

第16回日本エイズ学会

Interactive Session

症例から学ぶ HIV感染症診療のコツ

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Case 1

- 45 yo White Male**
- Diagnosed on routine insurance examination**
- PMHx remarkable for HTN, diet controlled**
- No medications**
- Understands treatment issues and wants to begin therapy if you think it is appropriate**

If his viral load is 30,000 c/ml, which CD4 count would you recommend starting therapy?

- 750 cells / ul
- 500 cells / ul
- 350 cells / ul
- 300 cells / ul
- 250 cells / ul
- ≤ 200 cells /ul
- Would observe

If his initial CD4 count is 700 cells/ul, which viral load value would you recommend starting Rx?

- **1,000 c / ml**
- **5,000 c / ml**
- **10,000 c / ml**
- **30,000 c / ml**
- **100,000 c / ml**
- **300,000 c / ml**
- **1,000,000 c / ml**
- **Would observe (e.g, Every 2 months)**

His CD4 count is 284 cells/ul and his VL 72,000 c/ml. You recommend starting with:

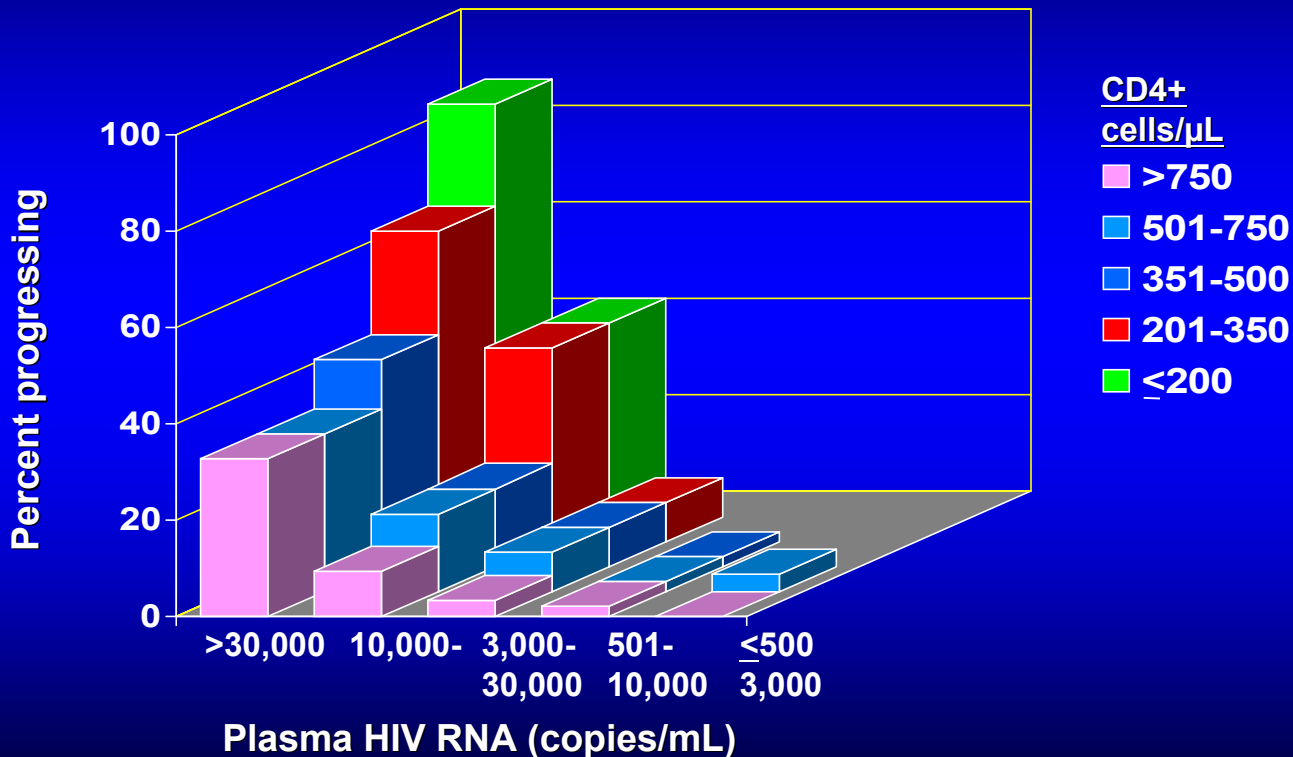
- **2 NRTIs and a PI**
- **2 NRTIs and a 'boosted' PI**
- **2 NRTIs and an NNRTI**
- **3 NRTIs**
- **NRTI + NNRTI + PI**
- **2 NRTIs and NtRTI (Tenofovir)**
- **No therapy now (A Holiday)**

His CD4 count is 34 cells/ul and his VL 284,000 c/ml.

You recommend starting with:

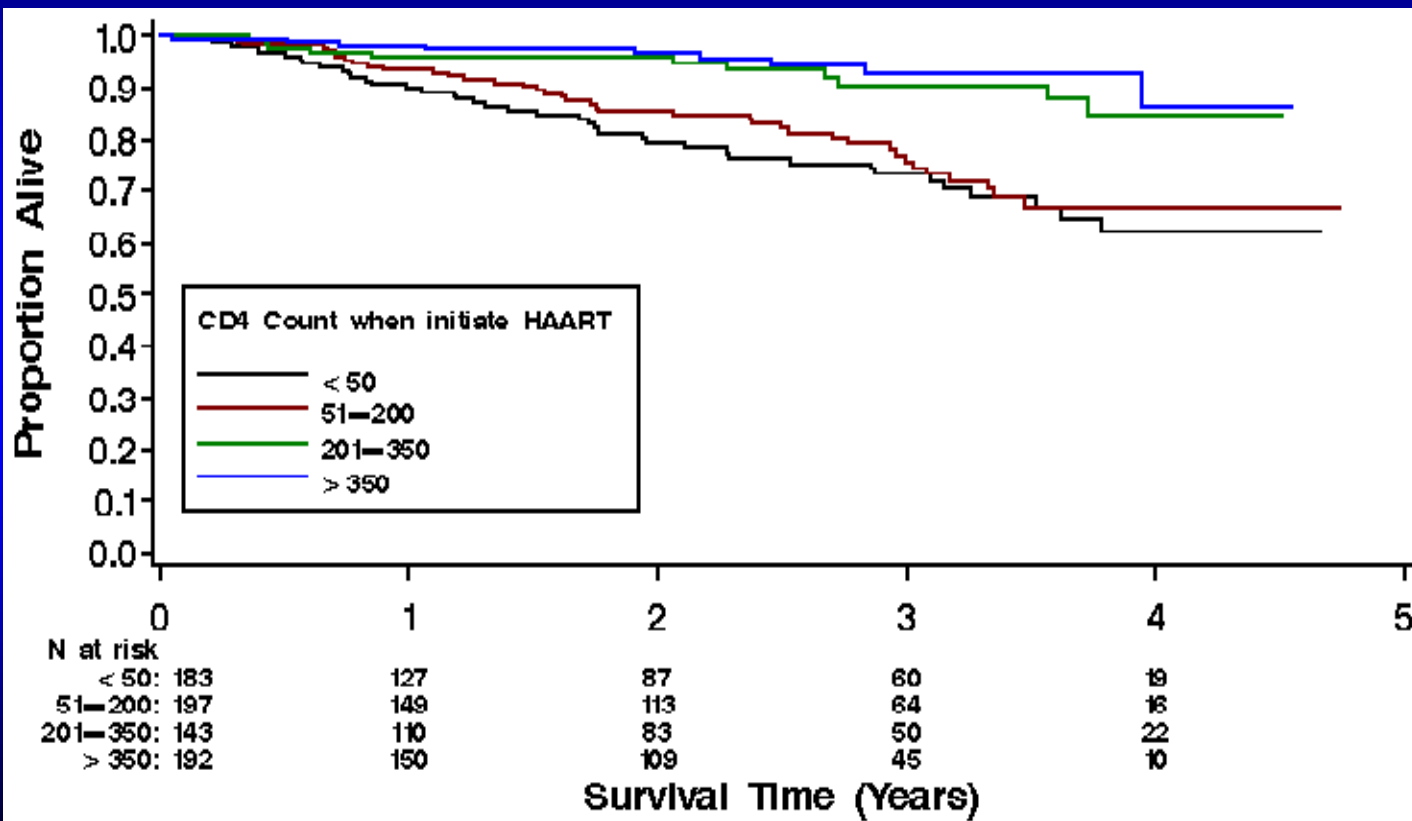
- **2 NRTIs and a PI**
- **2 NRTIs and a 'boosted' PI**
- **2 NRTIs and an NNRTI**
- **3 NRTIs**
- **NRTI + NNRTI + PI**
- **3 NRTIs and NtRTI (Tenofovir)**

Likelihood of Developing AIDS in 3 Years

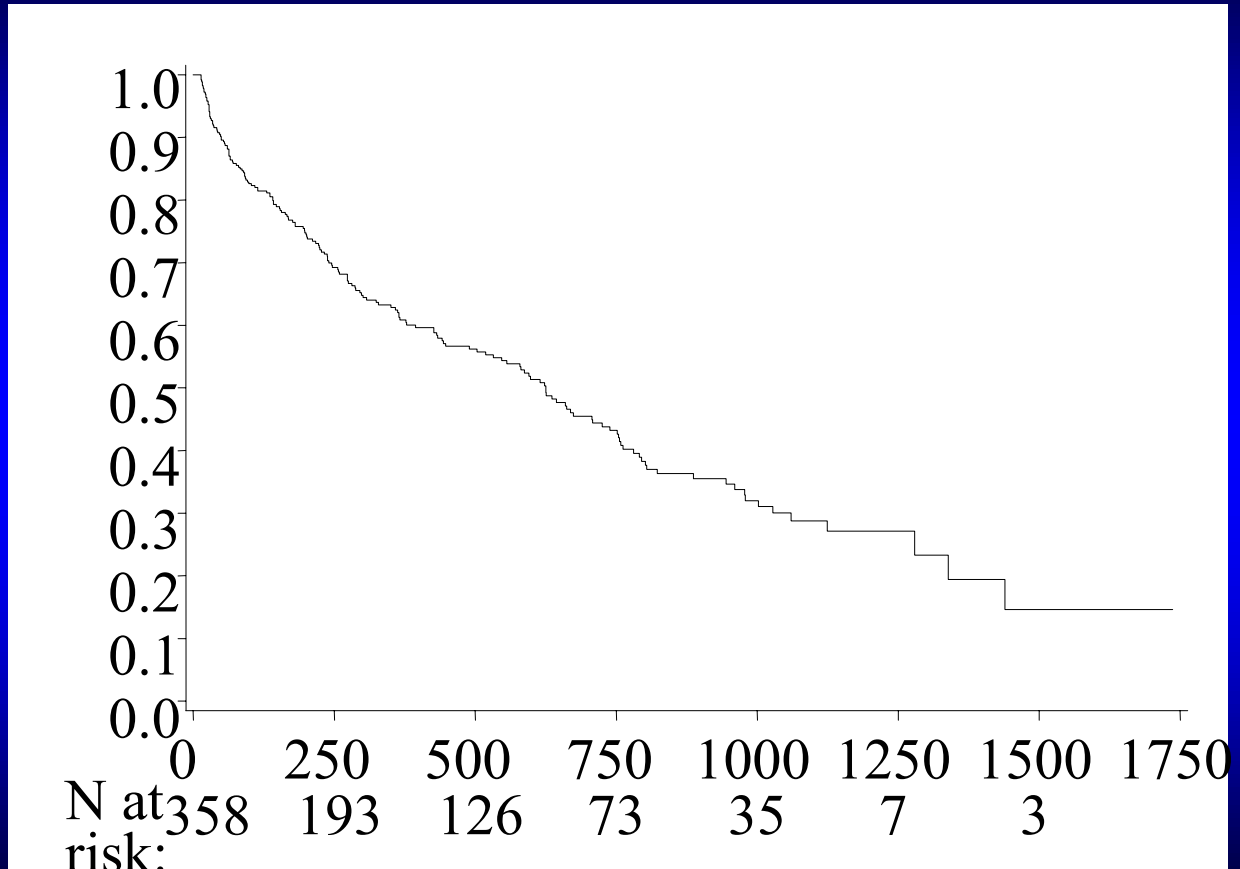


Adapted from: Mellors J et al. *Ann Intern Med.* 1997.

4 Year Survival in HAART Era



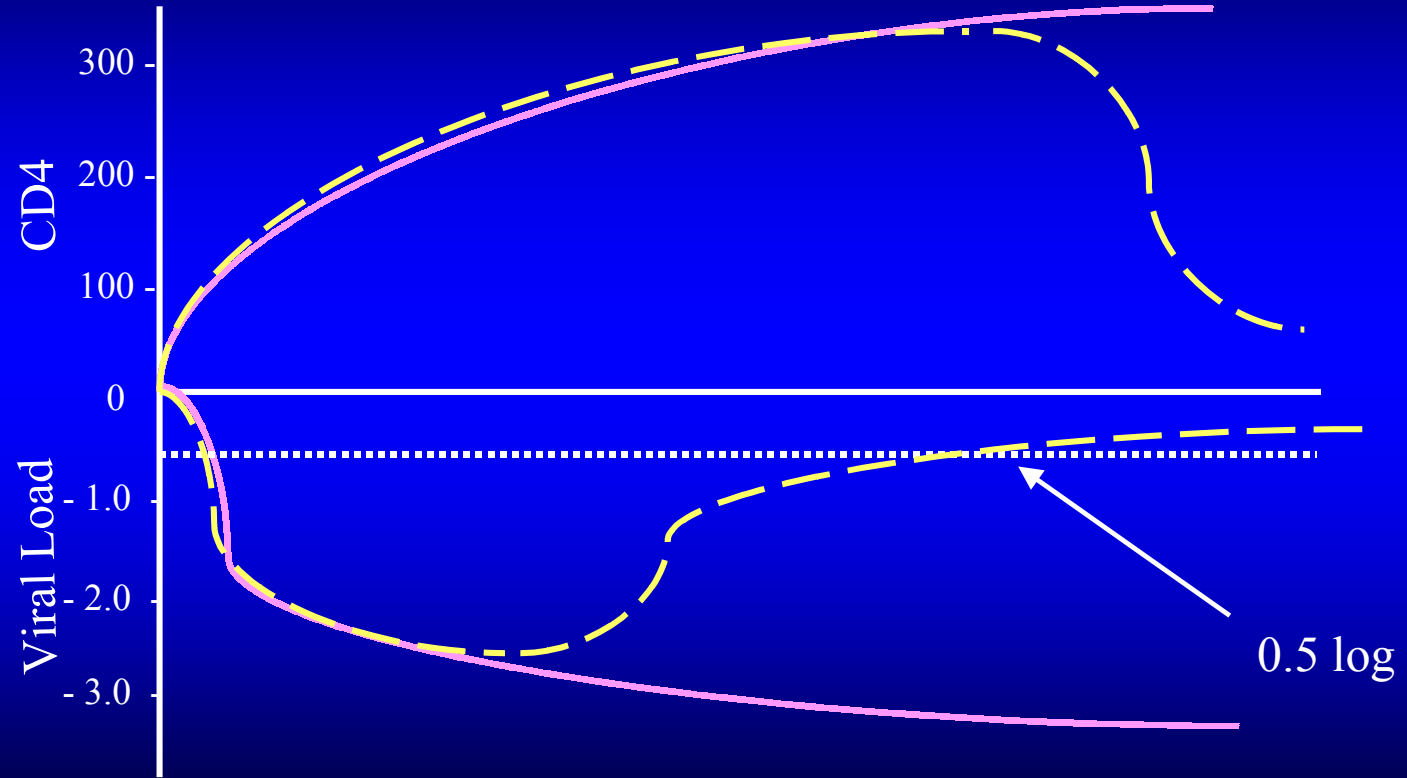
Durability of 1st Regimen



What is virologic failure?

- **Viral load > 50 copies / ml (confirmed)**
- **Viral load > 400 copies /ml (confirmed)**
- **Viral load < 1 log below baseline**
- **Viral load < 0.5 log below baseline**
- **Other**

What is Failure?



Case 2

- A 42 yo man is referred to you for management of his antiretroviral therapy. He was originally diagnosed 5 years ago and has been on several antiretroviral regimens, including:
 - 11/97 D4T / ddI/ NVP
 - 10 / 99 ZDV/ 3TC/ NFV

Case 2

- His viral load /CD4 results are as follows:
- 11/97 230,000 / 45 (ddI / D4T / NVP)
- 2/99 < 400 / 234
- 10/99 8480 / 265 (ZDV / 3TC / NFV)
- 5/00 <400 / 254
- 9/00 44,500 */ 220 (* confirmed)

Case 2

A genotypic resistance panel reveals the following mutations:

- RT:M41L, T215Y, K219Q, Y181C
- Protease:D30N, I84V, L90M

Case 2

Which of the following drugs should be used in the next regimen:

- ZDV
- D4T
- Abacavir
- Efavirenz
- Indinavir
- Tenofovir

Case 2

His viral load /CD4 results are as follows:

- 9/00 44,500 */ 220 (* confirmed)
- 10/00 ABC/D4T/IDV/rit
- 1/01 <400 / 350
- 4/01 32,600/ 300
- 7/01 83,000/ 290
- 10/ 01 134,000 / 230
- 9/ 02 178,000 / 170

Case 2

His local physician ordered a genotypic resistance panel. It revealed the following mutations:

**RT: M41L, T215Y, M184V, K219Q,
Y181C**

**Protease: L10F, D30N, G48V, I82V, L84M,
L90M**

Which of the following drugs should be used in the next regimen:

- ZDV
- D4T
- ddl
- ABC
- Efavirenz
- Indinavir
- SQV
- LPV
- APV
- TNV

A phenotype reveals:

ZDV	18 fold	SQV	30 fold
D4T	2.5 fold	RTV	40 fold
3TC	80 fold	IDV	40 fold
ABC	4.5 fold	NFV	60 fold
ddI	3 fold	APV	8 fold
ddC	5 fold	LPV	15 fold
NVP	90 fold	TNV	6 fold
EFV	30 fold		
DLV	80 fold		

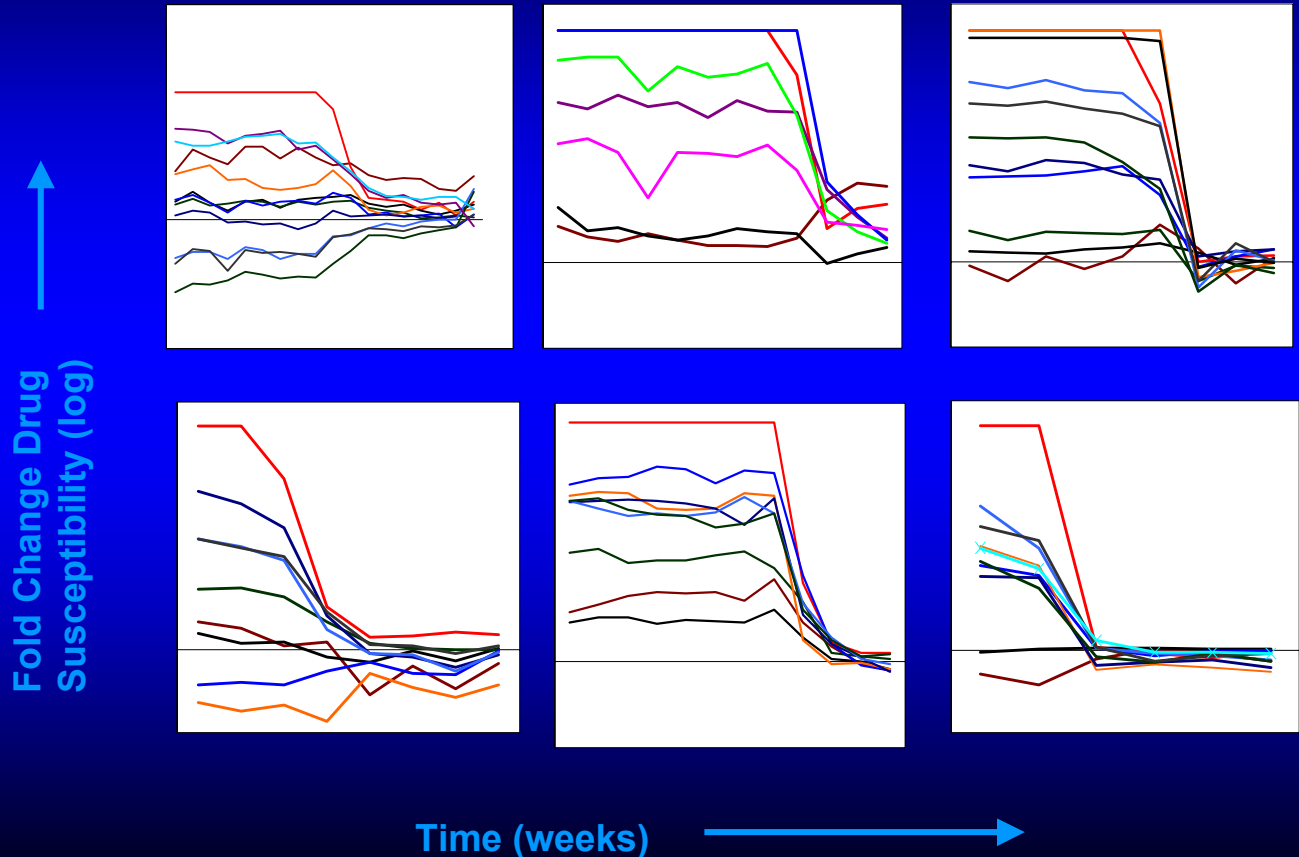
Which of the following drugs should be used in the next regimen:

- ZDV
- D4T
- ddl
- ABC
- Efavirenz
- Indinavir
- SQV
- LPV
- APV
- TNV

As a management strategy, is it a good idea to use a drug holiday in this setting to 'reset' the virus back to wild-type for better outcome?

- **Yes**
- **No**

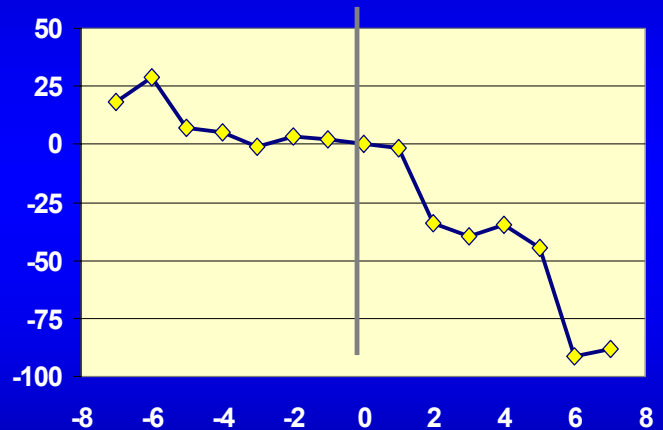
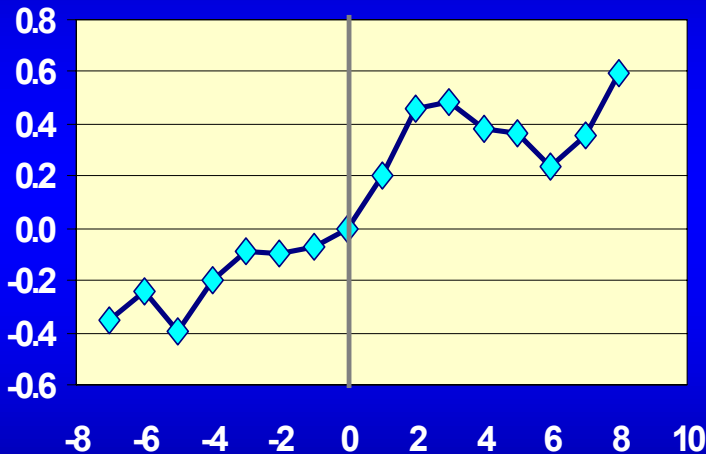
Change in Drug Susceptibility Over Time (n=6)



Change in HIV RNA and CD4 (STI) Before and After Switch in Phenotypic Susceptibility (n=16)

Change HIV RNA¹

Change CD4



Weeks Before and After WT
Switch

¹3 subjects excluded from HIV RNA analysis because
baseline levels near upper limit of quantification

32 Year Old White Female

- Diagnosed HIV+ December 1995
- Initial CD4 520; HIV RNA 10,900
- March 1996 started on stavudine / lamivudine and indinavir
- Tolerated well except 1 episode nephrolithiasis in 1999
- HIV RNA < 50 for 4 years;
Current CD4 840

She has heard about the long-term complications of HAART therapy, is very concerned and wants your advice.

You recommend:

- **“Stay the course, change would not be prudent” (George Herbert “W” Bush)**
- **Substitute a NNRTI for Indinavir**
- **Substitute zidovudine for stavudine**
- **Substitute both a NNRTI and zidovudine for indinavir and stavudine**
- **Stop her current therapy and observe**
- **Tell her “Predictions are always difficult ...especially when they involve the future” (J. Danforth Quayle)**

Next Case

- A 22 yo HIV-infected woman delivered a healthy baby (HIV-negative) 2 months ago.
- Diagnosed HIV+ during a routine prenatal workup.
- CD4 count at that time was 540 cells/ul; VL 12,000.
- She was started on ZDV / 3TC / Nevirapine
- At the time of delivery, her VL <50 and CD4 count 870 cells/ul.
- She is not breast feeding

She does not have a strong opinion about her ART.

At this time you recommend:

- **Continue treatment**
- **Stop therapy**
- **Phone a friend**

42 year old Male

- Diagnosed 11/99
- CD4 count 43 cells/ul; VL =233,000
- Started on ZDV/3TC/SQV/rit
- VL < 50 copies for last year
- CD4 = 87 cells/ul

He returns and asks why his CD4 count is not higher and whether there is anything you can do. You recommend:

- **No change in therapy**
- **A Drug Holiday**
- **Substitute Efavirenz for SQV/rit**
- **Intensify Rx with (add) Tenofovir**
- **Substitute Efavirenz for ZDV/3TC**
- **rIL-2 (3 million units qD X 5 days every 2 months)**

For HIV /HCV co-infected patients, which of the following is true:

- Alcohol consumption of < 1-2 drinks a day (40 mg ETOH) is generally not harmful
- Response rates of genotype 1 and genotype 2/3 infection to IFN Rx are ~ same
- Hepatitis A and B vaccinations induce a hyperactive immune response and speed progression of fibrosis
- Rates of drug-related liver disease are ~ same as non-HCV patients
- All of the above are true
- None of the above are true

Next Case...

- 52 year old Black male
- First diagnosed April 1998
- Initial VL 36,000 c / ml
- Initial CD4 253 cells/ul
- Wanted to start Rx

- Started on: D4T 40 mg bid; 3TC 150 mg bid; Indinavir 800 mg tid**
- Week 16, VL < 50 c/mL; CD4 448 cells/ ul**
- Week 60, complains of mild burning pain in lower extremities and increased abdominal girth.**
- He also had intermittent nausea, fatigue, some SOB with exertion (denies chest pain)**

Lab Results

(week 60; Fasting)

- VL < 50 c/ml
- CD4 420 cells/ul
- WBC 5,600 normal differential
- PCV 41%
- Na 142 K 4.1
- Cl 100 HCO₃ 20
- Cr 0.9 BUN 21
- Glu 172 AST 36
- ALT 30 Alk phos 134
- TAG 487
- Chol 218
- TB 2.2 (1.7 indirect)

You recommend:

- **Continue Current Therapy; Reevaluate in 2 weeks**
- **Substitute Tenofovir for D4T**
- **Reduce D4T dose to 30 mg bid**
- **Substitute EFV for IDV**
- **Change entire regimen to EFV, ABC, 3TC**
- **Stop antiretroviral therapy**

Next Case...

- **37 yo Male smoker, diagnosed with HIV 18 months ago**
- **CD4 103 cells/ul; VL 104,000 c/ml**
- **Started on D4T / 3TC / LPV / r**
- **Current CD4 325 cells/ul; VL <50 c/ml**
- **TG = 1047 mg/dl; Chol 237 mg/dl (HDL 35)**

At this point you recommend:

- **Observe for another 3 months with diet and exercise alone**
- **Start a 'statin' agent**
- **Start a fibrate**
- **Substitute NVP for LPV/r**
- **Substitute ABC for D4T**
- **Some other option**

Next Case, with a twist...

- 37 yo Male smoker, diagnosed with HIV 18 months ago
- CD4 103 cells/ul; VL 104,000 c/ml
- Started on D4T / 3TC / EFV
- Current CD4 325 cells/ul; VL <50 c/ml
- TG = 420 mg/dl; Chol 237 mg/dl (HDL 35)

At this point you recommend:

- **Observe for another 3 months with diet and exercise alone**
- **Start a 'statin' agent**
- **Start a fibrate**
- **Substitute NVP for EFV**
- **Substitute ABC for D4T**
- **Some other option**

Next Case, shaken not stirred...

- 37 yo Male smoker, diagnosed with HIV 18 months ago
- CD4 103 cells/ul; VL 104,000 c/ml
- Started on D4T / 3TC / EFV
- Current CD4 325 cells/ul; VL <50 c/ml
- TG = 425 mg/dl; Chol 187 mg/dl (HDL 35)
- Complains of facial fat loss

At this point you recommend:

- **Observe for another 3 months, encourage him to eat more and exercise**
- **Start growth hormone therapy**
- **Substitute NVP for EFV**
- **Substitute ABC for D4T**
- **Refer to a plastic surgeon for implants**
- **Some other option**

Efavirenz Switch Studies : 2NRTI + PI

→ 2NRTI + Efavirenz

N	Follow Up	TAGs	Chol	Glu/IR	Body Change
33	40 wks	NC	NC	NC	NC
39	24 wks	~↑	NC	NC	NC
43	24 wks	~↑	NC	-	NC
25	24 wks	~↓	NC	-	NC
25	24 wks	~↑	~↑	↓	~↓ VAT
165	24 wks	-	NC	-	-
27	36 wks	~↓	~↓	~↓	NC
56	24 wks	↓	↑HDL	-	NC
45	48 wks	↓	~↓	-	-
20	24 wks	NC	NC	NC	NC
93	52 wks	↓	NC	↓	↓ WHR ↓ VAT
41	52 wks	-	-	NC	-
100	52 wks	↓	↓	-	NC

Nevirapine Switch Studies : 2NRTI + PI →2NRTI + Nevirapine

N	Follow Up	TAGs	Chol	Glu/IR	Body Change
23	24 wks	↓	↓	↓	↓ WHR
138	24 wks	~↓	~↓	-	~↓
60	36 wks	↓	↓	NC	NC
80	24 wks	↓	↓	NC	↓ VAT
116	12 wks	~↓	NC	↓	NC
40	48 wks	↓	NC	↓	NC
26	24 wks	↓	↓	-	NC
63	60 wks	↓	NC	-	NC
68	24 wks	~↓	NC	-	-

Nucleoside Switch Studies : D4T → ZDV or ABC

N	Follow Up	TAGs	Chol	Glu/IR	Body Change
59	36 wks	↓	NC	NC	↓ SAT VAT NC
211	24 wks	~↓	↓	↓	-
163	52 wks	↓	↓	-	-
105	45 wks	~↓	~↓	-	-

Treatment Interruption Studies

N	Follow Up	TAGs	Chol	Glu/IR	Body Change
26	7 wks	↓	↓	NC	NC