Economic Burden of Tyrosine Kinase Inhibitor Treatment Failure in Chronic Myeloid Leukemia

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Abstract

To understand the economic burden of tyrosine kinase inhibitor (TKI) treatment failure in chronic myeloid leukemia (CML), episodes of TKI treatment failure in the 1 year after initiation were matched to those without failure. Failures had significantly higher health care resource use and costs. The high economic burden of TKI treatment failure reinforces the importance of optimal management in CML.

Background: The economic burden of tyrosine kinase inhibitor (TKI) treatment failure in chronic myeloid leukemia (CML) is not well understood. The objective of this study was to quantify the economic burden associated with treatment failure versus successfully remaining on TKI therapy. **Methods:** Treatment episodes for adult CML patients initiating a TKI of interest (imatinib, dasatinib, or nilotinib; index TKI) during July 1, 2008, to December 31, 2011, with continuous enrollment for $\geq$ 120 days before and 1 year after the initiation were identified from the IMS PharMetrics Plus Health Plan Claims Database. Eligible episodes of TKI treatment failure were matched to those without failure using propensity scores based on patients' baseline demographic and clinical characteristics. Treatment failure was defined as a switch to a nonindex TKI or discontinuation (gap in pharmacy claims $\geq$ 60 days) of index TKI over the 1-year follow-up. Mean all-cause health care resource utilization and costs per episode (in 2012 US dollars) over follow-up were compared between failures and nonfailures. **Results:** Among 1774 eligible episodes, 547 failures were matched to 547 nonfailures. Failures had fewer TKI prescription fills but higher utilization of all other services versus nonfailures. Consequently, failures incurred lower pharmacy costs ($51,238 vs. $72,450; Δ−$21,212) but higher medical costs ($52,619 vs. $18,180; Δ$34,439) than nonfailures, resulting in higher total costs ($103,857 vs. $90,630; Δ$13,227) (all $P < .05$). **Conclusion:** Total health care costs are higher for episodes of TKI treatment failure than those of ongoing treatment, largely as a result of costly medical (nonpharmacologic) services. Avoiding treatment failure by optimal CML management may reduce health care costs.

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Introduction

Chronic myeloid leukemia (CML) is a hematologic condition characterized by clonal expansion of pluripotent hematopoietic stem cells containing the active *BCR-ABL* fusion gene produced by a reciprocal translocation of the *ABL1* gene to the *BCR* gene.[1] With the approval of imatinib in 2002,[2] orally administered tyrosine kinase inhibitors (TKIs) have transformed the survival and prognosis in CML patients.[3] Second-generation TKIs (dasatinib and nilotinib) were initially approved in 2006 and 2007, respectively, for use in patients with disease that was resistant or intolerant to prior therapy, and received approval for use in first-line (1L) patients in 2010.[4,5] By the end of 2012, 2 more TKIs were available for resistant or intolerant CML patients, bosutinib and ponatinib.[6,7] According to National Comprehensive Cancer Network guidelines, the treatment paradigm relevant to the time of our analysis (ending in 2012) recommended treatment with a TKI approved in 1L, followed by use of an alternate second-generation TKI in second-line (2L) therapy.[8] In

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third-line (3L) therapy, investigational therapies or allogeneic hematopoietic stem cell transplantation (HSCT) were recommended. Before the introduction of TKIs, HSCT was a standard treatment option for CML, but it is now generally reserved for patients with disease that fails to respond optimally to TKIs.[9]

TKI treatment failure, in the form of resistance or intolerance to TKI therapy, is a significant challenge in CML management.[10-12] In clinical trials, resistance or intolerance is evident from trial discontinuation rates, which vary by TKI type and line of therapy. Reports indicate 14% to 33% of cases fail to respond to 1L therapy with imatinib, and about 25% fail 1L therapy with a second-generation TKI.[13-16] In 2L therapy, failure rates range from 41% to 61% in disease treated with a second-generation TKI.[17,18] Third-line therapy failures are not as well documented; reports project the incidence of failure to be 44% to 82% with a second-generation TKI.[19] These high discontinuation rates suggest a substantial potential burden of treatment failure.

Given that a variety of TKI options are now available at each therapy line with different efficacy, safety, and cost profiles, it is important to understand the economic value of a more efficacious or tolerable therapy by quantifying the economic consequences of treatment failure. Quantifying the real-world economic burden of TKI treatment failure may provide clinicians and health care administrators with valuable data to identify optimal strategies for managing CML. Real-world data not only reflect actual clinical practice but comprehensively capture health services and associated costs.

Despite their value, real-world estimates of the cost of TKI treatment failure are few. The majority of existing economic literature in CML focuses on health care resource utilization (HCRU) and costs among CML patients as a whole, or for patients who receive specific treatments (eg, 1L imatinib) rather than on the costs of failure.[20-23] No studies have quantified the excess burden of TKI treatment failure relative to successfully continuing treatment with a TKI.

The objective of this study was to quantify the burden of treatment failure by comparing 1-year HCRU and costs between 2 matched groups receiving TKI treatment for CML: those experiencing treatment failure in the 1 year after initiating a TKI of interest (imatinib, dasatinib, or nilotinib) versus those who successfully continued to receive TKI treatment over this period.

Methods

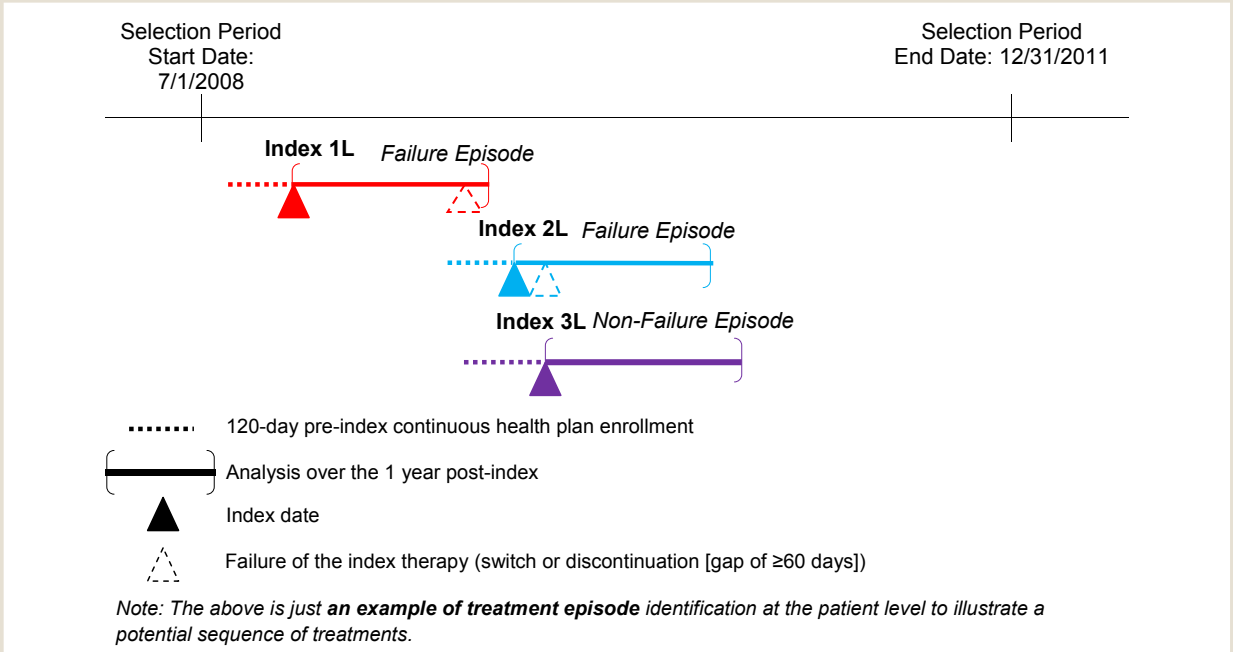
Data Source

This retrospective database analysis utilized data from the IMS PharMetrics Plus Health Plan Claims Database from March 1, 2008, to December 31, 2012. The database comprises adjudicated administrative claims data for more than 150 million unique health plan members; it is nationally representative of the commercially insured US population in terms of age and gender.

Study Design

To maximize the use of available data, the analysis was conducted at the treatment episode level; an episode was identified as a unique course of TKI treatment from initiation between July 1, 2008, and December 31, 2011 (selection period; Figure 1). A patient with multiple TKIs initiated in the selection period could have multiple treatment episodes in the study. All TKIs with an approved indication for CML treatment during the selection period were included as TKIs of interest (1L imatinib, 1L/2L/3L dasatinib and nilotinib).

Figure 1 Study Design at Episode Level



Abbreviations: 1L = first line; 2L = second line; 3L = third line.