Exploratory Research in Clinical and Social Pharmacy 7 (2022) 100163

Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop

Implementation of a model integrating primary and oncology pharmacists' care for patients taking oral anticancer agents (OAA)

Karen B. Farris [a,*], Tiffany Cadwallader [b], Joel Farley [c], Katie Gatwood [d], Emily Mackler [e], Justin Gatwood [f]

[a] University of Michigan College of Pharmacy, 428 Church Street, Ann Arbor, MI 48103, United States of America
[b] Auburn University Harrison School of Pharmacy, Walker Bldg, 2315, Auburn, AL 36849, United States of America
[c] University of Minnesota College of Pharmacy, 308 SE Harvard St, Minneapolis, MI 55455, United States of America
[d] Vanderbilt University Medical Center, Department of Pharmacy, 1211 Medical Center Drive, Nashville, TN 37232, United States of America
[e] University of Michigan, POEM (Pharmacists Optimizing Oncology Care Excellence in Michigan), 2500 Green Road, Suite 100, Ann Arbor, MI 48105, United States of America
[f] University of Tennessee Health Science Center College of Pharmacy, 302 S Perimeter Park Dr, Nashville, TN 37211, United States of America

ARTICLE INFO

Keywords:
Oral anticancer agents
Multiple chronic conditions
Pharmacists coordinated care oncology model

ABSTRACT

Improvements in chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM) treatment options have increased the 5-year survival rates for patients with these hematologic malignancies. In addition to cancer management, these patients may need help to manage multiple chronic conditions (MCC). The overall objective of this study is to examine the impact and implementation of a model that coordinates care between oncology and primary care pharmacists for people taking an oral anti-cancer agent (OAAs) and medications for comorbid chronic conditions. This is a multi-center, prospective, single-arm pilot study that will recruit up to 40 patients from Michigan Medicine and Vanderbilt University Medical Center (VUMC). Eligible participants will be 18 years of age or older, prescribed an OAA, have a diagnosis of either CML, CLL or MM, and be diagnosed with and taking medication for at least two specified chronic conditions. The Pharmacists Coordinated Care Oncology Model (PCOM) is a two-month intervention that builds upon current pharmacist clinical responsibilities. Generally, participants will complete a patient-reported outcome measure at 2 and 6 weeks post-OAA initiation that is sent to their oncology pharmacist, and they will also receive a comprehensive medication review at week 4 from a primary care pharmacist for their chronic medications. The pharmacists will communicate about the results via electronic medical record (EMR) and intervene if necessary. The primary endpoints are (1) dose-adjusted OAA proportion of days covered (PDC), and (2) PDC for chronic condition medications. PDCs will be determined via prescription records. The association of OAA and chronic medication PDCs will be quantified via correlation and chi-squared tests. The association between symptom experience and OAA adherence will be examined via correlation analyses. For implementation, characteristics of patient participants, feasibility, acceptability, adoption, fidelity, and trialability will be described. Data will be collected via EMR and pharmacist and patient interviews. Median/IQR for acceptability, adoption and fidelity will be reported, and patient interviews will be analyzed using a grounded theory approach and pharmacist interviews will be analyzed using thematic analyses.

Introduction

Improvements in treatment options for chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM) have led to double-digit increases in 5-year survival rates for these hematological malignancies over the past 40 years.[1] Patients with CML, CLL, MM, and other cancers are living longer, and this increased survival rate has changed the management strategies for these cancers, including being treated with more widely available oral anticancer agents (OAA). Importantly, a wide range of estimates about medication adherence to OAAs exists.[2–9] Adherence rates outside of clinical trials vary between 50 and 70%.[10,11] It is also known that the therapeutic window for OAAs, where the benefit is balanced with the side effects, may be narrow, and an adherence rate of ≥90% has been associated with improved clinical outcomes in multiple cancer diagnoses.[12,13]

In addition to managing an OAA, patients with hematological malignancies may also require management of other chronic conditions for which medication adherence is central to improving the odds of long-term survival.[2,14–16] Using nationally representative data from the National Health Interview Survey, Changchuan, et al. showed that multiple chronic

* Corresponding author at: University of Michigan, 428 Church Street, Ann Arbor, MI 48109-1065, United States of America.
E-mail addresses: kfarris@umich.edu (K.B. Farris), tjc0049@auburn.edu (T. Cadwallader), farl0032@umn.edu (J. Farley), katie.s.gatwood@vumc.org (K. Gatwood), estunteg@umich.edu (E. Mackler), jgatwood@uthsc.edu (J. Gatwood).

http://dx.doi.org/10.1016/j.rcsop.2022.100163
Received 19 November 2021Received in revised form 21 June 2022Accepted 26 July 2022
Available online xxxx

conditions (MCC) increased in cancer survivors from 23.6% in 2002 to 29.6% in 2018 (p trend <0.01), and this was more common in persons 18 to 44 years old and who were African-American. Importantly, many chronic conditions require medications for treatment.[17] Initiating an OAA in patients with MCC increases the complexity of the medication regimen and requires managing greater medication burden. Previously, it was observed that OAAs for patients with CML, CLL, or MM coincided with significant reductions in adherence to medications for comorbid MCCs, potentially placing these patients at increased risk for detrimental health outcomes.[3] In addition, Gatwood and colleagues reported 7.0%–17.6% reductions in 6-month medication adherence to chronic medications among patients with CML, CLL, or MM once an OAA was initiated.[4] Additional analyses are needed to confirm this phenomenon and to determine the extent to which MCC medication nonadherence may impact clinical outcomes once OAAs are initiated.

OAA therapy requires excellent medication adherence to achieve optimal outcomes, but challenging side effects can impact treatment. When added alongside therapy for MCC, medication problems may arise, and symptom burden is likely to play a significant role. Patient-reported outcome measures (PROM) have been developed and implemented in oncology practice to manage potential symptom burden. In previous work in Michigan oncology practices, 56% of patients taking OAAs reported moderate to severe symptoms, 23% reported 4 or more moderate to severe symptoms, and 30% of respondents reported some level of non-adherence to their oral oncolytic.[18,19] The combination of OAAs and medications for MCC among patients with cancer and MCC requires greater monitoring of medications. PROMs can facilitate longitudinal, objective measurements of the patient experience and can be used in conjunction with patient-reported adherence measures to examine symptom burden and OAA adherence..

Increasing evidence demonstrates the value that pharmacists can bring to care teams managing complex medication regimens in patients with MCC.[20,21] A care model to administer PROM and perform a comprehensive medication review (CMR) in patients with MCC on OAA was piloted by a practice in the Michigan Oncology Quality Consortium.[18] A CMR is defined as "a systematic process of collecting patient-specific information, assessing medication therapies to identify medication-related problems, developing a prioritized list of medication-related problems, and creating a plan to resolve them with the patient, caregiver and/or prescriber".[22] This model showed that 1 in 5 individuals taking an OAA with MCC were referred into the pharmacists' disease management programs for better chronic disease control. This was needed primarily for hypertension but also for diabetes, and this is likely due to the impact of OAAs on blood pressure control and/or patients requiring greater support after their cancer diagnosis to understand the importance of their chronic condition medications. Implementation of this model on a larger scale is necessary to initiate a rigorous evaluation of its implementation, uptake, and impact on outcomes in this patient population. PROM data, particularly focused on OAAs, can help identify patients at risk of experiencing problems with their medications, while a primary care pharmacists' CMR can help reveal and resolve specific medication issues, particularly with MCC medications. In addition, it is critical to more fully understand how patients are able to manage their medications during their cancer diagnosis as well as understand their role in navigating primary and specialty care. Oncology and primary care pharmacists may help bridge a gap between their care providers.[23,24]

The overall objective of this study is to examine the impact and acceptability of care coordination between oncology and primary care pharmacists on medications, symptoms, and disease management for people taking OAAs for hematologic cancers and with MCCs. The objective will be achieved by addressing the following aims:

1. Evaluate the impact of the Pharmacists Coordinated Care Oncology Model (PCOM) on patients' medication-focused outcomes, including number and type of medication changes, proportion of days covered (PDC) for OAA and chronic medications, time on OAA therapy and selected chronic disease outcomes.
2. Monitor the implementation of PCOM, assessing characteristics of participants, feasibility, acceptability, adoption, and fidelity.
3. Understand patient perceptions of coordinating care via PCOM and elucidate patient beliefs regarding OAA use and possible changes in medication adherence.
4. Assess pharmacists' perceptions of PCOM in terms of feasibility, appropriateness, and acceptability.

The data from this pilot study will serve as the basis for developing and more rigorously evaluating an implementation intervention and quantify the impact of PCOM on duration of therapy to OAAs and disease control for MCCs.

Methods

Study design

This is a multi-center, prospective, single-arm pilot study that will recruit up to 40 patients and up to 13 pharmacists from Michigan Medicine and Vanderbilt University Medical Center (VUMC). The study sites will recruit participants simultaneously, and implementation data will be collected at both sites (Table 2). These numbers will allow us to understand the potential impact of PCOM, its implementation, as well as participants' perceptions of the model. IRB approval at both study sites will be obtained.

Study population

The inclusion criteria for patient participants include: age ≥ 18 years; has a primary care physician (PCP); diagnosis of either CLL/SLL, CML, or MM; initiating an OAA, either for the first time or a change from a previous OAA; diagnosis of two or more chronic conditions for which medications are being taken; taking at least 2 chronic medications; willing to complete online surveys; and willing and able to provide informed consent. At least one of the chronic conditions and a medication for it must include diabetes, hypertension, hyperlipidemia, congestive heart failure, depression/anxiety, gastroesophageal reflux disease, or chronic obstructive pulmonary disease. Those who are non-English speaking or who have a concurrent diagnosis of type 1 diabetes due to concern of adherence measurement of insulin using claims data and human immunodeficiency virus due to high level of adherence required will be excluded.

To recruit participants, patients prescribed an OAA at Michigan Medicine or VUMC will be assessed for eligibility by pharmacists working within the oral chemotherapy program of their respective institution. As a part of standard care, these pharmacists counsel patients on their OAA, and this visit will be used by the pharmacists to make eligible patients aware of the study. Names and contact information of eligible and interested patients will be compiled and sent securely to a research assistant (RA) at the University of Michigan or VUMC. Patients will be contacted by the RA using phone, email, and/or text to set a time to conduct the study recruitment meeting. Potential participants will be contacted at the set day and time to provide further information about the study, confirm eligibility, and obtain verbal consent if willing to participate. After verbal consent, patients will be emailed a link to review and electronically sign the full consent. Participants will also be asked if they are willing to be contacted again, after CMR completion, to participate in an interview. Participants that agree to be contacted regarding interviews will be called by an RA to obtain verbal consent for this portion of the study 4–6 months after completion of initial PROM and schedule a time convenient for the interview. Recruitment (asked, refused) and extent of study participation will be determined.

All pharmacists who participate in this study will be asked to complete surveys and be interviewed at 3 intervals, after completing 5, 10 and 20 participants. At Michigan Medicine, all pharmacists performing the CMRs will be board-certified ambulatory care primary care pharmacists; a specialty pharmacy pharmacist or oncology pharmacist will assist with recruitment and the oncology pharmacist will communicate with the primary care pharmacist, when needed. At VUMC, all pharmacists performing the CMRs

will be from the VUMC retail pharmacy, and an oncology pharmacist, chosen by the site PI, will also be involved. Pharmacists will provide informed consent at the first interview. They will be emailed by the RA from their respective institutions twice to complete the three brief surveys and set times for three online interviews.

Intervention

PCOM is an intervention (Fig. 1) that builds upon what pharmacists currently do in their clinics, and the intervention focuses on patients who are receiving active OAA treatment and have MCC – all of which require oral medications. The intervention will be delivered following the initiation of or a change to a new OAA. The total time for the intervention is 2.5 h over 2 months. Generally, participants complete two PROMs for their OAA and receive a CMR for their chronic medications.

The PROM is a short survey that uses the validated Edmonton Symptom Assessment Scale (ESAS) to evaluate patients' symptom severity from 0 (none) to 10 (worst possible).[19,25] Symptom burden is classified as follows: 1–3 mild, 4–6 moderate, and 7–10 severe. The PROM monitors the following symptoms: pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, well-being, constipation, diarrhea, tingling/ numbness, mouth sores, and rash. In addition to symptom assessment, the PROM asks about patients' confidence in self-management of and ability to recognize the need to seek medical care for symptoms using a 0 (not confident) to 10 (confident) scale and includes a health literacy item. Patient adherence is assessed using a single item with a four-week reference period by asking them to rate their ability to take their OAA as prescribed as either excellent, very good, good, fair, or poor.[26–28] This item is included so clinical pharmacists may explore when adherence is not self-reported as excellent. Reasons for not taking OAAs are also solicited and include experiencing side effects, financial issues, and forgetfulness.[28] Oncology pharmacists will receive a summary report that highlights which symptoms are 7 or greater, 4 or greater and when medication adherence is less than excellent. The oncology pharmacist is expected to follow-up as soon as possible for symptoms that are 7 or greater and will follow-up within several days for the other situations.

The CMR is a process where pharmacists conduct one visit to obtain a complete medication list; assess patient understanding of medications; evaluate each medication for safety, effectiveness, use, and cost; and evaluate symptoms, labs, or clinical outcomes (e.g., hemoglobin A1c or blood pressure) for disease control. Based on the findings, pharmacists may call/email physicians for recommended medication changes. Pharmacists then deliver interventions in a second visit to patients, that generally includes approved medication changes as well as education. Primary care pharmacists will document the medication problems, interventions, and referrals for each participant. Diabetes, hypertension, and hyperlipidemia were selected because these conditions are managed by primary care pharmacists using collaborative practice agreements at the University Michigan. [22,29]

Participants will be sent the first PROM within two weeks of initiating an OAA and complete the second PROM about six weeks after initiating an OAA. A reminder email will be sent if they have not completed it within one week. Completed data from the first PROM will be entered into the electronic medical record (EMR) or REDCap, and it will trigger an in-basket message or automatic relay to the pharmacists that will conduct the CMR. The pharmacist or his/her trainee will contact participants to set the date for the CMR, typically about one month after the OAA is initiated. This pharmacist will schedule a second CMR visit if needed. The oncology and primary care pharmacists will intentionally communicate via the EMR about the medications used for diseases and symptoms to optimize patient use of medications.

Data collection

The specific data, source, and time of collection are outlined in Table 1.

PDC

PDC is the primary outcome for the study and includes: (1) dose-adjusted PDC for OAA and (2) PDC for chronic condition medications. PDC for 6 months will be determined from prescription claims for all participants. These claims will either be accessed via EMR or from pharmacies, with signed data release forms from participants. PDC is calculated as the ratio of the sum of days covered to the number of days in timeframe and reported as a percentage for the 6-month period following OAA initiation.[30] An 80% PDC threshold will be used to determine adherence for chronic condition medications as this is the accepted threshold for adherence to most chronic disease medications; however, continuous measures will be reported to examine the impact on lower levels of medication use (e.g., 60% and higher indicating adherence). For OAAs, data from the EMR for dose changes will be aligned with the refill data to calculate a dose-adjusted PDC. For OAAs, the dosing regimens may be complex and side effects may cause subsequent changes in dosing or timing of doses, so a dose-adjusted PDC must be computed to recognize that the dose changed but medication is available.

Other medication use variables

Days on OAA therapy will be gathered and OAA persistence will calculated for 6 months. The number, type, and reason/s for medication changes will be obtained, and any referrals or visits recommended and scheduled will be quantified. Medication use variables will be taken from the EMR, pharmacy records, and/or specialty pharmacy at 2 or 6 months.

Clinical outcomes

Selected chronic disease outcomes, including blood pressure, A1c, and lipid levels, will be obtained from the EMR and CMR at 2 months. These outcomes were selected for this evaluation because they are managed by primary care pharmacists using collaborative practice agreements at the University of Michigan.

Implementation

The characteristics of patient participants, feasibility, acceptability, adoption, fidelity, and trialability will be determined at both sites (Table 2).[31] Data will be collected via EMR, pharmacists, the completed PROMs, and/or the CMRs.

Patient interviews

A semi-structured interview guide will be used to solicit patients' perceptions of care coordination via PCOM and elucidate their beliefs regarding OAA use and possible changes in medication adherence (Table 3). Generally, the interview guide asks patients/participants about seeking primary care after their cancer diagnosis, how OAA treatment impacted their health and other medication use, and how/whether they think PCOM is helpful/supportive. It is likely that new ideas will be generated during the interviews, and the question guide can be changed over time to ensure that data saturation is achieved. An interview using online video or telephone (patient preference) will be scheduled approximately 60 days after OAA initiation, after all the intervention elements have been completed. The interviews will be conducted by the PI or a trained RA using the interview guide. The interview will be one contact, is expected to last between 30 and 40 min, and will be recorded and transcribed. In this study, all participants will be interviewed about primary care and OAA until data saturation is reached (anticipated after ~25 interviews).

Pharmacist interviews

Pharmacists' perceptions of PCOM will be captured using REDCap to gather three psychometrically-assessed measures, including the Acceptability of Intervention Measure (AIM), the Intervention Appropriateness Measure (IAM), and the Feasibility Intervention Measure (FIM) from Weiner and colleagues.[31] The short 4-item version of the AIM, IAM, and FIM with 5-point ordinal response options provided (completely agree to completely disagree) will be used. These validated measures will be collected from pharmacists after 5, 10 and 20 participants have been completed at both

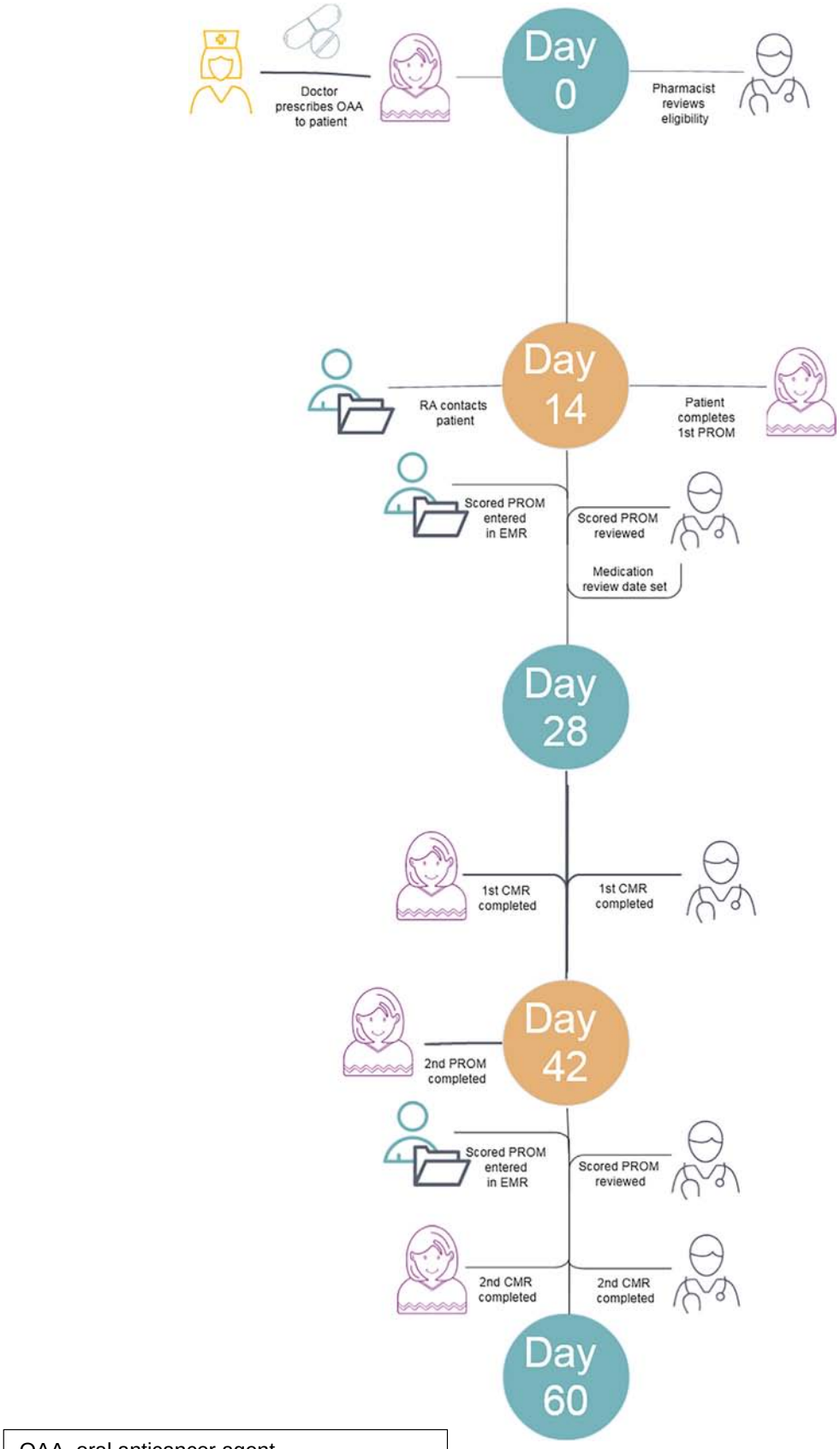

Fig. 1. Timeline for intervention components. Our conflicts of interest include the funding of this study by AstraZeneca, with an independent investigator grant to the University of Tennessee Center for Health Sciences.

Table 1
Medication use and chronic disease outcomes.

Medication use variables	Source	Data collection Time
Medication changes – number, type, and reason	Electronic Medical Record (EMR)	2 months
Referrals or visits recommended and scheduled arising from CMR	EMR	2 months
Refill dates and quantity to calculate PDC (proportion of days covered) for chronic medications	EMR and pharmacy records	6 months
Refill dates and quantity for medication Oral anticancer agent (OAA) Proportion days covered (PDC)	EMR and Specialty pharmacy	6 months
Days on OAA therapy (persistence)	EMR and Specialty pharmacy	6 months
Selected chronic disease clinical outcomes		
Blood pressure, if applicable	EMR and Comprehensive Medication Review (CMR)	2 months
Hemoglobin A1c, if applicable	EMR and CMR	2 months
Cholesterol, HDL, LDL, if applicable	EMR and CMR	2 months

sites. These measures have been psychometrically established for reliability and validity using confirmatory factor analysis. [31]

Formative and final interview guides for pharmacists will be used to gather pharmacist perceptions of implementing PCOM. An interview using online video will be scheduled after 5, 10 and 20 patients at both sites. The formative interview guide will be used for the first two interviews and the final interview guide will be used after all participants are completed. Topics to be addressed during the interviews include acceptability, feasibility, and appropriateness, and provide important detail and context for the quantitative surveys.

Each patient participant will receive $100, $25 when they complete the first PROM, $25 after they complete the second PROM, and $50 for the final interview. Each pharmacist will be paid $50 at the end of the study for completing interviews and surveys, as a gesture of appreciation.

Analysis

The University of Tennessee Health Science Center (UTHSC) is the coordinating center for analysis. Data from the University of Michigan and VUMC will be transferred to UTHSC study personnel using HIPAA compliant, secure data transfer software. UTHSC will receive uniquely identified data but the file linking patient identifiers and participant study number will be maintained at Michigan Medicine and VUMC.

PDC

The primary outcomes are (1) dose-adjusted OAA PDC and (2) PDC for chronic condition medications, and means and confidence intervals will be reported. The association of OAA and chronic medication PDC will be quantified via correlation and chi-squared tests. The association between the measures of symptom experience will be examined with adherence and

Table 2
Demographics and Result Statistics Measurements at Each Study Site.

Variables	Source	Data collection
Demographics		
Age	Elecronic Medical Record (EMR)	Baseline
Gender	EMR	Baseline
Race	EMR	Baseline
Ethnicity	EMR and Patient Reported Outcome Measure (PROM)	Baseline
Education	EMR and PROM	Baseline
Marital status	EMR	Baseline
Residential classification	EMR and PROM	Baseline
Insurance type/status	EMR	Baseline
Clinical		
Diagnoses	EMR	Baseline
Medications	EMR and Comprehensive Medication Review (CMR)	Baseline and at CMR
Cancer type	EMR	Baseline
Feasibility		
Days until oncology pharmacist reviews PROM	EMR	First 10 patients
Days until primary care pharmacist sets date for CMR	EMR	First 10 patients
Days until primary care completion of CMR	EMR	First 10 patients
Date and content of communications between oncology and primary care pharmacists	EMR	First 10 patients
Intervention Appropriateness Measure (survey)	Pharmacists	After 5, 10 and 20 patients
Feasibility Intervention Measure (survey)	Pharmacists	After 5, 10 and 20 patients
Acceptability		
Acceptability of Intervention Measure (survey)	Pharmacists	After 5, 10 and 20 patients
Adoption		
Percent of patients with 2 completed PROMS	EMR	After intervention
Percent of patients with completed CMR	EMR	After intervention
Fidelity		
Percent of patients where oncology pharmacist reviewed PROMs within 1 day	EMR	After 10 and 20 patients
Percent of patients with scheduled CMR within one week of first PROM result	EMR	After 10 and 20 patients
Percent of CMRs where note was routed to oncology pharmacist	EMR	After 10 and 20 patients
Percent of CMR notes that oncology pharmacist reviewed	EMR	After 10 and 20 patients
Trialability		
Patient symptoms	PROM into EMR	~2 weeks and 6 weeks
Self-reported OAA medication adherence	PROM into EMR	~2 weeks and 6 weeks

Table 3
Patient and pharmacist interview question guides.

Patient participants.
Primary care

- How often have you needed to schedule an appointment with your PCP since your cancer diagnosis? What do you think would prompt you to do this?
- How do you feel about seeing your PCP after being diagnosed with cancer?
- What role do you feel your PCP should have in supporting your chronic conditions during your cancer treatment?
- What did you expect from your PCP following your cancer diagnosis?
  - Probe: Have your expectations changed since you were first diagnosed?
- To what extent do you think your PCP and oncologist communicate with each other?

OAA treatment

- What concerns did you have about starting oral cancer treatment?
- How did starting your oral cancer medication impact your medications for your [heart, blood pressure, diabetes, etc.]?
  - Probe: What effect, if any, did starting your oral cancer medications have on your [heart, blood pressure, diabetes, etc.] medications?
- How have side effects arising from your oral cancer medications affected your ability to take your [heart, blood pressure, diabetes, etc.] medications?
- How has treating side effects arising from your oral cancer medications affected your abilities to take medications for [heart, blood pressure, diabetes, etc.]?
- Do you feel your medications for your chronic conditions are as important as your medications for cancer? Why or why not?

Over the past few months you have been asked questions about your OAA and you talked with a primary care pharmacist about all of your medications. This referral to primary care about all of your medications is new in cancer care. We would like to ask you some questions about it.

- How did you feel about completing the questions about symptoms/OAA adherence? Easy/difficult/lengthy/too detailed/not detailed enough/etc.?
- How did you like speaking to a pharmacist about your medications? Why/why not?
- How did you feel this support addressed your medication issues adequately? Why/why not?
- What changes would you want to see implemented in this process?

Pharmacist participants.
Pharmacist Formative Question Guide.
Over the past few months, you have been working in PCOM for patients with CML, CLL and MM. In PCOM, patients receiving OAAs completed a PROM twice and also received a CMR from a primary care pharmacist.

- [Acceptability] How easy or difficult was it to.....
  - identify eligible patients for PCOM? Why?
  - incorporate the PROM results into your workflow? Why?
  - provide the referral to the primary care pharmacist? Why?
  - set the CMR date? Why?
  - review the CMR note? Why?
  - communicate between oncology/primary care pharmacist? Why?
  - incorporate necessary medication changes into your workflow with the appropriate team/physician and get them implemented? Why?
- [Feasibility] What would make it more feasible to ....
  - identify eligible patients for PCOM? Why?
  - incorporate the PROM into your workflow? Why?
  - provide the referral to the primary care pharmacist? Why?
  - set the CMR date? Why?
  - review the CMR note? Why?
  - communicate between oncology/primary care pharmacist? Why?
  - incorporate necessary medication changes into your workflow with the appropriate team/physician and get them implemented? Why?
- [Process Map] How can we rearrange the components of the PCOM intervention – two PROMs, CMR, numerous MiChart communications, patient contact/scheduling - to make it easier to complete?
- [Appropriateness] How was the information from the PROM and/or CMR helpful in your care for your patients?

Pharmacist Final Question Guide

- We developed a summary model or map of what you've been doing the past few months. Please review it.
  - Probe: What needs to be changed? Clarified?
- Do you feel PCOM is an effective way to identify patients struggling with symptoms and/or non-adherence? Why/why not?
- Do you feel PCOM is an effective way to help patients increase their adherence? Why/why not?
- What did you like about PCOM?
- What did you dislike about PCOM?
- How do you feel PCOM was perceived by patients? oncologists or oncology office personnel? primary care physicians?

persistence to OAA via correlation analyses, appropriate to the level of measurement/recoding of the variable. The association between self-reported adherence at 2 and 6 weeks and length of time on OAA therapy will be examined via correlation. Three groups will be characterized via baseline demographic characteristics using chi-square analyses or *t*-tests and include (1) participants with a dose-adjusted OAA PDC > 95% vs lower, (2) chronic medication PDC >80% vs lower, and (3) symptom ratings >4 vs lower.

Other medication use variables

Using CMR data, medication problems, recommendations, and changes will be described, using the PQA Medication Therapy Problem Categories Framework.[32] The percent of individuals referred for additional follow-up for disease control of chronic conditions will be quantified. OAA persistence will be reported as mean and standard deviation.

Clinical outcomes

The percent of participants with controlled blood pressure of <140/90 for all participants, A1c, and lipid levels will be reported at 2 and 6 months.

Implementation

The characteristics of patient participants, feasibility, acceptability, adoption, fidelity, and trialability will be reported using descriptive statistics.

Patient interviews

All patient interviews will be recorded, transcribed, and analyzed by members of the study team. An evolved grounded theory approach for the patient data will be used, where coding is defined as open, axial, and selective, because this approach enables a process or theoretical model to be developed or for hypotheses to be generated. PCOM is a new model, and it is possible that these analyses can generate new hypotheses, new processes, and new theoretical constructs, based upon patients' views. Thus, a grounded theory approach is needed. In grounded theory, three phases of data analysis are used including open, axial, and selective coding.[33] Memoing will be used to consider codes and concepts. A code book will be developed using the first 6 interviews that can be used to code subsequent interviews; however, new codes may emerge. These first six interviews will be analyzed by two team members, who will meet and come to consensus on the open and axial codes, again recognizing that new codes could emerge. Thereafter, the interviews will be coded by one team member and new codes will prompt a meeting to agree upon new codes. Axial coding is a stage where codes are integrated to evolve concepts. Selective coding will then result in the core category, which portrays the central thesis of the analyses, and will be done collaboratively by the two team members. A pictorial process will be created that shows the key themes and/or concepts identified in the analyses and the hypothesized relationships that can be tested in future work. We will use 4 participants who were interviewed to review our final core category and pictorial process for validation.

Pharmacist interviews

The quantitative implementation outcomes analyses will be descriptive in nature. There are 4 items each for the three implementation surveys completed by the pharmacists and include appropriateness, acceptability, and feasibility. The 4 items will be averaged, and the median/IQR and modes will be graphically displayed over time. Other quantitative measures of implementation will be derived from the EMR for feasibility, adoption, and fidelity. These data will be reported as frequency distributions and/or median/IQR.

The pharmacist interviews will be recorded and thematically analyzed by members of the study team, with particular attention to feasibility and acceptability of the model. The first three interviews will be analyzed by two team members, who will meet and come to consensus on the codes and generate a code book. This code book will be used to analyze subsequent interviews, and any new codes will generate a meeting to achieve consensus. Codes may be collapsed into larger themes that can be used to improve the efficiency and effectiveness of the intervention, where possible. Grounded theory is not used for these data because the interviews are focused on implementation issues rather than concepts related to medication management.

Discussion

The increased use of OAAs in cancer treatment necessitates a model like PCOM for patient monitoring. The care provided to patients must also shift wholly from the cancer center and infusion setting to that which also supports patient self-care management.[34,35] Positive outcomes in patient satisfaction, severity of side effects, treatment discontinuation, unscheduled hospital admissions, and death were achieved when OAA patients received care via an intensive clinical pharmacy model.[21] While all oncology practices may not be able to integrate pharmacists into their practices, proactive monitoring via PROMs and a CMR can likely improve medication outcomes.[36] Side effects, either experienced or fear of side effects, are the primary reason for OAA nonadherence, which compromises clinical outcomes.[37–39] PCOM is a model that proactively evaluates and manages patients' symptom burden while taking OAAs and considers their MCC medications as well.

Conducting pilot studies to understand the issues related to inclusion criteria, recruitment, intervention delivery, and responsive outcomes are paramount before larger studies are planned and grant applications are submitted. These results will allow an understanding of where adaptations in the model and/or study procedures may be warranted. Importantly, results will also determine how patients respond to the study and the PCOM model. Using grounded theory to analyze interviews from patient participants can also provide critical understanding about medication management, roles of providers in OAA management, and hypothese for future study.

In considering potential obstacles, the study will aid in learning how the intervention can be better integrated into the EMR for greater efficiency and/or how communication across pharmacists can be facilitated. Understanding of the potential difficulties in recruitment and data collection will be obtained, and different approaches used, if needed.

The limitations of this research include the lack of a randomized control group to establish efficacy of PCOM. While the sample size is small, it is consistent with a single group pilot study. It is possible that a one-time CMR in the study time-frame may not be sufficient to identify all medication-related problems that develop with the addition of a new oral anti-cancer medication. Only three clinical outcomes were included, thus not every chronic condition used in the inclusion criteria was considered as a clinical outcome, and it is possible that a positive or negative impact will be missed. The patient interviews will be done with participants in the study and theoretical sampling using patient characteristics will not be done. This number of participants, however, is likely to result in the saturation of all concepts.

Conclusion

Unique models of care to improve medication adherence among patients who take both OAAs and have MCCs are needed. Clinical pharmacists routinely work in clinic settings and provide patient education, disease monitoring, and support for side effects and symptoms. Thus, PCOM is proposed as an approach between oncology and primary care pharmacists, as a means to improve medication, symptom, and disease management of patients with MCC who are also receiving active treatment with OAAs.

Acknowledgements

Funding: This work was supported by a grant from Astra Zeneca to the University of Tennessee Center for Health Sciences, Nashville, TN, with subawards to the University of Michigan and Vanderbilt University. The funding source had no role in determining the study design or results, but adverse events for their own pharmaceutical products will be reported to them. They encouraged publication of the protocol and study results.

References

1. Noone A, Howlader N, Krapcho M, et al. *SEER Cancer Statistics Review, 1975–2015*. Bethesda, MD: National Cancer Institute. April 2018. https://seer.cancer.gov/csr/1975_2015/. based on November 2017 SEER data submission, posted to the SEER web site.
2. Song X, Cong Z, Wilson K. Real-world treatment patterns, comorbidities, and disease-related complications in patients with multiple myeloma in the United States. Curr Med Res Opin 2016;32:95-103.
3. Dashputre AA, Gatwood K, Schmidt J, Gatwood J. Impact of oral oncolytic initiation on medication adherence for pre-existing comorbid chronic conditions. J Oncol Pharm Pract 2020;26:835–845.
4. Greer JA, Amoyal N, Nisotel L, et al. A systematic review of adherence to oral antineoplastic therapies. Oncologist 2016;21(3):354–376.
5. Chari A, Bhor M, Eldjerou L, et al. Treatment patterns and medication adherence among patients diagnosed with multiple myeloma and treated with panobinostat. Future Oncol 2018;14:2149–2160.
6. Cransac A, Aho S, Chretien ML, Giroud M, Caillot D, Boulin M. Adherence to immunomodulatory drugs in patients with multiple myeloma. PLoS One 2019;14(3), e0214446.
7. Patel K, Sudhir VS, Kabadi S, et al. 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;25:1897–1906.
8. Yood MU, Oliveria SA, Cziraky M, Hirji I, Hamdan M, Davis C. Adherence to treatment with second-line therapies, dasatinib and nilotinib, in patients with chronic myeloid leukemia. Curr Med Res Opin 2012;28:213–219.
9. Ward MA, Fang G, Richards KL, et al. Comparative evaluation of patients newly initiating first-generation versus second-generation tyrosine kinase inhibitors for chronic myeloid leukemia and medication adherence, health services utilization, and healthcare costs. Curr Med Res Opin 2015;31(2):289–297.
10. Ruddy K, Mayer E, Partridge A. Patient adherence and persistence with oral anticancer treatment. CA Cancer J Clin 2009;59:56–66.

11. McCue DA, Lohr LK, Pick AM. Improving adherence to oral cancer therapy in clinical practice. Pharmacother 2014;34:481–494.
12. Muluneh B, Schneider M, Faso A, et al. Improved adherence rates and clinical outcomes of an integrated, closed-loop, pharmacist-led Oral chemotherapy management program. J Oncol Pract 2018;14:e324–e334.
13. 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.
14. Gay F, Palumbo A. Management of disease- and treatment-related complications in patients with multiple myeloma. Med Oncol 2010;27(suppl 1):S43–S52.
15. Jabbour E, Makenbaeva D, Lingohr-Smith M, et al. Use of real-world claim databases to assess prevalence of comorbid conditions relevant to the treatment of chronic myelogenous leukemia based on National Comprehensive Network Treatment Guidelines. Clin Lymphoma Myeloma Leuk 2015;15:797–802.
16. Strati P, Parikh SA, Chaffee KG, et al. Relationship between co-morbidities at diagnosis, survival and ultimate cause of death in patients with chronic lymphocytic leukaemia (CLL): a prospective cohort study. Br J Haematol 2017;178:394–402.
17. Jiang C, Wang H, Wang Q, Zheng B, Shapiro CL. Cancer survivors with multiple chronic conditions: a rising challenge – trend analysis from National Health Interview Survey. 2020;38(15 suppl), e24089.
18. Mackler E, Petersen L, Severson J, et al. Implementing a method for evaluating patient-reported outcomes associated with oral oncolytic therapy. J Oncol Pract 2017;13:e395–e400.
19. Hui D, Bruera E. The Edmonton symptom assessment system 25 years later: past, present and future developments. J Pain Symptom Manag 2017;53:630–643.
20. Santschi V, Chiolero A, Burnand B, Colosimo AL, Paradis G. Impact of pharmacist care in the management of cardiovascular disease risk factors. Arch Intern Med 2011;171:1441–1453.
21. Dürr P, Schlichtig K, Kelz C, et al. The randomized AMBORA trial: impact of pharmacological/pharmaceutical care on medication safety and patient-reported outcomes during treatment with new oral anticancer agents. J Clin Oncol 2021;39:1983–1994.
22. Fact Sheet Summary of 2019 MTM Programs. Centers for Medicare and Medicaid Services (2020) Programs. Retrieved from: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/CY2019-MTM-Fact-Sheet.pdf. Accessed 06 08 21.
23. Wallner LP, Li Y, Furgal AKC, et al. Patient preferences for primary care provider roles in breast cancer survivorship care. J Clin Oncol 2017;35:2942–2948.
24. O'Toole E, Step MM, Engehardt K, Lewis S, Rose JH. The role of primary care physicians in advance cancer care: perspectives of older patients and their oncologists. J Am Geriatr Soc 2009;57(Supp 2):S265–S268.
25. Watanabe SM, Nekolaichuk CL, Beaumont C. The Edmonton symptom assessment system, a proposed tool for distress screening in cancer patients: development and refinement. Psychooncology 2012;21:977–985.
26. Feldman BJ, Fredericksen RJ, Crane PK, et al. Evaluation of the single-item self-rating adherence scale for use in routine clinical care of people living with HIV. AIDS Behav 2013;17:307–318.
27. Lu M, Safren SA, Skolnik PR, et al. Optimal recall period and response task for self-reported HIV medication adherence. AIDS Behav 2008;12:86–94.
28. Unni EJ, Farris KB. Development of a new scale to measure self-reported medication nonadherence. Res Soc Adm Pharm 2015;11:e133–e143.
29. Yoo A, Fennelly JE, Renauer MM, et al. Comprehensive medication review service by embedded pharmacists in primary care: Innovations and impact. J Am Pharm Assoc 2021. https://doi.org/10.1016/j.japh.2021.09.015. 021 Oct 2;S1544-3191(21)00385-X.
30. Canfield SL, Zuckerman A, Anguiano RH, et al. Navigating the wild west of medication adherence reporting in specialty pharmacy. J Mdg Care Spec Pharm 2019;25:1073–1077.
31. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. Implement Sci 2017;12:108.
32. PQA, Pharmacy Quality Alliance. Medication Management Services. https://www.pqaalliance.org/medication-management-services. Accessed 03 10 22.
33. Tie YC, Birks M, Francis K. Grounded theory research: a design framework for novice researchers. SAGE Open Med 2019;7.2050312118822927.
34. Weingart SN, Brown E, Bach PB, et al. NCCN task force report: oral chemotherapy. J Natl Compr Cancer Netw 2008;6(suppl 3):S1–14.
35. Krzyzanowska MK, Powis M. Extending the quality and safety agenda from parenteral to oral chemotherapy. J Oncol Pract 2015;11:198–201.
36. Mierzynska J, Piccinin C, Pe M, et al. Prognostic value of patient-reported outcomes from international randomised clinical trials on cancer: a systematic review. Lancet Oncol 2019;20:e685–e698.
37. Salgado TM, Mackler E, Severson JA, et al. The relationship between patient activation, confidence to self-manage side effects, and adherence to oral oncolytics: a pilot study with Michigan oncology practices. Support Care Cancer 2017;25:1797–1807.
38. Zerillo JA, Goldenberg BA, Kotecha RR, Tewari AK, Jacobson JO, Krzyzanowska MK. Interventions to improve oral chemotherapy safety and quality: a systematic review. JAMA Oncol 2018;4:105–117.
39. Nhean S, Kostoff D, Yang JJ, Vogel V, Rybkin II. Impact of oral chemotherapy management program on capecitabine toxicity management. JCO Oncol Pract 2021;26, OP2000947.