Cost-Utility Analysis of Dasatinib and Nilotinib in Patients With Chronic Myeloid Leukemia Refractory to First-Line Treatment With Imatinib in Thailand

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ABSTRACT

Background: Recently, the second-generation tyrosine kinase inhibitors dasatinib and nilotinib have emerged as alternative treatments in patients with chronic myeloid leukemia (CML) who are resistant to or intolerant of imatinib.

Objective: This article aimed to assess the cost utility and budget impact of using dasatinib or nilotinib, rather than high-dose (800-mg/d) imatinib, in patients with chronic phase (CP) CML who are resistant to standard-dose (400-mg/d) imatinib in Thailand.

Methods: A Markov simulation model was developed and used to estimate the lifetime costs and outcomes of treating patients aged ≥38 years with CP-CML. The efficacy parameters were synthesized from a systematic review. Utilities using the European Quality of Life–5 Dimensions tool and costs were obtained from the Thai CML population. Costs and outcomes were compared and presented as the incremental cost-effectiveness ratio in 2011 Thai baht (THB) per quality-adjusted life year (QALY) gained. One-way and probabilistic sensitivity analyses were performed to estimate parameter uncertainty.

Results: From a societal perspective, treatment with dasatinib was found to yield more QALYs (2.13) at a lower cost (THB 1,631,331) per person than high-dose imatinib. Nilotinib treatment was also found to be more cost-effective than high-dose imatinib, producing an incremental cost-effectiveness ratio of THB 83,328 per QALY gained. This treatment option also resulted in the highest number of QALYs gained of all of the treatment options. The costs of providing dasatinib, nilotinib, and high-dose imatinib were estimated at THB 5 billion, THB 6 billion, and THB 7 billion, respectively.

Conclusions: Treatment with dasatinib or nilotinib is likely to be more cost-effective than treatment with high-dose imatinib in CP-CML patients who do not respond positively to standard-dose imatinib in the Thai context. Dasatinib was found to be more cost-effective than nilotinib. (*Clin Ther*. 2014;36:534–543) © 2014 Elsevier HS Journals, Inc. All rights reserved.

Key words: chronic myeloid leukemia, cost-utility analysis, dasatinib, imatinib, leukemia, nilotinib, Thailand.

INTRODUCTION

Chronic myeloid leukemia (CML) is a malignant disorder characterized by abnormal proliferation of white blood cells. CML can be diagnosed by the presence of the Philadelphia chromosome, which results from a reciprocal translocation between chromosomes 9 and 22.[1] The new fusion gene, *BCR-ABL*, has been identified as the key factor in the development of CML. The disease is classified into 3 phases: (1) the chronic phase (CP); (2) the accelerated phase (AP); and (3) the blast phase (BP). Most patients are diagnosed with CML when the disease is in CP, which is generally asymptomatic. However, patients may show some symptoms, such as malaise, weight loss, and an enlarged spleen, during this phase, in

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which they may remain for 3 to 5 years.[2,3] Without treatment, the disease will progress from CP to AP, a more aggressive phase characterized by high proportions of blast cells (20%–30%), promyelocytes (>20%), and basophils (>20%). AP lasts ~4 to 6 months, after which most patients move into BP. During BP, CML takes on its most aggressive form, characterized by a high proportion of blast cells (>30%) in the peripheral blood or bone marrow. Patients may experience fever, fatigue, bone pain, and infections. Median survival in patients with BP-CML ranges from 3 to 6 months.[3] The incidence of CML in Thailand is ~0.5 case per 100,000 population per year.[4] Most new diagnoses of CML in Thailand are made in patients aged between 38 and 42 years.[5]

In the past decade, imatinib, the first available tyrosine kinase inhibitor (TKI), has been used widely as a first-line treatment of newly diagnosed CML.[6] Despite the high efficacy of imatinib, ~20% to 30% of patients with CML are resistant to or intolerant of the drug, and half of cases are due to a genetic mutation in the ABL domain.[7–9] Recently, the second-generation TKIs dasatinib and nilotinib have emerged and have been used as alternative treatments in patients with CML who are resistant to or intolerant of imatinib. Several experimental clinical studies have revealed that dasatinib or nilotinib use has a higher success rate than does the use of high-dose imatinib,[7,10,11] and the US Food and Drug Administration has recently approved the use of dasatinib and nilotinib as first-line treatments of newly diagnosed CML.[12] Economic evaluation studies have found that dasatinib offers good value-for-money in patients with CML who are imatinib resistant or intolerant in Sweden,[8] as well as nilotinib does in the United Kingdom. As a result, there are growing calls from Thai clinicians to include dasatinib and nilotinib in the National List of Essential Medicines (NLEM). Given the differences in health care infrastructure and economic parameters between Thailand and Sweden/United Kingdom, the data available from those economic evaluations might not be applicable for decision making in Thailand. This study aims to assess whether these 2 treatments are cost-effective in the Thai context, and the results will be used to inform decisions regarding the coverage of these drugs in the NLEM.

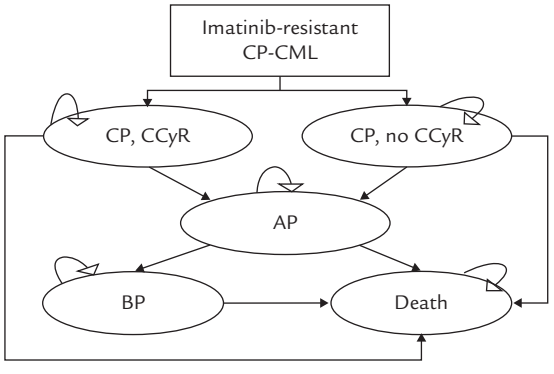

Figure 1. Structure of the Markov model. AP = accelerated phase; BP = blast phase; CCyR = complete cytogenetic response; CML = chronic myeloid leukemia; CP = chronic phase.

MATERIALS AND METHODS

Markov Model

A Markov model with a 2-month cycle length was developed based on typical treatment of patients with CP-CML, consisting of 5 initial health states: (1) CP with a *complete cytogenetic response* (CCyR), defined as no Ph-positive metaphases found in the bone marrow[13]; (2) CP without CCyR; (3) AP; (4) BP; and (5) death (Figure 1). In this Markov model, a cohort of patients with CP-CML aged ≥38 years (the median age of patients with CML in Thailand[5]) who failed to respond to first-line imatinib 400 mg/d were followed until death. Because this study focused on the costs and outcomes of CML treatment in patients in CP, it was assumed that patients who progressed to other phases would receive similar treatment. Because dasatinib 100 mg/d, nilotinib 800 mg/d, and high-dose imatinib (800 mg/d) are each used to treat patients in AP, the model assumed that the 3 treatments would be equally likely choices in patients who progressed to AP. In patients in BP, however, there is only 1 routine treatment—hydroxyurea 2000–3000 mg/d. The model took a societal perspective, meaning that the costs shouldered by both provider and household were taken into account. Future costs and outcomes were discounted at a rate of 3% per annum.

Model Input Parameters

Efficacy Data

The treatments were deemed *effective* if a patient experienced CCyR. The efficacy of each treatment was

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