Original Article

Breast Cancer Patients' Insurance Status and Residence Zip Code Correlate With Early Discontinuation of Endocrine Therapy: An Analysis of the ECOG-ACRIN TAILORx Trial

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BACKGROUND: Early discontinuation is a substantial barrier to the delivery of endocrine therapies (ETs) and may influence recurrence and survival. The authors investigated the association between early discontinuation of ET and social determinants of health, including insurance coverage and the neighborhood deprivation index (NDI), which was measured on the basis of patients' zip codes, in breast cancer. **METHODS:** In this retrospective analysis of a prospective randomized clinical trial (Trial Assigning Individualized Options for Treatment), women with hormone receptor–positive, human epidermal growth factor receptor 2–negative breast cancer who started ET within a year of study entry were included. Early discontinuation was calculated as stopping ET within 4 years of its start for reasons other than distant recurrence or death via Kaplan-Meier estimates. A Cox proportional hazards joint model was used to analyze the association between early discontinuation of ET and factors such as the study-entry insurance and NDI, with adjustments made for other variables. **RESULTS:** Of the included 9475 women (mean age, 55.6 years; White race, 84%), 58.0% had private insurance, whereas 11.7% had Medicare, 5.8% had Medicaid, 3.8% were self-pay, and 19.1% were treated at international sites. The early discontinuation rate was 12.3%. Compared with those with private insurance, patients with Medicaid (hazard ratio [HR], 1.53; 95% confidence interval [CI], 1.23-1.92) and self-pay patients (HR, 1.65; 95% CI, 1.25-2.17) had higher early discontinuation. Participants with a first-quartile NDI (highest deprivation) had a higher probability of discontinuation than those with a fourth-quartile NDI (lowest deprivation; HR, 1.34; 95% CI, 1.11-1.62). **CONCLUSIONS:** Patients' insurance and zip code at study entry play roles in adherence to ET, with uninsured and underinsured patients having a high rate of treatment nonadherence. Early identification of patients at risk may improve adherence to therapy. ***Cancer* 2021;127:2545-2552**. © *2021 American Cancer Society*.

LAY SUMMARY:

- In this retrospective analysis of 9475 women with breast cancer participating in a clinical trial (Trial Assigning Individualized Options for Treatment), Medicaid and self-pay patients (compared with those with private insurance) and those in the highest quartile of neighborhood deprivation scores (compared with those in the lowest quartile) had a higher probability of early discontinuation of endocrine therapy.
- These social determinants of health assume larger importance with the expected increase in unemployment rates and loss of insurance coverage in the aftermath of the coronavirus disease 2019 pandemic. Early identification of patients at risk and enrollment in insurance optimization programs may improve the persistence of therapy.

KEYWORDS: adherence, breast cancer, endocrine therapy, insurance, social determinants of health.

INTRODUCTION

Breast cancer is the most common cancer in American women with more than 268,600 new cases in 2019.[1] Approximately 75% of patients present with hormone receptor–positive breast cancers; for these patients, 5 years of adjuvant endocrine therapy (ET) substantially reduces the risks of locoregional and distant recurrence, contralateral breast cancer, death from breast cancer, and, therefore, death from any cause.[2-5]

The Trial Assigning Individualized Options for Treatment (TAILORx) was a prospective trial designed to assess the application of the 21-gene recurrence score to hormone receptor–positive, human epidermal growth factor receptor 2–negative, axillary node–negative breast cancer.[6] The results showed that ET alone was noninferior to adjuvant chemotherapy plus ET in patients with a recurrence score of 11 to 25.[6]

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Nonadherence and early discontinuation are substantial barriers to the delivery of ETs and may result in recurrence and mortality.[2] Nonadherence is defined as any incident when doses are missed, extra doses are taken, or doses are taken in the wrong quantity or at the wrong time. Early discontinuation is defined as when a patient stops a medication earlier than the period for which it is prescribed.[7] Approximately 30% to 60% of patients receiving ET are nonadherent to some degree,[8-15] and nonadherence may increase over time.[14] In adjuvant breast cancer clinical trials with longer follow-up (≥4 years), ET was prematurely discontinued by approximately 23% to 36% of the study participants.[16,17]

Several factors have been suggested as predictors of nonadherence and early discontinuation of ET, including extremes of age,[18,19] African American race,[20-24] greater comorbidities,[18,19,25] postmenopausal status,[12] cognitive impairment, disease-related and treatment-related factors (eg, type of surgery, receipt of adjuvant chemotherapy,[26] and greater treatment side effects),[18,19] low recurrence risk perception,[19] lack of provider communication regarding the importance of ET,[18,19] follow-up care with a general practitioner versus a cancer specialist,[18,19] increased out-of-pocket costs,[18] low social support,[18,19,25] and low socioeconomic status (SES).[27-29] Social determinants of health incorporate economic stability (eg, income and insurance), the built environment (eg, zip code/geography), and health system factors (access to and quality of care).[30] These have been hypothesized to shape health behavior, and they contribute to health outcomes. For example, affordability is a significant factor in patients' nonadherence to medication regimens or early discontinuation of therapy, as evidenced by higher rates of nonadherence and early discontinuation among patients with higher ET prescription copayments or those who received brand-name drugs versus generic equivalents.[31]

We aimed to investigate the association between early discontinuation of ET and social determinants of health, namely insurance coverage and the neighborhood deprivation index (NDI), at study entry among patients enrolled in the TAILORx trial.

MATERIALS AND METHODS

Study Protocol

TAILORx was a prospective, National Cancer Institute–funded clinical trial that was coordinated by the Eastern Cooperative Oncology Group (ECOG) and subsequently the ECOG-ACRIN Cancer Research Group. It was approved by the National Cancer Institute's central institutional review board and the appropriate local institutional review board. TAILORx is registered at ClinicalTrials.gov (NCT00310180). Data from ECOG-ACRIN clinical trials are available to researchers by directly contacting ECOG-ACRIN.

Women were required to provide written informed consent, including a willingness to have treatment assigned or randomized on the basis of recurrence score results. Women with a recurrence score of 10 or lower were assigned to receive ET only (arm A), and women with a score of 26 or higher were assigned to receive chemotherapy plus ET (arm D). Women with a midrange score of 11 to 25 underwent randomization and were assigned to receive either ET alone (arm B) or chemotherapy plus ET (arm C). Additional details regarding the study protocol have been previously reported.[6,32,33] For the current study, which is a post hoc analysis of the TAILORx trial, patients with breast cancer enrolled in the TAILORx trial who started ET within 1 year and 3 weeks of study entry were included. The additional 3 weeks conservatively accounted for variations in the initiation of the second follow-up reporting period for patients in arms A and D. This time frame resulted in the inclusion of an additional 50 participants.

Sociodemographic and Clinical Variables

The insurance status at study entry was determined with standard categories collected for all National Clinical Trials Network studies at the time of registration. The NDI was calculated with the Agency for Healthcare Research and Quality SES index.[34] The index is a weighted combination of the percentage of households with a mean number of 1 person or more per room, the median value of owner-occupied values, the percentage living below the poverty level, the median household income, the percentage 25 years old or older with a bachelor's degree or higher, the percentage 25 years old or older with less than a 12th-grade education, and the percentage 16 years old or older in the labor force who are unemployed. It is scaled to the US population to lie between 0 and 100, with a higher number indicative of greater neighborhood deprivation.[34] Previous studies have used this index to represent a geographical area–based measure of the socioeconomic deprivation experienced according to the neighborhood.[35,36] The NDI was computed by linkage of patients' 5-digit zip codes at the time of registration (for a subset of cases for whom the data were available) to county-level data

with the 2016-2017 Health Resource and Services Administration Area Health Resources File, which includes data on population characteristics and economics.[37] When a zip code represented multiple counties, for each component variable in the NDI, aggregate means and totals from those multiple counties were used to represent the county-level estimates for that zip code. Participants were grouped by NDI quartile. The index was not calculated for cases with unknown zip codes or those from Puerto Rico or international sites. Lower values for the NDI represent lower neighborhood aggregate SES and higher neighborhood deprivation.

Additional variables included arm assignment, age, race, menopausal status, tumor size, histologic grade, progesterone receptor expression, recurrence score, and first ET medication.

Study End Point

The primary end point was early discontinuation of ET, which was defined as stopping the medication within 4 years of its start (1416 days) for reasons other than distant recurrence or death. The start time of ET was not always similar to the time of study entry in the TAILORx trial. Because patients could have started ET up to 1 year after study entry, some early termination events could have occurred up to 5 years after registration. Patients who were lost to follow-up or withdrew from the study within 4 years of starting therapy but reported receipt of ET on their last follow-up were analyzed as still on ET with duration censored. Because many patients appear to have enrolled in TAILORx to test for the Oncotype score and the treatments involved were widely available standard of care, withdrawal from the study was not assumed to imply stopping treatment. However, we further performed a sensitivity analysis categorizing patients who were lost to follow-up or withdrew from the study within 4 years of starting ET as those with early treatment discontinuation. Because exact durations and reasons for discontinuation of medication were not recorded, if distant recurrence or death occurred within 3 months of the last dose, then the reason for discontinuation was assumed to be distant recurrence/death, and the duration was censored at that point.

Statistical Analyses

For categorical variables, frequencies and percentages are reported, and for continuous variables, means and standard deviations are reported. The early discontinuation rates were calculated with Kaplan-Meier estimates and are reported as frequencies and percentages. Cox proportional hazards models were used after it had been ensured that the proportional hazards assumption was met to analyze the association between various individual factors and the rate of early discontinuation of therapy. A joint model incorporating the major factors, including insurance, NDI, arm assignment, age, race, menopausal status, tumor size, progesterone receptor expression, recurrent score, and first ET medication, was also fit. Overall tests comparing the levels, hazard ratios (HRs), and 95% confidence intervals (CIs) are reported for each factor. P values $< .05$ were considered statistically significant.

RESULTS

Study Population

A total of 10,253 eligible women were registered between April 7, 2006, and October 6, 2010. Among 9719 eligible patients with follow-up information who were included in the main analysis set, 9475 started ET within 1 year and 3 weeks of entry. The baseline demographics of the included patients are shown in Table 1. A total of 58.0% had private insurance, whereas 11.7% had Medicare, 5.8% had Medicaid, 0.9% had military/Veterans Affairs insurance, 3.8% were self-pay, and 19.1% were recruited from international sites with an unknown insurance status, including Canada (n = 872), Ireland (n = 663), Peru (n = 254), Australia (n = 20), and New Zealand (n = 5).

Early Discontinuation Rate

Table 2 shows Kaplan-Meier early discontinuation rates for ET and early study withdrawals with ET reported to be taken in the last follow-up (censored ET durations). The discontinuation rate of ET increased over time from 2.6% during the first year to 4.0% during the fourth year after the start of treatment. Overall, the early discontinuation rate was 12.3% within 4 years of the start. Notably, 6.2% of the participants withdrew from the study or were lost to follow-up within 4 years after the start of ET. These patients were assumed to have continued their ET between their last follow-up and the time of study withdrawal or loss to follow-up.

Social Determinants of Health and Nonadherence

Table 3 shows the Kaplan-Meier estimates of early discontinuation rates for 2 variables related to social determinants of health—insurance and NDI—with adjustments for other variables. Compared with participants with

TABLE 1. Baseline Demographics of the TAILORx Cohort With an Endocrine Therapy Start Within 1 Year and 3 Weeks of Study Entry (n = 9475)

Characteristic	Value
Study arm, No. (%)	
Arm A (RS, 0-10; assigned endocrine therapy)	1577 (16.6)
Arm B (RS, 11-25; randomized to endocrine therapy)	3361 (35.5)
Arm C (RS, 11-25; randomized to endocrine therapy + chemotherapy)	3221 (34.0)
Arm D (RS, 26-100; assigned endocrine therapy + chemotherapy)	1316 (13.9)
Receipt of chemotherapy, No. (%)	
Arm C or D, received chemotherapy	3894 (41.1)
Arm C or D, no chemotherapy[a]	643 (6.8)
Arm A or B, received chemotherapy[a]	188 (2.0)
Arm A or B, no chemotherapy	4750 (50.1)
Age, mean (SD), y	55.6 (9.1)
Race, No. (%)	
White	7992 (84.3)
Black	668 (7.1)
Asian	398 (4.2)
Other/not specified	417 (4.4)
Ethnicity, No. (%)	
Hispanic	861 (9.1)
Not Hispanic	7445 (78.6)
Not specified	1169 (12.3)
Insurance status, No. (%)	
Private	5491 (58.0)
Medicare	1104 (11.7)
Medicaid	549 (5.8)
Military/VA	82 (0.9)
None (self-pay)	360 (3.8)
International	1814 (19.1)
Other/unknown	75 (0.8)
NDI (value range), No. (%)	
Quartile 1, highest deprivation (≤51.53)	1907 (20.1)
Quartile 2 (51.54-53.53)	1846 (19.5)
Quartile 3 (53.54-56.48)	1873 (19.8)
Quartile 4, lowest deprivation (>56.48)	1873 (19.8)
US zip code unknown or US territory (Puerto Rico)	162 (1.7)
International	1814 (19.1)
Menopausal status, No. (%)	
Premenopausal	3202 (33.8)
Postmenopausal	6273 (66.2)
Tumor size in largest dimension, No. (%)	
≤2 cm	7085 (74.8)
>2 cm	2388 (25.2)
Histologic grade of tumor, No. (%)	
Low	2441 (25.8)
Intermediate	5132 (54.2)
High	1620 (17.1)
Unknown	282 (2.9)
Progesterone receptor expression, No. (%)	
Negative	914 (9.6)
Positive	8357 (88.2)
Unknown	204 (2.2)
Oncotype DX RS, No. (%)	
≤10	1577 (16.6)
11-25	6582 (69.6)
>25	1316 (13.8)
First endocrine therapy, No. (%)	
AI	5546 (58.5)
Tamoxifen	3576 (37.7)
Tamoxifen and AI	68 (0.7)
Ovarian function suppression	249 (2.6)
Other	36 (0.4)

Abbreviations: AI, aromatase inhibitor; NDI, neighborhood deprivation index; RS, recurrence score; SD, standard deviation; TAILORx, Trial Assigning Individualized Options for Treatment; VA, Veterans Affairs.
[a]Reflects patients who did not adhere to their assigned treatment arm.

private insurance, those with Medicaid (HR, 1.53; 95% CI, 1.23-1.92) and those who self-paid (HR, 1.65; 95% CI, 1.25-2.17) had a higher probability of discontinuing ET within 4 years of its start. There was no significant difference in early discontinuation rates between patients with Medicare and patients with private insurance (Fig. 1). A sensitivity analysis including the 6.2% of participants (n = 282) who withdrew from the study or were lost to follow-up within 4 years after the start of ET as early discontinuers of therapy did not change the result (data not presented).

Furthermore, participants with a first-quartile NDI (highest deprivation) had a higher probability of discontinuation than those with a fourth-quartile NDI (lowest deprivation; HR, 1.34; 95% CI, 1.11-1.62). Overall, the probability of early discontinuation increased as neighborhood deprivation increased.

Other Factors Associated With an Early Discontinuation Rate

In addition to the insurance status and NDI at study entry, there were several other factors associated with the early discontinuation rate (Table 3). No receipt of chemotherapy was significantly associated with a higher probability of early discontinuation of ET. Increasing age (compared with an age ≤ 40 years), Black and Asian race (compared with White race), and higher recurrence scores were significantly associated with a lower probability of early discontinuation of ET.

DISCUSSION

Our retrospective analysis of women with breast cancer who were enrolled in the TAILORx trial and started on ET has shown that patients' insurance type and NDI at study entry are independent factors associated with early discontinuation. Among US participants, patients who were self-paying or had Medicaid and those who lived in neighborhoods with the highest deprivation level (ie, the first NDI quartile) were more likely to stop ET early. Notably, patients were recruited between April 2006 and October 2010. With the Affordable Care Act going into effect in January 2010, only a small proportion of the participants likely had Affordable Care Act exchange insurance coverage, and such information is not available.

Our study showed a 12.3% early discontinuation rate for ET within 4 years of its start for patients participating in the TAILORx trial. The parent study did not collect patient-reported reasons for early discontinuation. Prior studies reported a 5-year early discontinuation rate

TABLE 2. Kaplan-Meier Rates of Early Discontinuation and Early Withdrawal/Loss to Follow-Up for the Study Population (n = 9475)

Time From Start of Endocrine Therapy, y	Stopping Endocrine Therapy, No. (%)	Withdrawal From Study or Loss to Follow-Up With Report of Endocrine Therapy in Last Follow-Up, No. (%)
0-1	243 (2.6)	136 (1.4)
1-2	260 (2.8)	145 (1.5)
2-3	269 (2.9)	136 (1.4)
3-4	353 (4.0)	168 (1.8)
Total	1125 (12.3)	585 (6.2)

ranging from 20% to 48%.[18,19,38] The variability in the method for measuring early discontinuation, among other reasons, may contribute to the wide range of reported rates.

Our results for economic factors associated with early discontinuation are mostly consistent with prior studies, with self-pay and Medicaid insurance and residence in neighborhoods with higher deprivation levels associated with higher rates of early discontinuation.[27-29] The uninsured face barriers for prescription medications due to high out-of-pocket responsibilities. The average out-of-pocket cost for a month's supply of ET ranges from $70 (tamoxifen) to $505 (aromatase inhibitors) for self-pay patients without coupons or prescription assistance.[39] As the literature has established, the Medicaid population is also at higher risk for early discontinuation because of lesser coverage of routine care, heterogeneous coverage of costs of clinical trial participation,[40] and potentially lower financial or other reserves among this population.[27-29]

TAILORx did not include data on income or education. Neighborhood deprivation may be a proxy for participant SES. In addition, neighborhood influences access to care. In the absence of patient-level SES, we cannot tease apart the contributions of patient and neighborhood SES to the early discontinuation of ET in this population. However, after we had controlled for insurance status, a more direct proxy for individual-level resources, the NDI remained a significant correlate of early hormone therapy discontinuation, and this suggests independent effects of the built environment on health behavior and, consequently, health outcome.

The TAILORx trial did not include patients older than 75 years old. However, unlike prior studies,[12,26] the current study found that postmenopausal status and receipt of chemotherapy were associated with lower rates of early discontinuation. We assume that some degree of higher rates of early discontinuation in premenopausal women likely correlates with higher rates of early discontinuation seen in patients younger than 50 years. However, in the multivariable model, the association of both factors with early discontinuation remained independently significant. The higher probability of early discontinuation of ET among patients with lower recurrence scores in our study might be explained by lower recurrence risk perception among these patients, which is consistent with prior studies.[19] Conversely, receipt of chemotherapy exerts an opposite effect and reduces early discontinuation, perhaps because of higher recurrence risk perception or a desire to avoid chemotherapy in the future.

Finally, in the current study, Black and Asian participants (compared with White participants) had a lower probability of early discontinuation of ET. Prior studies have shown that among patients with sporadic (non–high-risk) breast cancer, Asians have higher odds of using ET than non-Hispanic Whites and African Americans.[21,41] Although in some studies Black women, compared with White women, have been shown to have a higher likelihood of early discontinuation,[20-24] we observed the opposite correlation after controlling for the neighborhood and insurance effects. We hypothesize that the previously demonstrated race effect on early discontinuation may be due to or otherwise accounted for in the NDI in our multivariable analysis.[42] In a recent study of TAILORx participants, compared with White women, Black women had worse clinical outcomes (eg, recurrence rates and survival).[43] Our study findings suggest that these disparities do not seem to be due to differences in ET adherence. Future analyses of clinical outcomes that include the NDI may be informative. The striking reversal of the expected pattern of early discontinuation of hormone therapy among Black women after we controlled for neighborhood characteristics strongly suggests the need for a routine longitudinal collection of variables representing social determinants of health. Such clinical and trial data may more fully explain the variations in health behavior and health outcomes currently attributed to race.

Our study has implications for clinical practice. To counteract increasing medication costs, pharmacy benefit

TABLE 3. Kaplan-Meier Early Discontinuation Rates for Endocrine Therapy and Hazard Ratios From a Joint Model

	Ratio	95% CI	*P*
Arm assignment with receipt of chemotherapy			
Arm C (RS, 11-25) or D (RS, 26-100), received chemotherapy	Reference		
Arm C (RS, 11-25) or D (RS, 26-100), no chemotherapy	1.71	1.37-2.14	.000003
Arm A (RS, 0-10) or B (RS, 11-25), received chemotherapy	1.03	0.66-1.61	.89
Arm A (RS, 0-10) or B (RS, 11-25), no chemotherapy	1.18	1.01-1.38	.03
Age			
≤40 y	Reference		
41-50 y	0.70	0.54-0.89	.005
51-60 y	0.52	0.39-0.70	.00001
61-70 y	0.46	0.34-0.64	.000003
≥71 y	0.57	0.38-0.86	.008
Race			
White	Reference		
Black	0.73	0.57-0.93	.01
Asian	0.50	0.34-0.75	.0007
Other or unknown	1.07	0.79-1.45	.65
Ethnicity			
Non-Hispanic	Reference		
Hispanic	0.87	0.70-1.09	.23
Ethnicity not reported	0.82	0.66-1.02	.07
Insurance type (US participants only)			
Private	Reference		
Medicare	1.10	0.88-1.37	.41
Medicaid	1.53	1.23-1.92	.0002
Military/VA	0.80	0.38-1.69	.56
None	1.65	1.25-2.17	.0003
Other or unknown	0.84	0.40-1.78	.65
NDI			
Quartile 1, highest deprivation	1.34	1.11-1.62	.003
Quartile 2	1.12	0.92-1.36	.26
Quartile 3	1.23	1.01-1.49	.04
Quartile 4, lowest deprivation	Reference		
Unknown	1.10	0.66-1.85	.71
International participant[a]	0.98	0.79-1.22	.84
Menopausal status			
Premenopausal	Reference		
Postmenopausal	1.08	0.87-1.34	.48
Tumor size in largest dimension			
≤2.0 cm	Reference		
>2.0 cm	1.06	0.93-1.22	.38
Progesterone receptor expression			
Negative	Reference		
Positive	0.75	0.61-0.91	.004
Unknown	0.51	0.28-0.92	.03
Oncotype DX RS			
≤10	Reference		
11-25	0.80	0.67-0.94	.007
>25	0.83	0.63-1.08	.16
First endocrine therapy			
AI	Reference		
Tamoxifen	1.00	0.84-1.20	.96
Tamoxifen and AI	1.27	0.70-2.32	.44
Ovarian function suppression	1.05	0.72-1.54	.81
Other	3.68	1.35-10.06	.01

Abbreviations: AI, aromatase inhibitor; CI, confidence interval; NDI, neighborhood deprivation index; RS, recurrence score; VA, Veterans Affairs.
[a]Compared with a US participant with private insurance in the lowest deprivation quartile.

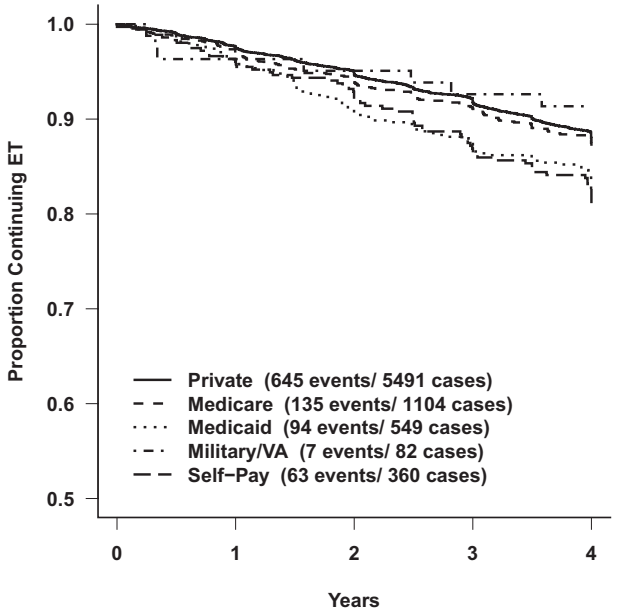

Figure 1. Early discontinuation rates for ET by type of insurance. ET indicates endocrine therapy; VA, Veterans Affairs.

plans have added additional tiers of drugs, increased copayment rates and deductibles, excluded some drugs from coverage, and increased preauthorization requirements.[44] Additional efforts should be made to implement initiatives such as price transparency, insurance optimization, and financial navigation to mitigate the patient-borne effects of cost sharing.[45-47] Enactment of parity laws and efforts to limit ET out-of-pocket costs may also affect medication adherence.[48] Additional efforts such as coordination of transportation for clinic visits and use of telemedicine and personalized culturally tailored interventions may improve early discontinuation due to limited access to health care. Finally, culturally sensitive outreach and education on the consequences of early discontinuation, as well as available resources on improving insurance coverage and access, might be helpful in mitigating early discontinuation and in building trust in the health system, particularly in communities of color. These recommendations may be particularly salient with the economic shock related to coronavirus disease 2019[49] and expected increase in unemployment rates, insurance coverage loss, and potential downward social mobility further influencing early discontinuation.

Our study has several limitations. First, the early discontinuation rate was calculated on the basis of the report of receipt or nonreceipt of medication in the last follow-up. Because exact durations and reasons for

discontinuation of ET were not recorded, if distant recurrence or death occurred within 3 months of last ET, then the reason for discontinuation was assumed to be distant recurrence/death. Second, we analyzed only the association between early discontinuation and insurance and NDI at study entry. It is possible that a patient's insurance or place of residence changed over the 5 years, and the impact of these changes on the discontinuation rate was not assessed. In other settings, transitions between coverage types can positively (eg, individuals transitioning from Medicaid only to more generous dual Medicare-Medicare coverage) or negatively (eg, women with the spousal transition to Medicare) influence health access and quality.[50,51] Liu et al[52] estimated that 25.6% relocate after their first cancer diagnosis. Although the relative neighborhood deprivation levels before and after relocation were not assessed, poverty and a lack of health insurance correlated with relocation and suggested downward neighborhood mobility. TAILORx did not collect data for treatment side effects. Therefore, we did not assess the correlation between side effects and early ET discontinuation. Participants in clinical trials differ from the general patient population, and this limits the generalizability of our results.

In summary, patients' insurance status and zip code play important roles in the persistence of ET use, with uninsured and Medicaid patients and participants who live in neighborhoods with high deprivation levels having a high rate of early discontinuation of therapy. Early identification of patients at risk, enrollment in insurance optimization programs, and culturally appropriate recurrence risk reduction education may improve the persistence of therapy.

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CONFLICT OF INTEREST DISCLOSURES

David Cella is the president of FACIT.org. Lynne I. Wagner reports personal fees from Celgene and Athenex outside the submitted work; her spouse manages his stock portfolio, which occasionally includes stocks from pharmaceutical companies (Johnson & Johnson and Eli Lilly), but she is not involved in stock purchases or any decisions. Ruth C. Carlos receives salary support as editor-in-chief of the *Journal of American College of Radiology* and travel support from the GE Radiology Research Academic Fellowship as the board of review chair. The other authors made no disclosures.

AUTHOR CONTRIBUTIONS

Gelareh Sadigh: Methodology, writing–original draft, and writing–review and editing. **Robert J. Gray:** Data curation and formal analysis, methodology, and writing–review and editing. **Joseph A. Sparano:** Funding acquisition, investigation, methodology, and writing–review and editing. **Betina Yanez:** Methodology and writing–review and editing. **Sofia F. Garcia:** Methodology and writing–review and editing. **Lava R. Timsina:** Methodology and writing–review and editing. **George W. Sledge:** Methodology and writing–review and editing. **David Cella:** Methodology and writing–review and editing. **Lynne I. Wagner:** Methodology and writing–review and editing. **Ruth C. Carlos:** Conceptualization, methodology, and writing–review and editing.

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