Comparing the cost-effectiveness of first-line HAART regimens

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OBJECTIVES

- To compare the cost effectiveness of lopinavir/ritonavir (LPV/r) vs. efavirenz (EFV) based regimens for the treatment of antiretroviral naïve patients over a 5 year horizon
- Measure the incremental cost per quality adjusted life year (QALY) that would be expected over the subsequent 5 years
- Assess the sensitivity of these results to model assumptions

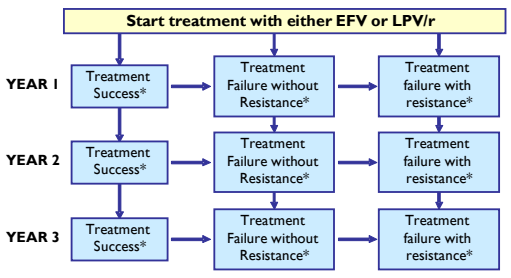
INTRODUCTIONS

- EFV and LPV/r are 2 of the first-line antiretroviral agents, in combination with 2 nucleoside/nucleotide agents, that are recommended by the Department of Health and Human Services Guidelines (DHHS)

METHODS

- Virtual cohort of treatment naïve HIV-infected patients over a 5 year-time horizon, starting one of the DHHS recommended regimens: LPV/r or EFV-based
- At the end of each year, patients could enter one of four mutually exclusive states, as shown in Figure 1: treatment success, treatment failure without resistance, treatment failure with resistance, and death

Figure 1: Markov Chain



Etc. for 5 years

*Death is possible from every state

Table 1: Clinical Parameters for Markov Model

Probabilities of treatment failure and resistance were derived from a meta-analysis of randomized clinical trials

Quality of life attributed to various states of living with HIV was based on a study by Schackman *et al.*

Probabilities of death from the various states were found in the HOMER cohort.

Parameter	Median	Low	High	Source
Probability of Failure on LPV/r (12 m)	0.275	0.241	0.308	Bishai et al, 2007, RE model
Subsequent Probability of Failure on LPV/r	0.1375	0.121	0.154	Bishai et al, 2007, RE model
Probability (Resistance | LPV/r, Failure)	0.26	0.21	0.324	Riddler et al, 2006, SA range from Bishai et al 2007
Probability of Failure on EFV (12 m)	0.252	0.19	0.41	Bishai et al, 2007, RE model
Subsequent Probability of Failure on EFV	0.126	0.09	0.20	Bishai et al, 2007, RE model
Probability (Resistance | EFV, Failure)	0.59	0.48	0.79	Riddler et al, 2006, SA range from Bishai et al 2007
Probability of Death if ARV Success	0.044	0.022	0.077	Hogg et al, 2006
Probability of Death if ARV Failure	0.084	0.059	0.118	Hogg et al, 2006
Probability of Death if Resistance	0.146	0.10	0.28	Hogg et al, 2006
Quality of Life if Success	0.866	0.825	0.907	Schackman et al, 2002
Quality of Life if Failure	0.736	0.722	0.749	Schackman et al, 2002

Table 2: Cost Parameters for Markov Model

Costs derived from Drug Topics Red Book [1] and expert clinician opinion on salvage regimens initiated after treatment failure and resistance development

Parameter	Median	Low	High	Source
Cost of LPV/r Success (Annual)	$17,113	$13,690	$20,536	Bishai et al, 2007
Cost of LPV/r Failure w/o Resistance (Annual)	$21,061	$16,848	$25,273	Bishai et al, 2007
Cost if Resistance after LPV/r (Annual)	$30,628	$24,502	$36,753	Bishai et al, 2007
Cost of EFV Success (Annual)	$14,424	$11,540	$17,309	Bishai et al, 2007
Cost of EFV Failure w/o Resistance (Annual)	$21,061	$16,848	$25,273	Bishai et al, 2007
Cost if Resistance after EFV (Annual)	$34,518	$27,615	$41,422	Bishai et al, 2007
Discount Rate	0.030	0	0.06	

[1] Thomson Healthcare, 2006

SENSITIVITY ANALYSIS

- Univariate analysis for a plausible range of each parameter for effects on cost, quality of life, and incremental cost-effectiveness ratio (ICER)
  - Repeated with wide range for each parameter
- Multivariate analysis from 1000 iterative draws

RESULTS

- Over five years, average costs associated with starting on LPV/r are $76,311, while the average costs associated with starting on EFV are $75,997
  - Difference of $314
- The LPV/r regimen provides 0.01 additional QALYs (3 days) over five years

Sensitivity Analysis Results

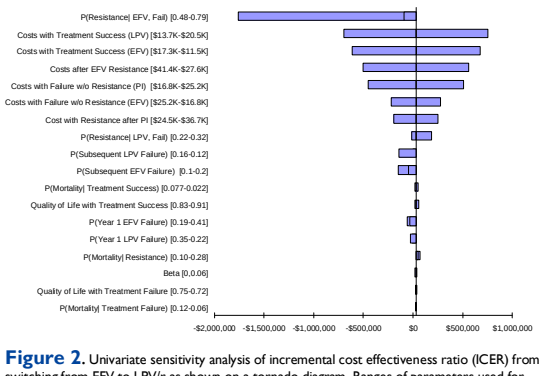


Figure 2. Univariate sensitivity analysis of incremental cost effectiveness ratio (ICER) from switching from EFV to LPV/r as shown on a tornado diagram. Ranges of parameters used for sensitivity testing shown in square brackets with value supporting left margin of tornado bar given first. Negative values mean that choosing LPV/r saves money per QALY. Positive values mean that choosing LPV/r requires spending money to produce QALYs

RESULTS CONT'D

- The results of multivariate sensitivity analysis are shown in Figure 3, which plots incremental costs and incremental QALY estimates emerging in 1000 iterations of the model
- Probabilities were beta distributions with medians, 5th percentile and 95th percentile as shown in Table 1. Costs were log normally distributed with 5th percentile and medians as per Tables 1&2
- Of the 1000 iterations, 280 fell in quadrant I (QALYs+, Costs+), 177 fell in quadrant II (QALYs-, Costs+), 138 fell in quadrant III (QALYs-,Costs-), and 335 fell in quadrant IV (QALYs+, Costs -)
- There were 70 iterations that fell exactly on the vertical axis implying zero difference in QALYs between the two drugs.

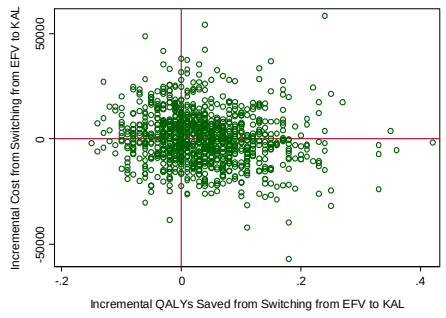


Figure 3. Multivariate sensitivity analysis from 1000 iterative draws. Each point on the graph plots the incremental cost on the y-axis and the incremental QALYS on the x-axis from one of the iterations.

Table 3: Parameter Values that Create Complete Equivalence Between EFV and LPV/r in Cost or QALYS

	Cost Equivalence	QALY Equivalence
P(Resistance| EFV, Fail) [0.59]	0.61	0.50
P(Resistance| LPV/r, Fail) [0.27]]	0.23	0.36
Cost of LPV/r Success (Annual) [$17.11K]	$16,974	NA
Cost of LPV/r Failure w/o Resistance (Annual) [$21K]	$20,802	NA
Cost if Resistance after LPV/r (Annual) [$30.6K]	$29,825	NA
Cost of EFV Success (Annual) [$14.4K]	$14,556	NA
Cost of EFV Failure w/o Resistance (Annual) [$21K]	$21,564	NA
Cost if Resistance after EFV(Annual) [$34.5K]	$34,900	NA
Probability of Failure on LPV/r (12 m) [0.28]	$0	0.29
Subsequent Probability of Failure on LPV/r [0.14]	<0	0.15
Probability of Failure on EFV (12 m) [0.25]	0.26	0.24
Subsequent Probability of Failure on EFV [0.13]	0.13	0.11
Probability of Death if ARV Success [0.04]	0.21	<0
Probability of Death if ARV Failure [0.08]	0.10	0.10
Probability of Death if Resistance [0.15]	0.14	0.13
Beta [0.03]	<0	0.22
Quality of Life with Treatment Success [0.87]	NA	>1
Quality of Life with Treatment Failure [0.74]	NA	0.67

LIMITATIONS

- Our results are limited by the assumptions of the model that did not include early or late side effects and costs of opportunistic infections
- Due to limited data on quality of life among HIV-1 infected individuals with antiretroviral drug resistance, quality of life was assumed equal for those who failed treatment with and without drug resistance
- If there is an unfavorable effect of antiretroviral drug resistance on quality of life, this assumption is biased in favor of EFV since LPV/r use leads to drug resistance less often than EFV use
- The model does not include PI mutations due to the very low likelihood of PI resistance developing during LPV/r-based treatment
- We have limited our study to focus on first-line antiretrovirals. With the availability of newer drugs assumptions incorporated into future models may change

DISCUSSION

- The anticipated difference between LPV/r and EFV in cost and QALYs over a five year horizon is small
- Although LPV/r is priced higher than EFV per day of therapy, the higher likelihood of spending time in a high cost, drug resistant state on an EFV-based regimen offsets nearly all of the price advantage
- The model of costs enables one to conclude that once the higher costs of time spent with resistant virus strains are factored in, both drugs appear to have equivalent costs to the medical system over a five year horizon

SUMMARY

- Over a 5 year horizon, nearly all of the higher acquisition costs of LPV/r are offset by savings from preventing entry into more costly states of virological failure and resistance
- The findings are robust to changes in parameter values
- Our cost-effectiveness model provides evidence to support the DHHS guidelines; drug regimens are equivalent from a cost perspective

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