Poster board number : 614

The Cost-effectiveness of Genotype Testing for Primary Resistance in Brazil

Paula M. Luz[1], Bethany L. Morris[2,3], Beatriz Grinsztejn[1], Kenneth A. Freedberg[2,3,4,5,6,7], Valdilea G. Veloso[1], Rochelle P. Walensky[2,3,4,5,8], Yoriko M. Nakamura[2,3], Paul E. Sax[5,8], Claudio J. Struchiner[1], A. David Paltiel[9]

[1]The Instituto de Pesquisa Clinica Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil; [2]Division of General Medicine, [3]The Medical Practice Evaluation Center, and [4]Division of Infectious Disease, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, [5]Harvard University Center for AIDS Research, [6]Department of Epidemiology, Boston University School of Public Health, [7]Department of Health Policy and Management, Harvard School of Public Health, [8]Division of Infectious Disease, Brigham and Women's Hospital — all in Boston, MA; [9]Yale School of Public Health, New Haven, CT.

Supported by : The National Council of Technological and Scientific Development (CNPq) and the Research Funding Agency of the State of Rio de Janeiro (FAPERJ) (Brazil), The National Institute of Allergy and Infectious Diseases (UM1 AI068636 and R01 AI058736) (USA)

Paula Mendes Luz, MD, PhD
Evandro Chagas Clinical Research Institute
Oswaldo Cruz Foundation
Avenida Brasil 4365
Rio de Janeiro 21040-360, Brazil
Phone: +55 21 2270 7064
Fax: +55 21 2270 7064
Email: paula.luz@ipec.fiocruz.br

BACKGROUND

- The Brazilian government has guaranteed universal provision of antiretroviral therapy (ART), free of charge, to human immunodeficiency virus (HIV)-infected individuals since 1996.
- Current HIV treatment guidelines in Brazil, a middle-income country, are comprehensive regarding ART initiation, lab monitoring, salvage regimens, and genotype testing after ART failure.
- Current guidelines do not recommend genotype testing for primary resistance in ART-naïve patients, though other studies have shown the cost-effectiveness of this strategy in resource-rich countries.

OBJECTIVE

- We sought to evaluate the clinical impact and cost-effectiveness of HIV genotype-resistance testing prior to 1st-line ART initiation in Brazil.

METHODS

Analytic Overview

- We used a previously published microsimulation model of HIV disease and treatment, populated with data from Brazil, to project the clinical and economic outcomes, discounted 3%/year, of performing a genotype test to detect non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance prior to first-line ART initiation in Brazil.
- We implemented two strategies (Figure 1), each weighted by the prevalence of primary resistance (4.4%):
  1. *No genotype:* no genotype testing prior to 1st-line ART initiation, an approximation of the current standard of care in Brazil
  2. *Genotype*: genotype testing prior to 1st-line ART initiation

The Cost Effectiveness of Preventing AIDS Complications (CEPAC) International Model

- CEPAC is a state-transition, first-order Monte Carlo microsimulation model of HIV infection incorporating natural history, disease progression, and treatment.
- Patients are drawn from initial distributions of age, sex, CD4 count, and HIV RNA level. HIV RNA level and CD4 count determine the rate of CD4 decline, which increases the risk of morbidity and mortality; ART reverses this decline.

The HIV Clinical Cohort at the Evandro Chagas Clinical Research Institute (IPEC)

- IPEC is located in Rio de Janeiro, Brazil and is one of Brazil's largest HIV research institutes.
- Cohort and natural history parameters for the model were derived from treatment-naïve HIV-infected adults presenting to HIV care at IPEC between 2000 and 2010.

METHODS (CONT'D)

Figure 1. Decision tree diagram for the analysis of HIV genotype testing in Brazil

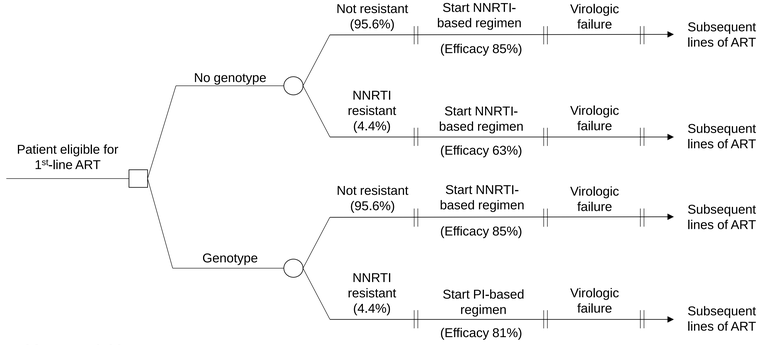


Table 1. Model input parameters

Variable	Base case value		Reference
Cohort Characteristics			IPEC HIV Clinical Cohort
Age, mean years (SD)	36 (10)		
Male sex, (%)	69%		
Initial CD4 count, mean cells/μL (SD)	347 (300)		
Prevalence of NNRTI resistance (%)	4.4%		Sprinz *AIDS Res. Hum. Retroviruses* 2009
ART Efficacy and Loss to Follow-up			
Adherence distribution			Sax *PLoS One* 2012
% with adherence >95%	45.0		
% with adherence between 50 and 95%	54.5		
% with adherence <50%	0.5		
HIV RNA suppression at 24 weeks (%) and mean CD4 gain for suppressed patients at 12 months(cells/μL)	HIV RNA suppression	Mean CD4 gain	Derived from:
1st-line NNRTI regimen without NNRTI resistance	85%	197	Campbell *PLoS Med* 2012
1st-line NNRTI regimen with NNRTI resistance	63%	197	Campbell *PLoS Med* 2012 and Goodman *AIDS* 2011
1st-line PI regimen with NNRTI resistance	81%	197	Molina *Lancet* 2008
2nd-line PI regimen	80%	197	Cahn *AIDS* 2011
3rd-line INSTI-containing regimen	75%	148	Steigbigel *N Engl J Med* 2008
4th-line 2nd generation NNRTI-containing regimen	70%	107	Madruga *Lancet* 2007 and Katlama *AIDS* 2009
5th-line CCR5-containing regimen	60%	141	Gulick *N Engl J Med* 2008 and Lalezari *CROI* 2007
Loss to Follow-up (/100 PY)			
Rate of loss to follow-up, overall average	4.1		IPEC HIV Clinical Cohort
Rate of return to care, overall average	81.8		IPEC HIV Clinical Cohort
Probability of late failure, average of all arms (/100 PY)	1.5		
Costs (2012 USD)			
Test costs, per test			Formal data request, Brazilian Ministry of Health
CD4	20		
HIV RNA	23		
Genotype	230		
Antiretroviral therapy, annual			Formal data request, Brazilian Ministry of Health
NNRTI regimen	1,400		
PI regimen as 1st-line ART	2,200		
PI regimen as 2nd-line ART	1,800		
INSTI-containing regimen	12,800		
2nd generation NNRTI-containing regimen	13,400		
CCR5-containing regimen	6,700		
Range of outpatient costs, annual	5-55		Formal data request, Brazilian Ministry of Health

PY: person year; USD: United States dollar; PI: protease inhibitor; INSTI: integrase inhibitor; CCR5: C-C chemokine receptor type 5; NNRTI: nonnucleoside reverse transcriptase inhibitor

Parameters not shown due to limited space include: HIV RNA distribution; baseline CD4 decline; monthly probabilities of opportunistic infection (OI) and chronic AIDS death; OI mortality probabilities; virologic failure rate after 6 months; annual routine care costs; acute OI costs; and mortality costs.

RESULTS

Table 2. Base case results for an analysis of HIV genotype testing in Brazil

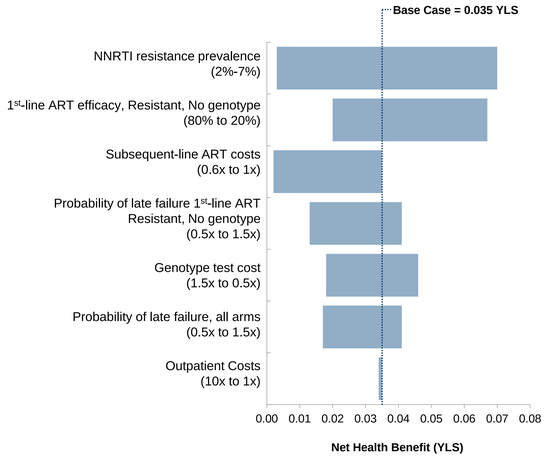
	Discounted Cost (2012 USD)	Undiscounted LE (months)	Discounted LE (months)	NHB[a] (YLS)	ICER[b] ($/YLS)
Cohort-based outcomes					
No NNRTI resistance *No genotype*	43,980	389.4	221.6		
No NNRTI resistance *Genotype*	44,290	389.4	221.6		
NNRTI resistance *No genotype*	67,200	381.1	217.7		
NNRTI resistance *Genotype*	55,130	388.5	221.2		
Population-wide outcomes, weighted by the prevalence of resistance (4.4%)					
No genotype	45,000	389.0	221.4	--	--
Genotype	44,770	389.4	221.6	0.035	Cost-saving

USD: United States dollar; LE: life expectancy; NHB: net health benefit; YLS: year of life saved; ICER: incremental cost-effectiveness ratio

[a] The willingness-to-pay threshold is assumed to be 1x the per capita Gross Domestic Product of the Brazil (2012 per capita GDP = $12,300). NHB = $(LE_{Genotype} - LE_{No\ genotype}) - \frac{(Cost_{Genotype}\text{-}Cost_{No\ genotype})}{(\text{Willingness to pay threshold})}$

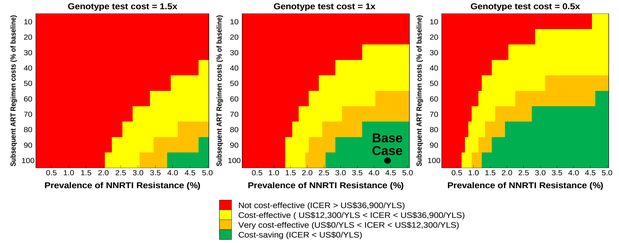
[b] The incremental cost-effectiveness ratio (ICER), reported in 2012 US dollars per life-year saved, was calculated as the incremental difference in cost divided by the incremental difference in life-years. By convention, a strategy that costs less and yields greater life expectancy compared to the reference strategy is labeled cost-saving and no ICER is reported.

Figure 2. Univariate sensitivity analysis tornado plot of select parameters



- Each horizontal bar represents the range of net health benefit produced by varying a given model parameter across the parameter ranges in parentheses.
- The vertical line represents the base case net health benefit for the *Genotype* strategy.
- A larger net health benefit indicates parameter variation that makes the *Genotype* strategy more favorable.

Figure 3. Multivariate sensitivity analysis



- Parameters varied simultaneously were genotype test cost, primary NNRTI resistance prevalence, and subsequent-line ART costs.

LIMITATIONS

- We assumed a constant prevalence of primary NNRTI-resistance across the country.
- Data on ART adherence and HIV RNA suppression were not derived from Brazilian sources.

CONCLUSIONS

- Genotype-resistance testing prior to 1st-line ART initiation in Brazil, a middle-income country, will both improve survival and decrease overall costs of HIV care and is, thus, cost-saving.
- The cost-saving results were robust when varying multiple parameters over their plausible ranges.
- Initial genotype-resistance testing for ART-naïve individuals should be incorporated into HIV treatment guidelines and the standard of care in Brazil.