

Perspectives on Adherence and Persistence With Oral Medications for Cancer Treatment

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As oral cancer therapies are developed, a high degree of persistence and adherence is necessary for optimal outcomes. Ensuring persistence, continuing treatment for the prescribed duration, and adherence—taking medication as prescribed—has been a challenge to patient management and health care cost containment in real-world settings.¹ It may appear as though persistence and adherence to oral cancer therapies is superior to that observed with oral noncancer therapies.² Indeed, patients with cancer tend to be highly motivated, to prefer oral therapies, and to exhibit high persistence and adherence in clinical trials.³ However, emerging real-world data indicate otherwise.

Persistency rates for oral cancer medications are generally lower in real-world settings compared with in clinical trials (Table 1),⁴⁻²⁰ especially for chronically administered medications. Persistence with tamoxifen at 3.9 years was 71.7% in the Arimidex, Tamoxifen Alone or in Combination (ATAC) trial,⁶ but persistence was only 64.8% at 3.5 years among women identified in a pharmacy database.⁵ The difference may be more pronounced in the elderly.^{9,12} Similarly, persistence with letrozole was 84% at 4.25 years in the Breast International Group 1-98 trial,⁵ but it was only 77% at 1 year in an analysis of two large-claims databases (data on file, Novartis, East Hanover, NJ). This difference remains despite inclusion of 23% of patients with a \geq 30-day treatment gap (Figure 1). Differences were not limited to patients with breast cancer. In the IRIS (International Randomized Study of Interferon Versus ST1571) trial, patients with chronic myelogenous leukemia (CML) persisted with imatinib at a rate of 91% at 19 months.⁴ By contrast, real-world persistence at 12 and 24 months among patients with CML and GI stromal tumors was 56% and 41%, respectively, when dosing gaps \geq 30 days were disallowed (data on file, Novartis, East Hanover, NJ). In addition, pharmacy records from 4,043 patients demonstrated a decrease in imatinib persistence from 100% to 23% between months 4 and 14 of treatment.²¹

There is less information on adherence compared with persistence in clinical trials. In the adherence companion study 60104 to Cancer and Leukemia Group B 49907, adherence to capecitabine in elderly patients with breast cancer was 78% during the prescribed six cycles of therapy.¹⁸ In the real world, a 96.7% adherence was observed.²⁰ However, capecitabine is not a chronic therapy, and in this study, adherence was measured for only 44.3 days (two cycles). The majority of adherence data is from the real-world setting, and these have shown variability (Table 1). Analysis of

claims data demonstrated 89% adherence to imatinib among patients with CML at 1 year when unlimited dosing gaps were allowed (data on file, Novartis, East Hanover, NJ). It was 78% at 2 years according to pharmacy records.²¹ Among patients with breast cancer, 54% to 80% of patients receiving hormonal therapy have been shown to adhere to treatment (data on file, Novartis, East Hanover, NJ).⁷

Poor adherence could potentially lead to serious clinical and economic consequences.²²⁻²⁵ In a study of tamoxifen-treated patients with breast cancer, lower than 80% adherence at 2.4 years was associated with an increased risk of death.²⁶ Furthermore, 90% of highly adherent patients with CML achieved a major cytogenetic response versus 60% of less adherent patients.²⁷ Adherence to imatinib of more than 90% and \leq 90% were associated with 94.5% and 28.4% probability, respectively, of a major molecular response at 6 years.²⁷ In the ADAGIO (Adherence Assessment With Gleevec: Indicators and Outcome) study, complete cytogenetic response was correlated with fewer treatment gaps during a 90-day period among patients with CML.²⁴

Nonadherence may be associated with increased resource use and costs. Patients with lower than 85% adherence during the first-year of imatinib therapy had higher inpatient costs, nonimatinib pharmacy costs, and outpatient costs compared with those with \geq 85% adherence.²⁵ Thus, physicians should identify barriers to persistence and adherence and develop strategies to optimize therapeutic benefits, especially when therapy may be prolonged.

Factors associated with nonadherence include disease complexity, poor communication, use of retail pharmacies, higher copayments, patient perceptions and motivations, and many others.^{28,29} Education, improved dosing, and good communication may increase adherence rates.³⁰ Strategies include emphasizing the value of the prescribed regimen, simplifying the regimen, encouraging use of medication-taking systems, obtaining caregiver assistance, and reinforcing desirable behavior. When nonpersistence and nonadherence are measured together, the extent of the problem is magnified. A recent study demonstrated that only 49% of patients with breast cancer took adjuvant hormonal therapy at the prescribed schedule and duration. Thus, minimizing the potential negative impact of nonadherence and nonpersistence seems prudent, given patients' preference for oral cancer therapies. Physicians, policy makers, and health plans need to develop effective strategies that drive adherence and persistence to ensure that patients derive the best

Table 1. Variability in Adherence and Persistence Rates in Clinical Trials and the Real-World Setting

Therapy	Persistence*				Adherence			
	Clinical Trial Setting		Real-World Setting		Clinical Trial Setting		Real-World Setting	
	% of Patients	Duration (years)	% of Patients	Duration (years)	% of Patients	Duration (years)	% of Patients	Duration (years)
Imatinib (CML)	91 ⁴	1.67 ⁴	56 [†]	1 [†]	NA	NA	89% rate of adherence ^{†‡}	1 [†]
			41 [†]	2 [†]				
Letrozole (breast cancer)	84 ⁵	4.3 ⁵	77 [†]	1 [†]	NA	NA	54 ^{†§}	1 [†]
Anastrozole (breast cancer)	75.9 ⁶	3.9 ⁶	NA	NA	NA	NA	69 ^{7¶}	1 ⁷
							69-78 ^{8¶}	1 ⁸
							50-68 ^{9¶}	3 ⁸
Tamoxifen (breast cancer)	71.7 ⁶	3.9 ⁶	77.9 ¹⁰	1 ¹⁰	NA	NA	80 ^{7¶}	1 ⁷
	84 ⁵	4.3 ⁵	64.8 ¹⁰	3.5 ¹⁰			77 ^{13¶}	1 ¹³
	77 ⁹	5 ⁹	≥ age 65 years:	≥ age 65 years:				
			83 ¹¹	2 ¹¹				
Aromatase inhibitors (breast cancer)			93 ¹⁴	1.3 ¹⁴				
Hormonal therapy (breast cancer)			68 ¹⁵	4.5 ¹⁵			72 ^{15†}	4.5 ¹⁵
Aromatase inhibitors and tamoxifen (breast cancer)			94 ¹⁶	1 ¹⁶				
			77 ¹⁶	55 ¹⁶				
Antiestrogen therapy (breast cancer)							≤ age 40 years: 37 ^{17†}	≤ age 40 years: 2.3 ¹⁷
Capecitabine (breast or breast/colon cancers)	83 ¹⁸	0.35 ¹⁸			78 ^{18¶}	0.35 ¹⁸	96.7% rate of adherence ²⁰	0.12 ²⁰
					96 ¹⁹	0.29 ¹⁹		

Abbreviations: CML, chronic myelogenous leukemia; NA, not applicable; MEMS, microelectric monitoring system.

* Continued treatment. In clinical trials, patients who discontinued therapy as a result of recurrence or death were considered to persist with therapy.

† Data on file, Novartis, Summit, NJ.

‡ Days supplied divided by days elapsed.

§ Patients with a treatment gap of 0-29 days.

¶ ≥ 80% medication possession ratio or doses recorded by MEMS.

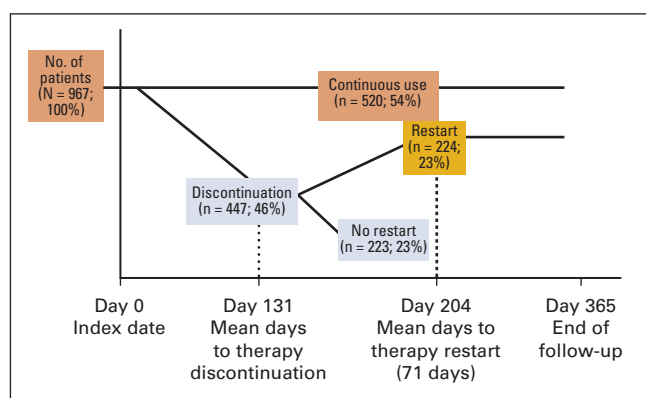


Figure 1. The patients who persisted with letrozole either continued therapy (54%) or had a therapy gap but reinitiated treatment by the end of the year (23%; data on file, Novartis, East Hanover, NJ).

therapeutic outcomes while reducing resource use and health care costs.

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