düzeyinde_*Karlsson AC et al. 2004*

EACS Guidelines 2020

v.10.1

EACS European AIDS Clinical Society

Virological Failure

Definition

- **INCOMPLETE SUPPRESSION:** HIV-VL > 200 copies/mL at 6 months[i] after starting therapy in PLWH not previously on ART
- **REBOUND:** confirmed HIV-VL > 50 copies/mL in PLWH with previously undetectable HIV-VL

Management of virological failure (VF)

If HIV-VL > 50 and < 200 copies/mL:

- Check for adherence
- Check HIV-VL 1 to 2 months later[ii]
- If genotype not possible, consider changing regimen based on past treatment and resistance history

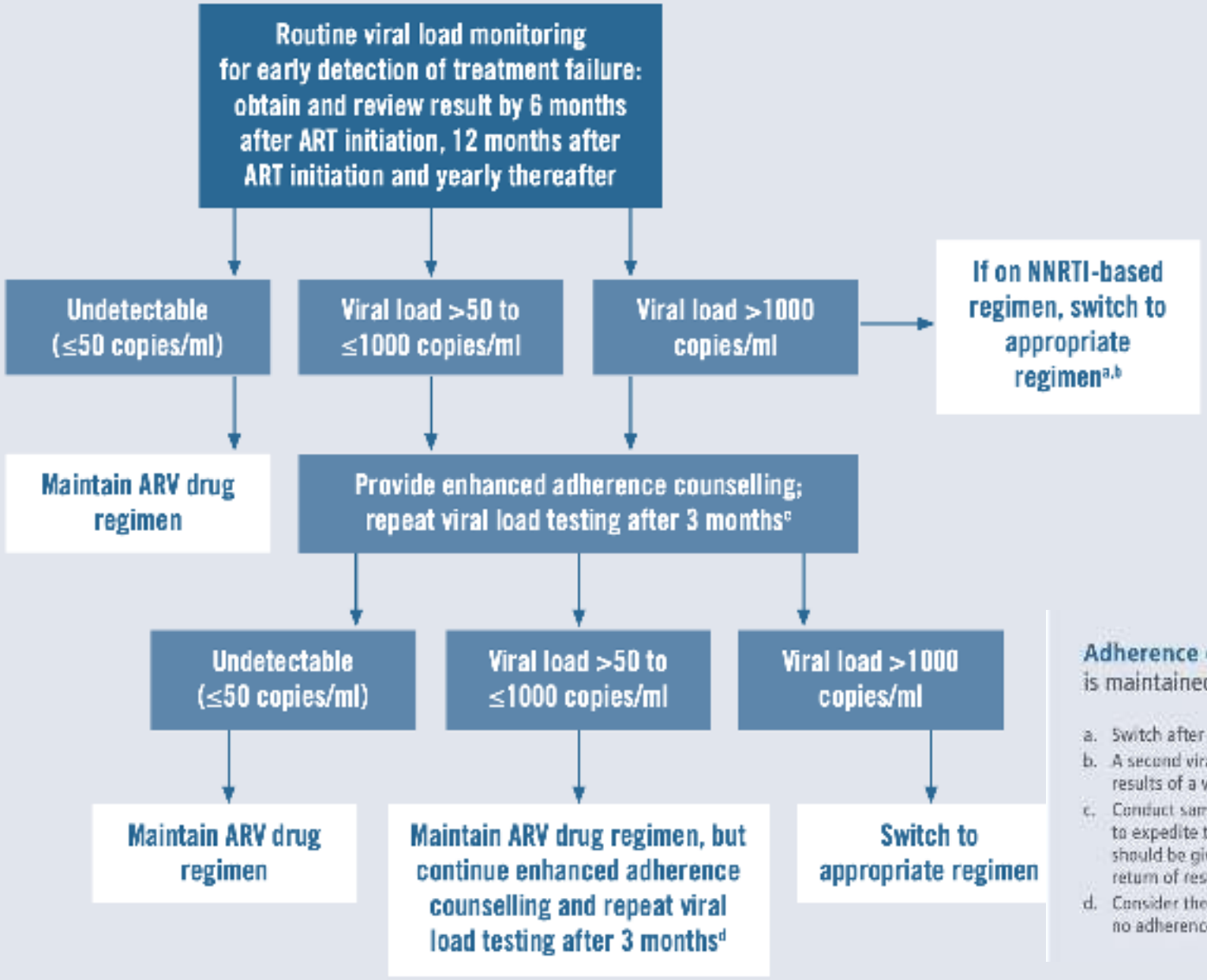
If HIV-VL confirmed > 200 copies/mL:

- Change regimen as soon as possible. What to change will depend on the resistance testing results
- If no resistance mutations found: re-check for adherence, perform TDM
- If resistance mutations found: switch to a suppressive regimen based on drug history; multidisciplinary expert discussion advised
- Goal of new regimen: HIV-VL < 50 copies/mL within 6 months

i. In PLWH with very high baseline HIV-VL (> 100,000-500,000 copies/mL), achieving viral suppression may take longer than 6 months
ii. In the absence of resistance and in persons fully adherent to treatment, consider non-suppressible viremia due to cellular proliferation [17]

17. Halvas EK, Joseph K , Brandt L et al. Nonsuppressible viremia on ART from large cell clones carrying intact proviruses. CROI 2019. Oral abstract 23

Fig 1. Treatment monitoring algorithm



Adherence counselling should be provided at all visits to ensure that viral suppression is maintained or given priority throughout care

a. Switch after a single elevated viral load should be considered if treatment experience is likely.
b. A second viral load may be considered before regimen switch if DTG-based regimens are unavailable and the results of a viral load test can be returned and acted on rapidly.
c. Conduct same-day testing using point-of-care viral load testing for a repeat viral load test, where available, to expedite the return of results. If not available, viral load specimens and results for a repeat viral load should be given priority across the laboratory referral process (including specimen collection, testing and return of results). See subsection 3.2.
d. Consider therapy switch for those receiving NNRTI-based regimens and based on clinical considerations and no adherence concerns.

World Health Organization

UPDATED RECOMMENDATIONS ON

HIV PREVENTION, INFANT DIAGNOSIS, ANTIRETROVIRAL INITIATION AND MONITORING

MARCH 2021

Virolojik başarısızlığa genel yaklaşım

- Yaklaşım bireyselleştirilmeli
  - ART geçmişi
  - ilaç direnci (güncel ve arşiv)
  - virolojik başarısızlık süresi
  - plazma viremi düzeyi
- İlk yapılacak virolojik başarısızlığı doğrulamak!
- Uyumu sorgula ve gider
- İlaç-ilaç ve ilaç-besin etkileşimlerini sorgula, irdele, gider

Clinical INFO HIV.gov, 12-2019

HIV-RNA
> alt saptama eşiği - <200 kopya/mL

- Düşük düzey viremi
- Bu düzeylerde seyreden virüs yükü genelde ilaç değişikliği gerektirmez
- İlaç direnci gelişme olasılığı düşük
- Mevcut ART kombinasyonu ile devam et
  - ≤3 ayda bir viral yük bak
- Direnç testi bu düzeyde genelde çalışmaz
  - DNA genotiplendirme

Clinical INFO HIV.gov, 12-2019

Clinical Infectious Diseases

MAJOR ARTICLE

EDITOR'S CHOICE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

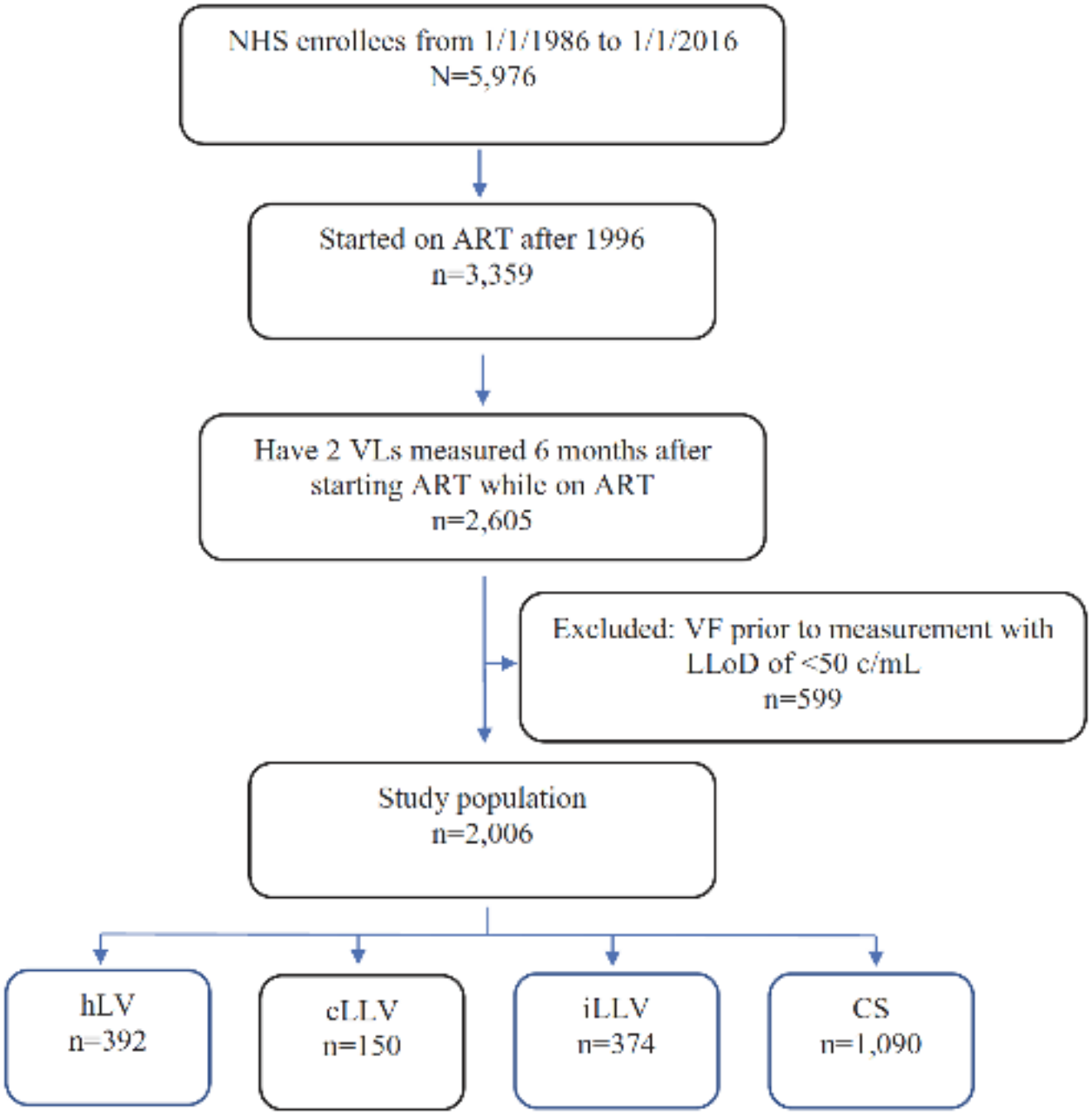
OXFORD

Persistent Low-level Viremia While on Antiretroviral Therapy Is an Independent Risk Factor for Virologic Failure

Christie Joya,[1,2] Seung Hyun Won,[1,3] Christina Schofield,[1,4] Tahaniyat Lalani,[1,3,5] Ryan C. Maves,[1,6] Karl Kronmann,[1,5] Robert Deiss,[1] Jason Okulicz,[1,7] Brian K. Agan,[1,3] and Anuradha Ganesan[1,2,3]

[1]Infectious Disease Clinical Research Program, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, [2]Division of Infectious Diseases, Walter Reed National Military Medical Center, and [3]The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, Maryland; [4]Division of Infectious Diseases, Madigan Army Medical Center, Tacoma, Washington; [5]Division of Infectious Diseases, Naval Medical Center Portsmouth, Virginia; [6]Division of Infectious Diseases, Naval Medical Center San Diego, California; and [7]Infectious Disease Service, San Antonio Military Medical Center, Texas

CID 2019:69 (15 December)



- HIV-positive Department of Defense beneficiaries
- En az 2 kez viral yük <50 c/mL
- Virolojik başarısızlık:
  teyit edilmiş viral yük ≥200 c/mL veya herhangi bir >1000 c/mL
- 4 birbirini dışlayan grup
  - hLV: high-level viremia
    200-1000 c/mL
  - LLV: low-level viremia
    50-199 c/mL
    - intermittent: ölçümlerin <%25'inde
    - persistent: geri kalan, ≥%25
  - CS: continuously suppressed

Table 2. Categorization of Subjects by Virologic Status

	Total	Virologic Failure	No Virologic Failure	
	(N = 2006)	(n = 383) %19	(n = 1623)	*P* Value
hLV, n (%)	392 (19.5)	182 (47.5)	210 (12.9)	<.0001
pLLV, n (%) %46	150 (7.5)	52 (13.6)	98 (6.0)	<.0001
iLLV, n (%)	374 (18.6)	22 (5.7)	352 (21.7)	<.0001
CS, n (%)	1090 (54.3)	127 (33.2)	963 (59.3)	<.0001

Table 4. Factors Associated With Virologic Failure

	Unadjusted HR		Adjusted HR	
Risk Factor	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
LLV (Ref. CS)				
hLV	3.08 (2.42–3.93)	<.0001	2.29 (1.78–2.96)	<.0001
pLLV	3.89 (2.74–5.52)	<.0001	3.46 (2.42–4.93)	<.0001
iLLV	0.34 (.22–.54)	<.0001	0.33 (.21–.52)	<.0001
Male	1.01 (.67–1.53)	.96	1.18 (.78–1.80)	.43
Race (Ref. white)				
Black	1.31 (1.05–1.65)	.02	1.33 (1.06–1.68)	.02
Hispanic/Other	0.81 (.57–1.15)	.24	1.03 (.72–1.47)	.87
Age at ART initiation[a] (per 10 year increase)	0.88 (.78–1.00)	.04	0.70 (.61–.82)	<.0001
Log viral load at ART initiation (copies/mL) (per log increase)	0.95 (.85–1.05)	.31	1.15 (1.02–1.30)	.02
Antiretroviral use prior to ART	2.64 (2.12–3.27)	<.0001	1.79 (1.34–2.38)	<.0001
Time from HIV diagnosis to ART initiation (per year increase)	1.05 (1.03–1.07)	<.0001	1.03 (1.00–1.06)	.06
CD4 counts[a] (per 100 cells/uL increase)	0.94 (.90–.98)	.002	0.97 (.93–1.01)	.14
ART regimen[a] (Ref. Unboosted PI)				
Boosted PI	0.70 (.50–1.00)	.05	0.96 (.67–1.37)	.81
INSTI	0.16 (.08–.31)	<.0001	0.26 (.13–.53)	<.001
NNRTI	0.45 (.35–.58)	<.0001	0.68 (.51–.90)	.007
Other combinations	0.95 (.68–1.34)	.78	1.18 (.83–1.66)	.36

Sonuç ve Tartışma

- 50-199 k/mL arası sebat eden viral yük virolojik başarısızlıkla ilişkili
  - bu durum saptandığında ilaç uyumu, farmakokinetik etkileşimler değerlendirilmeli
- 200-999 k/mL arası tek değer bile virolojik başarısızlıkla ilişkili
- Arada sırada olan 50-199 k/mL arası viral yük ise koruyucu
  - çoğu *blip* (sıçrama)
  - viral yük testi daha sık yapılmış
    - sağlık bakımı ile temas daha sık olduğundan uyumsuzluk giderilmiş olabilir
    - "engagement and retention"
  - immünolojik fayda
- Bu çalışmada ilaç uyumu değerlendirmeye katılmamış!

www.medscape.com

COMMENTARY

Low-Level Viremia in HIV: When Should We Worry?

Paul E. Sax, MD

March 11, 2020

- 50-200 k/mL arası viral yükün virolojik başarısızlıkla ilişkili olduğunu gösteren ve göstermeyen çalışmalar var
- Ara sıra olan LLV (yani *blip*) VF'yi öngördürmüyor
- Sebat eden LLV→ VF için OR 3.46
  - düşük ilaç düzeyi? ilaç uyumu, farmakokinetik etkileşim
- Ancak
  - 100% ilaç uyumu olup bir türlü LLV'sini düzeltemediğimiz hastalar?
  - Dolayısıyla **2 grup LLV'li hasta**; uyum sorunu olan ve olmayan
  - Uyum sorunu olmayan grup
    - çok yüksek rezerv ve zaman zaman çoğalmayan virüs salınımı?
    - bu grup nasıl yönetilmeli? → uyumu hallet ve yüksek genetik bariyerli rejim kullan!

Persistent HIV-1 Viremia on Antiretroviral Therapy: Measurement and Mechanisms

Jana L. Jacobs, Elias K. Halvas, Melissa A. Tosiano and John W. Mellors*

Division of Infectious Diseases, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, United States

MINI REVIEW
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doi: 10.3389/fmicb.2019.02383

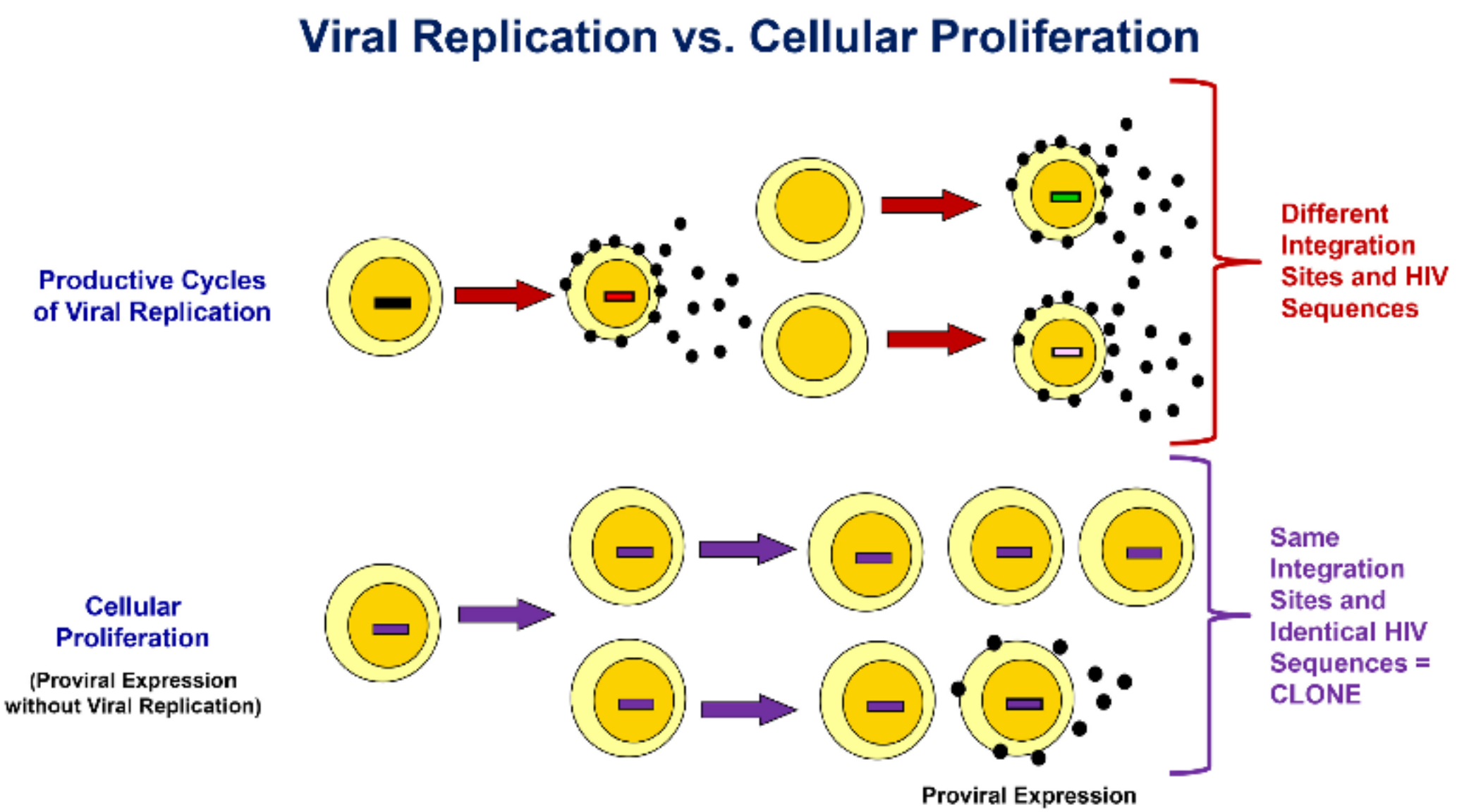

FIGURE 1 | Differentiating Viral Replication From Clonal Expansion with Proviral Expression as the Source of Persistent Viremia on ART. Integration site and HIV sequence analyses can be used to assess the origin of proviral expansion and/or viremia. Productive cycles of viral replication result in both genetic heterogeneity due to errors introduced by reverse transcriptase, and variation in the chromosomal integration site of the HIV provirus. Conversely, clonal expansion results in identical chromosomal HIV integration sites in cell progeny, identical proviral sequences, and identical viral sequences from the subset of cell in the clone that produce virus. See text for more details.

The Journal of Clinical Investigation

CLINICAL MEDICINE

HIV-1 viremia not suppressible by antiretroviral therapy can originate from large T cell clones producing infectious virus

Elias K. Halvas,[1] Kevin W. Joseph,[1] Leah D. Brandt,[1] Shuang Guo,[2] Michele D. Sobolewski,[1] Jana L. Jacobs,[1] Camille Tumiotto,[1] John K. Bui,[3] Joshua C. Cyktor,[1] Brandon F. Keele,[4] Gene D. Morse,[5] Michael J. Bale,[6] Wei Shao,[7] Mary F. Kearney,[6] John M. Coffin,[8] Jason W. Rausch,[9] Xiaolin Wu,[2] Stephen H. Hughes,[6] and John W. Mellors[1]

[1]Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA. [2]Leidos Biomedical Research, Inc., Frederick, Maryland, USA. [3]New York-Presbyterian Hospital/Weill Cornell Medical Center, Weill Department of Medicine, New York, New York, USA. [4]AIDS and Cancer Virus Program, Frederick National Laboratory for Cancer Research, Frederick, Maryland, USA. [5]NYS Center of Excellence in Bioinformatics and Life Sciences, Translational Pharmacology Research Core, University at Buffalo, Buffalo, New York, USA. [6]HIV Dynamics and Replication Program, National Cancer Institute, Frederick, Maryland, USA. [7]Advanced Biomedical Computing Science, Frederick National Laboratory for Cancer Research (FNLCR), Frederick, Maryland, USA. [8]Department of Molecular Biology and Microbiology, Tufts University, Boston, Massachusetts, USA. [9]Basic Research Laboratory, Center for Cancer Research, National Cancer Institute, Frederick, Maryland, USA.

November 2020

J Clin Invest. 2020;130(11):5847-5857.

Table 2. Immunologic and virologic characteristics of donors referred for nonsuppressible viremia

Donor ID	Pre-ART Plasma HIV-1 RNA (cps/mL)	Nadir CD4⁺ T Cells (cells/mm³)	Current CD4⁺ T Cells (cells/mm³)	Plasma HIV-1 RNA at Referral (cps/mL)[A]	HIV-1 DNA (cps/10⁶ PBMCs)[B]	Cell-Associated HIV-1 RNA (cps/10⁶ PBMCs)[B]	IUPM[C]
R-09	97,000	105	380	197	1,533	139	18.1
C-03	16,700,000	10	416	62	2,505	1,162	1.4
C-02	30,375	286	1,022	184	373	29	0.1
F-07	117,068	314	1,023	52	1,603	1,112	3.8
K-01	147,189	133	533	68	1,383	74	0.6
P-08	604,000	172	444	106	1,056	382	0.4
T-05	197,826	299	1,105	113	650	109	0.4
A-06	1,877,100	251	831	43	1,825	630	0.2
Median	**172,506**	**212**	**682**	**87**	**1,458**	**261**	**0.5**

[A]Plasma HIV-1 RNA copies/mL at time of referral determined by FDA-approved Roche CAP/CTM v2.0 or Abbott M2000 platforms. [B]HIV-1 DNA and cell-associated RNA copies/million peripheral blood mononuclear cells (PMBCs) measured by quantitative polymerase chain reaction (22). [C]Infectious units per million (IUPM) total CD4⁺ T cells by quantitative viral outgrowth assay (qVOA) (23, 24).

Years of detectable viremia= median 4.1 (range 1.3 - 5.2)

Table 3. Single-genome sequence matches between plasma HIV-1 RNA, proviruses, and viral outgrowth cultures

Donor ID	Identical Plasma HIV-1 RNA Sequences[A]	Proviral Sequences Matching Dominant Plasma HIV-1 RNA Sequences (% matching)[B]	qVOA p24+ Wells with Matching Sequences in Plasma HIV-1 RNA[C,D]	Proviral Sequences Matching Dominant qVOA HIV-1 RNA Sequences (% matching)[E]
R-09	50.0%	10.7%	100% (10/10)	10.7%
C-03	63.3%	2.9%	66.7% (2/3)	2.9%
C-02	90.7%	7.5%	100% (3/3)	7.5%
F-07	53.8%	0.3%	0% (0/4)	3.0%
K-01	37.5%	3.9%	0% (0/4)	<3.9%
P-08	100%	8.0%	0% (0/3)	<8.0%
T-05	76.7%	<0.7%	0% (0/3)	<0.7%
A-06	48.4%	<0.7%	0% (0/2)	<0.7%

[A]Percentage of all HIV-1 RNA single-genome sequences from plasma (1.3 kb of *gag-pro-pol*) that are identical or differ by 1 to 2 bases from the group of identical sequences. [B]Identical proviruses (single-genome sequences) in PBMCs that match HIV-1 RNA sequences from plasma (1.3 kb of *gag-pro-pol*). [C]Quantitative viral outgrowth (qVOA) HIV-1 RNA single-genome sequences (1.3 kb of *gag-pro-pol*). [D]Percentage and number of *gag* p24 antigen–positive (p24+) qVOA wells with identical sequences that match plasma HIV-1 RNA sequences (1.3 kb of *gag-pro-pol*). [E]Percentage of total proviral HIV-1 DNA single-genome sequences that match identical qVOA HIV-1 RNA single-genome sequences (1.3 kb of *gag-pro-pol*). Bold indicates that the proviruses in clonally expanded cells are intact (replication-competent) and either contribute to persistent infectious viremia (C-02, C-03, R-09) or can be induced ex vivo (F-07) to produce infectious virus (qVOA).

Sonuç

- 8 hastanın her birinin plazmasındaki HIV-1 genomik RNA'nın dizisi birbirinin aynı
- Aynılığı zamanla değişmiyor ve direnç geliştirmiyor
- 4 hastada plazmadaki dizi ile virüs kültüründeki dizi aynı yani çoğalabilen (replication-competent) virüs
- Klonların (replicone) büyüklüğü 50 – 350 milyon hücre
  enfekte hücrelerin %0.03 - %1.1
- Baskılanamayan virüs enfeksiyoz olabilir ve ART kesildiğinde viral geri tepmeye neden olur
- Replicone'ların yok edilmesi veya kontrol edilmesi için yeni yol bulunmalı!
  - *Bu durum ART değiştirerek veya kuvvetlendirerek giderilemiyor*

The Journal of Clinical Investigation

COMMENTARY

Nonsuppressible HIV-1 viremia: a reflection of how the reservoir persists

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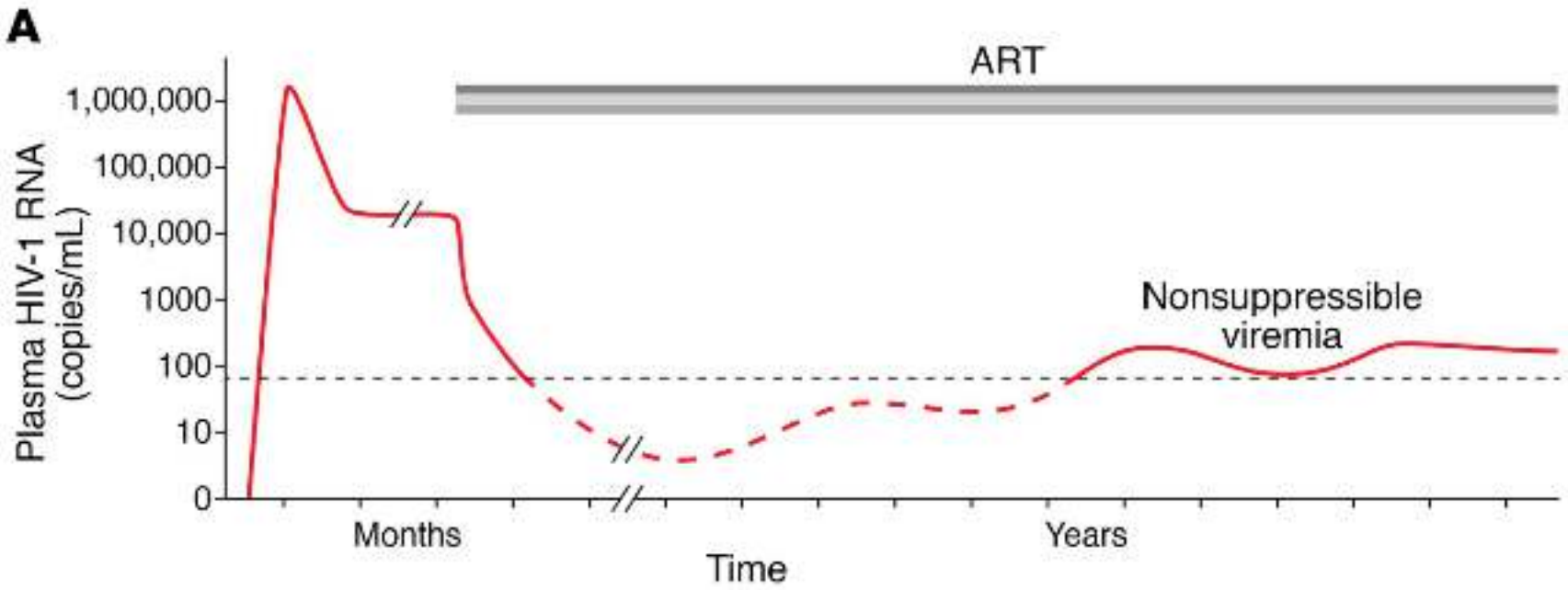

Figure 1. Nonsuppressible viremia can result from large clones of infected cells. (A) Plasma virus

Much evidence suggests that ART regimens cause a complete block in new infection of susceptible cells (reviewed in ref. 11), and therefore this rapid decay in viremia reflects the turnover of cells that were infected at the time treatment was started (2). Interestingly, although ART suppresses

13). It appears that ART simply reduces viremia to a new steady-state level that is slightly below the limit of detection of clinical assays (Figure 1A). This trace level of residual viremia is often in the range of 1–3 copies/mL (13, 14). The residual viremia

copies/mL (13, 14). The residual viremia appears to represent virus that originates from the latent reservoir rather than ongoing cycles of replication because it cannot be further reduced by intensifying treatment (15, 16).

This viremia cannot be suppressed by ART, which continues to block new infection of susceptible cells but not virus release from previously infected cells.

RESEARCH ARTICLE

Switch to second-line versus continued first-line antiretroviral therapy for patients with low-level HIV-1 viremia: An open-label randomized controlled trial in Lesotho

Alain Amstutz[1,2,3], Bienvenu Lengo Nsakala[4], Fiona Vanobberghen[1,2], Josephine Muhairwe[4], Tracy Renée Glass[1,2], Tilo Namane[5], Tlali Mpholo[6], Manuel Battegay[2,3], Thomas Klimkait[7], Niklaus Daniel Labhardt[1,2,3]*

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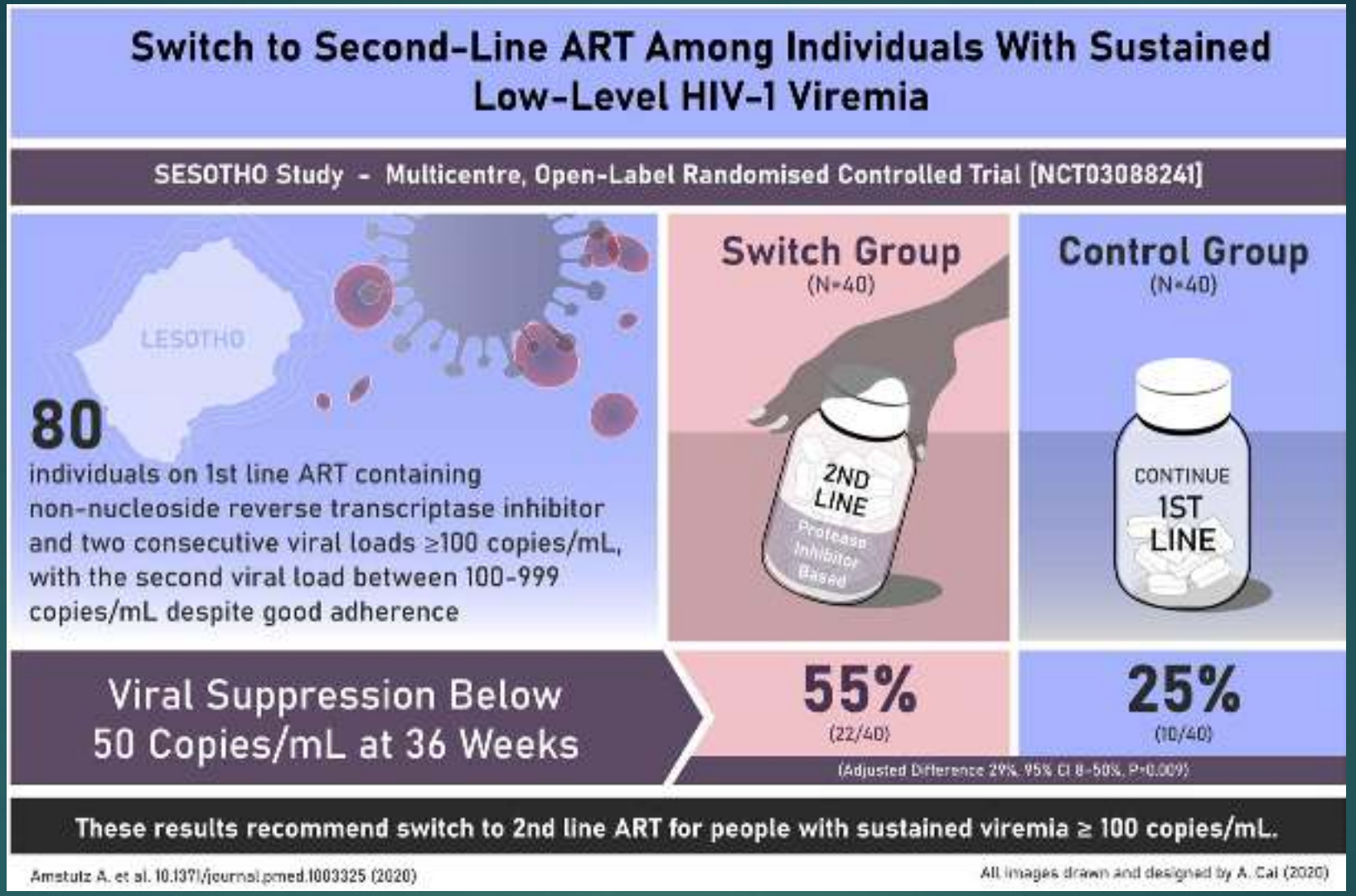

Table 1. Clinical and biomedical baseline characteristics of trial participants.

	Control group (n = 40)	Switch group (n = 40)	Total (n = 80)
HIV VL, copies/mL	391 (190–638) [113–990]	300 (125–679) [102–950]	347 (170–648) [102–990]
HIV VL 100–599 copies/mL	29 (73%)	27 (68%)	56 (70%)
HIV VL 600–999 copies/mL	11 (28%)	13 (33%)	24 (30%)

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PLoS MEDICINE

The Effect of Raltegravir Intensification on Low-level Residual Viremia in HIV-Infected Patients on Antiretroviral Therapy: A Randomized Controlled Trial

Rajesh T. Gandhi[1]*, Lu Zheng[2], Ronald J. Bosch[2], Ellen S. Chan[2], David M. Margolis[3], Sarah Read[4], Beatrice Kallungal[5], Sarah Palmer[6], Kathy Medvik[7], Michael M. Lederman[7], Nadia Alatrakchi[8], Jeffrey M. Jacobson[9], Ann Wiegand[10], Mary Kearney[10], John M. Coffin[11], John W. Mellors[12], Joseph J. Eron[3], on behalf of the AIDS Clinical Trials Group A5244 team

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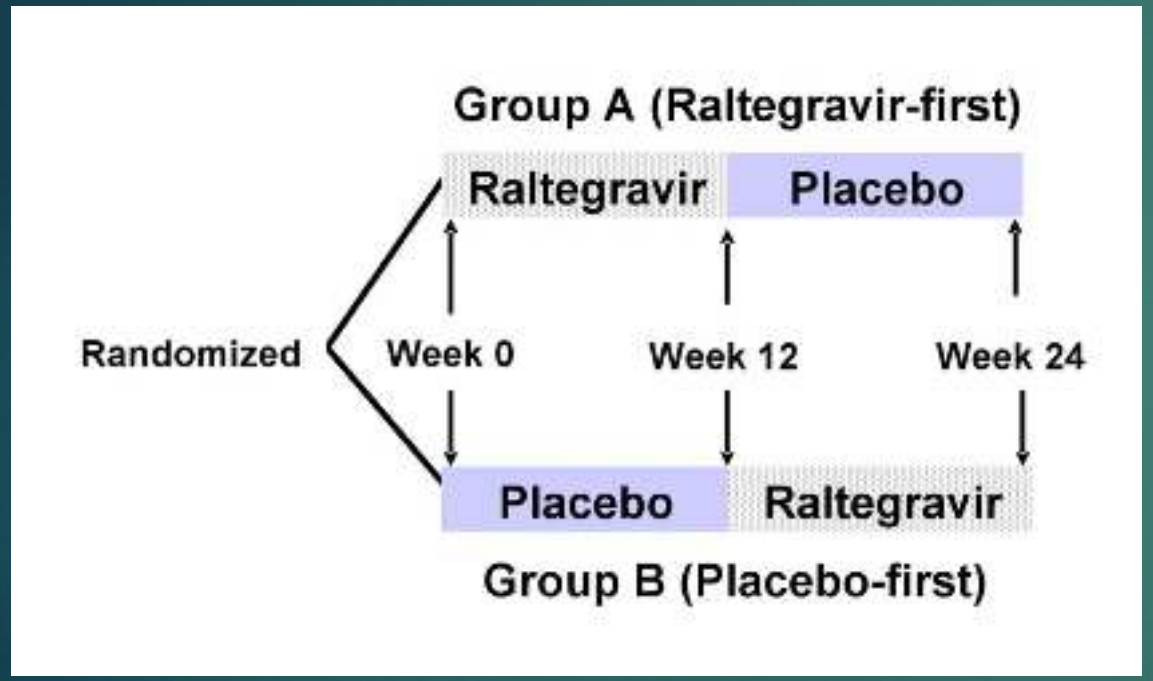
ART'nin raltegravir ile güçlendirilmesi düşük düzey viremiyi azaltmadı



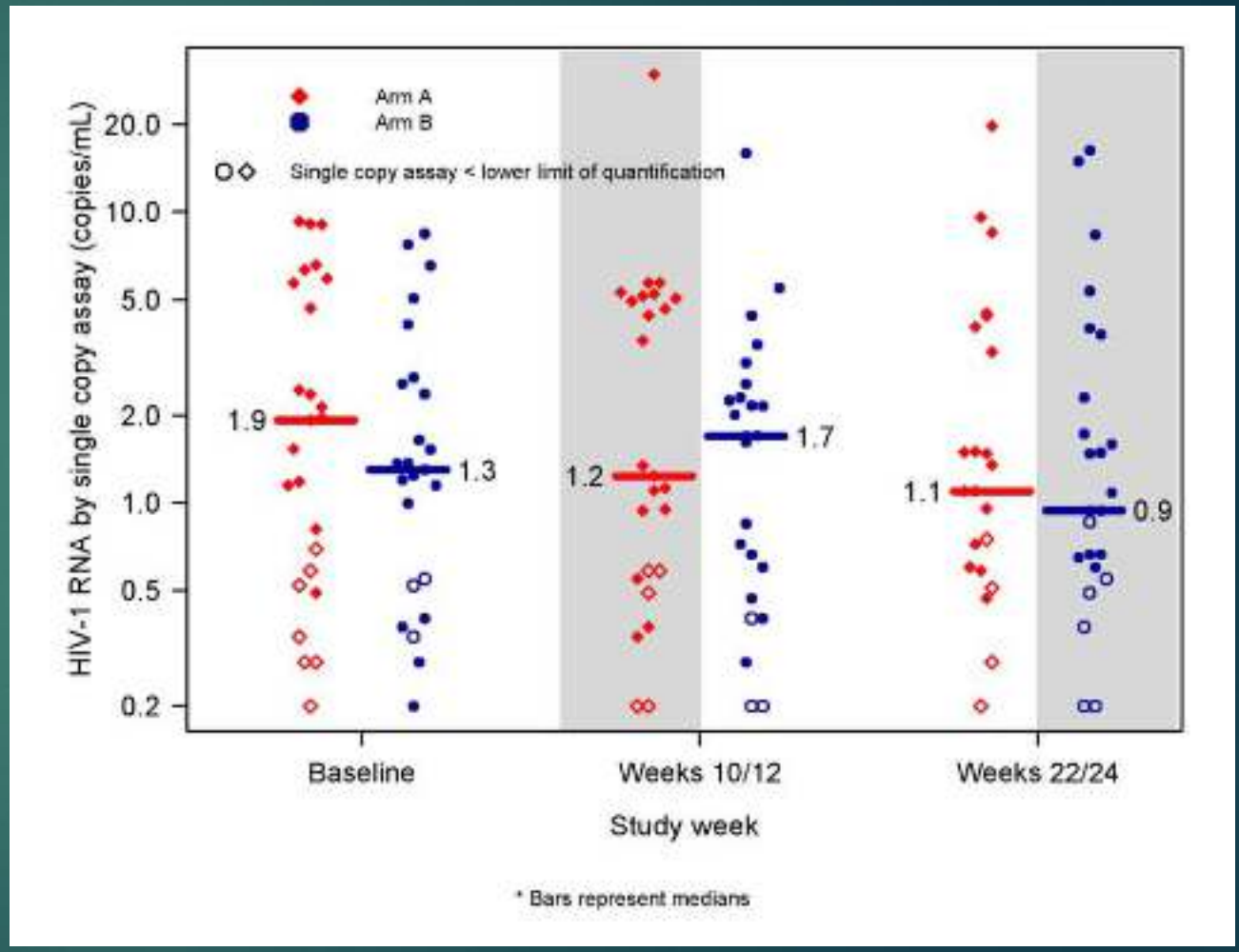


Figure 3. No reduction in low-level residual viremia after raltegravir intensification.

Düşük Düzey Viremi: Anlamı, Yönetimi ÖZET

- Düşük düzey viremi
  - ART ile <50 kopya/mL düzeyine indirdikten sonra virüs yükünün 50-200 kopya/mL arasında sebat etmesi
- İlaç uyumu, ilaç-ilaç, ilaç-besin problemlerini irdele ve gider
- Direnç testi (hücresel HIV-1 DNA)
- Terapötik ilaç düzeyi
- Yüksek genetik bariyerli rejime geç
- Eğer kandaki ilaç düzeyi yeterli ise bu durum viral replikasyondan daha çok proviral ekspresyonu gösterir ve ART değiştirmenin ya da kuvvetlendirmenin faydası olmaz

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