Cost and Efficiency Analysis of Raltegravir Versus Atazanavir/r or Darunavir/r for Treatment-Naive Adults With HIV-1 Infection in Spain

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BACKGROUND

- For treatment-naive individuals with human immunodeficiency virus (HIV-1) infection, commonly used treatments include the following:
  - Raltegravir (RAL) 400 mg twice daily
  - Atazanavir/ritonavir (ATV/r) 300 mg/100 mg once daily
  - Darunavir/ritonavir (DRV/r) 800 mg/100 mg once daily
- The AIDS Clinical Trial Group (ACTG) 5257 clinical trial is an independent head-to-head study (1,809 participants) comparing the efficacy and tolerability of these treatments when used in combination with emtricitabine/tenofovir DF (FTC/TDF) (200 mg/300 mg* once daily) among treatment-naive adults in the United States (US) with HIV-1 infection.
- At 96 weeks of follow-up, the RAL regimen exhibited favorable results compared with the ATV/r and DRV/r regimens in a composite endpoint combining virologic efficacy and tolerability.[1,2]

* While the listed dosing of TDF is different in Spain (245 mg) than in the US (300 mg), this difference is due to the fact that Spain does not include the weight of fumarate in the TDF molecular weight calculation. Therefore, the actual dosing is the same in both countries. The dosing of TDF will be referred to as 245 mg for the remainder of this analysis.

OBJECTIVE

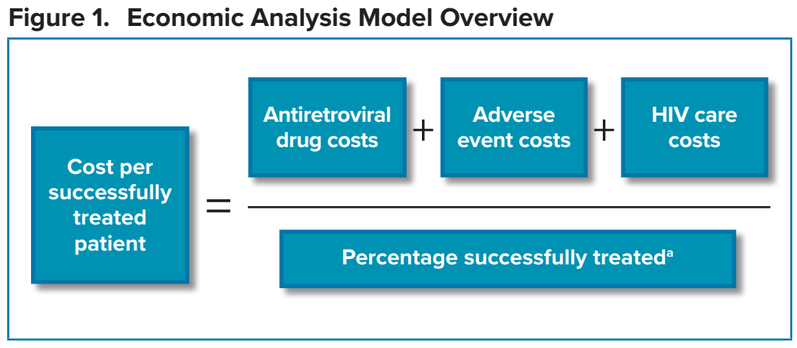
- The objective of this study was to estimate the efficiency, as measured by the cost per successfully treated patient, associated with the three antiretroviral regimens examined in the ACTG 5257 clinical trial from a Spanish perspective.

METHODS

Model Overview

- The economic model followed a cohort of treatment-naive individuals with HIV-1 infection from baseline through 96 weeks as they progressed through treatment in the ACTG 5257 clinical trial.
- As individuals progressed, the model tracked the costs incurred and estimated per-person costs by category and in aggregate for each first-line regimen.
- The model then estimated the total cost per successfully treated patient for each treatment arm. In this analysis, individuals who did not discontinue treatment due to virologic or tolerability failure (i.e., the trial's composite endpoint) for 96 weeks were considered successfully treated (Figure 1).

Figure 1. Economic Analysis Model Overview

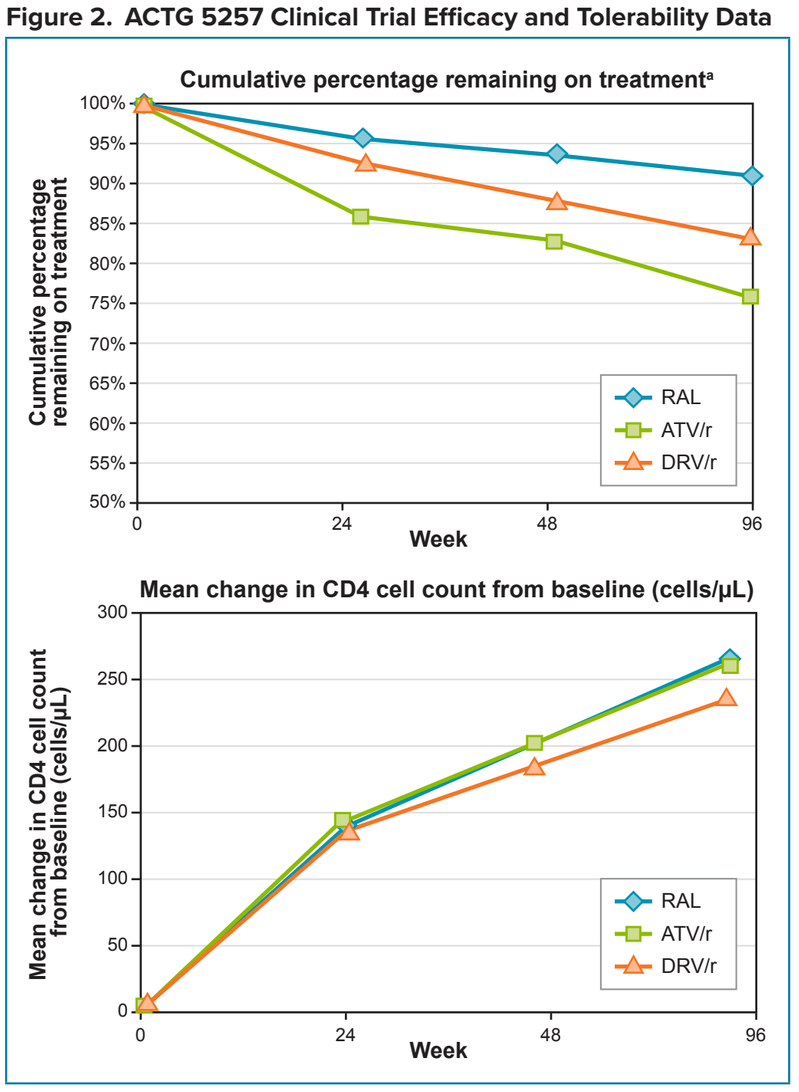


[a] Percentage of patients who remained on their ACTG 5257 clinical study drug for the entire modeled time horizon. In the base-case analysis, treatment discontinuation was based on the ACTG 5257 trial composite endpoint (i.e., discontinuation for virologic or tolerability failure).

Input Parameters

- Baseline characteristics for the modeled cohort were taken from the ACTG 5257 clinical trial.[1]
- Efficacy and tolerability data were taken from the ACTG 5257 clinical trial[1,2] to transition the modeled cohort between CD4 cell-count ranges and to alternative regimens after first-line regimen discontinuation (Figure 2).
- Total daily regimen costs for each comparator first-line regimen and substitution regimen were based on hospital costs (i.e., wholesaler selling price, which accounts for mandatory and commercial discounts) with additional Royal Decree-Law 8/2010 mandatory deductions applied (Table 1).[3]
- Grade 2, 3, and 4 adverse events with an incidence of at least 5% in any arm of the ACTG 5257 clinical trial were included.[1] The model applied a per-episode cost by event severity[4,5] and assumed the cost was incurred within the first 48 weeks of treatment (Table 1).
- HIV care costs included costs for disease monitoring and the treatment and prevention of opportunistic and other infections (Table 2).[6]

Figure 2. ACTG 5257 Clinical Trial Efficacy and Tolerability Data



[a] In the base-case analysis, treatment discontinuation was based on the ACTG 5257 trial composite endpoint (i.e., discontinuation for virologic or tolerability failure). Other trial endpoints were examined in scenario analysis.

Table 1. Antiretroviral Drug and Adverse Event Management Costs

Regimen	Cost Per Day		Adverse Event Management Costs[b]
	Study Regimen	Substitution Regimen[a]	
RAL 400 mg BID + FTC/TDF 200 mg/245 mg QD	€24.87	€23.75	€351
ATV 300 mg QD + RTV 100 mg QD + FTC/TDF 200 mg/245 mg QD	€24.12	€23.58	€618
DRV 800 mg QD + RTV 100 mg QD + FTC/TDF 200 mg/245 mg QD	€24.09	€22.69	€370

BID = twice daily; QD = once daily; RTV = ritonavir.

[a] Individuals who discontinued their study regimen in the model were transitioned primarily to other study regimens and also to various other substitution regimens based on the percentage of participants who switched to each regimen in the trial.[1,2] The weighted average substitution regimen cost was calculated based on these percentages.

[b] Adverse event management costs represent weighted averages of adverse event incidence (grade 2, 3, and 4) from the ACTG 5257 clinical trial[1] and per-episode costs by event severity, inflated when necessary to 2015 euros.[4,5,7]

Table 2. HIV Care Costs

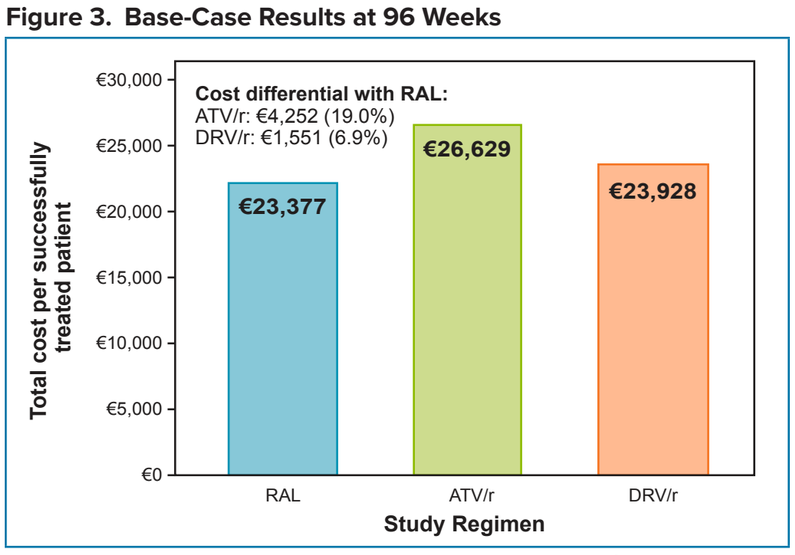
CD4 Cell-Count Range	Inpatient	Outpatient	Non-HIV Medications	Total
< 50	€834	€1,675	€391	€2,900
50-199	€834	€1,675	€267	€2,776
200-349	€1,014	€1,521	€101	€2,636
350-499	€1,014	€1,521	€101	€2,636
≥ 500	€170	€1,336	€102	€1,608

Note: Costs were taken from Lopez-Bastida et al.[6] and inflated from 2003 to 2015 euros.[7]

RESULTS

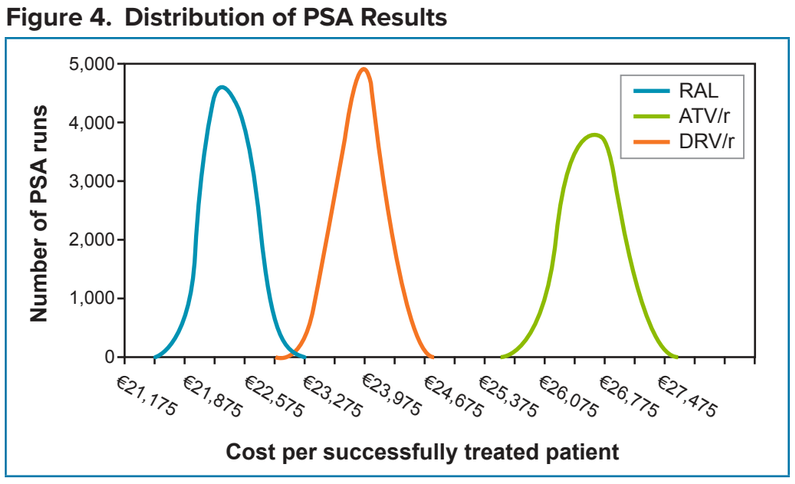
- RAL had the lowest total cost per successfully treated patient after 96 weeks of treatment compared with DRV/r and ATV/r when each was used in combination with FTC/TDF (Figure 3).
- RAL had the lowest total cost per successfully treated patient in all scenarios tested (alternate trial endpoint for regimen discontinuation, shorter time horizon, no discounting, without adverse event costs, and without HIV care costs).
- 100% of probabilistic sensitivity analysis (PSA) runs found RAL to have the lowest total cost per successfully treated patient (Figure 4).

Figure 3. Base-Case Results at 96 Weeks



Note: All cost outcomes were discounted at an annual rate of 3.0%.[8]

Figure 4. Distribution of PSA Results



Note: For ease of interpretation, this figure has been drawn as a continuous representation of a traditional histogram.

LIMITATIONS

- This analysis was limited to the first-line regimens included in the ACTG 5257 clinical trial and did not incorporate other common first-line regimens.
- The ACTG 5257 clinical trial included US participants only, which may not be fully representative of a Spanish population.
- Cost outcomes were estimated through 96 weeks only; potential long-term benefits of RAL (e.g., potential long-term benefits of RAL's favorable lipid profile, as reported in the ACTG 5257 clinical trial) were not captured.

DISCUSSION AND CONCLUSIONS

- RAL has the lowest total cost per successfully treated patient when compared with ATV/r and DRV/r for treatment-naive adults with HIV-1 infection in Spain.
- These results were found to be robust in sensitivity and scenario analyses.
- This economic evidence complements the known clinical benefits of RAL as reported in the ACTG 5257 clinical trial.

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