

## PAPER

# Do treatment patterns alter beliefs cancer patients hold regarding oral oncolytic agents?

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## Abstract

**Objective:** Cancer patients, particularly those prescribed with oral oncolytic medications, face treatment side effects and temporary and permanent stoppages of treatment. This research examines how events during treatment affect patients' beliefs regarding oral oncolytic medications.

**Methods:** A total of 272 cancer patients initiating 1 of 28 oral oncolytic agents were followed for 12 weeks. Assessments of Beliefs About Medications Questionnaire, symptoms, physical function, and depression measures were performed during telephone interviews at intake (medication start) and 4, 8, and 12 weeks. Electronic medical record audits identified dates of temporary and permanent medication stoppages. Linear mixed-effects models were used for longitudinal analyses of the Beliefs About Medications Questionnaire scores in relation to patient characteristics, symptom severity, and medication stoppages.

**Results:** Over the initial 12 weeks, beliefs about the necessity of oral medications have increased, concerns have decreased, and interference of medications with daily lives has increased. Permanent stoppage of a medication predicted significant declines in beliefs about its necessity over time. Male patients, those less educated, those reporting higher symptom severity, and those experiencing temporary stoppages had greater concerns. Interference of medications with daily life was higher for males, increased with higher symptom severity, and differed by drug category.

**Conclusions:** Patients' beliefs in the necessity of their oral medication were affected only by a permanent drug stoppage. Symptom severity, education, and patient sex affected patients' beliefs about their concerns with their medications and the interference medications posed for their daily lives. Interventions may need to target the distinct dimensions of beliefs during treatment with oral oncolytic agents.

## KEYWORDS

cancer, late stage disease, medication beliefs, medication stoppages, oncology, oral oncolytic medications, symptoms

## 1 | BACKGROUND

Patients with advanced cancers for whom earlier lines of treatment have failed are frequently prescribed with oral oncolytic agents including oral cytotoxic drugs, inhibitors directed at cell surface receptors, and those targeted at the tumor microenvironment.<sup>1</sup> A number of features set these medications apart from medications for other chronic

conditions. Oral oncolytic medications are typically expensive with a cost of hundreds of United States (US) dollars per dose and, although covered by many health insurances in the US, require out-of-pocket costs that could be in thousands of dollars. These medications may produce severe symptoms and side effects that patients experience at home without frequent contacts with oncology professionals. In response to these symptoms and side effects, oncologists may adjust

the dose by temporarily stopping the medication or permanent discontinuation of the oral oncolytic agent. This research focuses on examining factors that influence patients' beliefs about oral oncolytic medications as they proceed through the first weeks of treatment.

Horne and colleagues<sup>2,3</sup> developed measures of patients' beliefs regarding the necessity of their medications and concerns that arise from their impact on functioning and health. The Beliefs about Medicines Questionnaire (BMQ) is grounded in social cognition as expressed through the health belief model and assesses patients' positive outcome expectancy (benefits from treatment) and the accompanying concerns regarding the use of medications and their interference with daily activities.<sup>4-6</sup> Patients' scores on the necessity and concerns subscales have been found to be associated with their levels of adherence<sup>2,7-9</sup> as well as with their sex, symptom reports, duration of treatment, number of medications, and depression.<sup>7,10-17</sup>

This research examines how events arising during the course of treatment together with patients' factors alter beliefs regarding the necessity and concerns attributed to their medications. Identifying the effects of these events and patient factors could inform the development and tailoring of interventions to support adherence to and persistence of oral oncolytic treatment.

This report is based on the secondary analysis of data from a recently completed trial of an intervention to improve adherence and symptom management among patients' newly prescribed oral oncolytic medication.<sup>18</sup> Briefly, adherence was high and did not differ by trial arm, while symptoms were improved in the experimental arm. The important feature of this trial is the timing of data collection beginning with the initiation of the new oral oncolytic agent and through the first 12 weeks. We assess these data to determine how medication beliefs change over these initial 12 weeks and how patient, disease, and treatment factors influence the beliefs over time.

## 2 | METHODS

### 2.1 | Design and sample

A total of 272 patients were accrued from 6 national cancer institute-designated comprehensive cancer centers in the US (Figure 1). The study was approved by the Institutional Review Board (IRB) of Michigan State University (IRB# 13-076 M) and the IRBs of each cancer center. All patients had had health insurance coverage that was private and/or government-sponsored (Medicaid, Veterans Administration, Medicare for those 65 years of age or older). Patients were identified when first prescribed at least 1 of 28 oral anticancer agents approved by the Food and Drug Administration. Recruiters at each cancer center were trained in how to approach patients and introduce the study. Eligible patients were cognitively intact; had a Karnofsky score of 50 or higher or an ECOG score of 0 to 2; had a landline or cellular telephone; were able to speak and read English; and had appropriate level of hearing for telephone contacts. If patients agreed to participate, they signed the consent form and received a folder with complete study information including who to call with questions. Recruiters entered all patient information and drug name and dosage into a secure electronic tracking system, and interviewers

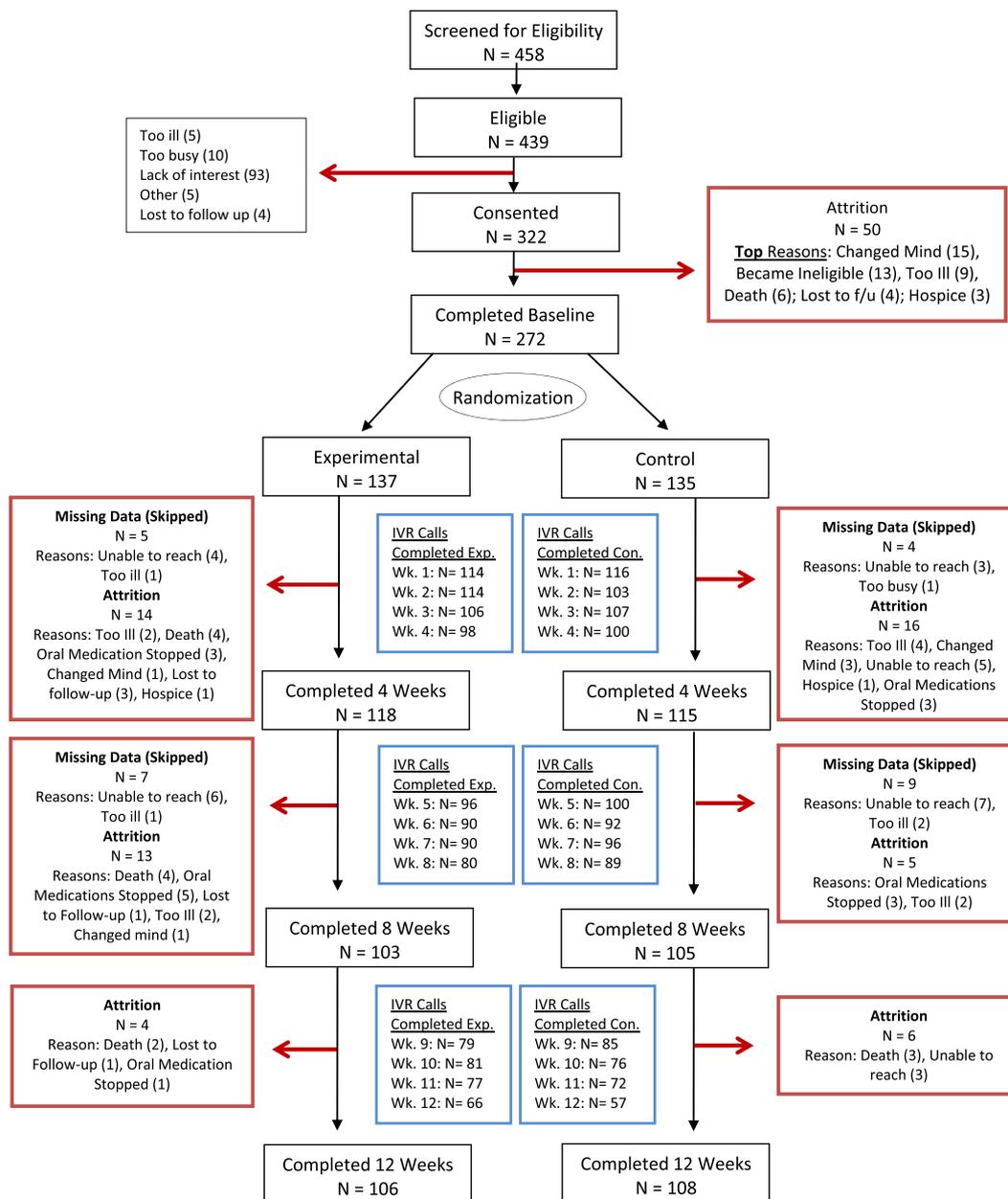
conducted baseline interviews shortly after patients had received their medication from the specialty pharmacy and started taking it. Following the intake interview, patients were randomized to either the experimental or control arm. A minimization program was used to balance treatment arms by accrual location, cancer site, continuous vs intermittent dosage, concurrent intravenous chemotherapy, and depression. All patients received interviews at 4, 8, and 12 weeks and weekly automated calls to assess symptoms and adherence to their oral oncolytic agents. Patients randomized to the experimental arm received daily telephone reminders to take their medications and a printed copy of the *Medication Management and Symptom Management Toolkit* (toolkit). During weekly calls, patients in the experimental arm were advised to consult the toolkit for each symptom they scored at a 4 or higher in severity on a 0 to 10 scale. This toolkit described 18 common symptoms associated with cancer and treatment using oral anticancer agents. It was organized by frequently asked questions and presented evidence-based advice on how to manage the symptom and when (at what severity levels) to inform the oncologist. The toolkit also offered suggestions on managing oral anticancer medication and enhancing adherence.

### 2.2 | Measures

All measures were administered at intake, 4, 8, and 12 weeks, with the exception of demographics and comorbid conditions, which were assessed at intake only. If oral cancer medication was stopped, and the patient did not take the medication in any of the 4-week period between interviews, medication-related instruments including the BMQ were not administered.

#### 2.2.1 | Beliefs about medicines (BMQ)

Originally, the instrument contained 10 items,<sup>3</sup> each rated on a 1-to-5 (strongly agree to strongly disagree) scale. Five items loaded onto the *necessity* subscale and 5 onto the *concerns* subscale. In 2004, the 11th item was added, focusing on unpleasant side effects.<sup>19</sup> For this research, 11 items were included, each with reference to "oral cancer medications." All items were submitted to an exploratory factor analysis at each of the 4 observations. Five necessity items were loaded consistently on the *necessity* subscale at each observation. However, at each observation, the original concern items separated into 2 unique subscales, one of which was labeled the *concerns* subscale, and the other one was labeled *interference* subscale. The *concerns* subscale included worry about having to take medications, worry about long-term effects, "medications are a mystery to me," and worry about becoming too dependent. The *interference* subscale comprised of 1 item from the original *concerns* subscale ("my medications disrupt my life") and 1 item from the later version of the instrument ("my medications give me unpleasant side effects"). Factor loadings for these 3 subscales remained stable at each of the 4 time points. Therefore, 3 subscale scores—*necessity*, *concerns*, and *interference*—were computed at each observation by averaging the corresponding item scores. Reverse scoring of items assured that higher scores on each subscale indicated greater necessity, concerns, or interference. The internal consistency reliability (Cronbach alphas) for each subscale at 4 time



**FIGURE 1** Oral adherence consort table. IVR, interactive voice response

points was .76, .81, .83, and .87 for necessity; .64, .68, .66, and .67 for concerns; and .75, .80, .70, and .75 for interference.

### 2.2.2 | Symptoms

The presence, severity, and interference with daily activities were measured for 18 prevalent symptoms including pain fatigue, sleep disturbance, anxiety, weakness, headaches, skin rash, numbness or tingling, redness or peeling in hands or feet, swelling of hands and feet, joint/muscle pain, mouth sores, lack of appetite, nausea or vomiting, diarrhea, constipation, cough, and shortness of breath. Patients indicated if they had experienced the symptom in the past 7 days and, if yes, rated severity of the symptom on a scale from 1 to 9 and interference of that symptom with daily activities on a scale of 0 (did not interfere) to 9 (interfered completely). Summed symptom severity and summed symptom interference indices were derived across the array of symptoms.

### 2.2.3 | Depressive symptoms

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression (CES-D) 20-item scale.<sup>20</sup> Cronbach alpha exceeded .90 in this sample.

### 2.2.4 | Physical function

Physical function was measured<sup>21,22</sup> using the Patient Reported Outcomes Measurement Information System Short Form 10 (Cronbach alpha exceeded .90).

### 2.2.5 | Demographic characteristics

Demographic characteristics including age, sex, race, ethnicity, and level of education were obtained during baseline interview. Level of education was summarized as high school or less, some to 4-year college education, or graduate/professional degree.

### 2.2.6 | Comorbid conditions treated with medications

Comorbid conditions treated with medications at intake into the trial were identified via electronic medical record (EMR) audits. The medications documented in the EMR prior to the prescription date for the oral oncolytic medication were used to identify the corresponding comorbid conditions. Based on the purpose of the drug, conditions included cardiovascular problems, chronic lung disease, asthma, kidney disease, diabetes, depression, and arthritis. If multiple medications were prescribed for the same condition, the condition was counted once.

### 2.2.7 | Oral oncolytic agents

Oral oncolytic agents were collapsed into 4 categories: cytotoxic agents, kinase inhibitors, sex hormone inhibitors, and others (see Appendix A). Dosages of these oral oncolytic medications were either continuous (taken every day) or intermittent (medication taken followed by rest periods).

### 2.2.8 | Treatment stoppages

Treatment stoppages were based on start date as documented in the EMR and then assigned to a corresponding 4-week time: baseline to weeks 4, 4 to 8, or 8 to 12. Temporary stoppages were differentiated from permanent stoppages based on information in the EMR for each oral oncolytic agent. Patients could experience multiple temporary stoppages but only 1 permanent stoppage. Temporary or permanent stoppage during each 4-week period was defined by at least one of the drugs in the protocol being stopped temporarily or permanently, respectively, in that period. We were unable to identify dose reductions in a uniform manner across sample for 2 reasons. First, reductions had to be calculated for each drug among multiple ones taken by a patient. Second, many oncolytic agents had intermittent dosing (3 weeks on 1 week off), and dose reductions could occur via directing the patient to take a smaller dose or by extending or adding rest periods.

## 3 | STATISTICAL ANALYSIS

The distributions of the BMQ subscale scores and other variables were summarized with descriptive statistics. Correlations among the BMQ subscales were computed at each time point. Longitudinal mixed-effects models were used to relate 4 repeated measures (baseline, 4, 8, and 12 weeks) of each of the 3 BMQ subscale scores to the following fixed explanatory variables: patient's age, sex, drug category, level of education, number of comorbid conditions treated with medications at intake, and trial arm. Since the intervention was not directed at beliefs about medications, we did not expect differences by trial arm but, nevertheless, adjusted for it in this secondary analysis. Time was entered as a categorical variable with levels—intake: 4, 8, and 12 weeks—to model potentially nonlinear patterns in the BMQ scores over time. Summed symptom severity as calculated at baseline 4, 8, and 12 weeks was entered as a time-varying covariate. Next, the presence or absence of permanent or temporary stoppages in each observation period (1 stoppage variable at a time) was added as a time-varying covariate.

Finally, we explored adding the physical function and CES-D scores as additional time-varying factors to gauge their effects on the BMQ over and above symptom severity. Least square means of the BMQ subscale scores according to time and drug category were output from the mixed models, and differences among them were tested. All statistical tests were 2-sided. The analyses were conducted in SAS 9.4.

## 4 | RESULTS

The sample had equal representation of males and females, and a mean age of 61 years (Table 1). At intake, health insurance covered oral oncolytic medication for 89% of patients. Fifty three percent of patients had out-of-pocket cost at intake (median \$25, range \$1-\$8300). Cytotoxic agents and kinase inhibitors accounted for most 28 oral agents prescribed at intake. Of 27 patients on sex hormone inhibitors, 26 were men with prostate cancer over 60 years of age. The average number of comorbid conditions treated with medications at intake was 3.38, with an average of 12 medications prescribed to patients for those conditions (Table 1).

Based on the unadjusted means of the BMQ subscales (Table 1), patients' beliefs about the *necessity* and *interference* of their oral anti-cancer medications rise over the 12 weeks while *concerns* decline. Each subscale appears to assess a unique construct. Necessity did not correlate with either *concerns* or *interference*, with Pearson correlation coefficients below 0.20 at each observation. Correlations between *interference* and *concerns* were 0.36 at intake, 0.28 at week 4, 0.31 at week 8, and 0.43 at week 12.

The highest rate of temporary stoppages of the oral agents was in the first 4 weeks of treatment (22%) then declined for the subsequent two 4-week periods. In contrast, permanent stoppages of oral agents were fairly stable with a slight decline from 11% in the first 4 weeks to 8% during weeks 8 to 12 (Table 1).

The multivariable longitudinal model for the *necessity* scores revealed that they were significantly higher at week 12 compared to intake, with the adjusted mean difference of 0.11, standard error of 0.05, and  $P = .02$  (first panel of Table 2). Level of education was a significant predictor of perceived necessity; those with some to completed college had lower *necessity* scores than those with graduate or professional degrees or high school or less education. Patients on cytotoxic agents reported lowest *necessity* scores compared to other drug classes. Permanent stoppages of oral agents had a strong negative effect on necessity beliefs, with significant reductions in perceived necessity following oral agent stoppages (mean reduction of 0.50, standard error = 0.10,  $P < .01$ , Table 2). Age, sex, number of comorbid conditions treated with medications, trial arm, and symptom severity did not affect *necessity* over and above education, time, drug category, and permanent stoppages.

*Concerns* declined significantly over the first 4 weeks following oral agent initiation then remained stable over time (Figure 2 and Table 2). Male patients, those less educated, and those who reported greater symptom severity and temporary stoppages were more concerned about the impact of their medications. In contrast, patients

**TABLE 1** Descriptive statistics for the study sample

Characteristic	N (%)
<b>Intake (N = 272)</b>	
Sex	
Male	136 (50%)
Female	136 (50%)
Race	
African American	22 (8%)
Caucasian	241 (89%)
Other/unknown	9 (3%)
Ethnicity	
Hispanic or Latino	5 (2%)
Not Hispanic or Latino	260 (95%)
Unknown	7 (3%)
Level of education	
High school or less	71 (26%)
Some college or completed college	150 (55%)
Graduate or professional degree	49 (18%)
Unknown	2 (1%)
Health insurance coverage for oral oncolytic medication	
Yes	241 (89%)
No	18 (6%)
Don't know	13 (5%)
Drug category	
Cytotoxic agents	95 (35%)
Kinase inhibitors	127 (47%)
Sex hormone inhibitors	27 (10%)
Other	23 (8%)
Site of cancer	
Breast	57 (21%)
Colorectal	41 (15%)
GI	17 (6%)
Leukemia	16 (6%)
Liver	12 (4%)
Lung	10 (4%)
Lymphoma	3 (1%)
Melanoma	8 (3%)
Myeloma	7 (3%)
Pancreatic	27 (10%)
Prostate	26 (10%)
Renal	24 (9%)
Sarcoma	15 (5%)
Brain	2 (1%)
Esophageal	3 (1%)
Other	4 (1%)
Study group	
Experimental	137 (50%)
Control	135 (50%)
Characteristic	Mean (StDev)
Age	61.38 (12.22)
Number of comorbid conditions treated with medications	3.38 (1.99)

(Continues)

**TABLE 1** (Continued)

Characteristic	Mean (StDev)
Number of medications other than oral oncolytics prescribed at intake or during the study	11.81 (5.90)
Out-of-pocket cost for oral oncolytic medication	257.82 (925.53)
BMQ necessity	3.70 (0.70)
BMQ concerns	2.66 (0.78)
BMQ interference	2.50 (0.97)
Symptom severity	24.76 (22.00)
Physical function	45.20 (7.87)
CES-D	9.76 (8.97)
<b>Week 4 (N = 233 completed interview, N = 222 completed BMQ)</b>	
BMQ necessity	3.62 (0.77)
BMQ concerns	2.51 (0.76)
BMQ interference	2.67 (1.1)
Symptom severity	22.61 (21.43)
Physical function	44.94 (8.39)
CES-D	9.69 (8.75)
Had a temporary drug stoppage, N (%) <sup>a</sup>	57 (22%)
Had a permanent drug stoppage, N (%) <sup>a</sup>	28 (11%)
<b>Week 8 (N = 208 completed interview, N = 186 completed BMQ)</b>	
BMQ necessity	3.72 (0.77)
BMQ concerns	2.47 (0.77)
BMQ interference	2.63 (1.00)
Symptom severity	18.82 (16.18)
Physical function	45.35 (7.92)
CES-D	9.15 (8.21)
Had a temporary drug stoppage, N (%) <sup>a</sup>	30 (12%)
Had a permanent drug stoppage, N (%) <sup>a</sup>	24 (9%)
<b>Week 12 (N = 214 completed interview, N = 164 completed BMQ)</b>	
BMQ necessity	3.80 (0.87)
BMQ concerns	2.47 (0.77)
BMQ interference	2.62 (1.04)
Symptom severity	17.99 (17.58)
Physical function	45.58 (8.45)
CES-D	9.52 (8.83)
Had a temporary drug stoppage, N (%) <sup>a</sup>	12 (5%)
Had a permanent drug stoppage, N (%) <sup>a</sup>	18 (8%)

Abbreviations: BMQ, Beliefs About Medications Questionnaire; CES-D, Center for Epidemiologic Studies Depression.

<sup>a</sup>Percent is out of the number of patients with available medical record audit data for each period: N = 272 at intake, N = 265 at week 4, N = 255 at week 8, and N = 234 at week 12.

whose treatment was not interrupted had fewer concerns regarding the impact of their medications.

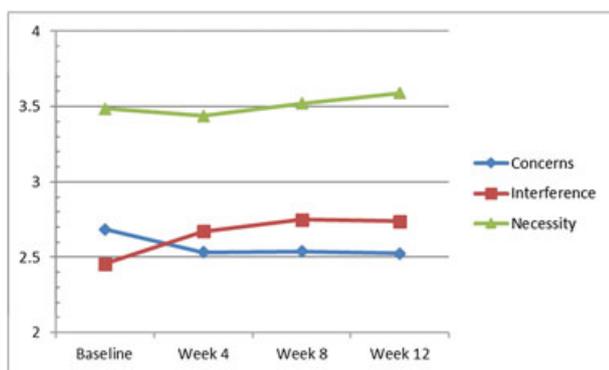
*Interference* scores increased significantly between baseline and week 4 then were relatively stable between weeks 4 and 12 (Figure 2 and Table 2). Higher symptom severity and male sex were associated with greater interference.

When physical function and CES-D scores were added to the longitudinal models as time-varying covariates, they were not significant and did not appreciably change the effects of other variables, therefore were not included in the final models.

**TABLE 2** Longitudinal models for BMQ subscales: coefficients, SEs, and significance of the effects of the explanatory variables

Explanatory Variable	Necessity			Concerns			Interference		
	Coefficient (SE)	T	P	Coefficient (SE)	T	P	Coefficient (SE)	T	P
Age	-0.0027 (0.28)	-0.80	0.42	0.0011 (0.003)	0.33	.74	0.0009 (0.004)	0.23	.82
Number of comorbid conditions	-0.02 (0.02)	-0.98	0.33	0.02 (0.02)	0.84	.40	0.03 (0.02)	1.62	.11
Sex									
Male	-0.13 (0.08)	-1.60	0.11	0.20 (0.08)	2.57	.01	0.17 (0.09)	1.95	.05
Female (ref)									
Trial arm									
Experimental	0.09 (0.08)	1.21	0.23	-0.05 (0.07)	-0.72	.47	-0.05 (0.08)	-0.58	.56
Control (ref)									
Symptom severity	0.0005 (0.001)	0.35	0.73	0.006 (0.0013)	4.54	<.01	0.02 (0.002)	13.24	<.01
Time									
Week 4	-0.04 (0.05)	-0.84	0.39	-0.15 (0.05)	-2.87	<.01	0.23 (0.07)	3.23	<.01
Week 8	0.04 (0.06)	0.66	0.51	-0.14 (0.06)	-2.28	.02	0.31 (0.08)	3.80	<.02
Week 12	0.11 (0.05)	2.28	0.02	-0.16 (0.04)	-3.49	<.01	0.29 (0.07)	4.33	<.01
Intake (ref)									
Drug category									
Cytotoxic agents	-0.25 (0.14)	-1.73	0.08	-0.14 (0.14)	-0.99	.32	0.55 (0.15)	3.61	<.01
Kinase inhibitors	-0.07 (0.14)	-0.48	0.60	0.07 (0.14)	0.54	.60	0.45 (0.15)	3.01	<.01
Other	0.01 (0.18)	2.34	0.94	-0.11 (0.18)	-0.62	.54	0.51 (0.19)	2.61	.01
Sex hormone inhibitors (ref)									
Oral agent stoppage									
Yes	Permanent: -0.50 (0.10)	-5.18	<.01	Temporary: 0.15 (0.06)	2.54	.01	Permanent: 0.20 (0.14)	1.46	.16
No (ref)									
Education									
Graduate or professional degree	-0.06 (0.12)	-0.51	0.61	-0.60 (0.11)	-5.33	<.01	-0.24 (0.12)	-1.90	.06
Some or completed college	-0.22 (0.10)	-2.39	0.02	-0.22 (0.09)	-2.47	.01	0.02 (0.10)	0.26	.80
High school or less (ref)									

Abbreviations: BMQ, Beliefs About Medications Questionnaire; SE, standard error.

**FIGURE 2** Least square means for the Beliefs About Medications Questionnaire necessity, concerns, and interference at 4 time points

## 5 | DISCUSSION

A new generation of oral oncolytic agents is transforming cancer treatment. At least a quarter (1/4) of all cancer agents in development are oral agents. Therefore, it is important to understand how events arising

during treatment with oral oncolytic agents affect patients' beliefs regarding the necessity, concerns, and interference they attribute to these medications. Consistent with other findings,<sup>23</sup> the 3 subscales have low to moderate interscale correlations, indicating that they reflect distinct constructs that change differently over time.

Patients' beliefs in the necessity of their medications did not change in the first 4 weeks then increased significantly between weeks 4 and 12. Concerns about medications declined in the first 4 weeks, with no change in weeks 8 to 12, and beliefs about medication interference steadily increased over time. With respect to necessity, the initial 4 weeks following the initiation of treatment appeared to be a time for deliberation. Following this initial period, patients altered their beliefs (stronger beliefs in the necessity of their medications, except for those where the medications were stopped; fewer concerns about its impact on future health; and a realization that the medications interfere with daily activities). However, changes in these beliefs are grounded in the events surrounding treatment. As symptom severity worsens, patients report greater concerns about how medications may affect their future health. Increasing symptom severity does not appear to affect beliefs about

necessity and may indicate that the treatment is working, and thus, medication is necessary to manage the cancer.

This research is among the first to show how patients' beliefs in the necessity of their medications decline when medications are withdrawn by the physician. Consistent with several cross-sectional studies of beliefs about different medication types,<sup>16,24</sup> we found that treatment interruptions may give rise to concerns that oral oncolytic agents are no longer managing their disease. At least 2 lines of explanation might be pursued. First, patients' beliefs regarding a medication may be mediated by oncologists' views of its efficacy. This explanation<sup>25</sup> points to the pivotal role that oncologists play in defining the necessity of treatment. Second, once stopped, patients may disavow the necessity of their medication as a form of reducing cognitive dissonance. While speculative, these explanations may guide future research regarding abrupt shift in necessity once cancer treatments are stopped.

Patients' concerns prompted by treatment interruption may produce a different type of reaction than concerns resulting from worsening symptoms. Interruptions suggest to patients that the medication is not tolerable while increasing symptoms may engender mixed reactions; on one hand, symptoms may indicate that the drug is working but concerns may be rising because patients may be unable to endure the consequences of the medication. Similar lines of research using other chronic diseases have reported how lack of self-efficacy was related to beliefs about necessity and concerns.<sup>13,26</sup> These data indicate that concerns regarding oral agents arise from different sources. Future research needs to explore how patients interpret and act upon concerns depending upon the factors that gave rise to them.

Regarding the effects of other factors on beliefs, differences according to sex and level of education were found, but comorbidity did not affect beliefs over and above other factors in longitudinal models. These findings are in contrast with those in type 2 diabetes, where differences in necessity beliefs by sex and comorbid conditions were found among patients on antihypertensive medications.<sup>26</sup> Lack of differences by sex and comorbidity in this study could be because of the difference in populations and the fact that oral oncolytic medications are often prescribed as the last available line of treatment. On the other hand, our findings on the influence of education on beliefs are similar to those reported among people with asthma.<sup>27</sup>

Finally, there were no effects of the adherence reminder and symptom management intervention on beliefs over and above symptom severity. This finding was expected because the intervention was not directed toward altering beliefs.

## 6 | CONCLUSIONS

In summary, patients' beliefs about the necessity of their cancer treatments are high, increase over time, and decline only when medications are permanently stopped. Male patients, those who report increasing severity of their symptoms, and those who experience temporary stoppages of their medications report increased concerns and interference of their medications with their lives. Since these factors remain significant in the multivariable model, they represent relatively independent contributions toward patients' level of concern.

## 6.1 | Limitations

The small numbers of racial and ethnic minorities limited assessment of how these variables affected beliefs. The follow-up period was very short given the long-term treatment among patients on these medications. Finally, during this short period, adherence was high and had little variation, which precluded the examination of the effects of beliefs on adherence.

## 6.2 | Clinical implications

Oncologists could be made aware of how medication adjustment occurs over time, introduce supportive and end-of-life care, and present it as a valuable next line of cancer management. Providers of supportive and end-of-life care could address patient beliefs about oral oncolytic medications as part of comprehensive patient care as patients move toward the end of life.

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## APPENDIX

### ORAL AGENT DRUG CATEGORIES

Cytotoxics	
Temodar (temozolomide)	7 (2.6)
Lonsurf (tipiracil and trifluridine)	1 (0.3)
Xeloda (capecitabine)	92 (33.8)
Kinase inhibitors	
BRC-ABL tyrosine kinase inhibitor	
Bosulif (bosutinib)	1 (0.3)
Gleevec (imatinib)	6 (1.8)
Sprycel (dasatinib)	2 (0.7)
Tasigna (nilotinib)	1 (0.3)
VEGF/VEGFR inhibitor	
Inlyta (Axitinib)	3 (1.1)
Nexavar (Sorafenib)	11 (4.0)
Sutent (Sunitinib)	8 (2.9)
Votrient (Pazopanib)	22 (8.1)
Lenvima (Lenvatinib)	1 (0.3)
Stivarga (Regorafenib)	9 (3.3)
EGFR HER2/neu	
Tarceva (erlotinib)	5 (1.8)
Gilotrif (afatinib)	1 (0.3)
Tykerb (lapatinib)	1 (0.3)
ALK inhibitor	
Xalkori (crizotinib)	4 (1.5)
Zykadia (ceritinib)	1 (0.3)
BRAF inhibitor	
Tafinlar (dabrafenib)	7 (2.6)
Phosphoinositide 3-kinase inhibitor	
Zydelig (idelalisib)	1 (0.3)
CDK inhibitor	
Ibrance (palbociclib)	36 (13.2)
Bruton tyrosine kinase inhibitor	
Imbruvica (ibrutinib)	7 (2.6)
Sex hormone inhibitors	
Xtandi (enzalutamide)	18 (6.6)
Zytiga (abiraterone acetate)	11 (4.0)
Other	
IMIDS	
Revlimid (lenalidomide)	10 (3.7)
Pomalyst (pomalidomide)	1 (0.3)
mTOR inhibitors	
Afinitor (everolimus)	11 (4.0)
PARP inhibitor	
Lynparza (olaparib)	1 (0.3)

Abbreviations: ALK, anaplastic lymphoma kinase; CDK, cyclin dependent kinase; EGFR, epidermal growth factor receptor; IMIDS, immunomodulatory; mTOR, mechanistic target of rapamycin; PARP, poly adenosine diphosphate ribose polymerase; VEGF, vascular endothelial growth factor; VEGFR, vascular endothelial growth factor receptor.