GENERIC DARUNAVIR AND DOLUTEGRAVIR ARE COST-EFFECTIVE IN SECOND-LINE ART

2194

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BACKGROUND

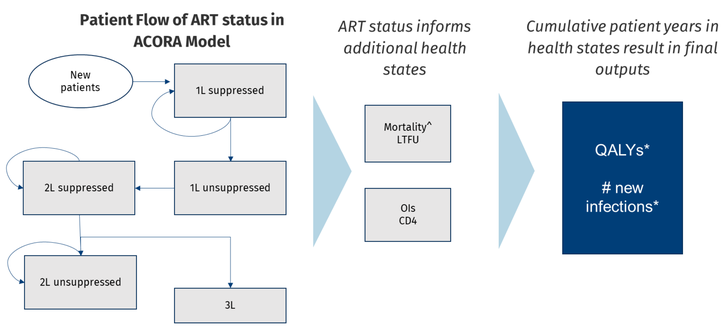
This analysis evaluates the cost-effectiveness of replacing lopinavir-ritonavir (LPV/r) and atazanavir-ritonavir (ATV/r) with darunavir-ritonavir (DRV/r) and dolutegravir (DTG) in second-line treatment in resource-limited settings.

There will be greater need for second-line (2L) antiretroviral therapy (ART) as HIV treatment programs mature. The best-in-class protease inhibitor (PI), DRV/r became available in 2021 as a generic fixed-dose combination (FDC) at a lower cost than LPV/r. This, together with use of DTG in 2L, offers opportunities to replace the currently used PIs to optimize 2L regimens offering improved health outcomes and cost effectiveness.

METHODS

We used an internally developed model - the Applied Cost and Outcomes Research Analysis (ACORA) model, designed to model program costs and patient outcomes through health states to conduct cost effectiveness analysis

- Deterministic Markovian state-transition model built in R.
- Outcomes include health outcomes: quality adjusted life years (QALYs), mortality, new infections, opportunistic infections (OIs), adverse events (AEs) and costs: ARVs, Labs, human resources (HR), OI treatment.
- Utility weights from the Global Burden of Diseases and 3% discounting were used.
- The model was parameterized with published and programmatic data. Drug failure and discontinuation profiles used clinical trial studies: ARTEMIS, FLAMINGO, ACTG 5257 and ICONA.



*HIV transmission rates per 100PYs are applied to health states off ART/discontinued, and if on ART – suppressed or unsuppressed. *Attia et. al. - Sexual transmission of HIV according to viral load and antiretroviral therapy: a systematic review and meta-analysis. 2009*
^ Mortality is dependent on CD4 band and ART status. *Parameters adapted from Optima Consortium for Decision Science / Optima HIV model*

METHODS (continued)

We conducted a 10-year forecast using quarterly time-steps and defined 4 scenarios:

- Standard of Care (SOC): uses ATV/r and LPV/r in 2L;
- C1: switches LPV/r to DRV/r;
- C2: switches both ATV/r and LPV/r to DRV/r;
- C3: uses DTG for a non-nucleoside reverse transcriptase inhibitor 1L failures and DRV/r for DTG 1L failures.

The analysis considered a hypothetical sub-Saharan African country with 1,000,000 existing ART patients, 94% on first-line (1L) and 6% on 2L, and 100,000 new patients initiating ART each year; the SOC was either 80% LPV/r and 20% ATV/r (LPV/r dominant setting), or the opposite (ATV/r dominant setting). Costs (measured in USD) and QALYs are restricted to patients who migrate to 2L. Incremental cost effectiveness ratios (ICER) are presented.

Incorporating DRV/r and DTG as preferred second-line treatment options can provide cost effective improvements in health outcomes as well as cost-saving opportunities.

RESULTS

- **Utilizing DTG in 2L, along with DRV/r as the PI (C3) shows savings of 20% and 10%** over the SOC for the LPV/r dominant and ATV/r dominant analysis, respectively.
- Replacing ATV/r with DRV/r increases costs by 17% when ATV/r is dominant but is expected to be cost effective in most resource limited settings with an ICER of $1688.

Strategy C3 was cost-saving and maximized QALYs in both LPV/r- and ATV/r-dominant scenarios (see table below). Strategies C1 and C2 resulted in higher costs and QALYs than SOC, with ICERs ranging from $34 to $1688 USD per additional QALY.

	Scenario	Total Cost (USD million)	Total QALYs (thousands)	ICER compared with SOC (Δ$/ΔQALY)
Lopinavir dominant	SOC	$ 416	974	
	C1 – DRV/r for LPV/r	$ 417	1,006	$ 34
	C2 – DRV/r for LPV/r and ATV/r	$ 432	1,013	$ 411
	C3 - DTG in 2L (DRV/r if DTG in 1L)	$ 333	1,019	cost-saving
Atazanavir dominant	SOC	$ 368	976	
	C1 – DRV/r for LPV/r	$ 372	983	$ 481
	C2 – DRV/r for LPV/r and ATV/r	$ 432	1,013	$ 1,688
	C3 - DTG in 2L (DRV/r if DTG in 1L)	$ 333	1,019	cost-saving

* Costs and QALYs over 10-years forecasted

CONCLUSIONS

- Introducing DRV/r into 2L and increasing use of DTG for eligible patients will improve the quality of treatment for 2L patients and offer financial savings.
- These findings provide empirical evidence of optimizing country programs' ARV policies that directly impact health improvements to patients.

Clinical trials have shown that DRV/r is more effective with an improved tolerability profile compared to the two most commonly used PIs. However, prior to 2021 without a **quality assured, generic fixed-dose combination available**, this ARV was cost prohibitive for programs in resource limited settings. With a generic now available at a lower cost than LPV/r, it is clear that guidelines should implement this switch. Replacing DRV/r with ATV/r will result in higher treatment costs, but this can be offset by optimizing DTG in 2L use and through improved outcomes.

Countries rely on evidence-based findings to help provide recommendations to treatment policy decisions. Cost-effectiveness analysis examines both costs and health outcomes to assess if additional costs are worth the expected health improvements. In this analysis we used both a LPV/r dominant and an ATV/r dominant settings to show options for countries to understand the implications that relate to their own current program portfolio.

ADDITIONAL KEY INFORMATION

This work will be highlighted in an upcoming publication. Contact authors with questions:
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