# Milestones in the Era of Effective HIV Treatment

June 24, 2016 By Benjamin Ryan

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The first HIV med, Retrovir (zidovudine, or AZT), was approved in 1987. Over the next few years, additional antiretrovirals (ARVs) were introduced in the same drug class (nucleoside reverse transcriptase inhibitors, also known as NRTIs, or nukes). But using only one or two meds from the same drug class wasn't enough to fully suppress the virus, and the crisis period of the epidemic raged on. In December 1995, the first protease inhibitor (PI), Invirase (saquinavir), was approved, and a new era of combination therapy was set to begin. Here's a timeline of the highlights:

1996

- The first viral load test is approved.
- The first non-nucleoside reverse transcriptase inhibitor (NNRTI, or non-nuke), Viramune (nevirapine), is approved.
- Norvir (ritonavir), a PI that would become a booster of other ARVs, is approved.
- At the 11th International AIDS Conference in Vancouver, numerous studies demonstrate the efficacy of triple-combination antiretroviral (ARV) treatment, ushering in the era of what was

then called highly active antiretroviral treatment, or HAART.

1997

- The first combination ARV tablet, Combivir (zidovudine/lamivudine), is approved.
- AIDS-related deaths drop 47 percent in one year.

1998

- The U.S. Department of Health and Human Services issues the first federal HIV treatment guidelines, recommending treatment for those with fewer than 500 CD4s, in keeping with the "hit early, hit hard" philosophy of the time.

2001

- In an about-face, U.S. treatment guidelines switch to recommending starting ARVs when CD4s have dropped to 200 or below.
- Viread (tenofovir disoproxil fumarate, or TDF), which comes with bone and kidney toxicities, is approved and goes on to become the most widely prescribed ARV.

2002

- The Global Fund to Fight AIDS, Tuberculosis and Malaria in developing nations is launched.

2003

- The first entry inhibitor, the injectable Fuzeon (enfuvirtide), is approved.
- President George W. Bush launches the U.S. President's Emergency Plan for AIDS Relief, or PEPFAR, pledging to spend $15 billion to combat the disease in poorer nations in five years.

2006

- The first once-daily, single-tablet ARV regimen, Atripla (efavirenz/TDF/emtricitabine), is approved.
- The SMART trial is stopped early. The expansive global study investigated whether interrupting HIV treatment could reduce the risk of diseases thought to be the result of ARV toxicities. But those who interrupted treatment actually had worse health outcomes. The surprise findings

spur research into the link between HIV, chronic inflammation and non-AIDS-defining conditions such as heart disease.

2007

- The first integrase inhibitor, Isentress (raltegravir), is approved.
- The first oral entry inhibitor, Selzentry (maraviroc), is approved.

2008

- As HIV treatments improve, U.S. treatment guidelines up the CD4 threshold for starting ARVs to 350.

2010

- As San Francisco recommends HIV treatment regardless of CD4 count, U.S. guidelines advise starting ARVs when CD4s drop to 500, while the threshold set by the World Health Organization (WHO) is 350 CD4s.

2011

- The HPTN 052 study finds that starting ARVs reduces the risk of transmitting HIV through heterosexual sex by 96 percent, launching the treatment-as-prevention (TasP) era.

2012

- U.S. guidelines recommend treatment for all people living with HIV, regardless of their CD4 count.
- The FDA approves Truvada (TDF/emtricitabine) for use as pre-exposure prophylaxis (PrEP).

2013

- UNAIDS reports that global AIDS-related deaths have fallen 30 percent since peaking in 2005.
- WHO recommends treatment once CD4s hit 500 or below.

2014

- Interim results from the ongoing PARTNER study find that there have been no transmissions

between partners in gay or straight mixed-HIV-status couples in which the HIV-positive partner has an undetectable viral load. Researchers estimate that the actual transmission risk may be close to zero, or in fact zero.

2015

- The placebo arm of the global START trial is terminated early when it becomes clear that there is a lower risk of various negative health outcomes associated with starting ARVs when CD4s are above 500 compared with waiting until they hit 350. In response, WHO supports treatment for all, regardless of CD4 count.
- Genvoya (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide, or TAF) is the first approved combination tablet to include an updated version of tenofovir that is safer for bones and kidneys.

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