Original Article

An Automated Intervention Did Not Improve Adherence to Oral Oncolytic Agents While Managing Symptoms: Results From a Two-Arm Randomized Controlled Trial

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Abstract

Context. An increasing number of oral cancer treatments require patient adherence and symptom self-management.

Objectives. The report presents the effects of a medication reminder and symptom management intervention directed at patients initiating new oral oncolytic agents.

Methods. Patients ($N = 272$) were recruited at six comprehensive cancer centers, interviewed over the telephone after oral agent initiation, and randomized to either standard care or a medication reminder and symptom management intervention. In the intervention arm, the automated system called patients daily to remind them about taking their medications and weekly to assess 18 symptoms and refer patients to a printed *Medication Management and Symptom Management Toolkit*. Severity of 18 symptoms was also assessed during telephone interviews at Week 4 (midintervention), Week 8 (postintervention), and Week 12 (follow-up). Adherence was measured using the relative dose intensity, the ratio of dose taken by patient out of dose prescribed by the oncologist, and assessed using pill counts at Weeks 4, 8, and 12 and prescribing information from medical records.

Results. The relative dose intensity was high and did not differ by trial arm. Symptom severity was significantly lower ($P < 0.01$) in the experimental arm at Week 8 but not at Weeks 4 or 12.

Conclusion. Adherence may be less of a problem than originally anticipated, and intervention was not efficacious possibly because of already high rates of patient adherence to oral oncolytic medication during first 12 weeks. Longer follow-up in future research may identify subgroups of patients who need interventions to sustain adherence. J Pain Symptom Manage 2018;56:727–735.

Key Words

Cancer, oral agents, symptom management, adherence

Introduction

An increasing number of cancer treatments are now approved in oral form. Many of these drugs have complicated dosing schedules and require adherence rates of greater than 80% to the Food and Drug Administration (FDA)-approved dosing to achieve a therapeutic effect.[1] The transition from infusion chemotherapy to an oral route has significant implications for patients. In exchange for eliminating the need for frequent trips and extended time in infusion units, patients must adhere to their medication regimens and recognize early on the need to manage their symptoms and side effects with less reliance on

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interactions with oncology professionals. This article reports the results from a 12-week two-arm randomized trial that tested a telephone adherence and symptom management intervention among patients newly prescribed oral oncolytic agents. If randomized to the intervention arm, patients received telephone daily reminders to take their medication tailored to the specific medication regimen. In addition, each week, telephone symptom assessment was performed for all patients, and those in the intervention arm were asked to use strategies from the printed symptom management toolkit for symptoms above predefined threshold. The following research questions were addressed. First, when compared against standard care and symptom assessments only, did patients who received the reminder and symptom management intervention have better adherence to the medication in the first 12 weeks? Second, did patients who received the reminder and symptom management intervention report lower symptom severity over 12 weeks? Third, are lower symptoms associated with better adherence?

Patient adherence to medications is influenced by multiple factors that lie between the provider prescription and patient consumption.[2–7] This research considers the relative dose intensity (RDI), a ratio of dose consumed by the patient to the dose prescribed by the oncologist.[8–10] Unlike medications for other chronic conditions, where dosing is established and remains relatively stable over time, dosing of oral oncolytic agents may undergo adjustments by oncologists because of patients' conditions and treatment-related symptoms and side effects. As a result, the prescribed doses may change over time creating new challenges for patient adherence and necessitating dynamic calculations of the RDI that account for dose changes. These changes also warrant the considerations of the dose consumed by patients out of the FDA-recommended dose and examining symptoms as a potential factor influencing adherence.

Methods

Sample

For this trial, patients were recruited between 2013 and 2017 from six National Cancer Institute-designated comprehensive cancer centers. The institutional review boards at each cancer center approved this trial. The inclusion criteria were as follows: 21 years or older, Eastern Cooperative Oncology Group score of 0–2 or Karnofsky score of ≥50, able to read and speak English, had a cellular or a landline telephone, and a new prescription of any one of 33 FDA-approved oral oncolytic agents selected according to their FDA approval and emerging use in treating prevalent cancers (Table 1; 28 agents prescribed to consented patients). Patients were excluded if they were prescribed preventive and adjuvant medications for breast cancer, such as tamoxifen, raloxifene, and aromatase inhibitors. The rationale for enrolling patients at the time of initiation of the oral agent was to intervene at the time when patients were forming a new medication-taking behavior to prevent suboptimal adherence. Based on their mechanisms of action, oral oncolytic agents were collapsed into four categories: cytotoxic agents, kinase inhibitors, sex hormone inhibitors, and others. Dosages of these oral oncolytic medications were either continuous (taken every day) or intermittent with cycles, which included days when a medication was to be

Table 1
Oral Agents With Counts and Percents of Patients Out of the Total Sample ($N = 272$) for Each Drug

Cytotoxics	
Temozolomide	7 (2.6)
Tipiracil & trifluridine	1 (0.3)
Capecitabine	92 (33.8)
Kinase inhibitors	
BRC-ABL tyrosine kinase inhibitor	
Bosutinib	1 (0.3)
Imatinib	6 (1.8)
Dasatinib	2 (0.7)
Nilotinib	1 (0.3)
VEGF/VEGFR inhibitor	
Axitinib	3 (1.1)
Sorafenib	11 (4.0)
Sunitinib	8 (2.9)
Pazopanib	22 (8.1)
Lenvatinib	1 (0.3)
Regorafenib	9 (3.3)
EGFR HER2/neu	
Erlotinib	5 (1.8)
Afatinib	1 (0.3)
Lapatinib	1 (0.3)
ALK inhibitor	
Crizotinib	4 (1.5)
Ceritinib	1 (0.3)
BRAF inhibitor	
Dabrafenib	7 (2.6)
Phosphoinositide 3-kinase inhibitor	
Idelalisib	1 (0.3)
Cyclin-dependent kinase inhibitor	
Palbociclib	36 (13.2)
Bruton's tyrosine kinase inhibitor	
Ibrutinib	7 (2.6)
Sex hormone inhibitors	
Enzalutamide	18 (6.6)
Abiraterone acetate	11 (4.0)
Other	
Immunomodulatory	
Lenalidomide	10 (3.7)
Pomalidomide	1 (0.3)
mTOR inhibitors	
Everolimus	11 (4.0)
Poly(ADP-ribose) polymerase inhibitor	
Olaparib	1 (0.3)

BRC-ABL = Breakpoint cluster region—Abelson; VEGF/EGFR = Vascular endothelial growth factor—epidermal growth factor receptor; HER2/neu = human epidermal growth factor receptor 2; ALK = anaplastic lymphoma kinase; mTOR = mammalian target of rapamycin; ADP = Adenosine diphosphate ribose.

taken followed by rest periods. Nurses, clinical pharmacists, or premedical students approached patients who were scheduled to initiate oral agents, verified eligibility criteria, explained the study, and obtained informed consent.

Trial Design

Recruiters collaborated with cancer center medical oncologists who identified patients initiating one of the selected oral agents. Recruiters approached patients, explained the study, and gave consented patients a folder with a copy of their consent form, a passcode patients selected for telephone calls, and numbers to call if they had questions or encountered problems. Patients indicated a preferred time that they wished to be called. Recruiters collected information on dosage, frequency, and cycle of the oral agent, and then forwarded this information to the study office. These data were used to program the interactive voice response (IVR) system that made daily medication reminder calls to patients randomized to the intervention arm.

After enrollment, patients completed a baseline interview within one to three days of starting their oral oncolytic medication. After the initial interview, patients were randomized to either the intervention or the standard care control arm using a minimization algorithm that was run from the central study office to ensure concealment. The algorithm balanced trial arms for recruitment location, site of cancer, regimen complexity (continuous vs. intermittent dosing), concurrent IV chemotherapy, and level of depressive symptoms, which are known to affect adherence[8] to medications for chronic conditions and enactment of self-management strategies.[11] Subsequent interview data were collected via telephone at Week 4 (trial midpoint), Week 8 (trial endpoint), and Week 12 (follow-up). Interviewers were blinded to trial arm assignment.

Adherence and Symptom Management Intervention

Patients randomized to the intervention arm received daily adherence reminder calls and weekly symptom assessment and management calls delivered by an IVR system.

Adherence Reminders. Each daily reminder call, delivered via a professionally recorded voice, began with a question of whether the oncologist stopped the medication. If yes, all calls were stopped, and the project manager contacted the site to determine if the oral agent stoppage was permanent or temporary. If a patient's response was no, then the patient was reminded to take his or her oral agent(s) for that day. If a medication had a scheduled rest period, the reminder call was not placed. The goal of the daily reminder intervention was to help patients adopt the behavior of taking the medication as prescribed through establishment of a routine. At the beginning of Week 5, patients had the option of continuing daily calls or reducing calls to every other day.

Symptom Assessment and Management. During Weeks 2–8, patients in both arms were queried by the IVR as to whether they had taken their medications as prescribed and whether they experienced any of 18 cancer-related or treatment-related symptoms. If a symptom was present, its severity was assessed on a one to nine scale. For each of the first eight weekly calls, patients in the intervention arm who reported any symptom at a severity of ≥4 (threshold) were referred to the *Medication Management and Symptom Management Toolkit* (the toolkit),[12] which was mailed to them after randomization. The threshold of four was selected based on the National Comprehensive Cancer Network for symptom monitoring and management.[13] The toolkit, written at an eighth grade level, uses a frequently asked question format, defines the symptom, its possible causes, and lists specific evidence-based strategies patients can use to alleviate the symptom.[12–14] Separate sections of the toolkit were devoted to oral cancer medication management (adherence, storage, disposal, travel, and financial assistance). The adherence section emphasized the importance of taking medication as prescribed by the physician, tips for patients on how to maintain adherence, and lists of problems for which patients should contact their oncologist.

Control Condition. Patients randomized to the control arm received weekly standard care and symptom assessment calls delivered by an IVR system.

Measures

Adherence. Dose taken for each of three 4-week periods (intake to Week 4, Week 5–8, and Week 9–12) was determined based on pill counts and prescription label information on the bottle at time of enrollment, Weeks 4, 8, and 12, accounting for the number of refills and number of pills per bottle. During four-, eight-, and 12-week interviews, patients were asked to pour pills on a clean napkin, use a kitchen utensil to count pills, report the count to the interviewer, and to return pills to their container. Similarly, patients reported information on script labels and counted medications in each blister pack. Dose prescribed for each of the three 4-week periods was determined based on the health record information, accounting for cycling, dose changes, and temporary and permanent stoppages in each 4-week period. For example, if medication was stopped for one of four weeks, the prescribed dose was based on three weeks when patient was directed to

take the medication by the oncologist. The RDI, ratio of dose taken to dose prescribed (primary outcome), was then calculated for each four-week period to reflect patient's medication-taking behavior. To facilitate the interpretation of the RDI, we have also calculated the ratio of dose taken to the FDA-approved dose. The difference between the RDI and the ratio of dose taken to FDA-approved dose is in the denominator: for the RDI, physician-directed stoppages and dose changes were subtracted to arrive at what the patients were dynamically directed to take by the physicians; whereas the FDA-recommended dose was fixed and based on the medication insert information.

Symptoms. Eighteen symptoms were assessed during interviews, and weekly calls were selected based on their reported frequency in the inserts for the selected oral agents and prevalence in our prior research studies:[15–18] pain, fatigue, sleep disturbance, anxiety, weakness, headaches, skin rash, numbness or tingling, redness or peeling in hands or feet, swelling, joint pain, mouth sores, lack of appetite, nausea or vomiting, diarrhea, constipation, cough, and shortness of breath. Patients were asked if, in the past seven days, they had experienced each symptom and, if yes, to rate its severity on a scale from one to nine resulting in a summed severity index ranging from 9 to 162. This index was the secondary outcome of the trial and analyzed at Weeks 4, 8, and 12. To facilitate the interpretation, we have also analyzed the number of symptoms at four or higher (threshold used in the symptom management intervention) at Weeks 4, 8, and 12.

Sociodemographic measures were obtained during baseline interview. Depressive symptoms were assessed during interviews using the Center for Epidemiologic Studies—Depression 20-item scale.[19] Cronbach's alpha exceeded 0.90 in this sample.

Sample Size

The study was powered using both the continuous RDI and indicator of underadherence defined as RDI <0.80.[20] For planning purposes, we used the projected underadherence rate of 35% and its reduction to 18% for the intervention arm, based on our preliminary work and the literature.[21,22] For power of 0.80 or greater in two-sided tests comparing two independent proportions (underadherence rate by trial arm) at 0.05 level of significance, the sample size required to detect this difference was 105 patients per arm. To account for projected 23% attrition, we planned to randomize 274 patients. When adherence was measured using approximately continuous RDI measure, the sample size of 105 per arm was sufficient to detect mean RDI arm differences of 0.39 of the SD at any one time point. For the secondary outcome of symptom severity, the analysis plan included the adjustment for symptom severity at intake, which led to a detectable effect size of 0.36 of the SD at each time point. Detectable effect sizes were even larger in longitudinal analyses that included three repeated measures.

Statistical Analyses

Distributions of the adherence and symptom severity measures were evaluated. Proportions of underadherent patients for each of three 4-week periods were compared using Fisher's exact test. Three repeated measures of the RDI and ratio of consumed to FDA-recommended dose (baseline to Week 4, Weeks 5–8, and Weeks 9–12) were analyzed using longitudinal linear mixed-effects (LME) model with the first-order autoregressive covariance structure. The LME modeling generalizes classical analysis of repeated measures and allows for the modified intent to treat approach under data missing at random assumption, so that all patients who completed at least one postrandomization assessment (Weeks 4, 8, or 12) were included, with no need for imputations under missing at random. The following covariates were entered in the LME models: trial arm, time, and trial arm by time interaction, and factors used to balance randomization. We have also adjusted for the drug category to control for different types of oral oncolytic medications prescribed to patients. The least square means by trial arm were output from the LME models at each time, and differences by trial arm were tested at each time point. To gauge the robustness of findings, the comparisons of the adjusted least square means were complemented by the comparisons of the unadjusted means using the two-sample t-tests.

Similar analytic approach was used to evaluate three repeated measures of the summed symptom severity index and the number of symptoms above threshold at Weeks 4, 8, and 12, with baseline version of each symptom outcome included as a covariate in the respective model.

Finally, to explore the relationship between symptom severity and adherence, repeated symptom measures at intake and Weeks 4 and 8 were entered as a time-varying covariate into the LME models for the repeated measures of RDI described previously. The direction and significance of the association was determined based on the model coefficient for the symptom variable.

Results

The mean sample age was 61 (SD 12), and 50% were males (Table 2).

A total of 233 patients completed Week 4; six patients who skipped Week 4 completed Week 8 or 12,

Table 2
Descriptive Statistics for the Sample at Baseline

Characteristic	Experimental Arm, *N* (%)	Control Arm, *N* (%)
Sex		
Male	67 (49)	69 (51)
Race		
African American	10 (7.3)	12 (9)
Caucasian	127 (92.7)	120 (89)
Other/unknown	0 (0)	3 (2)
Ethnicity		
Hispanic or Latino	2 (1.5)	3 (2)
Level of education		
High school or less	31 (22.6)	40 (29.6)
Some or completed college	79 (57.7)	71 (52.6)
Graduate or professional degree	25 (18.2)	24 (17.8)
Unknown	2 (1.5)	0 (0)
Drug category		
Cytotoxic agents	50 (36.5)	45 (33.3)
Kinase inhibitors	64 (46.7)	63 (46.7)
Sex hormone inhibitors	14 (10.2)	13 (9.6)
Other	9 (6.6)	14 (10.4)
Site of cancer		
Breast	27 (20)	30 (22)
Colorectal	21 (15)	20 (15)
Gastrointestinal	7 (5)	10 (7)
Leukemia	9 (6.5)	7 (5)
Liver	8 (6)	4 (3)
Lung	5 (4)	5 (4)
Lymphoma	2 (1.5)	1 (0.7)
Melanoma	6 (4)	2 (1.5)
Myeloma	3 (2)	4 (3)
Pancreatic	12 (9)	15 (11)
Prostate	13 (9.5)	13 (10)
Renal	15 (11)	9 (7)
Sarcoma	4 (3)	11 (8)
Brain	1 (0.5)	1 (0.7)
Esophageal	2 (1.5)	1 (0.7)
Other	2 (1.5)	2 (1.4)
	Mean (SD)	
Age	60.60 (12.6)	62.20 (11.9)
Number of symptoms above threshold	3.12 (3.06)	3.39 (3.27)
Summed symptom severity	22.58 (21.26)	24.36 (22.47)

thus 239 patients were analyzed in the LME models (intervention: $N = 122$; control: $N = 117$). Among those who dropped out, no differences by trial arm were found on sociodemographic, disease, treatment characteristics, or symptom severity at baseline. After the initial four weeks of daily reminders, 40% of patients in the intervention arm chose to continue with daily reminders, 38% switched to every other day, and 22% requested that their calls be stopped because they were remembering to take their oral oncolytic medications. According to patient requests, the reminder schedule was adjusted, but the symptom management part of the intervention proceeded as planned. There were no differences in RDI at Weeks 5–8 or 9–12 among patients according to their choice of frequency of daily reminders after four weeks.

More than 70% of patients completed their weekly calls (Fig. 1). Of those who completed the call each week, more than one-third said that they had used the toolkit during previous week. Approximately 75% of patients reported using the toolkit at each of Weeks 2–8, had at least one symptom above threshold during the previous week, and the remaining 25% used the toolkit although their symptoms were below four in severity. Among patients who did not use the toolkit, more than 75% stated that the reason was that their symptoms were not bothersome.

Only one patient was underadherent (RDI <0.8) at Week 4; eight patients (four in each arm) were underadherent at Week 8; and none were underadherent at Week 12, with no differences by trial arm. The analyses of the continuous RDI yielded the same conclusion of high RDI with no differences by trial arm (Table 3). The ratios of dose taken to dose directed by the oncologists (accounting for interruptions) averaged 89%–96% in both unadjusted and adjusted longitudinal analyses. The ratio of dose taken by patients to the FDA-recommended dose averaged 69%–75% (Table 3).

Symptom severity was significantly lower in the experimental arm at Week 8 (immediately after intervention) but not at Week 4 (midintervention) or Week 12 (follow-up) (Table 4). The results for the mean number of symptoms above threshold were similar, with the experimental arm having on average one fewer symptom than the control arm at Week 8. For both symptom severity index and number of symptoms, differences between trial arm at Week 8 were about one-third of the SD at baseline, which is often deemed clinically significant in patient-reported outcomes literature.[23] This difference was reduced at Week 12 (Table 4).

Finally, the association between symptom severity and adherence was in the expected direction, that is, more severe symptoms at the beginning of the four-week period (intake, Week 4, or Week 8) were associated with lower RDI over the subsequent four weeks, but this association was not statistically significant for either the summed severity index or the number of symptoms over threshold.

Discussion

This research considered patient's adherence to their prescribed dose of new oral oncolytic medication. The RDI was high according to the existing standards.[1] Consistent with other research that reported high rates of adherence to oral oncolytic medications,[24–26] this intervention failed to improve already high adherence observed among patients who received standard instructions and care. Data

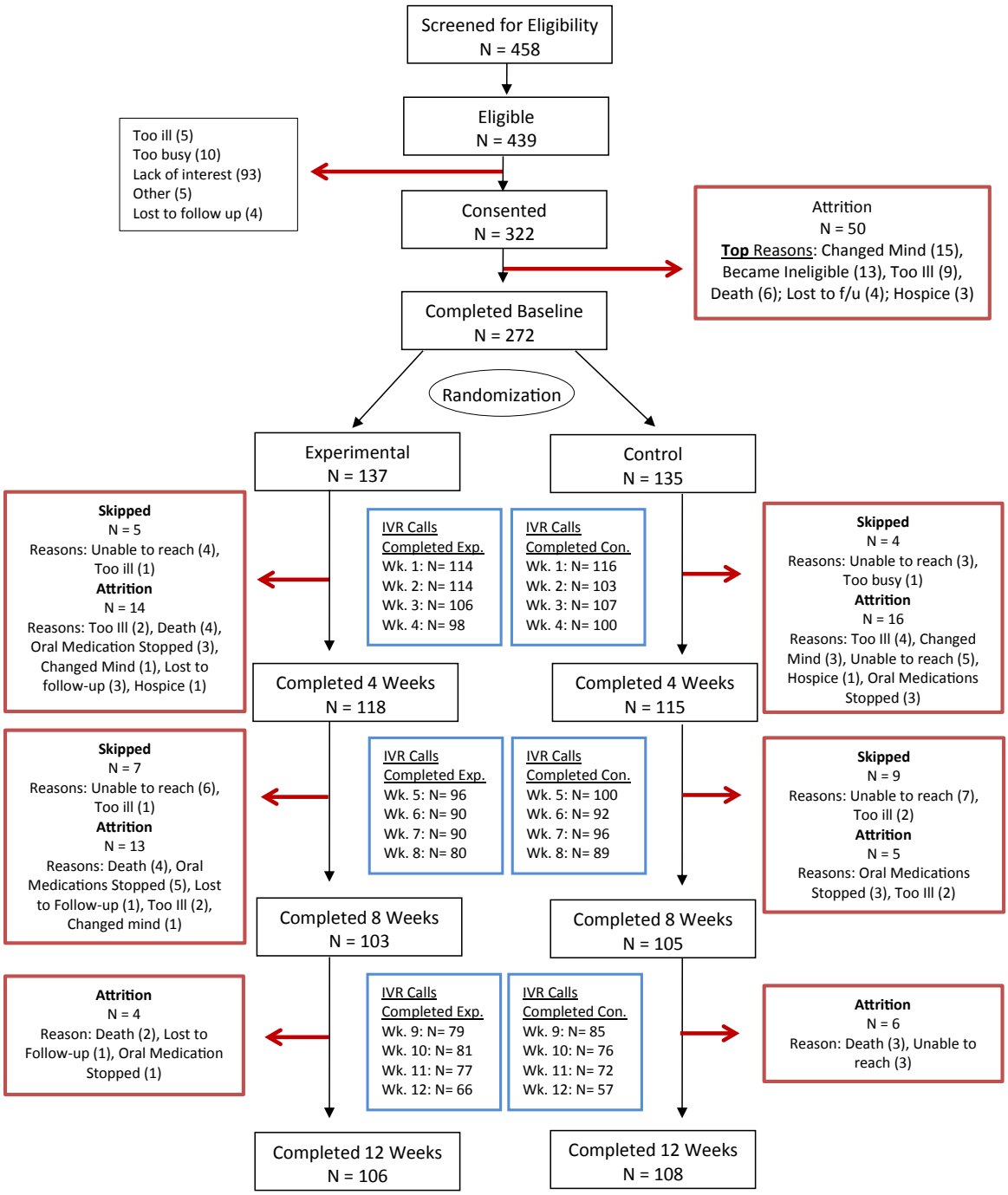

Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) diagram. IVR = interactive voice response.

from this trial indicate that patients had no difficulty remembering to take their medications, and high RDI was sustained during the first three 4-week periods, despite dose adjustments ordered by the oncologists and the complexity of the regimens.

This finding differs from lower adherence rates to medications reported for other chronic conditions.[27,28] Moreover, it was in contrast with the higher nonadherence rates found in our pilot data, which were used to inform this trial. One possible explanation is that patients in the pilot study[21,22] were further into their course of treatment and could have been more likely not to adhere to their regimen compared with these patients who were initiating treatment. Second, pilot work adherence was measured using patient self-report, and measurement did not start at the time of medication initiation, which could have led to biased estimates. Third, in this trial, patients were

Table 3
Unadjusted and Adjusted Means of RDI and Ratio of Dose Taken to FDA-Approved Dose by Trial Arm and Period

	Unadjusted			Adjusted		
	Experimental Arm	Control Arm	95% CI for Trial Arm Difference	Experimental Arm	Control Arm	95% CI for Trial Arm Difference
Dose per Time Period	Mean (SE)		*P*	Mean (SE)		*P*
Baseline to Week 4						
RDI	0.94 (0.01)	0.95 (0.01)	−0.03, 0.01 0.35	0.94 (0.01)	0.95 (0.01)	−0.04, 0.02 0.44
Ratio of dose taken to FDA-approved dose	0.75 (0.03)	0.82 (0.03)	−0.14, 0.02 0.11	0.75 (0.03)	0.80 (0.03)	−0.13, 0.02 0.16
Weeks 5–8						
RDI	0.96 (0.01)	0.97 (0.01)	−0.10, 0.03 0.33	0.95 (0.01)	0.97 (0.01)	−0.04, 0.02 0.50
Ratio of dose taken to FDA-approved dose	0.75 (0.033)	0.77 (0.04)	−0.11, 0.07 0.59	0.73 (0.03)	0.76 (0.03)	−0.11, 0.06 0.53
Weeks 9–12						
RDI	0.89 (0.03)	0.92 (0.03)	−0.11, 0.07 0.62	0.90 (0.02)	0.92 (0.02)	−0.07, 0.03 0.39
Ratio of dose taken to FDA-approved dose	0.75 (0.06)	0.73 (0.06)	−0.15, 0.19 0.81	0.69 (0.05)	0.73 (0.05)	−0.15, 0.09 0.58

RDI = relative dose intensity; FDA = Food and Drug Administration.

queried weekly as to their adherence; this alone may have been adequate to sustain high rates of adherence and render daily reminders unnecessary. Future work might consider a run-in period with monitoring of adherence followed by enrollment of only those patients who demonstrate declining adherence. This would address two questions, where currently there is little evidence: what patient, disease, and treatment characteristics are associated with earlier declines in adherence; and what is the minimal intervention needed to restore and sustain therapeutically effective levels of adherence.

Compared with standard care, the self-management intervention lowered symptom severity at Week 8, but this effect was not sustained at Week 12. This finding is in contrast with our past work where a similar intervention had sustained effects.[18] The symptom management intervention reduced severity and number of symptoms at Week 8, but once the intervention concluded, patients were not able to sustain ongoing self-management. Reasons for this could be advanced disease for which oral agents represent the last available line of treatment and prior treatments leading to reduced efficacy of self-care strategies.

A common theme in systematic reviews of strategies to improve adherence among oral oncolytic medications is the low quality of the studies.[24,29,30] This trial overcame some of these weaknesses. Patients were recruited from multiple centers, objective measures of adherence were used, and use of IVR systems assured

Table 4
Unadjusted and Adjusted Means of Symptom Outcomes by Trial Arm and Period

	Unadjusted			Adjusted		
	Experimental Arm	Control Arm	95% CI for Trial Arm Difference	Experimental Arm	Control Arm	95% CI for Trial Arm Difference
Symptom Assessments per Time Period	Mean (SE)		*P*	Mean (SE)		*P*
Week 4						
Number of symptoms above threshold	2.58 (0.28)	3.04 (0.29)	−1.26, 0.34 0.26	2.46 (0.24)	2.84 (0.24)	−0.97, 0.21 0.21
Summed symptom severity	20.51 (1.98)	22.86 (1.94)	−7.82, 3.11 0.40	19.26 (1.57)	21.74 (1.60)	−6.02, 1.83 0.21
Week 8						
Number of symptoms above threshold	1.88 (0.23)	2.83 (0.26)	−1.63, −0.26 <0.01	1.91 (0.24)	2.72 (0.24)	−1.41, −0.19 0.01
Summed symptom severity	14.56 (1.38)	20.93 (1.70)	−10.70, −2.04 <0.01	14.62 (1.65)	20.20 (1.65)	−9.53, −1.38 <0.01
Week 12						
Number of symptoms above threshold	2.18 (0.28)	2.36 (0.25)	−0.91, 0.56 0.64	1.94 (0.24)	2.35 (0.24)	−1.02, 0.21 0.19
Summed symptom severity	16.70 (1.79)	17.35 (1.55)	−5.32, 4.03 0.78	14.98 (1.63)	17.47 (1.63)	−6.75, 1.40 0.22

consistent assessment and intervention delivery. Multiple drugs were incorporated into the design to extend generalizability of findings over and above a single agent or class of agents. Our analyses involved three periods since patients' initiation of new oral oncolytic agents.

Against these strengths, several important limitations are recognized. First, pill counts may not be the best measure of adherence, especially in large studies where counts are conducted monthly and via telephone. In this study, actual pill counts were less of a problem than tracking refills and the combining of existing oral medications with newly received vials of medications.[31] Because we were most interested in establishing adherence and self-management behaviors after the initiation of treatment, this study did not follow patients' extended course of treatments, and thus we do not know their ultimate outcomes or have clinical evidence to define disease progression.

In conclusion, this study confirms other reports of high rates of patient adherence to oral oncolytic medications.[24,26,29,32] Adherence may be less of a problem than originally anticipated.[33] Symptom management requires ongoing support and appears not sustainable by patients alone.

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