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Real-world risk of recurrence among patients diagnosed with stage II-III HR+/HER2− early breast cancer treated with endocrine therapy in the US

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KEY FINDINGS & CONCLUSIONS

- This real-world study demonstrated differences in patient profiles and treatment patterns across two large oncology practices (community and academic)
  - Overall, disease characteristics were similar between the community and academic settings
  - In the academic setting, patients tended to be younger, and more patients with N0 disease received genomic testing for risk
  - Use of chemotherapy and extended ET was relatively high in the academic practice, which could be attributed to the younger patient demographic in this setting
  - Among premenopausal patients, AI as first ET was more prevalent in the academic setting
- Considerable and cumulative risk of recurrence was observed up to 7 years after initiating adjuvant ET and even during the adjuvant treatment period (median follow-up: 6.3 years)
- While the risk in patients with N+ disease is well established, patients with N0 high-risk disease (similar to NATALEE criteria[4]) have a comparable prognosis and exhibited a similar and substantial risk of recurrence
- Collectively, these findings emphasize an unmet need for effective treatments and strategies that may help patients adhere to treatment and gain maximal therapeutic benefit

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INTRODUCTION

- Among patients with hormone receptor–positive and human epidermal growth factor receptor 2–negative (HR+/HER2−) early-stage breast cancer (EBC), the current standard of care in the adjuvant setting involves use of endocrine therapy (ET; plus ovarian function suppression for premenopausal patients) with or without chemotherapy[1]
- Clinical care has been evolving over the last decade, with growing evidence and follow-up data on optimizing local and systemic therapies
  - Although several meta-analyses on risk of recurrence have been published, there is a lack of data on outcomes of patients initiating ET in the last decade, in which practice patterns for patients with EBC have changed considerably[2,3]
  - New targeted therapies added to ET, such as the cyclin-dependent kinase 4/6 inhibitors abemaciclib and ribociclib, have improved recurrence and disease-free survival outcomes in these patients in clinical trials[4-6]
- The objective of this analysis was to assess patient demographics and clinical characteristics, treatment patterns, and clinical outcomes, including RW risk of recurrence, among patients with HR+/HER2− EBC who received treatment with adjuvant ET in routine clinical settings at large oncology practices in the US

METHODS

Study design

- A retrospective, noninterventional cohort study of patients treated at large academic (Memorial Sloan Kettering Cancer Center) and community (Tennessee Oncology) practices was conducted (**Figure 1**)

Data collection and analysis

- Patients were randomly selected in order to generate equal distribution by year of adjuvant ET initiation, which allowed inclusion of patients with longer potential follow-up and more contemporaneous data while reducing selection bias
- Medical records were abstracted for patients who initiated adjuvant ET during the study index period (January 1, 2012, to December 31, 2018) and met other sample selection criteria (**Table 1**). Data were extracted using a customized structured electronic data collection form
- Descriptive analyses were conducted to summarize patient demographics, clinical characteristics, treatment patterns, invasive disease-free survival (iDFS) and distant relapse-free survival (DRFS). iDFS and DRFS were defined based on the Standardized Definitions for Efficacy End Points (STEEP) criteria[7]
- The Kaplan-Meier method was used to estimate iDFS and DRFS from the start of adjuvant ET

Figure 1. Study Design

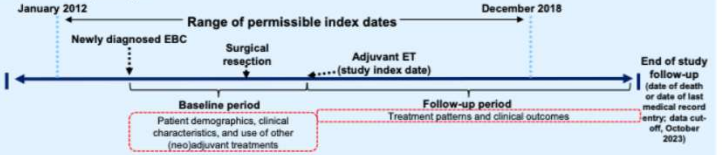


Table 1. Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
• Female patients ≥18 years with a diagnosis of adenocarcinoma of the breast	• Participation in an interventional clinical trial evaluating (neo)adjuvant systemic therapy in patients with EBC
• HR+ and HER2− status per ASCO/CAP guidelines	• Initial diagnosis of AJCC anatomic stage I disease
• Underwent surgical resection for BC and initiated adjuvant ET (with or without chemotherapy) between January 1, 2012, and December 31, 2018	• Initial diagnosis of AJCC anatomic stage IV (distant metastases) or unresectable (local/regional) advanced BC
• Anatomic stage II or III (*AJCC 8th edition*) BC at initial diagnosis from January 1, 2012, through December 31, 2018	
• Information available on all treatments from initial BC diagnosis onward and baseline characteristics before initial BC diagnosis	

AJCC, American Joint Committee on Cancer; ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BC, breast cancer; EBC, early breast cancer; ET, endocrine therapy; HER2−, human epidermal growth factor receptor-negative; HR+, hormone receptor-positive.

RESULTS

- Data were collected on 992 eligible patients (academic, 496; community, 496; median follow-up 6.3 years) (**Table 2**)
- A similar distribution across stage and nodal status was observed in both settings; most patients had stage II disease (76.7%) and 1 to 3 positive lymph nodes (N1) (46.8%); 35.8% of patients had node-negative (N0) tumors
- Patients in the academic vs community setting were younger (mean age, 55 years vs 60 years) and included a higher proportion of pre- or perimenopausal women (43% vs 26%, respectively)
- More patients with N0 disease received oncotype testing in the academic (79.9%) vs community (58.0%) practices (**Table 3**)

Table 2. Patient Demographics and Clinical Characteristics

	Overall (N=992)	Community setting (n=496)	Academic setting (n=496)
Median age at initial BC diagnosis, years	58.0	60.0	54.0
Race, n (%)			
Asian or Native Hawaiian/other Pacific Islander	48 (4.8)	7 (1.4)	41 (8.3)
Black or African American	98 (9.9)	50 (10.1)	48 (9.7)
White or Caucasian	762 (76.8)	430 (86.7)	352 (71.0)
Other or race unknown	64 (6.5)	9 (1.8)	55 (11.1)
Primary health insurance at last follow-up, n (%)			
Commercial	508 (51.2)	156 (31.5)	352 (71.0)
Medicare	367 (37.0)	263 (53.0)	104 (21.0)
Medicaid	40 (4.0)	35 (7.1)	5 (1.0)
Other/uninsured/unknown	77 (7.8)	42 (8.5)	35 (7.1)
Stage (*AJCC 8th edition*) at initial BC diagnosis, n (%)			
0A	502 (50.6)	248 (50.0)	254 (51.2)
IIB	259 (26.1)	137 (27.6)	122 (24.6)
IIA	153 (15.4)	79 (15.9)	74 (14.9)
IIIB	23 (2.3)	14 (2.8)	9 (1.8)
IIIC	55 (5.5)	18 (3.6)	37 (7.5)
Nodal status by tumor size, n (%)			
N0			
T2N0	322 (32.5)	157 (31.7)	165 (33.3)
T3N0	28 (2.8)	15 (3.0)	13 (2.6)
T4N0	5 (0.5)	4 (0.8)	1 (0.2)
N1			
T1N1	180 (18.1)	91 (18.3)	89 (17.9)
T2N1	231 (23.3)	122 (24.6)	109 (22.0)
T3N1	43 (4.3)	25 (5.0)	18 (3.6)
T4N1	10 (1.0)	4 (0.8)	6 (1.2)
N2/N3			
T1N2/N3	42 (4.2)	12 (2.4)	30 (6.0)
T2N2/N3	91 (9.2)	47 (9.5)	44 (8.9)
T3N2/N3	29 (2.9)	10 (2.0)	19 (3.8)
T4N2/N3	10 (1.0)	8 (1.6)	2 (0.4)
T2N0 by grade (percentage of T2N0 subgroup)[a], n			
T2N0G1	43 (13.4)	38 (24.2)	5 (3.0)
T2N0G2	179 (55.6)	81 (51.6)	98 (59.4)
T2N0G3	92 (28.6)	38 (24.2)	54 (32.7)

AJCC, American Joint Committee on Cancer; BC, breast cancer; G, grade; N, nodal status; T, tumor size.
[a] Grade was unknown for 8 T2N0 patients in the academic setting.

Table 3. Oncotype Testing by Nodal Status

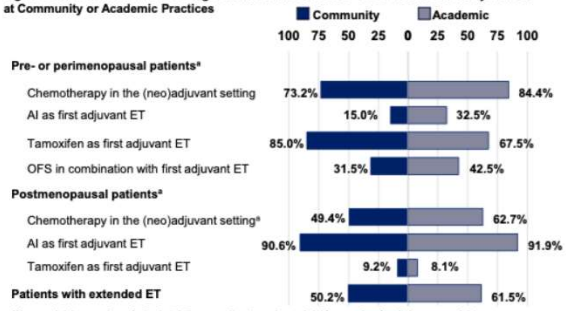
	Community setting (n=496)			Academic setting (n=496)		
	T2N0 (n=157)	T3N0/T4N0 (n=19)	N1 (n=242)	T2N0 (n=165)	T3N0/T4N0 (n=14)	N1 (n=222)
Oncotype performed, n (%)						
Yes	95 (60.5)	7 (36.8)	91 (37.6)	132 (80.0)	11 (78.6)	42 (18.9)
Test not performed/risk unknown	62 (39.5)	12 (63.2)	151 (62.4)	33 (20.0)	3 (21.4)	180 (81.1)
Oncotype RS risk status, n (%)[a]						
Low or medium risk (RS 0-25)	73 (76.8)	7 (100.0)	74 (81.3)	110 (83.3)	11 (100.0)	36 (85.7)
High risk (RS 26-100)	22 (23.2)	0	16 (17.6)	22 (16.7)	0	6 (14.3)

N, node; RS, recurrence score; T, tumor.
[a] All ages.

Treatment patterns among patients with HR+/HER2− EBC treated with adjuvant ET in community and academic settings

- Overall, (neo)adjuvant chemotherapy was less common (54.6% vs 72.0%) and fewer patients received extended ET of ≥5 years (50.2% vs 61.5%) in the community vs academic setting, respectively (**Figure 2**)
- Among pre- or perimenopausal patients, aromatase inhibitor (AI) as first ET was given at a lower rate in the community setting (15.0%) compared with the academic setting (32.5%), while use of AI as first ET was similar between settings (90.6% and 91.9%) in postmenopausal patients

Figure 2. Treatment Patterns Among Patients With HR+/HER2− EBC Treated With Adjuvant ET at Community or Academic Practices

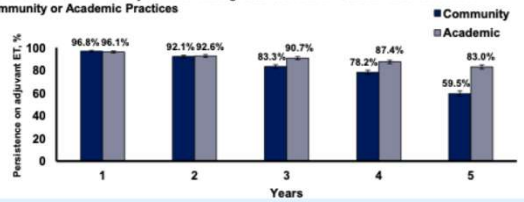


[a]Menopausal status was unknown for 9 patients in the community setting and are excluded from reporting of results by menopausal status.

Persistence on adjuvant ET was >80% in both settings during the initial years

- At 5 years, persistence in the community setting dropped to 59.5% (standard error [SE], 2.3%), while in the academic setting, it remained at 83.0% (SE, 1.8%) (**Figure 3**)

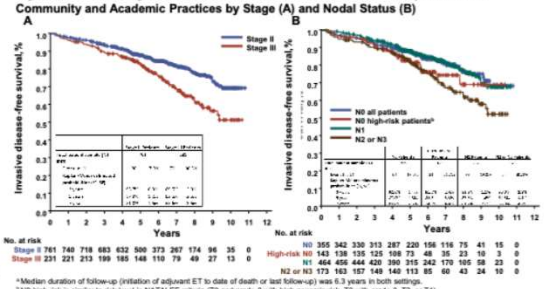
Figure 3. Persistence on Adjuvant ET Among Patients With HR+/HER2− EBC Treated at Community or Academic Practices



Disease-free survival outcomes by stage and nodal status

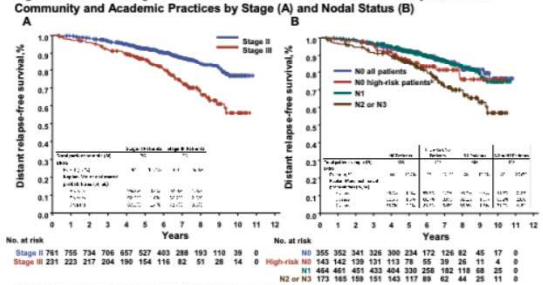
- For patients with stage II and III disease in both settings (combined data) risk of recurrence accumulated over a short period of time (**Figures 4** and **5**)
- Patients with N0 high-risk disease had a 25.7% risk of invasive disease over 7 years (**Figure 4B**), with a corresponding risk of distant disease of 18.8% (**Figure 5B**)

Figure 4. iDFS[a] Among Patients With HR+/HER2− EBC Treated With Adjuvant ET at Community and Academic Practices by Stage (A) and Nodal Status (B)



[a]Median duration of follow-up (initiation of adjuvant ET to date of death or last follow-up) was 6.3 years in both settings.
[b]N0-high risk is similar to risk level in NATALEE criteria (T2 and grade 2 with high genomic risk, T2 with grade 3, T3, or T4).

Figure 5. DRFS[a] Among Patients With HR+/HER2− EBC Treated With Adjuvant ET at Community and Academic Practices by Stage (A) and Nodal Status (B)



[a]Median duration of follow-up (initiation of adjuvant ET to date of death or last follow-up) was 6.3 years at both practices.
[b]N0-high risk is similar to risk level in NATALEE criteria (T2 and grade 2 with high genomic risk, T2 with grade 3, T3, or T4).

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