Breast Cancer in Young Women

Dr. Kate Lathrop, MD

2020 TAYA Conference

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Financial Disclosure

- I have a salary and contracted research with Ausio Pharmaceuticals and consulting fees from Encore Education. These relationships will not impact my ability to present an unbiased presentation.

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Breast Cancer in Young Women: A Case Study

- Maria is a 28 y.o. Hispanic woman who noticed a mass in left breast while showering 8 months ago. Over that period, the mass increased in size and became tender and painful.
- She then had a left mammogram that showed a 5.7 heterogenous shadowing mass with irregular margins with a lobulated lymph node with thickened cortex measuring up to 7 mm.
- Left breast and lymph node biopsy revealed Invasive Ductal Carcioma, grade 3 of 3, ER 70% PR 35% and Her2 3+ in the breast and axilla lymph node.

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Breast Cancer in Young Women: A Case Study

REPRODUCTIVE HISTORY: menarche at age 13. No parity. Currently using a progesterone implant in her arm for contraception x 6 years

PAST MEDICAL HISTORY: Hyperlipidemia.

PAST SURGICAL HISTORY: rhinoplasty.

SOCIAL HISTORY: Never smoked. No alcohol or Illicit drug use

FAMILY HISTORY: Breast Cancer in her aunt, age 40

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Breast cancer in the "Very Young" What's the Worry?

Being young (<35 years) at diagnosis:

- Associated with a less favorable prognosis
- Recurrence hazard and age is continuous with a 4% decrease in recurrence and a 2% decrease in cancer-specific death for every year of increase in age
- Less than 35: risk of death increases by 5% for every 1-year decrease in age
- Age 35–50 years: no significant correlation between risk of death and age

de la Rochefordiere, A. Age as prognostic factor in premenopausal breast carcinoma, Lancet 1993
Han W, Kang SY, Breast Cancer Res Treat, 2010

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Breast cancer in the "Very Young" What's the Worry?

The biology is significantly different:

- Higher prevalence of tumors of high grade
- Less likely to be hormone receptor positive
- Higher percentages of tumors with vascular invasion
- More likely to be HER2-overexpressed
- More Triple Negative tumors

G. Cancello, Annuals of Oncology, Oct 2010

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Assessing Genetic Risks

TESTING CRITERIA FOR HIGH-PENETRANCE BREAST AND/OR OVARIAN CANCER SUSCEPTIBILITY GENES
(This often includes *BRCA1, BRCA2, CDH1, PALB2, PTEN,* and *TP53* among others. See GENE-A for a more complete li

Testing is clinically indicated in the following scenarios:

1. Individuals with any blood relative with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene
2. Individuals meeting the criteria below but with previous limited testing (eg, single gene and/or absent deletion duplication analysis) interested in pursuing multi-gene testing
3. *Personal history of cancer*
   - Breast cancer with at least one of the following:
     - Diagnosed at age ≤45 y; or
     - Diagnosed at age 46–50 y with:
       - Unknown or limited family history; or
       - A second breast cancer diagnosed at any age; or
       - ≥1 close blood relative[e] with breast, ovarian, pancreatic, or high-grade (Gleason score ≥7) or intraductal prostate cancer at any age
     - Diagnosed at age ≤60 y with triple-negative breast cancer;
     - Diagnosed at any age with:
       - Ashkenazi Jewish ancestry; or
       - ≥1 close blood relative[e] with breast cancer at age ≤50 y or ovarian, pancreatic, or metastatic or intraductal prostate cancer at any age; or
       - ≥3 total diagnoses of breast cancer in patient and/or close blood relatives[e]
     - Diagnosed at any age with male breast cancer
   - Epithelial ovarian cancer[f] (including fallopian tube cancer or peritoneal cancer) at any age
   - Exocrine pancreatic cancer at any age[g] (See CRIT-3)
   - Metastatic or intraductal prostate cancer at any age[h]
   - High-grade (Gleason score ≥7) prostate cancer with:
     - Ashkenazi Jewish ancestry; or
     - ≥1 close relative[e] with breast cancer at age ≤50 y or ovarian, pancreatic, or metastatic or intraductal prostate cancer at any age; or
     - ≥2 close relatives[e] with breast or prostate cancer (any grade) at any age.
   - A mutation identified on tumor genomic testing that has clinical implications if also identified in the germline
   - To aid in systemic therapy decision-making, such as for HER2-negative metastatic breast cancer[i]
4. *Family history of cancer*
   - An affected or unaffected individual with a first- or second-degree blood relative meeting any of the criteria listed above (except individuals who meet criteria only for systemic therapy decision-making)[j]
   - An affected or unaffected individual who otherwise does not meet the criteria above but has a probability >5% of a *BRCA1/2* pathogenic variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, PennII)[k]

Assessing Genetic Risks

LI-FRAUMENI SYNDROME MANAGEMENT IN ADULTS

BREAST CANCER RISK FOR WOMEN

- Breast awareness[a] starting at age 18 y.
- Clinical breast exam, every 6–12 mo, starting at age 20 y.[b]
- Breast screening
  - Age 20–29[b] y, annual breast MRI[c] screening with contrast.[d]
  - Age 30–75 y, annual breast MRI[c] screening with contrast and mammogram with consideration of tomosynthesis.
  - Age >75 y, management should be considered on an individual basis.
  - For women with a *TP53* pathogenic/likely pathogenic variant who are treated for breast cancer, and who have not had a bilateral mastectomy, screening with annual breast MRI and mammogram with consideration of tomosynthesis should continue as described above.
- Discuss option of risk-reducing mastectomy
  - Counseling should include a discussion regarding degree of protection, reconstruction options, and risks. In addition, the family history and residual breast cancer risk with age and life expectancy should be considered during counseling.
- Address psychosocial and quality-of-life aspects of undergoing risk-reducing mastectomy.

OTHER CANCER RISKS

- Comprehensive physical exam including neurologic examination with high index of suspicion for rare cancers and second malignancies in cancer survivors every 6–12 mo.
- Colonoscopy and upper endoscopy every 2–5 y starting at 25 y or 5 y before the earliest known colon cancer in the family (whichever comes first).
- Annual dermatologic examination starting at 18 y.
- Annual whole body MRI[e,f,g] (category 2B).
- Annual brain MRI (category 2B) may be performed as part of the whole body MRI or as a separate exam.

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Reconstruction Challenges: Young Women are Different

- Competing priorities - Parenting, work, or recreational activities influence timing and type of reconstruction.
- Experience greater psychological morbidity and poorer quality of life than older women.
- Breast anatomy and physiology and overall medical condition generally allow more reconstructive options
- Young breast cancer survivors maybe less sexually active
- More body image and sexual problems than healthy women in their same age range.
- Related to both to side effects of breast cancer treatment and to difficulties with mental health and partner relationships

Lee, Breast Disease, vol. 23, no. 1, pp. 47-52, 2006
Fobair, Psycho-Oncology15: 579–594 (2006)

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Fertility Preservation

VOLUME 36 · NUMBER 19 · JULY 1, 2018
JOURNAL OF CLINICAL ONCOLOGY REVIEW ARTICLE

Gonadotropin-Releasing Hormone Agonists During Chemotherapy for Preservation of Ovarian Function and Fertility in Premenopausal Patients With Early Breast Cancer: A Systematic Review and Meta-Analysis of Individual Patient–Level Data

Matteo Lambertini, Halle C.F. Moore, Robert C.F. Leonard, Sibylle Loibl, Pamela Munster, Marco Bruzzone, Luca Boni, Joseph M. Unger, Richard A. Anderson, Keyur Mehta, Susan Minton, Francesca Poggio, Kathy S. Albain, Douglas J.A. Adamson, Bernd Gerber, Amy Cripps, Gianfilippo Bertelli, Sabine Seiler, Marcello Ceppi, Ann H. Partridge, and Lucia Del Mastro

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Fertility Preservation

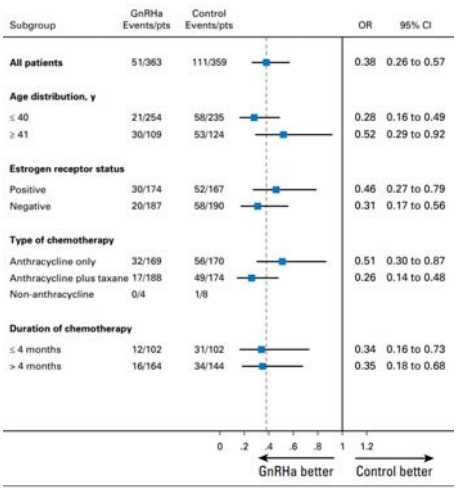
- Meta-analysis of individual patient data from five randomized clinical trials (PROMISE-GIM6, POEMS/SWOG S0230, Angelo Celtic Group OPTION, GBG-37 ZORO, and a Moffitt Cancer Center-led trial)
- Premature ovarian insufficiency rate in the GnRHa group was 14.1% vs 30.9% in the control group
- Patients in the GnRHa group had 62% less risk to develop premature ovarian insufficiency as compared to those treated with chemotherapy alone.
- Patients in the GnRHa group had 1- and 2-year amenorrhea rates of 36.8% and 18.2%, respectively. One- and 2-year amenorrhea rates in the control group were 40.4% and 30%, respectively.
- Thirty-seven patients in the GnRHa group had at least one post-treatment pregnancy during the follow-up period vs 20 patients in the control group.

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

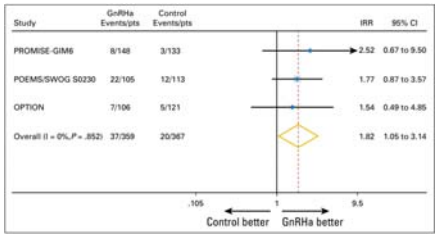
Lambertini et al, J Clin Oncol 36:1981-1990, 2018

Fertility Preservation

Premature ovarian insufficiency



Post treatment Pregnancies



Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Hormonal Therapy Selection

VOLUME 35 · NUMBER 27 · SEPTEMBER 20, 2017

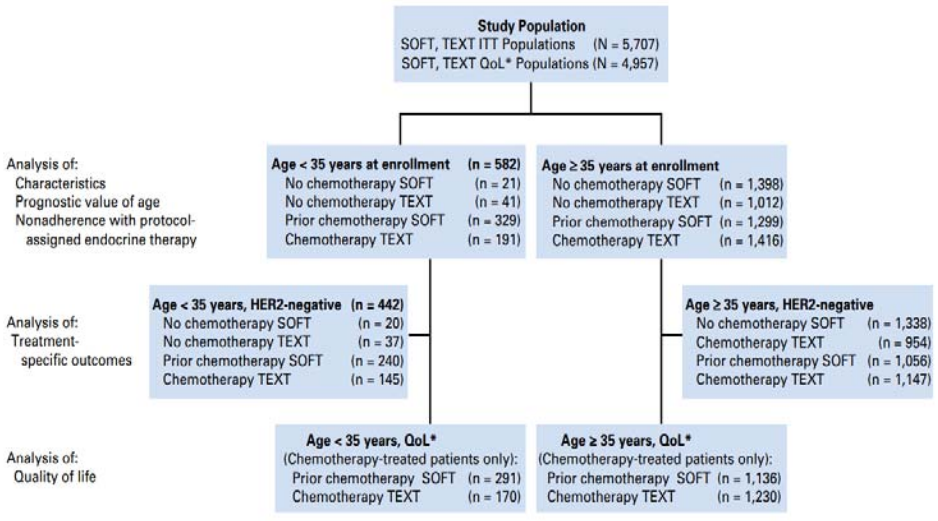
JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

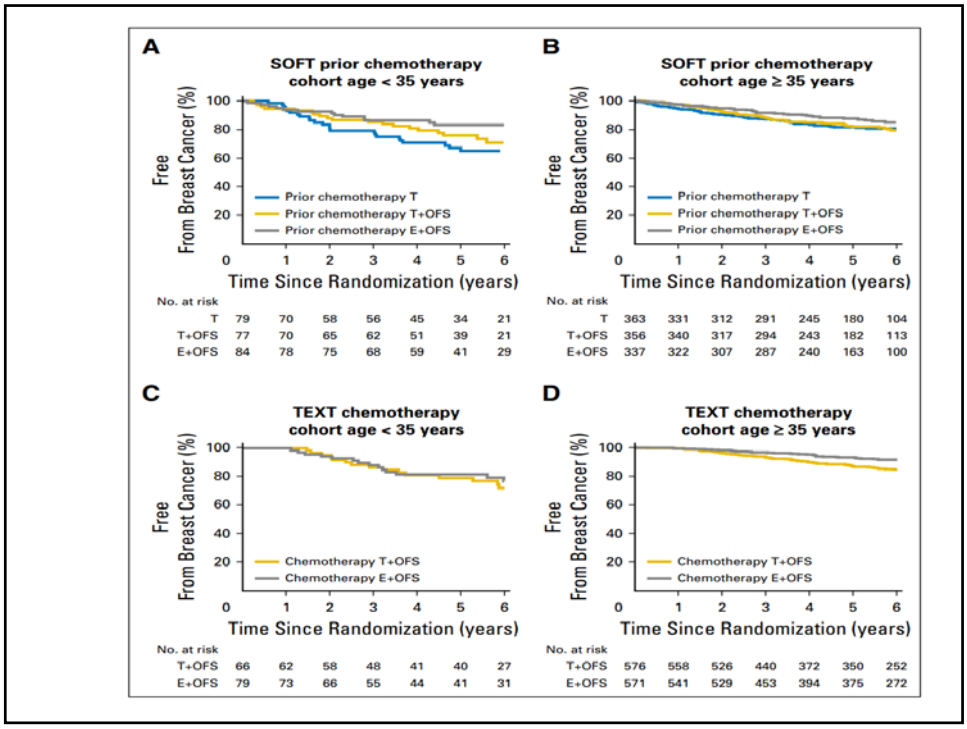
Treatment Efficacy, Adherence, and Quality of Life Among Women Younger Than 35 Years in the International Breast Cancer Study Group TEXT and SOFT Adjuvant Endocrine Therapy Trials

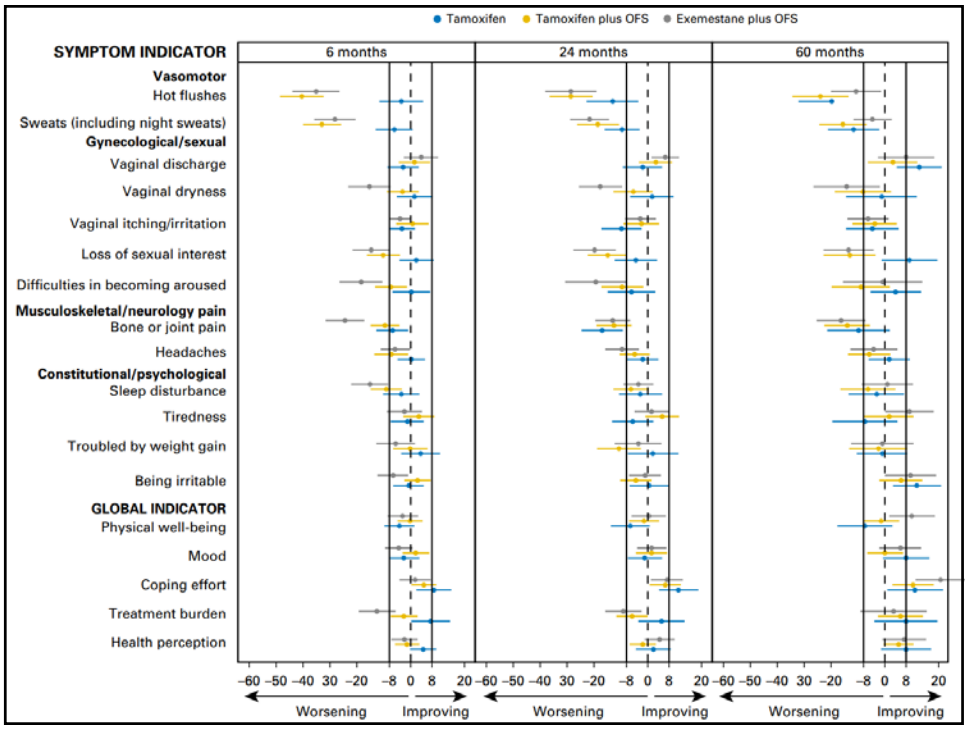
Poornima Saha, Meredith M. Regan, Olivia Pagani, Prudence A. Francis, Barbara A. Walley, Karin Ribi, Jürg Bernhard, Weixiu Luo, Henry L. Gómez, Harold J. Burstein, Vani Parmar, Roberto Torres, Josephine Stewart, Meritxell Bellet, Antonia Perelló, Faysal Dane, Antonio Moreira, Daniel Vorobiof, Michelle Nottage, Karen N. Price, Alan S. Coates, Aron Goldhirsch, Richard D. Gelber, Marco Colleoni, and Gini F. Fleming; for the SOFT and TEXT Investigators and the International Breast Cancer Study Group

Mays Cancer Center
UT Health San Antonio | MD Anderson Cancer Center

Hormonal Therapy Selection







Hormonal Therapy Selection

The NEW ENGLAND JOURNAL of MEDICINE

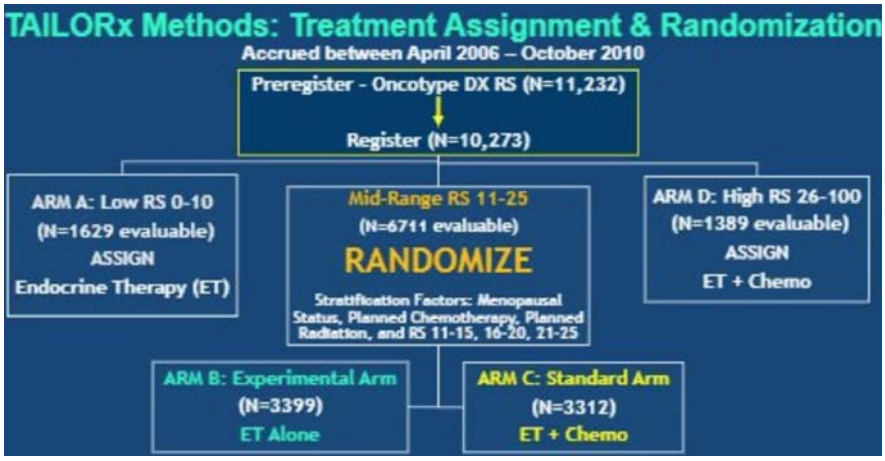
ESTABLISHED IN 1812 JUNE 20, 2019 VOL. 380 NO. 25

Clinical and Genomic Risk to Guide the Use of Adjuvant Therapy for Breast Cancer

J.A. Sparano, R.J. Gray, P.M. Ravdin, D.F. Makower, K.I. Pritchard, K.S. Albain, D.F. Hayes, C.E. Geyer, Jr., E.C. Dees, M.P. Goetz, J.A. Olson, Jr., T. Lively, S.S. Badve, T.J. Saphner, L.I. Wagner, T.J. Whelan, M.J. Ellis, S. Paik, W.C. Wood, M.M. Keane, H.L.G. Moreno, P.S. Reddy, T.F. Goggins, I.A. Mayer, A.M. Brufsky, D.L. Toppmeyer, V.G. Kaklamani, J.L. Berenberg, J. Abrams, and G.W. Sledge, Jr.

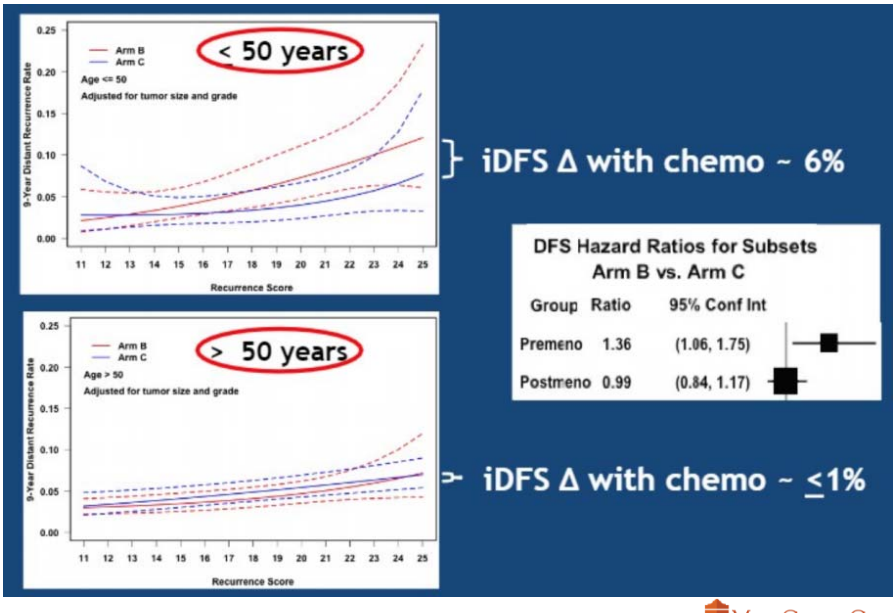
Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Hormonal Therapy Selection



Sparano, ASCO 2019

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center



Carey, ASCO 2019

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center

Hormonal Therapy Selection

Subgroup	No. of Patients	No. of Events	Hazard Ratio for Recurrence, Second Primary Cancer, or Death (95% CI)	No. of Distant Recurrences	Hazard Ratio for Distant Recurrence (95% CI)
All patients	9427				
Endocrine therapy					
Low recurrence score (0–10)	1572	176		30	
Intermediate recurrence score (11–25)	3282	422		127	
Chemoendocrine therapy					
Intermediate recurrence score (11–25)	3214	389		113	
High recurrence score (26–100)	1359	184		96	
>50 Yr of age	6469				
Endocrine therapy					
Low recurrence score (0–10)	1160	135		23	
Intermediate recurrence score (11–25)	2182	273		74	
Chemoendocrine therapy					
Intermediate recurrence score (11–25)	2171	292		79	
High recurrence score (26–100)	956	133		65	
≤50 Yr of age	2958				
Endocrine therapy					
Low recurrence score (0–10)	412	41		7	
Intermediate recurrence score (11–25)	1100	149		53	
Chemoendocrine therapy					
Intermediate recurrence score (11–25)	1043	97		34	
High recurrence score (26–100)	403	51		31	

Hormonal Therapy Selection

Recurrence Score® (RS) Result	Distant Recurrence Risk at 9 Years	Group Average Absolute Chemotherapy (CT) Benefit*
21	With AI or TAM Alone 7% 95% CI (6%, 9%) TAILORx	RS 11-25 All Ages <1% 95% CI (-1%, 2%) TAILORx

Decision on individual treatment especially around the RS 25 cutoff may consider other clinical factors.

AI = Aromatase Inhibitor / TAM = Tamoxifen
CI = Confidence Intervals

*For estimated CT benefit for individual RS results, see page 2.

Exploratory Subgroup Analysis for TAILORx and NSABP B-20:
Absolute CT Benefit for Distant Recurrence by Age and RS Result

Age	RS 0-10	RS 11-15	RS 16-20	RS 21-25	RS 26-100
>50 years	No CT Benefit (<1%)				>15% CT Benefit
≤50 years	No CT Benefit (<1%)		~1.6% CT Benefit	~6.5% CT Benefit	>15% CT Benefit

Questions...

Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center