

The association between patient satisfaction with information and adherence to oral anticancer agents

J Oncol Pharm Practice
2023, Vol. 29(3) 637–645
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/10781552221077258
journals.sagepub.com/home/opp



Eward J Melis¹ , Jeannette EF Zwart-van Rijkom¹, Toine CG Egberts^{1,2}, Bart JF van den Bemt^{3,4,5}, Petronella O Witteveen⁶ and Helga Gardarsdottir^{1,2}

Abstract

Introduction: Adherence to anticancer agents is a critical factor in achieving adequate clinical response, and became a major challenge for patients and caregivers since the increased substitution of parenteral cytostatic by oral drugs. One of the factors that influences adherence is how well informed patients are about their therapy. This study assesses the association between patient satisfaction with information about oral anticancer agents and adherence.

Materials and Methods: This study was conducted among patients (≥ 18 years) who began oral anticancer therapy. Patients satisfaction with information and adherence were assessed using validated questionnaires. Adherence was also assessed using refill data. Logistic regression was applied to assess the association between overall patient satisfaction with information and both self-reported adherence and adherence based on an MPR value of above 80%.

Results: In total, 124 patients were included in the study. The median (IQR) satisfaction with information was 15.0(4) on a scale of 0–17. Eighty-two percent of participants reported adherence, while the refill data demonstrated that 64.5% of patients had an adherence rate of 80% or higher. Overall satisfaction with information was not significantly associated with self-reported adherence (OR adj 0.98 [95% CI 0.85–1.15]) or refill-based adherence (OR adj 1.11 [95% CI 0.99–1.24]).

Conclusion: The findings indicate no significant relationship between patient satisfaction with information and adherence. The population was highly satisfied with information about the oral anticancer agents, which indicates a high level of satisfaction with usual care. However, the refill data reveals that 35.5% of patients were not adherent.

Keywords

Oral anticancer agent, oral anticancer therapy, cancer, adherence, satisfaction with information

Date received: 12 January 2021; revised: 10 January 2022; accepted: 13 January 2022

Introduction

Patients receiving anticancer therapy are traditionally treated in hospitals, where they receive intravenously administered anticancer drugs. However, over the past decades oral anticancer drugs have become available and increasingly substitute parenteral use.^{1,2} Whereas parenteral anti-cancer agents are usually administered by healthcare professionals in a specialized care setting, OAA users themselves are responsible for drug intake and adherence is not self-evident. Although home administration of OAAs has been well received by patients,^{3–5} it has also resulted in new challenges for health care professionals with regards to treatment adherence. A systematic review shows that non-adherence to OAA almost always leads to poorer

¹Department of Clinical Pharmacy, University Medical Center Utrecht, Utrecht, The Netherlands

²Division of Pharmaco-epidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands

³Department of Pharmacy, Sint Maartenskliniek, Nijmegen, The Netherlands

⁴Department of Pharmacy, Radboud University Medical Centre, Nijmegen, The Netherlands

⁵Department of Clinical Pharmacy and Toxicology, Maastricht University Medical Centre, Maastricht, The Netherlands

⁶Department of Medical Oncology, University Medical Center Utrecht, Utrecht, The Netherlands

Corresponding author:

Helga Gardarsdottir, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Universiteitsweg 99, 3584 CG Utrecht, The Netherlands.

Email: H.Gardarsdottir@uu.nl

health outcomes.⁶ For example studies on adherence in patients with chronic myeloid leukemia (CML) have identified adherence to imatinib as the critical factor to reach adequate response.⁷ Poor adherence to ibrutinib among patients with non-Hodgkin lymphoma of chronic lymphocytic leukemia is also associated with significantly worse rates of progression-free survival and overall survival.⁸ Poor adherence to endocrine therapy among women with breast cancer has similarly been associated with an increased risk of death.⁹ Moreover, from a pharmaco-economic perspective, adherence and effective use is particularly important given the high costs of the new OAs.¹⁰

Adherence to OAs has been reported to generally vary between 23 and 100%.^{11–13} Many factors can influence adherence to medication, such as the number of medications used, type of disease, beliefs about medicine, side effects of the treatment and how well informed patients are about their therapy.^{12,14,15} An important indicator of the quality of provided information about medication is the extent to which a patient is satisfied with the information. Assessing patient satisfaction with information can be accomplished through the use of validated questionnaires, such as the Satisfaction with Information about Medication Scale (SIMS).¹⁶

There are several existing studies addressing the relationship between patient satisfaction with information and adherence to OAA. However, the results to date are not unambiguous and are difficult to compare due to the differing methodologies used to measure satisfaction with information and adherence. According to existing findings, patients receiving oral anticancer therapy for different cancer types,¹⁷ CML patients using imatinib¹⁸ and capecitabine users¹⁹ who were more satisfied about the information they received about their medication reported better adherence than those who were unsatisfied with the information. However, a multicenter study including cancer patients using different OAs did not find a relation between satisfaction with information and adherence.¹² In addition, CML patients using nilotinib who are more satisfied with information do not report better adherence.²⁰

The aim of this study is to assess the association between patient satisfaction with information and adherence to OAA in patients treated in a large Dutch university hospital.

Materials and methods

Setting, design and study population

This retrospective study was conducted in the outpatient pharmacy of the University Medical Center Utrecht (UMCU), a large university hospital in the Netherlands with 1042 beds.²¹ Patients were eligible for inclusion if they were ≥ 18 years and started oral anticancer treatment

between May 2015 and September 2016. All patients were treated by a medical oncologist or hematologist at the UMCU and received the prescribed OAA from the UMCU outpatient pharmacy. These OAs can only be dispensed from the outpatient pharmacy of the hospital due to special governmental regulation.^{22,23} In the UMCU, physicians, physician assistants, pharmacists and pharmacy technicians provide information about the medication.

The information about medication use was derived from the UMCU outpatient pharmacy electronic information system, and the information about cancer diagnoses, treatment history and other co-morbidities was derived from the electronic hospital medical information system. Data was only collected on the use of OAA, not taking into account other medications that patients may have used. Medication was coded using the Anatomical Therapeutic Chemical (ATC) class system.²⁴ An OAA is defined as an oncolytic medicine for oral ingestion (see Appendix 1), including antineoplastic agents (ATC code L01, e.g. capecitabine and imatinib), enzalutamide (ATC L02BB04) and other immunosuppressants (ATC L04AX, e.g. lenalidomide).

A patient was defined as a starter if an OAA had not been dispensed to that patient during the 12 months prior to inclusion. Before inviting patients, the electronic hospital medical information system was consulted for information concerning whether the patient was terminal or had died; in such cases, patients were not invited for participation. Patients who were treated with the OAA for other non-cancer diseases were also excluded.

Eligible patients received a letter with information about the study, an informed consent form and a questionnaire about personal characteristics such as level of education. In addition, they received the (SIMS) and the Medication Adherence Rating Scale (MARS). When patients did not respond within four weeks, they received a reminder by mail. The time between start of treatment and receiving the questionnaires varied and was included in the analysis as a covariate.

Outcome measures

The primary outcome in this study was adherence to the OAs. Adherence was measured using two methods: self-reporting and pharmacy refill data. Self-reported adherence was assessed using the (MARS).²⁵ The MARS score ranged between 5 and 25. Patients were considered to be adherent if they never engaged in any form of non-adherent behavior (MARS score of 25). Refill-base adherence was calculated using the medication possession ratio (MPR) during the six months following treatment initiation.^{26,27} The MPR is the number of days for which medication was dispensed in a particular period, divided by the total number of days in

the period. The denominator was fixed at 182 days. The numerator for OAAs intended for continuous use was calculated as the number of days of dispensed medication. The numerator for OAAs intended for cyclical use was calculated as the number of days of dispensed medication plus the number of prescribed resting days. The duration of the last dispensing was cut off if it exceeded the study end date at six months. If a patient used a combination of different OAAs, the MPR was calculated for the agent with the highest number of medication days (see Appendix 2 for the different dosing regimens in this study). The MPR was assessed in two ways: by using the continuous MPR value in % as well as a dichotomous value (adherent vs. non-adherent). The dichotomous definition defined those with MPR values of 80% or higher as adherent.

Satisfaction with information

The SIMS questionnaire was used to assess patient satisfaction with the information provided about various aspects of the prescribed OAA.^{16,28} The SIMS questionnaire contains 17 questions (see Appendix 3). The answers “about right” and “not needed” received a score of 1 point (satisfied) and “too much,” “too little” and “not received” received a score of 0 points (dissatisfied). Summing all questionnaire items resulted in an overall satisfaction score (ranging from 0 to 17). A higher value indicates a higher level of satisfaction with the received information about the OAA.

Two items were added to the standard SIMS questionnaire: 1) “Each question requested specification of who had provided the (physicians, physician assistants or pharmacists/pharmacy technicians)” and 2) “Did you receive information about the optimal intake moment for your medicines?” This question was added because practice has demonstrated that patients often have doubts about the correct intake time; this question was not included in the calculation of overall satisfaction.

The number of information providers per question ranged from 0 to 3. These scores were summed for each patient, resulting in the variable “Score number information providers” (ranging from 0 to 51). For example, a patient who reported for 10 questions that he had received information from the physician and for seven questions from the physician and pharmacists would have a score of $10 \cdot 1 + 7 \cdot 2 = 24$.

Covariates

The covariates included in the analysis were age, gender, level of education (high, middle/low), tumor type (solid tumor, hematological malignancy), treatment (primary/recurrent), first-time use of any oral anticancer agent (yes/no), previously treated with intravenous anticancer therapy (yes/no), time on treatment at the moment of filling in

SIMS and MARS (months), monotherapy/combotherapy, dosing regimen on index date (continuous/cyclic/both) and number of information providers (0-13/14-17/18-24/25-51). The level of education was categorized into middle/low (secondary school/primary school/none) and high (college/university). Type of cancer was defined as solid tumor when the medication was prescribed by a medical oncologist and as hematological malignancy when the medication was prescribed by a hematologist. The time on treatment upon completion of the SIMS and MARS was defined as the time (number of months) between starting the therapy and filling in the questionnaires.

Data analysis

One researcher (J.G.) processed the questionnaires and a second researcher (S.T.) checked the processed data. Descriptive analysis was performed using proportions and medians with interquartile range (IQR). Logistic regression

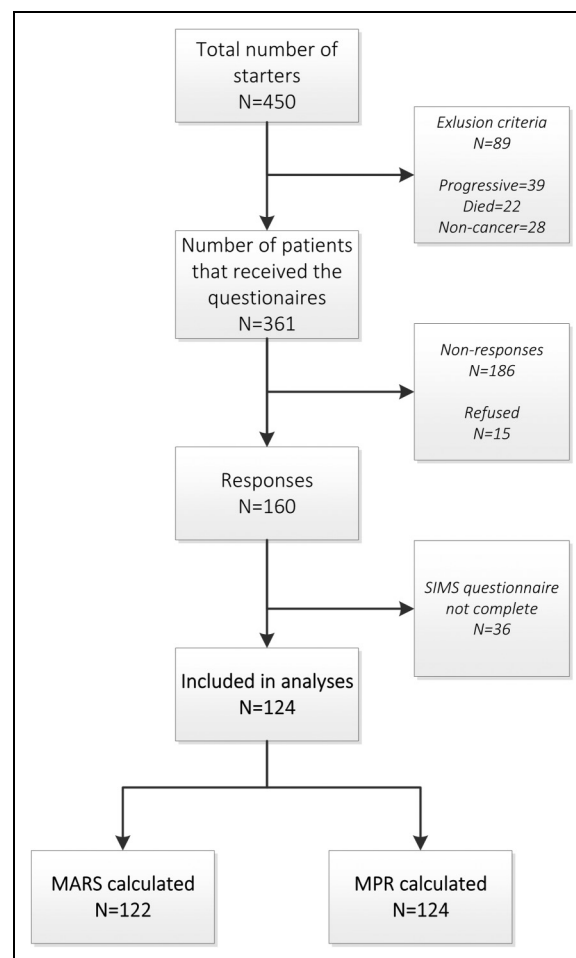


Figure 1. Flowchart of inclusion of patients initiating OAAs between May 2015 and September 2016.

was applied to assess the association between overall patient satisfaction with information and self-reported adherence and adherence based on an MPR value above 80%, resulting in odds ratios (OR) with 95% confidence intervals (CI). All covariates were tested in univariate logistic regression analyses. Covariates with a p-value below 0.2 in the univariate analyses were included in a multivariate logistic regression analysis.

The association between overall satisfaction and adherence defined by MPR value was assessed using linear regression analyses. All covariates were tested in the linear regression model and those with p-values below 0.2 were included in a multivariate linear regression analysis.

For each SIMS question, the association between satisfaction and adherence was assessed using logistic regression. This analysis was performed for self-reported adherence as well as refill-based adherence. Adjustments were made for multiple testing using the Bonferroni method. The result was only significant at a p-value of $0.05 / 36 = 0.001$. All analyses were performed using SPSS® Statistics version 21. The calculation of the MPR was performed using SAS® 9.4.

Ethics

The Medical Ethics Review Committee (METC) of the University Medical Centre Utrecht concluded that the Medical Research Involving Human Subjects Act (WMO) does not apply to this study; therefore, an official approval of this study by the METC was not required under the WMO (Ref 16/085C).

Results

Population

In total, 450 patients began OAA treatment during the study period. Eighty-nine patients did not meet the inclusion criteria (very progressive cancer $n = 39$, died $n = 22$ or non-cancer disease $n = 28$) and were therefore excluded, resulting in 361 eligible patients. Of the 361 eligible patients who were invited to participate, 36% ($n = 160$) responded. Of these, 36 patients were excluded because they did not complete the SIMS questionnaire. Of the remaining 124 patients, the MPR could be assessed for all patients; 122 (98%) filled in the MARS questionnaire (see Figure 1).

The mean (SD) age of the population was 60.7 (± 13.2) years, and 37.9% of the population was female (Table 1). Three-fourths of the patients were treated for a solid tumor and 39.5% of the patients were undergoing cancer treatment for the first time. Most patients (80.6%) were initiating an OAA for the first time. The median number of days for which OAA were dispensed was 156.

Satisfaction with information about OAA

The median overall satisfaction (IQR) score for the sample was 15.0(4) on a scale of 0–17. Patients with a higher score on the number of information providers were significantly more satisfied with the information they received; the median overall satisfaction scores for the four categories (0–13/14–17/18–24/25–51) were 14.0(7), 15.0(5), 15.0(3) and 17.0(2), respectively. Patients with a high level of education exhibited significantly lower SIMS scores than patients with a low/middle level of education, with a median of 15.0(5) compared to 16.0(3).

Table 1. Patient characteristics on index date.

| Characteristics | Number of patients (n = 124)(%) |
|---|------------------------------------|
| Age, mean (SD) years | 60.7 (± 13.2) |
| Gender | |
| Female | 47 (37.9%) |
| Male | 77 (62.1%) |
| Level of education | |
| High | 56 (45.2%) |
| Middle/low | 60 (48.4%) |
| Missing | 8 (6.4%) |
| Disease characteristics | |
| Tumor type | |
| Solid tumor | 94 (75.8%) |
| Hematological malignancy | 30 (24.2%) |
| Treatment | |
| Primary | 49 (39.5%) |
| Recurrent | 75 (60.5%) |
| Treatment characteristics | |
| First time use of oral anticancer agent | |
| Yes | 100 (80.6%) |
| No | 24 (19.4%) |
| Previously treated with intravenous anticancer therapy | |
| Yes | 36 (29.0%) |
| No | 88 (71.0%) |
| Time on treatment at filling in SIMS and MARS, mean (SD) months | 2.2 (2.3) |
| Monotherapy | 110 (88.7%) |
| Cytostatics | 77 (70.0%) |
| Targeted therapy | 33 (30.0%) |
| Combination therapy | 14 (11.3%) |
| Dosing regimen | |
| Continuous | 45 (36.3%) |
| Cyclic | 76 (61.3%) |
| Both | 3 (2.4%) |
| Information about treatment provided | |
| Score number of information providers | |
| 0–13 | 32 (25.8%) |
| 14–17 | 34 (27.4%) |
| 18–24 | 29 (23.4%) |
| 25–51 | 29 (23.4%) |

Adherence to oral anticancer drugs

Eighty-two percent of the patients reported that they were adherent to therapy. Meanwhile, the pharmacy dispensing records revealed a median MPR value of 86.1%, with 64.5% of patients having a MPR of 80% or higher. The MPR as a continuous variable demonstrated a left-skewed distribution.

Association between overall satisfaction with information about OAA and adherence

Overall satisfaction (median) did not differ between adherent patients and non-adherent patients (as determined by self-reporting and refill data). Figure 2(a) and (b) depict this comparison. The relation between overall satisfaction with information and adherence based on pharmacy dispensing data is depicted in Figure 2(c); this relationship is not significant.

As outlined in Table 2, overall patient satisfaction with information is not significantly associated with self-reported adherence (OR adj 0.98 [95% CI 0.85–1.15]). “Score number information providers per question” is the only covariate with a p-value below 0.2 and was included in the multivariate logistic model along with “Gender” and “Age.” Furthermore, no significant association was found between overall patient satisfaction with information and adherence based on dispensing data (MPR>80%; OR adj 1.11 [95% CI 0.99–1.24]). The covariates with a p-value below 0.2 are “Tumor type,” “Time on treatment at filling in SIMS and MARS” and “Monotherapy/Combination therapy.” These variables were included in the multivariate analysis along with “Gender” and “Age.” A higher age is significantly associated with lower adherence (OR 0.96 [95% CI 0.93–0.99]).

The association between satisfaction and adherence, measured through MPR as a continuous variable, was assessed with a linear regression model. The covariates “Gender,” “Age,” “Monotherapy/combination therapy” and “Dosing Regimen” resulted in a p-value below 0.2 and were included in the multivariate linear regression model. In this model, the overall satisfaction is not significantly associated with adherence (B 1.05 [95% CI = -0.51–2.61]).

Association between satisfaction and adherence per SIMS question

Adherence according to self-report or based on prescription data (MPR>80%) for each SIMS question is shown in Figure 3. When adjusting for multiple testing, no significant effect is found for any question.

Discussion

This study assessed the association between patient satisfaction with information and adherence to OAAs. No significant relationship was found between satisfaction with information and adherence. In general, the study population was highly satisfied with the received information. The median satisfaction score was 15.0 on a scale of 1–17. This finding suggests a high level of satisfaction with the usual care. As a result, it is difficult to find a significant effect of satisfaction with information on adherence.

The level of self-reported adherence in the study was 82%. Patients were considered to be adherent if they reported not to engage in any type of non-adherent. Even with this strict standard, the reported adherence was high, which resulted in little contrast in the data. Moreover, previous literature has reported that the MARS questionnaire over-reports adherence, including in the oncological domain.²⁹

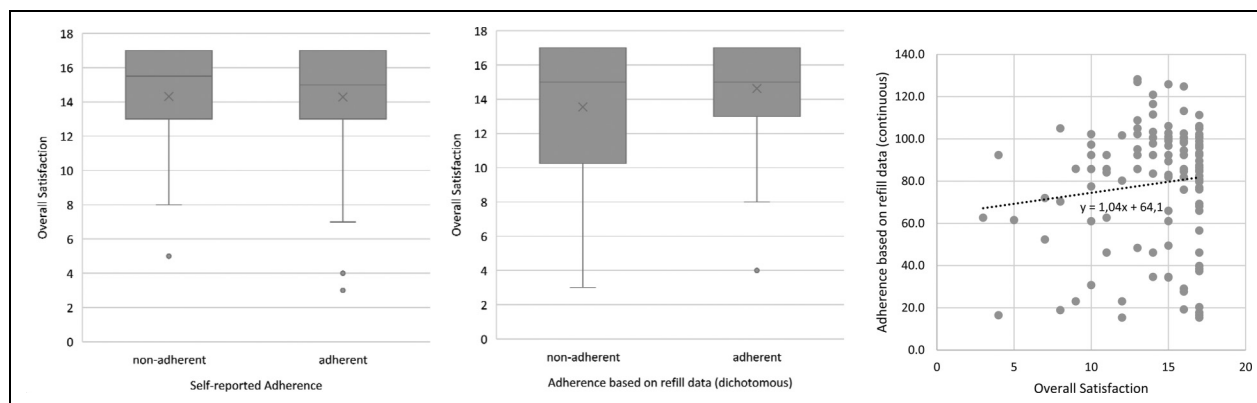


Figure 2. (a) boxplot of self-reported adherence vs. overall satisfaction with information (median values). (b) Boxplot of adherence based on refill data (dichotomous) vs. overall satisfaction with information (median values). (c) Scatterplot of overall satisfaction with information vs. adherence based on refill data (continuous).

Table 2. Association between overall satisfaction and adherence to OAA.

| | Self-reported adherence (MARS = 25) | | | | Adherence based on refill data (MPR >80%) | | | |
|--|-------------------------------------|------------|------|-----------|---|------------|------|------------|
| | OR | | Adj. | | OR | | Adj. | |
| | OR | 95% CI | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Overall satisfaction | 1.00 | 0.86–1.15 | 0.98 | 0.85–1.15 | 1.11 | 0.99–1.24 | 1.09 | 0.96–1.23 |
| Female | 1.03 | 0.39–2.68 | 0.90 | 0.34–2.41 | 1.11 | 0.52–2.37 | 1.06 | 0.46–2.43 |
| Age | 0.98 | 0.95–1.02 | 0.99 | 0.95–1.02 | 0.96 | 0.93–0.99* | 0.97 | 0.94–1.00 |
| <i>Level of education</i> | | | | | | | | |
| High | 1.00 | | | | 1.00 | | | |
| Missing | 0.43 | 0.07–2.58 | | | 1.67 | 0.31–9.04 | | |
| Middle/Low | 0.68 | 0.26–1.82 | | | 0.96 | 0.45–2.05 | | |
| Hematological malignity | 1.13 | 0.38–3.39 | | | 0.54 | 0.23–1.24 | 0.57 | 0.22–1.43 |
| Recurrent treatment | 0.82 | 0.32–2.14 | | | 1.27 | 0.60–2.68 | | |
| Previously treated with oral anticancer agent | 1.13 | 0.34–3.70 | | | 1.12 | 0.44–2.89 | | |
| Previously treated with intravenous anticancer therapy | 1.93 | 0.60–6.18 | | | 0.69 | 0.31–1.53 | | |
| Time on treatment at filling in SIMS and MARS | 0.92 | 0.76–1.12 | | | 1.18 | 0.98–1.43 | 1.21 | 1.00–1.48 |
| Combination therapy | 3.14 | 0.39–25.35 | | | 3.71 | 0.79–17.38 | 3.62 | 0.73–18.00 |
| <i>Dosing regimen</i> | | | | | | | | |
| Continuous | 1.00 | | | | 1.00 | | | |
| Cyclic | 1.28 | 0.50–3.31 | | | 1.1 | 0.51–2.37 | | |
| Both | nb | | | | nb | | | |
| <i>Score number of information providers</i> | | | | | | | | |
| 0–13 | 1.00 | | | | 1.00 | | | |
| 14–17 | 1.95 | 0.56–6.77 | 1.81 | 0.51–6.47 | 0.83 | 0.30–2.33 | | |
| 18–24 | 3.01 | 0.71–12.73 | 2.89 | 0.66– | 1.01 | 0.34–2.99 | | |
| | | | | 12.62 | | | | |
| 25–51 | 1.33 | 0.40–4.45 | 1.17 | 0.31–4.51 | 0.56 | 0.20–1.59 | | |

The mean adherence level in the study based on refill data was 78.9%. Patients with an adherence level based on refill data of less than 80% were considered to be non-adherent. According to this definition, a considerable number of patients (35.5%) were non-adherent. This proportion is comparable to other studies among oncologic patients.¹¹ These findings confirm that adherence to OAAs is an issue of concern. More research is needed to identify strategies to improve adherence to OAAs.

It is difficult to find a clear relationship between patient satisfaction with information and adherence to OAAs with the chosen measurement methods. There are previous studies that have found a positive correlation and others that have found no correlation. For example, a large multicenter study among CML patients using imatinib (n = 413) found that patients who desire more information are significantly more likely to be non-adherent.¹⁸ A single-center study of adherence among users of capecitabine (n = 113) similarly found that patients with a higher overall level of satisfaction with information adhered more often to their OAAs than patients with lower levels of satisfaction.¹⁹ However, in contrast, a multicenter study (N = 68) of satisfaction with information on adherence to nilotinib among

CML patients found that adherent and non-adherent patients did not differ in terms of satisfaction with information.²⁰ An additional study (n = 216) conducted in four university hospitals the Netherlands assessed factors that influence adherence to OAA and did not find an association between satisfaction and adherence.¹² The researchers in this study specifically measured satisfaction with information using the SIMS questionnaire and assessed adherence dichotomously using a pill-count method. The sample population in the study used a wide range of OAAs, for both solid tumors and hematologic malignities. Thus, a possible explanation for the findings is the heterogeneity of the sample population. The existing literature indicates that, in addition to providing information, many other factors influence adherence, such as socio-demographic factors, the dosing regimen, beliefs about medication and comorbidities.^{12,30–32} The more heterogeneous the study population, the more varied is the effect of such other factors on adherence. In studies with a relatively homogenous population (e.g. only capecitabine or imatinib users), a relationship between satisfaction with information and adherence can be established, while that was not the case in the aforementioned study among users of different OAAs.

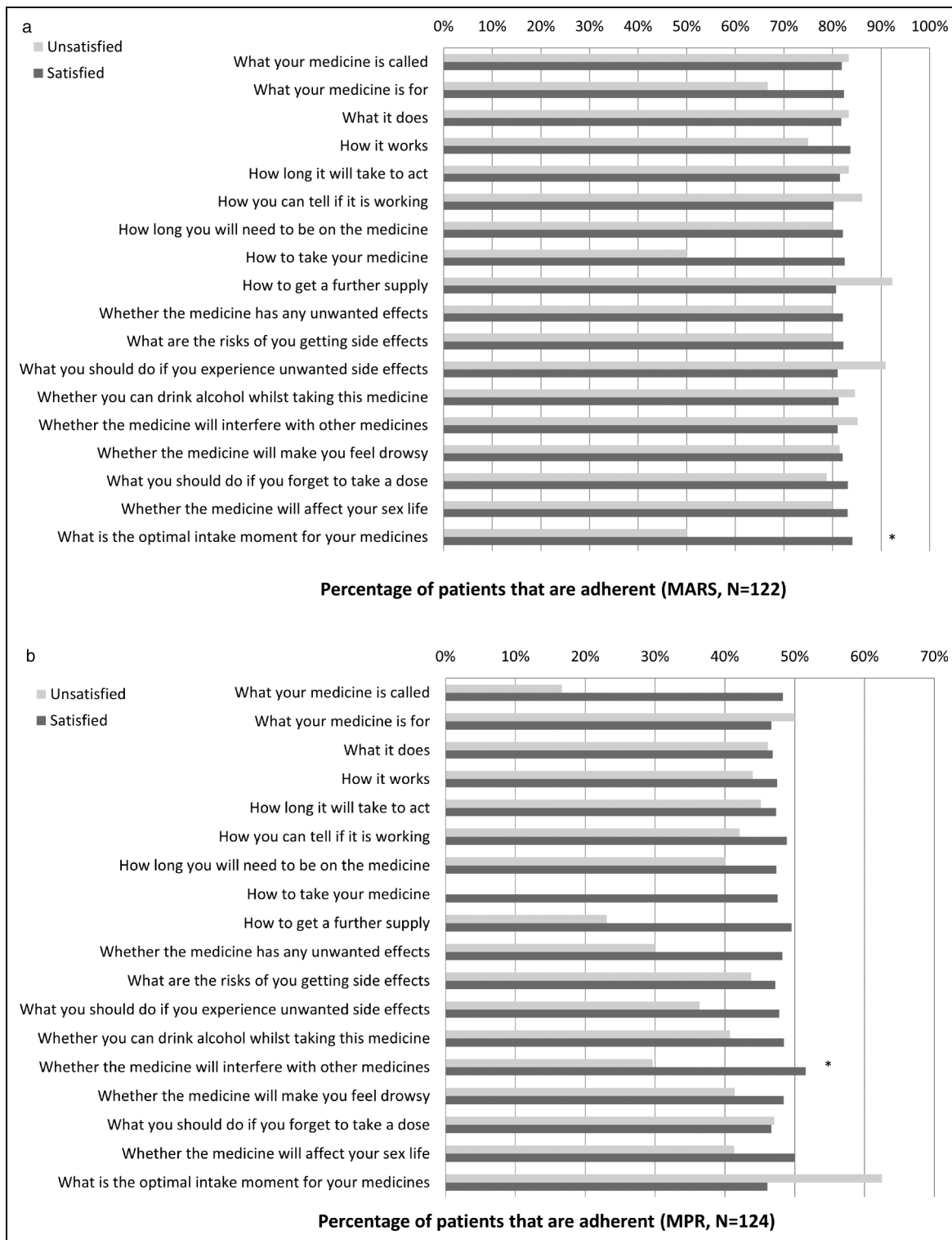


Figure 3. Patients adherence to OAA, satisfied versus unsatisfied patients. (a) By means of self-report based. (b) On the basis of refill data.

The sample population in the present study consists of users of a wide range of different OAAs, with many different oncologic and hematologic indications. However, this context closely resembles daily clinical practice. In addition, the patients received information from many different health-care providers. Moreover, the patients may have been in different stages of their disease. However, the study population was too small to conduct analyses of subgroups. In addition, a negative correlation has been reported for adherence and duration of treatment, e.g. adherence to treatment decreases the longer duration of the treatment lasts.³³ Comorbidity and subsequent polypharmacy can affect adherence,³⁴ however, this was not taken into account in the present study.

Strengths and limitations

A significant strength of our study was the use of two different methods to measure adherence in patients initiating OAA treatment in daily clinical practice. A further strength was the gathered insights in regards to specific patient characteristics, such as cancer type and primary or recurrent treatment. Such characteristics are relevant because they may affect adherence.

A limitation of this study was the heterogeneous population which made it difficult to measure an effect of satisfaction with information on adherence to OAAs. A further limitation was the relative small sample size and low response rate (about 40%). In addition this was a single-center study; therefore, the results cannot be generalized to the entire population of interest

Conclusion

No significant relationship is found between patient satisfaction with information and adherence to OAAs. The sample population was highly satisfied with information about OAAs, which indicates a high level of satisfaction with the usual care. The refill data indicates that 35.5% of patients were not adherent, which points to an issue of concern. Future research should focus on developing and implementing interventions to improve adherence in cancer patients. These interventions should put the patient at the center and include a multidisciplinary approach.

Acknowledgements

We thank Josine Groenendijk and Sandy To for processing the questionnaires and checking the processed data.


Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

ORCID iD

Eward J Melis  <https://orcid.org/0000-0003-1528-3544>

Supplemental Material

Supplemental material for this article is available online

References

1. Kircher SM, Meeker CR, Nimeiri H, et al. The parity paradigm: can legislation help reduce the cost burden of oral anticancer medications? *Value Health* 2016; 19: 88–98.
2. Benjamin L, Maroun R, Maurel F, et al. Patterns of use of oral anticancer treatments in France: a retrospective analysis of cancer treatments given ORally from 2004 to 2012 (Re-ACTOR study). *Curr Med Res Opin* 2015; 31: 323–332.
3. Eek D, Krohe M, Mazar I, et al. Patient-reported preferences for oral versus intravenous administration for the treatment of cancer: a review of the literature. *Patient Prefer Adherence* 2016; 10: 1609–1621.
4. Jensen LH, Osterlind K and Rytter C. Randomized cross-over study of patient preference for oral or intravenous vinorelbine in combination with carboplatin in the treatment of advanced NSCLC. *Lung Cancer* 2008; 62: 85–91.
5. Schott S, Schneeweiss A, Reinhardt J, et al. Acceptance of oral chemotherapy in breast cancer patients - a survey study. *BMC Cancer* 2011; 11: 129.
6. McGrady ME and Pai ALH. A systematic review of rates, outcomes, and predictors of medication non-adherence Among adolescents and young adults with cancer. *J Adolesc Young Adult Oncol* 2019; 8: 485–494.
7. Marin D, Bazeos A, Mahon FX, et al. Adherence is the critical factor for achieving molecular responses in patients with chronic myeloid leukemia who achieve complete cytogenetic responses on imatinib. *J Clin Oncol* 2010; 28: 2381–2388.
8. Williams AM, Baran AM, Casulo C, et al. Ibrutinib dose adherence and therapeutic efficacy in non-hodgkin lymphoma: a single-center experience. *Clin Lymphoma Myeloma Leuk* 2019; 19: 41–47.
9. Winn AN and Dusetzina SB. The association between trajectories of endocrine therapy adherence and mortality among women with breast cancer. *Pharmacoepidemiol Drug Saf* 2016; 25: 953–959.
10. Bekker CL, Melis EJ, Egberts ACG, et al. Quantity and economic value of unused oral anti-cancer and biological disease-modifying anti-rheumatic drugs among outpatient pharmacy patients who discontinue therapy. *Res Social Adm Pharm* 2019; 15: 100–105.
11. Huang WC, Chen CY, Lin SJ, et al. Medication adherence to oral anticancer drugs: systematic review. *Expert Rev Anticancer Ther* 2016; 16: 423–432.
12. Timmers L, Boons CC, Kropff F, et al. Adherence and patients' experiences with the use of oral anticancer agents. *Acta Oncol* 2014; 53: 259–267.

13. Krikorian S, Pories S, Tataronis G, et al. Adherence to oral chemotherapy: challenges and opportunities. *J Oncol Pharm Pract* 2019; 25: 1590–1598.
14. Verbrugghe M, Verhaeghe S, Lauwaert K, et al. Determinants and associated factors influencing medication adherence and persistence to oral anticancer drugs: a systematic review. *Cancer Treat Rev* 2013; 39: 610–621.
15. Mathes T, Pieper D, Antoine SL, et al. Adherence influencing factors in patients taking oral anticancer agents: a systematic review. *Cancer Epidemiol* 2014; 38: 214–226.
16. Horne R, Hankins M and Jenkins R. The satisfaction with information about medicines scale (SIMS): a new measurement tool for audit and research. *Qual Health Care* 2001; 10: 135–140.
17. Jacobs JM, Pensak NA, Sporn NJ, et al. Treatment satisfaction and adherence to oral chemotherapy in patients With cancer. *J Oncol Pract* 2017; 13: e474–ee85.
18. Efficace F, Baccarani M, Rosti G, et al. Investigating factors associated with adherence behaviour in patients with chronic myeloid leukemia: an observational patient-centered outcome study. *Br J Cancer* 2012; 107: 904–909.
19. Zahrina AK, Norsa'adah B, Hassan NB, et al. Adherence to capecitabine treatment and contributing factors among cancer patients in Malaysia. *Asian Pac J Cancer Prev* 2014; 15: 9225–9232.
20. Boons C, Tromp V, Neppelenbroek NJM, et al. Satisfaction with information on nilotinib treatment in chronic myeloid leukemia patients. *Acta Oncol* 2019; 58: 891–896.
21. Utrecht Jaarverslag UMC 2020: UMC Utrecht; 2020. updated 2020: <https://publicaties.umcutrecht.nl/het-umc-utrecht-in-2020/umc-utrecht-2020-in-beeld>
22. Stand van zaken van de overheveling medisch-specialistische geneesmiddelen in 2013; Rijksoverheid; 2012; updated 2012. <https://www.tweedekamer.nl/kamerstukken/detail?id=2012Z10482&did=2012D22118>
23. Kamerbrief Correcties overheveling specialistische geneesmiddelen 2015; Rijksoverheid; 2015; updated 2015. https://www.tweedekamer.nl/kamerstukken/brieven_regering/detail?id=2015Z09472&did=2015D19366
24. WHO ATC/DDD Index 2017: WHO Collaborating Centre for Drug Statistics Methodology; 2017 [updated 2017].
25. Chan AHY, Horne R, Hankins M and Chisari C. The Medication Adherence Report Scale: A measurement tool for eliciting patients' reports of nonadherence. *Br J Clin Pharmacol* 2020; 86(7): 1281–1288.
26. Patel K, Sudhir VS, Kabadi S, Huang JC, Porwal S, Thakkar K and Pagel JM. Impact of dosing frequency (once daily or twice daily) on patient adherence to oral targeted therapies for hematologic malignancies: a retrospective cohort study among managed care enrollees. *J Oncol Pharm Pract* 2019; 25(8): 1897–1906.
27. Middendorff G, Elsey R, Lounsbury B, et al. Impact of a specialty pharmacy case management service on adherence in patients receiving oral antineoplastic agents. *J Oncol Pharm Pract* 2018; 24: 371–378.
28. Mahler C, Hermann K, Horne R, et al. Patients' beliefs about medicines in a primary care setting in Germany. *J Eval Clin Pract* 2012; 18: 409–413.
29. Alsous M, Abu Farha R, Alefishat E, et al. Adherence to 6-mercaptopurine in children and adolescents with acute lymphoblastic leukemia. *PLoS One* 2017; 12: e0183119.
30. Kumar K, Raza K, Nightingale P, et al. Determinants of adherence to disease modifying anti-rheumatic drugs in white British and south asian patients with rheumatoid arthritis: a cross sectional study. *BMC Musculoskelet Disord* 2015; 16: 396.
31. Chua XHJ, Lim S, Lim FP, et al. Factors influencing medication adherence in patients with gout: a descriptive correlational study. *J Clin Nurs* 2018; 27: e213–ee22.
32. Smaje A, Weston-Clark M, Raj R, et al. Factors associated with medication adherence in older patients: a systematic review. *Aging Med (Milton)* 2018; 1: 254–266.
33. Chen Y, Wu X, Xian X, et al. Adherence to oral chemotherapy among colorectal cancer patients: a longitudinal study. *Eur J Oncol Nurs* 2020; 48: 101822.
34. Gellad WF, Grenard JL and Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity. *Am J Geriatr Pharmacother* 2011; 9: 11–23.