Med Clin (Barc). 2015;144(9):389–396

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Original article

Cost-per-responder analysis comparing romiplostim to rituximab in the treatment of adult primary immune thrombocytopenia in Spain☆

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ARTICLE INFO

Article history:
Received 18 April 2013
Accepted 28 November 2013
Available online 31 December 2015

Keywords:
Idiopathic thrombocytopenic purpura
Costs and costs analysis
Rituximab
Romiplostim

ABSTRACT

Background and objective: Romiplostim, a thrombopoietin-receptor agonist, is approved for second-line use in idiopathic thrombocytopenic purpura (ITP) patients where surgery is contraindicated. Anti-CD20 rituximab, an immunosuppressant, is currently used off-label. This analysis compared the cost per responder for romiplostim versus rituximab in Spain.
Materials and method: A decision analytic model was constructed to estimate the 6-month cost per responding patient (achieving a platelet count $\geq 50 \times 10^9$/L) according to the most robust published data. A systematic literature review was performed to extract response rates from phase 3 randomised controlled trials. Romiplostim patients received weekly injections; rituximab patients received 4 weekly intravenous infusions. Medical resource costs were obtained from Spanish reimbursement lists. Treatment non-responders incurred bleeding-related event (BRE) management costs as reported in clinical trials. Medical resource utilisation and clinical practice were based on Spanish treatment guidelines and validated by local clinical experts.
Results: The literature review identified phase 3 romiplostim trials with a response rate of 83%. Due to a lack of phase 3 controlled rituximab trials, a systematic review of studies was selected as the best source, reporting a response rate of 62.5%. The mean cost per patient for romiplostim was €16,289 and €13,459 for rituximab. Rituximab resulted in a 10% higher cost per responder (€21,535 versus €19,625 for romiplostim). Romiplostim use reduced drug administration, intravenous immunoglobulin, and bleeding-related costs compared to rituximab.
Conclusions: Due to its high level of efficacy leading to lower BRE costs, romiplostim represents an efficient use of resources for adult ITP patients in the Spanish Healthcare System.

Coste por paciente con respuesta a romiplostim y rituximab en el tratamiento de la trombocitopenia inmune primaria en España

Palabras clave:
Púrpura trombocitopénica idiopática
Costes y análisis de costes
Rituximab
Romiplostim

RESUMEN

Fundamento y objetivo: Romiplostim, agonista del receptor de la trombopoyetina, está aprobado para el tratamiento de segunda línea en pacientes con trombocitopenia inmune primaria (PTI). El tratamiento con rituximab no es infrecuente, aunque esta indicación no esté recogida en la ficha técnica. Este análisis compara el coste por paciente respondedor a romiplostim frente a rituximab en España.

☆ Please cite this article as: López MF, Mingot ME, Valcárcel D, Vicente García V, Perrin A, Campos Tapias I. Coste por paciente con respuesta a romiplostim y rituximab en el tratamiento de la trombocitopenia inmune primaria en España. Med Clin (Barc). 2015;144:389–396.
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2387-0206/

Materiales y método: Se ha diseñado un modelo para estimar el coste de 6 meses de tratamiento por paciente que responde (recuento plaquetario $\geq 50 \times 10^9$/L). Este modelo toma las referencias conforme a los datos publicados más sólidos. Los pacientes tratados con romiplostim recibieron inyecciones semanales; los pacientes tratados con rituximab recibieron 4 infusiones intravenosas semanales. Los precios se obtuvieron de las listas de reembolso españolas. Los pacientes sin respuesta incurrieron en gastos por el tratamiento de episodios relacionados con sangrado (ERS), tal como se notificó en los ensayos clínicos. La utilización de recursos médicos y la práctica clínica se basaron en las guías de tratamiento españolas y fueron validadas por expertos locales.
Resultados: Las tasas de respuesta para romiplostim y rituximab fueron del 83 y 62,5%, y el coste medio por paciente fue de 16.289 € y13.459 €, respectivamente. Con rituximab el coste por paciente respondedor fue un 10% superior (21.535 €) comparado con romiplostim (19.625 €). Romiplostim redujo el coste de administración de fármacos, el uso de inmunoglobulina intravenosa y los costes relacionados con ERS comparado con rituximab.
Conclusiones: Romiplostim representaría una opción terapéutica eficiente en comparación con rituximab para el tratamiento de pacientes adultos con PTI crónica en el Sistema Nacional de Salud español.

Introduction

Primary immune thrombocytopenia, also known as idiopathic thrombocytopenic purpura (ITP), is an acquired autoimmune disease characterised by isolated thrombocytopenia, with a peripheral platelet count $<100 \times 10^9$/L. Diagnosis of ITP is made by exclusion when there are no other identifiable causes. The disease is characterised by increased platelet destruction mediated by autoantibodies and a deficiency in their production.[1] Although incidence rates vary widely in the published literature, ITP is generally considered a rare disease.[2] In recent publications, an incidence of 3.9 for every 100,000 persons/year is estimated.[2,3] The number of affected persons is small, and patients with platelet counts higher than 50×10^9/L rarely need treatment[1]; however, this disorder may have major clinical and economic consequences, especially those related to haemorrhages and the deterioration of quality of life (QoL). Although many patients experience no symptoms or only minor haematomas, other cases may experience severe haemorrhages that may be intracranial, gastrointestinal or extensive mucocutaneous haemorrhages.[1] In addition, the physical symptoms are the main factor involved in the deterioration of QoL, and patients with ITP obtain bad scores on scales that assess aspects such as discomfort, psychological symptoms, fear, reduced social activity or reduced ability to work.[4,5]

Corticosteroids (occasionally administered together with intravenous immunoglobulin [IV Ig]) are the standard first-line of treatment; however, in refractory patients or patients with relapses, the second-line treatment was preferably limited to splenectomy until a few years ago.

Romiplostim is a thrombopoietin receptor agonist indicated for splenectomised adult patients with chronic ITP who are refractory to other medications (such as corticosteroids and IV Ig), or as a second-line treatment for non-splenectomised adult patients for whom surgery is contraindicated.[6] Thrombopoietin receptor agonists increase platelet production through the activation of the thrombopoietin receptor, which is the key mediator of platelet production.[1,7] Rituximab, a chimeric anti-CD20 monoclonal antibody, is indicated in adult patients with non-Hodgkin's lymphoma, chronic lymphocytic leukaemia and rheumatoid arthritis,[8] and, although it is not indicated in the manufacturer's technical data sheet, it is frequently used as a second-line treatment in adults with ITP.[1,7] Its main mechanism of action is characterised by a depletion of B lymphocytes with CD20+, which are involved in platelet destruction, mediated by immune mechanisms through the production of antiplatelet autoantibodies.

It has been reported that the treatment of chronic ITP in adults is expensive, particularly in patients with a severe form of the disease.[9] At present, the cost-consequence ratio of romiplostim and rituximab in patients with ITP in Spain is unknown. This has prompted us to conduct this analysis in order to assess clinical and economic implications and, in particular, to estimate the response rate and cost per patient for these two agents.

Methods

Structure of the economic model

A cost-consequence model was designed (Fig. 1) to compare the total direct costs of patients treated with romiplostim and rituximab. The parameters of the model considered drug costs, treatment duration, effectiveness of therapeutic alternatives and the use of healthcare resources. The cost-consequence analysis was chosen to present the results in a disaggregated manner, which allows the observer to independently assign the importance of the consequences for each alternative. These analyses are becoming more highly appreciated and are being applied more often in countries where the number of health technology assessments are increasing; in addition, they are usually more comprehensible to healthcare decision-makers compared to other types of pharmacoeconomic analyses.[10] The model was developed from the perspective of the Spanish National Healthcare System; therefore, only direct health costs were considered. The results and costs of patients (refractory to the first-line treatment) treated with romiplostim or rituximab were assessed. Splenectomy was not considered a third alternative in the decision-making process, since those patients, who were suitable candidates for splenectomy, would already have undergone the procedure. The analysis aimed at assessing the costs associated with each treatment intervention, including drug costs, medical visits, laboratory tests and costs related to treatments for bleeding-related episodes (BRE) in patients who did not respond. The proportion of patients whose platelet response was attributable to either of the treatments was determined 8 weeks following the start of treatment, based on international treatment guidelines.[1] As described by Weitz et al.,[11] based on a pooled data analysis of the romiplostim and placebo groups in the pivotal romiplostim trials, the patients who did not respond experienced BREs, which agglutinated the patients with bleeding episodes and those who needed rescue medication. The severity of a BRE was defined by the need for hospitalisation and the use of rescue medication.[11] The BREs were classified as ambulatory BREs and BREs that required hospitalisation. For the 18-week period contemplated in the model (the period in which patients were classified depending on whether or not they responded to the treatment), the risk of BREs was calculated using the number of BREs and the number of weeks per patient of follow-up.[11]