

CASE STUDY

Improving HIV treatment outcomes for patients on second-line therapy through optimal regimen uptake

ACCESS TO BETTER TOLERATED, MORE CONVENIENT REGIMENS FOR HIV TREATMENT PROMOTES ADHERENCE AND LEADS TO BETTER PATIENT OUTCOMES. CHAI IS WORKING TO ENSURE AFFORDABLE PRICING AND TO ADDRESS DEMAND-SIDE BARRIERS TO ACCESS. INCREASED UPTAKE OF OPTIMAL SECOND-LINE REGIMENS IN UGANDA AND NIGERIA HAS IMPROVED HIV TREATMENT AND WILL DELIVER \$6.5 MILLION IN SAVINGS BY 2018.

OVERVIEW

As antiretroviral therapy (ART) programs continue to expand and mature across low- and middle-income countries (LMICs), accessibility to effective, tolerable, and affordable regimens is becoming increasingly important. This is particularly true for the growing number of patients requiring second-line therapy. Until 2011, there was only one generically available option for a critical component of second-line therapy in LMICs. This formulation requires twice-daily dosing and can cause severe gastrointestinal problems, making adherence difficult. Access is also limited by the often prohibitively high cost to patients in LMICs; second-line therapies can be over three times the price of first-line treatment.

To avoid failing therapy and potentially transmitting second-line resistance, patients must adhere to treatment regimens. In addition, patients that fail second-line therapy are left with few options given the lack of third-line treatment in LMICs. For long-term adherence to be feasible, access to optimized regimens that improve the experience and convenience of treatment is critical. This can be accomplished in part by reducing pill burden and increasing access to drugs with fewer side effects.

With CHAI support and advocacy, an alternative second-line therapy, atazanavir boosted with ritonavir (ATV/r), was recommended as one of the two preferred options in the 2010 World Health Organization (WHO) treatment guidelines. The fixed-dose combination, which became generically available in 2011, offers clinical benefits over the predominant second-line drug, Kaletra (lopinavir boosted with ritonavir or LPV/r). ii,1

THEORY OF CHANGE

Adoption and uptake of optimal second-line regimens in key markets can demonstrate clinical and programmatic benefits and catalyze scale-up across other national programs. Increasing market share for optimal products secures supply sustainablity and increased volumes have the potential to drive future price reductions.

IMPACT

Nigeria and Uganda have experienced rapid product uptake, with 26% and 33% of second-line patients on ATV/r, respectively, after only two years of availability. This promotes retention in care and better treatment outcomes and will deliver approximately \$6.5 million in savings through 2018. At current levels, ATV/r uptake across CHAI countries for this same period is expected to deliver additional cost savings of approximately \$12.8 million. There remains significant opportunity to increase product uptake, with the potential to significantly increase savings.

EMERGING POWER PARTNERSHIPS

Mylan Laboratories in India (formerly Matrix) participated in CHAI's annual ceiling price agreements in 2010, enabling significant price reductions for ATV/r. Mylan's success has prompted additional suppliers to apply for and gain regulatory approval.

KEY PARTNERS

- DFID UNITAID GFATM

BENEFITS OF ATV/r OVER LPV/r:

- Efficacy and safety: ATV/r offers comparable efficacy, lower risk of elevated cholesterol, fewer toxicities, fewer gastrointestinal side effects, and is safe for use during pregnancy.
- Convenience: ATV/r reduces pill burden with once daily dosing, thereby supporting patient adherence.
- Cost: ATV/r has been 10-25% less expensive than LPV/r, enabling significant programmatic cost savings.
- Normative guidance: ATV/r is recommended by the WHO as one of two preferred options for second-line therapy and patients can be proactively switched from LPV/r to ATV/r. ATV/r is recommended above LPV/r in the US treatment guidelines.

ⁱ eg. CHAI ceiling price for first-line regimen (TDF/3TC/EFV) is \$130 per person per year (pppy),;second line regimen (AZT/3TC+LPV/r)is \$391 pppy.

ⁱⁱ According to a recent study, ATV/r may provide 30% mortality reduction and a 33% reduction in AIDS-defining illness or death versus LPV/r-based regimens.



As a result of CHAI's supply-side negotiations, ATV/r came to market at a lower price than alternative products, making ATV/r more accessible to LMICs and reducing the cost burden for resource-limited Ministries of Health (MOHs). Opportunities to optimize regimens with formulations that offer both a clinical and cost-saving benefit will enable LMICs to sustain the costs of maintaining large numbers of patients on effective, lifelong ART.

Based on the clinical and programmatic benefits offered by the newly available generic formulation, CHAI leveraged its unique position working at the juncture of global demand and supply to drive uptake of ATV/r in several key countries.

APPROACH

As part of the in-country work to drive uptake of optimal products, CHAI supported the national MOHs in both Uganda and Nigeria to expand access to ATV/r. CHAI's involvement spanned across early product adoption to roll-out processes, thus ensuring that product introduction resulted in uptake at the facility level.

Specifically, CHAI partnered with the MOH and other key stakeholders in Uganda and Nigeria to support the following activities:

Adopting ATV/r into national guidelines. Worked with the MOH and clinicians to provide relevant clinical and programmatic data to inform decision-making and revision of the national guidelines. Guidelines were revised to recommend ATV/r as the preferred option for all new second-line adult patients, and to proactively switch specific patient populations to ATV/r.

Ensuring smooth product introduction and transition. Created and implemented roll-out plans and training tools, including job aids and circulars on the benefits and usage of ATV/r, to be widely distributed to facilities.

Accelerating availability of ATV/r at all levels of the health system. Supported national medical stores with the inclusion of ATV/r in quantification, procurement, and supply planning activities. This helped to ensure that an adequate and constant supply of ATV/r was available to facilities.

Building clinician support for product uptake through improved clinical awareness and understanding. Identified key stakeholders and opinion leaders to champion the regimen; worked in collaboration to disseminate clinical and patient information and to address patient and prescriber concerns.

Driving uptake and utilization at ART sites. Conducted indepth Continuing Medical Education (CME) sessions with implementing partners to train healthcare workers on appropriate second-line regimens and detection of treatment failure. These sessions helped to increase healthcare worker confidence in prescribing ATV/r.

IMPACT

The introduction and scale-up of ATV/r in Uganda and Nigeria helped to provide higher quality care to nearly 18,000 patients by December 2014 and will result in combined total savings of \$6.5 million for the two national programs by 2018. iii,2

Additionally, patient benefits such as a reduced pill burden and fewer side effects will contribute to improved adherence, thereby reducing medical complications and risk of developing resistance. On a national level, ATV/r use has the potential to reduce morbidity and mortality, and contain the cost burden to HIV programs as a result of reduced treatment failure and transmission of drugresistant HIV.

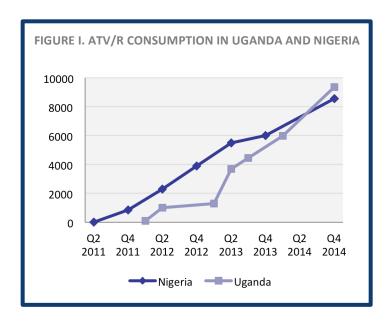
Product roll-out and sensitization work resulted in a vast increase in ATV/r demand in both countries; a trend that is expected to continue. In Uganda, the number of patients using ATV/r has increased over 90-fold since early 2012, accounting for 33% of second-line patients currently on ATV/r (Figure I). The CME sessions contributed to a 59% increase in ATV/r orders among covered facilities.

Driving uptake in Nigeria has been bolstered by work with a few key organizations that provide direct support to facilities, covering >90% of the second-line patient population. The number of second-line patients on ATV/r increased from a baseline of zero in mid-2011 to over 8,000 by the end of 2014 (Figure I).⁴ ATV/r is now the treatment for 26% of second-line patients in Nigeria compared to 0% in 2011.

As a result of initiating patients on ATV/r, cost savings related to product procurement in Uganda are conservatively projected at \$3 million by 2018. In Nigeria, these savings are estimated at \$3.5 million. In both cases, savings are based only upon patients currently receiving regimens with ATV/r, and are expected to increase as uptake continues to grow. These savings are only a partial measure of program benefit when the health impacts of better patient adherence is factored in.

iii ATV/r savings are based on CHAI 2013 Ceiling Price List and assumes consistent pricing over the 2014 – 2018 period.





LIMITATIONS AND LESSONS LEARNED

To encourage more widespread adoption, CHAI learned that gaining support from committed key opinion leaders, who are respected clinicians of ART treatment clinics, was key in building confidence of the broader clinical community and patients.

In regard to uptake, CHAI found that dedicated training sessions and facility-level chart reviews were more influential than general guideline trainings, where little time can be dedicated to ATV/r specifically. These trainings allow health care workers to share and discuss insights from individual ATV/r patient experiences. Patient acceptability was also a critical factor to gaining traction. The positive feedback from initial treatment groups helped to encourage reluctant patients and clinicians.

Lastly, collaboration with existing initiatives run by the MOH and key implementing partners were a cost-effective method of expanding outreach. These partnerships allowed for ongoing trainings and mentorship around ATV/r to be integrated as part of national training programs.

FUTURE OUTLOOK

Countries that have adopted ATV/r as the preferred treatment for adult second-line patients will see ongoing savings as patients are sustained on treatment in the coming years. As these programs expand, savings are expected to increase significantly. Additionally, as ATV/r gains market share, the relative price vs. LPV/r may reduce.

To replicate the success achieved in Uganda and Nigeria, CHAI has expanded this approach, resulting in more countries adopting ATV/r in national guidelines and conducting national roll-outs. Key coutries in various stages of driving uptake efforts include Tanzania and Ethiopia, with 35% and 31% of second-line patients on ATV/r, respectively, to date.

The priority for HIV programs continues to be successful retention of patients on first-line therapy, thereby reducing the need for costlier, more complicated second-line treatment. However, as the number of patients requiring second-line therapy grows, CHAI is continually monitoring the market and working with suppliers to identify emerging formulations that could improve the convenience, efficacy, and tolerability of second-line treatment. CHAI is also working with MOHs to scale-up viral load testing to enable better monitoring and detection of treatment failure, helping to ensure that patients are appropriately transitioned to second-line therapy. Lastly, CHAI is continuing to target price reductions and for existing and new second-line therapies as volumes increase.

REFERENCES

¹ HIV CAUSAL Collaboration, Cain L, et al. Boosted lopinavir vs. boosted atazanavir-containing regimens and immunologic, virologic and clinical outcomes: a prospective study of HIV-infected individuals in high-income countries. *Clin Infect Dis.* 2015; pii: ciu1167 [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/25567330. Accessed January 2015.

About the Clinton Health Access Initiative, Inc.

The Clinton Health Access Initiative, Inc. (CHAI) is a global health organization committed to strengthening integrated health systems and expanding access to care and treatment in the developing world. CHAI's solution-oriented approach focuses on improving market dynamics for medicines and diagnostics; lowering prices for treatment; accelerating access to lifesaving technologies; and helping governments build the capacity required for high-quality care and treatment programs. Though CHAI remains committed to its initial focus on HIV/AIDS; CHAI also has expanded its scope to work in the following program areas: HIV/AIDS and Tuberculosis (TB), Improving the Efficiency and Effectiveness of Healthcare Systems, Malaria, Human Resources for Health, Vaccines, and

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Contact Information

For more information on CHAI's HIV work, please contact: camole@clintonhealthaccess.org

² CHAI ATV/r savings calculations, December 2014.

³ National uptake data. Federal Ministry of Health, Republic of Uganda.

⁴ National uptake data. Federal Ministry of Health, Nigeria