

HIV Treatment 101

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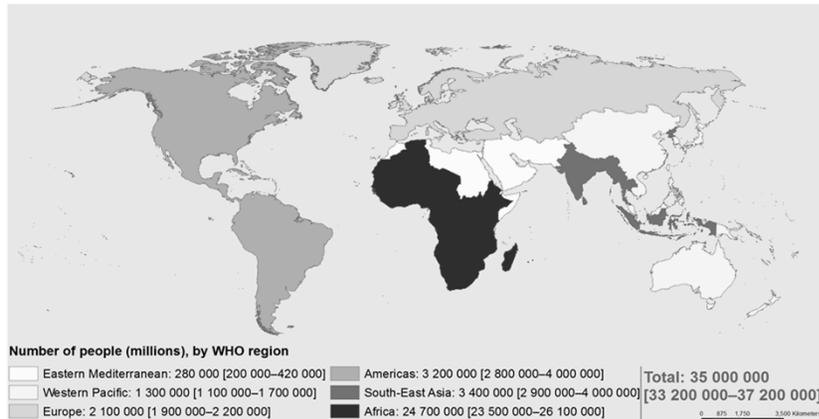


Objectives

- Epidemiology
- What is HIV?
- Common Labs
- Life Cycle
- Medication Classes
- Building an HIV regimen



Adults and children estimated to be living with HIV, 2013
By WHO region



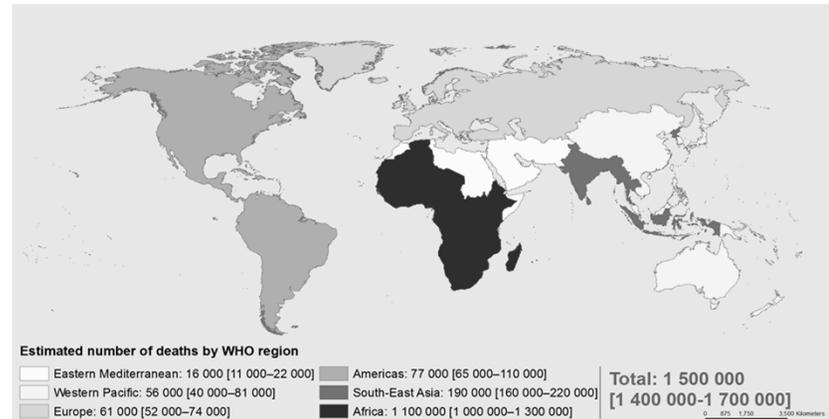
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Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSIS)
World Health Organization



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Estimated adult and child deaths from AIDS, 2013
By WHO region



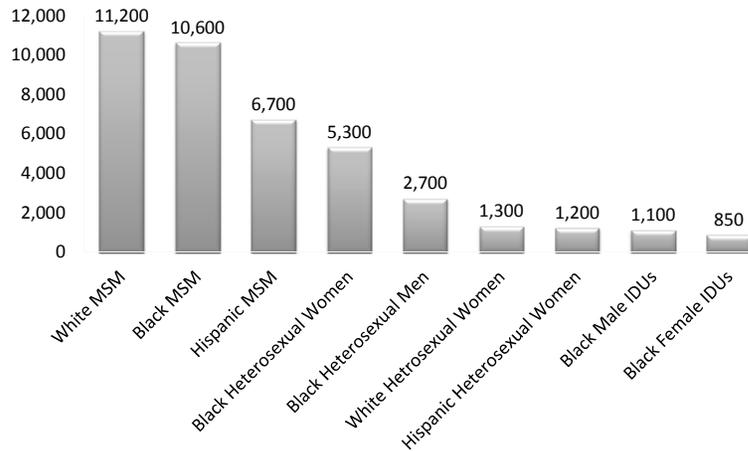
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New HIV Cases in the US (2010)

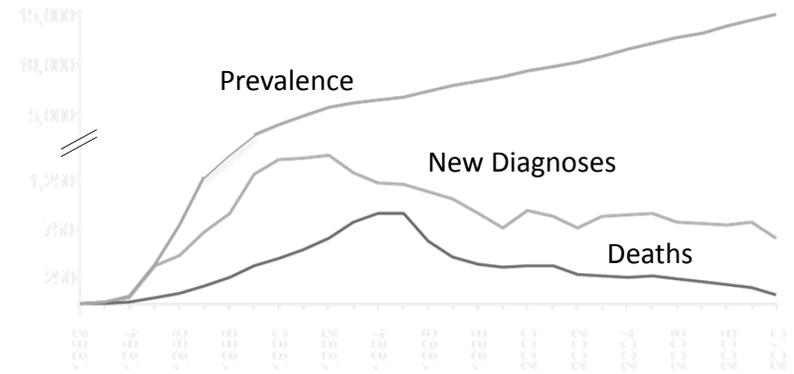


CDC HIV Incidence <http://www.cdc.gov/hiv/statistics/surveillance/incidence.html>



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Prevalence, Deaths, and Diagnoses in Michigan

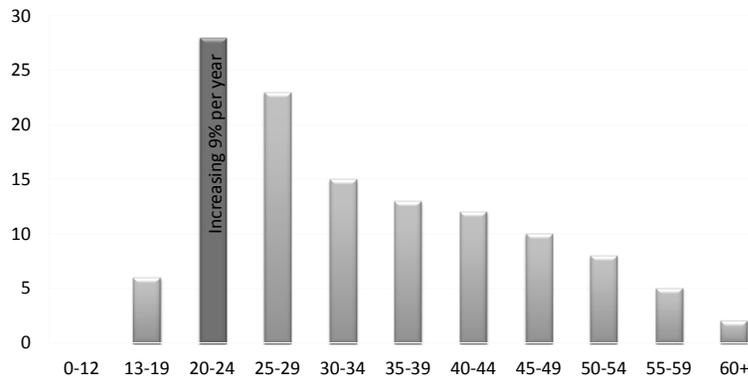


Epidemiologic Profile of HIV/AIDS in Michigan. July 2014 Annual HIV Surveillance Analysis. HIV/STD/VH/TB Epidemiology Section, Bureau of Epidemiology, MDCH. www.michigan.gov/hivstd.



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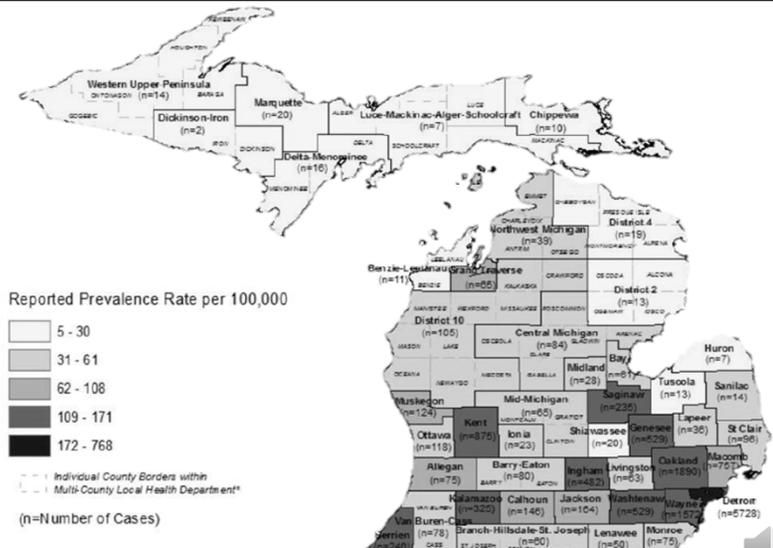
New HIV Cases in Michigan (2012)



Epidemiologic Profile of HIV/AIDS in Michigan. July 2014 Annual HIV Surveillance Analysis. HIV/STD/VH/TB Epidemiology Section, Bureau of Epidemiology, MDCH. www.michigan.gov/hivstd.



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Epidemiologic Profile of HIV/AIDS in Michigan. July 2014 Annual HIV Surveillance Analysis. HIV/STD/VH/TB Epidemiology Section, Bureau of Epidemiology, MDCH. www.michigan.gov/hivstd.



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What is HIV?

- Human – Only found in humans
- Immunodeficiency – Weakens immune system by destroying CD4 cells
- Virus – Reproduces by taking over a host cell

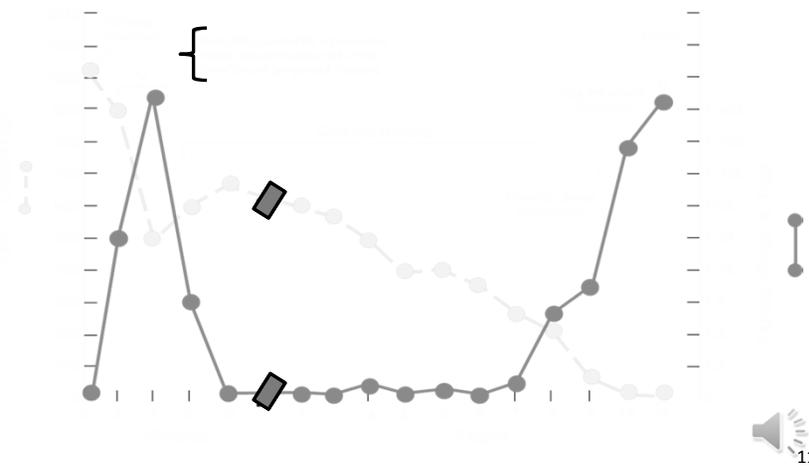


Common HIV Labs

- Viral Load
 - How much HIV is in the blood
 - Lower the better
- CD4 Count
 - How strong the immune system is
 - Higher the better
- Genotype
 - Has HIV found ways to avoid certain medications?
 - Resistance test



HIV Time Course

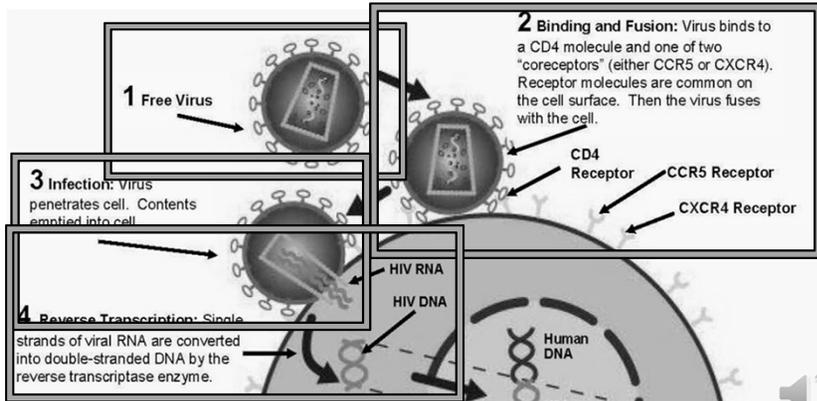


Goals of Therapy

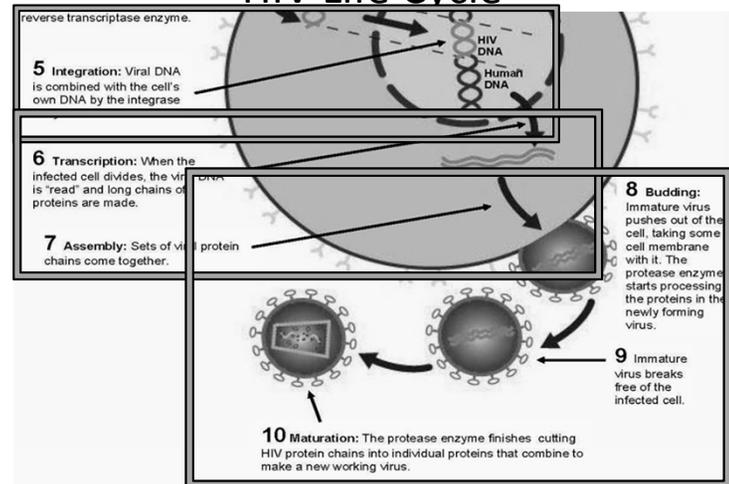
- Increase the CD4
 - Above 200, preferably above 500
- Decrease the VL
 - Non-detectable
- Improve quality of life
- Reduce secondary HIV related disease



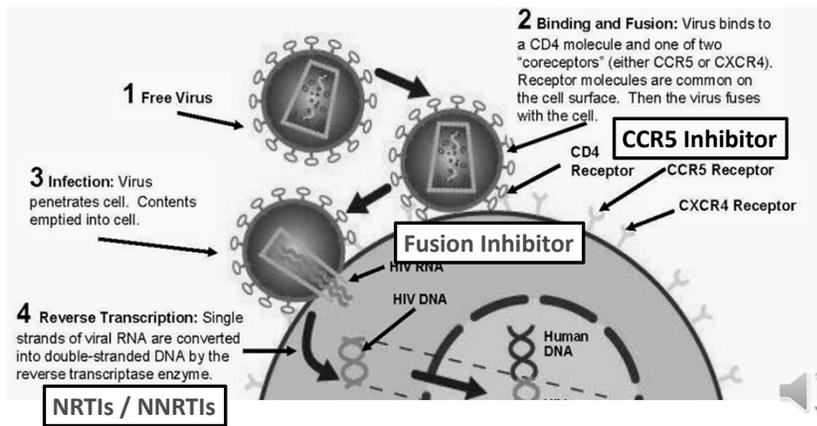
HIV Life Cycle



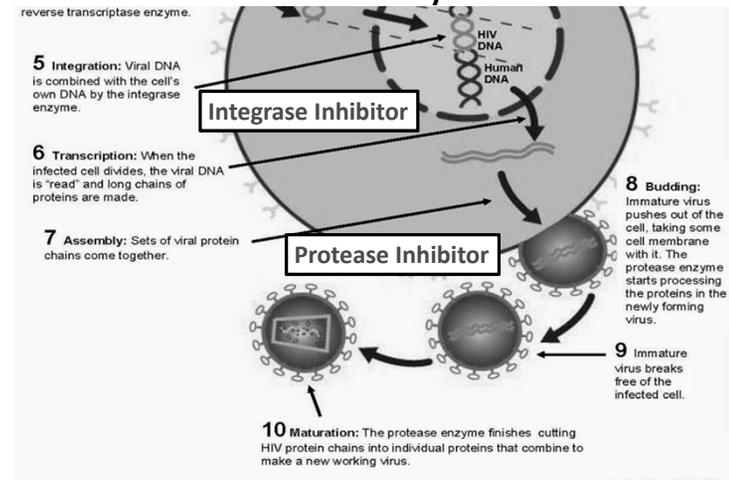
HIV Life Cycle



Antiretroviral Targets



HIV Life Cycle



FDA Approved Antiretrovirals

NRTIs	NNTRIs	PIs	Entry/Fusion Inhibitors
Combivir®	Edurant®	Aptivus®	Fuzeon®
Emtriva®	Intelence®	Crixivan®	Selzentry®
Epivir®	Rescriptor®	Evotaz®	
Epzicom®	Sustiva®	Invirase®	Single Tablet Regimens
Retrovir®	Viramune®	Kaletra®	Atripla®
Trizivir®		Lexiva®	Complera®
Truvada®	INSTIs	Norvir®	Stribild®
Videx®	ISENTRESS®	Prezista®	Triumeq®
Viread®	Tivicay®	Prezcobix®	
Zerit®	Vitekta®	Prezista®	
Ziagen®		Reyataz®	
		Viracept®	

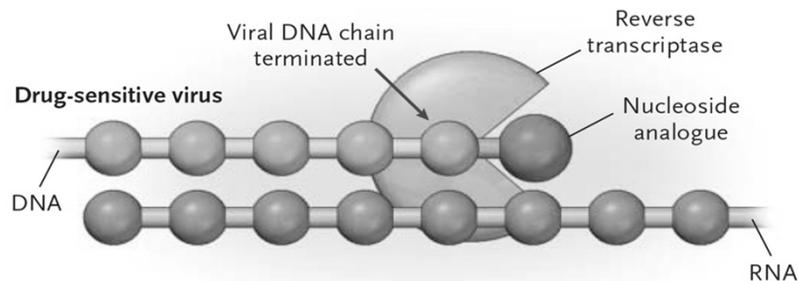


Nucleoside Reverse Transcriptase Inhibitors

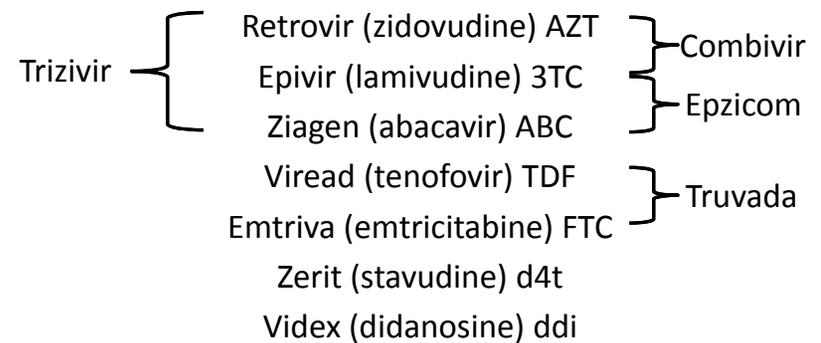
- When HIV copies itself it uses RNA as a template to make DNA
- The DNA stand is made up of multiple small building blocks
- NRTIs looks like these building blocks, but are shaped differently
- This difference in shape stops reverse transcriptase from working



Nucleoside Reverse Transcriptase Inhibitors



NRTIs: “Nukes”

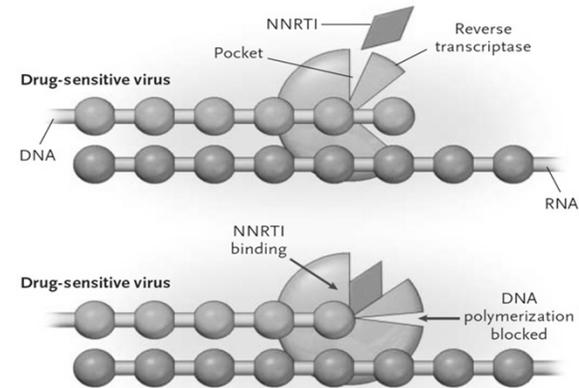


Non-Nucleoside Reverse Transcriptase Inhibitors

- When HIV copies itself it uses RNA as a template to make DNA
- NNRTIs stick to the enzyme responsible for making DNA out of RNA preventing it from working



Non-Nucleoside Reverse Transcriptase Inhibitors



Clavel F et al. N Engl J Med 2004;350:1023-35



NNRTIs: “Non-Nukes”

- Viramune (nevirapine) NVP
- Sustiva (efavirenz) EFV
- Rescriptor (delavirdine) DLV
- Intelence (etravirine) ETV
- Edurant (rilpivirine) RPV

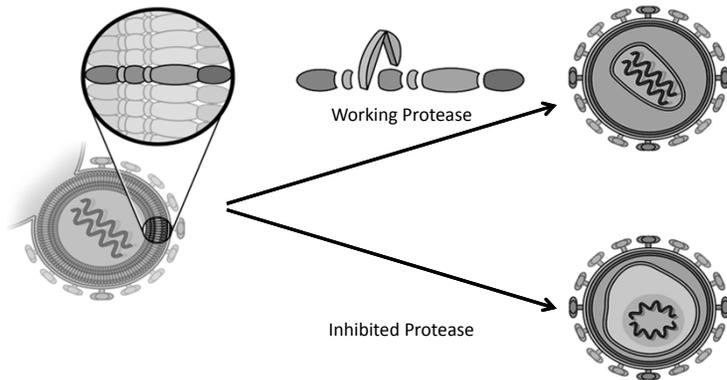


Protease Inhibitors

- When new HIV are made they start out as long protein chains
- Protease acts like a pair of scissors cutting these chains into parts so a mature virus can form
- Protease inhibitors bind to these “scissors” and prevent them from working



Protease Inhibitors



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PIs

- Invirase (saquinavir) SQV
- Crixivan (indinavir) IDV
- Norvir (ritonavir) RTV or /r
- Viracept (nelfinavir) NFV
- Kaletra (lopinavir/ritonavir) LPV/r
- Reyataz (atazanavir) ATV
 - Evotaz (atazanavir/cobicistat)
- Lexiva (fosamprenavir) FPV
- Aptivus (tipranavir) TPV
- Prezista (darunavir) DRV
 - Prezcofix (darunavir/cobicistat)

Yellow = Must be boosted



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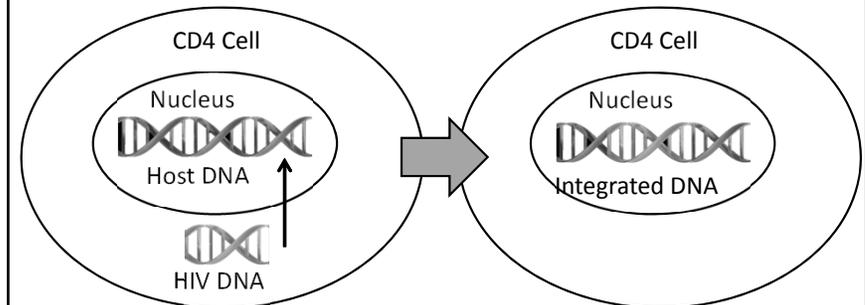
Integrase Inhibitors

- HIV uses human CD4 cells to make copies of itself
- In order to trick CD4 cells into doing this, it first must integrate its DNA in the human DNA
- HIV uses the integrase to do this
- Integrase inhibitors bind to this enzyme and prevent this process



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Integrase Inhibitors



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INSTIs

- Isentress (raltegravir) RAL
- Tivicay (dolutegravir) DTG
- Vitekta (elvitegravir) EVG



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CCR5 Inhibitor

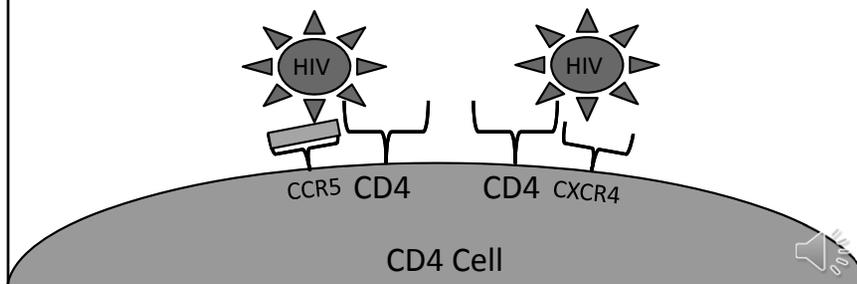
- HIV binds to the CD4 receptor to enter the cell
- This binding is not enough to enter the cell
- CD4 also requires binding to a co-receptor
- CCR5 inhibitors prevent HIV from binding to 1 of 2 possible co-receptors



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CCR5 Inhibitor

- Selzentry (maraviroc) MVC



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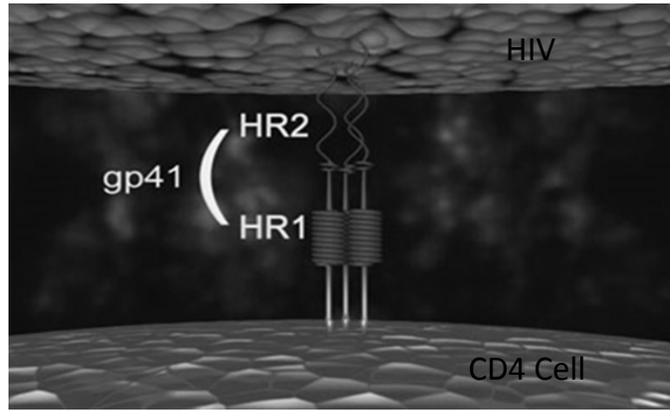
Fusion Inhibitor

- Once bound to the CD4 cell, HIV must fuse with the cell to release its contents into the cell
- Fusion inhibitors block HIV from fusing with the surface of the CD4 cell

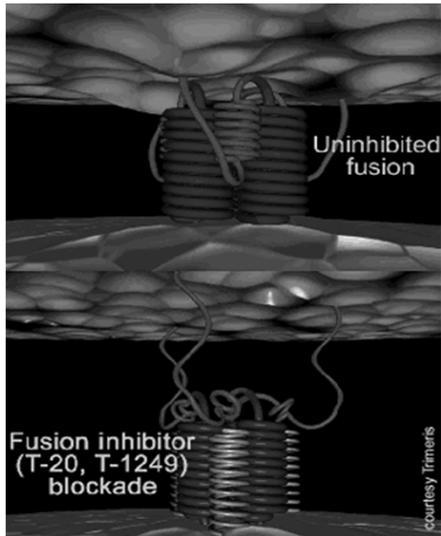
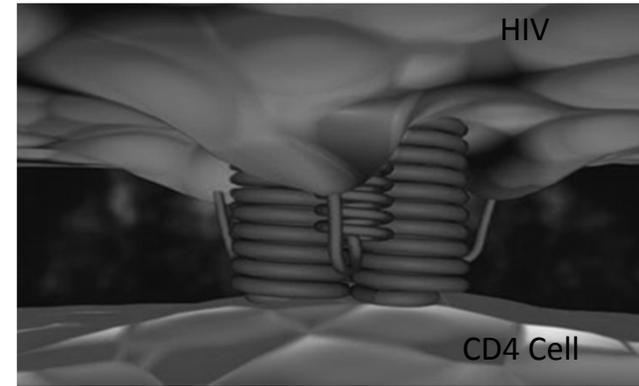


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Fusion Inhibitor



Fusion Inhibitor



Building an HIV regimen

- Three medication from at least 2 different classes
 - Never mono or dual therapy
 - NRTIs are the only class we routinely use more than 1 at a time
 - Ritonavir and Cobicistat do not count
- Number of medications does not have to match the number of pills



Single Tablet Regimens

- Atripla - 2006
 - Tenofovir/Emtricitabine/Efavirenz
 - NRTI/NRTI/NNRTI



- Complera - 2011
 - Tenofovir/Emtricitabine/Rilpivirine
 - NRTI/NRTI/NNRTI



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Single Tablet Regimens

- Stribild - 2012
 - Tenofovir/Emtricitabine/Cobicistat/Elvitegravir
 - NRTI/NRTI/Booster/INSTI



- Triumeq - 2014
 - Abacavir/Lamivudine/Dolutegravir
 - NRTI/NRTI/INSTI



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Simpler Regimens Over Time

Regimen	Dosing	Pill Burden
1996:	q8h: 10 pills/d	
1998	q12h: 5 pills/d	
2002	q12h: 3 pills/d	
2003	qd : 3 pills/d	
2004	qd: 2 pills/d	
2006	qd: 1 pill/d	



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