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Investigating factors associated with adherence behaviour in patients with chronic myeloid leukemia: an observational patient-centered outcome study

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BACKGROUND: Optimal adherence to imatinib therapy is of paramount importance to maximise treatment effectiveness in patients with chronic myeloid leukaemia (CML). The main objective of this study was to investigate patient-reported personal factors associated with adherence behaviour.

METHODS: Analysis was conducted on 413 CML patients receiving long-term therapy with imatinib. Adherence behaviour was measured with the Morisky Medication Adherence Scale and personal factors investigated included: quality of life, perceived social support, fatigue, symptom burden, psychological wellbeing and desire for additional information. Key socio-demographic and treatment-related factors were also taken into account. Univariate and multivariate logistic regression analyses were used to investigate factors associated with optimal adherence to therapy.

RESULTS: In all, 53% of patients reported an optimal adherence behaviour. The final multivariate model retained the following variables as independent predictors of optimal adherence to therapy: desire for more information (ref. no), odds ratio (OR) = 0.43 (95% confidence interval (CI), 0.29–0.66; $P < 0.001$), social support (higher score representing greater support), OR = 1.29 (95% CI, 1.11–1.49; $P < 0.001$) and concomitant drug burden (ref. no), OR = 1.82 (95% CI, 1.18–2.80; $P = 0.006$).

CONCLUSION: This study suggests that a higher level of social support, satisfaction with information received and concomitant drug burden are the main factors associated with greater adherence to long-term imatinib therapy.

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Imatinib was the first targeted therapy (TT) available for patients with chronic myeloid leukaemia (CML), providing major clinical advantages and better quality of life (QoL) outcomes compared with previous interferon-based treatments (Hahn *et al*, 2003; O'Brien *et al*, 2003). Typically, patients in treatment with imatinib are to take the drug indefinitely on a daily basis and ensuring an optimal adherence to treatment over the long-term period could be a challenge. According to a recent definition, proposed by an international panel of experts, adherence to medications is 'the process by which patients take their medications as prescribed' and this process has three main components: initiation, implementation and discontinuation (Vrijens *et al*, 2012).

Noens *et al* (2009) first showed that nonadherence to imatinib is associated with poorer response to treatment. More recently, Marin *et al* (2010) found a correlation between low adherence rate ($\leqslant$ to 90%) and 6-year probability to achieve a major molecular response (MMR) and a complete molecular response. These studies emphasise that strict adherence to the prescribed imatinib dose is of paramount importance to maximise treatment effectiveness in patients with CML.

The literature on potential reasons for nonadherence to oral anticancer treatments is scarce (Ruddy *et al*, 2009) and few data exist on reasons why CML patients might be nonadherent to imatinib therapy (Breccia *et al*, 2011; Eliasson *et al*, 2011). A number of factors can influence adherence to oral medication regimens (Partridge *et al*, 2002) and these not only include treatment-related aspects but also individual patient characteristics and personal factors (Ruddy *et al*, 2009).

Previous evidence in other medical conditions has shown that personal factors such as social support are strongly associated to adherence to therapy (DiMatteo, 2004a). Also, psychological aspects, subjective perceptions of QoL and side effects or information on disease and treatment have been found to be associated with adherence to therapy in various chronic medical conditions (Gordillo *et al*, 1999; Jackevicius *et al*, 2002; Krousel-Wood *et al*, 2004; DiMatteo, 2004a; Kripalani *et al*, 2007; Banta *et al*, 2009). We hypothesised that these factors could also

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be of importance in CML patients receiving long-term imatinib therapy. No study has fully investigated the concomitant role of personal factors as possible predictors of adherence behaviour in patients with CML using validated and standardised patient-reported questionnaires. The identification of such factors would be of value to physicians to help promptly identify those patients who are most in need of targeted interventions aimed at promoting a more stringent adherence behaviour.

The broad scope of this study was to examine whether social support, psychological wellbeing, QoL, fatigue and other treatment-related symptoms as well as satisfaction with information received are associated with adherence behaviour. Socio-demographic and clinical treatment-related factors were also considered. In particular, our main objective was that of profiling patients with an optimal adherence behaviour over the long-term period.

PATIENTS AND METHODS

Study design

In total, 448 CML patients were enrolled in a survivorship study involving 26 centres (Efficace *et al*, 2011). Investigation of factors associated with adherence to therapy was a secondary endpoint of the study and details on study procedure have been previously reported (Efficace *et al*, 2011). To be eligible for inclusion, patients had to be diagnosed in the early chronic phase of the disease and have been in treatment with imatinib for at least 3 years. Patients had to be in complete cytogenetic response (CCyR) at study entry. Ethic Committees of participating centres approved the study and all patients provided written informed consent.

Data collection and variables examined

Medication-taking behaviour Patients were categorised in two groups based on their medication-taking behaviour: adherers *vs* nonadherers. For this purpose, we used an adapted version of the self-reported Morisky Medication Adherence Scale (MMAS; Morisky *et al*, 1986). Patients were asked to answer the following questions: (1) Do you ever forget to take your medicine? (2) When you feel better do you sometimes stop taking your medicine? (3) Sometimes if you feel worse when you take the medicine, do you stop taking it? Each question had the following response categories: never, rarely, sometimes and often. Similarly to the original 4-item MMAS, patients who responded to all items as 'never' were considered as adherers (i.e., patients with an optimal adherence behaviour). All the other patients, responding at least, 'rarely', even to just one question, were considered as nonadherers. This latter category, of course, includes a wide range of patients with a suboptimal adherence behaviour, that is, those who might just occasionally miss few doses and those who might be recurrent nonadherers. However, for the purpose of this analysis the above classification was considered clinically relevant. All completed adherence surveys were anonymously returned to an independent data centre.

Socio-demographic and clinical factors Age, gender, education, marital status and concomitant drug burden were obtained through self-reports. Concomitant drug burden was defined as the assumption of additional drugs related to diseases other than CML (yes *vs* no). Baseline (i.e., at the time of diagnosis) clinical variables investigated included: the Eastern Cooperative Oncology Group (ECOG) performance status and Sokal risk classification. Clinical treatment variables examined were as follows: overall duration of therapy, time between start of therapy and CCyR and time from CCyR to study entry, and toxicity within 1 year from adherence evaluation. Also, intolerance to therapy was evaluated and this was defined as having changed imatinib dose (or temporarily discontinued treatment), at least once from treatment start to study entry, due to a toxic event (irrespective of types and grade).

Patient-reported personal factors

Social support: The Multidimensional Scale Of Perceived Social Support (MSPSS) was used. The MSPSS is a 12-item scale that evaluates perceptions of social support from three main sources: friends, family members and significant others (Zimet *et al*, 1990). Patients are asked to indicate their agreement with items on a 7-point Likert-type scale, ranging from very strongly disagree to very strongly agree. Total and subscale scores range from 1 to 7, with higher scores suggesting greater levels of perceived social support.

Quality of life: QoL was assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36; version 1). This robust psychometric questionnaire consists of 36 items yielding eight scales investigating physical and mental health-related aspects. Two summary scores, namely the physical component summary (PCS) and the mental component summary (MCS) are derived from a weighted combination of the eight scales. The PCS and MCS scores were used in this analysis (Ware and Sherbourne, 1992).

Desire of additional information: We investigated patients' satisfaction with information available at the time of the study participation in some key areas by asking patients whether they would have wished for more information on the following aspects: (1) disease; (2) side effects of therapy; and (3) impact of disease and side effects of therapy on their QoL. All three items had a possible dichotomous answer (yes *vs* no).

Fatigue and other treatment symptoms: Fatigue was evaluated with the FACIT Fatigue scale, which has undergone a rigorous validation process showing robust psychometric properties (Yellen *et al*, 1997). Other treatment-related symptoms, including oedema, abdominal discomfort, nausea, headache, diarrhoea, muscular cramps and musculoskeletal pain and skin problems were investigated with a previously reported *ad hoc* symptom measure (Efficace *et al*, 2010).

Psychological wellbeing: This was evaluated with the short form of the Psychological General Well-Being Index (PGWB-S) measuring the following psychological dimensions: anxiety, vitality, depressed mood, positive well-being and self-control (Grossi *et al*, 2006).

Statistical analysis

This analysis is based on 413 patients who returned a valid adherence questionnaire. Multivariate logistic regression analysis was used to investigate factors associated with optimal adherence. A first model examined the relation between adherence and socio-demographic/clinical variables, a second model between adherence and patient-reported personal factors. For each model, a first univariate analysis was performed to select the candidates for the multivariate model ($\alpha = 0.2$). Whereas multicollinearity was detected among selected candidates (variance inflation factor > 2), the model with lowest Akaike information criterion (AIC) was chosen among alternative stepwise regressions for each collinear variable ($\alpha = 0.05$). A final overall model was then selected via a stepwise process starting from the variables of previous two lowest AIC models ($\alpha = 0.05$). A bootstrap resampling procedure was used to investigate the replication stability of the final overall selected model (Efron and Tibshirani, 1993; Steyerberg *et al*, 2001). Bootstrapping has already been applied to logistic models in previous studies (Risselada *et al*, 2010; Suarthana *et al*, 2010). We generated 5000 samples each the same size of the original set of patients, by randomly sampling a patient within it and replacing him/her before sampling the next one. The same stepwise selection procedure was performed of a multivariate logistic model for each generated sample, starting from all variables considered for previous socio-clinical and patient-reported models without any

admission cutoff, after having checked for multicollinearity. The inclusion frequency of each variable in the final 5000 selected logistic models indicated the importance of its association with adherence behaviour. We also calculated the model selection probabilities on the basis of how many times a permissible model was selected in the bootstrap samples, looking for the most probable sets of variables. All analyses were performed with SAS v. 9.1.3 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Socio-demographic and clinical characteristics of the 413 patients analysed are reported in Table 1. Median age of patients was 57 years (range 20–87 years) and median duration of imatinib treatment was 5 years (range 3–9 years). According to our working definition, 53% of patients could be considered as adherers.

Socio-demographic and clinical factors associated with adherence

Univariate analysis showed that concomitant drug burden predicted a greater adherence to therapy ($P = 0.018$). The shorter the time since achieving CCyR was associated with greater adherence ($P = 0.019$). Median time since achieving CCyR in our sample was 4.42 years (range 0.17–8.67).

The best multivariate model identified the two following factors: concomitant drug burden (odds ratio (OR) = 1.653, 95% confidence interval (CI), 1.105–2.472) and time between CCyR and adherence evaluation (OR = 0.857, 95% CI, 0.748–0.983). Details are reported in Table 2.

Patient-reported personal factors associated with adherence

A higher mental health status ($P = 0.02$) and greater level of social support ($P < 0.001$) were associated with adherence in the univariate analysis. The desire for more information on all the three aspects investigated was also significant ($P < 0.001$). Three alternative multivariate models were fitted each including one type of desired information (i.e., disease, side effects and impact of both on QoL). The best multivariate model retained the two following factors: social support (OR = 1.290, 95% CI, 1.112–1.497) and desire for more information on the impact of disease and therapy on QoL (OR = 0.446, 95% CI, 0.292–0.682). Details are reported in Table 3.

Final multivariate model of factors associated with adherence

The final multivariate model identified concomitant drug burden, greater level of social support and satisfaction with information received (on the impact of therapy on one's QoL) as independent factors associated with optimal adherence (Table 4).

Table 1 Socio-demographic and clinical characteristics of study population ($n = 413$)

Variable	Total ($N = 413$)
Gender, N (%)	
Female	167 (40.44)
Male	246 (59.56)
Age at study entry (years)	
Median	56.83
Range	19.67–86.83
Education, N (%)	
Eight grade or less	188 (45.52)
High school	152 (36.8)
University degree or higher	70 (16.95)
Missing	3 (0.73)
Marital Status, N (%)	
Divorced	30 (7.26)
Single	42 (10.17)
Married/living together	304 (73.61)
Widow	31 (7.51)
Missing	6 (1.45)
ECOG performance status, N (%)	
0	278 (67.31)
⩾1	135 (32.69)
Sokal risk at diagnosis, N (%)	
Low (< 0.8)	217 (52.54)
Intermediate (0.8–1.2)	136 (32.93)
High (>1.2)	46 (11.14)
Missing	14 (3.39)
Concomitant drug burden, N (%)	
No	239 (57.87)
Yes	170 (41.16)
Missing	4 (0.97)
Duration of imatinib therapy (years)	
Mean (s.d.)	5.18 (1.48)
Median	5.08
Range	3.00–9.33

Abbreviation: ECOG = Eastern Cooperative Oncology Group.

Table 2 Logistic regression analysis of optimal adherence behaviour in relation to socio-demographic and clinical factors

	Univariate analysis		Multivariate analysis	
Variables	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Socio-demographic factors				
Age at study entry	1.012 (0.999; 1.026)	0.075	NA	NA
Education (ref. high)	1.456 (0.985; 2.154)	0.060	NA	NA
Gender (ref. male)	0.939 (0.634; 1.392)	0.755	NA	NA
Marital status (ref. married)	0.754 (0.482; 1.180)	0.217	NA	NA
Clinical factors				
ECOG performance status (ref. 0)	0.715 (0.474; 1.081)	0.111	NA	NA
Intolerance to imatinib (ref. no)	0.749 (0.485; 1.155)	0.191	NA	NA
Concomitant drug burden (ref. no)	1.617 (1.086; 2.408)	0.018	1.653 (1.105; 2.472)	0.014
Duration of therapy	0.897 (0.786; 1.023)	0.104	NA	NA
Time from CCyR to adherence evaluation	0.851 (0.744; 0.974)	0.019	0.857 (0.748; 0.983)	0.027
Time to CCyR	1.345 (0.950; 1.906)	0.095	NA	NA
Sokal risk (ref. low)	1.218 (0.820; 1.808)	0.329	NA	NA
Toxicities within 1 year from study entry (ref. no)	0.936 (0.583; 1.503)	0.784	NA	NA

Abbreviations: CCyR = complete cytogenetic response; CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; NA = not applicable; OR = odds ratio. Legend: only variables with $P < 0.2$ in univariate analysis were considered for inclusion in the starting multivariate model.

Table 3 Logistic regression analysis of optimal adherence behaviour in relation to patient-reported personal factors

	Univariate analysis		Multivariate analysis	
Variables	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Physical health	0.988 (0.968; 1.009)	0.268	NA	NA
Mental health	1.024 (1.003; 1.045)	0.023	NA	NA
Psychological well being[a]	1.030 (0.995; 1.066)	0.097	NA	NA
Fatigue	1.000 (0.979; 1.022)	0.988	NA	NA
Additional treatment-related symptoms[b]	0.988 (0.976; 1.000)	0.057	NA	NA
Global social support	1.305 (1.132; 1.505)	< 0.001	1.290 (1.112; 1.497)	<0.001
Desire for more information on:				
Disease (ref. no)	0.476 (0.321; 0.707)	< 0.001	NA	NA
Side effects of therapy (ref. no)	0.475 (0.320; 0.704)	< 0.001	NA	NA
Impact of disease and therapy on QoL (ref. no)	0.438 (0.295; 0.650)	< 0.001	0.446 (0.292; 0.682)	<0.001

Abbreviations: CI = confidence interval; NA = not applicable; OR = odds ratio; PGWB-S = the short form of the Psychological General Well-Being Index; QoL = quality of life. Legend: only variables with $P<0.2$ in univariate analysis were considered for inclusion in the starting multivariate model. [a]Overall sum score of the PGWB-S. [b]Overall mean symptom score (nausea, diarrhoea, oedema, skin problems, abdominal discomfort, musculoskeletal pain, headache and muscle cramps).

Table 4 Final multivariate model of factors associated with optimal adherence behaviour

Variable	**OR (95% CI)**	***P*-value**
Concomitant drug burden (ref. no)	1.823 (1.185; 2.804)	0.006
Global social support	1.290 (1.113; 1.495)	< 0.001
Desire for more information on the impact of disease and therapy on QoL (ref. no)	0.435 (0.286; 0.662)	< 0.001

Abbreviations: CI = confidence interval; OR = odds ratio, QoL = quality of life.

Supportive multivariate analysis

Our final multivariate model was the top one (i.e., the most selected one) out of all the 5000 bootstrap-generated simulation datasets. Also, the three highest inclusion frequencies were as follows: desire for more information on the impact of disease and therapy on QoL (93%), social support (89%) and assumption of concomitant drugs (71%). We note that these inclusion frequencies highlight the importance of a single variable being included as an independent factor in the model. Table 5 summarises findings from this additional supportive analysis.

DISCUSSION

This study suggests that a higher level of social support, satisfaction with information received and concomitant drug burden are the main factors associated with an optimal adherence to long-term imatinib therapy in CML patients.

Optimal adherence to imatinib therapy is crucial to maximise treatment effectiveness (Noens *et al*, 2009; Marin *et al*, 2010; Ibrahim *et al*, 2011), however, the ability of physicians to recognise nonadherence is poor (Osterberg and Blaschke, 2005). Given the paucity of data in the CML literature, we selected possible factors associated with adherence behaviour based on previous studies in other chronic medical conditions (DiMatteo, 2004a; Morisky *et al*, 2008). Our conceptual model was that of considering adherence behaviour in the centre of a process preceded by specific determinants and followed by specific health outcomes (Morisky and DiMatteo, 2011). The percentage of patients classified as nonadherers in our study (i.e., 47%) is high but seems broadly consistent with previous data indicating that between 25 and 50% of patients can be considered as nonadherent (Vermeire *et al*, 2001; DiMatteo, 2004b). Also, it is difficult to make comparisons regarding prevalence of nonadherence in other studies as this fluctuates as a function of methods used. However, our data support previous findings that adherence to imatinib therapy is far from optimal in CML patients (Noens *et al*, 2009). To our knowledge, only one study on a small cohort of 38 patients have found 'good' adherence to imatinib therapy (Jonsson *et al*, 2012).

Social support has been found to be associated with adherence in patients with HIV (Gordillo *et al*, 1999) and hypertension (Morisky and DiMatteo, 2011) as well as with other chronic medical conditions (DiMatteo, 2004a; Lett *et al*, 2005) and we

Table 5 Inclusion frequencies of single variables and top 10 models out of the 5000 bootstrap-generated data sets

	Inclusion frequency of single variables (%)[a]														
	20.3	**7.5**	**25.7**	**6.5**	**47.7**	**12.6**	**17.9**	**6.7**	**71.1**	**29.4**	**33.9**	**6.4**	**40.0**	**89.2**	**93.4**	
Top 10 Models[b]	**ASE**	**Gen**	**Edu**	**MS**	**ECOG**	**SKR**	**ITI**	**TWY**	**CD**	**TFCA**	**PCS**	**MCS**	**ATRS**	**GSS**	**IDTQ**	**%[c]**
1									√					√	√	5.9
2					√				√					√	√	3.0
3					√				√		√		√	√	√	2.5
4			√		√				√					√	√	2.2
5									√		√		√	√	√	2.0
6							√		√					√	√	1.9
7			√						√					√	√	1.8
8									√	√				√	√	1.8
9	√													√	√	1.5
10									√	√	√		√	√	√	1.4

Abbreviations: ASE = age at study entry; ATRS = additional treatment-related symptoms, i.e., overall mean symptom score (nausea, diarrhoea, oedema, skin problems, abdominal discomfort, musculoskeletal pain, headache, muscle cramps); CD = concomitant drug burden (ref. no); ECOG = Eastern Cooperative Oncology group performance status (ref. 0); edu = education (ref. high); gen = gender (ref. male); GSS = global social support; IDTQ = desire for more information on impact of disease and therapy on quality of life (ref. no); ITI = intolerance to imatinib (ref. no); MCS = mental health; MS = marital status (ref. married); PCS = physical health; SKR, Sokal risk (ref. low); TFCA = time from complete cytogenetic response to adherence evaluation; TWY = toxicities within 1 year at study entry (ref. no). [a]This percentage refers to the number of times a single variable was selected as an independent factor in multivariate analysis out of the 5000 bootstrap-generated samples. [b]Top 10 models out of the 5000 bootstrap-generated samples. An empty box means the variable was not selected in the model and the following symbol: √ means the variable was selected in the model. [c]This percentage refers to the number of times a given model was selected out of the 5000 bootstrap-generated samples.

report, for the first time, that this is also a key issue in patients with CML. Two broad types of social support have typically been investigated in previous adherence studies: 'structural' (e.g., marital status and living arrangements) and 'functional' (e.g., practical, emotional and family cohesiveness; DiMatteo, 2004a; Lett *et al*, 2005) and we investigated both constructs. Although marital status by itself was not significantly associated with adherence behaviour in our study, functional perceived social support as measured by the MSPSS did. Our findings are thus consistent with previous adherence studies indicating that functional social support, rather than structural, is a more prominent factor in determining adherence to therapy (DiMatteo, 2004a). The social support instrument used in our study (i.e., the MSPSS) is heavily focused in measuring the functional aspects of social support, by investigating the strength and the quality of patient's relationships with family members, friends and significant others in his/her life. It is thus possible to speculate, for example, that CML patients who can rely on stronger social networks are more likely to be reminded to take their drugs and stick with it over the long run. Also, they might be supported, through a number of other ways, in better coping with the burden of a lifelong therapy (DiMatteo, 2004a). Our findings should thus alert clinicians in exploring the level and quality of social support of their patients in their daily life as this could potentially provide additional insights on treatment outcomes.

Patients who were satisfied with information received with regard to the impact of therapy on their own QoL were more likely to be classified as adherers. This data complement previous evidence indicating an association between patients' knowledge of disease and treatment and adherence to therapy (Noens *et al*, 2009). Richardson *et al* (1990) showed that educational programs including information on disease and expected side effects were associated with better survival in patients with haematologic malignancies. Moon *et al* (2011) reported that a counselling programme, focusing also on the provision of information on QoL, was effective in improving compliance in CML patients receiving imatinib. However, scarce data is currently available on the effect of targeted therapies on CML patients' QoL (Efficace *et al*, 2012), thus current findings underscore the urgent need of more research on patients' QoL. A recent meta-analysis has clearly indicated that physician communication is an important predictor of patient adherence (Zolnierek and Dimatteo, 2009) and our data highlight the crucial role that physicians could potentially have in promoting adherence to therapy. For example, physician could proactively explore, during consultations, whether their patients want to know more.

Our results that a concomitant drug burden was associated with an optimal adherence to therapy lend support to previous data by Noens *et al* (2009) who showed an association between more medication to be taken daily and better adherence in CML patients undergoing imatinib therapy. This also seems consistent with earlier studies in patients with other diseases (Jackevicius *et al*, 2002). A qualitative study by Eliasson *et al* (2011) reported that adherent patients referred to taking imatinib as being part of their daily routine, hence, it would be possible to speculate that patients who are already taking medication for other diseases might be facilitated in fitting CML therapy into their regular overall medication-taking schedule.

Previous work has shown that some 30% of these patients-reported severe fatigue levels and that between 23 and 53% reported mild levels of other symptoms (Efficace *et al*, 2011). Thus, we investigated the association of these symptoms with adherence behaviour but did not find any significant relationships. Future longitudinal studies are required to fully ascertain the predictive role of patient-reported symptom burden on adherence from the very beginning of treatment.

Another finding that is noteworthy is that the shorter the time since achieving CCyR was associated with greater adherence in the multivariate analysis of socio-demographic and clinical data. Does this reflect that patients are 'fine' with having attained and maintaining CCyR and then become complacent and start being nonadherent? Previous qualitative research has also shown that patients tend to report an increase in intentional nonadherence behaviour over time (Eliasson *et al*, 2011), and our findings strongly support the need of prospective studies addressing this question.

This study has a number of strengths including a large sample size recruited in a multicenter study, and the use of validated patient-reported measures as possible predictors of adherence behaviour. Also, our additional sensitivity analysis confirmed the stability of the final multivariate model, thus strengthening the reliability of our findings.

This paper, however, also has potential limitations. First, we might have missed additional patient-related factors that have found to be related to adherence in patients with other diseases (Markkula *et al*, 2012). Second, we used an adapted version of the MMAS and third, it is possible that additional measures of adherence could have further contributed to a more sensitive definition of adherers *vs* nonadherers in our study. However, we note that as our patients were aware that their treating physicians would not have access to their answers, it is likely that their ratings reflected their actual behaviour in drug assumption. No gold standard exists for measuring adherence (Ruddy *et al*, 2009) and self-report methods provide a good estimate of medication adherence and also have potential advantages over other methods (Shi *et al*, 2010; Morisky and DiMatteo, 2011).

These potential limitations notwithstanding, we are confident our results extend findings of previous research on the relationships between poor adherence and CML treatment outcomes (Noens *et al*, 2009; Marin *et al*, 2010; Ibrahim *et al*, 2011) to suggest key potential determinants of adherence behaviour. Physicians are encouraged to pay special attention to factors identified in this study as they could help to promptly identify patients who might be at a heightened risk of nonadherence.

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Conflict of interest

Consultant or advisory role: FE and FrCo, (Bristol Myers Squibb), MiBa, MB, GR and MT, (Novartis and Bristol Myers Squibb). Research funding: FE and GR (Novartis). Honoraria: MiBa (Novartis, Bristol-Myers Squibb, Pfizer and Ariad); GA, GR and FC (Novartis and Bristol Myers Squibb). The remaining authors declare no conflict of interest.

Author contributions

Study concept: FE, MiBa and FM. Study design: FE, MiBa and FM. Data acquisition: FE, MiBa, GR, FrCo, FC, MB, GA,AI, ARR, SP, FG, MS, MT, MV and FM. Quality controls of data and algorithms: FrCo. Data analysis and interpretation: FE, MiBa, GR, FrCo, FC, MB, GA and FM. Statistical analysis: FrCo and FE. Manuscript preparation: FE. Manuscript editing: FE, MiBa, GR and FrCo. Manuscript review: FE, MiBa, GR, FrCo, FC, MB, GA,AI, ARR, SP, FG, MS, MT, MV and FM.

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