BACKGROUND

Adherence to the prescribed dose of tyrosine-kinase inhibitors (TKIs) is critical to maximize treatment effectiveness in chronic myeloid leukemia (CML). While patient-centered outcome studies are lacking in this area, literature has shown that a significant proportion of patients report both intentional and unintentional non-adherence.

STUDY OBJECTIVES

The main objective of this study was to identify risk factors that might predict intentional non-adherence to TKIs in CML.

PATIENTS AND METHODS

The CML Advocates Network, connecting 82 CML patient groups from 64 countries, conducted an international project investigating patterns of medication-taking behaviors of CML patients, supported by CML investigator groups in Italy. We sought to demonstrate the relationship between factors and adherence in this multinational cohort. A web-based survey was launched in 10 languages, enrolling CML patients from Sept 2011 to Jan 2013. The identified CML population was provided to a cohort of patients recruited in clinics in France, Germany and Italy, returned by patients in a pre-stamped envelope to an independent data center. Questions included potential factors associated with non-adherence as well as patients’ perception of disease and treatment burden. Based on previous literature and on clinical relevance, a pool of 16 candidate factors, potentially predicting intentional non-adherence, was selected for analysis. These included: frequency of CML medication, co-payment for CML treatment, and current TKI therapy. Adherence was measured by Morisky adherence scale. Patients who reported having skipped intentionally one or more doses over the last year were considered as “intentional non-adherers”. Differences between groups were tested by Chi-square, Wilcoxon-Mann-Whitney and Kruskal-Wallis test as appropriate. Multivariable logistic regression analysis was performed to examine the impact of pre-selected candidate factors on the probability of intentional non-adherence. Only those variables with p < 0.21 in univariate analysis were considered for inclusion in the multivariable model. Then, the same final set of admitted variables was used to fit two models to identify possible predictors of intentional non-adherence, based on line of therapy received by patients (i.e. first line or second and greater lines of therapy). Statistical significance level was set as p < 0.05 for all analyses.

RESULTS

This patient-led study is the largest study conducted to date on the influencers of non-adherence in CML. Overall, 2546 adult CML patients (47.6% female) under TKI treatment from 79 countries responded to the survey (Fig. 1). 2151 patients responded online, 396 questionnaires were returned on paper. No significant difference on intentional non-adherence was observed between paper or online responses. Only one third (33%) of patients reported a high level of adherence. Median age of patients was 51 years (range 19-86) and median time from diagnosis was 4 years (range 0-27) (Tab. 1). 61% were treated with imatinib (Fig. 3) and 39% in first line therapy (Fig. 4). Overall, 51.6% of all respondents reported having missed at least one dose unintentionally over the last year, and 19.3% did so intentionally. Out of 492 intentional non-adherent patients, 60% were on imatinib, 20% on nilotinib, 14% on dasatinib, 8% on other Therapy. Several factors predicted intentional non-adherence. In univariate analysis, the strongest predictors of TKI non-adherence were:

- More time to take CML medication (P < 0.001).
- Younger age (P = 0.015).
- Longer time since diagnosis (P < 0.001), lower satisfaction with information received from healthcare providers (P = 0.023), higher burden on social life (P < 0.001) and not being fully informed on the importance of adherence (P = 0.042) (Tab. 3). Non-adherence was lower when patients were told every dose was important to make the treatment work (P = 0.04). Overall, intentional non-adherers intended to avoid fatigue (13%), diarrhea and GI issues (11%), nausea (10%) and muscle pain (9%) (Fig. 5). For patients in second or greater lines of therapy (n = 98) all of the above factors were still statistically significant except for satisfaction with information received (Tab. 3). Being female (P = 0.001) also increased the likelihood of intentional non-adherence in this group.

CONCLUSION

Despite there is clear evidence that survival is close to that of the general population when CML is treated effectively in chronic phase with current therapies, every fifth CML patient deliberately skips doses. Key factors predicting intentional non-adherence can potentially help physicians and patient organizations to identify patients early who should be monitored more closely and informed about the importance of adherence. Managing side effects proactively also reduces reasons for intentional non-adherence.