2017 San Antonio Breast Cancer Symposium: Local Therapy Highlights

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Abstracts

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2. Axillary Dissection vs. No Axillary Dissection in Patients with cT1-T2N0M0 and only Micrometastasis in the Sentinel Node(s): Ten Year Results of the IBCSG 23-01 Trial (GS5-02)
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Abstracts

4. Primary Endocrine Therapy for ER-Positive Ductal Carcinoma in Situ (DCIS) CALGB 40903 (Alliance) (GS5-05)
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Appropriate margins for breast-conserving surgery in patients with early stage breast cancer: A meta-analysis

Frank Vicini, Vivek Verma, Harlan Sayles, Abram Recht, Chirag Shah

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Cleveland Clinic Taussig Cancer Institute
Beth Israel Deaconess Medical Center, Harvard Medical School,
UCLA Medical School, Radiation Oncology

Methods

- Conducted an updated meta-analysis of 38 studies with 55,302 patients to evaluate the influence of margin width on local recurrence in breast cancer patients treated with breast conserving surgery
- 3 Models:
  1) Negative vs. close (study specific pre-specified distance from margin) /positive
  2) Margin range: 0-2mm vs. 2-5mm vs. >5mm
  3) Negative vs. close (study specific pre-specified distance from margin) vs. positive

Results

1) Model 1: Negative vs. close (study specific pre-specified distance from margin) /positive
   - Negative Margin associated with lower local recurrence rates
2) Model 2: Margin range: 0-2mm vs. 2-5mm vs. >5mm
   - The larger the margin the lower the local recurrence rate
3) Model 3: Negative vs. close (study specific pre-specified distance from margin) vs. positive
   1) Lowest local recurrence rates seen with negative margins (when cutoff was 2mm and 5mm)

Take Home Message

- This study suggests that margins beyond no tumor at ink (greater than 2mm) may reduce rates of local recurrence and challenges the SSO guidelines
- Recommends considering re-excision in select patients to achieve greater margins

Limitations

- Studies date back to 1995 and findings may not be relevant to current practice with advances in treatment, imaging, pathologic analysis which may drive local recurrence rates down
- Each study did not serve as its own internal control because arms were added to each model depending on the margin status
- Threshold margins – actual surgery margins may not have been measured in individual studies, <1mm cutoff could have been considered negative whether it was 10 mm or 1mm margins

Axillary dissection vs. no axillary dissection in patients with cT1-T2 N0 breast cancer and micrometastases only in the sentinel node: ten-year results of the IBCSG 23-01 trial

Viviana Galimberti, MD
for the
International Breast Cancer Study Group

Background

- For patients with a metastatic sentinel node (SN), axillary dissection (AD) used to be the standard approach to the axilla
- Five-year results of 23-01 and 10-year results of Z0011 showed that, for patients with moderate axillary involvement, AD provided no advantage in terms of overall or disease-free survival, while axillary failure rates were low
- Updated follow-up of 23-01 was successful for 83% of patients who had not withdrawn

Study Design

- Eligible consenting patients – who could be scheduled for mastectomy or conservative surgery – were registered before surgery
- If tumor/nodal eligibility criteria met, randomized:-
  - Prior to amendment (June 2006): Tumor size ≤ 3 cm; unicentric; one micrometastatic (≤2 mm) sentinel node; no extracapsular extension or macrometastatic involvement
  - After amendment: Tumor size ≤ 5 cm; uni or multicentric; one or more micrometastatic (≤2 mm) sentinel nodes

Statistical Considerations

- Primary endpoint: invasive disease-free survival (DFS)
- Secondary endpoint: overall survival, incidence of reappearance of tumor in un-dissected axilla
- The non-inferiority margin for no-AD vs. AD was defined as a DFS hazard ratio (HR, no-AD relative to AD) of <1.25, and was assessed using a z-test applied to the log HR.

Patient and Tumor Characteristics

Characteristic	AD (n=464)	No AD (n=467)	Total (n=931)
Age, years; median (range)	53 (28–81)	54 (26–81)	54 (26–81)
Menopausal status			
Pre	204 (44%)	207 (44%)	411 (44%)
Post	260 (56%)	260 (56%)	520 (56%)
Pre-op sentinel node biopsy			
No	287 (62%)	286 (61%)	573 (62%)
Yes	177 (38%)	181 (39%)	358 (38%)
Sentinel node disease			
≤ 1 mm	323 (70%)	320 (69%)	643 (69%)
1.1–2.0 mm	131 (28%)	135 (29%)	266 (29%)
>2 mm	10 (2%)	11 (2%)	21 (2%)
Unknown	0	1 (<1%)	1 (<1%)

Patient and Tumor Characteristics

Characteristic	AD (n=464)	No AD (n=467)	Total (n=931)
Tumor size			
<2 cm	316 (68%)	322 (69%)	638 (69%)
2 cm to 2.9 cm	106 (23%)	112 (24%)	218 (23%)
≥3 cm	35 (8%)	28 (6%)	63 (7%)
Unknown	7 (2%)	5 (1%)	12 (1%)
Tumor grade			
Grade 1	118 (25%)	90 (19%)	208 (22%)
Grade 2	214 (46%)	241 (52%)	455 (49%)
Grade 3	129 (28%)	135 (29%)	264 (28%)
Unknown	3 (<1%)	1 (<1%)	4 (<1%)

90% ER+

75% PR+

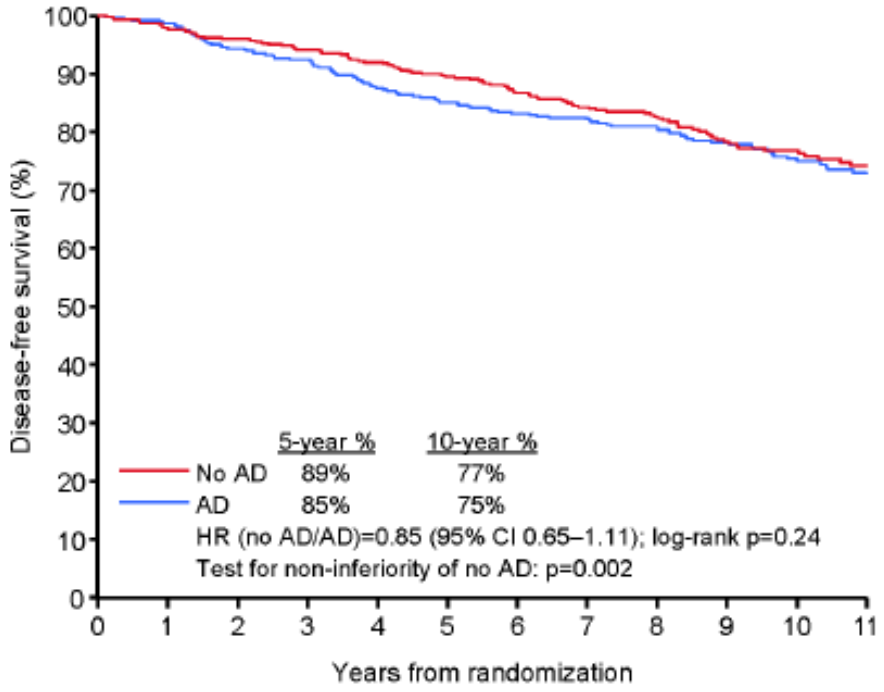
Local Treatment

Treatment	AD (n=464)	No AD (n=467)	Total (n=931)
Type of breast surgery			
Conservative	420 (91%)	425 (91%)	845 (91%)
Mastectomy	44 (9%)	42 (9%)	86 (9%)
Radiotherapy (BCS)			
No	10/420 (2%)	12/425 (3%)	22 (3%)
Yes	410/420 (98%)	413/425 (97%)	823 (97%)
Radiotherapy in mastectomy			
No	42/44 (95%)	39/42 (93%)	81 (94%)
Yes	2/44 (5%)	3/42 (7%)	5 (6%)

Systemic Treatment

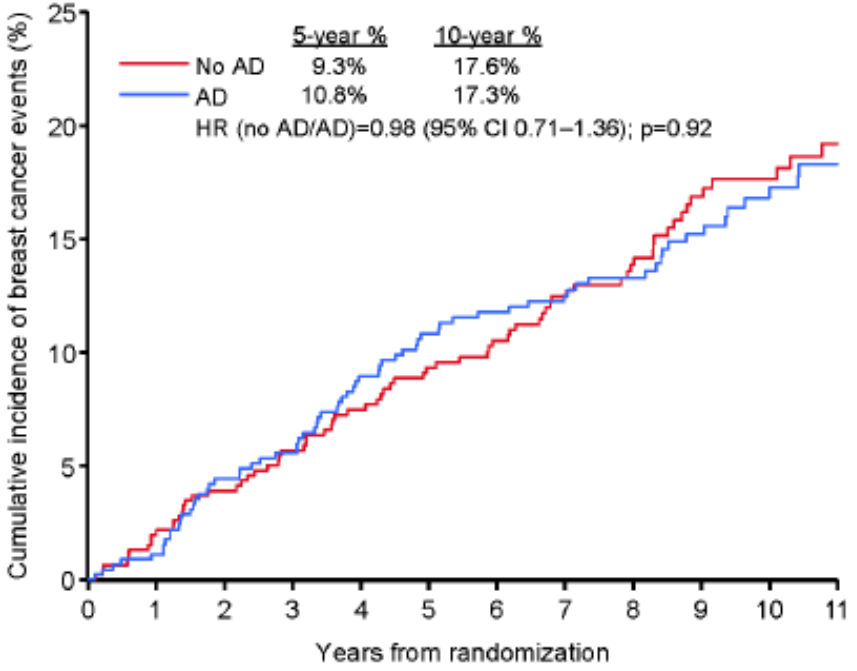
Treatment	AD (n=464)	No AD (n=467)
Any systemic therapy	441 (95%)	451 (97%)
Hormonal therapy only	292 (63%)	315 (67%)
Chemotherapy only	42 (9%)	33 (7%)
Combination therapy	107 (23%)	103 (22%)

Disease-Free Survival



Number at risk												
No AD	467	455	443	428	412	389	367	336	278	215	168	131
AD	464	456	433	419	392	371	353	335	282	231	169	130

Cumulative Incidence of Breast Cancer Events



Number at risk

No AD	467	455	443	428	412	389	367	336	278	215	168	131
AD	464	456	433	419	392	371	353	335	282	231	169	130

Disease-Free Survival Events and Deaths

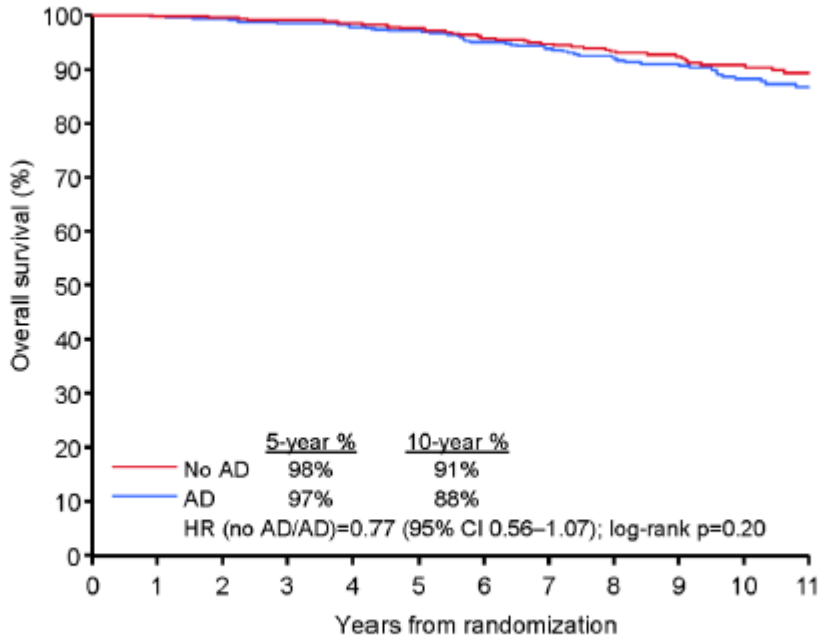
	AD (n=464)		No AD (n=467)	
Total DFS events	**117**	**25.2%**	**101**	**21.6%**
Breast cancer events	**75**	**16.2%**	**74**	**15.8%**
Local	13	2.8%	14	3.0%
Regional	3	0.6%	9	1.9%
Ipsilateral axillary events	**2**	**0.4%**	**8**	**1.7%**
Distant	47	10.1%	41	8.8%
Contralateral breast	12	2.6%	10	2.1%
Non-breast cancer events	**42**	**9.1%**	**27**	**5.8%**
Second (non-breast) primary	23	5.0%	17	3.6%
Death without prior cancer event	2	0.4%	6	1.3%
Death with unknown cancer status	17	3.7%	4	0.9%
Deaths	**58**	**12.5%**	**45**	**9.6%**

Disease-Free Survival Events According to Type of Surgery

	Mastectomy (n=86)		Breast conservation (n=845)	
Total DFS events	23 (26.7%)		195 (23.1%)	
Breast cancer events	17 (19.8%)		132 (15.6%)	
Ipsilateral axillary events	2		8	
	AD 1 (1.2%)	No AD 1 (1.2%)	AD 1 (0.1%)	No AD 7* (0.8%)
Non-breast cancer events	6 (7.0%)		63 (7.5%)	
Deaths	14 (16.3%)		89 (10.5%)	

*Five received intraoperative radiotherapy

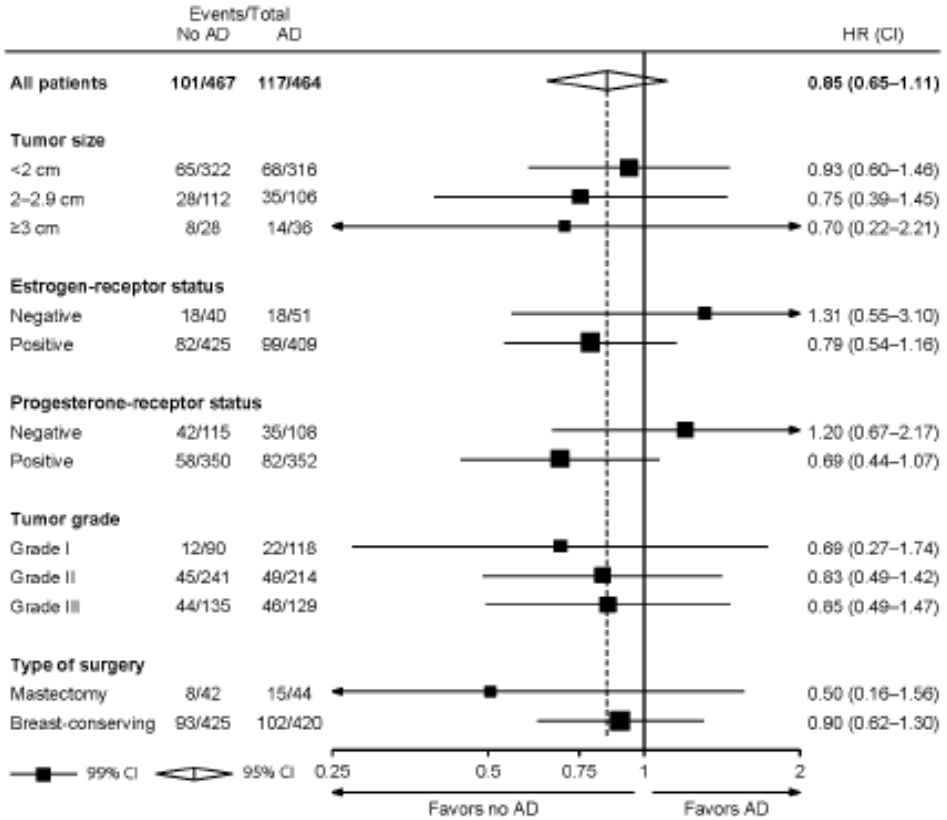
Overall Survival



Number at risk

No AD	467	464	460	451	441	424	405	375	314	257	197	158
AD	464	461	456	446	438	422	401	379	319	264	199	156

Subgroup Analysis of Disease-Free Survival



Conclusions

- Our findings are fully consistent with those of the Z0011 trial, which after 10 years found no differences between the AD and no AD groups for any endpoint in patients with moderate disease burden in the axilla, undergoing conservative breast surgery
- We also suggest that non AD is acceptable treatment in patients scheduled for mastectomy
- Our data fully support the change in clinical practice that started after the early published results
- No AD is now standard treatment in early breast cancer when the SN is only minimally involved

Take Home Message

- After a median f/u of 9.8 years, no difference between AD and no AD groups in DFS
- Rate of axillary failure was low at 1.7% in no AD arm
- Axillary dissection is not indicated in breast cancer patients treated with upfront breast conserving surgery and micrometastasis

Limitations

- Majority of patients had favorable, low risk tumors <2cm and 95% were ER+, 96% received systemic therapy
- Very few patients (9%) treated with mastectomy
- All breast conserving surgery patients in this study received radiation, but is radiation needed in postmastectomy patients with micromets who do not have AD?

Risk of Arm Morbidity after Local Therapy in Young Breast Cancer Survivors

A. Kuijer, MD, PhD

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L.S. Dominici, S.M. Rosenberg, J. Hu, S. Gelber, S. Di Lascio, J. Wong, K.J. Ruddy, R.M. Tamimi, L. Schapira, V.F. Borges, S.E. Come, K. Sprunck-Harrild, A.H. Partridge, T.A. King.

DANA-FARBER/BRIGHAM AND WOMEN'S CANCER CENTER

Study Objectives

- Assess the incidence of self-reported arm swelling and decreased range of motion among participants in the Young Womens Study
  - Breast Cancer Prevention Trial (BCPT) Symptom Checklist:
    - Have you experienced arm swelling/decreased range of motion on the side which you had surgery during the past 4 weeks (0=not at all; 4=extremely)
    - Surveys given at baseline (~4 mos after diagnosis), Q6 mos for 3 years, then annually
- Identify risk factors for the development of self-reported arm morbidity

Results: arm morbidity and breast surgery

- **13%** (n =136) of all patients reported arm swelling at 1 year
  - 11% of patients who underwent BCT
  - 14% of patients who underwent any mastectomy

- **33%** (n = 355) of all patients reported decreased ROM at 1 year
  - 32% of patients who underwent BCT
  - 34% of patients who underwent any mastectomy

Results: arm morbidity and local treatment

	Arm swelling (1 y)	*p*	Decreased ROM (1 y)	*p*
Breast conserving therapy				
SLNB (n = 191)	6%		31%	
ALND (n = 84)	25%	*<0.01*	37%	0.58
Any mastectomy without RT				
SLNB (n = 264)	4%		20%	
ALND (n = 59)	19%	*<0.01*	34%	0.12
Any mastectomy with RT				
SLNB (n = 79)	11%		41%	
ALND (n = 261)	25%	0.06	46%	0.68

Logistic regression arm swelling

		OR (95% CI)	*P-value*
Patient factors:			
BMI:	Overweight vs. normal weight	1.7 (1.1-2.7)	*0.03*
Financial status:	Comfortable vs. uncomfortable	0.6 (0.4-0.9)	*0.01*
Tumor factors:			
pT stage:	pT4 vs. pT1	4.2 (1.1-15.8)	*0.03*
pN stage:	pN1 vs. pN0	1.1 (0.5-2.2)	0.87
Treatment factors:			
Type of surgery:	Mastectomy + RT vs. BCT	1.1 (0.6-2.0)	0.70
	Mastectomy - RT vs. BCT	0.7 (0.4-1.4)	0.30
Axillary surgery:	ALND vs. SLNB	3.4 (1.8-6.4)	*<0.01*

Age, year of diagnosis, employment status, stage, breast reconstruction, chemotherapy and radiation were not associated with arm swelling

Logistic regression decreased ROM

		OR (95% CI)	*P-value*
Patient factors:			
BMI:	Overweight vs. normal weight	1.4 (1.0-2.1)	*0.05*
Tumor factors:			
pT stage:	pT4 vs. pT1	2.3 (0.5-10.4)	0.27
pN stage:	pN1 vs. pN0	1.6 (0.9- 2.9)	0.09
Treatment factors:			
Type of surgery:	Mastectomy + RT vs. BCT	2.1 (1.3-3.3)	<0.01
	Mastectomy - RT vs. BCT	0.78 (0.50-1.2)	0.30
Axillary surgery:	ALND vs. SLNB	1.1 (0.70-1.8)	0.65

Age, year of diagnosis, employment status, financial status, stage, breast reconstruction, chemotherapy and radiation were not associated with decreased ROM

Conclusions

- Young breast cancer survivors report high rates of arm morbidity in the first year of follow up

- ALND, increased BMI and less comfortable financial status were all independently associated with increased risk of self-reported arm swelling

- Patients receiving mastectomy with radiation therapy were twice as likely to experience decreased ROM at 1 year when compared to patients treated with BCT

- These findings highlight opportunities for pre-operative counseling, early referral to physical therapy and identification of resources for ongoing support for those at increased risk

- Attention to the risks and benefits of local therapy strategies, specifically BCT vs mastectomy, in this population is also warranted

Take Home Message

- Very high rates of mastectomy
- Increased BMI, ALND, and pT4 vs. T1 disease associated with higher rates of arm swelling
- Increased BMI and mastectomy + RT vs. BCT associated with decreased ROM

Limitations

- Data is limited to 1 year post breast cancer treatment
- Longer follow-up may show differences in arm morbidity
- All symptoms were patient reported and not objectively quantified

Phase II Single Arm Study of Preoperative letrozole for ER(+) Postmenopausal DCIS Alliance/CALGB 40903

E. Shelley Hwang[1], Terry Hyslop[1], Stephanie Duong[2], Isabelle Bedrosian[3], Dorota Wisner[4], Elissa Price[4], Abigail Caudle[3], Tina Hieken[2], Joseph Guenther[5], Cliff Hudis[6], Eric Winer[7], Alan P. Lyss[8], Diane Dickson-Witmer[9], Richard Hoefer[10], David W. Ollila[11], Maura Dickler[6], Timothy Hardman[1], Jeff Marks[1], Yunn-Yi Chen[4], Gregor Krings[4], Laura Esserman[4] and Nola Hylton[4]

[1]Duke University, Durham, NC; [2]Mayo Clinic, Rochester, MN; [3]MD Anderson, Houston, TX; [4]UCSF, San Francisco, CA; [5]St. Elizabeth Medical Center South, Edgewood, KY; [6]ASCO, Alexandria, VA; [7]Dana Farber Cancer Institute, Boston, MA; [8]Missouri Baptist Medical Center, [9]Christiana Care Health System, [10]Sentara Norfolk General Hospital, Norfolk, VA; [11]UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC.

Background

- Preoperative endocrine therapy improves rates of breast conservation in invasive breast cancer
- Endocrine therapy has been shown to decrease local recurrence rates of DCIS

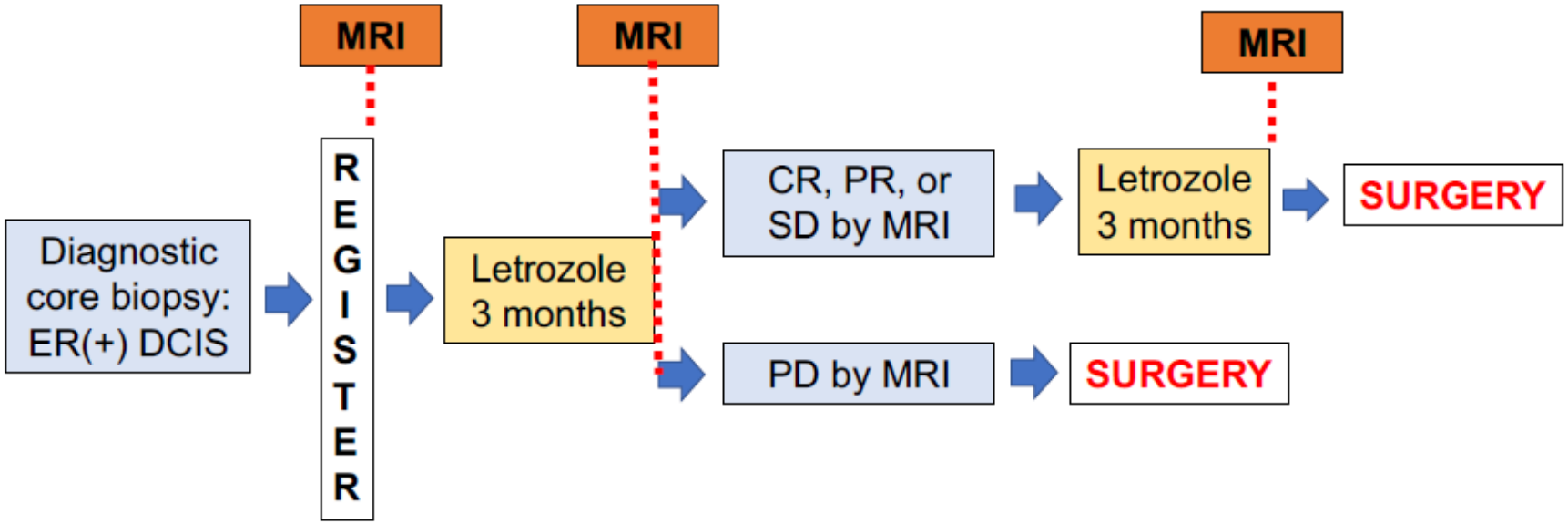
Study Questions

- Does ER+ DCIS respond to preoperative endocrine therapy?
- Can preoperative endocrine therapy result in pathologic complete response and potentially obviate need for surgery for DCIS?

Study Objectives

- Primary –
  - Use MRI to assess mean change in tumor volume from baseline to completion of preoperative letrozole in ER+ DCIS
- Secondary –
- To assess radiographic and pathologic outcomes of patients with DCIS treated with preoperative letrozole
- To determine if ER,PR, and Ki67 are altered with preoperative endocrine therapy

Study Schema



Study aim: to determine the radiologic changes associated with endocrine therapy alone in unresected (ER)-positive DCIS

Results

- N=77 patients who received treatment and 68 who completed all time points
- Mean of 33% reduction in DCIS volume after 3 months of letrozole
- Mean of 37% reduction in DCSI volume after 6 months of letrozole
- 82% of patients with > or <4.0cm of DCIS received lumpectomy
- ER, PR, and KI-67 expression decreased significantly by the time of surgery

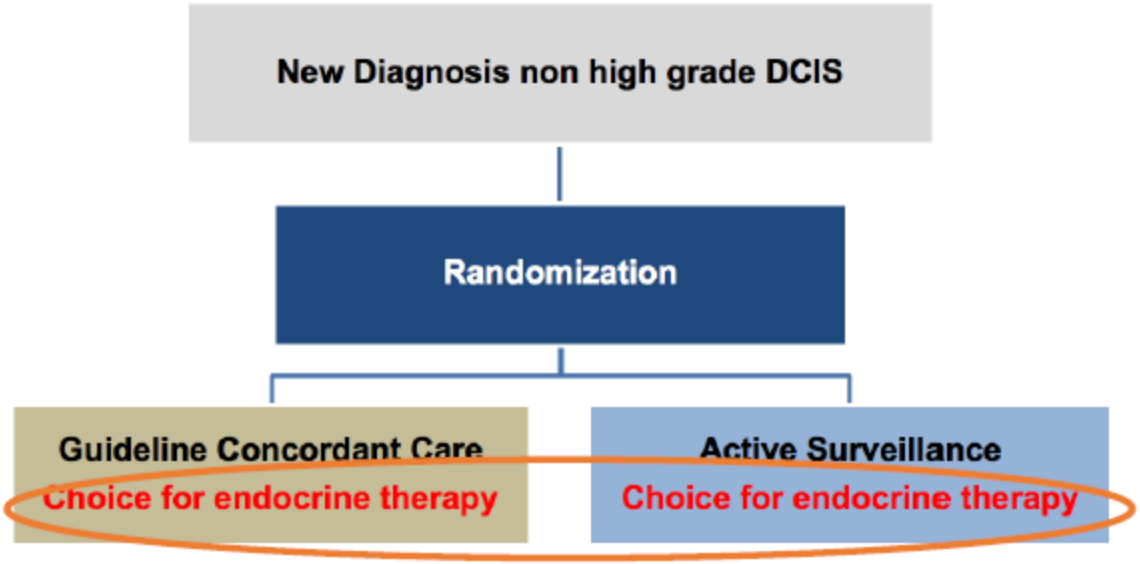
Results

- 51 (75%) of patients had DCIS only at time of surgery
- 7 (10%) had invasive cancer
- 6 (9%) had pCR, no evidence of DCIS or invasive cancer

Take Home Message

- Serial MRI was able to assess response to preoperative letrozole among DCIS patients
- Significant reduction in MRI enhancement (33%) seen after 3 months of letrozole
- 82% rate of successful lumpectomy even among patients with extensive calcifications
- Both invasive cancer and pathCR were seen at excision

COMET (Comparison of Operative to Monitoring or Endocrine Therapy) for low risk DCIS
RCT Study Design



Limitations

- Long term follow up in the setting of a randomized trial is needed
- Prevalence of skip lesions in DCIS
- Genomic analysis indicating which tumors are most amenable to neoadjuvant endocrine therapy is needed.

San Antonio Breast Cancer Symposium, December 5-9, 2017

Weight Loss and Breast Cancer Incidence in Postmenopausal Women

Chlebowski RT, Luo J, Anderson GL, Barrington W, Redding K, Simon MS, Manson JE, Rohan TE, Wactawski-Wende J, Lane D, Strickler H, Mosaver -Rahmani Y, Freudenheim JL, Saquib N, Stefanick ML

City of Hope National Medical Center
Women's Health Initiative Investigators

Background and Study Objectives

Background

While obesity is an established risk factor for postmenopausal breast cancer,[1,2] studies of weight loss and breast cancer provide inconsistent results [3]

Consequently, the current public health message is limited to "avoid body fatness"(International Association for Research on Cancer [IARC]) [3]

Study Objectives

To evaluate associations between weight change categories and breast cancer incidence in postmenopausal women participating in the Women's Health Initiative (WHI) Observational Study

Secondary analyses explored the association of weight loss and breast cancer incidence by weight loss intentionality

[1]Chlebowski RT, et al. J Clin Oncol 2002;20:1128-43
[2]Reeves GK, et al. BMJ 2007;335:1134-1143
[3]Lauby-Secretan B, et al. N Engl J Med 2016;375:794-8

Intentional Weight Loss and Endometrial Cancer Risk among 36,794 Postmenopausal Women after 11.4 Years (median) follow-up

% Weight Change	Endometrial cancers (N)	HR (95% CI)
Stable Weight (within ± 5%)	384	Reference
Weight gain (≥ 5%)	124	1.12 (0.92 to 1.38)
Weight loss (≥ 5%)	58	0.71 (0.54 to 0.95)
Intentional	33	0.60 (0.42 to 0.86)
Unintentional	25	0.94 (0.62 to 1.41)

Abbreviation: HR, hazard ratio

*Multivariable models adjusted for age at enrollment, race/ethnicity, education, smoking pack-years, recreational Physical activity, history of hormone therapy use, parity, age of menarche, age at first birth, family history of endometrial Cancer, and body mass index.

Luo, J , Chlebowski, RT, Hendryx M, et al. *J Clin Oncol 2017; 35*(11), 1189-1193.

Participants and Methods

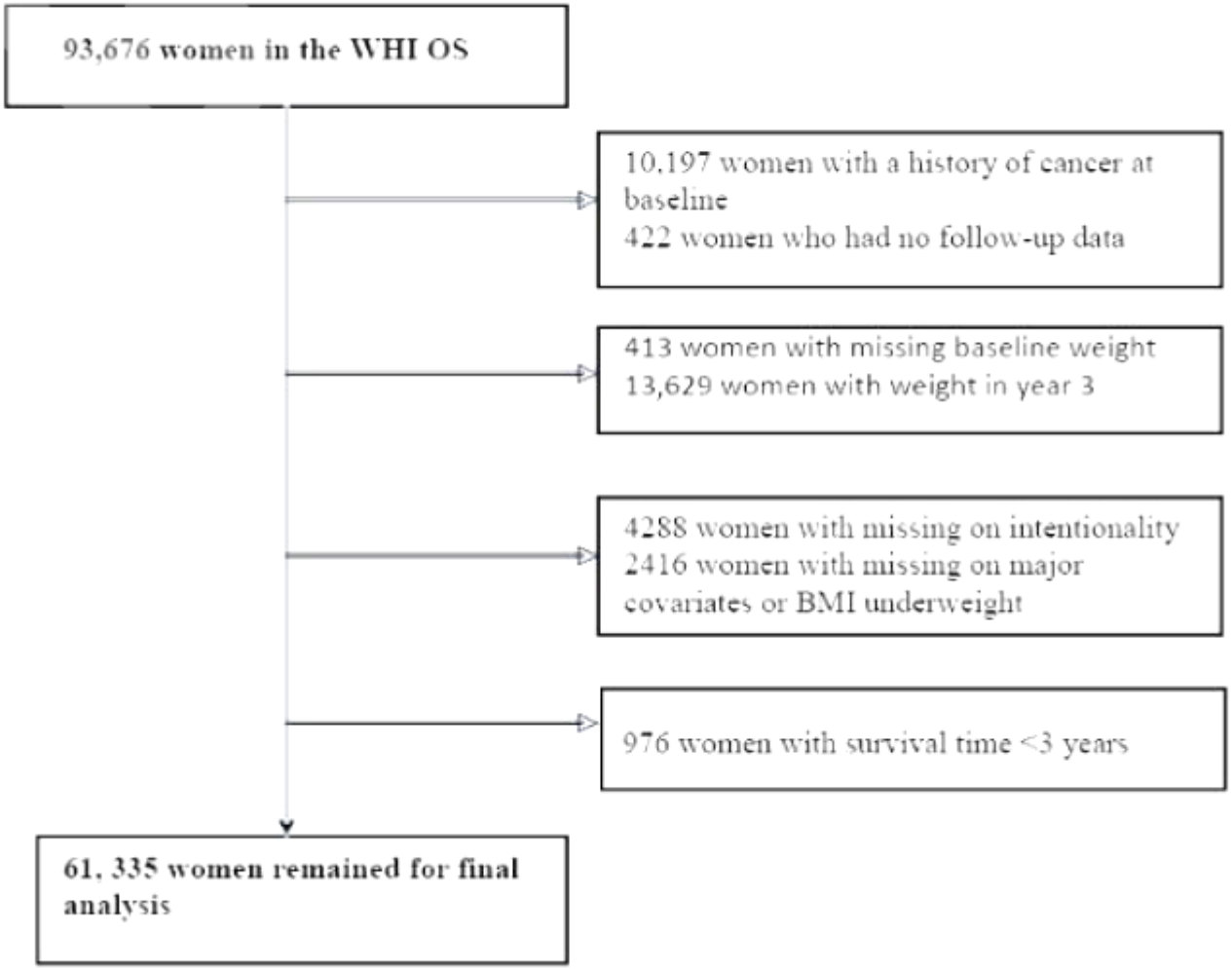
Participants in the Women's Health Initiative (WHI) Observational Study (n= 93,676)

- Postmenopausal, ages 50-79 years, with anticipated 3 year survival, recruited from 40 US Clinical Centers from 1993-1998
- 11.4 years mean follow-up through September 30, 2015

Measures

- Information on demographics, medical history and breast cancer risk factors collected at baseline by questionnaires
- Information on medication use collected at baseline during interviews including "in hand" medication container review.
- Mammograms were not protocol mandated but mammogram frequency wascllected annually

Flow Diagram of Participants Included in the Analysis



Measurements

- Measured height and weight at baseline and year 3, calculated body mass index (BMI kg/m^2)
- Weight change categories calculated as measured weight at year 3 subtracted from measured weight at baseline divided by measured weight at baseline:
  - Weight stable, ≤± 5% weight change
  - Weight gain ≥ 5% increase
  - Weight loss, ≥ 5% decrease
- Self-reported weight at year 6, not used in analyses
- At year 3, participants asked in a questionnaire
  - "In the past 2 years, did you gain or lose 5 or more pounds" (yes/no)
  - "Was the weight change intentional or unintentional " (yes/no)

Breast Cancer Ascertainment

- Incident invasive breast cancer cases ascertained at yearly contacts
- Confirmed after medical record and pathology report review by trained physician adjudicators at the local clinical centers
- Estrogen receptor (ER), progesterone receptor (PR) and Human Epidermal Growth Factor Receptor 2 (HER2) status was based on review of local laboratory reports
- Final adjudication and coding performed at WHI clinical Coordinating Center following SEER guidelines

Statistical Analyses

Baseline characteristics and tumor subtypes of the study population were described by 3-year weight change categories (weight stable, ≤± 5% weight change, weight gain ≥ 5% increase, weight loss, ≥ 5% decrease)

To estimate associations between weight change and weight loss by intentionality and breast cancer incidence, hazard ratios (HRs) and corresponding 95% confidence intervals (CI) were generated using multivariable-adjusted Cox proportional hazards models

A sensitivity analysis adjusted for mammogram frequency

Statistical Analyses (continued)

Multivariable-adjusted models adjusted for the Breast Cancer Risk Assessment Tool (BCRAT) score (BCRAT includes age at enrollment, race/ethnicity, age of menarche, age of the mother at the birth of her first live child, number of first-degree relatives with breast cancer, and the number of previous breast biopsies), education, smoking pack-years, recreational physical activity, alcohol consumption, history of hormone therapy use, parity, and BMI.

Weight change associations were examined in 4 subgroups defined by BMI (overweight, obese, normal), age group (50 <=70, 70+) race/ethnicity, and menopausal hormone therapy use (estrogen alone, estrogen plus progestin, none)

Baseline Characteristics by Weight Change Category

- Compared with the women with stable weight:
- Women who had ≥ 5% weight gain were more likely to be younger, Black and be heavier smokers (all $P < .01$)
- Women who had ≥ 5% weight loss were more likely to have higher BMI, but were less likely to be physically active or have used any menopausal hormone therapy (all $P < .01$)
- Other baseline characteristics including education, alcohol intake, history of estrogen alone or estrogen plus progestin, BCRAT risk score, bilateral oophorectomy, physical activity (MET-hrs/wk), BMI, and diabetes were similar among weight change category groups

Baseline Medication Use (%) by Weight loss Category

Weight change category	Metformin	NSAID
Stable Weight (within ± 5%) (n=41,139)	0.5%	8.7%
Weight gain (≥ 5%) (n=12,021)	0.7%	12.6%
Weight loss (≥ 5%) Intentional (n=4,829)	0.8%	10.3%
Weight loss (≥ 5%) Unintentional (n=3,346)	1.1%	12.2%

Metformin use rare

Measured Weight Change (pounds, mean, SD) by Weight loss Category Year 1- 3 (measured) and Year 3- 6 (self report)

Weight change category	Weight change Year 1-3	Weight change Year 3-6
Stable Weight (within ± 5%) (n=41,139)	+0.54 (4.07)	-2.80 (9.58)
Weight gain (≥ 5%) (n=12,021)	+18.51 (28.42)	-9.80 (31.33)
Weight loss (≥ 5%) Intentional (n=4,829)	-19.58 (27.12)	+2.55 (13.68)
Weight loss (≥ 5%) Unintentional (n=3,346)	-16.90 (18.69)	+1.82 (12.03)

Measured weight change from year 1-3 used in all analyses

Weight Change and Breast Cancer (n= 3,061) among 61,335 Postmenopausal Women after 11.4 Years (median) follow-up

- In multivariable–adjusted analyses, compared with the women with stable weight (n=41,139):
- Women who had ≥ 5% weight loss (n=8,175) had a significantly lower breast cancer incidence (HR 0.88 95% CI 0.78-0.98, P= 0.02)
- Adjustment for mammography frequency did not alter findings (HR 0.88 95% CI 0.78-0.99)
- Women who had ≥ 5% weight gain (n=12,021) did not have a higher overall breast cancer incidence (HR 1.02 95% CI 0.93-1.11). However, women with such weight gain had a significantly higher incidence of triple negative breast cancer (HR 1.54 95% CI 1.16-2.05)

Weight Change and Breast Cancer incidence including by Weight Loss Intentionality

% Weight change between baseline And Year 3	Breast cancer cases (N)	HR (95% CI) Multivariable-adjusted
Stable Weight (within ± 5%)	2,092	Reference
Weight gain (≥ 5%)	620	1.02 (0.93-1.11)
Weight loss (≥ 5%)	349	0.88 (0.78-0.98)
Intentional	229	0.91 (0.79-1.04)
Unintentional	120	0.82 (0.68-0.99)

Statistical test between intentional and unintentional weight loss groups found no significant difference (P=0.2)

Breast Cancer Characteristics by Weight Change Category

Characteristic	Stable Weight N=2092 (%)	Weight Gain N=620 (%)	Weight Loss		Weight Loss (overall) N=349 (%)	P value
			Intentional N=229 (%)	Unintentional N=120 (%)		
Histology						0.7
Ductal	62.9	64.5	62.4	72.5	65.9	
Lobular	11.8	10.0	11.4	8.3	10.3	
Ductal and lobular	14.1	14.2	15.3	10.8	13.8	
Other	11.3	11.3	10.9	8.3	10.0	
Estrogen/progesterone receptor						0.07
ER+PR+	68.2	69.2	61.6	70.8	64.8	
ER+PR-	13.3	11.1	16.2	15.0	15.8	
ER-PR-	11.3	14.5	14.4	10.0	12.9	
HER2 overexpression	10.9	11.0	10.9	10.8	10.9	0.4
Triple-negative tumor	7.2	11.0	9.6	6.7	8.6	0.02

Association Between Weight Change Category and Breast Cancer Risk by Stratifying Variable

		Weight Loss			
	Weight gain	Intentional	Unintentional	Weight loss (overall)	Interaction P value
Baseline BMI category					0.4
Normal weight	0.92 (0.80 1.06)	0.94 (0.72 1.24)	0.70 (0.50 0.96)	0.82 (0.66 1.02)	
Over weight	1.10 (0.95 1.28)	1.00 (0.80 1.25)	0.97 (0.72 1.30)	0.99 (0.82 1.19)	
Obese	1.07 (0.88 1.29)	0.86 (0.68 1.08)	0.82 (0.58 1.16)	0.85 (0.69 1.03)	
Age group					0.8
50-<70	1.03 (0.93 1.13)	0.89 (0.76 1.04)	0.77 (0.61 0.97)	0.85 (0.74 0.97)	
70+	0.97 (0.77 1.23)	0.99 (0.73 1.35)	0.91 (0.67 1.25)	0.95 (0.76 1.20)	
Hormone use					0.6
Never	0.99 (0.85 1.16)	0.80 (0.63 1.02)	0.78 (0.58 1.06)	0.79 (0.65 0.96)	
E-alone	1.14 (0.96 1.34)	1.02 (0.79 1.32)	0.92 (0.66 1.27)	0.98 (0.79 1.21)	
E+P	0.95 (0.81 1.12)	0.97 (0.75 1.24)	0.79 (0.54 1.15)	0.91 (0.73 1.13)	

Summary and Conclusions

In a large prospective study of postmenopausal women, compared to women with stable weight, women with weight loss of ≥ 5% were at a lower breast cancer risk

There was no significant difference in breast cancer findings by weight loss intentionality

These findings suggest that interventions in postmenopausal women designed to generate weight loss may reduce breast cancer risk.

Take Home Message

- Weight lost >/= 5% over a 3 year period was protective against breast cancer development among postmenopausal women
- Weight gain was not associated with a higher risk of breast cancer generally, but among patients who gain weight they had a higher incidence of triple negative breast cancers

Limitations

- No data presented on breast cancer specific survival
- Did not report on contribution of diet and exercise/physical activity to their findings
- Patients with missing data were not included
- Have not conducted analysis on 6 year data, which is self-reported

A validation of a DCIS biological risk profile in a randomized study for radiation therapy SweDCIS

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Background

- Radiation known to decrease local recurrence by 50% relatively following BCS, and 15% absolute risk reduction, no impact on mortality
- Traditional pathological risk factors associated with recurrence:
  - Size
  - Grade
  - Margins

Methods

- Validation of DCIS Biological Risk Signature in the SweDCIS randomized trial with 20 year follow-up
- DCIS Biological Risk Signature includes 4 clinical factors and 7 biological markers
  - Previously validated in a cohort of Kaiser patients and results presented at the 2016 SABCS
  - Decisions score (</=3 considered low risk, while >3 considered high risk)

Results

- Decision score >3 was prognostic of all recurrences (DCIS or invasive)
- Decision score </= 3 predicted was prognostic of only non-invasive recurrences
- Decision score >3 predicted for 9% absolute benefit of radiation
- No benefit of radiation seen in patients with decision score </=3

Take Home Message

- DCIS biological risk signature with decision score >3 appears to be both prognostic and predictive of benefit of radiation in DCIS patients treated with lumpectomy

Limitations

- Positive margins in 12% of patients
- High rates of local recurrence compared with patients treated in the modern era
- Prospective randomized trial using this biological risk profile and risk score would validate these findings
- Unclear how the clinical factors were incorporated with the biological factors and how they were weighed
- Unclear how the cutoff scores of 3 was determined

Thank you