Original Study

Current Practices in the Management of Chronic Myeloid Leukemia

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Abstract

A cross-sectional survey of board certified hematologists/oncologists was conducted to describe current chronic myeloid leukemia (CML) practice patterns and compare these self-reported practices with the clinical guidelines. Overall, the reported practice patterns regarding CML treatment were in accordance with guidelines; however, decisions also appear to be based on the attitudes, beliefs, and personal experience of the responding physicians.

Background: A previous survey of physician self-reported practice patterns in the management of CML was conducted in 2005. The National Comprehensive Cancer Network and European LeukemiaNet guidelines now include nilotinib and dasatinib in their treatment algorithms for CML. To assess these new guidelines, a cross-sectional survey of US hematologists and/or oncologists was conducted in December 2010 through an online survey. **Materials and Methods:** The survey had 43 questions consisting of items updated from the 2005 survey to reflect changes in clinical practice, tyrosine kinase inhibitor therapy, and current guidelines. **Results:** Analysis of the responses from 507 board certified medical oncologists/hematologists suggests that the use of imatinib 400 mg as an initial treatment option had decreased from 62% in 2005 to 52% in the 2010 survey. Currently, nearly 40% of physicians would choose either nilotinib or dasatinib as first-line treatment. From the surveyed physicians, achievement of at least a major molecular response (MMR) is the predominant treatment goal in chronic phase CML. **Conclusion:** This survey emphasizes the need for continued updates and education regarding optimal therapy, monitoring practices, and therapeutic end points in CML.

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Introduction

A survey was conducted between November 2005 and January 2006 to assess hematologists' and oncologists' self-reported treatment strategies for chronic myeloid leukemia (CML).[1] The results suggested that practice patterns of respondents were generally aligned with current guidelines and published clinical trials. However, there were some notable findings, including dosing discrepancies of tyrosine kinase inhibitors (TKI), confusion on the optimal timing of treatment decisions, and time points for evaluating therapeutic response. The survey results also suggested that the use of molecular monitoring was less than optimal, and a full appreciation of the differences between the qualitative and quantitative polymerase chain reaction (PCR) techniques was missing despite developments in real-time, reproducible, quantitative assays. The authors concluded that there were several areas where the practice of treating CML could be improved. Additionally, a recommendation was made to repeat the survey in the future to identify changing trends in treatment patterns.

In the 5 years since the original survey, practice has changed with respect to disease monitoring in CML and in the choice of first-line treatment options. In addition to the previously established standard of care, imatinib, the FDA granted approval for the use of nilotinib[2] (Tasigna; Novartis Pharmaceuticals Corp, East Hanover, NJ) and

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dasatinib[3] (Sprycel; Bristol-Myers Squibb Co, Princeton, NJ) based on the results of clinical studies supporting the use of these agents in the initial treatment of CML. Subsequently, the National Comprehensive Cancer Network (NCCN; 2010)[4] and European LeukemiaNet (ELN; 2009)[5] guideline recommendations were amended to include nilotinib and dasatinib into their treatment algorithms for newly diagnosed CML. In concert with these changes, the ELN guidelines[5] updated their definitions for imatinib response (optimal, failure, suboptimal) and warning prognostic factors in patients with chronic phase CML.

The purpose of this study was to re-evaluate self-reported management of CML among hematologists and/or oncologists within the United States given multiple changes in CML treatment options and response expectations in the past 5 years. This survey evaluates physicians' perceptions regarding current CML therapies, treatment associated issues such as toxicity and resistance, efficacy, ease of use of available treatments, barriers to optimal treatment, monitoring, and determination of treatment effectiveness. The results of this survey are discussed in relation to the original survey, current guidelines, and recent clinical trial outcomes.

Materials and Methods

This was a prospective United States-based, noninterventional, cross-sectional study conducted through an online survey in December 2010. The 43-question survey was expected to be completed in 20 minutes and consisted of items updated from the previous survey[1] to reflect new clinical evidence, change in clinical practice, and updated clinical guidelines. The survey was reviewed and approved by the investigators for content and clarity of the questions and instructions, and was pilot tested by Medefield, the survey company, to determine the length and feasibility of the survey. The survey questions and responses are available in the Supplementary Data.

The survey population included physicians who have registered with the survey company and had agreed to be contacted for the purposes of survey research. The survey company verified the credentials of physicians opting in for survey research through US medical education numbers and educational history (ie, diplomas). Physicians were eligible if they reported being a board certified hematologist, oncologist, or hematologist/oncologist; and treated at least 5 patients with CML outside of the context of a clinical trial in the past 2 years.

Five hundred seven physicians treating patients with CML were surveyed. The surveyed physicians represented the first 507 that qualified, from a population of US physicians who were registered with the survey company and who fit the criteria established by the survey (convenience sample).

The variables collected were descriptive in nature. As such, the frequency and percent of each response category was calculated. In addition, responses were examined by physician practice type.

Results

Survey Participant Characteristics

Eighty-two percent of the respondents specialized in hematology/oncology and the remaining 18% were in the field of medical oncology. The majority were in private practice (57.4%) followed by employment within a university or teaching institution (26.4%) or community or regional hospitals (14.6%). For more than 90% of respondents, it had been more than 6 years since completing their medical training and 89% had CML patients under their direct management at the time of the survey. Half of the respondents had patients enrolled in clinical trials (53.7%) ranging from 1 to more than than 20.

Initial Diagnosis and Workup

Participants were asked to respond to questions referring to diagnostic tests typically performed at initial patient workup. With multiple answers allowed, peripheral blood cell counts (84.6%) and bone marrow cytogenetics (83.4%) were cited as the most commonly obtained diagnostic tests when evaluating a patient with a consistent picture of CML (question [q.] 7). This was followed by bone marrow fluorescence in situ hybridization (FISH) (63.7%), peripheral blood FISH (59%), and quantitative reverse-transcriptase PCR (qRT-PCR) (57.2%).

For purposes of diagnosis, participants most frequently relied on bone marrow cytogenetics (65.5%), followed by bone marrow and peripheral blood FISH (each 48.1%), and peripheral blood cell counts (44.4%) (q. 8). qRT-PCR was included less often for purposes of diagnosis (36.7% peripheral blood qRT-PCR, 24.7% bone marrow qRT-PCR). When asked the frequency of including a bone marrow study at the initial diagnosis, 80% of survey respondents indicated that it is performed >90% of the time (q. 9).

Treatment Patterns by Patient Type

The survey contained several clinical scenarios for which the respondents were to choose their preferred treatment option. Two of the cases involved a newly diagnosed 40-year-old patient with chronic phase CML; 1 had an human leukocyte antigen-matched related sibling (q. 10) and the other an unrelated matched donor (q. 11). The third case was a newly diagnosed 60-year-old patient who was at high risk for transplantation complications because of comorbidities (q. 12). Approximately 60% of the respondents preferred to use imatinib and 40% preferred to use nilotinib/dasatinib as initial therapy in each of the cases. In the case with a matched related sibling, the opinion was split evenly as to whether an allogeneic stem cell transplant (allo-SCT) evaluation should be performed in addition to imatinib/nilotinib/dasatinib (q. 10). However, with an unrelated donor, more than 60% would not recommend allo-SCT evaluation at the onset of therapy (q. 11).

Treatment Goals and Monitoring

Seventy-two percent of respondents indicated that their primary goal for treatment response was major molecular response (MMR; 27.4%) or complete molecular response (CMR; 44.4%) for a newly diagnosed CML patient with TKI therapy (q. 13). Seventeen percent consider the achievement of complete cytogenetic response (CCyR) to be their primary goal in treating CML patients (Figure 1). Based on the respondents' primary treatment goal, the survey then queried the most critical time period to evaluate initial response to TKI therapy and the results are displayed in Figure 2 (q. 14).

Figure 3 illustrates when respondents indicated 'effective' initial treatment for newly diagnosed CML patients receiving TKI therapy among hematologic remission (HR), partial cytogenetic response (PCyR), CCyR, and MMR (q. 25).