Anti-retroviral options for Southern Africa

Wits HIV Research Unit

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Context…

- Major urban centre with infectious diseases expertise vs
- Regional hospital with untrained doctors
- Regional hospitals/clinics with intermittent doctors
- Regional clinics with nurses
- Regional health ‘facilities’ with non-nurses

Aims of regimens…

- Effective (all triple combinations good, durable)
- Sustainable (side effects, cost, infrastructure)
- Simple (food restrictions, dosing frequencies, pill burden)
- Tolerable (side effects)
- Safe (side effects) – for patient & easy for HCW diagnosis
- Acceptable (clinician agreement)

Considerations…

- High incidence of tuberculosis, interactions of rifampicin and ART
- Pregnancy-friendliness
- Ease of administration
- Side effect profile
- Other drugs
- Cost

TB and ART

- Very high incidence of TB in SA
- Rifampicin problem with most PI's and nevirapine
- Nucleosides OK, efavirenz OK (with dose modification)
- BUT – ART dramatically decreases incidence of TB ?a consideration

Pregnancy-friendly regimens

- NOT efavirenz
- NOT ddI/d4T in combination (?apart)
- ? New drugs
- Most old drugs OK
- Do we drive our protocols based on this?

Ease of administration…

- Twice daily possible
- Try to minimise food issues
- Problem with: ddI (needs empty stomach), indinavir (after meals), other PI's
- ?possibility of combination tablets
- ?future research re: once daily dose

Side effects…

- Gastro-intestinal tract side effects prominent
- ?choose drugs that have clinical indicators, rather than laboratory (ddI, d4T, 3TC, abacavir, efavirenz vs AZT, nevirapine, protease inhibitors)
- May need options for special groups eg: drivers, machine operators
- ?restrict number of variations, to allow HCW's to familiarise themselves with side-effects

Other drugs…

- Rifampicin discussed
- Antacids may decrease absorption
- P450 changes – azoles, cimetidine
- Cardiac: QTc - terfenidine, astemizole
- Contraceptive preparations

Cost

- Fluid, open to negotiation
- Nucleoside analogues: d4T cheapest, ddi cheap, ?AZT/3TC
- NNRTI's: Efav/nev very similar
- PI's: Ind with rit cheap, ?Kaletra, saquinavir mod expensive, nelfinavir prohibitive

Minimum suggested recommendations:

- Three drugs – two nucleosides and PI or NNRTI or abacavir
- Twice daily dosing

Suggested nucleoside combinations and problems

- d4T and 3TC - ?pregnancy problem
- AZT and 3TC – lab monitoring
- ddI and (d4T or AZT or 3TC) – food restrictions, pregnancy
- ddC – only with AZT, unpopular drug
- Abacavir – idiosyncratic drug reaction a big problem

Non-nucleoside analogues

- Nevirapine – not OK in TB, needs lab monitoring
- Efavirenz – pregnancy unfriendly

Protease inhibitors…

- Indinavir with ritonovir – kidney stones, water/food restrictions, problem in TB
- Kaletra (lopinavir/rit) – problem in TB
- Saquinavir/rit – problem in TB
- Nelfinavir – problem in TB

Easiest in my opinion…

- d4T/3TC/efavirenz for TB-friendliness, no monitoring
- AZT/3TC/PI for women who may/want to fall pregnant

- No nevirapine
- No abacavir, other than in places with skills

- BUT adherence, adherence, adherence – biggest challenge is to get trained HCW's to administer Rx in enabling environment to motivated patients