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REVIEW

Cost-effectiveness analysis of initial HIV treatment under Italian guidelines

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Giorgio L Colombo[1,2]
Vincenzo Colangeli[3]
Antonio Di Biagio[4]
Sergio Di Matteo[2]
Claudio Viscoli[4]
Pierluigi Viale[3]

[1]School of Pharmacy, University of Pavia, Pavia, Italy; [2]SAVE - Studi Analisi Valutazioni Economiche, Milan, Italy; [3]Clinica Malattie Infettive, Azienda Ospedaliera Sant'Orsola Malpighi Bologna, Alma Mater Studiorum, University of Bologna, Bologna, Italy; [4]Clinica Malattie Infettive dell'Ospedale San Martino di Genova, University of Genova, Genova, Italy

Introduction: Since the mid-1990s, highly active antiretroviral therapy (HAART) has modified the clinical course of human immunodeficiency virus (HIV) infection, reducing the rate of disease progression, the incidence of opportunistic infections, and mortality. The authors of this paper performed an economic analysis to estimate the cost-effectiveness of the HAART regimens in Italy for managing HIV-infected patients according to national guidelines.

Patients and methods: The incremental cost-effectiveness analysis was carried out by means of a Markov model, which through a decision-analytic approach, made it possible to compare the studied antiretroviral regimens. The population considered in the model consisted of adult subjects with HIV who received antiretroviral HAART treatment for the first time. The population considered in the analysis reflects the patients' characteristics according to one of the regional surveillance systems HIV/AIDS infection report currently operating in Italy. The analysis was carried out from the point of view of the Italian health care system. The considered outcome measures were quality-adjusted life years (QALYs) and direct health costs calculated for the year 2010. Both the outcomes (QALYs) and the costs were discounted by 3.5%. The time horizon adopted in the model was 10 years.

Results: The model shows, in terms of cost per gained QALY, single tablet regimen (STR) appeared to be the most cost-effective therapeutic choice (€22,017), followed by tenofovir (TDF) + lamivudine + efavirenz (EFV) (€24,526), and TDF/emtricitabine (FTC) + nevirapine (€26,416), and TDF + FTC + EFV (€26,558); the remaining strategies have an incremental cost-effectiveness ratio (ICER) value varying from €28,000 to €41,000 per QALY. The sensitivity analysis on the main variables confirmed the validity of the base case scenario.

Conclusion: STR is the most cost-effective treatment strategy, compared with the other therapeutic regimens recommended by the Italian guidelines. All the ICER values of the various regimens considered by the Italian guidelines were lower than the threshold value of €50,000 commonly accepted at the international level. The model developed represents a tool for policy makers and health care professionals to make short- and long-term cost projections and thus evaluate their impact on the available budgets for HIV patients.

Keywords: antiretroviral therapy regimens, single tablet regimens, STR, Markov model, quality-adjusted life years, QALYs, HAART

Introduction

According to UNAIDS, at the end of 2009, 33.3 million people worldwide were estimated to be living with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS).[1] In Italy, the surveillance of HIV/AIDS in the period 1985–2008 reported a total of 42,747 new HIV diagnoses. In 2007, there were 2012 new HIV diagnoses, equivalent to an incidence of 6.7 per 100,000 residents.[2]

Correspondence: Giorgio L Colombo
SAVE - Studi Analisi Valutazioni Economiche, Via Previati, 74 – 20149 Milan, Italy
Tel +39 0248519231
Fax +39 0273960369
Email giorgio.colombo@savestudi.it

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The economic burden of HIV infection is well recognized all around the world.[3,4] Its management involves the use of health care service for HIV treatment, the treatment of AIDS-associated symptoms and opportunistic infections, and other costs associated with morbidity/premature mortality of adult working patients. Since the mid-1990s, highly active antiretroviral therapy (HAART) has modified the clinical course of the HIV infection, reducing the rate of disease progression, the incidence of opportunistic infections, and mortality.[5,6] This prolonged survival has changed HIV infection into a chronic disease.[7] As a consequence, combination antiretroviral therapy has resulted in longer survival and a better quality of life for many HIV-infected patients.[8] The current therapeutic options available in Italy and Europe include more than 20 approved antiretroviral drugs divided into five classes: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors, fusion or entry inhibitors, and integrase inhibitors (InI). Each of these groups attacks HIV in a different way. The most common drug regimen (as HAART) given to people beginning treatment usually consists of two NRTIs combined with either an NNRTI, or a "boosted" protease inhibitor, or an InI.[9] Each drug varies greatly in terms of efficacy, resistance, pill burden, safety, and price. Considering the complexity of the disease, the Italian recommendations are invaluable in assisting physicians in electing the most favorable therapies. However, because HIV is a prolonged disease, the treatment of which may continue for many years, the need for regimens with potent antiviral activity, proven long-term safety, good adherence, and a low rate of antiviral resistance should also be evaluated in terms of lifetime costs. In a context of limited health care resources, pharmacoeconomic considerations are crucial to help policy makers make the most appropriate decisions on resource allocation. The authors of this paper therefore performed an economic analysis to estimate the cost-effectiveness of the HAART regimens in Italy for managing HIV-infected patients according to national guidelines.[9] They also estimated the impact of the disease on the quality of life of patients.

Patients and methods

The purpose of this study was to determine the incremental cost-effectiveness ratio (ICER) per (quality-adjusted) year of life gained for therapeutic combinations (regimens) based on drugs recommended by the Italian guidelines for the first-line treatment of patients with HIV.[9] The incremental cost-effectiveness analysis was carried out by means of a Markov model, which through a decision-analytic approach, made it possible to compare the studied antiretroviral regimens.[10] The analysis was carried out from the point of view of the Italian health care service (Servizio Sanitario Nazionale [SSN]). The considered outcome measures were quality-adjusted life years (QALYs) and direct health costs calculated for the year 2011. Both the outcomes (QALYs) and the costs were discounted by 3.5%.[11] The time horizon adopted in the model was 10 years. The antiretroviral regimens considered follow the latest Italian guidelines and represent the drug options that are more frequently used in the first-line treatment of patients with HIV.[9] The population considered in the model consisted of adult subjects with HIV who received antiretroviral HAART treatment for the first time; this hypothetical cohort reflects the patient characteristics according to one of the regional surveillance systems HIV/AIDS infection report currently operating in Italy.[12]

Structure of the model

The Markov model simulates the quality of life and the costs for an HIV patient for 10 years, starting from the administration of the initial treatment, through 1-year cycles, based on the administered antiretroviral therapy.[13] After entering the model and receiving one of the antiretroviral regimens, the patient can "move" through eight health states, defined by the CD4-cell count combined with the viremia levels (VL), one AIDS state and one death state (Figure 1).

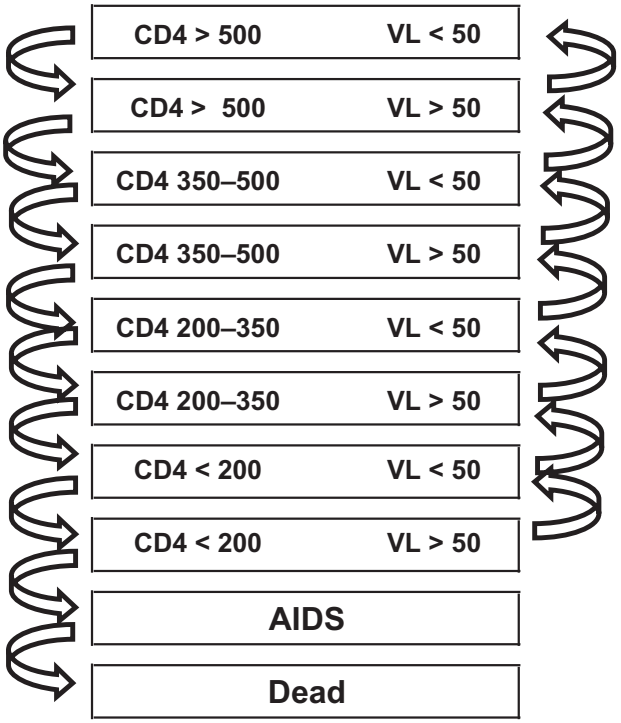

Figure 1 Structure of the Markov model.
Abbreviations: AIDS, acquired immunodeficiency syndrome; VL, viremia levels.

The model assigned patients responding to the antiretroviral therapy a viremia value lower than 50 copies, and allowed responders to move within the CD4 classification. In case of failure of the first-line treatment, the model presumed a viremia value >50 copies for the patients and CD4 values following the trend of the untreated population.[14] Nonresponders with a CD4 value <200 were changed to the AIDS state; patients were changed to the death state depending on their CD4 class, as shown in Table 1, and also 25% of patients with full-blown AIDS.[2] Finally, the model was completed with appropriate occurrence values to define probabilistic knots, and with precise cost estimates, in order to finalize the comparison, as described below. Modeling was undertaken using Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA).

Transition probabilities and outcomes

Tables 1 and 2 report the percentage distribution of patients considered in the model with respect to the CD4-cell count. The distribution draws on the observations on the HIV-AIDS infection situation in the Emilia Romagna region (epidemic update as of December 31, 2009). Table 3 shows the immunologic responses for each of the therapeutic regimens studied, as indicated in the Italian guidelines, and reports the bibliographical references. When data were not available, it was assumed that the response remained constant at the last observed value by applying the last value carried forward technique.

To evaluate cost-effectiveness, the ICER was used. When the value of a new therapeutic option needs to be assessed, the ICER provides the additional resources that have to be used to achieve the additional benefit: ICER is the difference in cost divided by the difference in effect between two alternatives. In this analysis, the direct costs and effectiveness of each regimen were compared with the direct costs and effectiveness of the disease natural history (absence of treatment).

Table 1 Patient distribution based on CD4-cell count and viremia and mortality per health state[13]

CD4-cell count	Viremia (VL)	HIV-linked mortality rate
>500 cells/μL	<50	0.40%
>500 cells/μL	≥50	0.40%
351–500 cells/μL	<50	0.40%
351–500 cells/μL	≥50	0.40%
201–350 cells/μL	<50	0.80%
201–350 cells/μL	≥50	0.80%
<200 cells/μL	<50	8.44%
<200 cells/μL	≥50	8.44%

Abbreviation: HIV, human immunodeficiency virus.

Table 2 Patient distribution based on CD4-cell count and viremia

CD4-cell count	Viremia (VL)	% distribution of patients[a] (base case)	% distribution of patients[b] (sensitivity analysis)
>500 cells/μL	<50	12.98%	3.25%
>500 cells/μL	≥50	12.98%	3.25%
351–500 cells/μL	<50	12.98%	7.00%
351–500 cells/μL	≥50	12.98%	7.00%
201–350 cells/μL	<50	16.36%	18.75%
201–350 cells/μL	≥50	16.36%	18.75%
<200 cells/μL	<50	7.70%	21.00%
<200 cells/μL	≥50	7.70%	21.00%

Notes: [a]Adapted from HIV-AIDS infection situation in the Emilia Romagna region (epidemic update as of December 31, 2009)[12]; [b]adapted from Gallant et al.[15]

The effectiveness indicators considered in this economic evaluation are the QALYs. Table 4 shows the utility values associated with the eight health states identified by the CD4-cell count. These values, published in the study by Simpson et al,[13] were calculated by means of the EuroQol-5 Dimensions (EQ-5D) questionnaire.[29] The permanence in the disease state (CD4 and viremia) was adjusted for the corresponding utility and then combined for the average expected lifetime, with the purpose to evaluate the years of survival adjusted for the quality of life.[30]

Resource consumption and costs

The resource consumption associated with the patients considered in the model is linked with the administration of the antiretroviral regimens and with other direct health costs, such as hospitalizations, medical examinations, laboratory tests, and so on. Table 5 shows the average annual costs for each first-line regimen. Dosages were calculated based on the Italian and British guidelines;[9,31] whereas the purchase costs of the pharmaceutical specialties were calculated based on the reimbursement price paid by the SSN, which takes into account the price updates effective from January 1, 2011.[32]

For every health state defined by the CD4-cell count, an additional health cost associated with patients was assumed, including a further consumption of health resources due to hospitalization, day hospital, general practitioner and specialist examinations, laboratory tests, and diagnostic procedures. Costs were estimated based on the results of the research by Garattini et al[33] (Table 6). The cost data stratified by CD4 were then actualized to 2010.[34,35]

Table 3 Efficacy data: immunologic response per different treatment regimen

	Treatment	Response rate										Source
		Year										
		1	2	3	4	5	6	7	8	9	10	
Atripla	TDF/FTC + EFV (single tablet regimen)	80.00%	67.00%	64.00%	64.00%	64.00%	64.00%	64.00%	64.00%	64.00%	64.00%	Gallant et al,[15] Pozniak et al,[16] Arribas et al[17]
Truvada + Sustiva	TDF/FTC + EFV	80.00%	67.00%	64.00%	64.00%	64.00%	64.00%	64.00%	64.00%	64.00%	64.00%	Gallant et al,[15] Pozniak et al,[16] Arribas et al[17]
Truvada + Reyataz + Norvir	TDF/FTC + ATV/r	78.00%	74.00%	74.00%	74.00%	74.00%	74.00%	74.00%	74.00%	74.00%	74.00%	Molina et al,[18] Molina et al[19]
Truvada + Viramune	TDF/FTC + NVP	66.80%	66.80%	66.80%	66.80%	66.80%	66.80%	66.80%	66.80%	66.80%	66.80%	Soriano et al[20]
Truvada + Prezista + Norvir	TDF/FTC + DRV/r	79.00%	79.00%	79.00%	79.00%	79.00%	79.00%	79.00%	79.00%	79.00%	79.00%	Mills et al[21]
Truvada + Kaletra + Norvir	TDF/FTC + LPV/r	76.00%	68.00%	68.00%	68.00%	68.00%	68.00%	68.00%	68.00%	68.00%	68.00%	Molina et al,[19] Molina et al[20]
Truvada + Isentress	TDF/FTC + RAL	86.10%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	Lennox et al,[22] Lennox et al[23]
Viread + Epivir + Sustiva	TDF + 3TC + EFV	76.30%	72.60%	69.70%	69.70%	69.70%	69.70%	69.70%	69.70%	69.70%	69.70%	Gallant et al[24]
Kivexa + Sustiva	ABC/3TC + EFV	59.00%	59.00%	59.00%	59.00%	59.00%	59.00%	59.00%	59.00%	59.00%	59.00%	Post et al[25]
Kivexa + Reyataz + Norvir	ABC/3TC + ATV/r	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	81.00%	Squires et al[26]
Kivexa + Kaletra + Norvir	ABC/3TC + LPV/r	68.00%	60.00%	60.00%	60.00%	60.00%	60.00%	60.00%	60.00%	60.00%	60.00%	Smith et al,[27] Pulido et al[28]

Note: Response rate refers to HIV RNA < 50 copies/mL.
Abbreviations: 3TC, lamivudine; ABC, abacavir; ATV/r, ritonavir-boosted atazanavir; DRV/r, ritonavir-boosted darunavir; EFV, efavirenz; FTC, emtricitabine; LPV/r, ritonavir-boosted lopinavir; NVP, nevirapine; RAL, raltegravir; TDF, tenofovir.

Sensitivity analysis

The sensitivity analysis verified the impact of a series of variations of the base case with a large influence on the obtained results.[9] A series of univariate analyses were carried out on some parameters of the simulation model, such as: virological response, HIV-associated mortality rate, and the initial distribution of patients based on the CD4-cell count. In particular, the allotment of patients per CD4-cell count was varied based on the evidence of the study by Gallant et al[36] and simulated for hypothetical seriousness scenarios. Each parameter was varied with respect to its 95% confidence interval.

Table 4 Utility values associated with the eight health states identified by the CD4-cell count[13]

CD4-cell count	Viremia (VL)	Utility
>500 cells/μL	<50	0.946
>500 cells/μL	≥50	0.946
351–500 cells/μL	<50	0.933
351–500 cells/μL	≥50	0.933
201–350 cells/μL	<50	0.931
201–350 cells/μL	≥50	0.931
<200 cells/μL	<50	0.830
<200 cells/μL	≥50	0.830

Results

Table 7 shows the average annual cost and the QALYs for a patient with HIV treated with each of the first-line antiretroviral regimens mentioned in the Italian guidelines. The simulation model shows that patients treated with a single tablet regimen (STR) (0.755 QALY/year) have a better quality of life, with a higher number of QALYs than with other therapeutic regimens, followed by tenofovir/

Table 5 Average annual costs for each first-line therapeutic regimen[35,36]

Treatment	Annual costs HAART treatment
TDF/FTC + EFV (single tablet regimen)	€7226
TDF/FTC + EFV	€7226
TDF/FTC + ATV/r	€9016
TDF/FTC + NVP	€6936
TDF/FTC + DRV/r	€10,167
TDF/FTC + LPV/r	€9294
TDF/FTC + RAL	€13156
TDF + 3TC + EFV	€6711
ABC/3TC + EFV	€6776
ABC/3TC + ATV/r	€8566
ABC/3TC + LPV/r	€8844

Abbreviations: 3TC, lamivudine; ABC, abacavir; ATV/r, ritonavir-boosted atazanavir; DRV/r, ritonavir-boosted darunavir; EFV, efavirenz; FTC, emtricitabine; LPV/r, ritonavir-boosted lopinavir; NVP, nevirapine; RAL, raltegravir; TDF, tenofovir.

emtricitabine (TDF/FTC) + raltegravir (0.735 QALY/year) and abacavir/lamivudine (ABC/3TC) + atazanavir/ritonavir (0.731 QALY/year). Table 7 shows the mean treatment cost for a patient with HIV based on the first-line antiretroviral regimen received. The TDF + 3TC + efavirenz (EFV) regimen (€8211) reveals a lower mean treatment cost, followed by TDF/FTC + nevirapine with €8231, ABC + 3TC + EFV with €8047, and TDF + FTC + EFV with €8551. Comparing the above mentioned costs and outcomes in incremental terms (ICER) with the no-treatment strategy, the STR appeared to be the most cost-effective therapeutic choice (€22,017), followed by TDF + 3TC + EFV (€24,526), TDF/FTC + nevirapine (€26,416), and TDF + FTC + EFV (€26,558); the remaining strategies have an ICER value varying from €28,000 to €41,000 per QALY.

The sensitivity analysis carried out on the main variables does not highlight significant variations with respect to the base case. For instance, including the discount rate (0%–5%) on costs and QALYs determines an increase of the ICER for all therapeutic regimens. On the other hand, it is worth noting that the cost per QALY decreases with the increase of the seriousness of the treated patient's disease (CD4), showing that severe-illness patients can benefit the most (Table 8).

Discussion

The therapeutic success against HIV is mainly due to the results obtained by scientific research, which allow finding drugs with a powerful antiviral activity. Since 1996, with the discovery of new classes of drugs and molecules which can thwart viral replication on various fronts, and especially with the introduction of combined therapies, the life expectancy and quality of life of people with HIV have enormously improved. Adding new antiretroviral STRs to conventional therapies can help physicians in the choice of the optimal treatment to administer HIV patients. Since STR is not the only available therapeutic alternative, it was deemed necessary to carry out a comparison with other antiretroviral regimens; therefore the analysis considered the regimens recommended, to a varying extent, by the Italian guidelines. The comparison was not limited to considering clinical effectiveness, but it also evaluated treatment costs. In particular, an incremental cost-effectiveness analysis was performed for each regimen, with respect to the no-treatment option, from the point of view of the Italian national health care system (SSN) and taking into account the national guidelines.[9] Such comparisons were carried out with the help of a Markov decision model over a 10-year time horizon. The model estimated QALYs as outcomes and direct health costs (drugs, medical examinations, hospitalizations, tests, and so on) as costs; these costs were attributed a value based on prices and rates as of 2010.

Table 6 Average annual cost per patient and health state expressed in CD4 (excluding HAART cost)[33]

	AIDS	CD4+ < 200	201 < CD4+ < 500	CD4+ > 501
Hospitalization and therapy	€2457	€771	€233	€43
Hospitalizations	€2121	€674	€196	€39
Laboratory tests	€149	€64	€19	€3
Diagnostic procedures	€187	€33	€19	€0
Day hospital	€6336	€2583	€2316	€1886
Accesses	€6279	€2557	€2300	€1877
Medical visits	€57	€25	€15	€9
Specialist examinations	€314	€348	€319	€299
Laboratory tests (outpatients)	€980	€950	€937	€859
Diagnostic procedures (outpatients)	€137	€80	€21	€28
Total cost	€10,225	€4732	€3827	€3115

Abbreviation: HAART, highly active antiretroviral therapy.

Table 7 Results: costs, QALYs and ICER of the base case scenario (10-year horizon)

Strength and evidence Italian GL		Treatment	Mean cost per patient	Mean QALYs per patient	Mean cost per QALYs	Delta cost	Delta QALYs	ICER QALYs
		Untreated	€3492	0.525	€6645			
AI		TDF/FTC + EFV (single tablet regimen)	€8551	0.755	€11,323	€5059	0.230	€22,017
AI	AI	TDF/FTC + EFV	€8551	0.716	€11,944	€5059	0.190	€26,558
AI	AI	TDF/FTC + ATV/r	€9479	0.722	€13,124	€5988	0.197	€30,412
AI	BI	TDF/FTC + NVP	€8231	0.705	€11,678	€4740	0.179	€26,416
AI	BI	TDF/FTC + DRV/r	€10,165	0.727	€13,977	€6674	0.202	€33,061
AI	BI	TDF/FTC + LPV/r	€9517	0.715	€13,312	€6026	0.190	€31,793
AI	BI	TDF/FTC + RAL	€12,174	0.735	€16,552	€8682	0.210	€41,328
BI	AI	TDF + 3TC + EFV	€8211	0.718	€11,438	€4719	0.192	€24,526
BI	AI	ABC/3TC + EFV	€8047	0.689	€11,682	€4555	0.163	€27,880
BI	AI	ABC/3TC + ATV/r	€9276	0.731	€12,695	€5784	0.205	€28,182
BI	BI	ABC/3TC + LPV/r	€9117	0.699	€13,047	€5626	0.173	€32,448

Abbreviations: 3TC, lamivudine; ABC, abacavir; ATV/r, ritonavir-boosted atazanavir; DRV/r, ritonavir-boosted darunavir; EFV, efavirenz; FTC, emtricitabine; GL, guidelines; ICER, incremental cost-effectiveness ratio; LPV/r, ritonavir-boosted lopinavir; NVP, nevirapine; QALY, quality-adjusted life year; RAL, raltegravir; TDF, tenofovir.

The results of the simulation model show that in terms of cost per gained QALY, STR is the most cost-effective treatment strategy, compared with the other therapeutic regimens recommended by the guidelines. All the ICER values of the various regimens considered by the Italian guidelines were lower than the threshold value of €50,000, commonly accepted at the international level.[36] This value has the purpose of expressing the willingness of the decision makers to pay in order to obtain additional health units, or the purpose of making new therapies available to citizens. Though no officially established threshold is available for Italy, it is worth noting that recent guidelines by the Italian Health Economics Association[9] recommend that a threshold of €25,000–40,000 be adopted. Other acceptable references of cost-effectiveness for the Italian context are €36,500 and €60,000 and have been calculated by two different authors.[37,38]

The favorable result of the STR is probably due to literature evidence showing a better adherence of the patients to STR, which determines an increase of the quality of life of patients with HIV.[39] However, it is now recognized that low adherence to antiretroviral drugs is strictly linked to the therapeutic regimen failure[40] and consequently to the indicators of the HIV-disease progression, such as virological failure,[41] insufficient immunologic reconstitution, the clinical progression of the disease, and lastly, death.[42,43] Adherence to therapy is not only necessary to obtain a therapeutic result in patients starting a treatment, but also to maintain an effective viral suppression in the course of time.[44]

The sensitivity analysis on the main variables confirmed the validity of the base case. It is worth noting, in particular, that the increasing seriousness of the patients' conditions (CD4-cell decrease) improves the incremental cost-effectiveness ratio with respect to the no-treatment strategy for all therapeutic regimens. This result is consistent with the indications of the Italian and international guidelines, suggesting the maximum evidence of outcomes in the treatment of patients with CD4-cell levels lower than 500.[9,31] Furthermore, the results of this present study are in line with other pharmacoeconomic analyses, in particular with the study of Ravasio[30] and with the more recent cost-utility analysis.[45,46] Also, the sensitivity analysis includes any reduction in price of drugs due to patent expiry. For example, with the assumption of a 3TC price reduction of 50% included into the TDF + 3TC + EFV regimen, the most cost-effective strategy remains the STR.

This study has a few limitations, the most important of which concerns the quality of data entered into the model; parameters such as efficacy, for example, are based on studies with a limited time-frame and hence may be inadequate for modeling the treatment of a chronic disease for a longer time. Other important limitations regard the transition probabilities, which were lacking in some cases and thus assumed to remain constant over time, and the utilities, which were derived from different literature sources and considered to be acceptable for an Italian population.[47] These assumptions were necessary to simplify the model or to take account of incomplete data into literature sources.

In addition to these limitations, the final result should be interpreted taking into account some others constraints. One constraint could be the adoption of a long-term simulation model (10 years) to compare the three alternative regimens, which was built on the basis of clinical information (now

Table 8 Results of one-way sensitivity analyses

Treatment	Base case[a]	Patient distribution[b]	Costs per CD4 (–20%)	Costs per CD4 (+20%)	Annual costs HAART treatment (–20%)	Annual costs HAART treatment (+20%)	Efficacy (–20%)	Efficacy (+20%)	LAM generic assumption (–50% current price)	Discount rate 0%	Discount rate 5%
TDF/FTC + EFV (single tablet regimen)	€22,017	€17,236	€22,836	€21,198	€16,795	€27,239	€24,696	€20,006	€22,017	€21,057	€22,447
TDF/FTC + EFV	€26,558	€19,914	€27,546	€25,570	€20,259	€32,857	€30,355	€23,834	€26,558	€25,148	€27,197
TDF/FTC + ATV/r	€30,412	€23,039	€31,370	€29,455	€23,373	€37,452	€33,462	€28,356	€30,412	€28,760	€31,162
TDF/FTC + NVP	€26,416	€19,715	€27,522	€25,310	€20,026	€32,805	€30,445	€23,499	€26,416	€24,925	€27,094
TDF/FTC + DRV/r	€33,061	€25,164	€33,989	€32,133	€25,521	€40,601	€35,295	€31,730	€33,061	€31,270	€33,874
TDF/FTC + LPV/r	€31,793	€23,961	€32,800	€30,785	€24,427	€39,159	€34,899	€29,738	€31,793	€30,032	€32,591
TDF/FTC + RAL	€41,328	€31,552	€42,195	€40,462	€32,196	€50,460	€42,193	€51,514	€41,328	€39,094	€42,340
TDF + 3TC + EFV	€24,526	€18,439	€25,513	€23,540	€18,634	€30,418	€28,395	€21,679	€22,756	€23,222	€25,119
ABC/3TC + EFV	€27,880	€20,532	€29,149	€26,611	€21,035	€34,725	€32,181	€24,815	€27,880	€26,226	€28,634
ABC/3TC + ATV/r	€28,182	€21,456	€29,088	€27,277	€21,641	€34,724	€31,094	€26,170	€28,182	€26,688	€28,861
ABC/3TC + LPV/r	€32,448	€24,179	€33,599	€31,296	€24,807	€40,089	€36,193	€29,916	€32,448	€30,576	€33,298

Notes: [a]Discount rate 3.5%; [b]data from Gallant et al.[15]

Abbreviations: 3TC, lamivudine; ABC, abacavir; ATV/r, ritonavir-boosted atazanavir; DRV/r, ritonavir-boosted darunavir; EFV, efavirenz; FTC, emtricitabine; LAM, lamivudine; LPV/r, ritonavir-boosted lopinavir; NVP, nevirapine; RAL, raltegravir; TDF, tenofovir.

available in the literature) referring to a short–medium period. This is justified by the fact that the evaluation of the benefits and costs of a health program needs synthesis tools capable of giving a representation of the reality to study which is as faithful as possible,[30] especially when the effects of the program have a time horizon with a long-term impact, or when the data sources are not homogenous (ie, they derive from administrative records, clinical studies, and meta-analyses). It is therefore necessary to use models, such as in the studied case, when the clinical trial (1) is incomplete or lacking (in this case, the necessary data for the economic evaluation derive from different and nonhomogeneous sources) and (2) only measures an intermediate result or a short-period follow-up (the model can be used to predict the possible final results).

It is worth highlighting, however, that the average cost emerging from this present study is substantially in line with a recent analysis of the real treatment costs for HIV patients.[48] The research work by Rizzardini et al,[48] developed starting from the administrative database of the reimbursements of the Lombardia region for the years 2004–2007, shows an average annual cost per patient of €9609. In this present study, the estimated average annual cost per patient is €9270. However, the difference between the two annual costs (–4%) depends on the fact that the average annual cost considered by Rizzardini et al represents patients in the real clinical practice, for instance including patients with hepatitis C virus infection and previously treated patients, but taking account of all costs during the years 2004 and 2007. With the analysis of naïve patients only, under the same terms used in the present analysis, the results of the two research studies would certainly converge.

To conclude, it is worth noting that the model developed is a dynamic instrument that can be adapted to various health care settings (overall in chronic disease, such as hepatitis B virus or HIV) in that it can be run using different input data (ie, efficacy, cost, and epidemiological data).[49] By allowing the simulation of different scenarios, it represents an invaluable tool for policy makers and health care professionals to make short- and long-term cost projections and thus evaluate their impact on the available budgets.

Disclosure

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