Patient- *versus* physician-reporting of symptoms and health status in chronic myeloid leukemia

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Online Appendix (full Patients and Methods section)

PATIENTS AND METHODS

Study Population and Procedures

We approached consecutive CML patients as part of a larger project on cancer survivorship involving 26 departments of hematology of university (n=16) and community (n=10) hospitals in Italy.[4] Patients were eligible if they were in treatment with first line imatinib for at least three years and in complete cytogenetic response (CCyR). Patients with major cognitive dysfunction or psychiatric conditions were excluded. To avoid any risk of convergence in item ratings, the study was designed to avoid that patients and their treating physicians were aware of each other's ratings. Physicians invited their patients to participate at the earliest follow-up visit following approval of the study in their center. Consenting patients were asked to complete a questionnaire at home and return it in a self-addressed, stamped envelope. All questionnaires were returned to an independent center for statistical analyses (i.e., GIMEMA Data Center). The physicians were asked to complete a questionnaire for each of their patients entering the study. This was done as close in time as possible to the time that the patient was asked to complete his/her questionnaire. Thus the physicians did not have access to their patients questionnaire responses.

The study was approved by the institutional review boards of all participating hospitals and all patients provided written informed consent.

Data Collection and variables examined

The questionnaire administered to patients and physicians included a checklist of 9 core symptoms developed specifically for patients treated with imatinib. Details on the development of this checklist have been reported previously.[17] Briefly, a literature search was performed to identify most relevant issues for this patient population using several electronic databases. The list of potential issues was then presented to health care professionals (including clinicians and research nurses) for feedback on appropriateness of content and breadth of coverage. The list was also pilot tested on a small sample of CML patients for further refinement and issues were then operationalised into specific questions. This checklist was then administered to a larger sample of CML patients receiving imatinib. The symptoms assessed were: abdominal discomfort, diarrhea, edema, fatigue, headache, muscle cramps, musculoskeletal pain, nausea and skin problems. The respondents were asked to report the severity of each of these symptoms during the past week on a four point Likert scale (i.e., "not at all", "a little", "quite a bit" and "very much"). Respondents were also asked to complete a single question on overall health status from the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)[18]: "In general you would say your health is?" with the response options: "excellent", "very good", "good", "fair" and "poor". This latter question was included because it been shown to be a valid measure of self-rated overall health.[19]

Additional patient variables collected included age, gender, dose of imatinib, and duration of care by the participating physician. Additional physician variables included age, gender, number of CML patients under direct management, overall number of years in practice and years of experience in treating CML patients, and how long each of their patients in the study had been under their management (i.e., one, two, three or more than three years). The date of questionnaire completion by both the patients and physicians was also recorded.

Statistical analysis

The assumption underlying our analysis was that the patients' self-reported outcomes were the benchmark against which the physicians' ratings should be compared. We computed differences in ratings for each symptom scale previously described and the overall health status as measured by the SF-36 questionnaire. Differences ranged from -3 to +3 and -4 to +4 respectively for symptoms and overall health status ratings, with a negative, null or positive value representing physicians' underestimation, agreement or overestimation of the patients' rating. For descriptive purposes, we grouped such differences in five classes,[14] representing proportions of agreement (difference=0) and either minor or major disagreement (difference = |1| and ≥ |2|, respectively). As such analysis showed that physician's underestimation was more frequent than overestimation for all symptoms, we focused on this side of physician-patient rating discrepancy (i.e., physician's underestimation). Thus, we examined the inner structure of physicians' underestimation by the relative frequencies of the corresponding ratings pairs. We also investigated the association between patient-rated and physician-rated symptoms and overall health status (patient-reported) by Kendall's Tau-b. Furthermore, we used a multilevel logistic regression analysis to investigate potential patient-related and physician-related predictors of physicians' underestimation of patients' symptom (α=0.05). The multilevel approach was chosen to account for the clustered nature of the data (i.e., each physician could evaluate more than one patient).[20] We applied Bonferroni correction to adjust for multiple testing. All analyses were performed with SAS Version 9.2 (SAS Institute Inc).

Online Appendix (Collaborators/Participating centers):

The following centers participated in this study, enrolling patients.

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