

Generic ART: Guidelines and Research

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Should HIV treatment
guidelines consider cost?

DHHS Guidelines and Cost

- When to start ART?: earlier vs. late
 - Freedberg NEJM 2001; Schackman Am J Pub Health 2001
 - Additional data needed for ↑ CD4 thresholds
- Resistance testing: GT vs. PT
 - Sax Clin Infect Dis 2005
- Tropism testing: GT vs. PT
- Relationship to non-adherence

DHHS Guidelines and Cost of ART

- Rx simplification: 2 PI + RTV
- PI monotherapy rationale
- maraviroc requires tropism testing

DHHS Guidelines: Cost Table

Appendix B Table 8:

Monthly Suggested Wholesale Price (SWP)

Antiretroviral Drug (Generic and Brand Names)	Strength	Dosing	Tabs/Capsules/mLs per Month	SWP ^a (Monthly)
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
abacavir				
• generic	300 mg tab	2 tabs daily	60 tabs	\$602.66
• Ziagen	300 mg tab	2 tabs daily	60 tabs	\$670.37
• Ziagen	20 mg/mL soln	30 mL daily	900 mL	\$674.60
didanosine delayed-release				
• generic	400 mg cap	1 cap daily	30 caps	\$368.72
• Videx EC	400 mg cap	1 cap daily	30 caps	\$478.08
emtricitabine				
• Emtriva	200 mg cap	1 cap daily	30 tabs	\$574.14
• Emtriva	10 mg/mL soln	24 mL daily	680 mL (28-day supply)	\$542.32
lamivudine				
• generic	300 mg tab	1 tab daily	30 tabs	\$429.66
• Epivir	300 mg tab	1 tab daily	30 tabs	\$498.89
• Epivir	10 mg/mL soln	30 mL daily	900 mL	\$498.90
stavudine				
• generic	40 mg cap	1 cap twice daily	60 caps	\$403.70
• Zerit	40 mg cap	1 cap twice daily	60 caps	\$512.62
tenofovir				
• Viread	300 mg tab	1 tab daily	30 tabs	\$998.80
zidovudine				
• generic	300 mg tab	1 tab twice daily	60 tabs	\$360.97
• Retrovir	300 mg tab	1 tab twice daily	60 tabs	\$557.83

French HIV Rx Guidelines (10/13)

www.sante.gouv.fr

- Initial treatment
 - RAL is listed as alternative
 - “Replace Atripla by...generic efavirenz plus generic lamivudine + (branded) tenofovir...”
- Suppressed patients on ART
 - On PI/r, switch to EFV or NVP
- PEP: Use PI/r-based regimens
- Commentary **Raffi and Reynes JAC 2014 (epub)**
 - “...economic considerations significantly influence and, in some instances, take precedence over scientific evidence...”

How should HIV treatment
guidelines consider generic
ART?

DHHS Guidelines and Generics

DRUG

- abacavir
- didanosine
- lamivudine
- nevirapine
- stavudine
- zidovudine
- zidovudine/lamivudine

DHHS DESIGNATION

- alternative
- (none)
- alternative
- other
- (none)
- alternative
- alternative

Next ART to Go Generic

DRUG

- atazanavir (2017)
- darunavir (2015)
- efavirenz (2015)
- emtricitabine (2015)
- tenofovir (2017)

DHHS DESIGNATION

- preferred
- preferred
- preferred
- preferred
- preferred

What are the advantages and disadvantages of generic ART?

COST IMPACT OF GENERIC ART

(Walensky et al., Ann Intern Med 2013;158:84)

Category	Cost*
EFV/TDF/FTC (branded ART)	\$15,300
EFV + TDF/FTC ("generic 2 pill")	\$11,600
EFV + TDF/3TC ("generic 3 pill")	\$ 9,200

*Estimated savings: \$920M/year (US)

What is the comparative data
on pill number and dosing
frequency for ART regimens?

Meta-Analysis

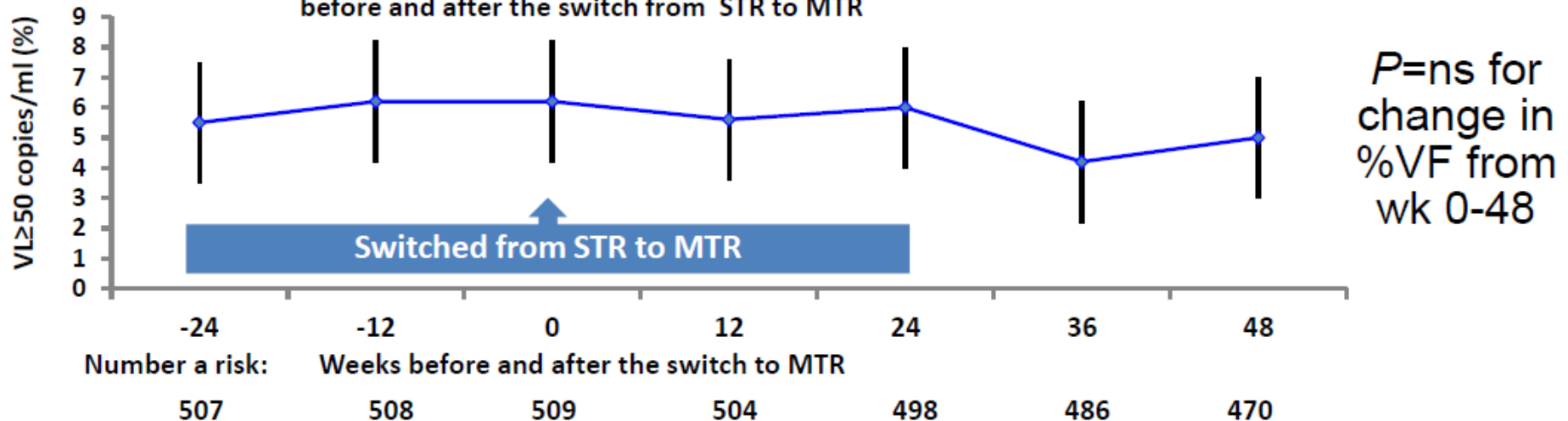
- 19 studies (N=6312 adult HIV+ naïve and experienced patients)
- Pill number
 - Negative and significant association between:
 - pill number and adherence for twice-daily but NOT once-daily regimens
 - pill number and virologic suppression for both once- and twice-daily regimens
- Dosing frequency
 - Adherence better for once- vs. twice-daily regimens
 - NO significant difference in virologic failure

What is the data on separating
the components of single-
tablet regimens (STR)?

Danish study

- Eligibility: TDF/FTC/EFV >1 year prior to change without known adherence issues
- Cohort: N=509 patients
 - 215 (42%) on first regimen
 - 478 (94%) changed to TDF + 3TC + EFV

Percentage with VL \geq 50 copies/ml and 95% CI at 12 weeks intervals before and after the switch from STR to MTR



Spanish study

- In 7/10, Balearic Islands Health Svc. ordered d/c of STR (reversed in 8/10)
- 75 patients replaced STR with individual components (vs. 150 who continued STR)
- Assessed adverse events and costs
- Results (over 120 days)
 - Rx related AE: 14 (19% of separate with 4 severe) vs. 2 (1% of STR) ($P < 0.001$)
 - Most neuropsychiatric at first visit after switch
 - Cost: €0.72/day more with separate vs. STR

What will be required for
generics to be recommended
in treatment guidelines?

What research must be done
to assess the role of generics
in treatment guidelines?