General Overview of Commercially Available Long-Acting Injectable Antiretroviral Therapy: In 5 Slides

Louisiana Commission on HIV and Hepatitis C
Education, Prevention, and Treatment

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Slide 1
Long Acting Cabotegravir (CAB-LA) for HIV Prevention

- Apretude ® 200 mg/mL (FDA Approved December 2021)
- Integrase Strand Transfer Inhibitor (INSTI)
  - Blocks Integrase (early event in the HIV life cycle)
  - When present in the bloodstream upon exposure to HIV, it blocks seroconversion
- Indication: at risks adults and adolescents weighing 35 kg or more to reduce the risk of sexually acquired HIV-1 infection.
- Clinical Trials:
  - **HPTN 083**: HIV incidence rate of 0.38% CAB versus 1.21% TDF/FTC; 66% fewer infections in CAB versus TDF/FTC; Post Hoc Analysis 68%. Statistically superior.
  - **HPTN 084**: HIV incidence rate of 0.21% CAB versus 1.79% TDF/FTC; 89% few infections with CAB versus TDF/FTC. Statistically superior.
- Administration/Dosing Schedule/Clinical Considerations
  - Intramuscular (IM) site. Ventrogluteal site is preferred.
  - Initiation: 600 mg (3 ML) IM X 2 doses one month apart.
  - Continuation injections: 600 mg IM every 2 months.
  - There is a 7-day window period before or after the injection date.
  - Follow up: HIV testing 4th gen Ag/Ab testing and HIV RNA testing is recommended upon initiation and before every injection.

Slide 2
Long Acting Cabotegravir/Rilpivirine (CAB/RPV) for HIV Treatment

- Cabenuva ® [cabotegravir 200 mg/mL; rilpivirine 300 mg/mL] (FDA Approved January 2021; February 2022)
- Integrase Strand Transfer Inhibitor (INSTI) plus Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)
  - INSTI: Blocks integrase (early event in the HIV life cycle)
  - NNRTI: NNRTIs work by BINDING reverse transcriptase keeping HIV from making a copy of itself.
- Indication: Approved for adolescents and adults 12 years or older and weighing 35 kg or more who are treatment experienced with no known resistance to either drug.
- Clinical Trials: ATLAS and FLAIR (2 randomized, open-label, multicenter, multinational phase 3 studies)
  - **ATLAS**: ART-experienced (randomized 1:1) to current antiretroviral regimen or to oral lead in (CAB/RPV) then to injection.
  - **FLAIR:** ART naïve/viremic >1000 copies/mL; induction ABC/3TC/DTG to viral suppression; then (randomized 1:1) to remain on ABC/3TC/DTG or to oral lead in (CAB/RPV) then to injection.
  - Monthly injections of CAB+RPV LA were noninferior to daily oral CAR for maintaining HIV-1 suppression
- Administration/Dosing Schedule/Clinical Considerations
  - Intramuscular (IM) site. Ventrogluteal site is preferred.
  - Initiation: 600 mg CAB (3ML)/900 mg (3ML) RPV IM X 2 doses one month apart.
  - Continuation injections: 600 mg/900 mg IM every 2 months.
  - There is a 7-day window period before or after the injection date.

Slide 3
Long-Acting Lenacapavir (LEN) for Heavily Treatment Experienced People Living with HIV (PLWH)

- Sunlenca ® lenacapavir 463.5mg/1.5 mL (FDA Approved December 2022)
- Capsid Inhibitor: disrupts HIV replication in multiple early to late processes.
  - Capsid: coating of proteins which houses the HIV viral genome.
  - Capsid inhibitors binds to the HIV capsid protein and disrupts:
    - Capsid core formation.
    - Virus assembly and release.
    - Nuclear transport.
- Indication: treatment of human immunodeficiency virus type 1 (HIV-1) infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.

Slide 4
LEN Continued

- Clinical Trials: Capella Study (Phase 3 Trial) enrolled patients with multidrug-resistant HIV-1 infection in two cohorts.
  - Cohort 1 (n=36 [24 LEN; 12 placebo]): randomized 2:1 (oral LEN or placebo in addition to their failing therapy for 14 days; during the maintenance period, starting on day 15, patients in the LEN group received subcutaneous LEN once every 6 months, and those in the placebo group received oral LEN followed by subcutaneous LEN; both groups also received optimized background therapy (OBT).
  - Cohort 2 (n=36): all the patients received open-label oral LEN with OBT on days 1 through 14; subcutaneous LEN was then administered once every 6 months starting on day 15.
  - The primary end point was the percentage of patients in cohort 1 who had a decrease of at least 0.5 $\log_{10}$ copies per milliliter in the viral load by day 15; a key secondary end point was a viral load of less than 50 copies per milliliter at week 26.
  - In patients with multi-drug-resistant HIV-1 infection, those who received LEN had a greater reduction from baseline in viral load than those who received placebo.

Slide 5
LEN Continued

- Administration/Dosing/Clinical Considerations
  - Administration/Dosing (Two Options): subcutaneous (SC) injection
    - LEN 600 mg orally PLUS 927 mg SC injection (Day 1); 600 mg oral (Day 2). Daily OBT.
    - LEN 600 mg orally (Day 1 and 2); 300 mg (Day 8); 927 mg SC (Day 15). Daily OBT.
    - Maintenance: 927 mg SC every 6 months (+/- 2 weeks) plus daily OBT.
  - Clinical Considerations
    - OBT is incredibly important. Lack of adherence to OBT could lead to LEN monotherapy and resistance.

References

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