Florida/Caribbean AIDS Education and Training Center

HIV CareLink

A Newsletter for HIV/AIDS Primary Care Providers

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Updated Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Released

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On November 3rd, 2008, updated **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents** developed by the Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents were released. This issue of HIV CareLink summarizes the major changes to the Guidelines which are available at http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf.

New Rating Scheme

- D (should usually not be offered) and E (should never be offered) ratings removed
- Ratings A, B, C used to rate the strength of a given statement with A being the strongest recommendation
- Quality of evidence
  - o I ranking now includes randomized trials with virologic endpoints (previously only included trials with clinical endpoints)
  - o II ranking includes non-randomized trials or observational cohort studies with long-term clinical outcomes
  - o III ranking remains *expert opinion*

Laboratory Monitoring

- New table provides schedule for baseline and periodic lab monitoring-summarized below, see Table 3 for full details
- Viral load (VL) and CD4
  - o VL changed from q3-4 mos to q3-6 mos (on or off ART)
  - o For pts on ART, consider 6 mos for VL/CD4 if virologicaly/immunologically stable x 2-3 yrs
  - o Check VL just prior to and 2-8 wks after starting or changing ART and q4-8 wks until undetectable
  - o CD4 remains q3-6 mos
- CBC with differential
  - o q3-6 mos (on or off ART)
  - o Check CBC with diff just prior to and 2-8 wks after ART initiation
- Fasting lipids
  - o Annually if normal (q6 mos if abnormal or borderline) at last assessment
- Fasting glucose
  - o If normal at last assessment check annually if not on ART or q6 mos if on ART. Check q3-6 mos if abnormal or borderline at last assessment.
- Urinalysis
  - o Baseline for all pts
  - o Annually for pts on tenofovir
  - o Q3-6 mos for pts with HIVAN
- Basic chemistry (preferably fasting), LFTs
  - o Na, K, HCO_3, Cl, BUN, Creatinine, AST, ALT, Tbili, Dbili q6-12 mos if off ART or q3-6 mos if on ART (some recommend phosphorus if on tenofovir)
  - o Estimate of renal function should include CrCl (Cockcroft-Gault equation) or GFR (MDRD equation)

What to Start in ART-naïve Patients

- Darunavir (Prezista®)/ritonavir (RTV, Norvir®) qd *added as a preferred PI option* (see next page for more detailed information)
- Lopinavir/RTV (Kaletra®) qd changed from alternative to preferred PI option

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- Abacavir/lamivudine (Epzicom®) changed from preferred to alternative NRTI component due to ↑ risk of MI in pts with high cardiac risk and potency concerns in pts with VL > 100,000 copies/mL
- Unboosted atazanavir (ATV, Reyataz®), didanosine (Videx EC®) + [lamivudine (Epivir®) or emtricitabine (Emtriva®)] not recommended due to efficacy concerns
- Neither nelfinavir (Viracept®) nor indinavir (Crixivan®) recommended for initial tx

ART Components Not Recommended
- Etravirine (ETR, Intelence™) should not be used with an unboosted PI
- ETR should not be used with RTV-boosted ATV, fosamprenavir (Lexiva®), tipranavir (Aptivus®)

New Section on Regimen Simplification
- Change in ART to ↓ pill burden or dosing frequency, ↑ tolerability, and/or ↓ food/fluid requirements
- Consider simplification when:
  - o Receiving ART no longer recommended as preferred or alternative options for initial tx
  - o Regimen chosen in setting of ART failure when there was incomplete resistance or drug-drug interaction data
  - o Regimen chosen prior to availability of newer ART options that may be easier to take and/or better tolerated

Darunavir (DRV, Prezista®)/RTV QD Approved for ART-naïve

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- On October 21st 2008, FDA approved qd regimen of RTV-boosted DRV for ART-naïve pts
- Dosing in ART-naïve patients
  - o DRV 800 mg (2-400 mg tabs) + RTV 100 mg (1 capsule) po qd with food
  - o New 400 mg tablet approved and available in pharmacies
  - o Cost: The monthly wholesale acquisition cost is $822.12, plus cost of 100 mg ritonavir
- Dosing in ART-experienced patients
  - o DRV 600 mg (1 tab) + RTV 100 mg (1 cap) po bid with food
  - o 300 mg tab no longer being manufactured
  - o FDA granted traditional approval of DRV/RTV bid in ART-exp pts

ART-naïve Indication Based on Results of ARTEMIS Study
- DRV/RTV 800 mg/100 mg qd compared to LPV/RTV 800 mg/200 mg total daily dose (either qd or bid) both with tenofovir/ emtricitabine (Truvada®) in ART-naïve pts

Baseline Characteristics (selected)

	DRV/RTV	LPV/RTV
N	343	346
Female, n (%)	104 (30)	105 (30)
Age, years[1]	36 (9)	35 (9)
Black, n (%)	80 (23)	71 (21)
Hispanic, n (%)	77 (22)	77 (22)
HIV-RNA[2] (range)	70,800 (835-5,580,000)	62,100 (677-4,580,000)
CD4[3] (range)	228 (4-750)	218 (2-714)
HBV/HCV, n (%)	43 (13)	48 (14)
CD4 < 200, n (%)	141 (41)	148 (43)
HIV-RNA ≥ 100K, n (%)	117 (34)	120 (35)

[1] Mean (± SD)
[2] Median, copies/mL
[3] Median, cells/mm^3

- Results-96 week analysis
  - o 79% of DRV/RTV and 71% of LPV/RTV pts achieved VL < 50 copies/mL
    - ▪ Diff = 8.3% with 95% CI (1.8-14.7), ITT-TLOVR, p=0.012
  - o Less Grade 2-4 diarrhea with DRV/RTV (4% vs. 11% with LPV/RTV, p<0.001)
  - o Smaller median % ↑ in Trigs (12% vs. 50%, p < 0.001) and TC (15% vs. 23%, p<0.001) with DRV/RTV compared to LPV/RTV

Reference:
1. Mills A, Nelson M, Jayaweera D, et al. Efficacy and safety of darunavir/ritonavir 800/100 mg once-daily versus lopinavir/ritonavir in treatment-naive, HIV-1-infected patients at 96 weeks: ARTEMIS (TMC114-C211). Program and abstracts of the 48th Annual ICAAC/IDSA 46th Annual Meeting; October 25-28, 2008; Washington, DC. Abstract H-1250c. More detailed summary available online at http://www.clinicalcareoptions.com/HIV/Conference%20Coverage/Washington%202008/Tracks/First-Line/Capsules/1250c.aspx
(Must enter your clinicalcareoptions.com login for link to function)