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Longitudinal Adherence to Aromatase Inhibitors over 5 Years in Postmenopausal Early-Stage Breast Cancer

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INTRODUCTION

- Aromatase inhibitors (AIs) are the recommended standard adjuvant therapy for postmenopausal women with hormone-receptor positive (HR+), non-metastatic breast cancer following surgery.
- Suboptimal adherence to AIs remains in the real-world setting, which could reduce the clinical effectiveness, increasing the risk of breast cancer recurrence and cancer-related mortality.

OBJECTIVE

- To describe the longitudinal adherence trajectories to AIs over a 5-year treatment course.
- To identify factors associated with suboptimal adherence rates of AI among postmenopausal women with early-stage breast cancer in the United States (US)

METHODS

Data Source

- Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked database (2007-2020)

Patient Population

- Inclusion Criteria
  - Female patients diagnosed with HR+ stage I-III breast cancer (≥66 years of age at diagnosis)
  - New use of adjuvant AI (anastrozole, letrozole, or exemestane) within 1 year of breast cancer diagnosis. (index date as date of initiation)
  - Breast cancer as the first and only primary cancer prior to index date
  - Continuous enrollment in Medicare Part A, B, and D, and without HMO at least 1 year before index date
- Exclusion Criteria
  - Surgery between breast cancer diagnosis and index date (mastectomy or lumpectomy)
  - Having any tamoxifen prescription after index date

Adherence Measurement

- Continuous monthly proportion days covered (PDC) of AI prescriptions during the 5 years after index date
  - 60 periods over 5 years, with 0-100% for each period
  - Stockpiling: pushed forward the start of early filled to the first day after the end of current supply
- Measurement period
  - Until end of the month preceding censoring event or 5 years after index date
- Censoring event (earliest of):
  - Death
  - Disenrollment
  - Second cancer (based on SEER registry)
  - Cancer progression: initiation of chemotherapy or radiotherapy ≥120 days after index; OR second breast cancer surgery except reconstructive surgery ≥180 days after first breast cancer surgery; OR cancer recurrence after index date with ≥1 inpatient or ≥2 outpatient ICD diagnosis

Statistical Analysis

- Group-based trajectory model (GBTM)
  - 2-5 groups using quadratic polynomial dropout model
  - Selection criteria: (1) >5% in each group; (2) BIC closest to 0 with clinically distinguished groups; (3) log of twice difference in BIC between complex and simple model ≥2; (4) average posterior probability (APP) ≥0.7; (5) odds correct classification (OCC) ≥5
- Factors associated with group membership
  - Multinomial logistic regression to determine the adjusted odds ratio (highest adherence group as reference)

RESULTS

Figure 1. 5-group trajectory model of AI adherence

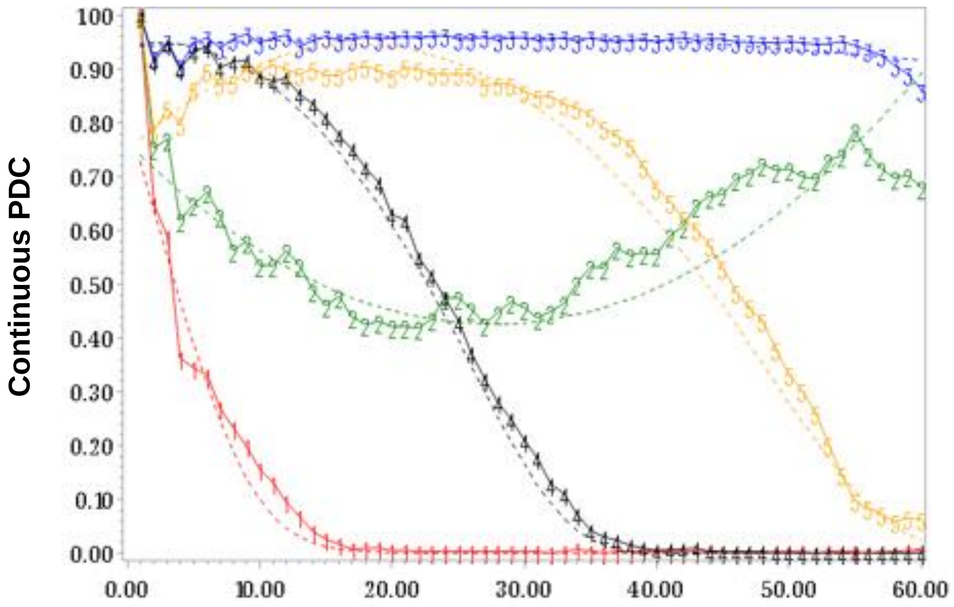

Table 1. Characteristics and criteria of the 5-group trajectory model

Trajectory Groups	Group Probability (n=10919)	APP	OCC
Rapid Decline (Red)	10.5% (1147)	~1.0	3.79*10^69
Decline then Increase (Green)	5.0% (526)	0.9	7.77*10^94
Gradual Decline (Black)	16.0% (2154)	0.7	3.27*10^67
Flat then Decline (Yellow)	7.8% (768)	0.9	1.85*10^59
Consistently High (Blue)	60.7% (6324)	0.9	1.57*10^53

Table 2. Associations between patient characteristics and adherence trajectory membership

Trajectory Groups	Rapid Decline	Decline then Increase	Gradual Decline	Flat then Decline	Consistently High
Characteristics	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age					
66-75 years	Reference	Reference	Reference	Reference	Reference
76-85 years	**1.53** (1.32 – 1.77)	1.10 (0.89 – 1.34)	1.08 (0.96 – 1.21)	**1.51** (1.27 – 1.78)	Reference
>85 years	**2.35** (1.81 – 3.05)	1.14 (0.75 – 1.74)	**1.41** (1.12 – 1.77)	**2.23** (1.64 – 3.03)	Reference
Prior Emergency Room Visit					
0	Reference	Reference	Reference	Reference	Reference
1	**1.23** (1.04 – 1.46)	1.16 (0.91 – 1.46)	1.08 (0.95 – 1.24)	1.13 (0.92 – 1.38)	Reference
2	**1.32** (1.00 – 1.74)	0.69 (0.44 – 1.08)	**1.32** (1.07 – 1.63)	1.12 (0.81 – 1.56)	Reference
3 or more	**1.55** (1.11 – 2.16)	1.32 (0.85 – 2.03)	**1.40** (1.07 – 1.83)	0.92 (0.59 – 1.42)	Reference
History of Chemotherapy					
No/Unknown	Reference	Reference	Reference	Reference	Reference
Yes	**1.33** (1.02 – 1.72)	**1.49** (1.06 – 2.09)	1.09 (0.92 – 1.30)	**1.34** (1.00 – 1.80)	Reference
History of Depression					
No	Reference	Reference	Reference	Reference	Reference
Yes	**1.31** (1.06 – 1.62)	**1.41** (1.06 – 1.89)	1.05 (0.88 – 1.26)	1.20 (0.93 – 1.55)	Reference
History of Lipid Lowering Agent					
No	Reference	Reference	Reference	Reference	Reference
Yes	**0.59** (0.49 – 0.7)	**0.78** (0.61 – 0.99)	**0.85** (0.74 – 0.98)	0.92 (0.75 – 1.14)	Reference

DISCUSSION

- This study revealed heterogenous adherence patterns to AI amongst postmenopausal women with early-stage breast cancer in the US along with potential factors associated with suboptimal adherence patterns.
- Recognizing these patterns and factors is crucial for developing interventions to enhance adherence to AI and ultimately optimize treatment outcomes.
- The findings of this study could potentially facilitate the implementation of strategies to effectively support at-risk patient groups.

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