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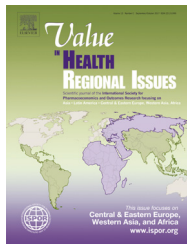

Cost Effectiveness of Dolutegravir as a First-Line Treatment Option in the HIV-1–Infected Treatment-Naive Patients in Russia

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ABSTRACT

Objectives: To evaluate the cost effectiveness of dolutegravir + abacavir/lamivudine (DTG + ABC/3TC) compared with raltegravir + abacavir/lamivudine (RAL + ABC/3TC) and ritonavir-boosted darunavir + abacavir/lamivudine (DRV/r + ABC/3TC) in HIV-1–infected treatment-naive patients in Russia. **Methods:** A dynamic Markov model was developed with five response states and six $CD4^+$-based health states. Efficacy estimated as probability of viral suppression (HIV RNA <50 copies/ml) at 48 weeks was obtained from a published network meta-analysis. Baseline cohort characteristics and health state utilities were informed using DTG phase 3 clinical trials. Health care resource use was obtained from literature and costed using published unit costs. Costs (presented in Russian rubles) included antiretroviral drug costs; HIV management costs such as routine care; costs of treating cardiovascular conditions, opportunistic infections, and drug-related adverse effects; and mortality costs. A patient lifetime analysis was conducted using the societal perspective. Outcomes were quality-adjusted life-years (QALYs), life-years, incremental cost per QALY ratio, and incremental cost per responder. **Results:** The viral suppression rate among patients receiving DTG + ABC/3TC was 71.7% compared with 65.2% for RAL + ABC/3TC and 59.6% for DRV/r + ABC/3TC. The mean duration of response per patient was 116.6 months for DTG + ABC/3TC, 108.6 months for RAL + ABC/3TC, and 98.9 months for DRV/r + ABC/3TC. Total discounted costs for treatment over patient lifetime were RUB 2.89, 5.32, and 4.38 million for DTG + ABC/3TC, RAL + ABC/3TC, and DRV/r + ABC/3TC, respectively. Lifetime discounted QALYs were 12.73 for patients on DTG + ABC/3TC and 12.72 each for patients on RAL + ABC/3TC and DRV/r + ABC/3TC. DTG + ABC/3TC thus dominated the other two alternatives. **Conclusions:** With lower costs, higher response rates, and comparable QALYs, DTG + ABC/3TC can be considered as a cost-effective alternative.

Key words: cost effectiveness, dolutegravir, economic analyses, HIV, Russia.

Introduction

Among the countries of Eastern Europe and Central Asia, Russia has the largest number of HIV-1 infection diagnoses, with an estimated 103,438 new HIV diagnoses in 2016 [1,2]. This group of newly diagnosed patients with HIV is growing at a rate of 10% each year [1]. Despite such a large number of patients living with HIV, just over a third (37.3%) had access to antiretroviral therapy (ART) in 2015, with lack of adequate funding for diagnosis and treatment being a major barrier [1]. In Russia, HIV treatment and prevention initiatives are funded by central and regional governments, with limited contribution from local and international charitable institutions. Care is delivered through HIV-specific centers, which are responsible for clinical research, monitoring and testing, HIV treatment, and counseling.

In 2016, the Russian government announced a strategy to combat the spread of HIV by improving access to ART, which was one of its strategic initiatives [1]. Nevertheless, inadequate funding has remained a challenge. Despite increasing state funding for HIV treatment and prevention over the last few years, the 2016 funding of $325 million was estimated to cover only a fifth of the target population [3]. Therefore, access to effective and cost-saving ART remains an important priority to achieve Russia's strategic objective of reducing AIDS-related deaths by 2020.

ART usually comprises three antiretroviral agents, two nucleoside reverse transcriptase inhibitors, commonly referred to as

Conflicts of interest: Y. S. Punekar and V. Chounta are employees of ViiV Healthcare and hold stocks in the company. E. K. Bukin was an employee of ViiV Healthcare at the time of this study and holds stocks in the company. G. Tremblay and S. A. Garib are employees of Purple Squirrel Economics and received payment from ViiV Healthcare for consultancy during the conduct of this study. J. Piercy and T. Holbrook are employees of Adelphi Real World and received payment from ViiV Healthcare for consultancy during the conduct of this study.

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backbone, and a third agent, often referred to as a core agent, from a different antiretroviral class. In Russia, current core agents used in treatment-naive patients include non–nucleoside reverse transcriptase inhibitors, protease inhibitors, and integrase inhibitors (INIs) including ritonavir-boosted darunavir (DRV/r) and raltegravir (RAL) [4]. Dolutegravir (DTG) is a second-generation INI with a higher barrier to resistance, which received regulatory approval in Russia in 2014. In its phase 3 clinical program among HIV-1–infected treatment-naive patients, DTG has demonstrated superiority to DRV/r and noninferiority to RAL, two commonly used ARTs in Russia [5–7]. With the introduction of DTG, the objective of this analysis was to assess the cost effectiveness of DTG + backbone compared with RAL + backbone and DRV/r + backbone for HIV-1–infected treatment-naive patients.

Methods

Model Design

A cost-effectiveness model was developed to estimate the clinical outcomes and costs of DTG + backbone compared with other core agents used in Russia with a societal perspective. DRV/r and RAL, the core agents most likely to be displaced by DTG, were selected as comparators.

The model framework was a dynamic Markov model (also called a semi-Markov model) with a series of disease health states along with transition probabilities for each state that characterize disease progression. The cycle length used in the model was 1 month and the overall time horizon was patient lifetime.

Model response states and health states

Patients in the model transitioned between the five response states. Responder states modeled included responder maintaining ART; nonresponder maintaining ART; discontinuation due to failure; discontinuation due to other reasons such as intolerance, toxicity, poor adherence, or simplification; and death. Responders, defined as proportion of patients achieving viral suppression (HIV-1 RNA <50 copies/ml), maintained their ART. Nonresponders were allowed to remain on ART for a period of 6 months, consistent with the real-world treatment practice in Russia. Each patient was classified into one of these response states estimated using network meta-analysis (NMA) by Patel et al. [8]. Patients in each response state, except death, were further divided into $CD4^+$-based health states (Fig. 1). Each patient's $CD4^+$ level was determined by the treatment used, the time on treatment, and the responder status. Responders were estimated to have higher $CD4^+$ levels compared with nonresponders. Among responders, some treatments were estimated to have better $CD4^+$ efficacy on the basis of NMA [8]. In addition, the time on treatment was also a key driver for the increase in $CD4^+$ levels because the model assumed a linear increase until patients reached the trial efficacy at weeks 48 and 96, after which the $CD4^+$ levels were expected to decrease [9]. Patients discontinuing their treatment were assumed to go back to their baseline $CD4^+$ levels. This was a conservative assumption used to illustrate no incremental treatment effect after treatment withdrawal [10].

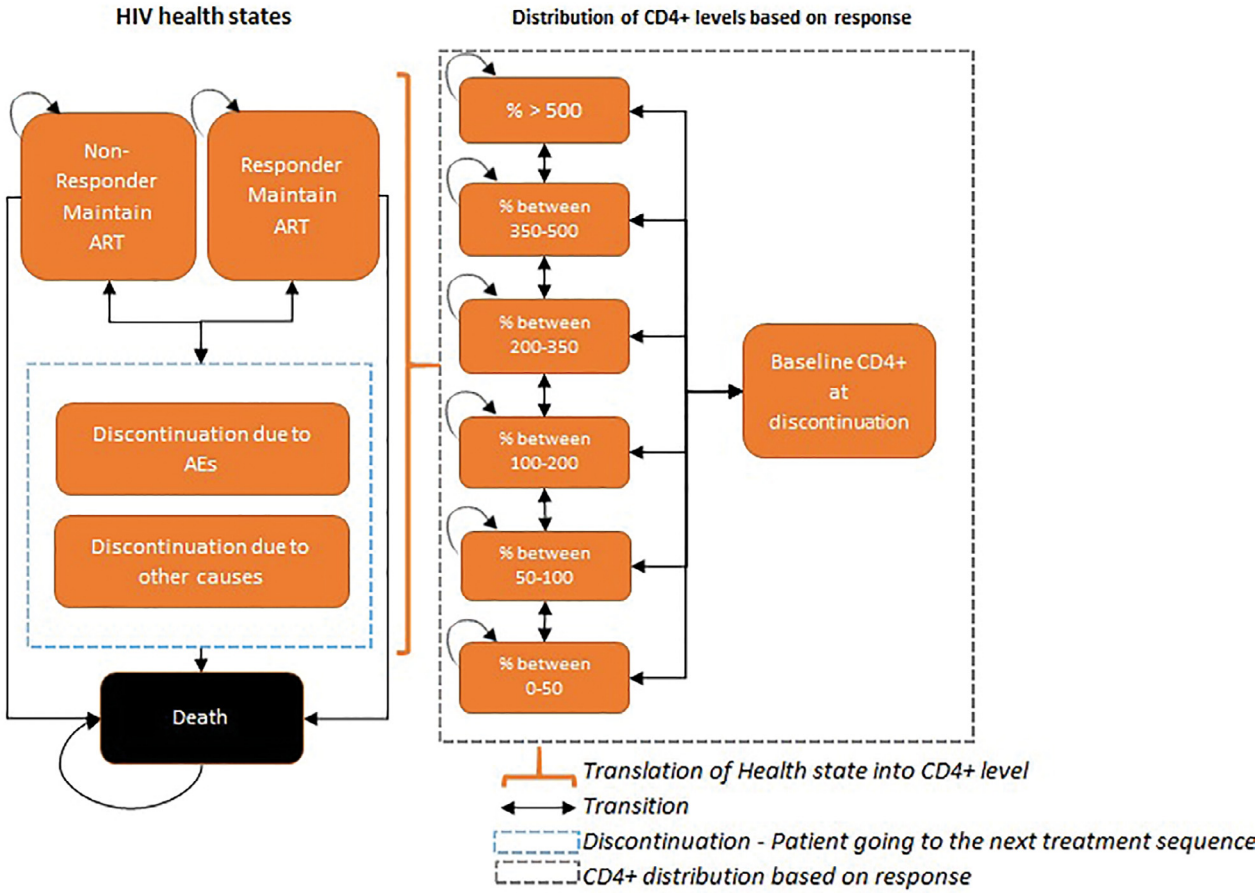

Fig. 1 – Model figure. AE, adverse event; ART, antiretroviral therapy.