

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 (ddl, 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



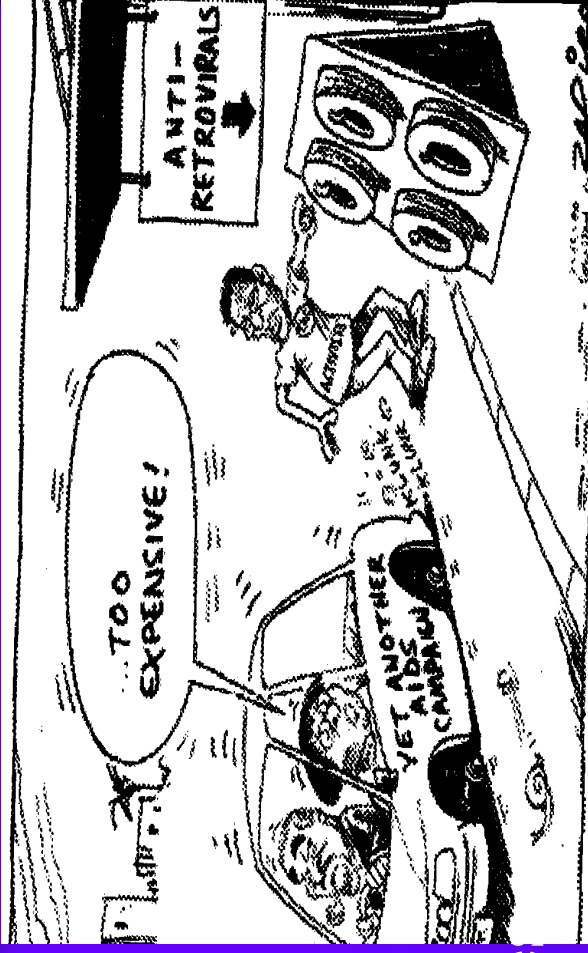
Other drugs...

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



Cost


- ◆ Fluid, open to negotiation
- ◆ Nucleoside analogue 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 ritonavir – 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

