Case Presentation 1

A 24 yo graduate student in physics is diagnosed with asymptomatic HIV infection. His CD4 cell count is 700/mm^3 and his plasma HIV-1 RNA level is 1500 c/mL. These values were confirmed on a second visit.

A full discussion of the potential benefits and risks of antiretroviral therapy is undertaken. The patient is amenable to therapy but is uncertain.

Clinical Decision Point

What do you recommend?

1. **Start IDV/ZDV/3TC**
2. **Start IDV/low-dose RTV/ZDV/3TC**
3. **Start NFV/d4T/3TC**
4. **Start NFV/d4T/ddI**
5. **Start NVP/ZDV (or d4T)/3TC**
6. **Start EFZ/ZDV (or d4T)/3TC**
7. **Start ABC/ZDV (or d4T)/3TC**
8. **Defer therapy and follow**

Course

The patient returns 3, 6, 9 and 12 months later. The patient has remained asymptomatic but the CD4 cell count has progressively fallen to 600/mm^3 and the plasma HIV-1 RNA level has risen to 4500 c/mL.

The patient is concerned but still on the fence about starting therapy.

Clinical Decision Point

What do you recommend?

1. **Start IDV/ZDV/3TC**
2. **Start IDV/low-dose RTV/ZDV/3TC**
3. **Start NFV/d4T/3TC**
4. **Start NFV/d4T/ddI**
5. **Start NVP/ZDV (or d4T)/3TC**
6. **Start EFZ/ZDV (or d4T)/3TC**
7. **Start ABC/ZDV (or d4T)/3TC**
8. **Defer therapy and follow**

Course

After lengthy discussion, therapy is started with ZDV/3TC (fixed dose combination) and EFZ. The patient complains of severe cognitive difficulties—wild dreams, a sense of confusion and difficulty concentrating.

His graduate studies are suffering and there is no improvement after 2-3 weeks of therapy.

Clinical Decision Point

What do you recommend?

1. **Continue the current regimen with encouragement that the symptom will abate**
2. **Continue ZDV/3TC and split the dose of efavirenz**
3. **Continue ZDV/3TC and substitute ABC for EFZ**
4. **Continue ZDV/3TC and Substitute NVP for EFZ**
5. **Discontinue all therapy**

Course

Option 3 is chosen and ABC is substituted for EFZ. The patient is initially fine but after 10 days he develops fever, myalgias, nausea, vomiting and mild rash.

Clinical Decision Point

What do you recommend?

1. **Immediately stop ABC**
2. **Immediately stop the entire regimen**
3. **Substitute nevirapine for ABC**
4. **Substitute nelfinavir for ABC**

Course

The entire regimen is stopped and the patient rapidly improves. It is now 7 days after all symptoms have resolved.

Clinical Decision Point

What do you recommend?

1. **Restart ZDV/3TC and substitute NVP for ABC**
2. **Restart ZDV/3TC and substitute NFV for ABC**
3. **Restart ABC/ZDV/3TC**

Course

NVP/ZDV/3TC is begun and the patient does well. The regimen is well tolerated, the CD4 cell count rises to 750/mm^3 and the plasma HIV-1 RNA falls to <50 c/mL.

Case Presentation 2

A 35 yo woman, unaware of her HIV status, presents with Pneumocystis carinii pneumonia.
She responds well to treatment and is seen in clinic to discuss the initiation of antiretroviral therapy. Her CD4 cell count is 10 and her plasma HIV-1 RNA level 1,000,000 c/mL at a stable point post resolution of her PCP.

After a full discussion of the issues, she is willing to begin therapy.

Clinical Decision Point

What do you recommend?

1. Start IDV/ZDV/3TC
2. Start IDV/low-dose RTV/ZDV/3TC
3. Start NFV/d4T/3TC
4. Start NFV/d4T/ddI
5. Start RTV/SQV (400/400)/d4T/3TC
6. Start IDV/EFZ/d4T/3TC
7. Start EFV/ZDV (or d4T)/3TC
8. Start ABC/ZDV (or d4T)/3TC

Course

Therapy is begun with IDV/low-dose RTV/ZDV/3TC. The regimen is well tolerated and adherence is excellent. The plasma HIV-1 RNA level is repeated at 4 weeks and is found to be 10,000 c/mL.

Clinical Decision Point

What do you recommend?

1. **Intensify therapy with ABC**
2. **Intensify therapy with EFZ**
3. **Intensify therapy with ddI/hydroxyurea**
4. **Continue the current regimen unchanged**
5. **Switch the entire regimen**

Course

IDV/low-dose RTV/ZDV/3TC is continued unchanged and the plasma HIV-1 RNA level progressively declines to <50 c/mL at week 12. The CD4 cell count has risen to 210/mm^3.

The patient is followed closely, is highly adherent to the regimen and the plasma HIV-1 RNA level is consistently <50 c/mL.

Course (Cont'd)

After 12 months of therapy, however, the plasma HIV-1 RNA level is 750 c/mL. It is repeated 3 weeks later and is 1,000 c/mL. Adherence has not changed and there have been no vaccinations or intercurrent illnesses.

Clinical Decision Point

What do you recommend?

1. **Intensify therapy with ABC**
2. **Intensify therapy with EFZ**
3. **Intensify with ddI/hydroxyurea**
4. **Continue the current regimen unchanged**
5. **Switch the entire regimen**
6. **Continue regimen and order resistance testing**
7. **Continue regimen and order trough indinavir level (assuming availability)**

Clinical Decision Point

The regimen was continued and a specimen for genotyping was sent. What do you expect the results to show?

1. Fully wild-type virus
2. The codon 70 and 215 ZDV-associated resistance mutations
3. The codon 82 PI-associated mutation
4. The codon 184 3TC-associated mutation
5. A combination of ZDV, 3TC, and IDV associated mutations

Clinical Decision Point

The results show an isolated M184V mutation.
At this point, your recommendation would be:

1. **Intensify therapy with ABC**
2. **Intensify therapy with EFZ**
3. **Intensify therapy with ABC plus EFZ**
4. **Continue the current regimen unchanged**
5. **Substitute ABC for 3TC**
6. **Substitute EFZ for 3TC**
7. **Substitute d4T/ddI for ZDV/3TC**
8. **Substitute d4T/ABC for ZDV/3TC**
9. **Switch the entire regimen**

Course

d4T/ABC is substituted for ZDV/3TC. The regimen is well tolerated and the plasma HIV-1 RNA level drops consistently below 50 c/mL.

Case Presentation 3

A 28 yo woman who is six weeks pregnant is found to be HIV positive at a routine prenatal visit. She is asymptomatic with respect to her HIV disease. Her CD4 cell count is 350/mm^3 and her plasma HIV-1 RNA level is 30,000 c/mL.

She is concerned about her own health and is willing to consider therapy but wants to avoid risk to the fetus if at all possible.

Clinical Decision Point

What do you recommend?

1. **Start therapy immediately**
2. **Defer therapy until the mid-second trimester**

Clinical Decision Point

If the CD4 cell count were 100/mm^3 and the plasma HIV-1 RNA level were 150,000 c/mL, what would you recommend?

1. Start therapy immediately
2. Defer therapy until mid-second trimester

Course

Return to the first scenario (CD4 cell count 350/mm^3; plasma HIV-1 RNA level 30,000 c/mL). The decision is made to defer initiation of therapy until the second trimester.

Clinical Decision Point

What do you recommend?

1. **Start ZDV**
2. **Start IDV/2 nRTIs**
3. **Start EFZ/2 nRTIs**
4. **Start NVP/2 nRTIs**
5. **Start ABC/2 nRTIs**

Clinical Decision Point

What dual nucleoside combination do you recommend?

1. ZDV/3TC
2. d4T/3TC
3. d4T/ddI
4. d4T/ZDV
5. ZDV/ddC
6. ZDV/ddI

Course

IDV/ZDV/3TC is started and is well tolerated. The CD4 cell count rises to 475/mm^3 and the plasma HIV-1 RNA level drops below 50 copies/mL. Delivery is uneventful and the baby remains HIV seronegative.

Case Presentation 4

A 30 yo man with a diet-controlled diabetes mellitus, mild hypercholesterolemia, and a strong family history of coronary artery disease is found to be HIV seropositive during an insurance physical.

His CD4 cell count is 250/mm^3 and the plasma HIV-1 RNA 120,000 c/mL. After consultation with his physician, he is eager to begin antiretroviral therapy.

Clinical Decision Point

What therapy would you start with?

1. **IDV/ZDV/3TC**
2. **IDV/low-dose RTV/ZDV/3TC**
3. **NFV/d4T/3TC**
4. **NFV/d4T/ddI**
5. **EFZ/ZDV(or d4T)/3TC**
6. **ABC/ZDV(or d4T)/3TC**
7. **IDV/ZDV/3TC w/ a planned switch to EFV/ZDV/3TC following successful suppression of the plasma HIV-1 RNA below 50 c/mL**
8. **IDV/ZDV/3TC w/ a planned to switch to ABC/ZDV/3TC following successful suppression of the plasma HIV-1 RNA below 50 c/mL**

Case 5: Initial Presentation

The patient is a 33 year old man who was initially diagnosed with HIV-1 infection in 1989

At the time of diagnosis, he was asymptomatic and had a CD4 cell count of 550 / mm3

Case 5: Course

He was followed on no antiretroviral therapy until 1993 when his CD4 cell count had fallen to 320/mm^3.

He was initially begun on zidovudine which he tolerated well.

The CD4 cell count peaked at 400/mm^3 five months later, but had fallen back to 300/mm^3 after a year of zidovudine therapy.

Case 5: Course

With the addition of didanosine his CD4 cell count rose to 420 / mm^3 and remained there for 2 years.

His plasma HIV-1 RNA level was first measured in 1995 and was found to be 85,000 copies / ml.

In 1996 he was entered on a clinical trial of saquinavir. He received AZT, ddC, and saquinavir until late 1997.

At study completion, his CD4 cell count was 250 / mm^3 and his plasma HIV-1 RNA level was 25,000 copies / ml.

Case 5: Course

In early 1998, his regimen was changed to D4T, 3TC, and Indinavir

By mid 1999 his plasma HIV-1 RNA level had fallen to 15,000 / mL and his CD4 cell count had risen 250 / mm^3

What therapeutic approach would you take?

Case 5: Decision Point 1

1. Sit tight since the CD4 cell count is stable or rising.
2. Change his regimen to D4T, adefovir, hydroxyurea, ritonavir, amprenavir, and efavirenz
3. Genotype his virus in preparation for a change in therapy.

Case 5: Course

A genotype is sent and returns with mutations at the following loci:

- RT: 74, 184
- PI: 10, 82, 90

Which of the following statements are true.

Case 5: Decision Point 2

1. The patient's virus is very likely to respond to AZT.
2. The patient's virus will not respond to abacavir.
3. The patient's virus will be susceptible to nelfinavir.
4. The patient's virus will respond to efavirenz.

Case 5: Course

The patient's virus is phenotyped and the following is noted:

NRTI's: The virus has wild type susceptibility to D4T and to AZT but shows a 4 fold reduction in susceptibility to ddI and abacavir. The virus is highly resistant to 3TC.

NNRTI's: The virus is fully susceptible to all NNRTI's

PI's: The 'fold" resistance to PI's is as follows: Saq: 2; Ind: 8; Rit: 8; Nel: 4; Amp: 2

Case 5: Course

The patient is treated with the following regimen:

- Ritonavir 200 mg bid
- Amprenavir 1200 mg bid
- Efavirenz 600 mg qhs
- D4T: 40 mg bid
- abacavir: 300 mg bid

Case 5: Course

The patient is lost to follow up for 4 months and returns with a plasma HIV-1 RNA level of 16,000 copies and a CD4 cell count of 210 / mm^3

He reports that the ritonavir made him sick to his stomach and that he did not take it after the first week.

He got a rash during the second week of therapy and stopped taking his abacavir. The rash resolved.

Which of the following is likely to be true?

Case 5: Decision Point 3

1. The failure to take the ritonavir allowed the efavirenz to reduce his amprenavir trough levels to the sub therapeutic range.
2. The virus is likely to have a K103N mutation.
3. The prospect of restarting abacavir should give the practitioner chest pain
4. All of the above are true

Case 5: Decision Point 4

Which of the options below is most attractive?

1. Restart the ritonavir and leave him on the current regimen.
2. Add adefovir, hydroxyurea, ddI, and AZT.
3. Stop all therapy to allow resistant virus to be replaced by wild type virus after a 2 month drug holiday.
4. Genotype the virus again and try another regimen.
5. Phenotype the virus again and try another regimen
6. Both 4. and 5.
7. Stop all drugs since he is not benefiting from therapy.

OI Prophylaxis Case Illustration 1

42 y.o. M diagnosed with HIV infection in 1985

- 4/96: d4T, 3TC, IDV; difficulty with adhering to Rx
- 6/96: CMV retinitis; nadir CD4+ 48 cells/μL
- 2/97: CD4+ 100 cells/μL, progression of CMV retinitis
- 3/97: Cidofovir--> IV GCV--> stable, started p.o. GCV
- 6/97: CD4+ 370 cells/μL; VL 1,038 copies/ml

What would you recommend for this patient?

OI Prophylaxis Case Illustration 1

1. Stop CMV maintenance therapy

2. Continue CMV maintenance therapy

3. Check CMV DNA PCR in blood and if positive continue CMV maintenance therapy

4. Check LPA responses to CMV Ag and if negative continue CMV maintenance therapy

OI Prophylaxis Case Illustration 1

Continued:

- **6/97-6/98: CD4+ count 370; GCV stopped; CMV retinitis progressed x 2**
- **5/99: CD4+ 550; CMV retinitis progressed; no LPA responses to CMV Ag; recovery of CMV from vitreous**
- **The pt remains on CMV maintenance Rx and has had 2 additional recurrences/progressions of CMV retinitis.**

OI Prophylaxis Case Illustration 2

41 y.o. M diagnosed with HIV infection in 5/97

- **5/97: Acute PCP; CD4+ < 10 cells/µL, on MAC prophylaxis with azithromycin 1200 mg once/week**
- **1/98: ZDV/3TC/NFV; VL 25,093 copies/ml, CD4+ 18**
- **5/98: Perirectal abscess; VL 375 copies/ml, CD4+ 48**
- **8/98: VL 70 copies/ml, CD4+ count 50 cells/µL**
- **11/98: VL < 20 copies/ml, CD4+ count 68 cells/µL**

What would you recommend for this patient?

OI Prophylaxis Case Illustration 2

1. Discontinue MAC prophylaxis (azithromycin)
2. Continue MAC prophylaxis with azithromycin
3. Check MAC BC and if negative discontinue azithromycin
4. Change antiretroviral therapy to determine if CD4+ count improves
5. Continue current antiretroviral therapy and stop MAC prophylaxis once CD4+ count increases to > 100/µL

OI Prophylaxis Case Illustration 2

Case continued:

- **12/98: MAC prophylaxis continued; localized pneumonia (+) MAC LN, endobronchial lesion, pericardial effusion with early signs of tamponade --> MAC Rx started with clarithromycin, ethambutol, rifabutin.**
- **MAC isolate resistant to clarithromycin; ciprofloxacin added and 6 week course of IV amikacin administered.**
- **Remains on MAC maintenance therapy with clarithromycin, ethambutol, rifabutin, cipro - symptoms and signs improved.**