Breast Cancer Risk Reduction Therapy

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RISK ASSESSMENT

Risk Categories

Women ages ≥ 35 years old[1], **and** one of the following:

- History of lobular carcinoma in situ (LCIS)[2]
- Atypical ductal hyperplasia (ADH)[2]
- Atypical lobular hyperplasia (ALH)[2]
- Estrogen receptor positive ductal carcinoma in situ (ER+ DCIS)
- Gail model 5 year breast cancer risk ≥ 1.7%
- Tyrer-Cuzick model 10 year breast cancer risk ≥ 5%
- Prior thoracic radiation therapy (XRT) at age 10-30 years old[3]

and

- Life expectancy ≥ 10 years

and

- No contraindications[4] to risk reduction therapy

Does patient meet criteria?

- Yes
- No → Patient not a candidate for risk reduction treatment

TREATMENT

Pre-menopausal → Tamoxifen

Post-menopausal:

- High risk lesions:
  - LCIS
  - ADH/ALH
  → Recommend one of the following:
  - Tamoxifen[5]
  - Raloxifene[5,6]
  - Aromatase inhibitors (AI)[7,8] (exemestane **or** anastrozole)
- ER+ DCIS → Recommend one of the following:
  - Aromatase inhibitors (AI)[9] (exemestane **or** anastrozole)[10]
  - Tamoxifen[5,11]
- Lifetime risk ≥ 20% by Gail or Tyrer-Cuzick models
- Prior thoracic XRT at age 10-30 years old[3]
  → Recommend one of the following:
  - Tamoxifen[5]
  - Raloxifene[5,6]
  - Aromatase inhibitors (AI)[8] (exemestane **or** anastrozole)
- Lifetime risk < 20% by Gail or Tyrer-Cuzick models → Assess balance of benefits and harms[12] and recommend one of the following:
  - Tamoxifen[5]
  - Raloxifene[5,6]
  - Aromatase inhibitors (AI)[8] (exemestane **or** anastrozole)

[1] Patients without breast prophylactic mastectomy (BPM)
[2] Primary benefit is seen in patients up to age 70 years old and may not be as great for those who are older
[3] Limited data regarding risk reduction therapies in women with prior thoracic XRT
[4] If prior history of a thromboembolic event, tamoxifen and raloxifene are contraindicated as an option due to increased risk. Adequately treated endometrial hyperplasia or early-stage endometrial cancer is not a contraindication to the use of tamoxifen.
[5] Standard dose of tamoxifen (20 mg daily) or raloxifene is recommended. If there are concerns about side effects, discuss low dose of tamoxifen (10 mg every other day) as initial treatment option. Standard dose of tamoxifen is preferred based on more robust data.
[6] Lower risk of uterine cancer but less long-term benefit
[7] Limited data regarding AIs in women with proliferative breast lesions
[8] Off-label (Not FDA approved) but evidence-based if tamoxifen is contraindicated or not tolerated
[9] Recommend anastrozole as first choice. If there are concerns about side effects or contraindications, patients can be offered standard dose of tamoxifen (20 mg daily) or low dose of tamoxifen (10 mg every other day).
[10] If patient is intolerant of tamoxifen, anastrozole, and exemestane, the use of letrozole may be considered
[11] In patients with an intact uterus, it may be preferred to use low dose of tamoxifen (10 mg every other day) due to decrease incidence of uterine cancers
[12] Tables that can be used to determine women for whom the benefits outweigh the risks can be found at Freedman, A. N., Yu, B., Gail, M. H., Costantino, J. P., Graubard, B. I., Vogel, V. G., … McCaskill-Stevens, W. (2011). Benefit/risk assessment for breast cancer chemoprevention with raloxifene or tamoxifen for women age 50 years or older. *Journal of Clinical Oncology, 29*(17), 2327.

Note: Recommended duration of treatment for a total of 5 years

- In cases where patient prefers decreased duration or cannot tolerate for the recommended duration of 5 years, it can be discussed with the patient that there is data for taking it for 3 years based on the low dose tamoxifen study
- Provider may consider continuing raloxifene beyond the 5 years.

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Department of Clinical Effectiveness V5
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DEVELOPMENT CREDITS

This risk reduction algorithm is based on majority expert opinion of the Breast Cancer Risk Reduction Therapy workgroup at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Core Development Team Leads

Therese Bevers, MD (Clinical Cancer Prevention)
Abenaa Brewster, MD (Clinical Cancer Prevention)

Workgroup Members

Banu Arun, MD (Breast Medical Oncology)
Powel Brown, MD, PhD (Clinical Cancer Prevention)
Joyce Dains, DrPH, APRN, FNP-BC (Nursing)
Olga N. Fleckenstein, BS♦
Ernest Hawk, MD (Clinical Cancer Prevention)
Thoa Kazantsev, MSN, RN, OCN♦
Ana Nelson, APRN, FNP-BC (Clinical Cancer Prevention)
Priya Thomas, MD (Clinical Cancer Prevention)

♦ Clinical Effectiveness Development Team

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