Adherence to endocrine prevention in patients with atypical hyperplasia and lobular carcinoma *in situ*: promising trends from real-world use of low-dose tamoxifen

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BACKGROUND

- Women with high-risk lesions (HRL) have an increased lifetime risk of developing breast cancer.[1]
- Endocrine prevention is a well-established and cost-effective preventative strategy for risk reduction in these patients.[2]
- In 2019, the TAM-01 trial addressed tolerability concerns by demonstrating that baby tamoxifen (5mg for 3 years) provides comparable risk reduction with fewer side effects.[3]
- Yet, studies show that endocrine prevention remains underutilized, with initiation rates as low as 14.8%.[4]

OBJECTIVES

To evaluate the factors associated with initiation and adherence to endocrine prevention by regimen in women with high risk lesions, including **atypical ductal hyperplasia** (ADH), **atypical lobular hyperplasia** (ALH), and classical **lobular carcinoma *in situ*** (LCIS)

METHODS

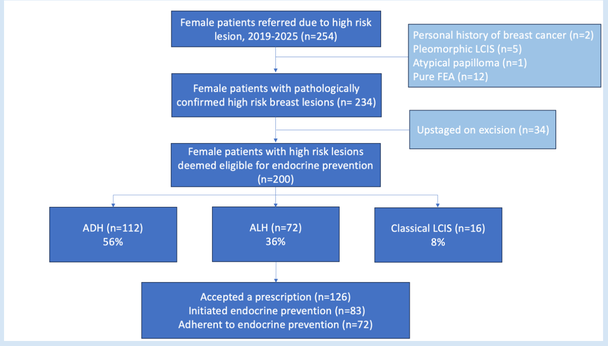


FIGURE 1: Cohort Selection We identified all female patients with a pathologically confirmed high risk breast lesion deemed eligible for endocrine prevention referred to our clinic between 2019-2025

METHODS

- **Study design:** Retrospective cohort study with prospectively collected data
- **Primary outcome**: To analyze the trends in initiation and adherence to endocrine prevention in eligible women with ADH, ALH, and LCIS
- **Statistical analysis:** Univariate analyses were performed using Chi-squared and Fisher's exact test to evaluate factors associated with adherence. Descriptive statistics were used to characterize demographic and clinical variables. P-values <0.05 used to indicate statistical significance.

COHORT CHARACTERISTICS

TABLE 1 Clinical Characteristics of patients with HRL (n=200)

Characteristic	
Age – n, (%)	
<40 years	10 (5.0)
41-50 years	51 (25.5)
51-60 years	82 (41.0)
61+ years	57 (28.5)
Race/ethnicity – n, (%)	
White	87 (43.5)
Black	5 (2.6)
Hispanic or Central/South American	6 (3.1)
Asian/Southeast Asian	18 (9.2)
North African/ Middle Eastern	17 (8.7)
Other	4 (2.0)
Unknown	63 (32.1)
High Risk Lesion (HRL) – n, (%)	
Atypical ductal hyperplasia	112 (56.0)
Atypical lobular hyperplasia	72 (36.0)
Lobular carcinoma in situ	16 (8.0)
Family History of Breast Cancer – n, (%)	
Yes, first or second degree relative	48 (24.0)
No	152 (76.0)
Parity – n, (%)	
Nulliparous	76 (38.0)
One or more pregnancy	124 (62.0)
Menopausal Status – n, (%)	
Premenopausal	63 (31.5)
Postmenopausal	137 (68.5)
Oral contraceptive use – n, (%)	
Yes	91 (45.5)
No	109 (54.5)
Hormone replacement therapy use – n, (%)	
Yes	27 (13.5)
No	173 (86.5)
ACR Type Breast Density – n, (% with breast density available)	
Type A (entirely fatty)	
Type B (scattered fibroglandular)	6 (3.5)
Type C (heterogeneously dense)	55 (32.4)
Type D (extremely dense)	81 (47.7)
	28 (16.5)
Surgical Excision Performed – n, (%)	
Yes	105 (52.5)
No	95 (47.5)
Concern about developing breast cancer – n, (%)	
Low	34 (17.0)
Moderate	48 (24.0)
High	98 (49.0)
Unknown	20 (10.0)

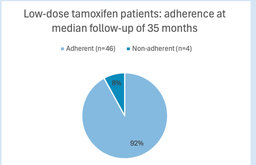
RESULTS

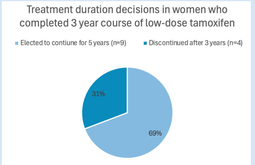
TABLE 2 Adherence to endocrine prevention in HRL patients who accepted a prescription (n=126)

Characteristic	No. accepted Rx (%)	No. who initiated Rx and remained adherent (% Rx)	p-value*
Total	126 (100)	72 (57.1%)	
Age – n, (%)			**0.046**
<50 years	34 (27.0)	15 (45.4)	
51-60 years	65 (51.6)	44 (67.7)	
61+ years	27 (21.4)	12 (44.4)	
High Risk Lesion (HRL) – n, (%)			0.11
Atypical ductal hyperplasia	63 (50.0)	31 (49.2)	
Atypical lobular hyperplasia	49 (38.9)	30 (61.2)	
Lobular carcinoma in situ	14 (11.1)	11 (78.6)	
Family History of Breast Cancer – n, (%)			**0.048**
Yes, first or second degree relative	31 (24.6)	22 (71.0)	
No	95 (75.4)	50 (52.6)	
Parity – n, (%)			0.70
Nulliparous	41 (32.5)	22 (53.7)	
One or more pregnancy	85 (67.5)	50 (58.8)	
Menopausal Status – n, (%)			0.13
Premenopausal	40 (31.8)	19 (47.5)	
Postmenopausal	86 (68.3)	53 (61.6)	
Oral contraceptive exposure – n, (%)			0.12
Yes	60 (47.6)	26 (63.6)	
No	66 (52.4)	30 (50.0)	
Hormone replacement therapy – n, (%)			**0.03**
Yes	17 (13.5)	6 (35.3)	
No	109 (86.5)	64 (58.7)	
ACR Type Breast Density – n, (% with breast density available)			0.32
Type A (entirely fatty)	3 (2.7)	2 (66.7)	
Type B (scattered fibroglandular)	30 (27.0)	19 (63.3)	
Type C (heterogeneously dense)	60 (54.1)	37 (61.7)	
Type D (extremely dense)	18 (16.2)	7 (38.9)	
Surgical Excision of their HRL – n, (%)			0.08
Yes	65 (51.6)	42 (64.6)	
No	61 (48.4)	30 (49.2)	
Medication Prescribed – n, (%)			0.94
Tamoxifen 5 mg	82 (65.1)	46 (56.1)	
Tamoxifen 20 mg	17 (13.5)	11 (64.7)	
Raloxifene 60 mg	21 (16.7)	11 (52.4)	
Anastrozole 1 mg/Exemestane 25 mg	6 (4.8)	3 (50.0)	
Concern about developing breast cancer – n, (%)			0.35
Low	15 (11.9)	6 (40.0)	
Moderate	20 (15.9)	12 (60.0)	
High	91 (72.2)	54 (59.3)	
Prior awareness of endocrine prevention – n, (%)			**0.03**
Yes	28 (22.2)	21 (75.0)	
No	98 (77.8)	51 (52.0)	

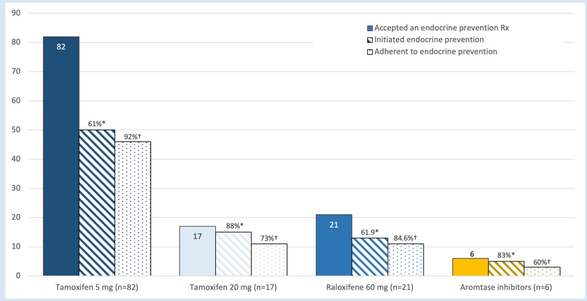
HRL High risk lesion; ***Rx*** prescription/prescribed; *Bold if statistically significant on Fisher exact test with p-value less than 0.05.

Low-dose tamoxifen analysis





RESULTS



Of note, no patients developed venous thromboembolism or endometrial cancer during follow-up

Reasons for non-adherence after initiation (n=11): vasomotor symptoms (n=3), gynecologic symptoms (n=3), musculoskeletal symptoms (n=2), dyspnea (n=1), or gastrointestinal side effects including nausea or abdominal pain (n=2).

FIGURE 2: Endocrine prevention uptake, initiation, and adherence by regimen. *Indicates the percentage of patients who initiated endocrine prevention after accepting an endocrine prevention prescription; †Indicates the percentage of patients who were adherent to treatment after initiating endocrine prevention; ***Rx*** endocrine prevention.

CONCLUSIONS

- Of the 200 female patients included in this study, 126 (63%) accepted a prescription and 83 (65.9%) of those patients initiated endocrine prevention;
- At median follow-up of 35 months, 72 (57.1%) remained adherent;
- Increased adherence was significantly associated with age, family history, and prior awareness of endocrine prevention;
- Prior or current hormone replacement therapy (HRT) use was negatively associated with adherence;
- In the subgroup of patients who initiated endocrine prevention, the overwhelming majority (77%) remained on treatment, with low rates of discontinuation due to side effects;
- Low-dose tamoxifen was the most popular endocrine prevention regimen prescribed; of the low-dose tamoxifen patients who completed a 3-year regimen, almost 70% elected to continue and complete a total 5-year course

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