

# Selecting Initial ART Regimens

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# Disclosure

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- None

# Objectives

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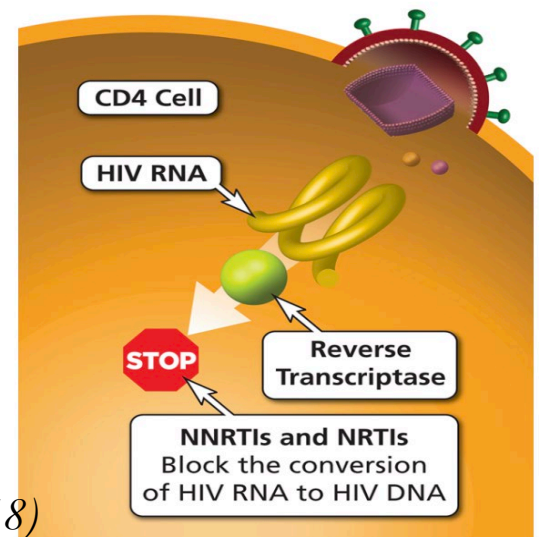
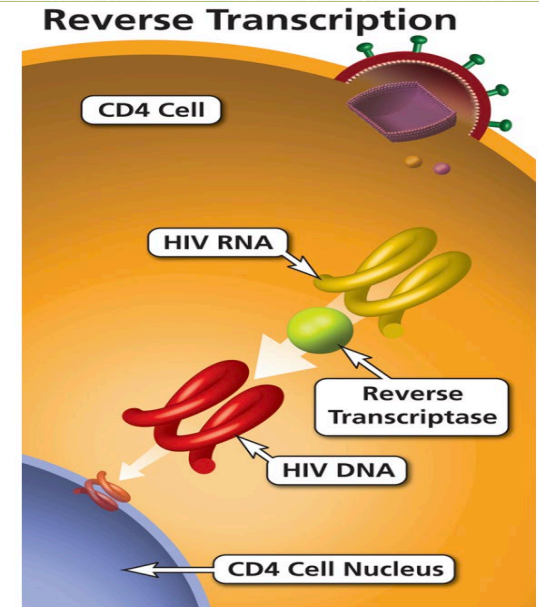
- After the completion of this activity, participants
  - Will recognize the HHS guidelines recommended initial ART regimens
  - Will identify factors affecting initial ART regimen
  - Will apply the recommendations in their own clinical practice

# Scenario-1

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- A 32 years old Caucasian male ( MSM) presents with diffuse lymphadenopathy, tonsillar enlargement, and severe thrombocytopenia. Based on the testing, he is found to have acute HIV ( Viral load of 134,000 copies/ml and CD4 of 367). He also has newly diagnosed syphilis, chlamydial throat infection, and chronic hepatitis C ( Elevated viral load). What is the best initial regimen ?
  - Dolutegravir + Tenofovir Alafenamide/Emtricitabine
  - Dolutegravir/Abacavir/Lamivudine
  - Rilpivirine/Tenofovir Alafenamide/Emtricitabine
  - Darunavir + Ritonavir + Tenofovir Alafenamide/Emtricitabine

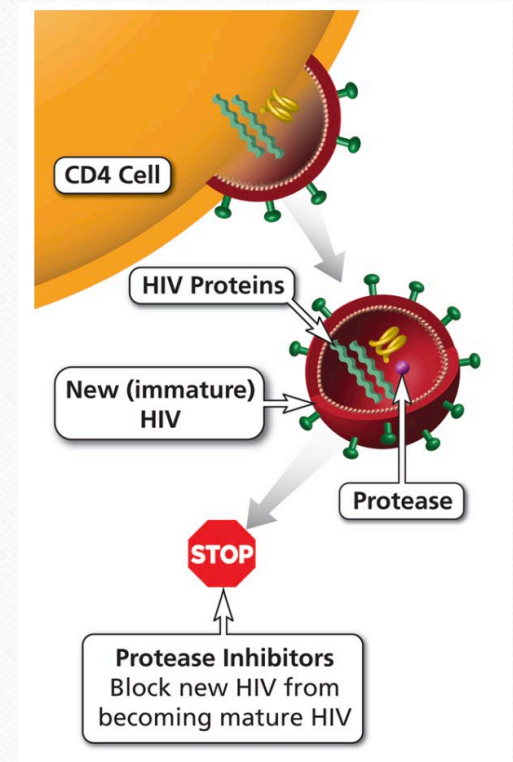
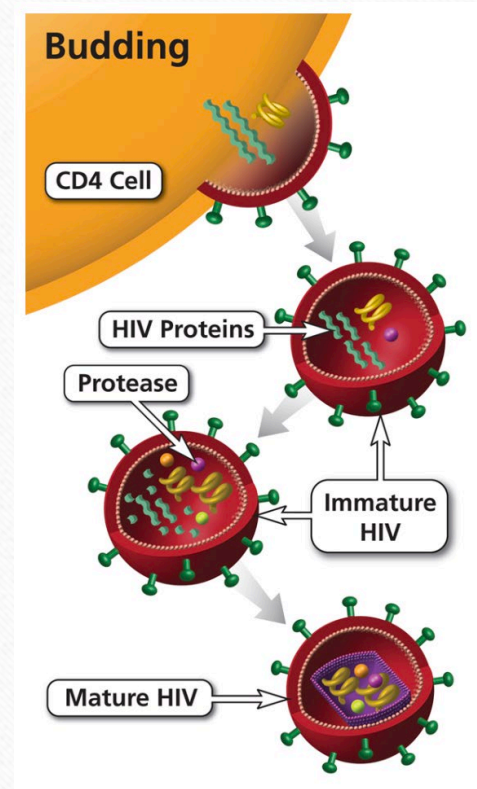
- Nucleoside Reverse Transcriptase Inhibitors ( NRTIs)
  - Zidovudine ( AZT or ZDV)
  - Stavudine ( d4T)
  - Didanosine ( ddI)
  - **Abacavir ( ABC)**
  - **Tenofovir ( Disoproxil Fumarate and Alafenamide) ( TDF, TAF)**
  - Lamivudine ( 3TC)
  - Emtricitabine ( FTC)
- Non-Nucleoside Reverse Transcriptase Inhibitors ( NNRTIs)
  - Nevirapine ( NVP)
  - Etravirine ( ETR)
  - **Efavirenz ( EFV)**
  - **Rilpivirine ( RPV)**
  - **Doravirine ( DOR)**



*Images: HHS guidelines ( last updated/ reviewed Oct 25<sup>th</sup> 2018)*

- Protease Inhibitors

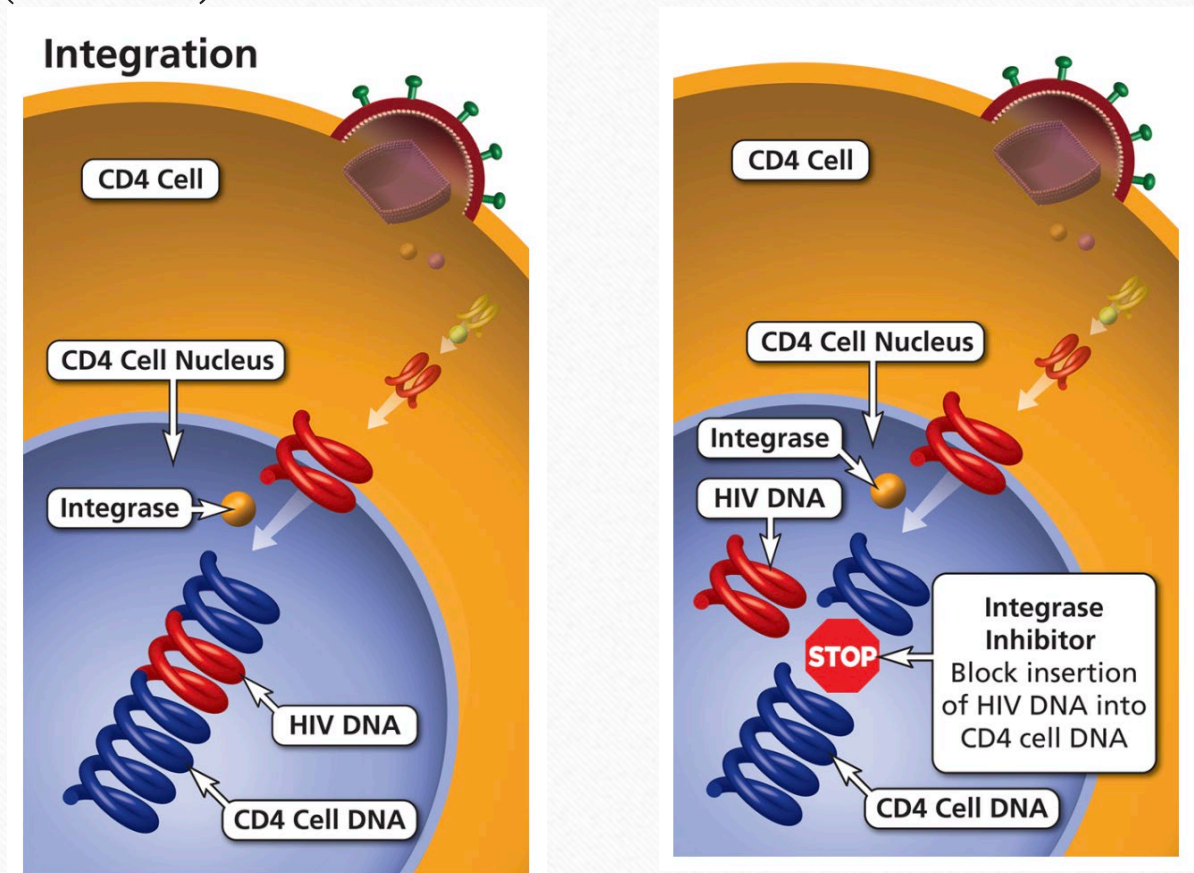
- Nelfinavir
- Saquinavir
- Lopinavir
- Indinavir
- Tipranavir
- Fosamprenavir
- **Darunavir**
- **Atazanavir**
- **Ritonavir**



*Images: HHS guidelines (last updated/ reviewed Oct 25<sup>th</sup> 2018)*

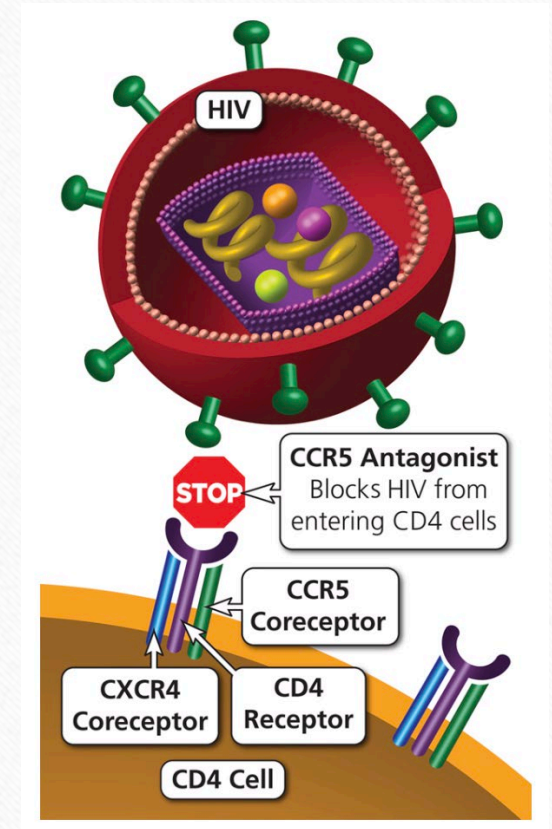
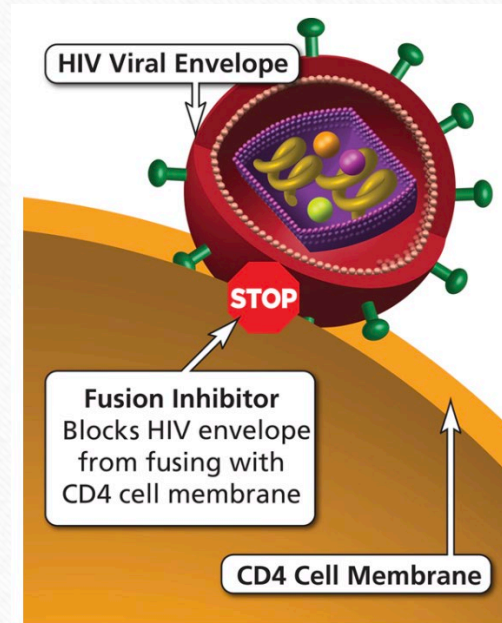
## Integrase Strand Transfer Inhibitors (INSTIs)

- Bictegravir
- Dolutegravir
- Elvitegravir
- Raltegravir



*Images: HHS guidelines (last updated/reviewed Oct 25<sup>th</sup> 2018)*

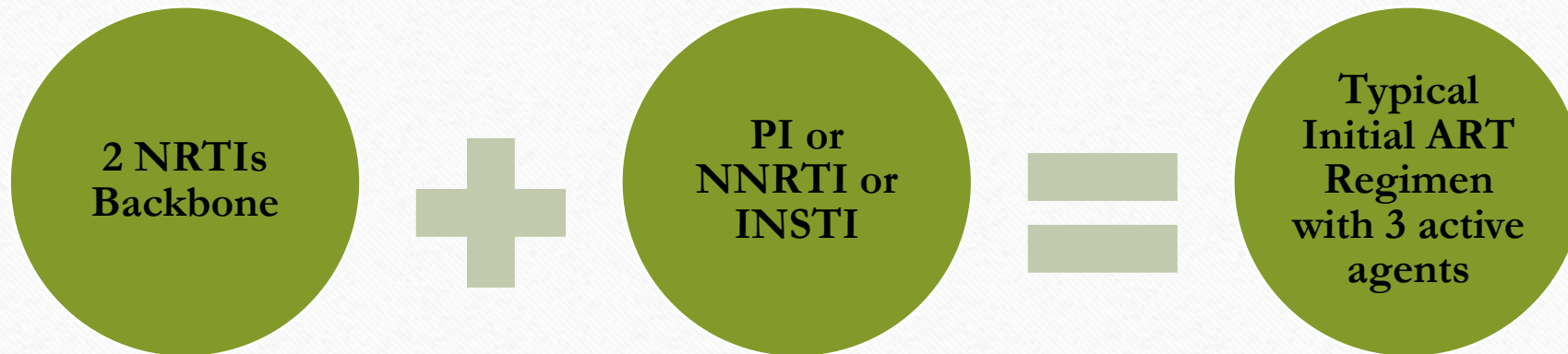
- Fusion Inhibitors
  - Enfuvirtide ( T-20)
- CCR5 Antagonists
  - Maraviroc ( MVC)
- Post-Attachment Inhibitors
  - Ibalizumab
- Pharmacokinetic Enhancers
  - Cobicistat ( COBI)



*Images: HHS guidelines ( last updated/ reviewed Oct 25<sup>th</sup> 2018)*



# A Typical Most Efficacious Regimen



## Goals of ART:

- Maximally and durably suppress plasma HIV RNA
- Restore and preserve immunologic function
- Reduce HIV-associated morbidity and prolong the duration and quality of survival
- Prevent HIV transmission

*HHS guidelines (last updated/reviewed Oct 25<sup>th</sup> 2018)*

## Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

### INSTI plus 2 NRTIs:

**Note:** For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.

- BIC/TAF/FTC (**AI**)
- DTG/ABC/3TC<sup>a</sup> (**AI**)—if HLA-B\*5701 negative
- DTG plus tenofovir<sup>b</sup>/FTC<sup>a</sup> (**AI** for both TAF/FTC and TDF/FTC)
- RAL<sup>c</sup> plus tenofovir<sup>b</sup>/FTC<sup>a</sup> (**BI** for TDF/FTC, **BII** for TAF/FTC)

## Recommended Initial Regimens in Certain Clinical Situations

These regimens are effective and tolerable but have some disadvantages when compared with the regimens listed above or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred (see Table 7 for examples).

### INSTI plus 2 NRTIs:

**Note:** For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.

- EVG/c/tenofovir<sup>b</sup>/FTC (**BI** for both TAF/FTC and TDF/FTC)
- RAL<sup>c</sup> plus ABC/3TC<sup>a</sup> (**CI**)—if HLA-B\*5701 negative and HIV RNA <100,000 copies/mL

### Boosted PI plus 2 NRTIs: (In general, boosted DRV is preferred over boosted ATV).

- (DRV/c or DRV/r) plus tenofovir<sup>b</sup>/FTC<sup>a</sup> (**AI**)
- (ATV/c or ATV/r) plus tenofovir<sup>b</sup>/FTC<sup>a</sup> (**BI**)
- (DRV/c or DRV/r) plus ABC/3TC<sup>a</sup> —if HLA-B\*5701 negative (**BII**)

### NNRTI plus 2 NRTIs:

- DOR/TDF<sup>b</sup>/3TC (**BI**) or DOR plus TAF<sup>b</sup>/FTC (**BIII**)
- EFV plus TDF<sup>b</sup>/FTC<sup>a</sup> (**BI** for EFV 600 mg/TDF/FTC or EFV 600 mg/TDF/3TC, **BII** for EFV 600 mg plus TAF/FTC)
- RPV/tenofovir<sup>b</sup>/FTC<sup>a</sup> (**BI**)—if HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm<sup>3</sup>

### Regimens to Consider when ABC, TAF, and TDF Cannot be Used or Are Not Optimal:

- DTG plus 3TC (**BI**)
- DRV/r plus RAL BID (**CI**)—if HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm<sup>3</sup>
- DRV/r once daily plus 3TC<sup>a</sup> (**CI**)

*HHS guidelines (last updated/reviewed Oct 25<sup>th</sup> 2018)*

- **Factors to consider before initial ART selection**

- Pretreatment viral load and CD4 count
- Genotype
- HLA-B\*5701 status
- Individual preferences
- Anticipated adherence to the regimen
- Comorbidities/coinfections and co-existing conditions
- Regimen's barrier to resistance
- Potential adverse effects
- Known or potential drug interactions
- Convenience (e.g., pill burden, dosing frequency, availability of fixed-dose combination (FDC) formulations, food requirements)
- Cost and access

*HHS guidelines (last updated/reviewed Oct 25<sup>th</sup> 2018)*

# Scenario-1

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  - A. Dolutegravir + Tenofovir Alafenamide/Emtricitabine
  - B. Dolutegravir/Abacavir/Lamivudine
  - C. Rilpivirine/Tenofovir Alafenamide/Emtricitabine
  - D. Darunavir + Ritonavir + Tenofovir Alafenamide/Emtricitabine

# Scenario-1

Urgency

Genotype/Resistance barrier

Viral load/CD4

HLA B\*5701

Potential interactions

- 
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    - A. Dolutegravir + Tenofovir Alafenamide/Emtricitabine**
    - B. Dolutegravir/Abacavir/Lamivudine
    - C. Rilpivirine/Tenofovir Alafenamide/Emtricitabine
    - D. Darunavir + Ritonavir + Tenofovir Alafenamide/Emtricitabine

## Scenario-2

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- A 29 years old female was recently diagnosed with HIV. Viral load is 150,000 copies/ml and CD4 is 344. She wants to conceive in near future and is sexually active with her boyfriend without using any contraceptives. Genotype is pending. HLA B\*5701 is negative. What is the best regimen ?
  - A. Bictegravir/Tenofovir Alafenamide/Emtricitabine
  - B. Dolutegravir/Abacavir/Lamivudine
  - C. Darunavir + Ritonavir + Tenofovir Disoproxil Fumarate/Emtricitabine

# Scenario-2

Potential co-existing condition  
Potential adverse effects

- 
- A 29 years old female was recently diagnosed with HIV. Viral load is 150,000 copies/ml and CD4 is 344. She wants to conceive in near future and is sexually active with her boyfriend without using any contraceptives. Genotype is pending. HLA B\*5701 is negative. What is the best regimen ?
    - A. Bictegravir/Tenofovir Alafenamide/Emtricitabine
    - B. Dolutegravir/Abacavir/Lamivudine
    - C. Darunavir + Ritonavir + Tenofovir Disoproxil Fumarate/Emtricitabine**



## Scenario-3

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- A 46 years old male ( IV drug user) is recently diagnosed with HIV ( Viral load of 85,000 and CD4 of 340). He was diagnosed with hepatitis B few months ago and has positive surface Ag on repeat testing now. HLA B\*5701 is negative. Genotype testing is pending. He has h/o non-compliance to medical care and medication intake. What is the best regimen?
  - A. Bictegravir/Tenofovir Alafenamide/Emtricitabine
  - B. Dolutegravir/Abacavir/Lamivudine
  - C. Raltegravir + Tenofovir Alafenamide/Emtricitabine
  - D. Rilpivirine/Tenofovir Alafenamide/Emtricitabine

# Scenario-3

Co-existing condition  
Compliance  
Genotype  
Resistance barrier

- 
- A 46 years old male ( IV drug user) is recently diagnosed with HIV ( Viral load of 85,000 and CD4 of 340). He was diagnosed with hepatitis B few months ago and has positive surface Ag on repeat testing now. HLA B\*5701 is negative. Genotype testing is pending. He has h/o non-compliance to medical care and medication intake. What is the best regimen?
    - A. Bictegravir/Tenofovir Alafenamide/Emtricitabine**
    - B. Dolutegravir/Abacavir/Lamivudine
    - C. Raltegravir + Tenofovir Alafenamide/Emtricitabine
    - D. Rilpivirine/Tenofovir Alafenamide/Emtricitabine

# Scenario-4

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- A 58 years old female has h/o osteopenia and stage IV renal disease. She was diagnosed with HIV several years ago but has not been on medications. Now she is willing to start ART but would like to keep the number of medications minimal. Viral load is 190,000 and CD4 is 98. Genotype showed no resistance. HLA B\*5701 is positive. What is the best regimen?
  - A. Bictegravir/Tenofovir Alafenamide/Emtricitabine
  - B. Dolutegravir/Abacavir/Lamivudine
  - C. Dolutegravir + Lamivudine
  - D. Darunavir + Ritonavir + Raltegravir

# Scenario-4

Co-existing conditions

Viral load/CD4

HLA B\*5701

Potential adverse effects

Convenience

- 
- A 58 years old female has h/o osteopenia and stage IV renal disease. She was diagnosed with HIV several years ago but has not been on medications. Now she is willing to start ART but would like to keep the number of medications minimal. Viral load is 190,000 and CD4 is 98. Genotype showed no resistance. HLA B\*5701 is positive. What is the best regimen?
    - A. Bictegravir/Tenofovir Alafenamide/Emtricitabine
    - B. Dolutegravir/Abacavir/Lamivudine
    - C. Dolutegravir + Lamivudine**
    - D. Darunavir + Ritonavir + Raltegravir

## Scenario-5 ( Time permitting)

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- A 48 years old male was diagnosed with HIV two years ago but has not been on treatment yet. He had a massive myocardial infarction last month and he was also found to have markedly elevated LDL and total cholesterol. He is currently on optimal medical management. He says he wants to start ART as he wants to “ take good care of my health now”. Viral load is 145,000 copies/ml and CD4 is 160. Genotype shows no resistance and HLA B\*5701 is negative. What is the best regimen?
  - A. Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine
  - B. Dolutegravir + Tenofovir Alafenamide/Emtricitabine
  - C. Dolutegravir/Abacavir/Lamivudine
  - D. Darunavir + Ritonavir + Tenofovir Alafenamide/Emtricitabine

## Scenario-5 ( Time permitting)

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  - A. Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine
  - B. Dolutegravir + Tenofovir Alafenamide/Emtricitabine**
  - C. Dolutegravir/Abacavir/Lamivudine
  - D. Darunavir + Ritonavir + Tenofovir Alafenamide/Emtricitabine

# Take Home Points

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- Follow the updated guidelines <https://aidsinfo.nih.gov/guidelines> ( New evidence continues to change the recommendations)
- Keep in mind !! ( Easy to make mistakes)
  - Pretreatment viral load and CD4
  - Genotype and resistance barrier
  - HLA-B\*5701 status
  - Co-existing conditions
  - Interactions, formulations, preferences, convenience, adherence
  - Availability

# Thank You !!!!

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- Questions ??