

Dünden Bugüne HIV Enfeksiyonu

Deniz Gökengin
Ege Üniversitesi Tıp Fakültesi
Enfeksiyon Hastalıkları ve Klinik
Mikrobiyoloji Anabilim Dalı

1981



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MMWR

Weekly

June 5, 1981 / 30(21):1-3

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Epidemiologic Notes and Reports

***Pneumocystis* Pneumonia -- Los Angeles**

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viremia. The serum complement-fixation CMV titer in October 1980 was 256; in May 1981 it was 32.* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and acyclovir. He died May 3, and postmortem examination showed residual *P. carinii* and CMV pneumonia, but no evidence of neoplasia.

Patient 2: A previously healthy 30-year-old man developed *p. carinii* pneumonia in April 1981 after a 5-month history of fever each day and of elevated liver-function tests, CMV viremia, and documented seroconversion to CMV, i.e., an acute-phase titer of 16 and a convalescent-phase titer of 28* in anticomplement immunofluorescence tests. Other features of his illness included leukopenia and mucosal candidiasis. His pneumonia responded to a course of intravenous TMP/SMX, but, as of the latest reports, he continues to have a fever each day.

Patient 3: A 30-year-old man was well until January 1981 when he developed esophageal and oral candidiasis that responded to Amphotericin B treatment. He was hospitalized in February 1981 for *P. carinii* pneumonia that responded to TMP/SMX. His esophageal candidiasis recurred after the pneumonia was diagnosed, and he was again given Amphotericin B. The CMV complement-fixation titer in March 1981 was 8. Material from an esophageal biopsy was positive for CMV.

1981

RARE CANCER SEEN IN 41 HOMOSEXUALS

Outbreak Occurs Among Men
in New York and California
—8 Died Inside 2 Years

By LAWRENCE K. ALTMAN

Doctors in New York and California have diagnosed among homosexual men 41 cases of a rare and often rapidly fatal form of cancer. Eight of the victims died less than 24 months after the diagnosis was made.

The cause of the outbreak is unknown, and there is as yet no evidence of contagion. But the doctors who have made the

**"What's it like
to have
Kaposi's
sarcoma?"**

It's a bummer."

It's a bummer being thirty years old and having cancer. It's a bummer being Jewish, Italian and gay. It's a bummer going through the medical procedures that doctors use to diagnose and treat cancer. It's a bummer having six or seven hundred thousands of dollars of dollars. It's a bummer not knowing what caused it. It's cancer, or it can be cured.

Now, it's a lucky job if there was. I don't feel sick. My cancer hasn't spread. I still function pretty much normally.

Now, I have a good support system — I have a therapist, understanding parents, lots of friends. There's health insurance and disability insurance.

Even so, I sometimes get real depressed. This thing could kill me — I killed two friends of mine, and hundreds of other brothers that I don't know personally. I don't want you to get it, too.

Are you thinking, "This can't happen to me"? I didn't think it could happen to me, either. But it did.

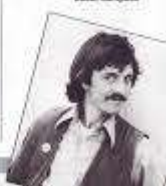
The scary thing that underlies AIDS and the other related diseases is that the patient's natural immune system's ability to fight off disease has somehow been weakened. No one knows for sure why this is happening. It is likely that chronic suppression may be very widespread in urban gay male communities.

How can you protect yourself? Well, I don't want to sound moralistic, but frequent use of "recreational drugs" lowers your immunity. So, too, does having sex with lots of different partners — besides sharing good times you're also likely to be sharing all kinds of germs.

If you see anything suspicious in the last line, slow down. Take care of yourself.

Yes, it's your own business, and only you can decide. But I want you all to be around for next year's Parade and Celebration! And the next.

Edith Campbell



A20 L

RARE CANCER SEEN IN 41 HOMOSEXUALS

Outbreak Occurs Among Men

A Pneumonia That Strikes Gay Males

A mysterious outbreak of a sometimes fatal pneumonia among gay men has occurred in San Francisco and several other major cities, it was revealed yesterday.

24 Eylül 1982

İlk kez **AIDS** terimi kullanıldı

1983



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January 07, 1983 / 31(52):697-8

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Epidemiologic Notes and Reports Immunodeficiency among Female Sexual Partners of Males with Acquired Immune Deficiency Syndrome (AIDS) -- New York

CDC has received reports of two females with cellular immunodeficiency who have been steady sexual partners of males with the acquired immune deficiency syndrome (AIDS).

Case 1: A 37-year-old black female began losing weight and developed malaise in June 1982. In July, she had oral candidiasis and generalized lymphadenopathy and then developed fever, non-productive cough, and diffuse interstitial pulmonary infiltrates. A transbronchial biopsy revealed *Pneumocystis carinii* pneumonia (PCP). Immunologic studies showed elevated immunoglobulin levels, lymphopenia, and an undetectable number of T-helper cells. She responded to antimicrobial therapy, but 3 months after hospital discharge had lymphadenopathy, oral candidiasis, and persistent depletion of T-helper cells.

The patient had no previous illnesses or therapy associated with immunosuppression. She admitted to moderate alcohol consumption, but denied intravenous (IV) drug abuse. Since 1976, she had lived with and had been the steady sexual partner of a male with a history of IV drug abuse. He developed oral candidiasis in March 1982 and in June had PCP. He had laboratory evidence of immune dysfunction typical of AIDS and died in November 1982.

Case 2: A 23-year-old Hispanic female was well until February 1982 when she developed generalized lymphadenopathy. Immunologic studies showed elevated immunoglobulin levels, lymphopenia, decreased T-helper cell numbers, and a depressed T-helper/T-suppressor cell ratio (0.82). Common infectious causes of lymphadenopathy were excluded by serologic testing. A lymph node biopsy showed lymphoid hyperplasia. The lymphadenopathy has persisted for almost a year; no etiology for it has been found.

The patient had no previous illnesses or therapy associated with immunosuppression and denied IV drug abuse. Since the summer of 1981, her only sexual partner has been a bisexual male who

1983



Robert Gallo
Institute of Human Virology



Luc Montagnier



Françoise Barre Sinoussi

Pasteur Enstitüsü

- 20 Mayıs 1983'de Luc Montagnier ve Françoise Barre Sinoussi AIDS etkenini izole ettiler (daha sonra LAV olarak adlandırıldı)
- Kasım 1983'de Robert Gallo AIDS etkenini izole etti (daha sonra HTLV III olarak adlandırıldı)²

¹Barre-Sinoussi F., et al. Science 1983

² Markham PD, et al. Ann N Y Acad Sci. 1984

1984

- Robert Gallo ve ekibi HTLV'yi saptayacak tanı testini keşfetti¹
- Robert Gallo ve Luc Montagnier ortak bir toplantı yaparak buldukları virüslerin birbirinin aynı olduğunu açıkladılar.²

¹Weiss SH et al. JAMA 2014

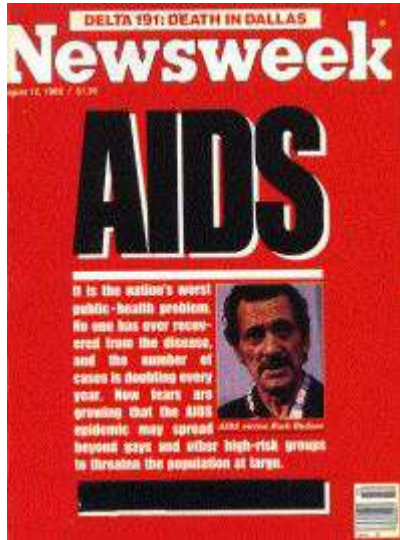
²www.aids.gov

1985



1. Uluslararası AIDS Konferansı Atlanta-Georgia¹

CDC kanların taranması konusunda bir kılavuz yayımladı.²



FDA ilk ticari ELISA testine onay verdi.¹

Rock Hudson AIDS nedeniyle öldü¹

¹www.aids.gov

²MMWR 34(1);1-5 1985

1986

AIDS etkeni virüsün adı **HIV** olarak belirlendi

1987



İlk antiretroviral ilaç FDA onayı aldı¹

WB tanı kiti FDA onayı aldı¹



AIDS Anma Battaniyesi Washington DC'de bir alışveriş merkezinde sergilendi

(1920 panel; günümüzde >48.000)²

AIDS'e karşı ilk aşı insanlar üzerinde denenmeye başlandı.³

¹US Food and Drug Administration. <https://www.fda.gov/ForPatients/Illness/HIVAIDS/History/ucm151074.htm#1987>

²www.aidsquilt.org

³www.aids.gov

1988



1 Aralık
Dünya AIDS Günü

1989



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MMWR

Supplements

June 16, 1989 / 38(5-5):1-9

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Guidelines for Prophylaxis Against *Pneumocystis carinii* Pneumonia for Persons Infected with Human Immunodeficiency Virus



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Supplements

June 23, 1989 / 38(5-6):3-37

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Guidelines for Prevention of Transmission of Human Immunodeficiency Virus and Hepatitis B Virus to Health-Care and Public-Safety Workers A Response to P.L. 100-607 The Health Omnibus Programs Extension Act of 1988

The material in this report was developed by the National Institute for Occupational Safety and Health in collaboration with the Center for Infectious Diseases, Centers for Disease Control.

introduction

1990

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MMWR

Recommendations and Reports

January 26, 1990 / 39(RR01);1-14

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Public Health Service statement on management of occupational exposure to human immunodeficiency virus, including considerations regarding zidovudine postexposure use

The PHS staff members listed below served as authors of this document. CENTERS FOR DISEASE CONTROL Coordinators Jacquelyn A. Polder, B.S.N., M.P.H. David M. Bell, M.D. Edward Baker, M.D., M.P.H. Kenneth Castro, M.D. Mary Chamberland, M.D., M.P.H. James Curran, M.D., M.P.H. Thomas Folks, Ph.D. Julia Garner, R.N., M.N. James Hughes, M.D. Harold Jaffe, M.D. William Jarvis, M.D. Ruthanne Marcus, M.P.H. William Martone, M.D., M.Sc. Robert Mullan, M.D. Gerald Schochetman, Ph.D. NATIONAL INSTITUTES OF HEALTH David Henderson, M.D. Deborah Katz, R.N., M.S. Charles Litterst, Ph.D. John McGowan, Ph.D. Linda ReckJack Whitescarver, Ph.D. FOOD AND DRUG ADMINISTRATION Janet Arrowsmith, M.D. Paul Beninger, M.D. HEALTH RESOURCES AND SERVICES ADMINISTRATION Samuel Matheny, M.D. INTRODUCTION

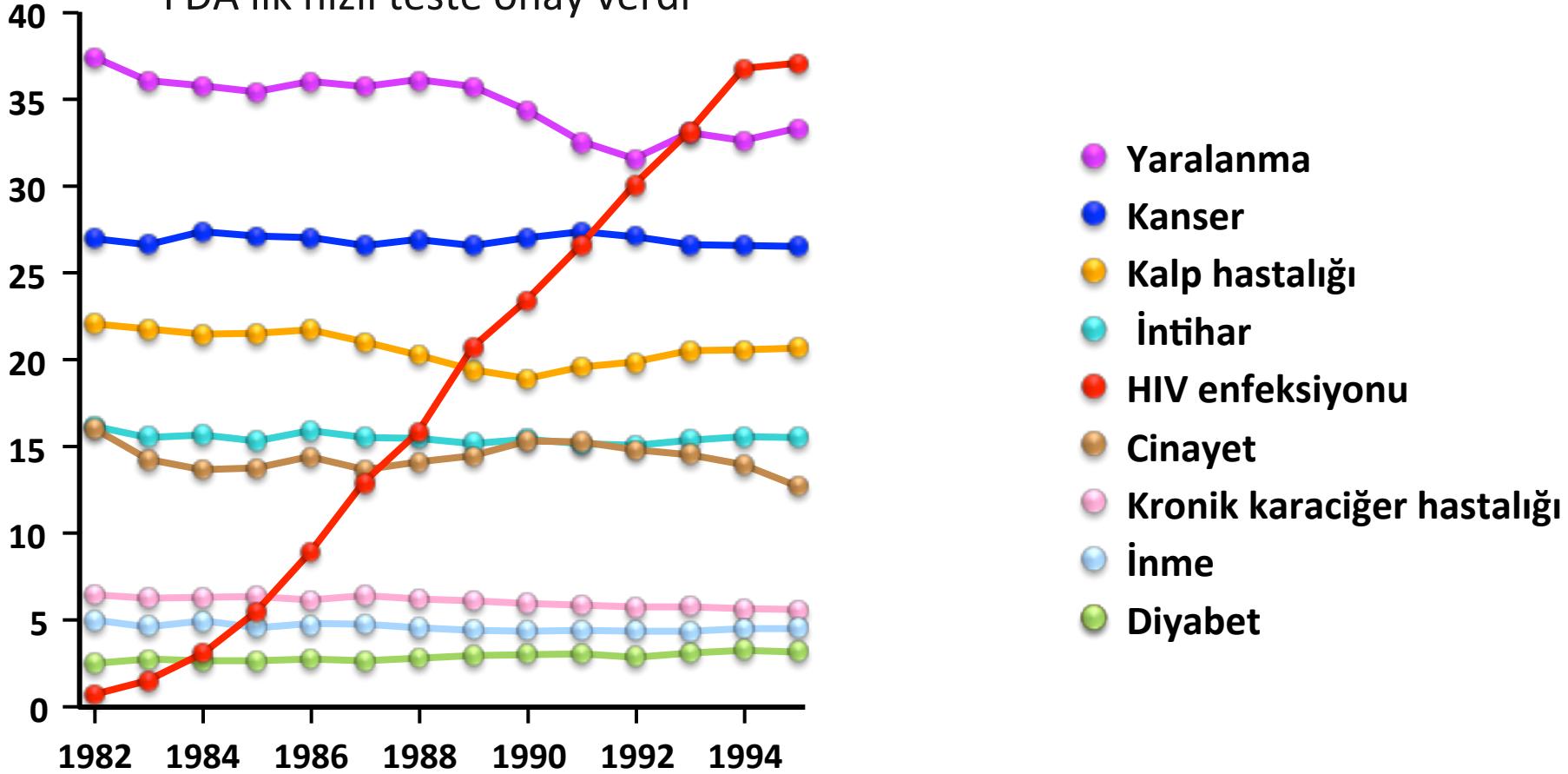


1991



1992

- ABD'de AIDS 25-44 yaş arasındaki **erkeklerde** bir numaralı ölüm nedeni oldu
- FDA ilk hızlı teste onay verdi



1993

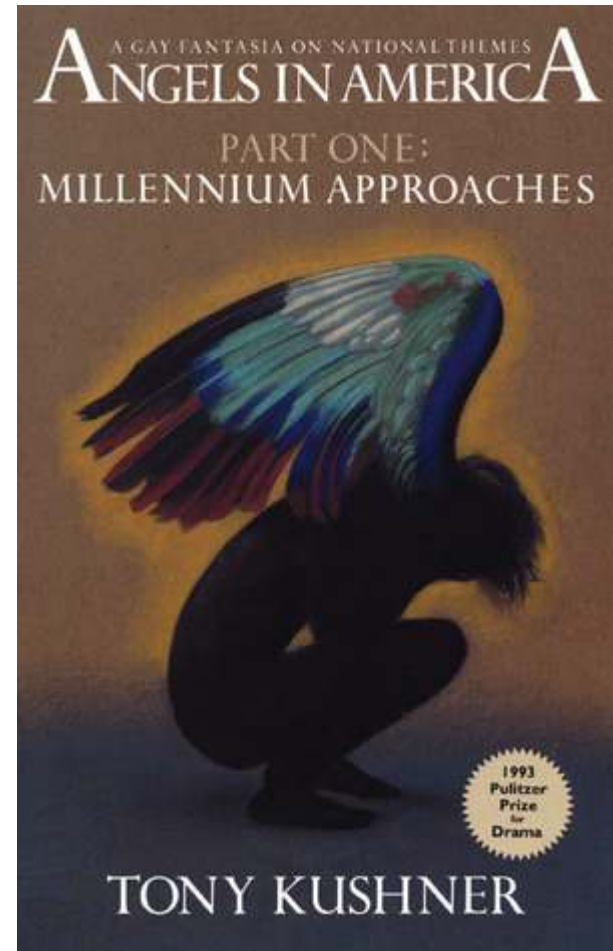




AIDS konulu ilk film
Philadelphia

www.aids.gov

1993

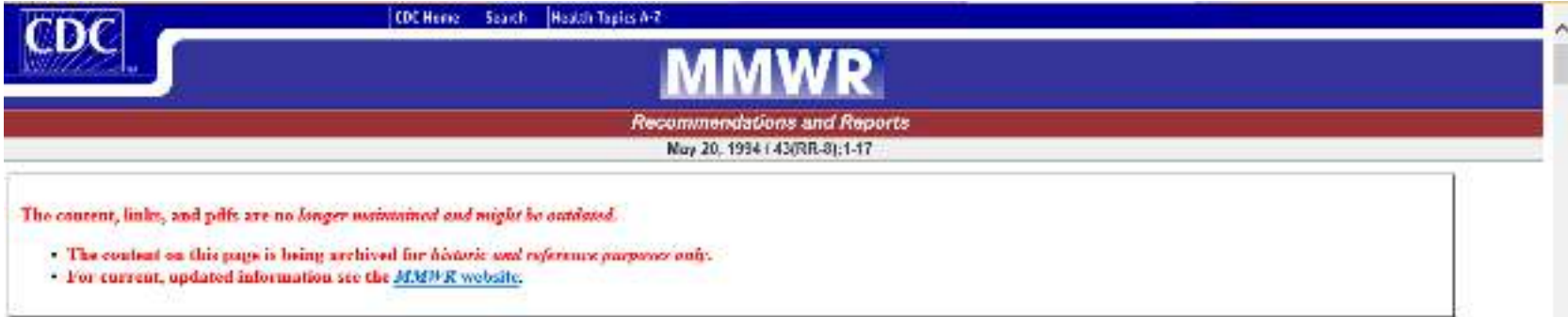


1994

AIDS ABD'de yaşayan 25-44 yaş arasındaki **tüm bireylerde** ölümün önde gelen nedeni oldu¹

Perinatal bulaşmanın önlenmesi için AZT kullanımı önerildi²

İlk tükürük testi FDA tarafından onaylandı³



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Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissue and Organs

The following CDC staff members prepared this report:

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Wanda K. Jones, Dr.P.H. Office of the Associate Director for HIV/AIDS

¹www.aids.gov

²CDC. MMWR Morb Mortal Wkly Rep. 1994

³US Food and Drug Administration. <https://www.fda.gov/ForPatients/Illness/HIVAIDS/History/ucm151079.htm#9>

1995

İlk proteaz inhibitörü FDA tarafından onaylandı¹



Dr. David Ho

«Hit early, hit hard»

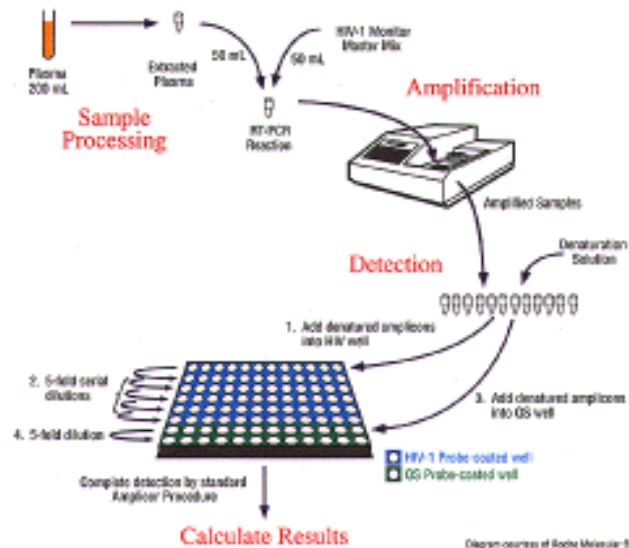
¹US Food and Drug Administration. <https://www.fda.gov/ForPatients/Illness/HIVAIDS/History/ucm151079.htm#9>

²Ho DD. New Engl J Infect 1995

1996



How Viral Load Is Measured by HIV RNA Assay



www.aids.gov

1996



Karma ART

1997



Karma ART standart tedavi yaklaşımı oldu¹

İlk karma preparat (Combivir) FDA onayı aldı²

CDC ABD'de ölümlerin azaldığını bildirdi³

Proteaz inhibitörlerine karşı direnç gelişmeye başladı¹

Dünya üzerinde HIV ile yaşayan 30 milyon insan olduğu tahmin ediliyor⁴

¹www.aids.gov

²US Food and Drug Administration. <https://www.fda.gov/ForPatients/Illness/HIVAIDS/History/ucm151079.htm#9>

³Centers for Disease Control and Prevention. www.cdc.gov.

⁴www.unaids.org

1998



Guidelines for the Use of Antiretroviral Agents in
HIV-1-Infected Adults and Adolescents

1999



HIV dünyada ölüm nedenleri arasında dördüncü, Afrika'da birinci sırada¹

Vaxgen aşı çalışması Tayland'da başlatıldı²

¹www.who.int

²www.aids.gov

2000



2015

**MILLENNIUM
DEVELOPMENT GOALS**



2001

Declaration of Commitment on HIV/AIDS

UNITED NATIONS GENERAL ASSEMBLY
SPECIAL SESSION ON HIV/AIDS
25 - 27 JUNE 2001



United Nations

1. İnsanların enfeksiyondan korunmak için ne yapmaları gerektiğini bilmelerini sağlamak
2. Anneden bebeğe bulaşı engellemek
3. Enfekte olan herkesin tedaviye ulaşmasını sağlamak
4. Hastalığa çare ve aşı bulmak için iki kat daha fazla çalışmak
5. Yaşamları AIDS nedeniyle sarsılmış tüm insanlara yardım etmek

<http://www.unaids.org>

2001

- Jenerik ilaç üreticilerinin az gelişmiş ülkeler için düşük fiyatlı ilaç üretimi
- Diğer firmaların az gelişmiş ülkeler için fiyatları düşürmeleri
- Doha Deklarasyonu— gelişmekte olan ülkelere jenerik ilaç satın alma ve üretme hakkının verilmesi



2002



The Global Fund

To Fight AIDS, Tuberculosis and Malaria

Hükümetler, sivil toplum örgütleri, özel sektör ve etkilenen toplumların ortaklığı ile kuruldu

www.theglobalfund.org

2002



Parmak kanında hızlı test kiti FDA onayı aldı¹

Yan etkiler ve artan ilaç direnci nedeniyle «hit early hit hard» stratejisi sorgulanmaya başlandı²

¹US Food and Drug Administration. <https://www.fda.gov/ForPatients/Illness/HIVAIDS/History/ucm151079.htm#9>

²www.aids.gov

2003



5 yıllık 15 milyon dolarlık plan



www.aids.gov
www.who.int

DSÖ üyesi 192 ülkenin işbirliği ile başlatıldı

2003

- Vaxgen Faz III çalışması sonlandı
 - Tayland'da 2546 DiİB
 - Kuzey Amerika ve Avrupa'da 5417 eşcinsel
- Plaseboya göre HIV enfeksiyonunda %3,8 oranında azalma
- Aşının koruyucu hiçbir etkisi yok

<http://www.vaxreport.org/Back-Issues/Pages/VaxGenreleasesresultsofThaiPhaseIIItrial.aspx>

Daniel J. DeNoon. Unsurprising and Surprising Results of VaxGen's HIV Vaccine Trial: An Expert Interview With Mark Feinberg, MD, PhD. Medscape. Feb 28, 2003.

2004

- Hızlı testte tükürük kullanımı FDA tarafından onaylandı
- FDA sabit dozlu kombinasyonların onay sürecini hızlandırdı

2005



The Global Fund

To Fight AIDS, Tuberculosis and Malaria



World Health
Organization



UNAIDS

Tedaviye ulaşan insan sayısı

2004 sonu itibariyle

700 000

www.theglobalfund.org

www.who.int

www.unaids.org

2006 HIV/AIDS'in 25. yılı



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Recommendations and Reports

September 22, 2006 / 55(RR14):1-17

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Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings

Prepared by

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³Northrup Grumman Information Technology (contractor with CDC)

2006

Anatomic Pathology / HIV-1 TARGET CELLS IN FORESKIN

HIV-1 Target Cells in Foreskins of African Men With Varying Histories of Sexually Transmitted Infections

Betty A. Donoval,¹ Alan L. Landay, PhD,² Stephen Moses, MD, PhD,³ Kawango Agot, PhD,⁴ J.O. Ndinya-Achola, MBChB,⁵ Edith A. Nyagaya,⁴ Ian MacLean, PhD,³ and Robert C. Bailey, PhD¹

Key Words: HIV-1; Foreskin; Circumcision; Immunohistochemistry

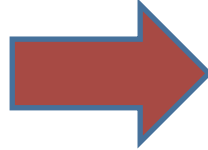
DOI: 10.1309/JVHQVDJDYKMS6EPH

CYBE olan (s:20) ve olmayan (s: 19) erkeklerin sünnet derileri incelenmiş
CYBE öyküsü olanlarda Langerhans hücreleri ve makrofajların sayısı daha yüksek
Sünnet derisinin mukozal yüzeyinde bulunan bu hücreler kişiyi HIV'e daha duyarlı kılıyor

2007

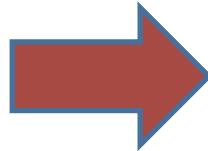
HIV ile yaşıyan bireylerin sayısında 2006'ya göre %16 azalma.

Angola
Hindistan
Mozambik
Nijerya



HIV epidemisine ilişkin kestirim yöntemlerinin deęiştirilmesi

Kenya
Zimbabve



Riskli davranışlardaki azalmaya baęlı olarak yeni enfeksiyon sayılarının azalması

Prevention of Rectal SHIV Transmission in Macaques by Daily or Intermittent Prophylaxis with Emtricitabine and Tenofovir

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Funding: Measurement of drug levels by RFS was supported in part by National Institutes of Health (NIH) Centers for AIDS Research (CFAR) grant 5P30-AI50409 and by the Department of Veterans Affairs. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: Authors JGGL, RAO, RJ, TMF, and WH are named in a US Government patent application related to methods for HIV prophylaxis.

Academic Editor: Andrew Carr, St. Vincent's Hospital, Australia

ABSTRACT

Background

In the absence of an effective vaccine, HIV continues to spread globally, emphasizing the need for novel strategies to limit its transmission. Pre-exposure prophylaxis (PrEP) with antiretroviral drugs could prove to be an effective intervention strategy if highly efficacious and cost-effective PrEP modalities are identified. We evaluated daily and intermittent PrEP regimens of increasing antiviral activity in a macaque model that closely resembles human transmission.

Methods and Findings

We used a repeat-exposure macaque model with 14 weekly rectal virus challenges. Three drug treatments were given once daily, each to a different group of six rhesus macaques

**Son 10 yılda
yeni enfeksiyonlarda
%17 azalma**

Dođu Asya'da %25 artış



2009



The NEW ENGLAND JOURNAL of MEDICINE

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CME ▶

ORIGINAL ARTICLE

BRIEF REPORT

Long-Term Control of HIV by *CCR5* Delta32/Delta32 Stem-Cell Transplantation

Gero Hütter, M.D., Daniel Nowak, M.D., Maximilian Mossner, B.S., Susanne Ganepola, M.D., Arne Müßig, M.D., Kristina Allers, Ph.D., Thomas Schneider, M.D., Ph.D., Jörg Hofmann, Ph.D., Claudia Kücherer, M.D., Olga Blau, M.D., Igor W. Blau, M.D., Wolf K. Hofmann, M.D., and Eckhard Thiel, M.D.

N Engl J Med 2009; 360:692-698 | [February 12, 2009](#) | DOI: 10.1056/NEJMoa0802905

2010



NIH Public Access

Author Manuscript

Science. Author manuscript; available in PMC 2011 September 3.

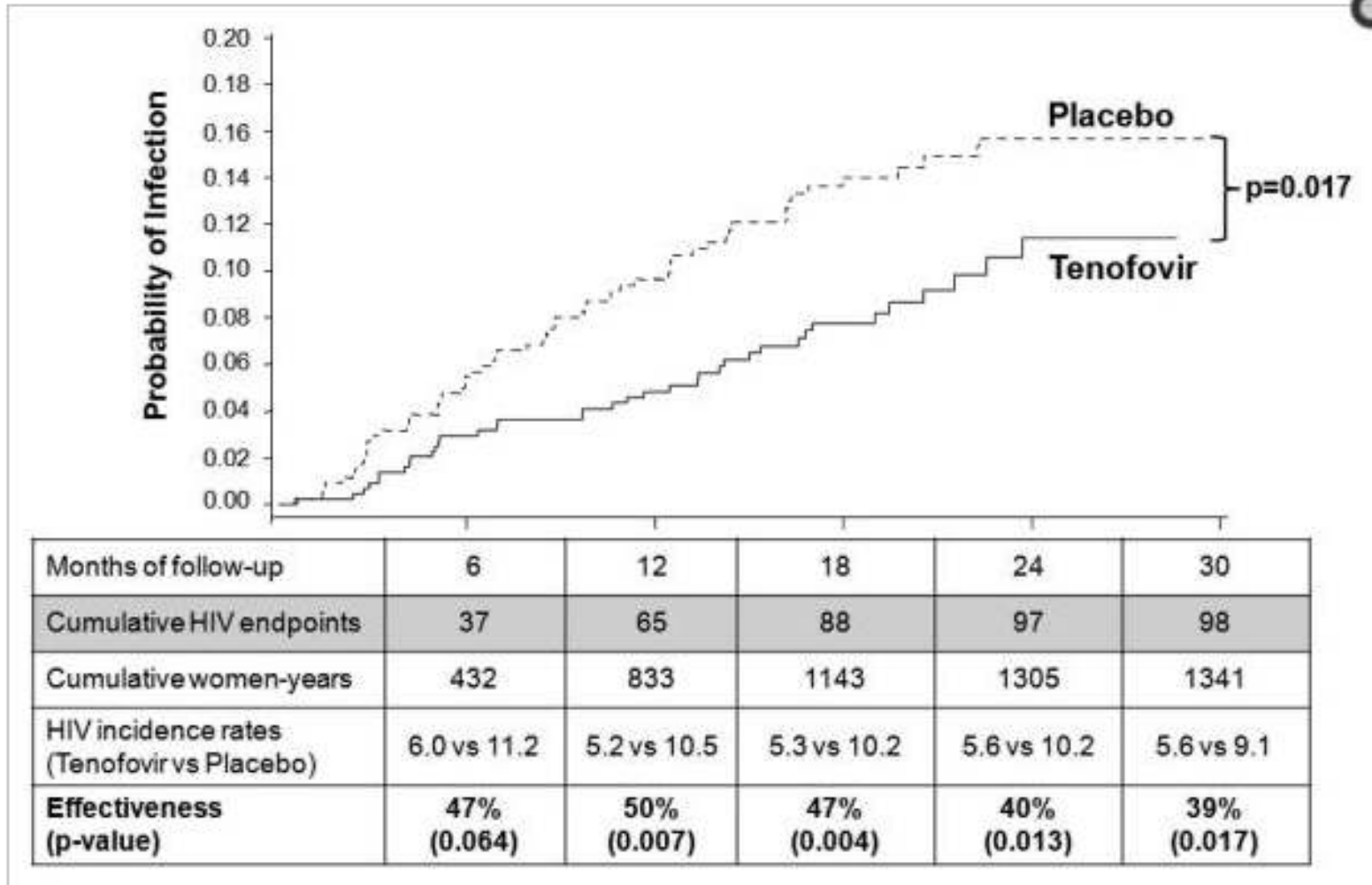
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Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

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HIV'in edinilme riskinde %39 (tam uyumla kullananlarda %54) azalma Figure 2



İnsidans TDF kolunda 5.6/100 kadın yılı, plasebo kolunda 9.1/100 kadın yılı

2010



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N Engl J Med. Author manuscript; available in PMC 2011 June 30.

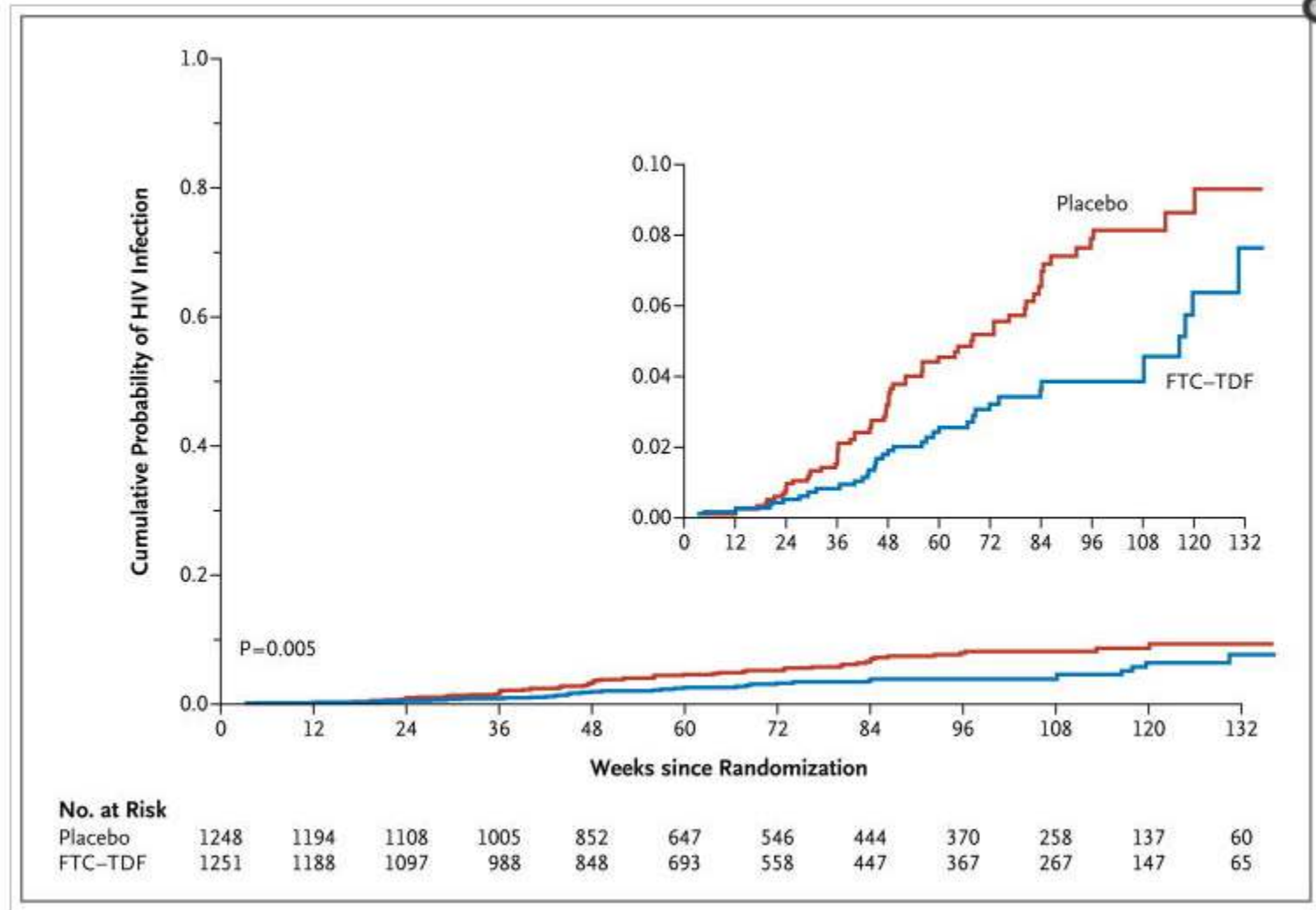
Published in final edited form as:

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Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm. D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martin Casapia, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr. P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B. Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R. Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D. for the iPrEx Study Team

Figure 2

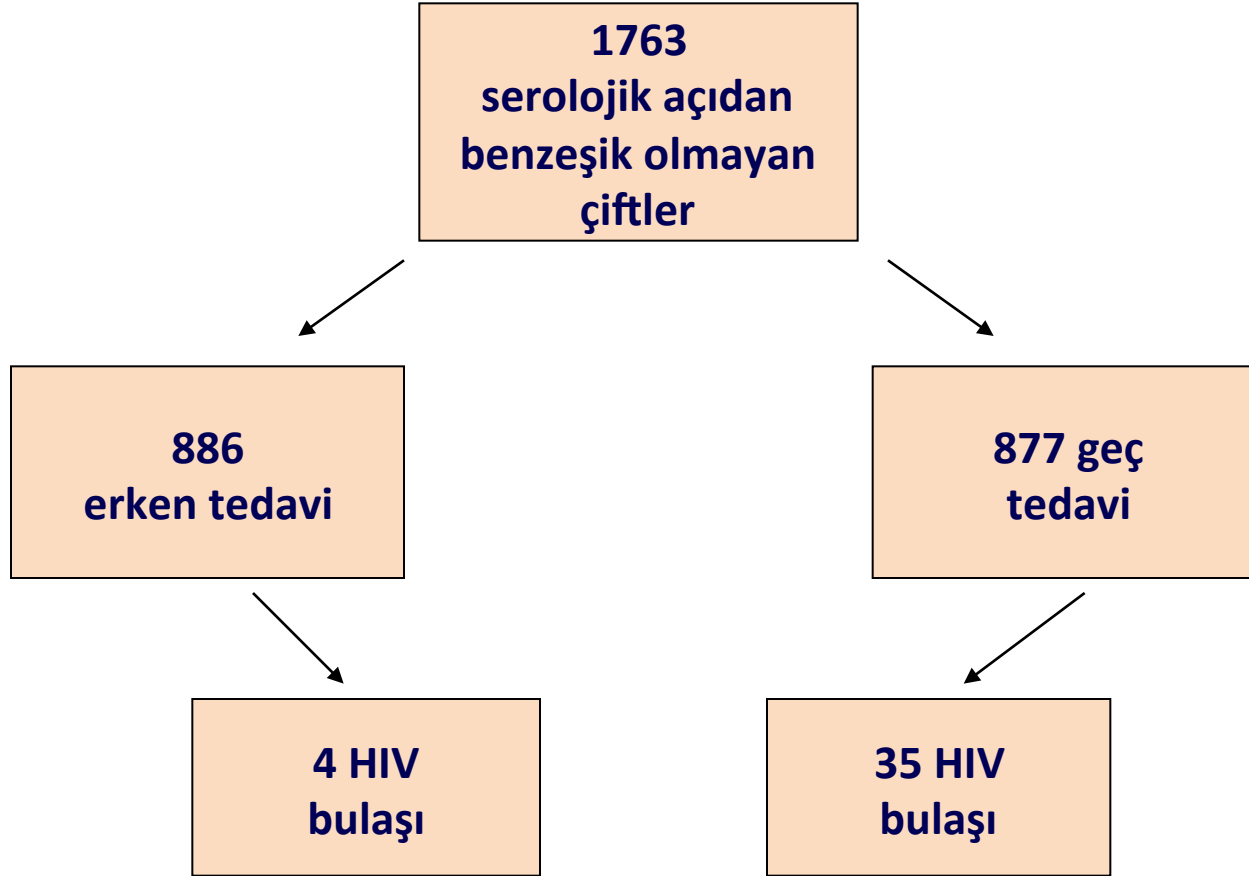


Kaplan–Meier Estimates of Time to HIV Infection (Modified Intention-to-Treat Population)

TDF-FTC alan grupta HIV enfeksiyonunda %44 azalma

2011

HPTN 052 alıřması



P=0.0001

(HPTN 052)

	Erken (s=886)	Geç (s=877)	
Başlangıçtaki CD4 ortanca (ÇDG)	442 (373–522)	428 (357–522)	
Başlangıçtaki viral yük ortanca ÇDG	4.4 (3.8–4.9)	4.4 (3.9–4.9)	
Yaş (indeks eş)	33	32	
Evli	%94	%95	
Korunmasız ilişki	%6	%8	
Bağlantılı geçişler (s)	1	27	HR 0.04 (%95 GA: 0.01–0.28)
DSÖ Evre IV olaylar, pulmoner TB, ağır bakteriyel enf. veya ölüm (s=hasta)	40 (her HY için 2.4)	65 (her HY için 4.0)	HR 0.59, %95 GA: (0.40, 0.88), p=0.01
TB (s=olay)	17	33	
Ekstrapulmoner TB (s)	3	17	p<0.002
Ölüm	10	13	HR 0.77, %95 GA: (0.34, 1.76), p>0.5
İstenmeyen olay	%24	%5	



2011

From www.bloodjournal.org by guest on November 27, 2016. For personal use only.

CLINICAL TRIALS AND OBSERVATIONS

Evidence for the cure of HIV infection by CCR5 Δ 32/ Δ 32 stem cell transplantation

Kristina Allers,¹ Gero Hütter,² Jörg Hofmann,³ Christoph Loddenkemper,⁴ Kathrin Rieger,² Eckhard Thiel,² and Thomas Schneider¹

¹Department of Gastroenterology, Infectious Diseases, and Rheumatology, Medical Clinic I, Campus Benjamin Franklin, Charité-University Medicine Berlin, Berlin, Germany; ²Department of Hematology, Oncology, and Transfusion Medicine, Medical Clinic III, Campus Benjamin Franklin, Charité-University Medicine Berlin, Berlin, Germany; ³Institute of Medical Virology, Helmut-Ruska-Haus, Campus Mitte, Charité-University Medicine Berlin, Berlin, Germany; and ⁴Institute of Pathology/Research Center ImmunoSciences (RCIS), Campus Benjamin Franklin, Charité-University Medicine Berlin, Berlin, Germany

2012



NIH Public Access Author Manuscript

N Engl J Med Author manuscript; available in PMC 2013 September 11.

Published in final edited form as:

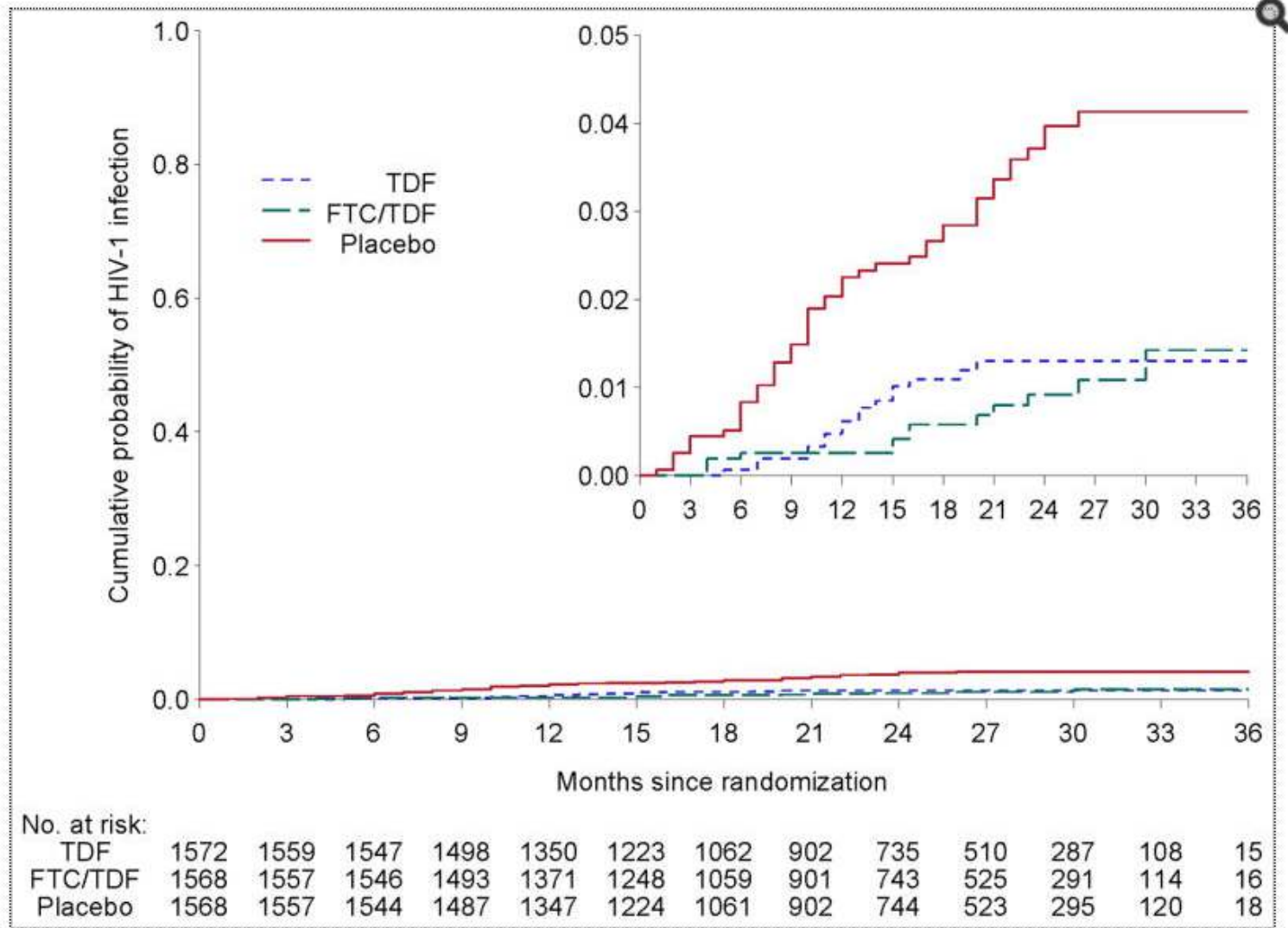
N Engl J Med. 2012 August 2; 367(5): 399–410. doi:10.1056/NEJMoal108524.

Antiretroviral Prophylaxis for HIV-1 Prevention among Heterosexual Men and Women

Jared M. Baeten, M.D., Ph.D., Deborah Donnell, Ph.D., Patrick Ndase, M.B., Ch.B., M.P.H., Nelly R. Mugo, M.B., Ch.B., M.P.H., James D. Campbell, M.D., M.S., Jonathan Wangisi, M.B., Ch.B., M.Sc., Jordan W. Tappero, M.D., M.P.H., Elizabeth A. Bukusi, M.B., Ch.B., Ph.D., Craig R. Cohen, M.D., M.P.H., Elly Katabira, M.B., Ch.B., Allan Ronald, M.D., Elioda Tumwesigye, M.B., Ch.B., M.S., Edwin Were, M.B., Ch.B., M.P.H., Kenneth H. Fife, M.D., Ph.D., James Kiarie, M.B., Ch.B., M.P.H., Carey Farquhar, M.D., M.P.H., Grace John-Stewart, M.D., Ph.D., Aloysious Kania, M.B., Ch.B., Josephine Odoyo, M.P.H., Akasiima Mucunguzi, M.B., Ch.B., Edith Nakku-Joloba, M.B., Ch.B., Ph.D., Rogers Twesigye, M.B., Ch.B., M.P.H., Kenneth Ngure, M.P.H., Cosmas Apaka, B.Sc., Harrison Tamoooh, M.B., Ch.B., Fridah Gabona, M.B., Ch.B., Andrew Mujugira, M.B., Ch.B., M.Sc., Dana Panteleeff, B.S., Katherine K. Thomas, M.S., Lara Kidoguchi, M.P.H., Meighan Krows, B.A., Jennifer Revall, B.A., Susan Morrison, M.D., M.P.H., Harald Haugen, M.S., Mira Emmanuel-Ogier, B.A., Lisa Ondrejcek, M.A., Robert W. Coombs, M.D., Ph.D., Lisa Frenkel, M.D., Craig Hendrix, M.D., Namandjé N. Bumpus, Ph.D., David Bangsberg, M.D., M.P.H., Jessica E. Haberer, M.D., M.P.H., Wendy S. Stevens, M.D., F.C.Path., Jairam R. Lingappa, M.D., Ph.D., and Connie Celum, M.D., M.P.H. for the Partners PrEP Study Team*

NIH-PA Author Manuscript

NIH-PA Author



Kaplan-Meier curve for the primary modified intention-to-treat analysis

Plaseboya göre HIV-1 insidansında TDF ile %67, TDF-FTC ile %75 azalma;
ilaç rejimleri arasındaki fark anlamlı değil

2012

Key Updates to Existing Sections

Following are key updates to existing sections of the guidelines.

Initiating Antiretroviral Therapy in Treatment-Naive Patients

The Panel updated its recommendations on initiation of ART in treatment-naive patients. The changes are primarily based on increasing evidence showing the harmful impact of ongoing HIV replication on AIDS and non-AIDS disease progression. In addition, the updated recommendations reflect emerging data showing the benefit of effective ART in preventing secondary transmission of HIV. The updated section includes more in-depth discussion on the rationale for these recommendations and on the risks and benefits of long-term ART.

The Panel's recommendations are listed below.

- ART is recommended for all HIV-infected individuals. The strength of this recommendation^a varies on the basis of pretreatment CD4 cell count:
 - CD4 count <350 cells/mm³ (AI)
 - CD4 count 350 to 500 cells/mm³ (AII)
 - CD4 count >500 cells/mm³ (BIII)
- Regardless of CD4 count, initiation of ART is strongly recommended for individuals with the following conditions:
 - Pregnancy (AI) (see [perinatal guidelines](#) for more detailed discussion)
 - History of an AIDS-defining illness (AI)
 - HIV-associated nephropathy (HIVAN) (AII)
 - HIV/hepatitis B virus (HBV) coinfection (AII)

2012

TDF+FTC temas öncesi korunmada kullanılmak üzere FDA onayı aldı



2013

Dünyada 35 milyon kişinin HIV ile yaşadığı tahmin ediliyor

2001-2013 arasında yeni HIV enfeksiyonları %38 azaldı

www.aids.gov
www.unaids.gov

2020'ye dek

90%

of all



living with HIV will
know their HIV
status

90%

of all



living with HIV will
receive sustained
antiretroviral
therapy

90%

of all



receiving
antiretroviral therapy
will have durable viral
suppression

2015

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 27, 2015

VOL. 373 NO. 9

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

ABSTRACT

BACKGROUND

Data from randomized trials are lacking on the benefits and risks of initiating antiretroviral therapy in patients with asymptomatic human immunodeficiency virus (HIV) infection who have a CD4+ count of more than 350 cells per cubic millimeter.

METHODS

We randomly assigned HIV-positive adults who had a CD4+ count of more than 500 cells per cubic millimeter to start antiretroviral therapy immediately (immediate-initiation group) or to defer it until the CD4+ count decreased to 350 cells per cubic millimeter or until the development of the acquired immunodeficiency syndrome (AIDS) or another condition that dictated the use of antiretroviral therapy (deferred-initiation group). The primary composite end point was any serious AIDS-related event, serious non-AIDS-related event, or death from any cause.

RESULTS

A total of 4685 patients were followed for a mean of 3.0 years. At study entry, the median HIV viral load was 12,759 copies per milliliter, and the median CD4+ count was 651 cells per cubic millimeter. On May 15, 2015, on the basis of an interim analysis, the data and safety monitoring board determined that the study question had been answered and recommended that patients in the deferred-initi-

The members of the writing group (Jens D. Lundgren, M.D. [cochair], Abdel G. Babiker, Ph.D. [cochair], Fred Gordin, M.D. [cochair], Sean Emery, Ph.D., Birgit Grund, Ph.D., Shweta Sharma, M.S., Anchalee Avihingsanon, M.D., David A. Cooper, M.D., Gerd Fätkenheuer, M.D., Josep M. Libre, M.D., Jean-Michel Molina, M.D., Paula Munderi, M.D., Mauro Schechter, M.D., Robin Wood, M.D., Karin L. Klingman, M.D., Simon Collins, H. Clifford Lane, M.D., Andrew N. Phillips, Ph.D., and James D. Neaton, Ph.D. [INSIGHT PI]) of the INSIGHT START Study Group assume responsibility for the overall content and integrity of this article. The affiliations of the members of the writing group are listed in the Appendix. Address reprint requests to Dr. Lundgren at the Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark, or at jens.lundgren@regionh.dk.



End Point	Immediate-Initiation Group (N=2326)		Deferred-Initiation Group (N=2359)		Hazard Ratio (95% CI) †	P Value
	no.	no./100 person-yr	no.	no./100 person-yr		
Composite primary end point	42	0.60	96	1.38	0.43 (0.30–0.62)	<0.001
Components of the primary end point						
Serious AIDS-related event	14	0.20	50	0.72	0.28 (0.15–0.50)	<0.001
Serious non-AIDS-related event	29	0.42	47	0.67	0.61 (0.38–0.97)	0.04
Death from any cause	12	0.17	21	0.30	0.58 (0.28–1.17)	0.13
Tuberculosis	6	0.09	20	0.28	0.29 (0.12–0.73)	0.008
Kaposi's sarcoma	1	0.01	11	0.16	0.09 (0.01–0.71)	0.02
Malignant lymphoma	3	0.04	10	0.14	0.30 (0.08–1.10)	0.07
Cancer not related to AIDS	9	0.13	18	0.26	0.50 (0.22–1.11)	0.09
Cardiovascular disease	12	0.17	14	0.20	0.84 (0.39–1.81)	0.65
Other secondary end points						
Grade 4 event ‡	73	1.06	73	1.05	1.01 (0.73–1.39)	0.97
Unscheduled hospitalization §	262	4.02	287	4.40	0.91 (0.77–1.08)	0.28
Grade 4 event, unscheduled hospitalization, or death from any cause	283	4.36	311	4.78	0.91 (0.77–1.07)	0.25
Most common grade 4 events, unscheduled hospitalization, or death from any cause ¶						
Bacterial infectious disorder	14	0.20	36	0.52	0.38 (0.20–0.70)	0.002
Bone or joint injury	17	0.24	11	0.16	1.55 (0.73–3.31)	0.26
Depressed mood disorder or disturbance	12	0.17	9	0.13	1.34 (0.57–3.19)	0.50
Infection with unspecified pathogen	64	0.93	65	0.94	0.99 (0.70–1.40)	0.96
Injury not elsewhere classified	11	0.16	22	0.31	0.50 (0.24–1.03)	0.06
Suicidal or self-injurious behavior not elsewhere classified	27	0.39	24	0.34	1.15 (0.66–1.99)	0.63
Viral infectious disorder	12	0.17	15	0.21	0.81 (0.38–1.72)	0.58
Grade 4 event, unscheduled hospitalization, or primary end point	295	4.56	355	5.52	0.82 (0.71–0.96)	0.01

Special Communication

**Antiretroviral Treatment of Adult HIV Infection
2014 Recommendations
of the International Antiviral Society-USA Panel**

Background: In addition to the published WHO antiretroviral treatment guidelines, the International Antiviral Society-USA Panel (IAS-USA Panel) published its 2014 recommendations for the antiretroviral treatment of HIV infection. The IAS-USA Panel's recommendations are based on the most up-to-date evidence, including data from clinical trials, observational studies, and expert opinion.

- Recommendation 1.1:** For individuals with HIV infection, treatment should be initiated with a fully suppressive first-line antiretroviral regimen consisting of two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), a third NRTI, and an integrase strand transfer inhibitor (INSTI).
- Recommendation 1.2:** For individuals with HIV infection, the first-line regimen should include a nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone with a third NRTI and an INSTI, through both oral and intravenous routes. The choice of INSTI should be based on the quality of evidence and the patient's clinical characteristics.
- Recommendation 1.3:** For individuals with HIV infection, the first-line regimen should include a nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone with a third NRTI and a protease inhibitor (PI), through both oral and intravenous routes. The choice of PI should be based on the quality of evidence and the patient's clinical characteristics.
- Recommendation 1.4:** For individuals with HIV infection, the first-line regimen should include a nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone with a third NRTI and a boosted protease inhibitor (PI), through both oral and intravenous routes. The choice of boosted PI should be based on the quality of evidence and the patient's clinical characteristics.
- Recommendation 1.5:** For individuals with HIV infection, the first-line regimen should include a nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone with a third NRTI and a non-nucleoside reverse transcriptase inhibitor (NNRTI), through both oral and intravenous routes. The choice of NNRTI should be based on the quality of evidence and the patient's clinical characteristics.


World Health Organization
 **English**




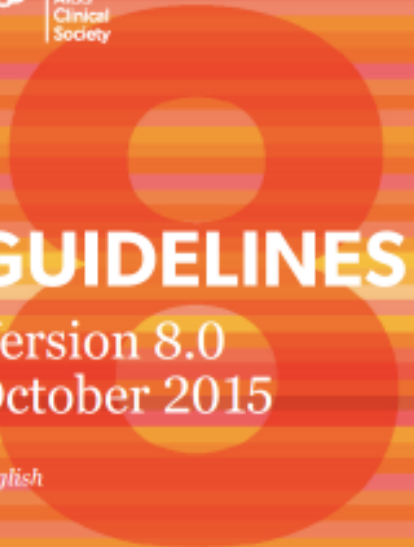
GUIDELINES 

**GUIDELINE ON WHEN
TO START ANTIRETROVIRAL
THERAPY AND
ON PRE-EXPOSURE
PROPHYLAXIS FOR HIV**

SEPTEMBER 2015



EACS
European
AIDS
Clinical
Society



GUIDELINES

Version 8.0
October 2015

English

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Statement by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents Regarding Results from the START and TEMPRANO Trials

The findings of the two trials (the START and TEMPRANO) were highly influential in determining the current standard of care for HIV infection. The findings of the START and TEMPRANO trials have been widely cited in the medical literature. The findings of the START and TEMPRANO trials have been widely cited in the medical literature. The findings of the START and TEMPRANO trials have been widely cited in the medical literature.

With the availability of the START and TEMPRANO trial results, the Panel's recommendation on when to start ART is now based on the findings of the START and TEMPRANO trials. However, the strength of the recommendation will be changed to a strong recommendation based on data from observational studies and expert opinion.

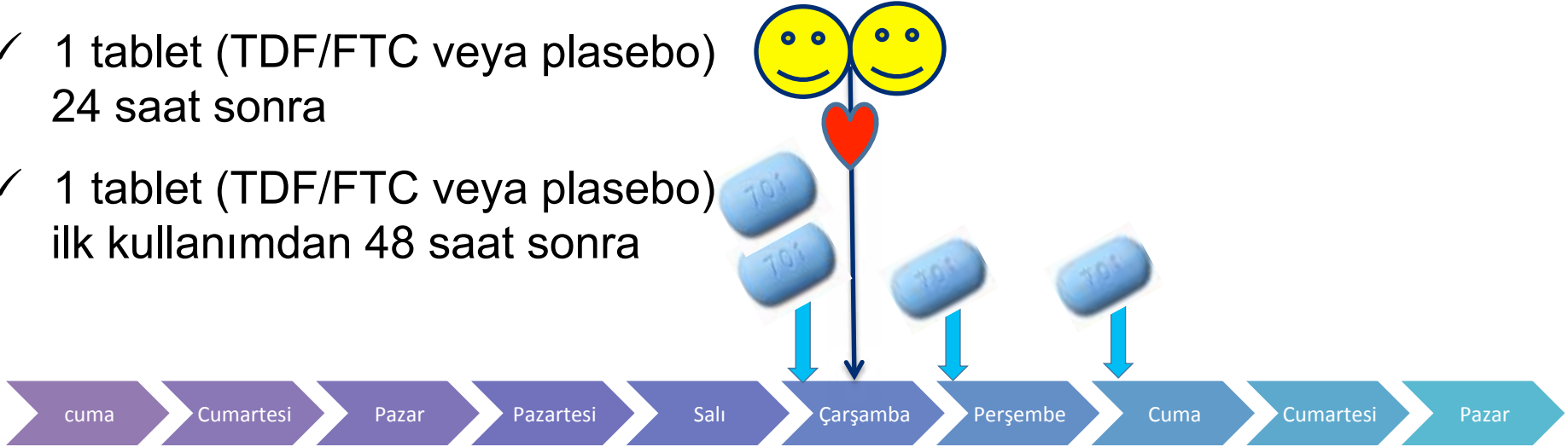
The additional benefit of not increasing the risk of HIV transmission further, and beyond the overall public health value of the recommendation, is the benefit of not increasing the risk of HIV transmission further, and beyond the overall public health value of the recommendation.

It should be noted that neither of these trials included data on the impact of pre-exposure prophylaxis (PrEP) on HIV transmission. However, the findings of the START and TEMPRANO trials have been widely cited in the medical literature. The findings of the START and TEMPRANO trials have been widely cited in the medical literature.

2015

IPERGAY Cinsel eylemle bağlantılı TÖP

- ✓ 2 tablet (TDF/FTC veya plasebo) seksten 2-24 saat önce
- ✓ 1 tablet (TDF/FTC veya plasebo) 24 saat sonra
- ✓ 1 tablet (TDF/FTC veya plasebo) ilk kullanımdan 48 saat sonra

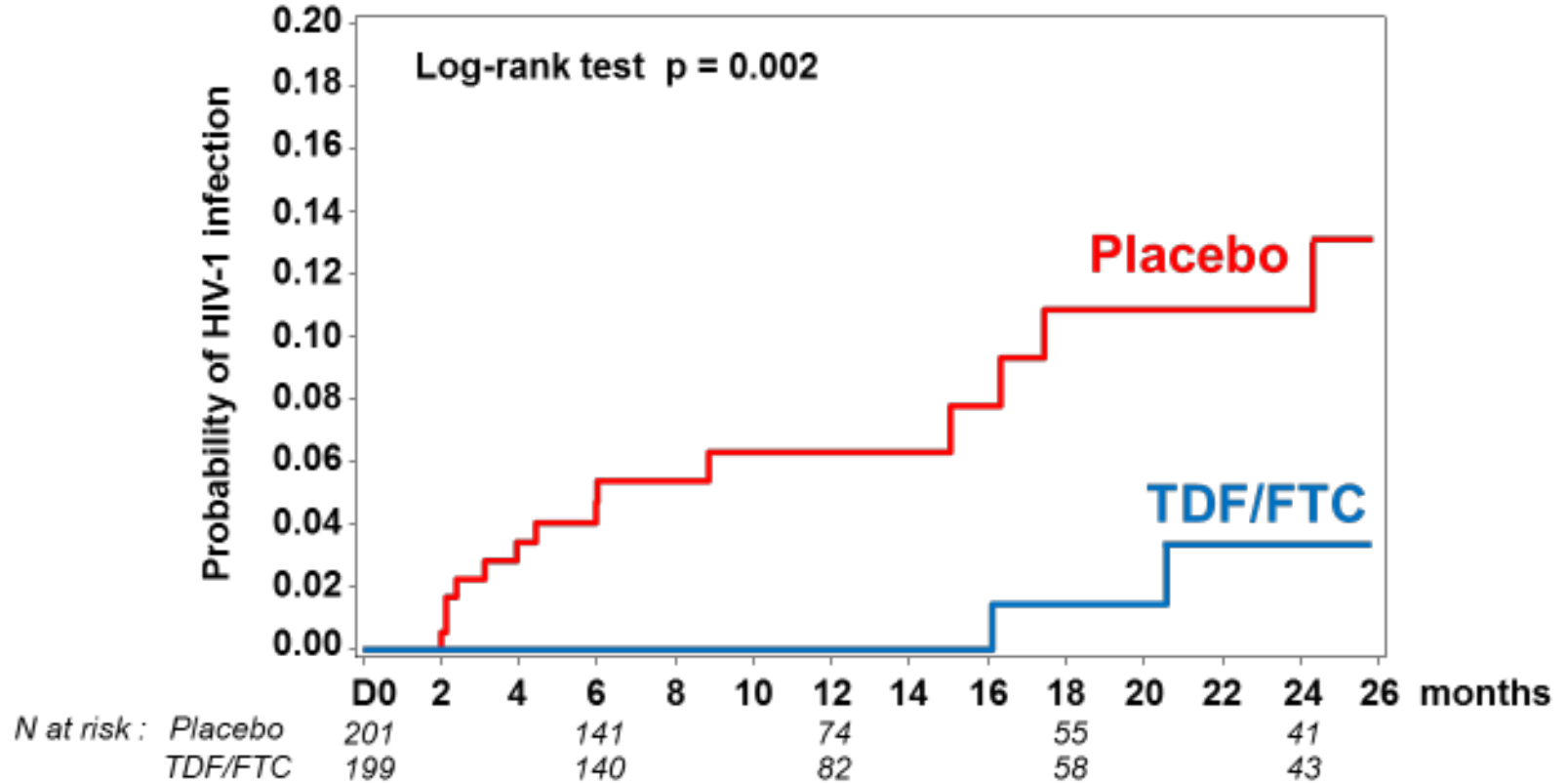


Tek cinsel ilişkiyi kapsamak için 3 gün içinde 4 tablet TDF/FTC



ipergay
ANRS
Intervention Préventive
de l'Exposition aux Risques
avec et pour les Gays

HIV-1 enfeksiyonuna kadar geçen zaman için KM kestirimleri (mITT toplumu)



Ortalama izlem süresi 13 ay: 16 katılımcıda yeni enfeksiyon
14 plasebo kolunda (insidans: 6,6 / 100 KY), **2 TDF/FTC kolunda** (insidans: 0,94 / 100 KY)
Direnç mutasyonu saptanmamış

HIV-1 insidansında %86 görece azalma (%95 GA: 40-99, $p=0,002$)
Bir enfeksiyonu önlemek için bir yıl boyunca tedavi edilmesi gereken kişi sayısı: **18**



**PRe-exposure Option for HIV
prevention in the UK: immediate or
Derferred**

<http://www.proud.mrc.ac.uk/>

HIV İnsidansı

Grup	Enf. sayısı	İzlem (KY)	İnsidans (her 100 KY)	%90 GA
Tüm grup	22	453	4,9	3,4–6,8
Hemen	3 (+2*)	239	1,3	0,4–3,0
Ertelenen	19 (+1**)	214	8,9	6,0–12,7

Etkinlik =%86 (%90 GA: %58 – 96)

P değeri =0,0002

Oran farkı =7,6 (%90 GA: 4,1 – 11,2)

Profilaksi alması gerekenler =13 (%90 GA: 9–25)

* 2 olgu ilk taramada pozitif bulunmuş

** 1 olgu ilk taramada pozitif bulunmuş

2016

Original Investigation

Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy

Alison J. Rodger, MD; Valentina Cambiano, PhD; Tina Bruun, RN; Pietro Vernazza, MD; Simon Collins; Jan van Lunzen, PhD; Giulio Maria Corbelli; Vicente Estrada, MD; Anna Maria Geretti, MD; Apostolos Beloukas, PhD; David Asboe, FRCP; Pompeyo Viciana, MD; Félix Gutiérrez, MD; Bonaventura Clotet, PhD; Christian Pradier, MD; Jan Gerstoft, MD; Rainer Weber, MD; Katarina Westling, MD; Gilles Wandeler, MD; Jan M. Prins, PhD; Armin Rieger, MD; Marcel Stoeckle, MD; Tim Kummerle, PhD; Teresa Bini, MD; Adriana Ammassari, MD; Richard Gilson, MD; Ivanka Krznaric, PhD; Matti Ristola, PhD; Robert Zangerle, MD; Pia Handberg, RN; Antonio Antela, PhD; Sris Allan, FRCP; Andrew N. Phillips, PhD; Jens Lundgren, MD; for the PARTNER Study Group

14 Avrupa ülkesinden 75 klinik

548 heteroseksüel çift
~36000 kondomsuz
cinsel ilişki

340 ESE
>22000 kondomsuz
cinsel ilişki

Bağlantılı geçiş hiç yok

**RISK OF SEXUAL TRANSMISSION OF HIV FROM A PERSON LIVING WITH
HIV WHO HAS AN UNDETECTABLE VIRAL LOAD**
Messaging Primer & Consensus Statement

(U)ndetectable=(U)ntransmissible
Belirlenemez viral yük=Bulaş yok

2017

RAPID COMMUNICATIONS

Fall in new HIV diagnoses among men who have sex with men (MSM) at selected London sexual health clinics since early 2015: testing or treatment or pre-exposure prophylaxis (PrEP)?

AE Brown^{1,2}, H Mohammed^{1,2}, D Ogaz¹, PD Kirwan¹, M Yung¹, SG Nash¹, M Furegato¹, G Hughes¹, N Connor¹, VC Delpech¹, ON Gill¹

1. HIV & STI Department, Centre for Infectious Disease Surveillance and Control (CIDSC), Public Health England, London, United Kingdom
2. These authors contributed equally to this work and share first authorship

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Citation style for this article:

Brown AE, Mohammed H, Ogaz D, Kirwan PD, Yung M, Nash SG, Furegato M, Hughes G, Connor N, Delpech VC, Gill ON. Fall in new HIV diagnoses among men who have sex with men (MSM) at selected London sexual health clinics since early 2015: testing or treatment or pre-exposure prophylaxis (PrEP)? *Euro Surveill.* 2017;22(25):pii=30553. DOI: <http://dx.doi.org/10.2807/1560-7917.ES.2017.22.25.30553>

Article submitted on 12 June 2017 / accepted on 20 June 2017 / published on 22 June 2017

Ekim 2015 Eylül 2016 arasında ESE’de HIV tanısında %32 azalma (Ekim 2014– Eylül 2015 dönemine kıyasla).

HIV testlerinde artış ve tanı alanlara hemen ART başlanması ve TÖP kullanılması ile bağlantılı

NEWS RELEASES

Monday, March 5, 2018

Broadly neutralizing antibody treatment may target viral reservoir in monkeys

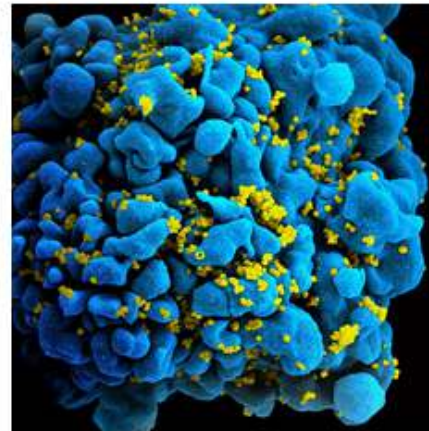
NIH-supported scientists find combination therapy suppresses HIV-like virus in primates.



After receiving a course of antiretroviral therapy for their HIV-like infection, approximately half of a group of monkeys infused with a broadly neutralizing antibody to HIV combined with an immune stimulatory compound suppressed the virus for six months without additional treatment, according to scientists supported in part by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. The therapy may have targeted the viral reservoir — populations of long-lived, latently infected cells that harbor the virus and that lead to resurgent viral replication when suppressive therapy is discontinued.

The new findings may inform strategies that attempt to achieve sustained, drug-free viral remission in people living with HIV. Researchers discussed their results today at a press conference at the 25th Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

"HIV excels at evading the immune system by hiding out in certain immune cells. The virus can be suppressed to very low levels with antiretroviral therapy, but quickly rebounds to high levels if a person stops taking medications as prescribed," said Anthony S. Fauci, M.D., NIAID Director. "The findings from this early stage research offer further evidence that achieving sustained viral remission without daily medication might be possible. This potential application is yet another



HIV-infected T cell. NIAID

Institute/Center

National Institute of Allergy and Infectious Diseases (NIAID)

Contact

Judith Lavelle
301-402-1663

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PGT121 Combined with GS-9620 Delays Viral Rebound in SHIV-Infected Rhesus Monkeys. E Borducchi, et al. Conference on Retroviruses and Opportunistic Infections, March 6, 2018.

Then Now Future

Fifteen years of progress and hope. But miles to go to end the AIDS epidemic by 2030—new milestones to reach, barriers to break and frontiers to cross.

People living with HIV on antiretroviral therapy

1 million
15 million
All people living with HIV

2001 2015 2030

New HIV infections

3 million
2 million
0.2 million

2001 2014 2030

AIDS-related deaths

2.0 million
1.2 million
0.2 million

2004 2014 2030

Investments for AIDS response

4.9 US\$ billion
21.7 US\$ billion
32 US\$ billion

2001 2015 2020



The
New England
Journal of Medicine

VOLUME 373

DECEMBER 3, 2015

NUMBER 23

Ending the HIV-AIDS Pandemic – Follow the Science

AS Fauci & HD Marston

*“...The science has spoken. There can now be
no excuse for inaction.”*



«...Bilim sözünü söyledi. Artık harekete geçmemenin hiçbir mazereti olamaz.»