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Original

Cost-effectiveness analysis of HLA-B*5701 typing in the prevention of hypersensitivity to abacavir in HIV+ patients in Spain

Diana Nieves Calatrava [a,*], Óscar de la Calle-Martín [b], José A. Iribarren-Loyarte [c], Antonio Rivero-Román [d], Laura García-Bujalance [e], Isabel Pérez-Escolano [e] and Max Brosa-Riestra [a]

[a] Oblikue Consulting, Barcelona, Spain
[b] Department of Immunology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
[c] Department of Infectious Diseases, Hospital de Donostia, San Sebastián, Spain
[d] Department of Infectious Diseases, Hospital Reina Sofía de Córdoba, Córdoba, Spain
[e] Department of Medicinal Product Evaluation and Healthcare Management, GlaxoSmithKline, Spain

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ABSTRACT

Introduction: Approximately 4% to 8% of patients with HIV-1 treated with abacavir present a hypersensitivity reaction (HSR). Various studies have shown a direct association between human leukocyte antigen (HLA)-B*5701 and HSR to abacavir. The objective of this study was to analyze whether systematic HLA-B*5701 testing to prevent HSR in patients treated with abacavir is a cost-effective option for the Spanish National Health System.

Methods: An analytical decision-making model was constructed as a decision tree model for a simulated cohort of 1000 HIV patients to evaluate whether HLA-B*5701 testing to prevent HSR to abacavir was cost effective compared with not performing the test. The parameters included in the model and the use of healthcare resources should the patient develop HSR were taken from the PREDICT-1 study and the opinion of clinical experts. The principal result obtained was the incremental cost per HSR avoided. The time horizon of the analysis was 6 months. All costs were expressed in 2008 Euros.

Results: The analysis showed that the total direct healthcare costs per patient were €1344 and €1322 with and without HLA-B*5701 testing respectively, and that 36 cases of HSR were prevented per 1000 screened patients. These results yielded a cost per HSR avoided of €630. The sensitivity analysis showed that the results were sensitive to the cost of the test, with an economic saving of €102 or a cost-effectiveness ratio of €4234.

Conclusions: The model predicts that generalized use of the HLA-B*5701 test before prescribing abacavir in HIV+ patients could represent an economic saving or a limited additional cost for the National Health System which may be counterbalanced by the benefits in terms of a lower incidence of HSR.

Análisis coste-efectividad del tipaje HLA-B*5701 en la prevención de la hipersensibilidad al tratamiento con abacavir en pacientes VIH+ en España

Palabras clave:
Coste efectividad
HLA-B*5701
Reacción hipersensibilidad
Abacavir
VIH
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RESUMEN

Introducción: Aproximadamente el 4 – 8% de los pacientes con VIH-1 tratados con abacavir presentan una reacción de hipersensibilidad (RHS). Diversos estudios han mostrado que existe una asociación directa entre el antígeno leucocitario humano (HLA)-B*5701 y la RHS a abacavir. El objetivo del presente estudio ha sido analizar si la realización sistemática del test HLA-B*5701 para prevenir la RHS en los pacientes tratados con abacavir es una opción coste-efectiva para el Sistema Nacional de Salud (SNS) español.

Métodos: Se realizó un modelo analítico de decisiones mediante un modelo de árbol de decisión para simular una cohorte de 1.000 pacientes con VIH en el que se comparó si la realización del test HLA-B*5701 para prevenir la RHS al tratamiento con abacavir era una opción coste-efectiva versus no realizar el test. Los parámetros introducidos en el modelo así como el uso de recursos sanitarios en caso de que el paciente desarrollase una RHS provenían del estudio PREDICT-1 y de la opinión de expertos clínicos. El resultado principal del studio fue el coste incremental por RHS evitada. El horizonte temporal del análisis fue de 6 meses. Todos los costes se expresaron en euros del año 2008.

Resultados: El análisis demostró que los costes sanitarios directos totales por paciente fueron 1.344 € y 1.322 € al realizar o no el test HLA-B*5701, respectivamente, evitando unos 36 casos de RHS por cada 1.000 pacientes cribados. Estos resultados dieron lugar a una razón de coste por RHS evitada de 630 €. El análisis

* Corresponding author.
E-mail address: diana.nieves@oblikue.com (D. Nieves Calatrava).

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de sensibilidad mostró que los resultados fueron sensibles al coste del test produciendo desde un ahorro económico de 102 € hasta una razón coste-efectividad de 4.234 €.

Conclusiones: El modelo predice que la generalización del uso del test HLA-B*5701 previamente a la prescripción de abacavir en los pacientes HIV+ podría suponer un ahorro económico o un coste adicional limitado para el SNS que puede verse compensado por los beneficios en términos de menor incidencia de RHS.

Introduction

Human immunodeficiency virus type 1 (HIV-1) infection has become one of the world's greatest public health problems. However, the use of highly active antiretroviral therapy (HAART) has decreased the morbidity and mortality associated with HIV infection.[1] HAART typically includes a regimen combining nucleoside reverse transcriptase inhibitors (NRTIs) with protease inhibitors or non-nucleoside reverse transcriptase inhibitors (NNRTIs).[2] Abacavir is a NRTI that has shown efficacy, few drug interactions, and a favorable long-term toxicity profile.[3,4] The most important adverse effect of abacavir that limits its use in therapy is that approximately 4% to 8%[5–7] of patients treated with abacavir present hypersensitivity to the drug, with an idiosyncratic systemic reaction including fever, rash, fatigue, and gastrointestinal and respiratory symptoms.[6] This hypersensitivity reaction (HSR) usually appears within 6 weeks of starting treatment,[6] its severity varies, and in 0.03% of patients it leads to death.[6] Therefore, abacavir is contraindicated in patients who develop a HSR. Although the precise mechanisms that produce the HSR are unknown, it has been suggested that genetic, immunological, and metabolic factors are involved.[8,9] Various studies have shown a direct association between human leukocyte antigen (HLA)-B*5701 and HSR to abacavir, as patients who present the HLA-B*5701 allele have a 100-fold greater risk of experiencing HSR when exposed to abacavir.[8,10–14] Systematic HLA-B*5701 typing before prescribing abacavir would therefore enable clinicians to determine susceptibility to HSR, thus increasing safety in the management of HIV+ patients.

HIV is the world's main infectious cause of death and produces a substantial economic burden for society;[15] thus, economic evaluations are useful to make appropriate treatment decisions based on clinical and financial grounds. Several studies have evaluated the cost-effectiveness of different HAART regimens previously.[16–18] Because abacavir is one of the NRTI included in HAART regimens recommended by Spanish HIV+ treatment guidelines, the present work aims to analyze whether systematic HLA-B*5701 testing to prevent HSR in patients who are candidates for abacavir treatment is a cost-effective option for the Spanish National Health System (NHS).

Methods

Type of analysis

A cost-effectiveness analysis was performed to compare the healthcare costs associated with performing the HLA-B*5701 test or not in HIV+ patients before they receive antiretroviral combinations containing abacavir, with the clinical benefit in terms of HSR avoided with the test. The study was based on an analytical decision-making model in which the results were expressed in relation to the incremental cost-effectiveness ratio of screening, as cost per HSR avoided.

Pharmacoeconomic model

A simulated cohort of HIV+ patients was built with a decision tree model to represent clinical practice, depending on whether the patients' susceptibility to treatment with abacavir was known or not. The model assumed that patients presenting a positive HLA-B*5701 test result would receive a HAART regimen that did not contain abacavir, whereas patients presenting a negative HLA-B*5701 test would receive HAART containing abacavir, and even then, could still present HSR (Fig. 1). The parameters included in the model and the use of healthcare resources should the patient develop HSR were taken from current literature[19,20] and the opinion of 3 clinical experts, obtained with a specific questionnaire. The first part of the questionnaire showed the assumptions of the cost-effectiveness model and

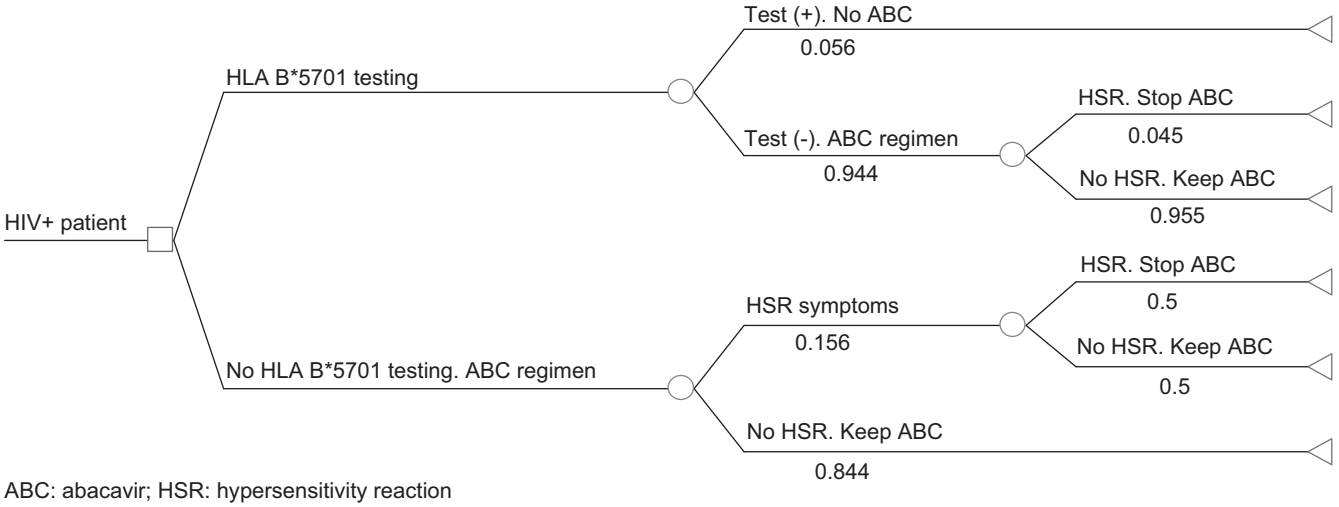

Fig. 1. Analytical decision-making model.