

13th Annual Conference of the
National HIV Nurses Association (NHVNA)



National HIV Nurses Association

Nicky Perry
Brighton and Sussex University
Hospitals NHS Trust

16-17 June 2011, Arena and Convention Centre, Liverpool

**Ten Key Lessons from HIV
Research**

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Brighton and Sussex
University Hospitals
NHS Trust

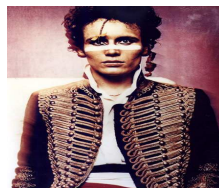
HIV epidemic at 30 years The Early Years



June 5th 1981



Jade Goody was born



Adam Ant was UK number 1 with Stand and Deliver

1981: Israel bombs Baghdad nuclear reactor

Israel shocks the world by destroying the Osirak nuclear plant near the Iraqi capital for fear it would be used to make atom bombs.

Pneumocystis Pneumonia --- Los Angeles - Microsoft Internet Explorer

Address http://www.cdc.gov/mmwr/preview/mmwrhtml/june_5.htm

CDC Home Search Health Topics A-Z

MMWR

Weekly

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

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.

Downloading picture <http://mhrcs.cdc.gov/b/ss/cdcgov/1/6.5-Pd-5/943723420536115?AQ8&srch=1&t=10/5/2011%2013%3A10%3A3%205%20-6>

start Microsoft Act... NHVNA 2011 Conference 2... Ten key lesso... FRINGE 16.5... Pneumocysts... EN Search Desktop 13:10

A Cluster of Kaposi's Sarcoma and Pneumocystis carinii Pneumonia among Homosexual Male Resident - Microsoft Internet Explorer

Address <http://www.cdc.gov/mmwr/preview/mmwrhtml/00001114.htm>

CDC Home Search Health Topics A-Z

MMWR

Weekly

June 18, 1982 / 31(23);305-7

A Cluster of Kaposi's Sarcoma and Pneumocystis carinii Pneumonia among Homosexual Male Residents of Los Angeles and Orange Counties, California

In the period June 1, 1981-April 12, 1982, CDC received reports of 19 cases of biopsy-confirmed Kaposi's sarcoma (KS) and/or Pneumocystis carinii pneumonia (PCP) among previously healthy homosexual male residents of Los Angeles and Orange counties, California. Following an unconfirmed report of possible associations among cases in southern California, interviews were conducted with all 8 of the patients still living and with the close friends of 7 of the other 11 patients who had died.

Data on sexual partners were obtained for 13 patients, 8 with KS and 5 with PCP. For any patient to be considered as a sexual contact of another person, the reported exposures of that patient had to be either substantiated or not denied by the other person involved in the relationship (or by a close friend of that person).

Within 5 years of the onset of symptoms, 9 patients (6 with KS and 3 with PCP) had had sexual contact with other patients with KS or PCP. Seven patients from Los Angeles County had had sexual contact with other patients from Los Angeles County, and 2 from Orange County had had sexual contact with 1 patient who was not a resident of California. Four of the 9 patients had been exposed to more than 1 patient who had KS or PCP. Three of the 6 patients with KS developed their symptoms after sexual contact with persons who already had symptoms of KS. One of these 3 patients developed symptoms of KS 9 months after sexual contact, another patient developed symptoms 13 months after contact, and a third patient developed symptoms 22 months after contact.

The other 4 patients in the group of 13 had no known sexual contact with reported cases. However, 1 patient with KS had an apparently healthy sexual partner in common with 2 persons with PCP; 1 patient with KS reported having had sexual contact with 2 friends of the non-Californian with KS; and 2 patients with PCP had most of their anonymous contacts (greater than or equal to 80%) with persons in bathhouses attended frequently by other persons in Los Angeles with KS or PCP.

Done, but with errors on page.

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Piecing things together..

- First link of HIV being blood borne virus
- Pattern of unusual symptoms in patients, the task force named the condition acquired immune deficiency syndrome (AIDS)
- Risk groups for HIV emerging
 - Heterosexuals
 - Infants of infected mothers
 - Haemophilliacs
 - Injecting Drug Users
- Fear and denial even among the medical profession to discuss HIV/AIDS

YG

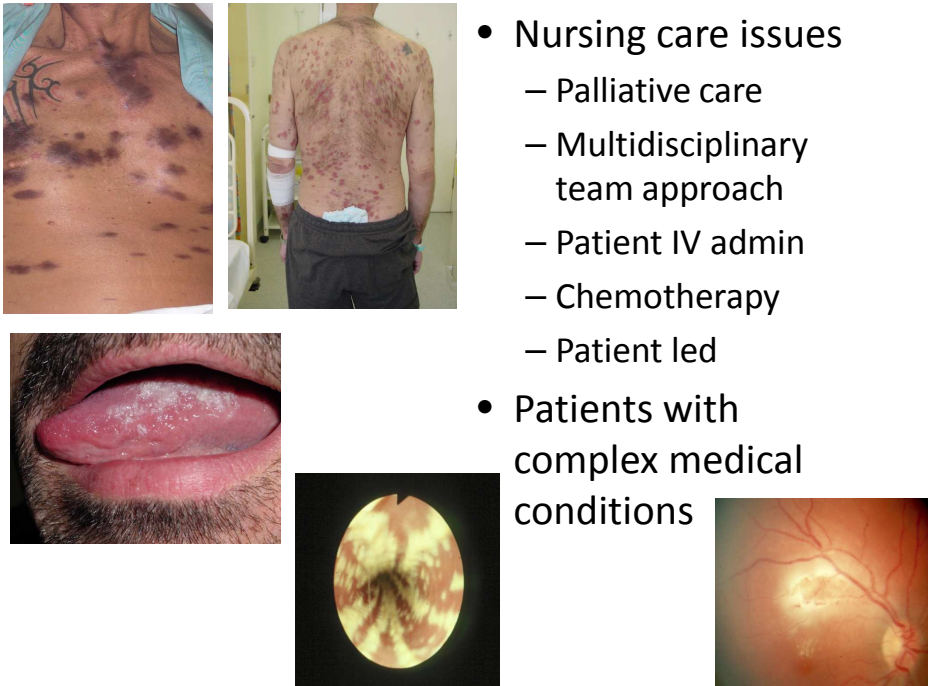
In 1984, Science published two separate articles in the same issue

- Robert Gallo claimed that a virus from an AIDS patient was strikingly similar in shape to other human T-cell viruses (HTLVs) and called his newly isolated virus HTLV-III
- Luc Montagnier isolated a virus from a gay man patient with swollen lymph nodes different from HTLV-I. They named their isolated virus lymphadenopathy-associated virus (LAV)
- HIV was chosen as a compromise between the two claims (LAV and HTLV-III) Montagnier was awarded half a Nobel Prize



Luc Montagnier (left) and Robert Gallo.

YG



- Nursing care issues
 - Palliative care
 - Multidisciplinary team approach
 - Patient IV admin
 - Chemotherapy
 - Patient led
- Patients with complex medical conditions

Lesson 1

1989 – ACTG 019

- Halted after 1 year
- AZT seemed to delay progression of disease



HIV epidemic at 30 years
The Middle Years





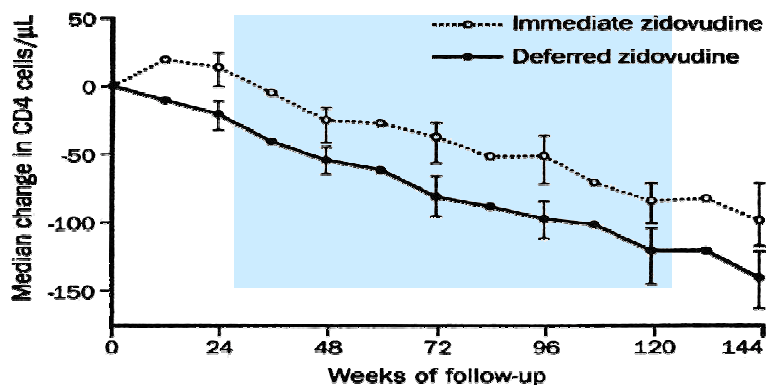
Lesson 2

Concorde Study

Concorde Study

Double-blind RCT:

- Immediate: (n=877) AZT 2004
- Deferred (PBO): (n=872) 'til ARC/AIDS/persistent low CD4



Number with results		Weeks of follow-up					
Immediate	721	695	643	592	557	482	
Deferred	730	703	638	594	560	468	

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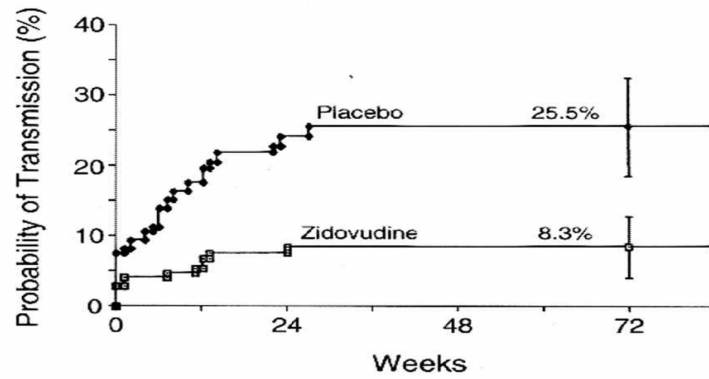
Concorde Coordinating Committee. Lancet 1994; 343(8902): 871-881.

Lesson 3

ACTG 076

Mother to Child Transmission

1994 a door is opened
Antiretrovirals work to prevent transmission!



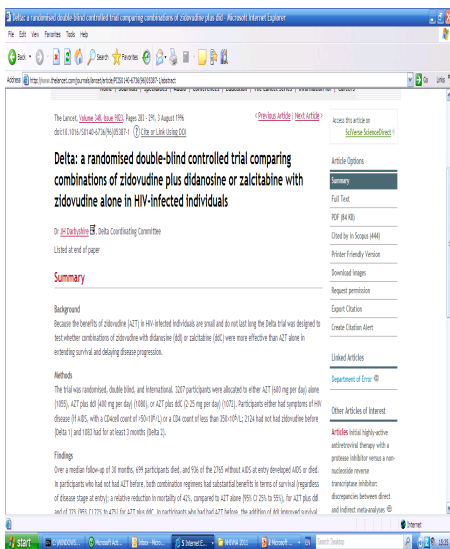
Placebo	183	84	42	37
Zidovudine	180	105	51	43

Connor EM, Sperling RS, Gelber R et al. for The Pediatric AIDS Clinical Trials Group **Protocol 076**
 Study Group *New England Journal of Medicine* 1994; 331:1173-1180.

Lesson 4

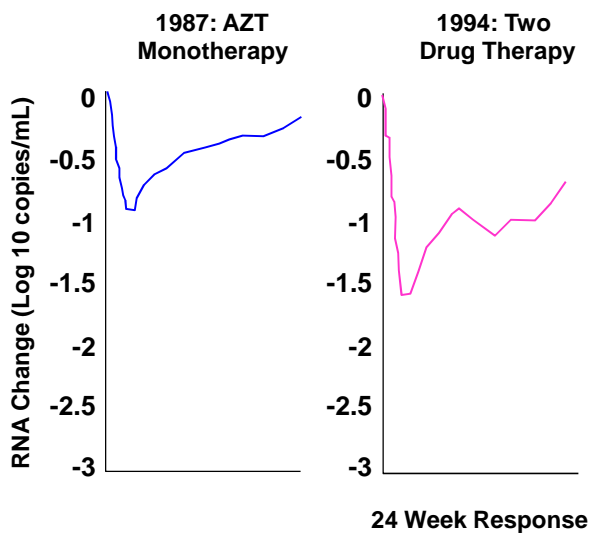
Combination therapy

Delta Study



Results

- 3,000 patients
- Prolongs life and delays disease progression



Lesson 5

Viral load testing
Protease Inhibitors
Triple Therapy

World AIDS Conference
Vancouver 1996....
...the era of triple-therapy with PIs
begins



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The Battle....



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Early PIs – dosing

- Saquinavir¹
 - 600mg TID
- Indinavir²
 - 800mg every 8 hours
- Ritonavir³
 - 600mg (liquid) BID

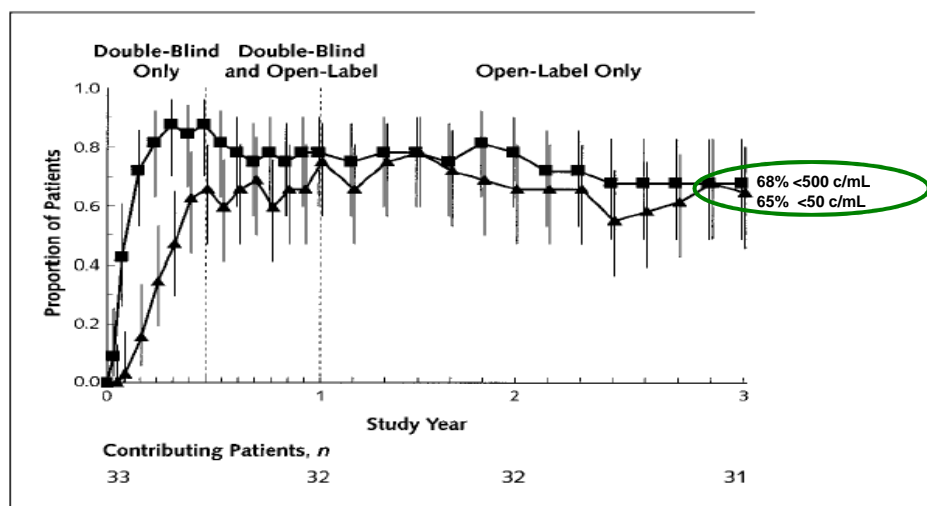
1. Vella S et al. *Antivir Ther* 1996;1(3):129-140.
2. Gulick RM et al. *N Engl J Med* 1997; 337(11): 734-739.
3. Cameron DW for the Advanced HIV Disease Ritonavir Study Group. *Lancet* 1998; 351: 543-549.

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Lesson 6

Protease Inhibitors work!

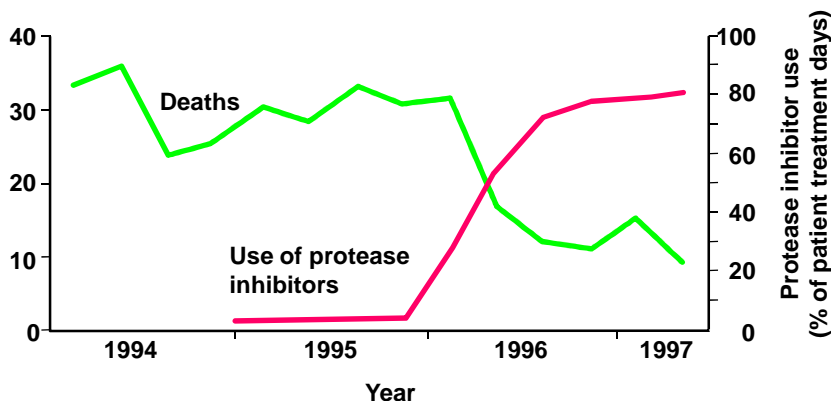
Figure 1. Proportion of patients with serum HIV RNA levels less than 500 copies/mL and less than 50 copies/mL during 3 years of treatment with indinavir, zidovudine, and lamivudine.



Squares represent proportions with levels less than 500 copies/mL; triangles represent proportions with levels less than 50 copies/mL; error bars represent 95% CIs.

Impact on Death

HIV-infected subjects with <100 CD4⁺ cells/mm³



N Engl J Med 1998; 338: 853-860

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U.S. House rejects homophobia
Hefley amendment to overturn executive order goes down to defeat.
page 19

Banner days
More on the just-completed Gay Games from Amsterdam.
page 22 - 23

Perversely pretty
Photographer Pierre Molinar in Santa Monica.
see Arts section

BAY AREA REPORTER

Vol. 28 • No. 33 • 13 August 1998

Serving the Gay & Lesbian Community for more than 27 years

No obits

by Timothy Rodrigues

Readers of the *Bay Area Reporter* who regularly scan the obituary page for familiar faces — friends, ex-lovers, former tricks, that gay you used to see at the gym who has not been around for a while — will have to forgo that ritual this week. No obituaries were filed with the paper for this issue, a first since the AIDS epidemic exploded in San Francisco's gay community.

That doesn't mean that there were no AIDS deaths in the past week; next week's issue may have more obits than usual. Nevertheless, after more than 17 years of struggle and death, and some weeks with as many as 21 obituaries printed in the *B.A.R.*, it seems a new ritual may be taking hold, and the community may be on the verge of a new era of the epidemic. Perhaps.

"It is certainly refreshing, and I think we deserve a break like that. By the same token, it is hard to imagine that it will last forever," Dana Van Gorden, director of gay and lesbian

health for the Department of Public Health (DPH), told the *B.A.R.* "We all deserve a little bit of respite," he continued.

Derek Gordon, director of communications for the San Francisco AIDS Foundation (SFAF), who has been living with HIV for many years, talked about scanning the obituary page, looking to see who died, and feeling "it was just a matter of time before I would see my own fate."

"Remember my granddaddy said he knew he was getting near death because he used to scan the obits," he told the *B.A.R.* "I used to think how tragic because I was doing the same thing at 30."

Gordon cautioned that the decrease in the number of obituaries reflects a parallel trend in his personal experience. He said he no longer feels the same sense of "demon and dagger," and added, "I don't have any (recent) obits to personally read."

Dick Fabich, AIDS policy adviser to Mayor Willie Brown, and someone who has lived with AIDS for many years, has had the opposite personal experience. He has recently had two close friends die of AIDS, something he says he has not

had to deal with for some time.

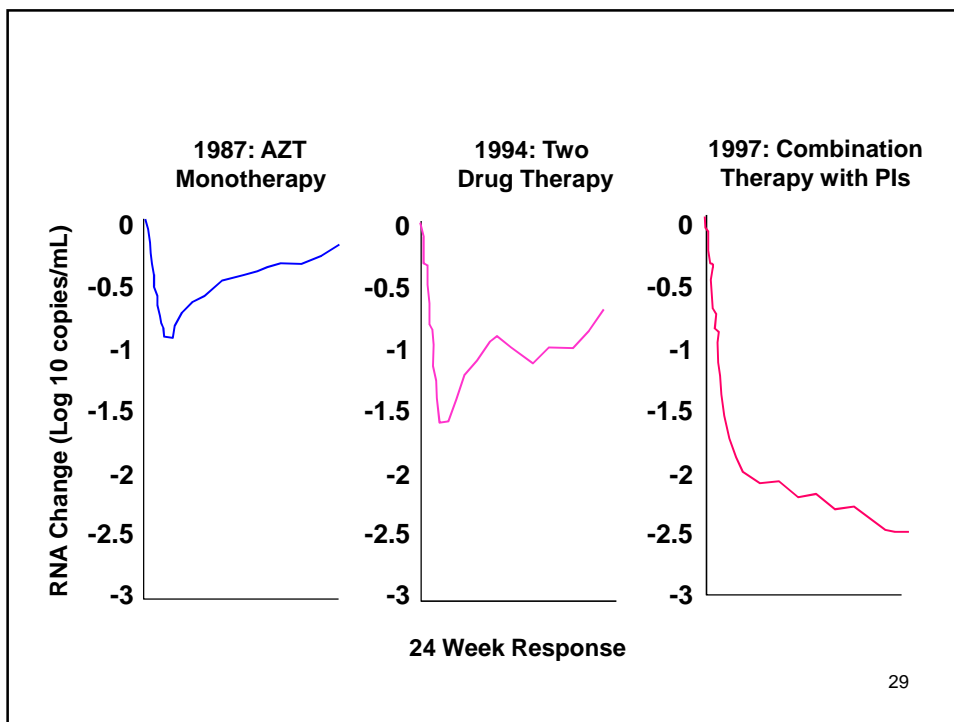
"I have frankly had a concern that we are seeing a shift in the opposite direction," he said, mentioning an increase in the number of people he knows who have died, gotten infected by HIV, or been diagnosed.

While acknowledging that the lack of obituaries is symbolically very important, Fabich warned that it is important not to overstate the situation and said there should be no loosening of efforts to fight the epidemic.

If current estimates are correct, 15 people may have been infected by HIV in the last week, and it is estimated that 15,000 people living in San Francisco are HIV-positive.

Although scientists, reporters, and government officials have commented that AIDS deaths have been declining since the introduction of new anti-HIV drug regimens, several of those mentioned mentioned that many people cannot obtain, choose not to take, or do not benefit from currently available treatment options. Also, the incidence of HIV/AIDS is increasing among youth, people of color, women, and the het-

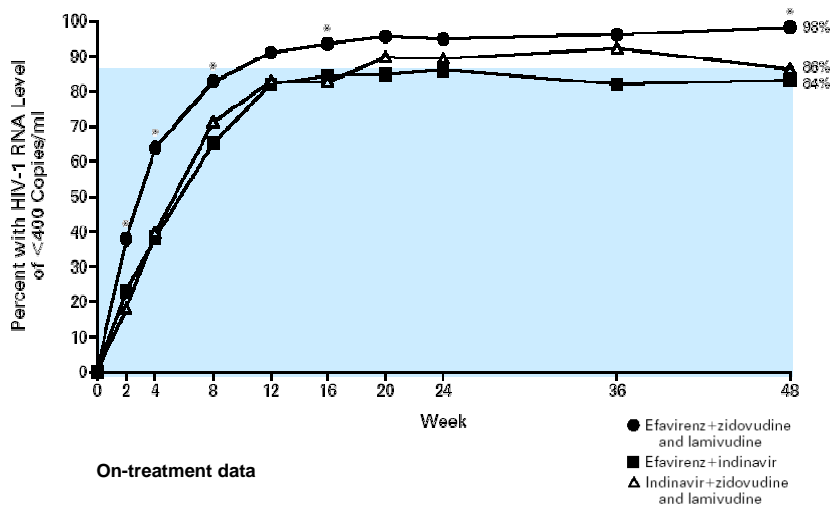
page 17



Lesson 7

The third class

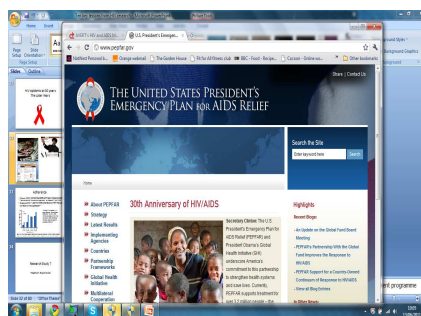
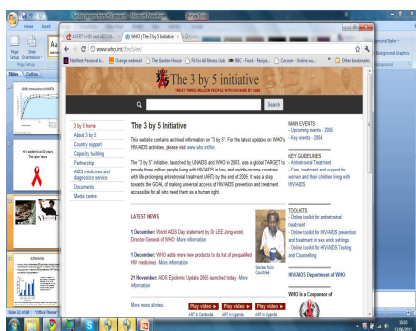
1998: Introduction of NNRTIs



32

Staszewski S et al. N Engl J Med 1999; 341(25): 1865-1873.

HIV epidemic at 30 years The Later Years

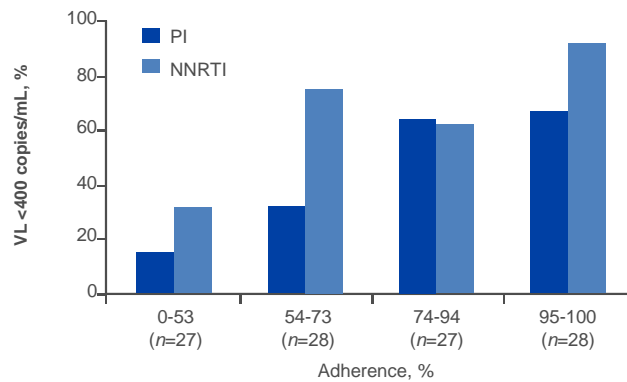


Adherence

- Paterson 2000 – “*adherence ≥ 95% optimises virologic outcome*”

¹ Based on data from Rx-experienced populations on unboosted PI and 2 NUCs²

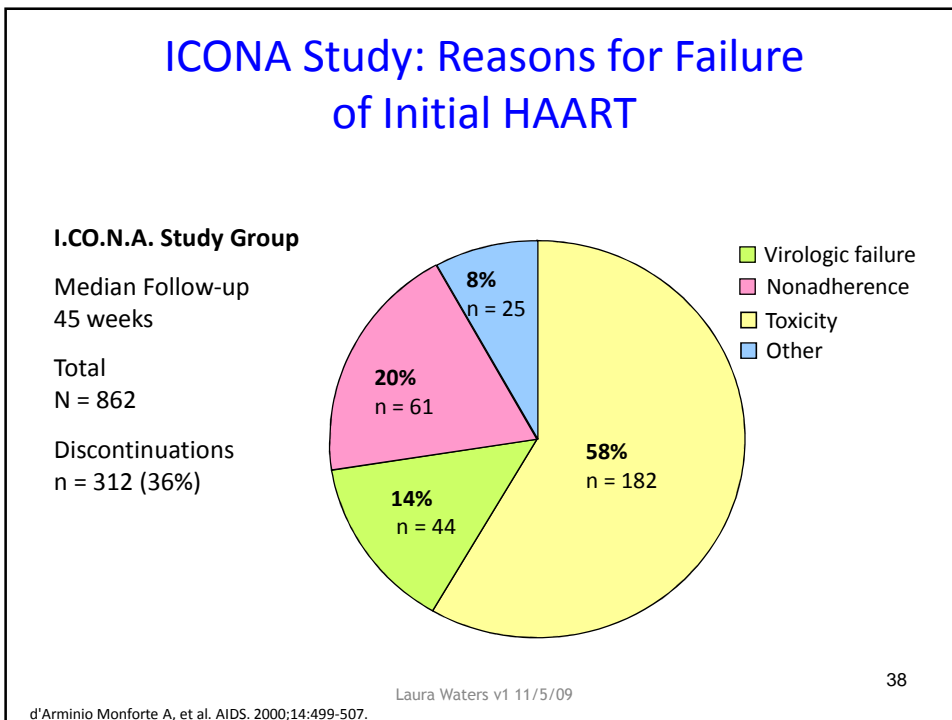
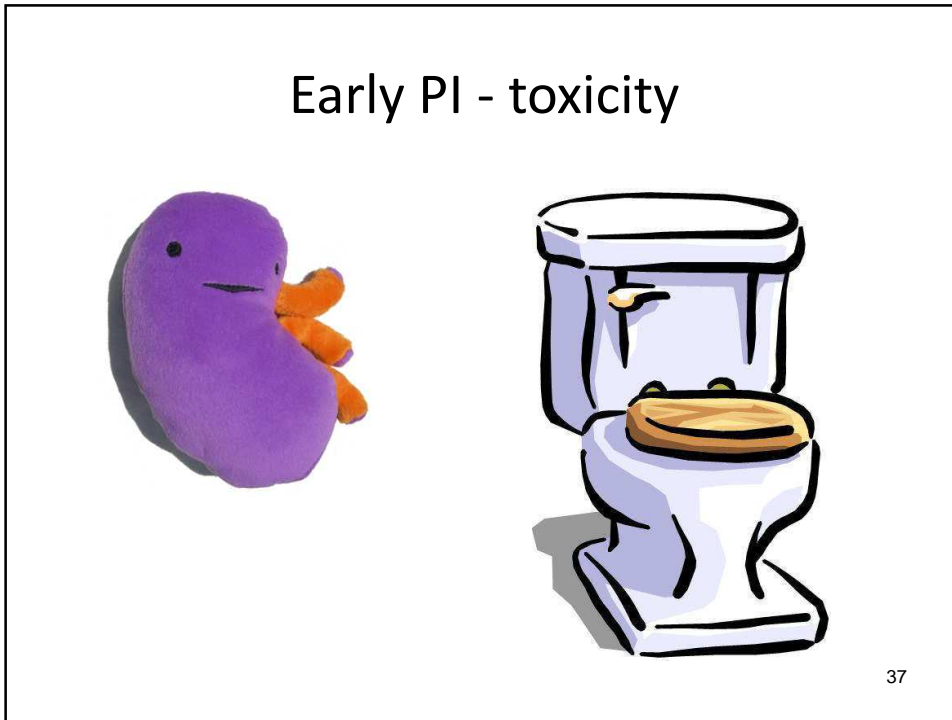
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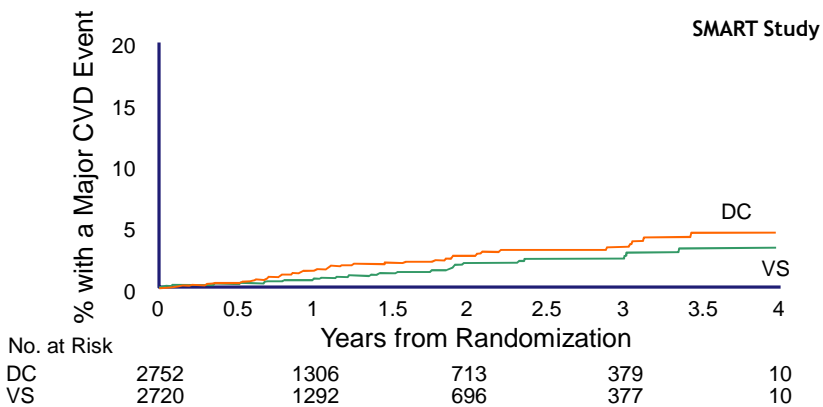
Data from 110 HIV-infected patients initiating 1st cART including an unboosted PI or NNRTI (efavirenz, nevirapine)
Adapted from: 1. Paterson DL et al. *Ann Intern Med* 2000; 133:21–30; 2. Bangsberg D et al. *Clin Infect Dis* 2006; 43:939–941.

Lesson 8

Emergence of new issues



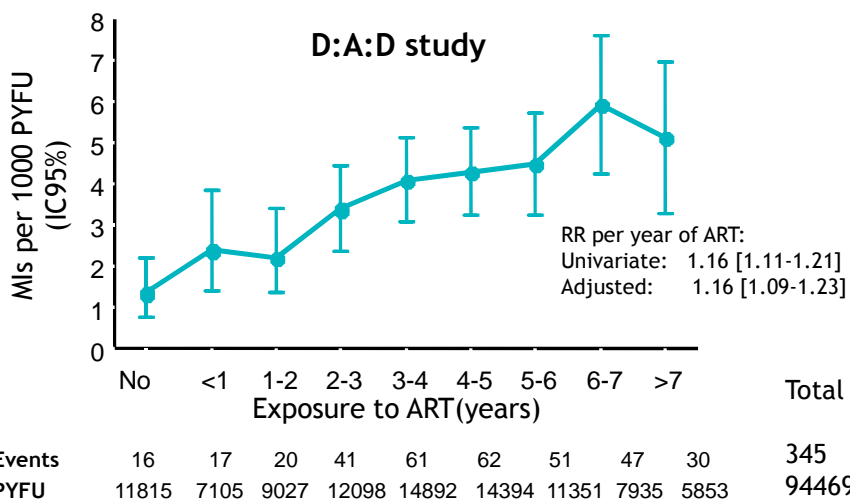
ART withdrawal increases the risk of CV disease due to acute effects of HIV viremia



- ART discontinuation associated with:
 - Increased immune activation (Tebas P et al. *PLoS ONE* 2008)
 - Increased adhesion molecules (Papasavvas E et al. *AIDS* 2008)
 - Increased inflammation (Seoane E et al. *J Acquir Immune Defic Syndr* 2008)

Phillips A, et al. 14th CROI, Los Angeles, CA, February 25-28, 2007. Abst. 41.

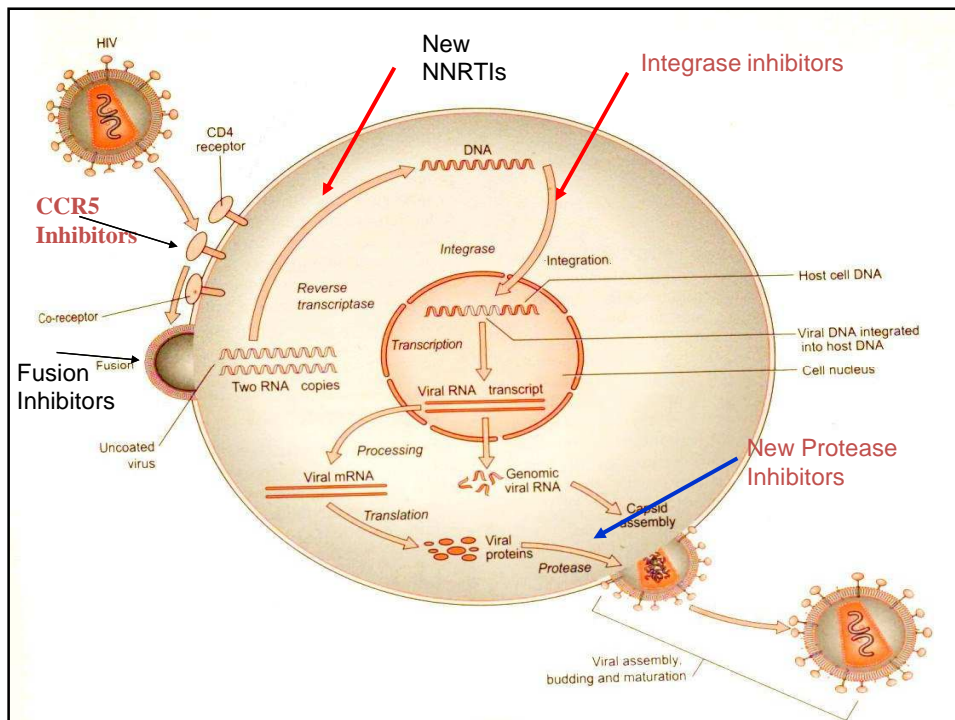
Largest observational study to date linked myocardial infarction to ART exposure

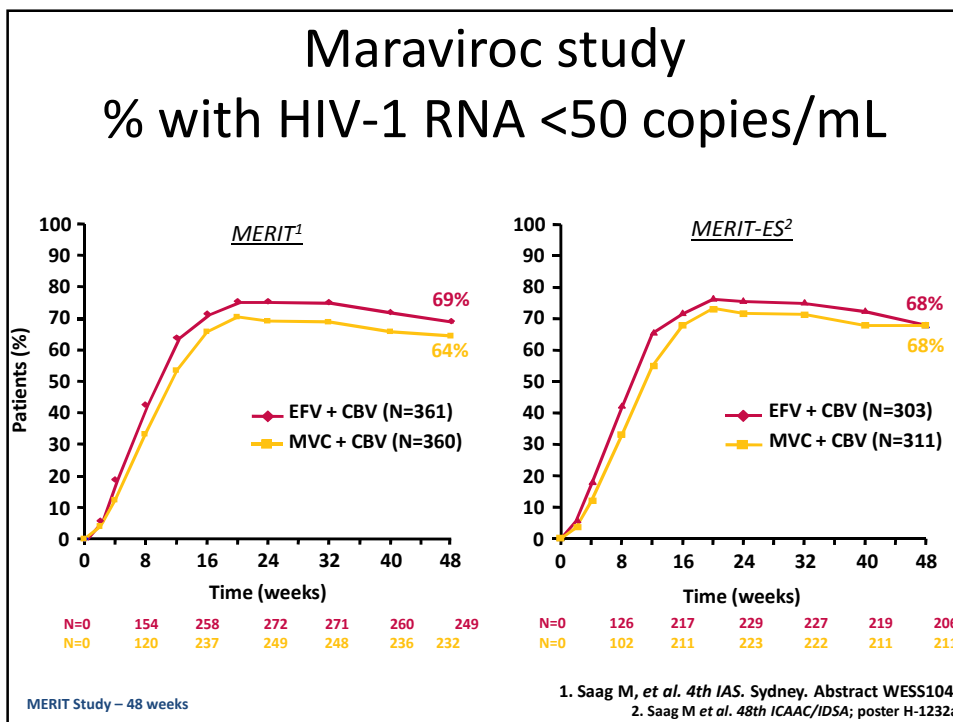
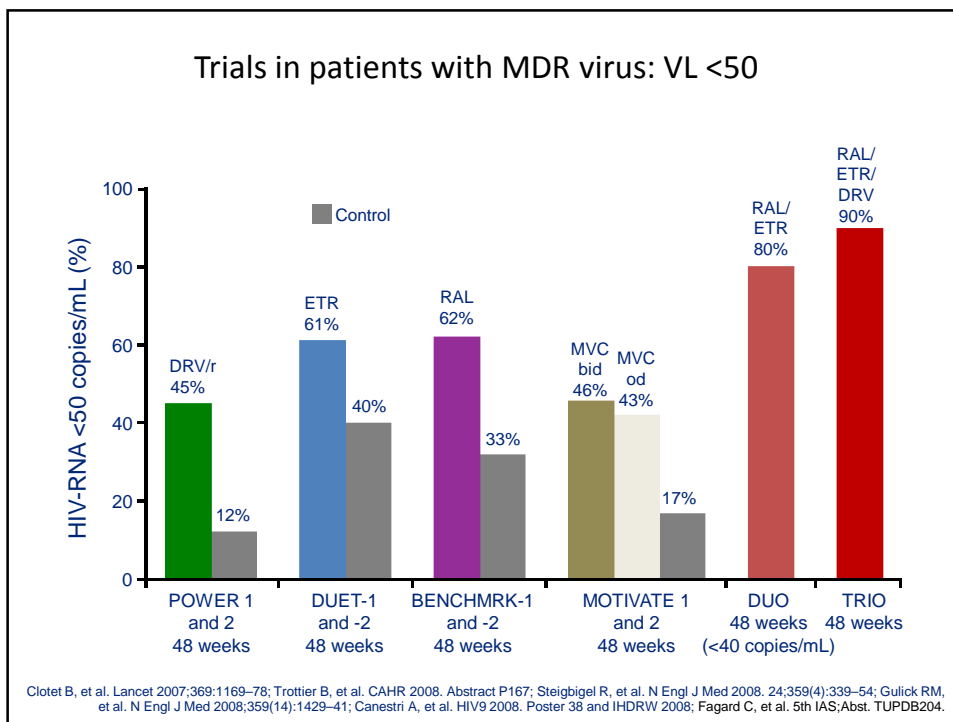


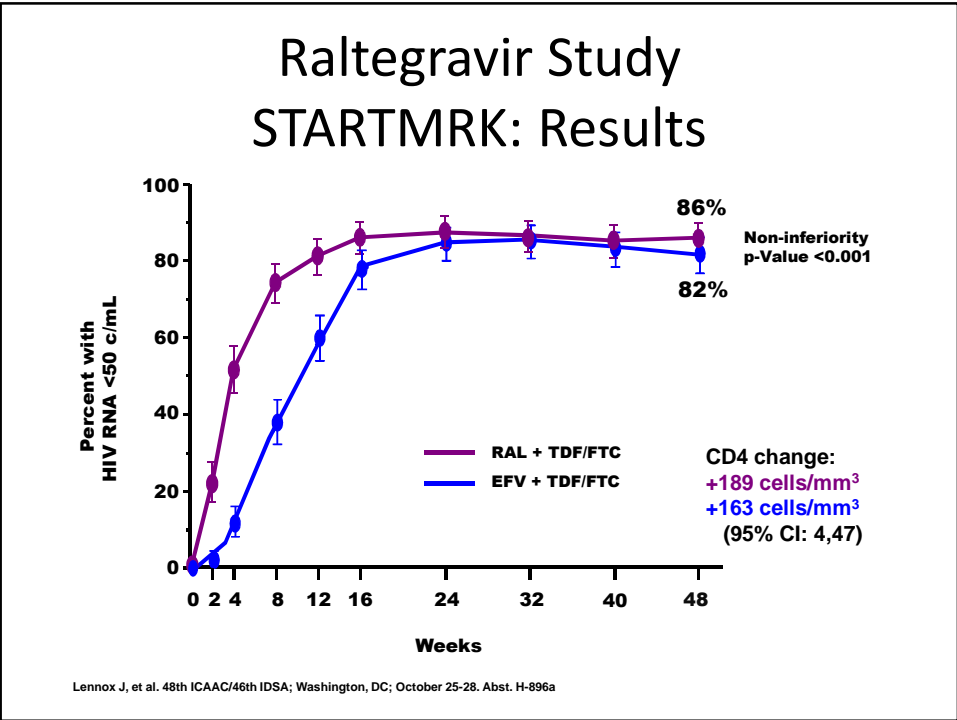
D:A:D study group. NEJM 2003; 349: 1993-2003

Lesson 9

Right drug, right time
New Classes







The ultimate goal (for now)

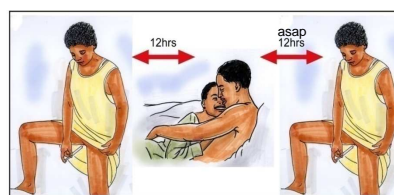
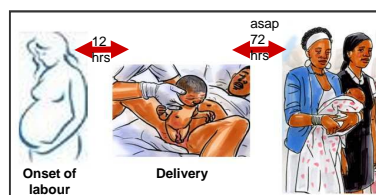


Lesson 10

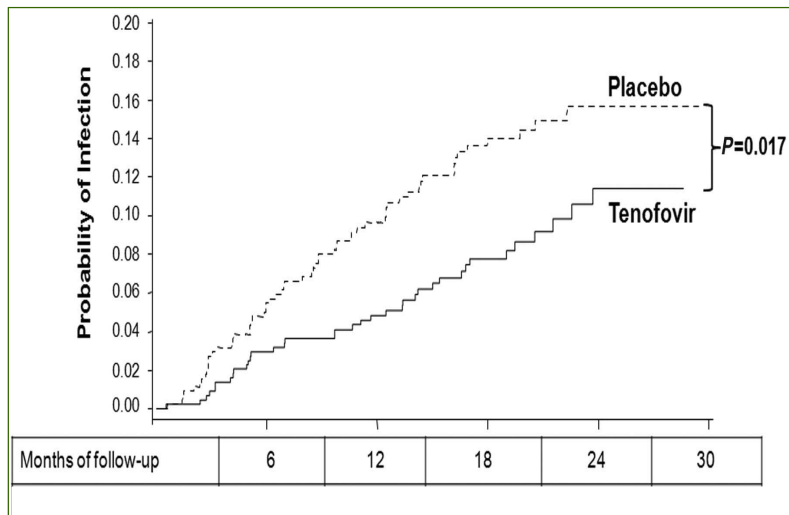
Prevention

CAPRISA 004 assessed the safety and effectiveness of 1% tenofovir gel

- BAT 24 coitally-related gel use
 - Insert 1 gel up to 12 hours **B**efore sex,
 - insert 1 gel as soon as possible within 12 hours **A**fter sex,
 - no more than **T**wo doses in **24** hours



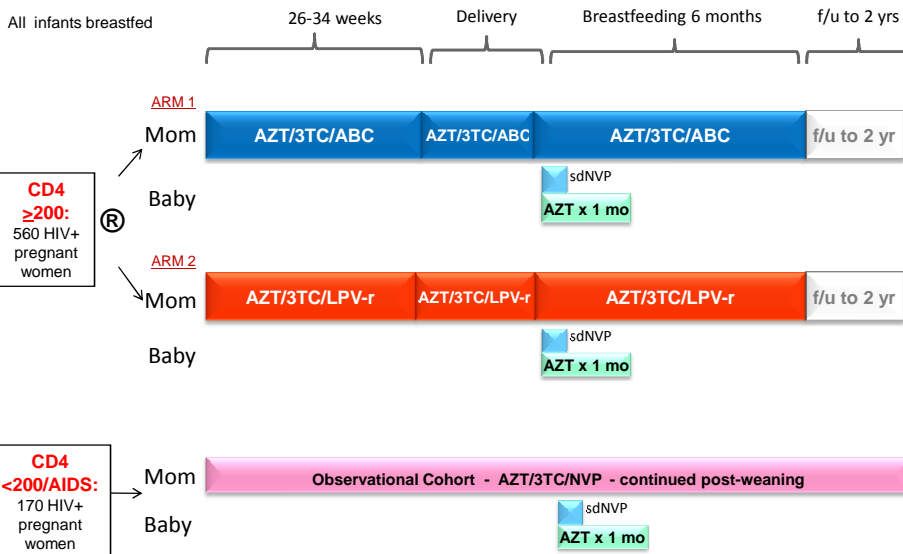
CAPRISA 004 study



Q. Abdool Karim et al., Science 329; 1168-1174 (2010)

Mma Bana: Compares 2 Maternal HAART Regimens: AP/IP/PP Intervention

Shapiro R et al. IAS, Capetown S Africa, July 2009, Abs. WE LB B101



Mma Bana: Primary MTCT Endpoint

Shapiro R et al. IAS, Capetown, South Africa, July 2009, Abs.

Infections among live-born infants, by maternal arm	Arm A (TZV) N=283	Arm B (KAL/CBV) N=270	Obs Arm (NVP/CBV) N=156
<i>In utero</i>	3 (1.1%)*	1 (0.4%)	1 (0.6%)
Intrapartum	0	0	0
Breastfeeding	2 (0.7%)	0	0
Total at 6 months	5 (1.8%)*	1 (0.4%)	1 (0.6%)

P=0.53

**Overall Transmission 1% (95% CI, 0.5-2.0%)
Through Age 6 Months**

Anti-HIV drugs prevent HIV infection, trial shows – if you take them

iPrEx Can a pill prevent HIV?

Every 11 seconds a person acquires HIV. While current HIV prevention methods help reduce transmission, they are not enough. New prevention methods to control rapidly within populations such as men who have sex with men (MSM), are needed to help HIV infection, and in geographic regions such as Africa, Asia and Latin America, where HIV spreading rapidly.

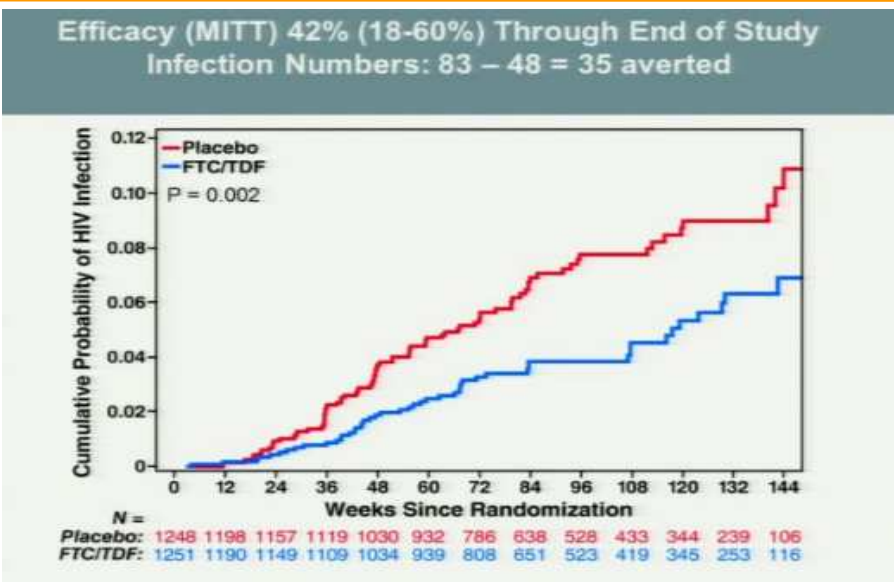
The world urgently needs **new HIV prevention options**

Global iPrEx is the first large efficacy study in MSM to evaluate whether an antiretroviral prevents HIV.

2,499 participants in total

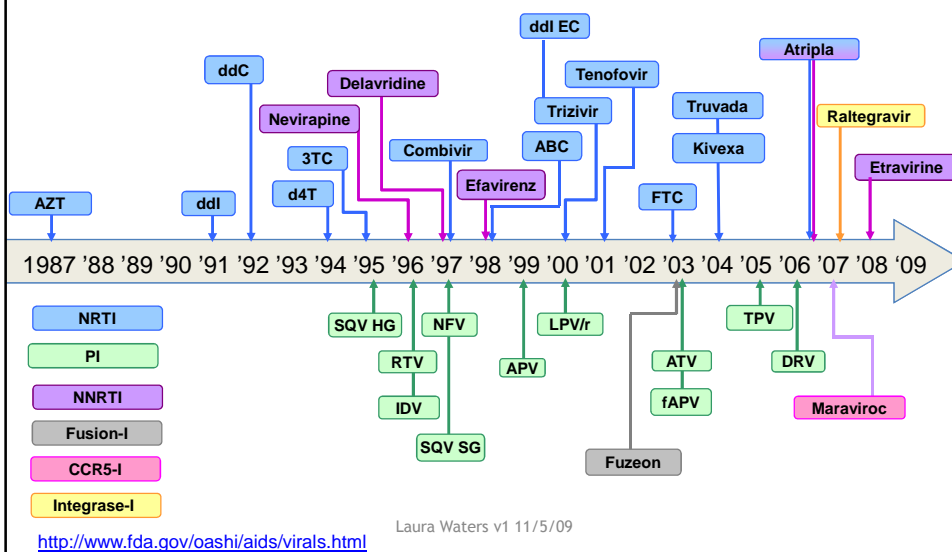
- 40% participants in USA
- 20% participants in THAILAND
- 40% participants in PERU
- 40% participants in SOUTH AFRICA

iPrEx, efficacy (CROI 2011; #92)



FDA: Approved Antiretrovirals

Between 1987 and 1995, 4 antiretrovirals were launched.
 Since 1995, 28 new products have been introduced.



Acknowledgements

Dr Laura Waters

Dr Martin Fisher

www.avert.org