Cost-effectiveness of the once-daily efavirenz/emtricitabine/tenofovir tablet compared with the once-daily elvitegravir/cobicistat/emtricitabine/tenofovir tablet as first-line antiretroviral therapy in HIV-infected adults in the US

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Background: February 2013 US treatment guidelines recommend the once-daily tablet of efavirenz/emtricitabine/tenofovir (Atripla®) as a preferred regimen and the once-daily tablet of elvitegravir/cobicistat/emtricitabine/tenofovir (Stribild™) as an alternative regimen for first-line treatment of human immunodeficiency virus (HIV). This study assessed the clinical and economic trade-offs involved in using Atripla compared with Stribild as first-line antiretroviral therapy in HIV-infected US adults.

Methods: A Markov cohort model was developed to project lifetime health-related outcomes, costs, quality-adjusted life years (QALYs), and cost-effectiveness of Stribild compared with Atripla as first-line antiretroviral therapy in HIV-1-infected US patients. Patients progressed in 12-week cycles through second-line, third-line, and nonsuppressive therapies, acquired immune deficiency syndrome, and death. Baseline characteristics and first-line virologic suppression, change in CD4 count, and adverse effects (lipid, central nervous system, rash, renal) were based on 48-week clinical trial results. These results demonstrated equivalent virologic suppression between the two regimens. Point estimates for virologic suppression (favoring Stribild) were used in the base case, and equivalency was used in the scenario analysis. Published sources and expert opinion were used to estimate costs, utilities, risk of acquired immune deficiency syndrome, mortality, subsequent-line CD4 count, clinical efficacy, and adverse events. Costs were reported in 2012 US dollars. Sensitivity analyses were conducted to assess robustness of results.

Results: Compared with patients initiating Atripla, patients initiating Stribild were estimated to have higher lifetime costs. Stribild added 0.041 QALYs over a lifetime at an additional cost of \$6,886, producing an incremental cost-effectiveness ratio of \$166,287/QALY gained. Results were most sensitive to first-line response rates, product costs, and likelihood of renal adverse events. When equivalent efficacy was assumed, Atripla dominated Stribild with lower costs and greater QALYs.

Conclusion: At a societal willingness to pay of \$100,000/QALY, Stribild was not cost-effective in the base case compared with Atripla for first-line HIV treatment.

Keywords: human immunodeficiency virus, cost-effectiveness, antiretroviral therapy

Introduction

February 2013 guidelines from the US Department of Health and Human Services include four preferred initial combination antiretroviral treatment regimens for

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antiretroviral-naïve human immunodeficiency virus type 1 (HIV-1)-infected patients who are not pregnant. These regimens incorporate as their “backbone” the nucleoside reverse transcriptase inhibitors (NRTIs) tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC). The regimens include one that is nonnucleoside reverse transcriptase inhibitor (NNRTI)-based, two that are protease inhibitor-based, and one that is integrase strand transfer inhibitor-based.¹

One of these preferred regimens, Atripla® (efavirenz/emtricitabine/tenofovir; Bristol-Myers Squibb, Princeton, NJ, USA; Gilead Sciences Inc, Foster City, CA, USA) is a once-daily single tablet combining the NNRTI regimen efavirenz with the NRTI backbone (TDF/FTC). Among the list of alternative regimens is Stribild™ (elvitegravir/cobicistat/emtricitabine/tenofovir; Gilead Sciences Inc), a recently introduced once-daily single-tablet integrase inhibitor composed of elvitegravir and cobicistat with the NRTI backbone (TDF/FTC). In a 48-week Phase III clinical trial of adults aged 18+ years, Atripla and Stribild were found to have similar clinical efficacy.² Adverse event rates for the two regimens were similar, except that patients receiving Atripla experienced more central nervous system reactions and rash, whereas those receiving Stribild experienced more renal events.

To better understand the potential trade-offs involved in choosing between these two agents, this analysis used decision-analytic modeling to evaluate the cost-effectiveness of Atripla compared with Stribild in first-line treatment for antiretroviral-naïve HIV-infected US adults.

Materials and methods

We developed a Markov cohort model that projected, from the payer perspective, the cost-effectiveness of using Atripla versus Stribild as first-line treatment in an antiretroviral-naïve HIV-infected US adult population (Figures 1 and 2). A Markov model is constructed of mutually exclusive and exhaustive health states, and patients are simulated through the health states at fixed intervals known as model cycles. Once the model has simulated all patients until death, outcomes (ie, costs and survival) are summed for the entire cohort.

Patients entered the model with baseline age, gender, race, and CD4 count estimated from the Phase III clinical trial population.² Trial participants were adults aged at least 18 years with:

- plasma HIV-1 RNA concentrations $\geq 5,000$ copies per mL
- estimated glomerular filtration rate of at least 70 mL per minute

Figure 1 Model schematic for health states of an antiretroviral therapy-naïve HIV-1-infected adult US population.

Abbreviations: AIDS, acquired immune deficiency syndrome; AKI, acute kidney injury; CKD, chronic kidney disease; HIV, human immunodeficiency virus.

Figure 2 Model schematic for adverse events^b in an antiretroviral therapy-naïve HIV-1-infected adult US population.

Notes: ^aRash, renal abnormalities, central nervous system symptoms, and other events causing discontinuation of treatment; ^bpatients who began to receive lipid-lowering therapy (because of elevated lipids) did not discontinue treatment and faced added costs of lipid-lowering therapy.

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; HIV, human immunodeficiency virus.

- aspartate and alanine aminotransferase concentrations of no more than five times the upper limit of normal
- total bilirubin of no more than 25.65 $\mu\text{mol/L}$ or a normal direct bilirubin, absolute neutrophil count of at least 1,000 cells per μL
- at least 50,000 platelets per μL
- hemoglobin concentration of at least 85 g/L
- a negative serum pregnancy test.

Patients with new acquired immune deficiency syndrome (AIDS)-defining disorders or serious infections within 30 days of screening were excluded. In total, 348 patients were included in the safety population for the Stribild arm of the trial, and 352 patients were included in the Atripla arm.

The Markov model incorporated 12-week cycles to accommodate the timing of HIV treatment cycles and the shorter nature of treatments for adverse events. During each 12-week model cycle, patients could respond to and continue their current treatment with or without elevated lipids, they could discontinue treatment due to adverse events or virologic failure, or they could die due to HIV infection, AIDS, acute kidney injury, chronic kidney disease, or other causes. Patients who discontinued initial treatment progressed through second-line and third-line treatments and nonsuppressive therapy, whereas those who experienced elevated lipid levels continued to receive their current HIV treatment and received lipid-lowering therapy (40 mg of atorvastatin once daily) until 6 months after progression to the next line of HIV therapy. Second-line treatment was defined as a market basket of either atazanavir or darunavir, each with ritonavir and two NRTIs. Third-line treatment and nonsuppressive therapy were defined as: 1) darunavir with ritonavir, efavirenz, and two NRTIs; or 2) maraviroc, raltegravir, and two NRTIs. For both lines, patients were equally divided between the treatment options.

For each model strategy (ie, Atripla or Stribild), we projected total costs, life years, quality-adjusted life years (QALYs), virologic response, AIDS events, and adverse events (rash, renal abnormalities, central nervous system symptoms, elevated lipids). QALYs allow for inclusion of the impact of treatments on health-related quality of life. Incremental costs, life years, and QALYs of Stribild compared with Atripla were calculated to estimate incremental cost-effectiveness ratios (ICERs), a measure of the value of an intervention. Costs were reported in 2012 US dollars, and both costs and clinical outcomes were estimated using a 3% annual discount rate to incorporate the diminishing value of cost and clinical outcomes in future years. The model was developed using TreeAge Pro 2012 (TreeAge Software Inc, Williamstown, MA, USA), a commonly used

modeling software which allows for comparison across treatment strategies.

Table 1 shows the characteristics of the model baseline patient population, which is based on the Phase III clinical trial population.² Age-specific and gender-specific all-cause mortality and HIV-specific and AIDS-specific mortality were based on national US data,^{3,4} and mortality associated with acute kidney injury and chronic kidney disease plus dialysis were based on estimates from the published literature.^{5,6} Virologic response and change in CD4 count were estimated from clinical trial data and published literature. CD4 counts were categorized and plateaued after 3 years.⁷⁻⁹ Although the clinical trial² showed equivalent virologic suppression between the two regimens, the more conservative point estimates (favoring Stribild) were used as model inputs. Clinical efficacy data are shown in Table 2.

Patients who progressed (due to virologic failure or a severe adverse event) through three lines of therapy and onto nonsuppressive regimens had a viral load of ≥ 50 copies/mL and CD4 counts that plateaued at their most recent prior value. Patients who received nonsuppressive therapy could progress to AIDS, at which point their CD4 counts were categorized from 0 to <50 cells/ mm^3 or 50 to ≤ 200 cells/ mm^3 (Table 2).^{10,11}

The model included the following adverse events: rash, renal abnormalities, central nervous system symptoms, elevated lipids causing initiation of lipid-lowering therapy, and other adverse events causing treatment discontinuation. Adverse events were defined as those causing treatment discontinuation except for elevated lipids, for which treatment continued with additional costs. Rates of adverse events were based on published literature and expert opinion (Table 3), and were included in the model after being converted to 12-week probabilities. Rash, central nervous system symptoms, and other adverse events causing treatment discontinuation occurred only during the first cycle of treatment; renal abnormalities and elevated lipids causing initiation of

Table 1 Model baseline population of antiretroviral therapy-naïve HIV-1-infected adult patients

Parameter	Estimate	Reference
Baseline patient population	Stribild™	Atripla® 2
Age, mean (SD), years	38 (10.4)	38 (10.6)
Percentage male, %	88	90
Nonwhite, %	39	36
Black/African American, %	30	26
CD4 count (cells/ mm^3), %		
≤ 200	12	15
201 to ≤ 350	32	27
351 to ≤ 500	32	39
> 500	23	20

Abbreviations: HIV, human immunodeficiency virus; SD, standard deviation.

Table 2 Model clinical efficacy estimates

Parameter	Estimate (per 12-week cycle) ^a	Reference
Mortality		
All-cause	Age, gender-specific	3
HIV ^b	0.9%	4
AIDS ^b	3.5%	4
Acute kidney injury	26.6%	5
Chronic kidney disease with dialysis ^c	1.9%	6
Probability of AIDS, given nonsuppressive regimens	1.8%	10
CD4 <50 cells/mm ³ (% among patients with AIDS) ^d	55.2%	11
Proportion achieving virologic response, mean (range per 12-week cycle)		
First-line		
Atripla®	0.81 (0.28–0.72)	20,21
Stribild™	0.85 (0.76–0.89)	20,21
Second-line	0.49 (0.41–0.57)	22,23
Third-line	0.51 (0.49–0.57)	10,24,25
Change in CD4 count, mean (range per 12-week cycle)		
First-line		
Atripla	263 (120–367)	2,7,8,9,21
Stribild	263 (140–426)	2,7,8,9,21
Second-line	105 (94–109)	7,8,9,26,27
Third-line	129 (79–147)	7,8,9,10,24,25

Notes: ^aValues are rounded; ^bexcess mortality in addition to all-cause; ^caverage annual mortality by race weighted using Stribild population distribution; ^dCD4 count ≤200 cells/mm³ among all patients with AIDS.

Abbreviations: AIDS, acquired immune deficiency syndrome; HIV, human immunodeficiency virus.

lipid-lowering therapy occurred at any time. Adverse events except for elevated lipids occurred at the end of week 8 of the 12-week model cycle, at which time patients discontinued treatment and took a 4-week drug holiday before initiating their subsequent line of therapy in the next cycle. Patients who initiated lipid-lowering therapy continued for 24 weeks (two model cycles) after discontinuing the HIV treatment that caused initiation of such therapy.

A proportion of patients with renal abnormalities experienced acute kidney injury and were at risk of developing chronic kidney disease and requiring hemodialysis (dialysis) in the cycle following the acute kidney injury event. The likelihood of acute kidney injury was based on patients experiencing renal failure in the clinical trial,² and the likelihood of chronic kidney disease plus dialysis was based on expert opinion. Patients with acute kidney injury who did not develop chronic kidney disease experienced added costs and decreased utility and proceeded to the next line of therapy. Those with chronic kidney disease also proceeded to the next line of therapy, and for all remaining model cycles remained on dialysis with utility decrements and added costs.

Table 3 Model adverse event^{a,b} rates by treatment

Parameter	Estimate ^a	Reference
CNS symptoms ^c		
Atripla®	1.8%	2
Stribild™	0.6%	2
Renal abnormalities		
Atripla	0%	2
Stribild		
No AKI	0.22%	2
AKI	0.14%	2
CKD with dialysis ^d	0.03%	Expert opinion
Rash ^c		
First-line		
Atripla	1.4%	2
Stribild	0%	2
Second-line	0.7%	22
Third-line	1.8%	22,25,28
Elevated lipids		
First-line		
Atripla	1.3%	29
Stribild	1.0%	29
Second-line	1.4%	26,27
Third-line	2.7%	25,26,30,31
Other events ^c		
First-line		
Atripla	0.5%	2
Stribild	0.5%	2
Second-line	0.4%	22
Third-line	0.7%	22,28

Notes: ^aValues are reported as probability per 12-week model cycle and are rounded; ^bdefined as events causing treatment discontinuation except for elevated lipids causing initiation of lipid-lowering therapy, for which treatment continues with an additional cost; ^cevents occur only during the first cycle of each line of therapy; ^dpatients with AKI may progress to CKD with dialysis only during the cycle following the acute AKI event.

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; CNS, central nervous system.

Costs per 12-week cycle are shown in Table 4 and were inflated to 2012 dollars using the Consumer Price Index.¹² The analysis was conducted from the payer perspective, with included costs as follows: product acquisition; baseline monitoring; and treatment for adverse events. Costs of productivity losses were not included.

Product acquisition costs were based on 30-day wholesale acquisition costs.¹³ A market basket of commonly used second-line and third-line treatment regimens was selected based on expert opinion, and nonsuppressive and third-line therapy regimens were assumed to be equivalent. Regimen dosing schedules were based on published guidelines.¹ To account for adjusted dosing of abacavir/lamivudine (ABC/3TC) in patients with stage V chronic kidney disease, 1% of patients within the NRTI market basket received the reduced ABC/3TC dosage recommended in the February 2013 guidelines.

Table 4 Model costs by treatment, patient monitoring characteristic, and adverse event

Parameter	Cost ^a	Distribution ^b	Reference
Product acquisition costs			
First-line			
Atripla®	4,918	Gamma	1, 13
Stribild™	6,559		
Second-line ^c	6,977		
Third-line ^d	9,092		
Patient monitoring costs ^e			
No virologic failure ^f	914	Gamma	32
Virologic failure			
CD4 ≥50 cells/mm ^{3,g}	1,561		
CD4 <50 cells/mm ^{3,h}	1,620		
Patient receiving new line of therapy ⁱ	113		
Cost of treating adverse events			
Rash	226	Gamma	32
Elevated lipids	186		13, 32
CNS symptoms	226		32
Renal abnormalities			
No acute kidney injury	914		32
Acute kidney injury	33,594		14, 32
Chronic kidney disease with dialysis	48,665		15
Other adverse events causing discontinuation	226		32

Notes: ^aAll costs are per 12-week cycle and are reported in 2012 US dollars; ^bdistributions used in probabilistic sensitivity analysis; ^csecond-line treatment defined as 50% receiving atazanavir with boosted ritonavir (atazanavir/r) and two NRTIs, 50% receiving darunavir with boosted ritonavir (darunavir/r) and two NRTIs; ^dthird-line treatment defined as 50% receiving darunavir/r + etravirine, 50% receiving maraviroc + raltegravir + optimized background therapy; ^eall cost estimates were averages of high and low managed care rates; ^{f,g,h}cost included baseline monitoring components, consisting of a 10-minute physician office visit, one blood draw, one chemistry panel, one complete blood count, one CD4 count, and one viral load assessment (ultrasensitive quantification); ⁱcost included baseline patient monitoring plus a 15-minute physician office visit, one blood draw, and one viral load assessment; ^jcost included baseline patient monitoring plus a 25-minute physician office visit, one blood draw, and one viral load assessment; ^kcost included a 15-minute physician office visit.

Abbreviations: CNS, central nervous system; NRTIs, nucleoside reverse transcriptase inhibitors.

In each cycle, patients underwent baseline monitoring consisting of a physician visit and laboratory workup. Patients with virologic failure underwent more intensive monitoring, and those who started a new line of therapy had an additional office visit to ensure medication compliance.

For each instance of rash, central nervous system symptoms, or renal abnormalities without acute kidney injury, patients had two office visits, the first to diagnose the adverse event and the second to determine when the patient was ready to begin the next line of treatment. Costs were applied during the cycle in which events occurred. Patients who required lipid-lowering therapy received one 40 mg atorvastatin tablet per day and incurred additional patient monitoring costs. Patients with renal abnormalities with acute kidney injury incurred a one-time acute kidney injury treatment cost¹⁴ and

the cost of two additional patient monitoring visits. Patients who progressed to chronic kidney disease with dialysis incurred costs in each remaining model cycle for inpatient and outpatient services, emergency department visits, and all other services.¹⁵

Utility weights for patients with HIV and AIDS were estimated from the literature¹⁶ and varied by CD4 count (Table 5). The impact of adverse events was applied as a utility decrement to the baseline HIV or AIDS utility weight during the cycle in which the adverse event occurred (which, for chronic kidney disease with dialysis, includes every subsequent model cycle). Because the specific adverse events grouped as “others causing treatment discontinuation” varied between treatments, no disutility was applied for these events.

In the base case, we evaluated the cost-effectiveness of the preferred and alternative first-line strategies in antiretroviral-naïve HIV-infected US adults. ICERs were calculated as the ratio of incremental costs to incremental QALYs and reported over a lifetime period. One-way and probabilistic sensitivity analyses were conducted to evaluate the impact of parameter uncertainty on model outcomes. In one-way sensitivity analyses, each parameter was varied individually at ±10% of the base case value. In the probabilistic sensitivity analyses, all parameters were varied simultaneously for 5,000 model iterations.

Results

Base case

When Stribild was compared with Atripla in the base case, lifetime costs were higher by \$6,886, life expectancy was

Table 5 Model utility estimates by CD4 count and adverse event

Parameter	Utility	Distribution ^a	Reference
CD4 count (cells/mm ³)			
		Beta	
>500	0.946		16
351 to ≤500	0.933		
201 to ≤350	0.931		
50 to ≤200	0.853		
<50	0.781		
Adverse events (disutilities)			
CNS symptoms	−0.043		33
Lipid-lowering therapy	0		Expert opinion
Rash	−0.034		33
Renal abnormalities			Expert opinion
No acute kidney injury	0		Expert opinion
Acute kidney injury ^b	−0.06		34
Chronic kidney disease with dialysis ^c	−0.06		34

Notes: ^aDistributions used in probabilistic sensitivity analysis; ^bdisutility is applied in the cycle in which the acute episode occurs; ^cdisutility is applied during cycle of initial diagnosis and all subsequent cycles.

Abbreviation: CNS, central nervous system.

higher by 0.0188 years, and quality-adjusted life expectancy was higher by 0.0414 QALY. This resulted in an ICER of \$166,287/QALY (Table 6). Without quality adjustment, this ICER increased to \$365,750/LY.

At 3 years, quality-adjusted survival was greater among patients receiving Atripla than among those receiving Stribild. Over a lifetime, Atripla patients experienced a greater number of adverse events than did Stribild patients. However, patients receiving Stribild experienced acute kidney injury or chronic kidney disease with dialysis, whereas those receiving Atripla did not.

For both strategies, HIV medications accounted for a large proportion of the total costs, totaling \$635,764 per patient for Atripla and \$637,296 per patient for Stribild. The costs for patients who were receiving first-line medication were higher for patients receiving Stribild (\$53,628) than for those receiving Atripla (\$28,486), but for both strategies most costs were accrued among patients receiving nonsupportive therapy or those with AIDS.

Sensitivity analyses

The tornado diagram (Figure 3) shows the impact of varying all parameters $\pm 10\%$ when comparing Stribild with Atripla. Results were most sensitive to first-line response rates of Stribild and Atripla, followed by the cost of Stribild. A 10% decrease in Stribild response or a 10% increase in Atripla response resulted in Atripla's costing less and being more effective than Stribild. A 10% increase in Stribild response or a 10% decrease in Atripla response caused the ICER to drop to just over \$20,000 and \$34,000/QALY, respectively. Varying Stribild costs resulted in ICERs ranging from \$65,487 to \$267,088/QALY, and when Atripla costs were varied, this range was \$109,898 to \$222,676/QALY. Subsequent treatment (ie, second-line and third-line and nonsuppressive therapy) costs had less impact on ICERs than first-line costs, whereas the costs and rates of adverse events other than renal failure had the least impact on results.

When all 49 parameters were varied simultaneously in probabilistic sensitivity analysis (Figure 4), results suggested that at a societal willingness to pay of \$50,000/QALY,

Stribild would be considered cost-effective 17.5% of the time. At a societal willingness to pay of \$100,000/QALY, Stribild would be cost-effective 27.6% of the time. Of the 5,000 model simulations, Stribild was dominated in 41.9%, whereas Atripla was dominated in 11.9%. Across all 5,000 iterations, the average incremental costs and QALY between the strategies was \$7,897 and 0.0256. This resulted in an ICER of \$308,296.

Scenario analyses were conducted to examine the impact of discounting and assumptions regarding chronic kidney disease risk and treatment efficacy. Without discounting, the ICER increased to \$207,273. When the risk of chronic kidney disease with dialysis among Stribild patients was assumed to be half that of base case, the ICER decreased to \$96,557/QALY. When Stribild and Atripla were assumed to have equivalent efficacy to reflect the noninferiority clinical trial findings, Atripla dominated Stribild (cost less than Stribild and provided greater life expectancy and quality-adjusted life expectancy), regardless of chronic kidney disease risk or discounting assumptions.

Discussion

In antiretroviral-naïve HIV-1-infected adult patients who were not pregnant, Stribild was not cost-effective compared with Atripla given a commonly used societal willingness to pay threshold of \$100,000.^{17–19} Although model results predicted that Stribild would provide a slight benefit in quality-adjusted life expectancy, the increased costs of Stribild led to an ICER of \$166,287. This suggests that using Stribild in this patient population is not an efficient use of economic resources compared with using Atripla.

The results of this model must be considered in light of its limitations. Efficacy inputs from the pivotal Phase III clinical trial² were based on point estimates rather than the trial's conclusion of Atripla's noninferior efficacy. When assuming equivalent efficacy in the scenario analysis, Atripla dominated Stribild, suggesting that our base case results may have overestimated Stribild's benefit. The risk of death due to chronic kidney disease with dialysis was based on a population of HIV-infected patients with chronic kidney disease,

Table 6 Summary results for Atripla versus Stribild^a

	Cost		Survival (years)		QALY		ICER (LY)	ICER (QALY)
	Lifetime	Δ	Lifetime	Δ	Lifetime	Δ		
Atripla™	\$726,728		16.8436		14.9565			
Stribild®	\$733,615	\$6,886	16.8625	0.0188	14.9979	0.0414	\$365,750	\$166,287

Notes: ^aIncorporating 3% annual discount rate for cost, LY, and QALY outcomes. All costs are reported in 2012 US dollars. All values are per person and rounded.

Abbreviations: ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year.

Figure 3 One-way sensitivity analyses.^{a,b}

Notes: ^aIncorporating 3% annual discount rate for cost, LY, and QALY outcomes. Results expressed in \$/QALY for Stribild™ compared with Atripla®; ^ball parameters were varied by $\pm 10\%$; ^cStribild™ had higher costs and lower QALYs than Atripla®.

Abbreviations: AE, adverse event; AIDS, acquired immune deficiency syndrome; AKI, acute kidney injury; CKD, chronic kidney disease; LY, life year; QALY, quality-adjusted life year.

among whom only a portion had end-stage renal disease. Our results may thus overestimate the benefit (and underestimate the ICER) of Stribild compared with Atripla. In addition, although the model only considered severe adverse events causing treatment discontinuation, our utility estimates were

derived from patients who also had less severe events. In this way, our model may have underestimated the quality of life decrement associated with adverse events; because the extent of bias could vary between events and therefore regimens, it is unclear how this may have impacted model ICERs.

Figure 4 Probabilistic sensitivity analyses.^a

Notes: ^aIncorporating 3% annual discount rate for cost, LY, and QALY outcomes. Results expressed in \$/QALY for Stribild™ compared with Atripla®. Blue dots represent ICERs when all parameters were varied simultaneously for 5,000 model simulations. Larger red box represents base case. Blue dotted line represents 95% confidence ellipse.

Abbreviations: IC, incremental cost; ICER, incremental cost-effectiveness ratio; IE, incremental effectiveness; QALY, quality-adjusted life year.

Because costs and QALYs are likely to accumulate at different rates for each strategy, model-predicted ICERs could differ for time horizons of less than a lifetime. Although such outcomes were not evaluated in this analysis, the lifetime results presented here are based on following patients through all lines of therapy and provide a complete depiction of the clinical and economic trade-offs between strategies. Finally, second-line and third-line therapies were defined as a market basket of products independent of initial treatment, which may oversimplify actual treatment patterns.

By reducing viral load with less renal toxicity and having a lower unit cost, Atripla was predicted in this model to lower rates of acute kidney injury and chronic kidney disease events and decrease total spending compared with Stribild. Using a US cost-effectiveness threshold of \$100,000/QALY, the cost of using Stribild is not an effective expenditure of resources compared with using Atripla in antiretroviral-naïve HIV-infected patients. As health care costs increase and more effort is put into controlling these costs, this knowledge may be useful to physicians, policymakers, and payers alike in their efforts at making clinically appropriate yet cost-conscious decisions.

Disclosure

Drs Correll and Juday are employees of Bristol-Myers Squibb. Ms Anene, Drs Bentley and Broder, and Mr Ortendahl are employees of Partnership for Health Analytic Research, LLC, which was paid by Bristol-Myers Squibb to conduct the research described in this manuscript.

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