Palliative and Supportive Care (2015), **13**, 255–263.

doi:10.1017/S1478951513001260

Lack of congruence between patients' and health professionals' perspectives of adherence to imatinib therapy in treatment of chronic myeloid leukemia: A qualitative study

SIMON WU, M.B.B.S./B.MED.SCI.,[1,2] DESMOND CHEE, M.B.B.S./B.MED.SCI.,[1,2] ANNA UGALDE, B.A., PH.D.,[1,3] PHYLLIS BUTOW, B.A., DIP.ED., M.CLIN.PSYCH., M.P.H., PH.D.,[4] JOHN SEYMOUR, M.B., B.S., F.R.A.C.P., PH.D.,[2,5] AND PENELOPE SCHOFIELD, B.SC., PH.D.[1,2,6]

[1]Department of Cancer Experiences Research, Peter MacCallum Cancer Center, East Melbourne, Victoria, Australia
[2]Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Parkville, Victoria, Australia
[3]Center for Palliative Care, St Vincent's Hospital Melbourne, Fitzroy, Victoria, Australia
[4]Department of Psychology, The University of Sydney, Sydney, New South Wales, Australia
[5]Department of Hematology, Peter MacCallum Cancer Center, East Melbourne, Victoria, Australia
[6]Sir Peter MacCallum Department of Oncology, The University of Melbourne, Parkville, Victoria, Australia

(RECEIVED October 20, 2013; ACCEPTED November 8, 2013)

ABSTRACT

Objective: Consistent use of imatinib is critical for treatment success in chronic myeloid leukemia, yet perfect adherence to the prescribed clinical regimen is reported to be as low as 14%. This study aimed to understand patients' experiences of chronic myeloid leukemia with a qualitative approach, including identified facilitators and barriers to adherence, drawing on patients' and health professionals' perspectives, recording comments made by patients and health professionals involved with the same treatment team.

Method: We recruited patients with chronic myeloid leukemia prescribed imatinib therapy and health professionals involved in their treatment from a specialized cancer center. Semi-structured qualitative interviews were recorded, transcribed, and manually analyzed using interpretive phenomenological analysis. Recruitment ceased upon saturation, with 16 patients and 10 health professionals (hematologists $n = 4$, nurses $n = 3$, pharmacists $n = 3$).

Results: Twelve patients reported at least one instance of nonadherence. Reasons for unintentional nonadherence included forgetfulness related to variations of routine and doctor–patient communication issues. Reasons for intentional nonadherence included desires to reduce dose-dependent side effects and insufficient support. Patients who reported higher nonadherence rates felt complacent following periods of sustained disease control or had received conflicting advice regarding nonadherence. Health professionals had difficulty in accurately evaluating medication adherence due to a lack of reliable measures, utilizing patient self-report and manifestations of suboptimal disease control to guide assessments.

Significance of Results: Adherence issues persist throughout the course of treatment. While high patient-reported nonadherence rates were recorded, health professionals were often unaware of the complex causes, compounded by an inadequacy of adherence assessment tools. Some patients reported nonadherence events because of insufficient education or lack of access to prompt medical guidance. These issues should be addressed to improve clinical practice.

KEYWORDS: Cancer, Adherence, Chronic myeloid leukemia, Qualitative, Imatinib

Address correspondence and reprint requests to: Penelope Schofield, Peter MacCallum Cancer Center, Locked Bag 1, A'Beckett Street, Victoria, 8006, Australia. E-mail: penelope.schofield@petermac.org.

INTRODUCTION

Imatinib therapy has revolutionized chronic myeloid leukemia (CML) treatment, greatly extending survival

(Druker et al., 2006; Kantarjian et al., 2006; Hehlmann et al., 2007). However, imatinib requires continuous daily use for optimal efficacy (Stone, 2004; Jabbour et al., 2008; Yoshida et al., 2011), and adherence to the regimen, defined as the extent of correspondence between a person's behavior and healthcare recommendations, is critical to treatment outcome (Sabate, 2003). Current adherence is reported to be suboptimal; over a 90-day period, a prospective Belgian study demonstrated perfect adherence in only 14% of patients with CML (Noens et al., 2009).

Moreover, a British clinical trial found that an adherence rate below 90% of doses is linked to suboptimal molecular response and increased risk of disease progression in patients who had achieved a cytogenetic remission (Marin et al., 2010; Ibrahim et al., 2011). A subsequent qualitative study involving 21 of the trial participants found that imatinib nonadherence could be attributed to a range of unintentional and intentional causes (Eliasson et al., 2011). Unintentional nonadherence was predominantly related to forgetting doses, while reasons for intentional nonadherence included side effects and lifestyle factors.

In an ongoing systematic review of existing interventions employed to improve medication adherence and treatment outcomes, improving adherence in other chronic conditions was considered complex and not cost effective (Haynes et al., 2008). The focus in CML should be on developing targeted interventions as appropriate to each patient (Efficace et al., 2013). Factors that are correlated with improved adherence include functional social support for patients, adequate information regarding management, and the use of multiple medications, speculated to be linked to preexisting routines for oral medication use (Efficace et al., 2012).

Patient education regarding oral chemotherapy use is delivered by doctors, nurses, and pharmacists, yet existing evidence suggests that health professionals (HPs) have poor skills when it comes to accurately identifying nonadherent patients, suggesting that additional assistance interventions are not currently targeted to the patients most in need (Williams, 2001; Hartigan, 2003; Noens et al., 2009).

The literature on the perspectives of HPs regarding treatment issues in CML, including adherence, has been limited to an online survey that supported the use of detailed counseling before commencement of treatment and ongoing patient–physician contact to improve adherence (Guilhot et al., 2010). In order to understand these perspectives in depth, it is necessary to conduct detailed interviews with health professionals with regard to treatment protocols and feasibility of adherence interventions.

Our qualitative study aimed to explore and compare patient experiences with HPs' perceptions regarding imatinib therapy for CML, including facilitators and barriers to adherence, identifying differences in perspective, to underpin the subsequent development of adherence-promotion strategies targeted to appropriate factors.

METHOD

Recruitment

The study was undertaken at a specialist cancer center in Australia (the Peter MacCallum Cancer Center). With ethics approval, two groups of participants were recruited: patients with CML and their treating HPs. The investigator (SW) was not involved in treatment of patients and had no other contact with participants. Interviewed health professionals were not involved in any other aspect of the study.

Inclusion criteria were: patients aged 18 years or over and proficient in English, a confirmed diagnosis of chronic-phase CML, at least three months of continuous treatment, and no evidence of drug resistance. Exclusion criteria were: patients who had cognitive or psychological difficulties, who were too unwell, or who had no further followups.

Data Collection

Consented participants were interviewed face to face by the first author (SW). Patients were consecutively recruited via patient lists filtered using criteria. Participants were consecutively recruited until saturation of themes, which was achieved after interviews with 16 of the 23 eligible patients and 10 HPs (hematologists $n = 4$, nurses $n = 3$, pharmacists $n = 3$). No one refused participation.

All interviews followed a standardized semistructured format at the cancer center. Separate interview schedules were developed for each group; however, similar issues were discussed. Patient interviews explored their experiences of ongoing imatinib treatment, including adherence. HP interviews collected their views regarding imatinib adherence and current CML treatment practices.

Data Analysis

The data collection and data analysis phases were concurrent. Audio recordings of interviews were transcribed and deidentified. Nonadherence was defined as any instance where a patient failed to administer the prescribed regimen as directed, including instances of a suboptimal dose, according to current guidelines (Baccarani et al., 2009).

https://doi.org/10.1017/S1478951513001260 Published online by Cambridge University Press

Analysis was performed using interpretive phenomenological analysis (IPA), which involves collecting accounts from participants regarding their interpretations of significant events or processes, or "phenomena" (Smith et al., 2009). Researchers were required to use their own conceptions to explore the participants' world in order to understand their perspectives. The IPA approach was chosen for its ability to draw themes strongly supported by the data, focusing on the study objectives and exploring the rationale behind participants' actions (Smith et al., 2009).

Analysis was completed manually by the interviewer (SW) to ensure consistency of interpretation and coding of data. Using a constant comparative approach, segments of each transcript were grouped into codes; a coding guide was developed that categorized the data into discrete themes.

To reduce the likelihood of subjective interpretations and ensure a rigorous analytical process, two transcripts were additionally reviewed by two other investigators (DC and PS) independently. Disagreements were discussed among the three investigators, leading to coding guide revisions. One investigator (DC) then independently coded another five randomly selected transcripts to confirm the comprehensiveness and discreteness of categories, with additional revisions. Transcripts were reread and recoded as required to reflect any changes. The interview schedules were refined for subsequent interviews to validate the refined codes. Finally, "axial coding" was employed to develop categories that subsumed many of the first-order concepts (Bryman & Burgess, 1994). Analysis ceased upon saturation.

RESULTS

The 16 patients interviewed had received imatinib therapy for a median of 35 months (range 6–113). Patient interviews lasted an average of 61 minutes (range 22–105). Eleven (69%) reported at least one instance of a suboptimal dose and another reported an overdose.

The 10 HPs interviewed had a median 5.5 years of clinical hematology practice (range 1–22). HPs within each professional group shared similar perspectives, and interviewing ceased once this became evident. HP interviews lasted an average of 32 minutes (range 20–51), as the focus was to gather expert perspectives in comparison to patient's in-depth personal experiences.

Participant demographics are shown in Table 1. Themes, subthemes, and representative quotes are given in Table 2.

Theme 1: Management of CML

Tolerating Treatment

Patients had varied experiences with imatinib. Many were asymptomatic of their CML at diagnosis, yet paradoxically experienced bothersome side effects from treatment. One doctor (HP6) acknowledged that side effects that "have quite a large impact on the quality of life of the patient would probably have the most effect" on adherence.

Table 1. *Participant demographics*

	Patients ($n = 16$)	HPs ($n=10$)		
		Doctors ($n = 4$)	Nurses ($n = 3$)	Pharmacists ($n = 3$)
Age (years)	52 (26–71)	42 (32–46)	31 (28–47)	31 (24–37)
Sex				
Male	9 (56%)	4 (100%)	0 (0%)	2 (67%)
Female	7 (44%)	0 (0%)	3 (100%)	1 (33%)
Treatment duration (months)	35 (6–113)			
Clinical experience (years)		9 (4–22)	5 (1–11)	5 (2–8)
Employment status				
Full time	6 (37%)	4 (100%)	2 (67%)	3 (100%)
Part time	4 (25%)	0 (0%)	1 (33%)	0 (0%)
Sick leave	1 (6%)	0 (0%)	0 (0%)	0 (0%)
Home duties	2 (13%)	0 (0%)	0 (0%)	0 (0%)
Retired	3 (19%)	0 (0%)	0 (0%)	0 (0%)
Residence				
Metropolitan	6 (37%)	4 (100%)	3 (100%)	3 (100%)
Regional/rural	10 (63%)	0 (0%)	0 (0%)	0 (0%)
Interview duration (minutes)	61 (22–105)	32 (20–51)		

Data are *n* (%) or median (range).

https://doi.org/10.1017/S1478951513001260 Published online by Cambridge University Press

Table 2. *Representative quotes*

Themes	Subthemes	Quotes
Theme 1: Management of CML	○ Tolerating treatment	Tiredness of colossal, you know—I've got a young family and just sort of trying to keep up with the daily routine of that is not easy. [PT1]
	○ Seeking assistance	Normal GPs just don't really realize or know too much about it; it's not their field. That's why I don't really bother talking to them about it. [PT8] They should be complaining [be]cause that's the only way that we would hear their problems. [HP5: pharmacist]
	○ Complementary and alternative medicine (CAM)	The drops that [the naturopath] gave me to put under my tongue, they sort of seemed to work for me (. . .) there's nothing wrong with having a go. [PT2]
Theme 2: Perspectives promoting adherence	○ Disease awareness	My understanding of it, if I don't take the drug I risk the leukemia coming back. [PT15]
	○ Downward comparison	When I first heard I had leukemia, you know, you say to yourself why me, well you know. But there's a lot of people in the world worse off than me, and I think myself lucky. [PT3]
Theme 3: Adherence behaviors & strategies	○ Patient education	I often sort of talk about routine, you know, talking about the fact that it is with a main meal and which main meal is the most consistent throughout your day. [HP4: pharmacist]
	○ Triggers	How do I remember to take it, um, well they're on top of the (. . .) they're just sitting on top of my fridge, and it's just second nature to me now. [PT15]
	○ Clinical practice improvements	Someone like an outreach pharmacist or a nurse could just give them a courtesy phone call and just say okay, so how many tablets do you think you've missed? [HP4: pharmacist]
Theme 4: Risks for nonadherence	○ Complacency	I get into the car, due to take off and remember about that, and I say, "Ah, only one day"; don't worry about that. [PT12]
	○ Inconsistency following nonadherence	I said I missed one and they said "Yeah, don't worry about it too much, just try and take them as soon as you can." So I'm not too worried about missing one [PT10]
	○ Poor adherence detection methods	We may well not be picking up side effects as early as we might; you can never be a hundred percent sure. [HP8: pharmacist] I forgot to take the medicine with me. I'm a little bit worried, but I say no it's too late now and I don't want to tell the doctor, I don't want to upset the doctor. [PT12]
Theme 5: Reasons for unintentional nonadherence	○ Forgetfulness	If I join my friend for tea and I decide to sleep over, right, and then I forgot that night and the next morning. [PT12]
	○ Poor communication	That's a big issue if you've got patients who don't speak English because it all comes to a head if you've worked out what the problem is and you need to get the script and get the tablets into them and there's a delay. [HP9: doctor]
Theme 6: Reasons for intentional nonadherence	○ Reducing drug impact on life	I went off my pills for three days, and for the wedding the food was beautiful and the wine was lovely and everything tasted so good [be]cause everything tastes so rotten when you're on Glivec. [PT14]
	○ Access to medical advice	I actually stopped taking the drug for a few days, you know, [be]cause I thought, "Well, this is lowering my immunity this drug [be]cause I know that is one of the side effects." [PT13]

Seeking Assistance

HPs believed that patient education facilitated swift reporting of treatment issues, allowing timely resolution. Generally, patients reported issues to their treating hematologist within a few hours if deemed urgent. However, perceptions of urgency varied between patients.

https://doi.org/10.1017/S1478951513001260 Published online by Cambridge University Press

As one patient described, "I do feel guilty ringing [the doctor] direct when it might be something that I consider small like (. . .) when I'm fasting, how am I [going to] take my drug?" (PT7). Another patient preferred to ask a nurse for assistance: "Your treating physician tends to be quite a busy person, naturally, so a lot of those questions can be directed to the nurse" (PT14). One doctor (HP10) noted, "there are a lot of resources around, but just making [patients] aware" was the issue.

Complementary and Alternative Medicine (CAM)

Nine patients reported use of oral CAM. Most commonly, patients consumed multivitamins, fish oil supplements, or probiotics aimed at improving general health, while three patients used numerous naturopathic remedies to manage side effects. Patients were aware of the potential for drug interactions with imatinib, so they "always check[ed] first" (PT7) with their hematologist before using CAM.

Theme 2: Perspectives Promoting Adherence and Drug-Taking

Disease Awareness

One nurse (HP1) warned patients that CML could be "a devastating disease that can lead to your death," using fear of disease progression as motivation for adherence. This appeared to be quite effective; one patient revealed being "too scared not to be on it, so I really, you know, I don't want to miss it" (PT6). Evidence of good test results also often provided positive motivation to sustaining adherence: "I'd been doing so well, why wouldn't I stay on it?" (PT13). One doctor (HP6) agreed with that viewpoint: "Patients accept quite a few significant side effects as long as the treatment seem[s] to be working."

Downward Comparison

Despite the side effects experienced, patients with CML noted that patients with other cancers had more burdensome experiences, suggesting downward comparisons. Downward comparison is a form of psychosocial self-evaluation and coping mechanism where patients compare themselves positively to others in worse circumstances (Taylor & Lobel, 1989; Stanton et al., 1999): "There's a lot more people worse off than me so [I] don't complain too much" (PT16). Another patient was "happy knowing there's a pill [she] can pop" (PT7), noting that other potential treatments were associated with reduced efficacy or greater toxicity. Generally, HPs evaluated imatinib therapy to be low-intensity treatment: "It's fairly low maintenance really from the clinician's point of view; it's not like they're having chemotherapy that requires coming in on a regular basis" (HP3: doctor).

Theme 3: Adherence Behaviors and Strategies

Patient Education

HPs believed patient education was the main strategy to encourage adherence, because as one nurse (HP7) put it, "Self-care management is absolutely crucial to helping compliance." HPs focused on educating about crucial management strategies to deal with significant tolerance issues. It was noted that multiple modes of education delivery are essential: "All of that can just go over their head, so the importance of providing written information to further consolidate, that is really important" (HP7: nurse).

Triggers

Patients would leave the drug in a visible location to act as a prompt: "I generally have it on the table for meals so I don't forget" (PT16). HPs encouraged patients to ingest imatinib with food in order to integrate drug taking with a consistent aspect of daily routine, which additionally had the benefit of minimizing gastrointestinal side effects. Other prompts mentioned included alarms, reminders from family, pillboxes, medication diaries, and organizing dose schedules to coordinate use of multiple medications. Four patients stored extra tablets in various locations: "I keep a couple in my work drawer so I've always got it wherever I am, so it's pretty hard for me to miss" (PT8).

Patients had full control of their drug-taking regime. If they had difficulty taking the drug at a certain time of day, some tried to improve their adherence by changing the timing of their routine. One patient tried taking imatinib in the morning, but explained, "I wouldn't be able to function during the day; just makes me feel too sick, so I take it at night, take a sleeping tablet and try to miss all the side effects" (PT15). Some patients taking more than one tablet daily split their dose. This provided an additional opportunity for patients to take their tablets in case they had forgotten earlier, also reducing dose-dependent side effects.

Clinical Practice Improvements

HPs noted a lack of systematic support outside patient–doctor consultations. One nurse (HP1) conceded that "we try and set [patients] up as best we can, but it's still that very ad hoc fashion," while a pharmacist (HP4) acknowledged that her contact with patients was "only a few minutes at a time."

https://doi.org/10.1017/S1478951513001260 Published online by Cambridge University Press

One doctor (HP9) suggested the establishment of "a specialist nurse, dedicated to the treatment of the disease and who can set up and monitor compliance." Pharmacists proposed a pharmacy outreach program to provide dedicated patient followup outside consultation times. However, HPs noted the prohibitive cost of these suggestions.

Theme 4: Risks for Nonadherence

Complacency

Patients were less concerned about nonadherence when they observed no consequences: "After I forgot and when I come to do blood test it's still okay; it's still zero; that's why [it does] not concern me much" (PT12). One pharmacist (HP8) stated, "If these patients have had [CML] for a while they're less receptive; they don't want to hear [the advice] again." Consequently, patient education to reinforce adherence could become diminishingly effective.

Inconsistent Advice Following Nonadherence

One nurse (HP1) asserted she was "blunt with them, saying, 'Look, even if you're missing a day or two days, you know, it's really [important]; this is something that needs to be taken constantly.'" However, some patients reported being told that nonadherence events were not serious. One patient recounted, "I've missed a couple of nights and I've rang like the research nurse and she said, 'Look, don't stress. It's only one night'" (PT15).

Poor Adherence Detection Methods

HPs were generally unaware of any widespread adherence issues amongst their patients: "There's general acceptance of the need to be on it, so they don't complain much." (HP10: doctor). However, two patients with ongoing instances of nonadherence did not report them, making it difficult to monitor nonadherence. One doctor (HP6) admitted, "I wouldn't be aware of [nonadherence] because I've never asked them specifically; I just ask them a very general open-ended question."

In fact, HPs explained that they only began to suspect poor adherence following a suboptimal response to treatment: "Unless you can see in their blood levels [that], 'Hey something fishy's going on,' (. . .) you have to take their word for it" (HP2: nurse).

Theme 5: Reasons for Unintentional Nonadherence

Forgetfulness Resulting from Disruptive Routines

Seven patients reported forgetfulness as a cause of nonadherence, primarily due to interruptions in their daily routines. One noted, "I suppose it's all into routine like and that's where sometimes if I'm distracted I can forget" (PT14). One doctor described a young patient where "there'll be occasions where he'll have a late night or something like that; he might miss an odd dose" (HP10: doctor).

Poor Communication

One doctor (HP9) recounted issues in educating a non-English-speaking patient: "Some of it was lost in translation, so we thought she was taking one dose and she was taking a different dose." Another patient had a poor understanding of the mechanism of imatinib and believed the drug could be "stored" in the body: "I reckon there's enough in my system to miss out one day" (PT2).

Moreover, patients were hesitant about approaching community-based HPs regarding CML-related concerns: "Sometimes when you're talking to the GPs or even chemists, like you know more about CML than they do" (PT14). For example, one general practitioner prescribed antibiotics to a patient that were known to interact with imatinib.

Finally, there were communication issues between HPs. Miscommunication between pharmacists and doctors occasionally led to drug supply problems.

Theme 6: Reasons for Intentional Nonadherence

Reducing Drug Impact on Life

One patient skipped doses to avoid taste disturbances during her daughter's wedding: "The food was beautiful (. . .) everything tasted so good [be]cause everything tastes so rotten when you're on Glivec" (PT4). One doctor (HP3) conceded that patients with side effects may potentially "stop [imatinib] until they come for their review."

Six patients were open to reducing their dose of imatinib or ceasing treatment altogether if it led to relief from side effects: "I was told (. . .) this is my lifeline, [but] I wonder if there's ever a time that I can have a break" (PT1). Importantly, patients stated they would only stop imatinib under their doctor's instruction.

Access to Medical Advice

Several otherwise adherent patients revealed they had intentionally skipped doses when they were concerned about significant side effects, but were unable to get prompt management advice: "When I vomited, the information wasn't there; do I take another dose, don't I, will I overdose?" (PT7). Notably, with

https://doi.org/10.1017/S1478951513001260 Published online by Cambridge University Press

appropriate advice, these patients reported no further instances of nonadherence.

DISCUSSION

This study is the first to compare patients' and HPs' insights regarding adherence and ongoing management of imatinib therapy. Interviews revealed only 31% of patients reporting perfect adherence, a level comparable to the 14 and 41% (36 out of 87 patients) in the major Belgian and British studies, respectively (Noens et al., 2009; Marin et al., 2010). There is no adherence rate threshold shown to ensure treatment efficacy, so perfect adherence remains the optimal target (Abraham & MacDonald, 2012).

The reasons proffered for nonadherence were similar to prior reports regarding oral chemotherapy (Eliasson et al., 2011). Unintentional nonadherence most commonly arose from forgetfulness related to disruptions to normal drug-taking routines. Intentional nonadherence was generally related to avoidance of side effects and difficulty getting prompt medical advice. Higher symptom severity has been linked to intentional non-adherence (Efficace et al., 2013).

The risk of nonadherence increases as patients lose motivation to maintain treatment, especially with the absence of immediately recognized repercussions, or if they misinterpret reassurance from HPs regarding missed doses, hence undermining previous warnings about the implications of nonadherence (Eliasson et al., 2011). It has been noted that treatment persistence in the absence of disease symptoms requires ongoing commitment and communication between patient and HP (Horne, 2006).

HPs were not always aware of patients' nonadherence. Detection of nonadherence was usually based on patient self-report; however, two patients admitted that they did not report nonadherence. Currently, the only objective methods of identifying poor adherence are to monitor for disease relapse via blood assays or plasma drug levels (Baccarani et al., 2009). The risk of imatinib failure increases with duration of nonadherence, so it is arguable that poor adherence is an issue long before relapse occurs (Ibrahim et al., 2011). Monitoring plasma imatinib concentrations to detect adherence is another alternative, but there is considerable variation in drug levels attained at a given imatinib dose among individual patients (Peng et al., 2004; Cortes et al., 2009). Further, maintenance of adherence is a better predictor of treatment efficacy than monitoring treatment based on plasma levels (Yoshida et al., 2011).

It has been proposed that adherence can be improved by combining a number of component interventions targeting a combination of cognitive, behavioral, and affective elements as opposed to single targets (Roter et al., 1998). Changing health-related behaviors can be described as involving three elements: (1) patient education, (2) motivation to change behavior, and (3) teaching skills to achieve change (Fisher & Fisher, 1992). Patient education involves raising awareness of the importance of adherence among patients and family members (Osterberg & Blaschke, 2005). Motivation is generated by follow-up discussions, acting as opportunities to speak to poor adherers while encouraging good adherers to maintain their behavior (Ruddy et al., 2009). The third element can vary with each patient; in patients who have been adherent to imatinib therapy, establishing reminders and incorporating drug taking into daily routine are among the techniques used (Eliasson et al., 2011). These strategies may not suit the whole spectrum of patients, so it is imperative to expand upon this knowledge and develop interventions appropriate for all patients using imatinib, which are customized to each patient's needs yet clinically and economically feasible to operate.

HPs interviewed emphasized patient education to motivate adherence by alerting patients to the risks of poorly controlled disease. However, even adherent patients intentionally skipped doses if there were difficulties accessing timely assistance or were unwilling to seek help if they perceived the issue as unimportant. Patients used downward comparison to cope with treatment, but this also meant they were reluctant to complain. Patients require education about knowing when and how to seek help, but additionally, the assistance needs to be readily available (Osterberg & Blaschke, 2005; Regnier Denois et al., 2011).

Some patients relied solely on hematologists for self-management advice because they were unaware of other forms of follow-up support. Specialist clinic nurses and pharmacists are well placed to meet patients' needs and facilitate adherence (Winkeljohn, 2010; Grossman, 2011). The use of mobile technology is one such option; there is evidence that patients can effectively manage their side effects by communicating with clinicians via mobile telephones (Kearney et al., 2009). This has the advantage of shorter response times and thus reducing the risk of missed doses. It can theoretically offer better adherence by daily communication with patients. Furthermore, some patients reported that community HPs had poor awareness of drug interactions, but with good communication from specialists general practitioners can contribute to maintaining continuity of care, bridging the gap between the specialist cancer center and patients' local environment (Murchie et al., 2009). Increasing patient awareness of auxiliary support services can ensure that patients' needs are met while relieving the care burden on hematologists.

https://doi.org/10.1017/S1478951513001260 Published online by Cambridge University Press

Ideally, HPs should be proactive in raising treatment concerns. CAM supplements, used by nine of our patients, are important to discuss, since imatinib pharmacokinetics can be affected by numerous substances (Jabbour et al., 2012). Patients were open to discussing CAM, but historically, these discussions are often impeded by numerous barriers during consultations (Schofield et al., 2003; Richardson et al., 2004; Monti & Yang, 2005; Broom & Adams, 2009). Guidelines on effectively discussing CAM use in consultations are available (Schofield et al., 2010).

Our qualitative study focused on defining the context for, as opposed to the frequency of, nonadherence and did not measure nonadherence objectively. Measuring the true adherence rate among patients could establish a set of feasible targets for intervention. This study should be repeated in nonspecialist hospital and community practice settings to analyze standards across healthcare settings regarding oral chemotherapy.

CONCLUSIONS

Patient education practices must be integrated with mechanisms to ensure that patients can receive support promptly, while improvements in patient followup are needed to reinforce education and motivate adherence. Detection currently relies on patient self-report, which is dependent on patients' ability to accurately recollect and willingness to disclose nonadherence. Improving patient–provider communication can reduce this issue to an extent, but there need to be systems that can objectively identify nonadherence early enough to minimize the risk of treatment failure.

These findings can inform the development of interventions to improve patient–HP communication and facilitate early detection of nonadherence. With the emergence of more oral chemotherapies, it is critical that we be able to accurately monitor adherence and that HPs and patients discuss key issues affecting adherence, leading to a shared commitment toward sustained disease control.

ACKNOWLEDGMENTS

The authors would like to thank the patients and health professionals at the Peter MacCallum Cancer Center for volunteering their time to make this study possible.

ETHICS APPROVAL

This study received institutional approval from the Peter MacCallum Ethics Committee.

FUNDING AND DISCLOSURES

This work was supported by a Peter MacCallum Cancer Foundation Grant. PS was supported by National Health and Medical Research Council Career Development Award ID 628563. JS has received honoraria as a member of the Novartis Advisory Board.

REFERENCES

Abraham, I. & MacDonald, K. (2012). Why are patients with chronic myeloid leukaemia (non-)adherent? *British Journal of Cancer*, *107*(6), 901–903.

Baccarani, M., Cortes, J., Pane, F., et al. (2009). Chronic myeloid leukemia: An update of concepts and management recommendations of European LeukemiaNet. *Journal of Clinical Oncology*, *27*(35), 6041–6051.

Broom, A. & Adams, J. (2009). Oncology clinicians' accounts of discussing complementary and alternative medicine with their patients. *Health (London)*, *13*(3), 317–336.

Bryman, A. & Burgess, R.G. (1994). *Analyzing qualitative data*. London: Routledge.

Cortes, J.E., Egorin, M.J., Guilhot, F., et al. (2009). Pharmacokinetic/pharmacodynamic correlation and blood-level testing in imatinib therapy for chronic myeloid leukemia. *Leukemia*, *23*(9), 1537–1544.

Druker, B.J., Guilhot, F., O'Brien, S.G., et al. (2006). Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia. *The New England Journal of Medicine*, *355*(23), 2408–2417.

Efficace, F., Baccarani, M., Rosti, G., et al. (2012). Investigating factors associated with adherence behaviour in patients with chronic myeloid leukemia: An observational patient-centered outcome study. *British Journal of Cancer*, *107*(6), 904–909.

Efficace, F., Rosti, G., Cottone, F., et al. (2013). Profiling chronic myeloid leukemia patients reporting intentional and unintentional non-adherence to lifelong therapy with tyrosine kinase inhibitors. *Leukemia Research* [Epub ahead of print]. http://dx.doi.org/10.1016/j.leukres.2013.07.003.

Eliasson, L., Clifford, S., Barber, N., et al. (2011). Exploring chronic myeloid leukemia patients' reasons for not adhering to the oral anticancer drug imatinib as prescribed. *Leukemia Research*, *35*(5), 626–630.

Fisher, J.D. & Fisher, W.A. (1992). Changing AIDS-risk behavior. *Psychological Bulletin*, *111*(3), 455–474.

Grossman, S. (2011). Management of type 2 diabetes mellitus in the elderly: Role of the pharmacist in a multidisciplinary health care team. *Journal of Multidisciplinary Healthcare*, *4*, 149–154.

Guilhot, F., Coombs, J., Zernovak, O., et al. (2010). A global retrospective and physician-based analysis of adherence to tyrosine kinase inhibitor (TKI) therapies for chronic myeloid leukemia (CML). *ASH Annual Meeting Abstracts*, *116*(21), 1514.

Hartigan, K. (2003). Patient education: The cornerstone of successful oral chemotherapy treatment. *Clinical Journal of Oncology Nursing*, *7*(6 Suppl.), 21–24.

Haynes, R.B., Ackloo, E., Sahota, N., et al. (2008). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews*, Apr. *16*(2), CD000011.

Hehlmann, R., Hochhaus, A. & Baccarani, M. (2007). Chronic myeloid leukaemia. *The Lancet*, *370*(9584), 342–350.

Horne, R. (2006). Compliance, adherence, and concordance: Implications for asthma treatment. *Chest*, *130*(1 Suppl.), 65S–S72.

Ibrahim, A.R., Eliasson, L., Apperley, J.F., et al. (2011). Poor adherence is the main reason for loss of CCyR and imatinib failure for chronic myeloid leukemia patients on long-term therapy. *Blood*, *117*(14), 3733–3736.

Jabbour, E., Cortes, J.E., Ghanem, H., et al. (2008). Targeted therapy in chronic myeloid leukemia. *Expert Review of Anticancer Therapy*, *8*(1), 99–110.

Jabbour, E., Saglio, G., Radich, J., et al. (2012). Adherence to BCR–ABL inhibitors: Issues for CML therapy. *Clinical Lymphoma, Myeloma & Leukemia*, *12*(4), 223–229.

Kantarjian, H.M., Talpaz, M., O'Brien, S., et al. (2006). Survival benefit with imatinib mesylate versus interferon-alpha-based regimens in newly diagnosed chronic-phase chronic myelogenous leukemia. *Blood*, *108*(6), 1835–1840.

Kearney, N., McCann, L., Norrie, J., et al. (2009). Evaluation of a mobile phone-based, advanced symptom management system (ASyMS) in the management of chemotherapy-related toxicity. *Supportive Care in Cancer*, *17*(4), 437–444.

Marin, D., Bazeos, A., Mahon, F.X., et al. (2010). Adherence is the critical factor for achieving molecular responses in patients with chronic myeloid leukemia who achieve complete cytogenetic responses on imatinib. *Journal of Clinical Oncology*, *28*(14), 2381–2388.

Monti, D.A. & Yang, J. (2005). Complementary medicine in chronic cancer care. *Seminars in Oncology*, *32*(2), 225–231.

Murchie, P., Delaney, E.K., Campbell, N.C., et al. (2009). GP-led melanoma follow-up: The practical experience of GPs. *Family Practice*, *26*(4), 317–324.

Noens, L., van Lierde, M.A., De Bock, R., et al. (2009). Prevalence, determinants, and outcomes of nonadherence to imatinib therapy in patients with chronic myeloid leukemia: The ADAGIO study. *Blood*, *113*(22), 5401–5411.

Osterberg, L. & Blaschke, T. (2005). Adherence to medication. *The New England Journal of Medicine*, *353*(5), 487–497.

Peng, B., Hayes, M., Resta, D., et al. (2004). Pharmacokinetics and pharmacodynamics of imatinib in a phase I trial with chronic myeloid leukemia patients. *Journal of Clinical Oncology*, *22*(5), 935–942.

Regnier, Denois V., Poirson, J., Nourissat, A., et al. (2011). Adherence with oral chemotherapy: Results from a qualitative study of the behaviour and representations of patients and oncologists. *European Journal of Cancer Care*, *20*, 520–527.

Richardson, M.A., Masse, L.C., Nanny, K., et al. (2004). Discrepant views of oncologists and cancer patients on complementary/alternative medicine. *Supportive Care in Cancer*, *12*(11), 797–804.

Roter, D.L., Hall, J.A., Merisca, R., et al. (1998). Effectiveness of interventions to improve patient compliance: A meta-analysis. *Medical Care*, *36*(8), 1138–1161.

Ruddy, K., Mayer, E. & Partridge, A. (2009). Patient adherence and persistence with oral anticancer treatment. *CA: A Cancer Journal for Clinicians*, *59*(1), 56–66.

Sabate, E. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: World Health Organization.

Schofield, P.E., Juraskova, I. & Butow, P.N. (2003). How oncologists discuss complementary therapy use with their patients: An audio-tape audit. *Supportive Care in Cancer*, *11*(6), 348–355.

Schofield, P., Diggens, J., Charleson, C., et al. (2010). Effectively discussing complementary and alternative medicine in a conventional oncology setting: Communication recommendations for clinicians. *Patient Education and Counseling*, *79*(2), 143–151.

Smith, J.A., Flowers, P. & Larkin, M. (2009). *Interpretive phenomenological analysis: Theory method and research*. London: Sage.

Stanton, A.L., Danoff-Burg, S., Cameron, C.L., et al. (1999). Social comparison and adjustment to breast cancer: An experimental examination of upward affiliation and downward evaluation. *Health Psychology*, *18*(2), 151–158.

Stone, R.M. (2004). Optimizing treatment of chronic myeloid leukemia: A rational approach. *The Oncologist*, *9*(3), 259–270.

Taylor, S.E. & Lobel, M. (1989). Social comparison activity under threat: Downward evaluation and upward contacts. *Psychological Review*, *96*(4), 569–575.

Williams, A.B. (2001). Adherence to HIV regimens: 10 vital lessons. *The American Journal of Nursing*, *101*(6), 37–43.

Winkeljohn, D. (2010). Adherence to oral cancer therapies: Nursing interventions. *Clinical Journal of Oncology Nursing*, *14*(4), 461–466.

Yoshida, C., Komeno, T., Hori, M., et al. (2011). Adherence to the standard dose of imatinib, rather than dose adjustment based on its plasma concentration, is critical to achieve a deep molecular response in patients with chronic myeloid leukemia. *International Journal of Hematology*, *93*(5), 618–623.