NCCN Guidelines® Updates: Breast Cancer

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Update to the Breast Cancer Guidelines-2016 Systemic Therapy

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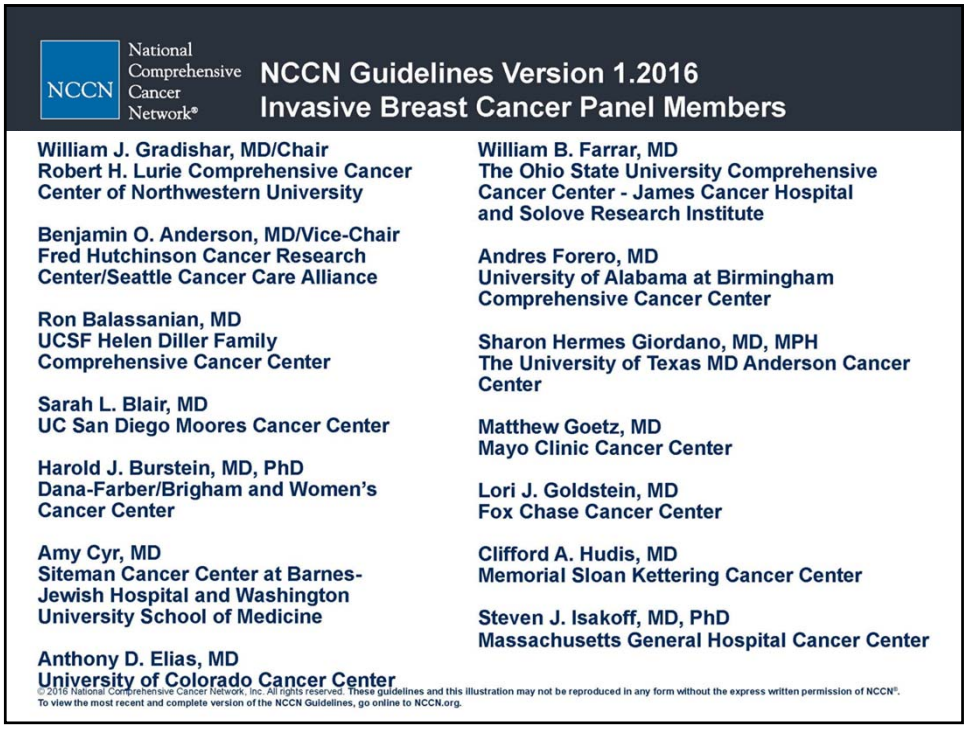

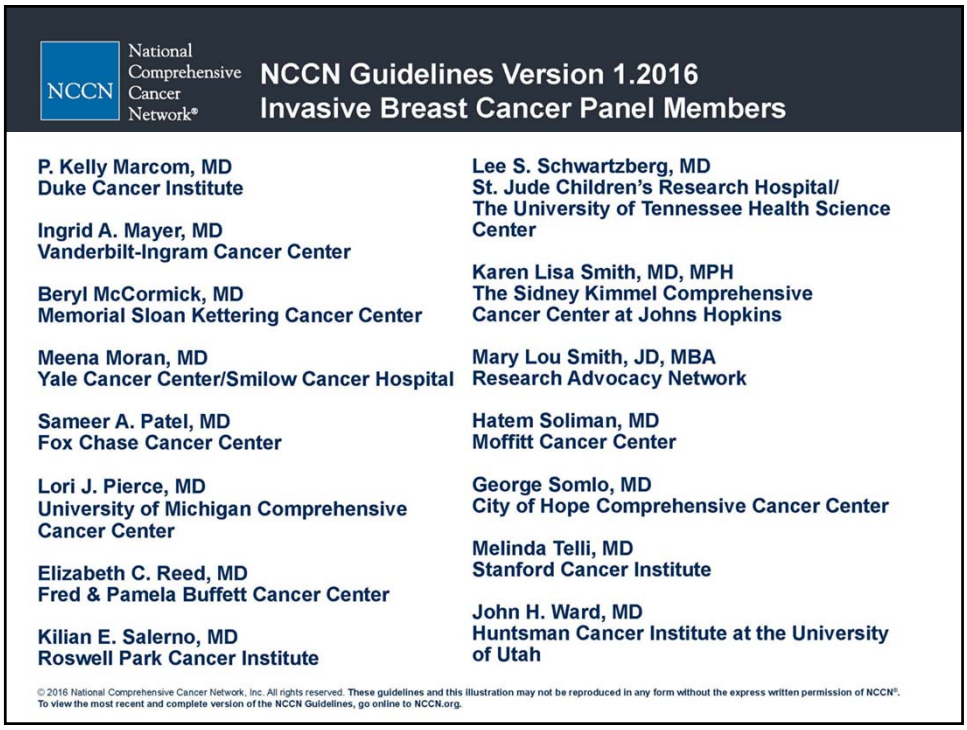

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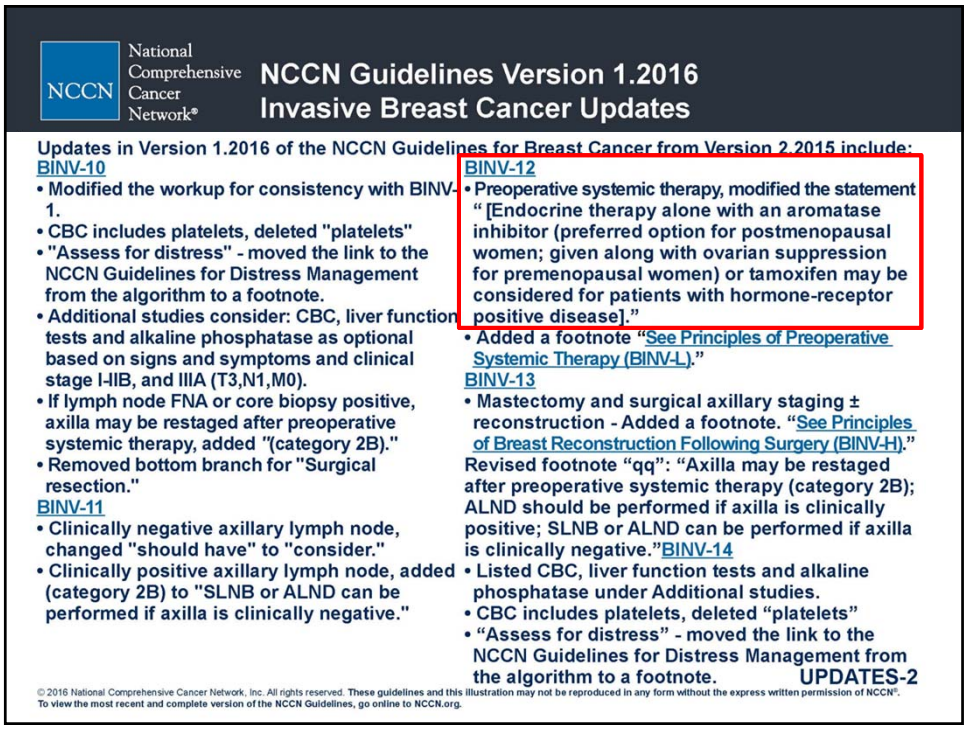
Outline

- Preoperative endocrine rx
- Optimizing adjuvant endocrine rx in pre- and postmenopausal women
- Preoperative HER2 –directed therapy
- New partners for endocrine rx in MBC
- Fertility



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NCCN Guidelines Version 1.2016
Invasive Breast Cancer Updates

Updates in Version 1.2016 of the NCCN Guidelines for Breast Cancer from Version 2.2015 include:

BINV-10
- Modified the workup for consistency with BINV-1.
- CBC includes platelets, deleted "platelets"
- "Assess for distress" - moved the link to the NCCN Guidelines for Distress Management from the algorithm to a footnote.
- Additional studies consider: CBC, liver function tests and alkaline phosphatase as optional based on signs and symptoms and clinical stage I-IIB, and IIIA (T3,N1,M0).
- If lymph node FNA or core biopsy positive, axilla may be restaged after preoperative systemic therapy, added "(category 2B)."
- Removed bottom branch for "Surgical resection."

BINV-11
- Clinically negative axillary lymph node, changed "should have" to "consider."
- Clinically positive axillary lymph node, added (category 2B) to "SLNB or ALND can be performed if axilla is clinically negative."

BINV-12
- Preoperative systemic therapy, modified the statement "[Endocrine therapy alone with an aromatase inhibitor (preferred option for postmenopausal women; given along with ovarian suppression for premenopausal women) or tamoxifen may be considered for patients with hormone-receptor positive disease]."
- Added a footnote "See Principles of Preoperative Systemic Therapy (BINV-L)."

BINV-13
- Mastectomy and surgical axillary staging ± reconstruction - Added a footnote. "See Principles of Breast Reconstruction Following Surgery (BINV-H)."

Revised footnote "qq": "Axilla may be restaged after preoperative systemic therapy (category 2B); ALND should be performed if axilla is clinically positive; SLNB or ALND can be performed if axilla is clinically negative."

BINV-14
- Listed CBC, liver function tests and alkaline phosphatase under Additional studies.
- CBC includes platelets, deleted "platelets"
- "Assess for distress" - moved the link to the NCCN Guidelines for Distress Management from the algorithm to a footnote.

UPDATES-2

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Who is Suitable for Neoadjuvant Endocrine Therapy?

- Selection paramount
  - **ER Rich Cancers (Allred 7+8)**
  - **Older postmenopausal women but also**
  - **Younger women with significant morbidities**

Neoadjuvant chemotherapy +/- anti –HER2 rx is increasingly successful in producing pCRs, BUT only in ER- and HER2-positive cancers

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ER vs Response to Neoadjuvant Chemotherapy

- 1731 patients neoadjuvant chemotherapy
- 1163 ER +; 556 ER-

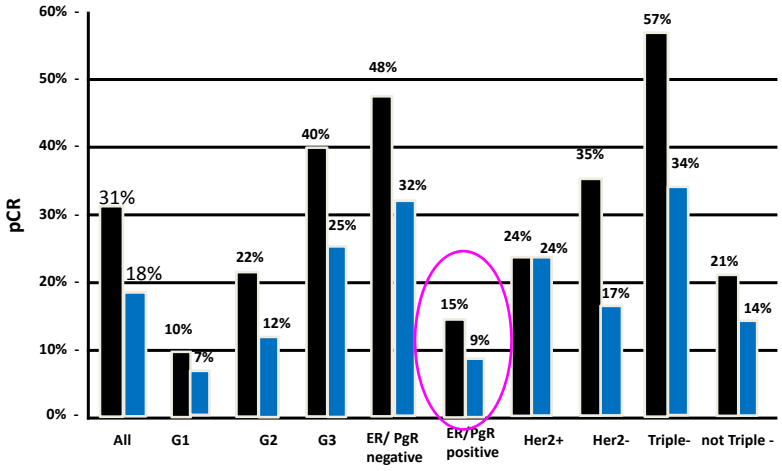
Path CR Rate

- 24% for ER-
- 8% for ER+

p <0.001

Guarneri et al JCO 2006: 24; 1037-44

Effect of Phenotype on pCR to Neoadjuvant Chemotherapy - GeparTrio



Huober J, et al. *Breast Cancer Res Treat.* 2010;124(1):133-140.

Age <40 – black bars
Age ≥40 – blue bars

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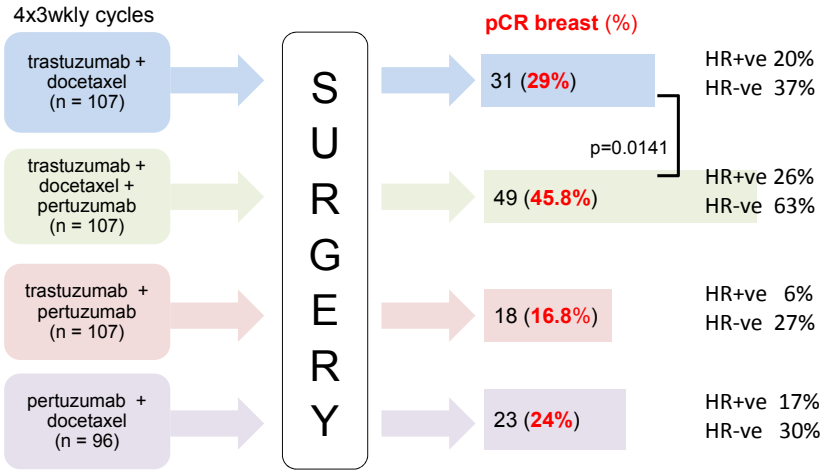
NeoSphere: Neoadjuvant Phase 2 Operable or Locally Advanced. >2cm (417pts)



Adjuvant FEC given to Arms A, B, D; adjuvant docetaxel given to Arm C; 1 year adjuvant trastuzumab was given to all arms.

Gianni L, *et al*. *Lancet Oncol* 2012; **13**:25–32

Not fully appreciated that pCR is not as important in predicting outcome of ER- positive cancers

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ER status, pCR and prognosis in patients receiving neoadjuvant chemotherapy for early breast cancer

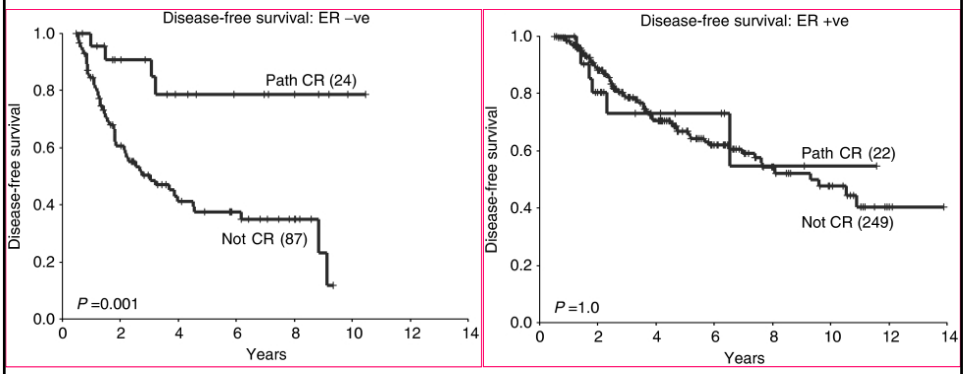
A E Ring, I E Smith, S Ashley, L G Fulford, and S R Lakhani

Br J Cancer. 2004; 91: 2012–2017

- 435 patients treated with neoadjuvant chemotherapy

DFS in Patients with ER– and ER+ Cancers vs pCR

ER Negative **ER Positive**



Ring et al Br J Cancer. 2004; 91: 2012–2017

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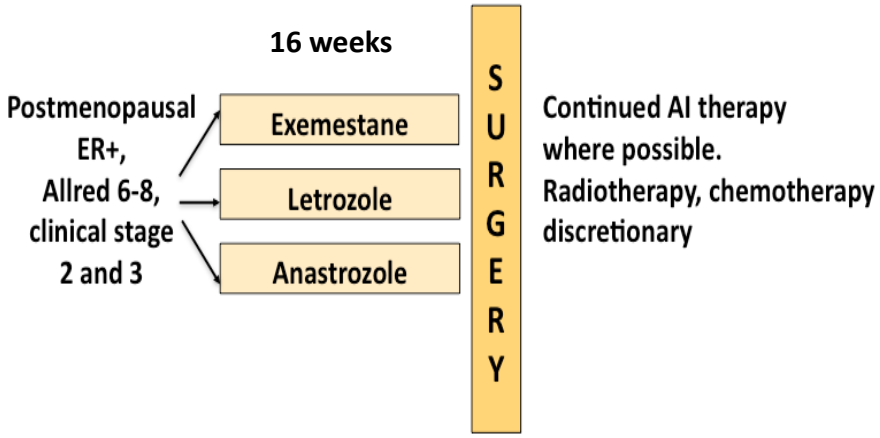
ACOSOG Z1031 Study Design Cohort A



National Institutes of Health. www.clinicaltrials.gov/ct/show/NCT00265759. Accessed April 13, 2011.

ACOSOG Z1031, Cohort A Clinical Responses

Clinical Response	Treatment Arm EXE (n = 124)	LET (n = 127)	ANA (n = 123)
Complete Response	25 (20%)	26 (21%)	20 (16%)
Partial Response	49 (40%)	66 (52%)	63 (51%)
Clinical Response rate	74/124 (60%)	92/127 (72%)	83/123 (68%)

All were ER rich with Allred scores of 6-8.

Olson JA, et al. Presented at: 2010 Breast Cancer Symposium; October 1-3, 2010; Washington, DC. Abstract 91.

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Invasive Breast Cancer Updates

Updates in Version 1.2016 of the NCCN Guidelines for Breast Cancer from Version 2.2015 include:

BINV-H (1 of 2)

- First paragraph, added the following "However, breast reconstruction should not interfere with the appropriate surgical management of the cancer or the scope of appropriate surgical treatment for this disease. Coordinating consultation and surgical treatment with a reconstructive surgeon should be executed within a reasonable time frame."
- Modified "Oncoplastic techniques for breast conservation can extend breast-conserving surgical options in situations where the resection by itself would likely yield an unacceptable cosmetic outcome."

BINV-H (2 of 2)

- Modified the statement "Evidence of nipple involvement such as Paget's disease or other nipple discharge associated with malignancy, and/or imaging findings suggesting malignant involvment of the nipple or subareolar tissues is a contraindicates nipple preservation."

BINV-I

- This page has been reorganized and updated.

BINV-J

- Changed tamoxifen for 5 y (category 1) ± ovarian suppression or ablation (category 2B) to a (category 1).
- Adjuvant endocrine therapy - premenopausal at diagnosis, added "or aromatase inhibitor for 5y + ovarian suppression or ablation (category 1)." With a new footnote " Aromatase inhibitor or tamoxifen for 5 y plus ovarian suppression should be considered, based on SOFT and TEXT clinical trial outcomes, for premenopausal women at higher risk of recurrence (i.e. young age, high grade tumor, lymph node involvement, Pagani, NEJM 2014, Prudence, NEJM 2014).Survival data still pending."

UPDATES-4

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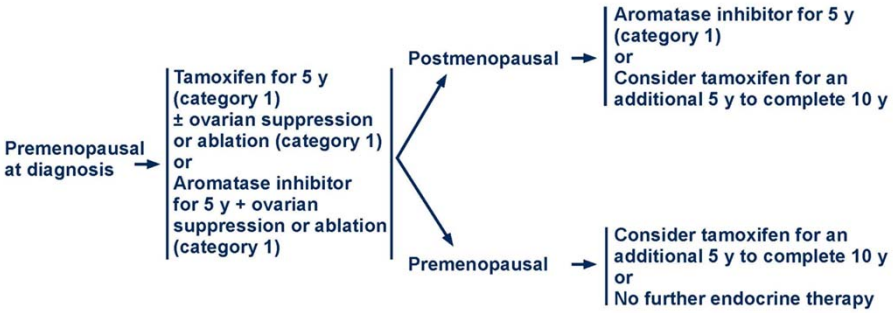
NCCN Guidelines Version 1.2016
Invasive Breast Cancer

ADJUVANT ENDOCRINE THERAPY



BINV-J

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Invasive Breast Cancer

ADJUVANT ENDOCRINE THERAPY

- Aromatase inhibitor for 5 y (category 1) or Tamoxifen for 2–3 y or Aromatase inhibitor for 2–3 y (category 1)
  - → Aromatase inhibitor to complete 5 y of endocrine therapy (category 1) or Up to 5 y of an aromatase inhibitor (category 2B)
  - → Tamoxifen to complete 5 y of endocrine therapy (category 1)
- Postmenopausal at diagnosis
  - → Tamoxifen for 4.5–6 y → Aromatase inhibitor for 5 y (category 1) or Consider tamoxifen for an additional 5 y to complete 10 y
- Women with a contraindication to aromatase inhibitors, who decline aromatase inhibitors, or who are intolerant of the aromatase inhibitors
  - → Tamoxifen for 5 y (category 1) or Consider tamoxifen for up to 10 y

BINV-J

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Early Stage Breast Cancer
Tamoxifen: 5 Years Vs. Not

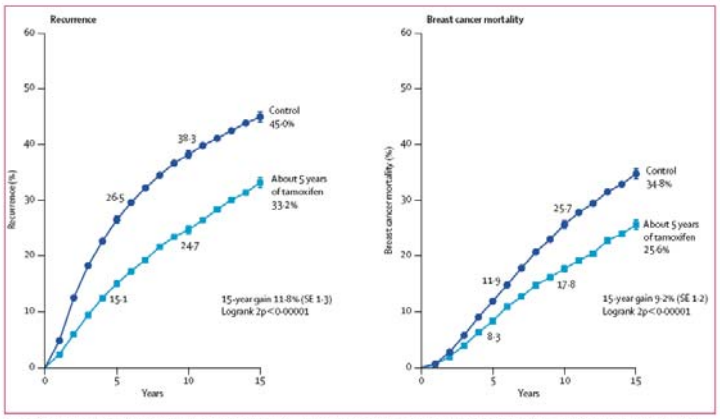

Figure 8: About 5 years of tamoxifen versus not in ER-positive (or ER-unknown) disease: 15-year probabilities of recurrence and of breast cancer mortality
10 386 women: 20% ER-unknown, 30% node-positive. Error bars are ±1SE.

- More than half of recurrences and deaths occur post-treatment

EBCTCG, Lancet 2005,365: 1687

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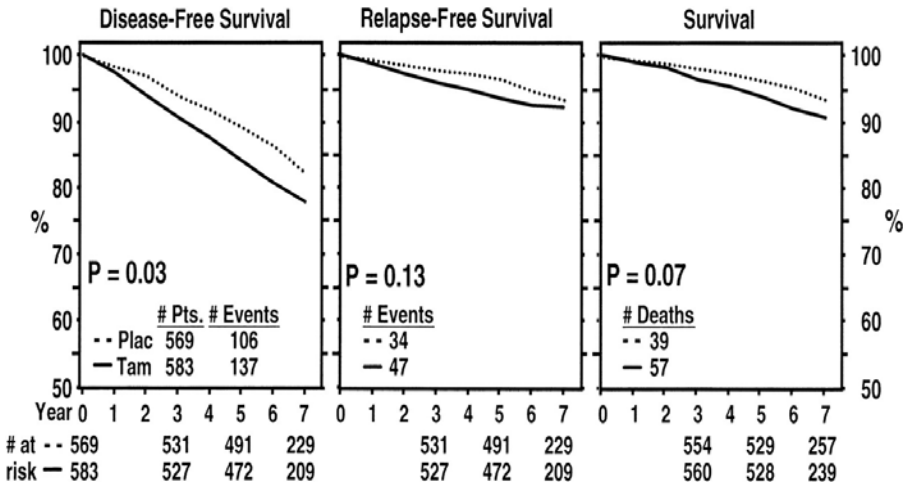
Tamoxifen

Why did we stop at 5 years anyway?

Duration of Tamoxifen: NSABP B-14

Fisher, et al. JNCI 2001;
median f/u 7 years post-rerandomization



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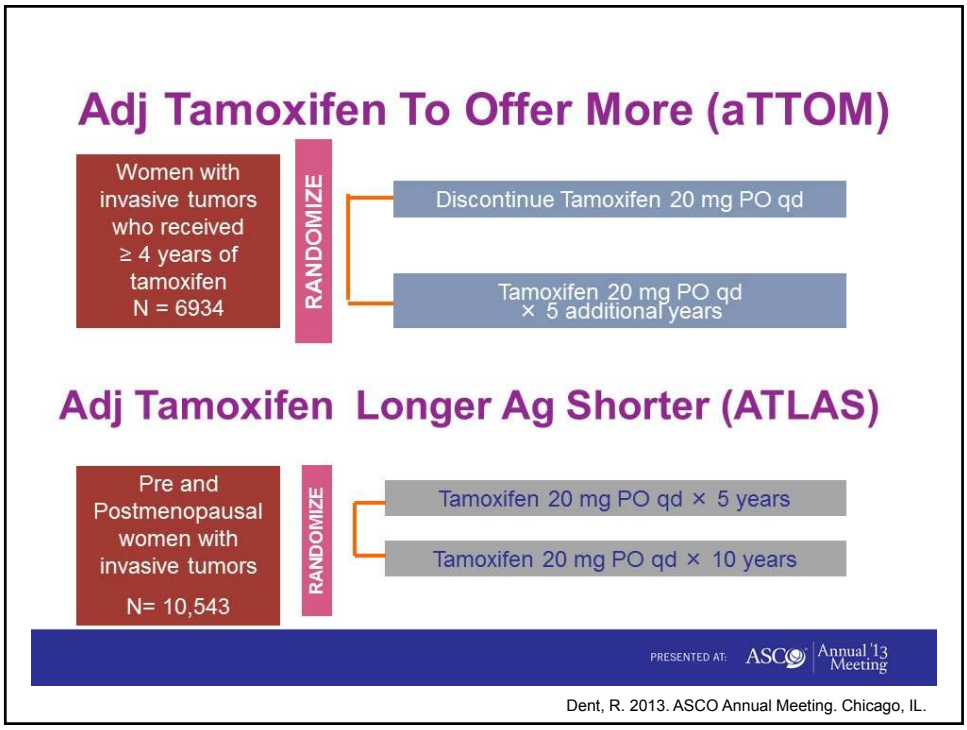
Duration of Adjuvant Endocrine Therapy: What Have ATLAS & aTTOM Taught Us?



Dent, R. 2013. ASCO Annual Meeting. Chicago, IL.

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Combined Outcomes in ATLAS and aTTom

	Breast Cancer Mortality	Overall Survival
Years 5 - 9	0.97 (0.84-1.15)	0.99 (0.89-1.10)
Years 10+	0.75 (0.65-0.86)*	0.84 (0.77-0.93)*
All Years	0.85 (0.77-0.94)*	0.91 (0.84-0.97)*

*$p < 0.05$ favoring 10 years

Gray, et al. Abstract 5. ASCO 2013

Adjuvant Endocrine Therapy Premenopausal Women

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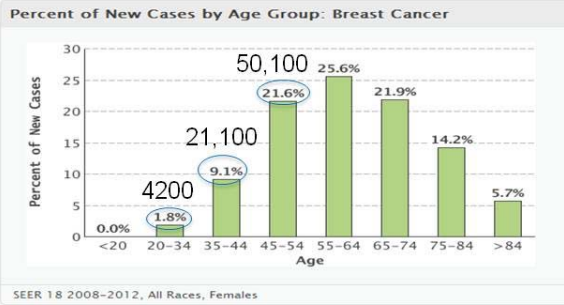
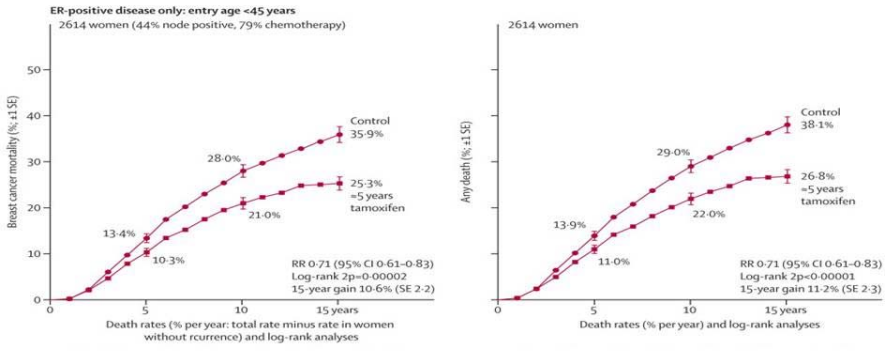
Breast Cancer in Premenopausal Women: The Scope of the Problem

- Most frequent cancer diagnosis in women worldwide
- In the US
  - ~75,340 ≤ age 54
  - ~25,270 ≤ age 44
- Most common cause of cancer death



15 year Outcome with 5 Years of Tamoxifen in < 45 Year Old Women



EBCTCG; The Lancet, Volume 378, Issue 9793, 2011, 771 - 784

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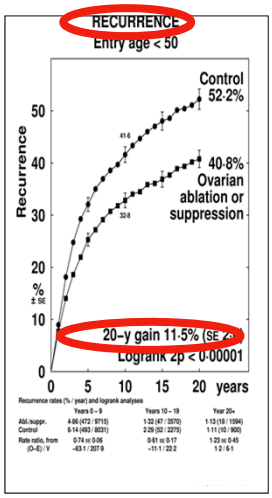
EBCTCG Ovarian Suppression/Ablation

2006 EBCTCG

- **OA/OS vs not**
- **No chemo**
- **Not selected for ER**



SOFT: SUPPRESSION of OVARIAN FUNCTION TRIAL
Premenopausal ER+ve and/or PR+ve Breast Cancer

3047 Patients Randomized in ITT (Dec 2003 - Jan 2011)

Primary Analysis (n= 2033)

Median follow-up=5.6 y

Two Patient Cohorts

No Chemotherapy (47%)

Premenopausal, within 12 weeks of surgery (Median time since surgery = **1.8 months**)

Prior Chemotherapy (53%)

Premenopausal* after completing chemotherapy; Randomization within 8 months of completion (Median time since surgery = **8.0 months**)

RANDOMIZE

- **Tamoxifen x 5y (n=1018)**
- **Tamoxifen+OFS x (n=1015) 5y**
- **Exemestane+OFS (n=1014) x 5y**

*According to locally-determined E_2 level in premenopausal range

OFS=ovarian function suppression (oophorectomy, triptorelin or XRT)

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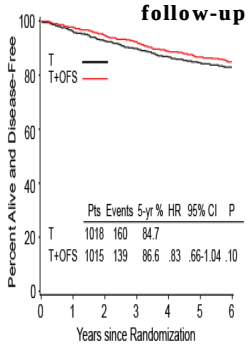
SOFT Primary Analysis: Disease-free Survival

5.6 years median follow-up

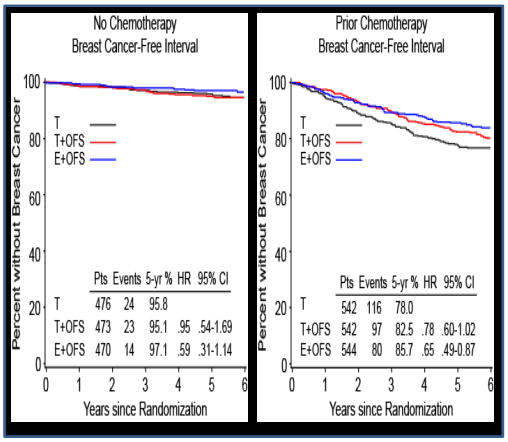


> 95% overall survival

Primary analysis in overall population not significant (p=0.10)
Multivariable Cox model HR=0.78 (95% CI 0.62-0.98) p=0.03

Francis et al, N Engl J Med, 2015

SOFT—Outcomes by Chemotherapy



No chemotherapy cohort selected for low risk features:
90% ≥ age 40yr, 91% node negative, 85% tumor ≤ 2cm, 41% grade 1

Francis et al, N Engl J Med, 2015

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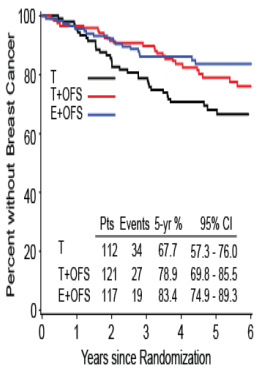
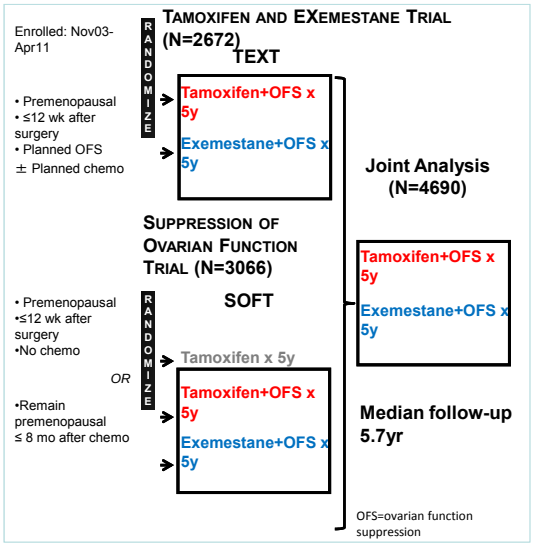
SOFT—Outcomes for Women < 35 yr



- **350 patients (11.5%) under age 35**
- **94% received chemotherapy in this age group**

Francis et al, N Engl J Med, 2015

TEXT and SOFT Joint Analysis



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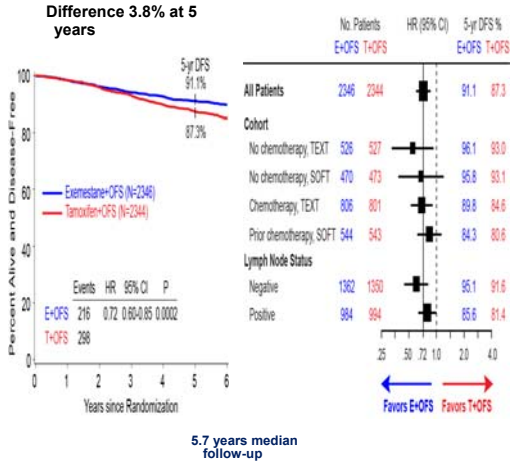
Exemestane+OFS Improved DFS



5.7 years median follow-up

Pagani et al, N Engl J Med, 2014

Joint Analysis of TEXT and SOFT

Exemestane + OFS vs Tamoxifen + OFS

Outcome	HR (95% CI)	P
DFS	0.72 (0.60-0.85)	0.0002
BCFI	0.66 (0.55-0.80)	<0.0001
DDFI	0.78 (0.62-0.97)	0.02
OS	1.14 (0.86-1.51)	0.37

Median Follow-up of 5.7 years

Pagani et al, N Engl J Med, 2014

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Predictable Adverse Events Profile

CTCAE V3.0 Grade 3-4	E + OFS	T + OFS
Musculoskeletal	11%	5.2%
Fracture	1.3%	0.8%
Cardiac	0.3%	0.1%
Thrombosis/ embolism	0.8%	1.9%
Dyspareunia	2.3%	1.4%
Premature discontinuation	16%	11%

Pagani et al, N Engl J Med, 2014

Patient Reported Outcomes in Joint Analysis

Symptom	OFS + Tamoxifen	OFS + Exemestane
Hot flashes/sweats	+	
Vaginal dryness		+
Loss of sexual interest		+
Difficulty with arousal		+
Bone/joint pain		+

"Changes in global QOL were small and similar between treatments over the 5 years"

Bernhard et al, Lancet Oncol, 2015

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Adjuvant Endocrine Therapy for Premenopausal Women

- **Consider use of OFS+Tamoxifen or OFS+AI for higher risk women like:**
  - **Chemotherapy recipients who remain premenopausal**
  - **Multiple positive nodes**
  - **Age < 35 yrs**
- **Optimal duration of OFS-based therapy uncertain-suggest 3-5 years**
- **Long term follow-up of pivotal trials for adherence, toxicity & benefit critical**

HER2+ Disease

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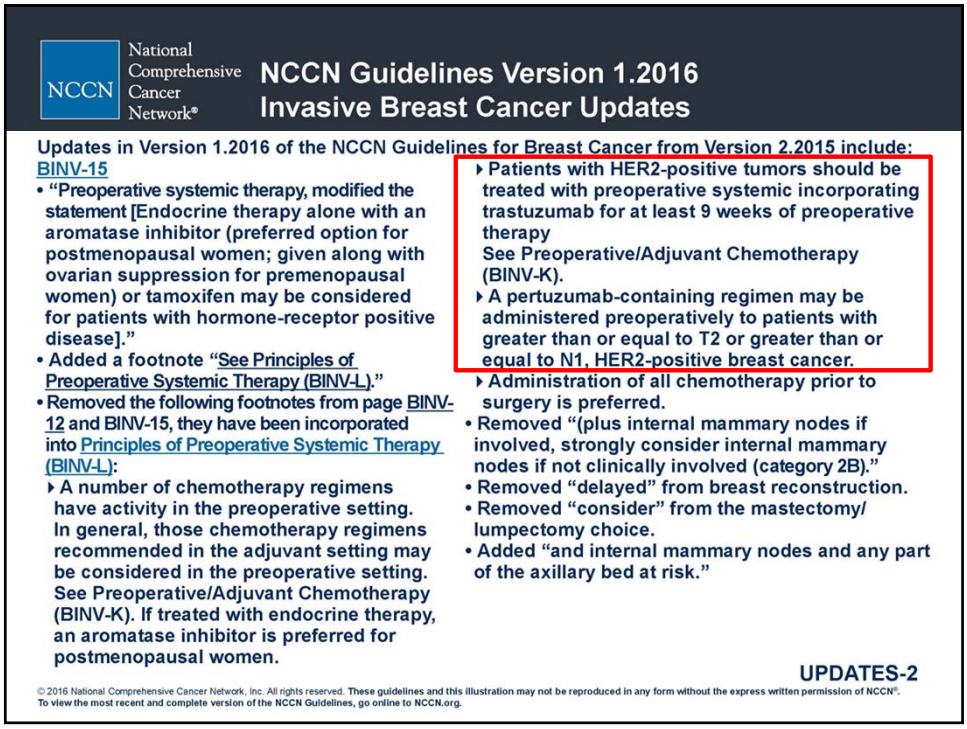

Does improving pCR

improve breast cancer outcomes?

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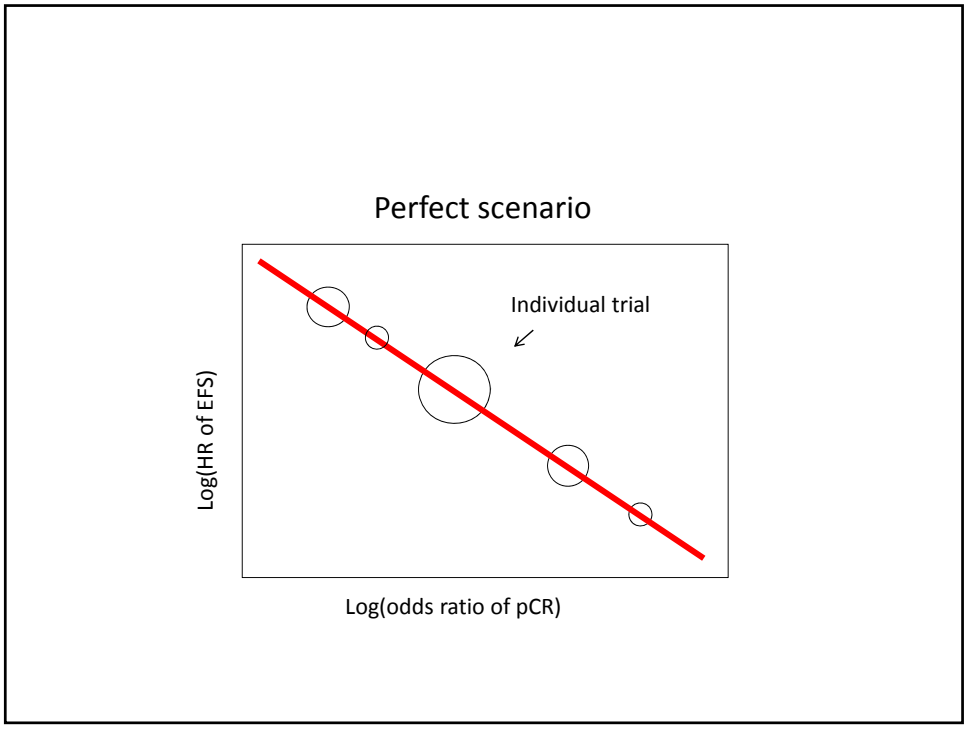

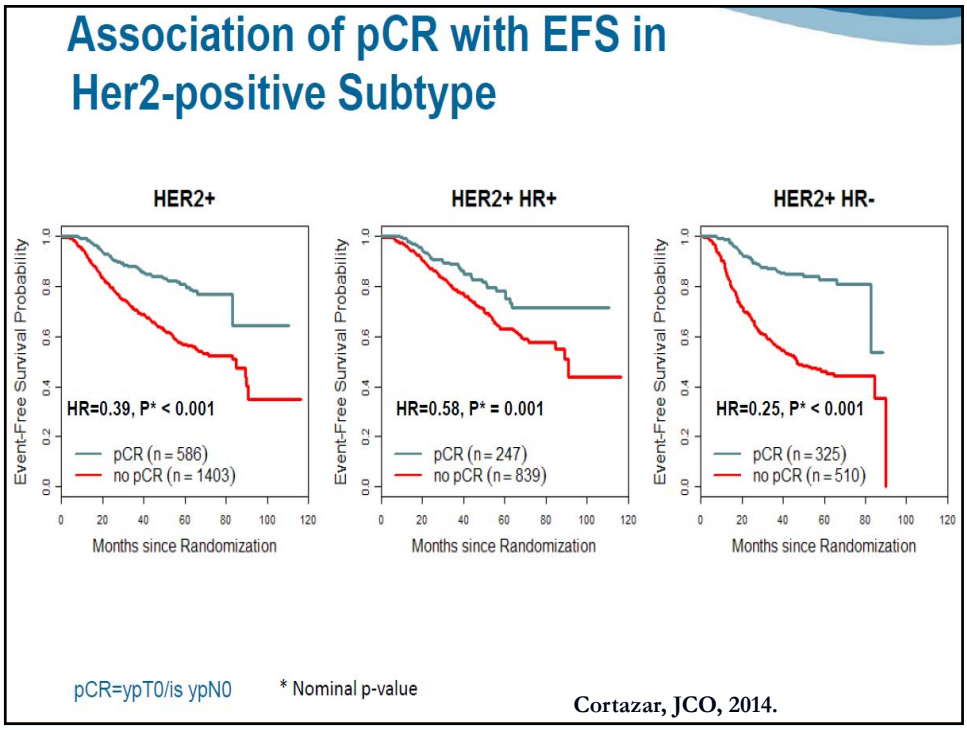

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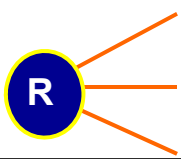
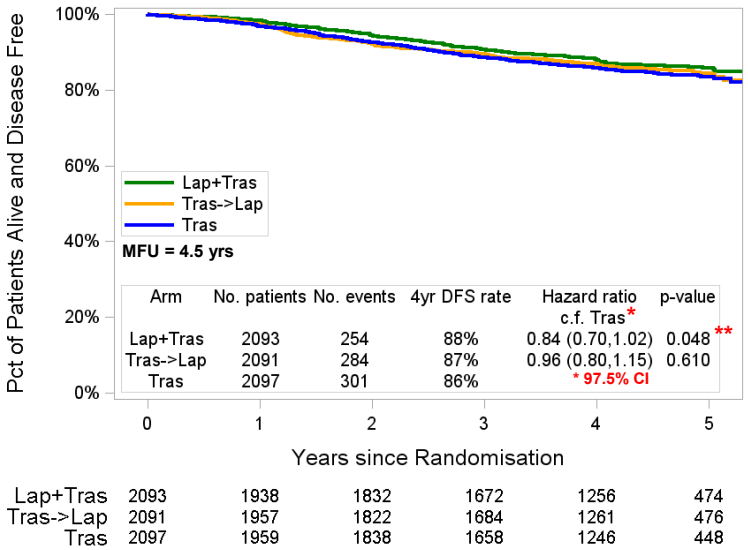
Pathologic Response in Neo-ALTTO



	Path CR (breast only)	Path CR (breast + LN)
Lapatinib + Paclitaxel	25%	20%
Trastuzumab + paclitaxel	29%	28%
Trast + Lap + paclitaxel	51%	47%

Baselga et al, Lancet 2012

ALTTO Trial: DFS Analysis



**p-value ≤ 0.025 required for statistical significance

Piccart et al, ASCO 2014

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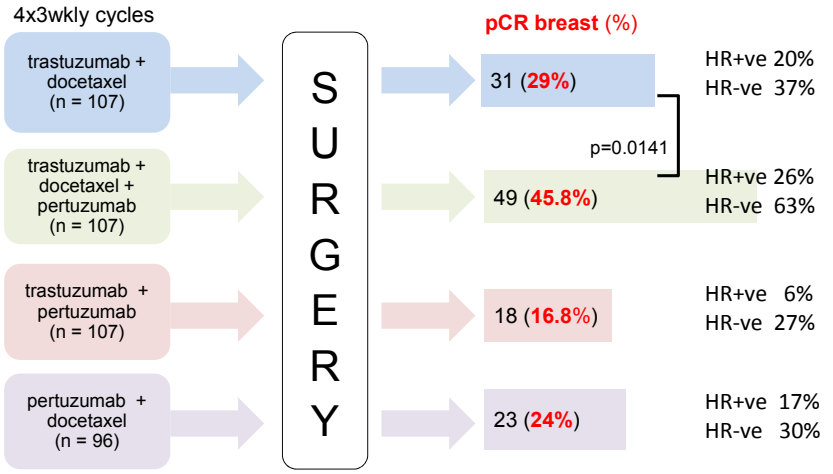
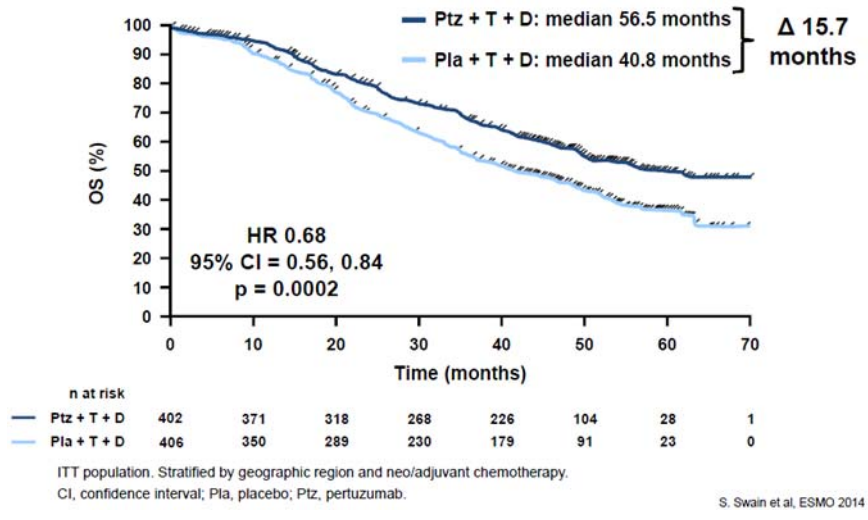
NeoSphere: Neoadjuvant Phase 2 Operable or Locally Advanced. >2cm (417pts)



Adjuvant FEC given to Arms A, B, D; adjuvant docetaxel given to Arm C; 1 year adjuvant trastuzumab was given to all arms.

Gianni L, *et al*. *Lancet Oncol* 2012; **13**:25–32

Final OS Analysis of CLEOPATRA sets a new paradigm of treatment of HER2+ MBC



ITT population. Stratified by geographic region and neo/adjuvant chemotherapy.
CI, confidence interval; Pla, placebo; Ptz, pertuzumab.

S. Swain et al, ESMO 2014

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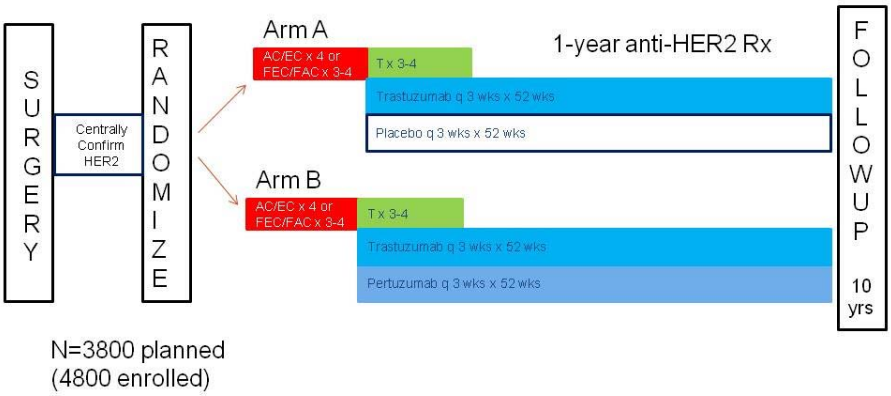
APHINITY: Randomized Adjuvant Phase 3 Trial



N=3800 planned
(4800 enrolled)

A=doxorubicin, E=epirubicin, C=cyclophosphamide, T=taxane (paclitaxel or docetaxel), F=5-fluorouracil, H=trastuzumab, P=pertuzumab

PRESENTED AT: ASCO Annual '15 Meeting

Reason to be encouraged

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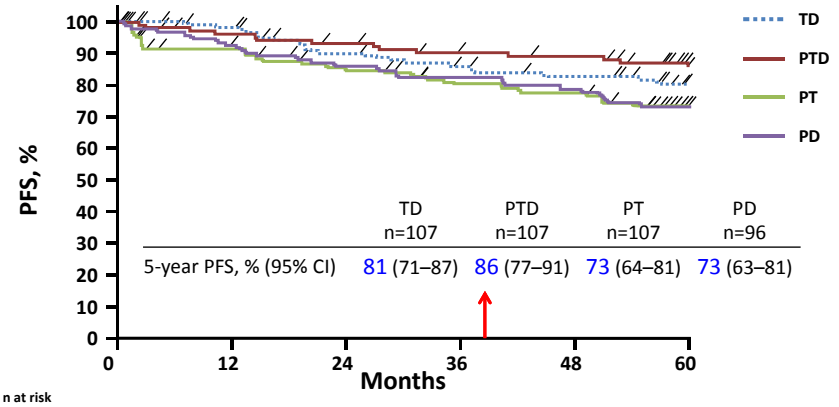
NEOSPHERE: PFS by All Treatment Arms
ASCO 2015 Update



	TD n=107	PTD n=107	PT n=107	PD n=96
5-year PFS, % (95% CI)	81 (71–87)	86 (77–91)	73 (64–81)	73 (63–81)

n at risk						
TD	107	101	89	83	78	58
PTD	107	99	94	88	86	63
PT	107	93	86	80	77	55
PD	96	85	76	72	69	57

Kaplan–Meier curves are truncated at 60 months (the end of scheduled follow-up). However, summary statistics shown here take into account all follow-up
Three late events occurred with PTD: two cases of progressive disease (PD) at 63 and 71 months, and one death due to an unrelated cerebrovascular accident without PD at 76 months

Gianni et al ASCO 2015

Case #1

- A 67 yo WF presents with newly diagnosed bone metastases. She was originally dx with a 3 cm IDC of the left breast 4 years earlier and underwent mastectomy. The tumor was ER+/PR+/HER2- and SLN were negative. A recurrence score was low. Treatment with anastrozole was initiated.

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Case #1

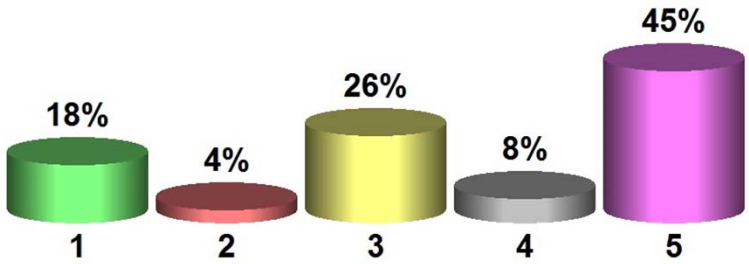
- She was doing well until recently when diffuse boney aches were noted not responding to NSAID
- Labs showed an elevated Alk Phos; a bone scan demonstrated several lytic lesions throughout the axial skeleton. CT CAP showed 2 suspicious 1 cm lesions in the liver
- A liver biopsy was consistent with the original dx and remained ER+

Audience Polling Results

Case #1

In addition to starting a bone agent (bisphosphonate or denosumab) and discontinuing anastrozole you would:

1. Start chemotherapy
2. Start an alternative AI
3. Start an alternative AI and add palbociclib
4. Start fulvestrant
5. Start fulvestrant and palbociclib



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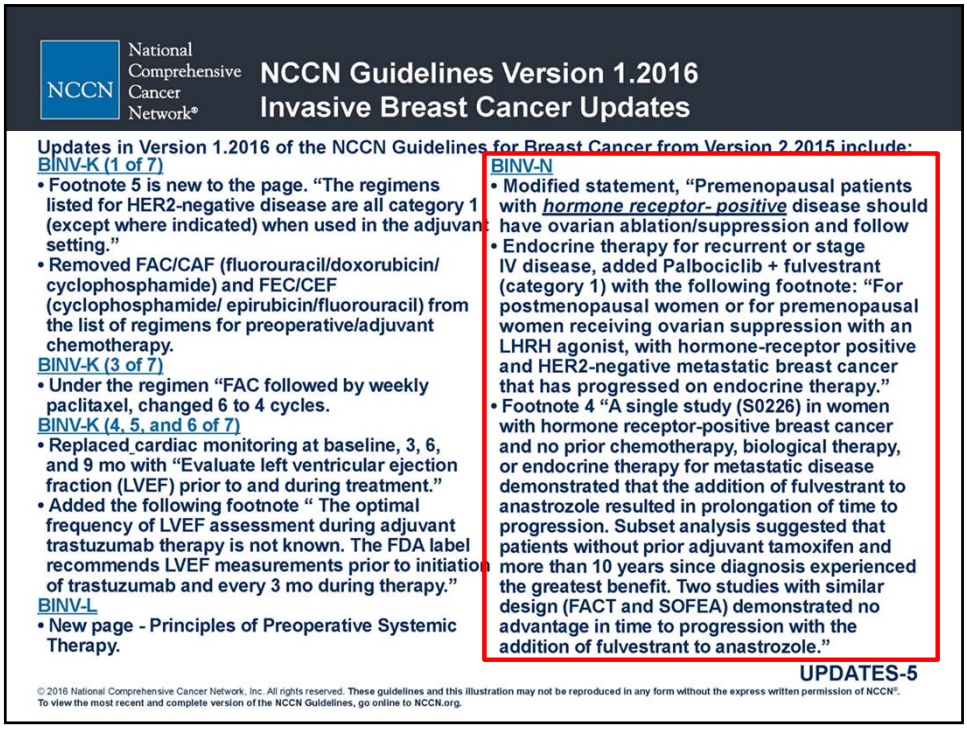

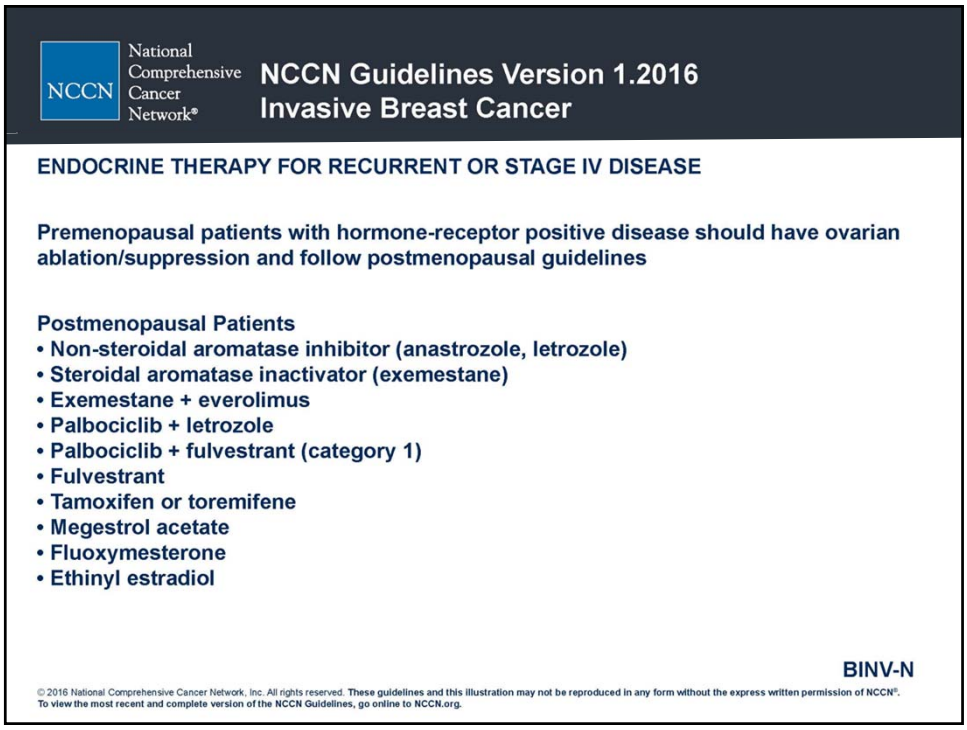

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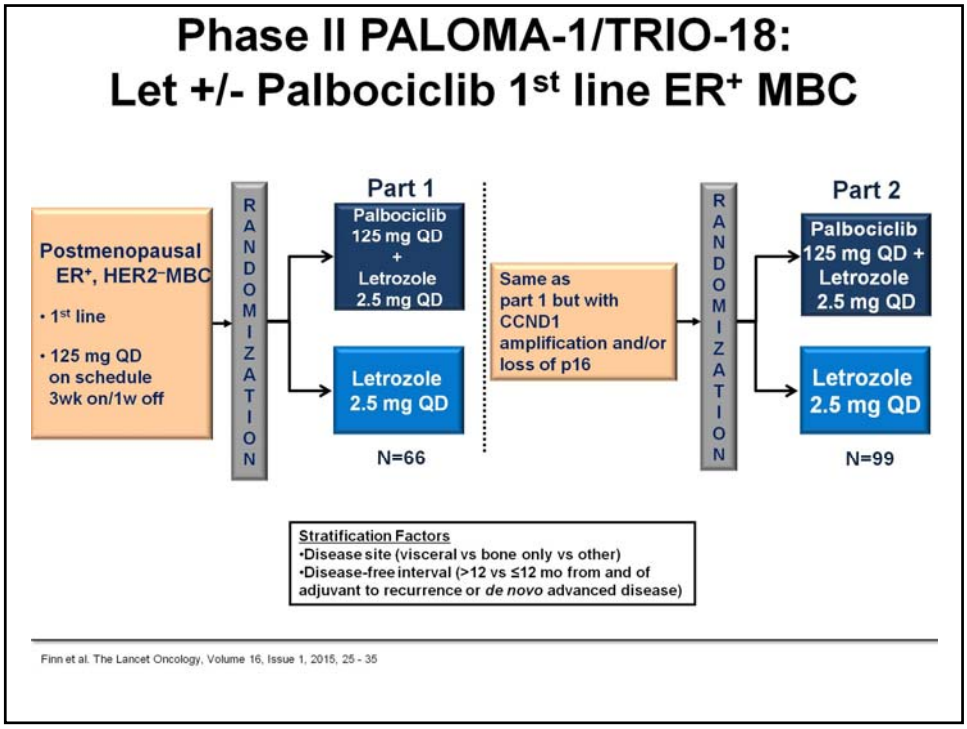

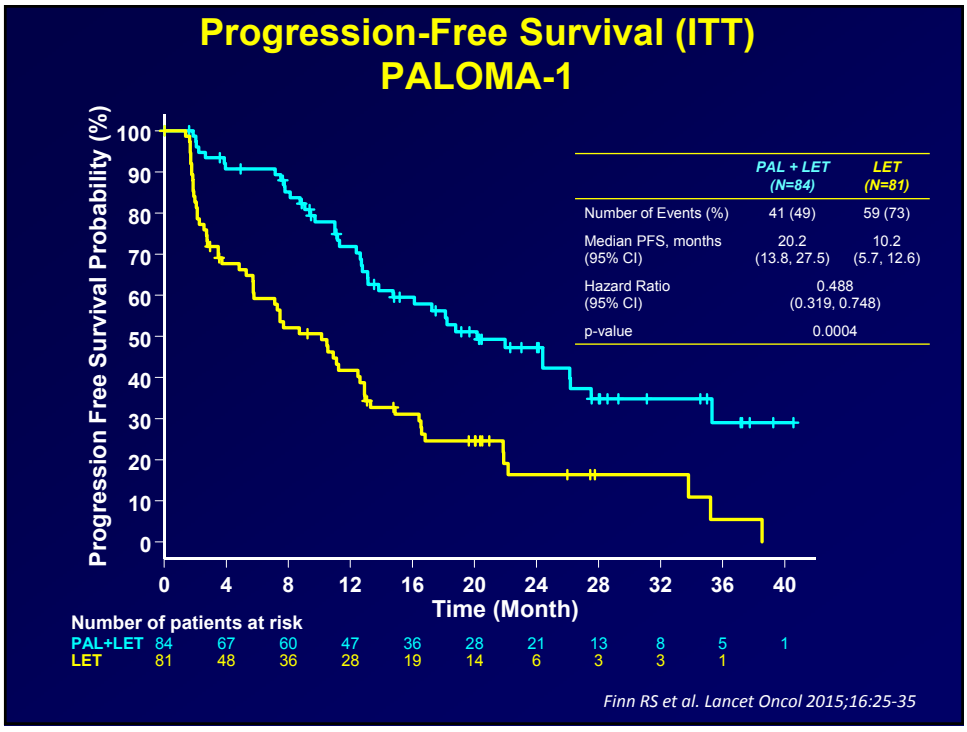

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PALOMA3: A Double-Blind, Phase III Trial of Fulvestrant with or without Palbociclib in Pre- and Post-Menopausal Women with Hormone Receptor-Positive, HER2-Negative Metastatic Breast Cancer that Progressed on Prior Endocrine Therapy

Turner NC et al. *Proc ASCO* 2015;Abstract LBA502.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 16, 2015 VOL. 373 NO. 3

Palbociclib in Hormone-Receptor–Positive Advanced Breast Cancer

Nicholas C. Turner, M.D., Ph.D., Jungsil Ro, M.D., Fabrice André, M.D., Ph.D., Sherene Loi, M.D., Ph.D., Sunil Verma, M.D., Hiroji Iwata, M.D., Nadia Harbeck, M.D., Sibylle Loibl, M.D., Cynthia Huang Bartlett, M.D., Ke Zhang, Ph.D., Carla Giorgetti, Ph.D., Sophia Randolph, M.D., Ph.D., Maria Koehler, M.D., Ph.D., and Massimo Cristofanilli, M.D.

Phase III PALOMA-3: Fulvestrant +/- Palbociclib 2nd line ER+ MBC

- HR+, HER2– ABC
- Pre-/peri-* or post-menopausal
- Progressed on prior endocrine therapy:
  - On or within 12 mo adjuvant
  - On therapy for ABC
- ≤1 prior chemotherapy regimen for advanced cancer

*All received goserelin.

2:1 Randomization
N=521

Stratification:
- Visceral metastases
- Sensitivity to prior hormonal therapy
- Pre-/peri- vs Post-menopausal

n=347 → Palbociclib (125 mg QD; 3 wks on/1 wk off) + Fulvestrant† (500 mg IM q4w)

n=174 → Placebo (3 wks on/ 1wk off) + Fulvestrant† (500 mg IM q4w)

- ***Post-menopausal patients must have progressed on prior aromatase inhibitor therapy.***

Nicholas Turner at 2015 ASCO Annual Meeting

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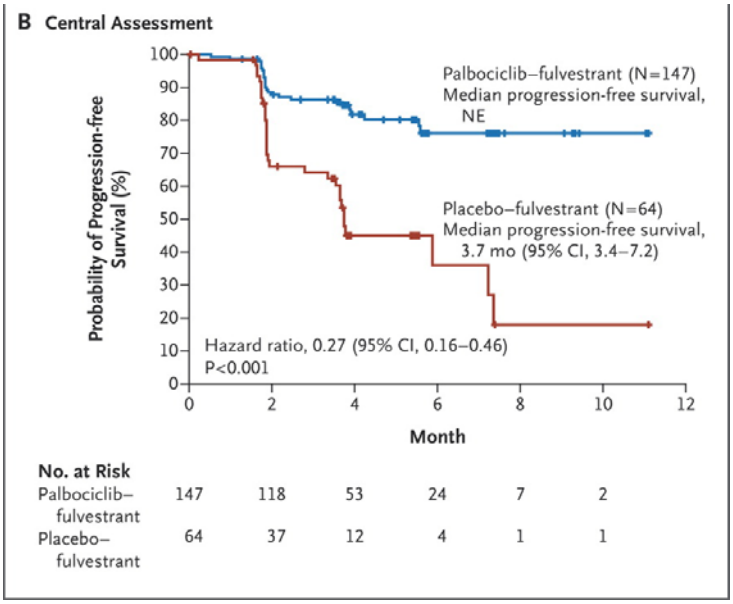

Turner NC et al. N Engl J Med 2015. DOI: 10.1056/NEJMoa1505270

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NCCN Guidelines Version 1.2016
Invasive Breast Cancer Updates

Updates in Version 1.2016 of the NCCN Guidelines for Breast Cancer from Version 2.2015 include:

BINV-C
- **Fertility and birth control, modified the first bullet: "All premenopausal patients should be informed about the potential impact of chemotherapy on fertility and asked about their desire for potential future pregnancies. Patients who may desire future pregnancies should be referred to fertility specialists before chemotherapy and/or endocrine therapy, to discuss the options based on patient specifics, disease stage and biology, (which determine the urgency and type and sequence of treatment). Timing and duration allowed for fertility preservation, options inclusive of oocyte and embryo cryopreservation as well as evolving technologies, and the probability of successful pregnancies subsequent to completion of breast cancer therapy are also to be discussed."**

BINV-D
- **Footnote 2: Removed the last sentence "However, only peritumoral injections map to the internal mammary lymph node(s).**

BINV-E
- **Replaced "Sentinel lymph node biopsy is the preferred method of axillary lymph node staging if there is an experienced sentinel node team and the patient is an appropriate sentinel lymph node biopsy candidate (See BINV-D)." with "Sentinel lymph node biopsy should be performed and is the preferred method of axillary lymph node staging if the patient is an appropriate sentinel lymph node biopsy candidate."**

BINV-F
- **Second paragraph, modified the last sentence "A boost to the tumor bed is recommended in patients at higher risk for recurrence."**

BINV-G
- **Absolute contraindications: added "Diffusely positive pathologic margins" and removed "Positive pathologic margin."**
- **Relative contraindications: added "Positive pathologic margin" and removed "Diffusely positive pathologic margins."**
- **Added a link to NCCN Guidelines for Genetic/ Familial High-Risk Assessment Breast and Ovarian.**

UPDATES-4

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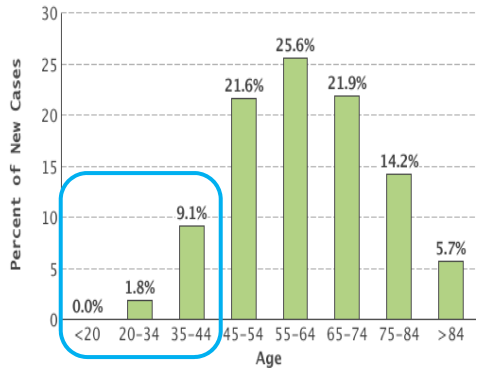
Many young women are diagnosed each year with breast cancer in the US

Percent of new cases by age



http://seer.cancer.gov/

>25,000 women < 45 years of age diagnosed each year

Treatment poses a risk of infertility

Professional guidelines highlight the need for clinicians to address fertility

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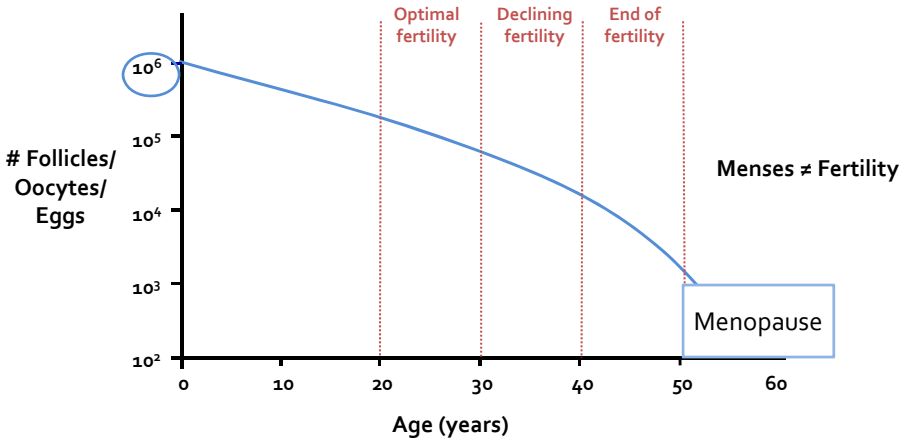
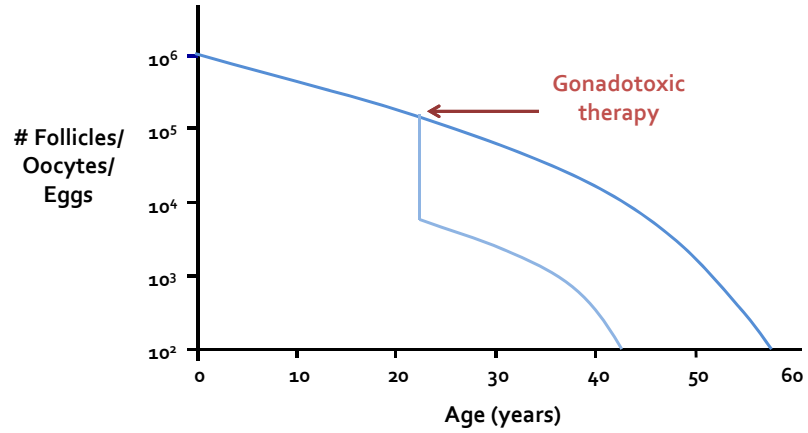
Effect of Age on Ovarian Reserve



Adapted from Faddy et al 1992

Effects of Treatment on Fertility

Depletion of ovarian follicle pool



Adapted from Faddy et al 1992

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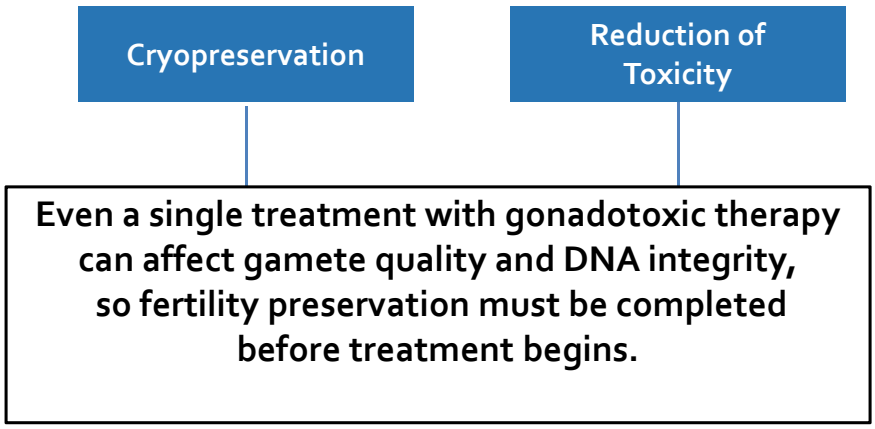
Fertility Preservation Options



Ovarian Suppression

- GnRH agonists: leuprolide, goserelin, triptorelin
- Mechanism of action is unclear
  - Suppression of FSH → ↓ follicle recruitment and maturation → protection from chemo destruction?
- Administered as a monthly injection
  - Start 1-2 weeks before first chemotherapy
- Will cause menopausal symptoms

Blumenfeld et al 2015; Del Mastro et al 2011; Lambertini et al 2015; Moore et al 2015

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Ovarian Suppression

- Results have been conflicting – investigational

  PROMISE (ER+)

  ↓ POF (8% vs 22%) ↑ pregnancies (5.4% vs 3%)

  POEMS (ER-)

  ↓ POF (8.9% vs 25.9%) ↑ pregnancies (21% vs 11%)

Blumenfeld et al 2015; Del Mastro et al 2011; Lambertini et al 2015; Moore et al 2015

NCCN Guidelines Updates: Breast Cancer

Kilian E. Salerno, MD

Director of Breast and Soft Tissue / Melanoma Radiation Oncology

Roswell Park Cancer Institute

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NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Breast Cancer

Version 1.2016

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

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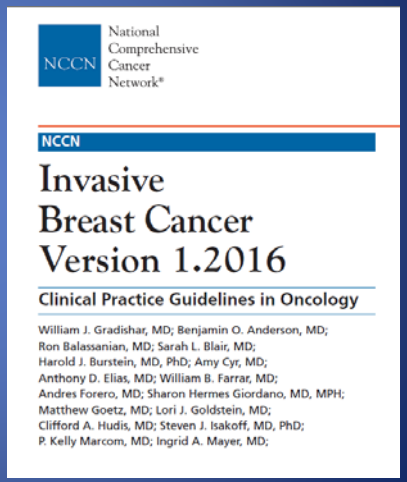
NCCN Guidelines Updates: Breast Cancer

- All changes to guidelines summarized
  - pages UPDATES-1 through UPDATES-5
- Locoregional therapy manuscript published in current issue of JNCCN (March 2016 issue)



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Locoregional Updates

- Outline
  - General principles of radiation
  - Guidelines updates
  - Regional nodal irradiation (RNI)
    - Which patients need RNI and to what extent?

Principles of Radiation Therapy

- Treatment options
  - Targets
  - Definitions
  - Techniques
- Optimizing treatment planning and delivery

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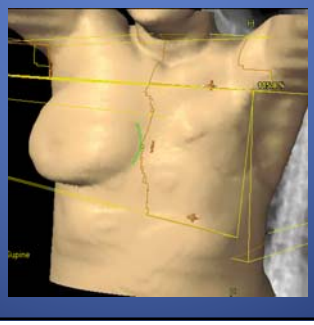
Radiation Treatment Options

TARGETS:

- Whole breast
- Partial breast
- Chest wall
- Regional nodes
  - SCV
  - ICV
  - Axilla at risk
  - IMNs
- Boost



Radiation Treatment Options

DOSE and FRACTIONATION

- Conventional Fractionation
  - 1.8-2 Gy per fraction to total dose 45-50 Gy
- Hypofractionation
  - Shorter course utilizing larger doses per fraction
  - >2 Gy per fraction to lower total dose
    - 40 - 42.5 Gy given in daily fxs for whole breast
    - 34 - 38.5 Gy given twice daily fxs for partial breast
- Accelerated course
  - Treatment over shorter time course

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Radiation Treatment Options

MODALITIES:

- External Beam
  - Photons
  - Electrons
- Brachytherapy
  - Radioactive source
  - Catheters/devices
- Intraoperative
  - Various means

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Invasive Breast Cancer

PRINCIPLES OF RADIATION THERAPY

Whole Breast Radiation:
Target definition is the breast tissue in entirety. The whole breast should receive a dose of 46–50 Gy in 23–25 fractions or 40–42.5 Gy in 15–16 fractions (hypofractionation is preferred). All dose schedules are given 5 days per week. A boost to the tumor bed is recommended in patients at higher risk for recurrence. Typical boost doses are 10–16 Gy in 4–8 fractions.

Chest Wall Radiation (including breast reconstruction):
The target includes the ipsilateral chest wall, mastectomy scar, and drain sites when indicated. Depending on whether the patient has had breast reconstruction or not, several techniques using photons and/or electrons are appropriate. CT-based treatment planning is encouraged in order to identify lung and heart volumes and minimize exposure of these organs. Dose is 46–50 Gy in 23–25 fractions to the chest wall +/- scar boost at 2 Gy per fraction to a total dose of approximately 60 Gy. All dose schedules are given 5 days per week. Special consideration should be given to the use of bolus material to ensure that the skin dose is adequate.

Regional Nodal Radiation:
Target delineation is best achieved by the use of CT-based treatment planning. For the paraclavicular and axillary nodes, prescription depth varies based on the patient anatomy. For internal mammary node identification, the internal mammary artery and vein can be used as a surrogate for the nodal location (as the nodes themselves are not usually visible on planning imaging). Based on the post-mastectomy radiation randomized studies and recent trials, radiation therapy of the internal mammary lymph nodes should be strongly considered when delivering regional nodal irradiation. CT treatment planning should be utilized when treating the internal mammary lymph nodal volume to evaluate dose to normal tissues, especially the heart and lung, and dose constraints respected. Dose is 46–50 Gy in 23–25 fractions to the regional nodal fields. All dose schedules are given 5 days per week.

BINV-I

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PRINCIPLES OF RADIATION THERAPY

Optimizing Delivery of Individual Therapy:
It is important to individualize radiation therapy planning and delivery. CT-based treatment planning is encouraged to delineate target volumes and adjacent organs at risk. Greater target dose homogeneity and sparing of normal tissues can be accomplished using compensators such as wedges, forward planning using segments, and intensity-modulated radiation therapy (IMRT). Respiratory control techniques including deep inspiration breath-hold and prone positioning may be used to try to further reduce dose to adjacent normal tissues, in particular heart and lung. Boost treatment in the setting of breast conservation can be delivered using enface electrons, photons, or brachytherapy. Chest wall scar boost when indicated is typically treated with electrons or photons. Verification of daily setup consistency is done with weekly imaging. In certain circumstances, more frequent imaging may be appropriate. Routine use of daily imaging is not recommended.

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Radiation Treatment Options

TECHNIQUES:

- Positioning
  - Supine vs Prone
- CT based planning
- 3D conformal vs IMRT
- Respiratory control with deep inspiration breath hold technique
  - "respiratory gating"

Prone breast positioning

Respiratory gating cube and glasses

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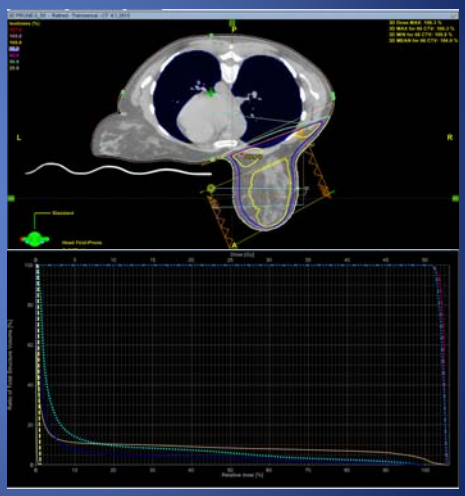
Use of Prone Positioning

Use of prone positioning

- Use in select patients with early stage disease
- Breast is target
- Minimize normal tissue doses and treatment toxicity



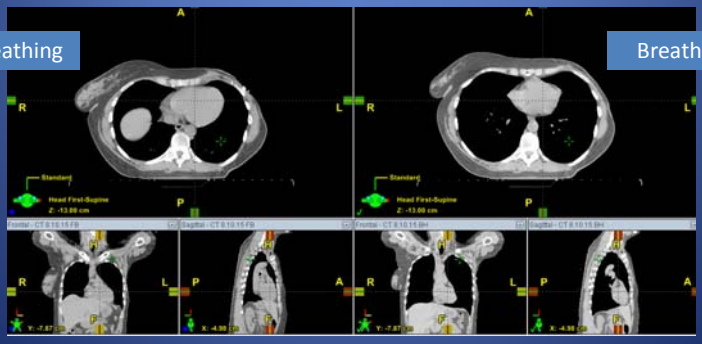
Use of "Respiratory Gating"

Breath hold technique

- Moderate deep inspiration
- Extra time, equipment, personnel, increased planning efforts and time for treatment

Free Breathing

Breath Hold



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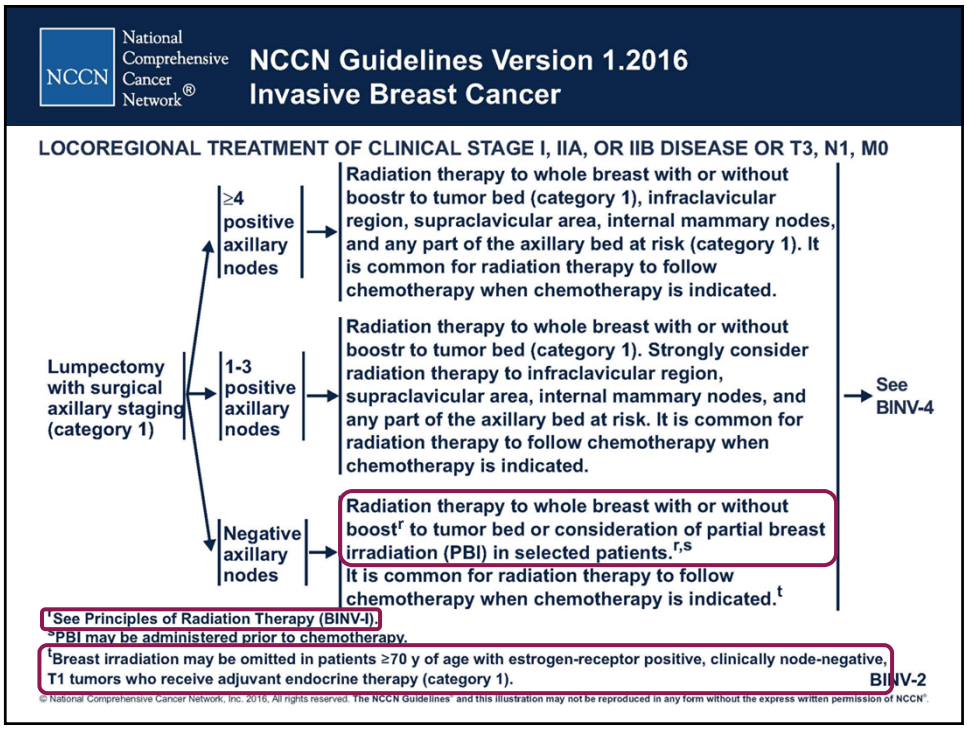
NCCN Guidelines Updates: Breast Cancer

- Adjuvant radiation options following breast conserving surgery
  - Hypofractionation
  - Accelerated Partial Breast Irradiation (APBI)
  - Omission of RT



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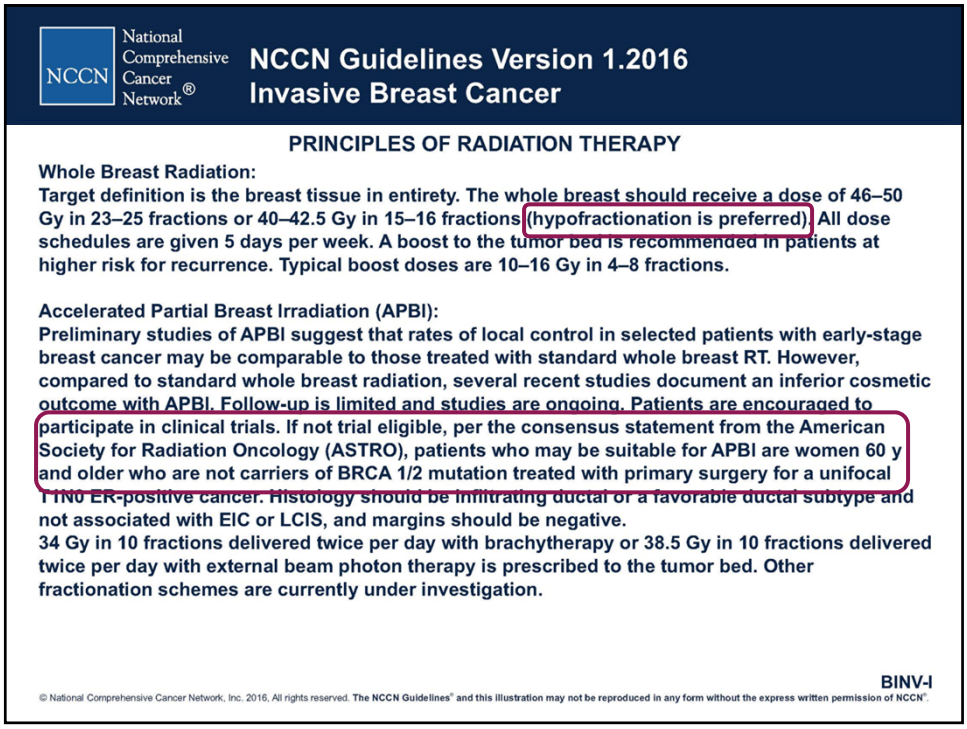

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Invasive Breast Cancer

PRINCIPLES OF RADIATION THERAPY

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Target definition is the breast tissue in entirety. The whole breast should receive a dose of 46–50 Gy in 23–25 fractions or 40–42.5 Gy in 15–16 fractions (hypofractionation is preferred). All dose schedules are given 5 days per week. A boost to the tumor bed is recommended in patients at higher risk for recurrence. Typical boost doses are 10–16 Gy in 4–8 fractions.

Accelerated Partial Breast Irradiation (APBI):
Preliminary studies of APBI suggest that rates of local control in selected patients with early-stage breast cancer may be comparable to those treated with standard whole breast RT. However, compared to standard whole breast radiation, several recent studies document an inferior cosmetic outcome with APBI. Follow-up is limited and studies are ongoing. Patients are encouraged to participate in clinical trials. If not trial eligible, per the consensus statement from the American Society for Radiation Oncology (ASTRO), patients who may be suitable for APBI are women 60 y and older who are not carriers of BRCA 1/2 mutation treated with primary surgery for a unifocal T1N0 ER-positive cancer. Histology should be infiltrating ductal or a favorable ductal subtype and not associated with EIC or LCIS, and margins should be negative.
34 Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions delivered twice per day with external beam photon therapy is prescribed to the tumor bed. Other fractionation schemes are currently under investigation.

BINV-I

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Hypofractionation

- *Whole breast radiation: why is hypofractionation now preferred in the guidelines?*
  - Long term results from Ontario and UK trials

    Canadian 42.5 Gy in 16 fractions, no boost
    START B 40 Gy in 15 fractions, ± boost

- At least equivalent or better disease outcomes
- At least equivalent or better cosmesis
- At least equivalent or better side effects

Whelan et al, NEJM 2010
Haviland et al, Lancet Oncol 2013

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Hypofractionation

- Who can be treated with hypofractionated whole breast irradiation?
- ASTRO Guidelines 2011
  (following Ontario publication but prior to UK)

Table 1. Evidence supports the equivalence of hypofractionated whole breast irradiation with conventionally fractionated whole breast irradiation for patients who satisfy all of these criteria*

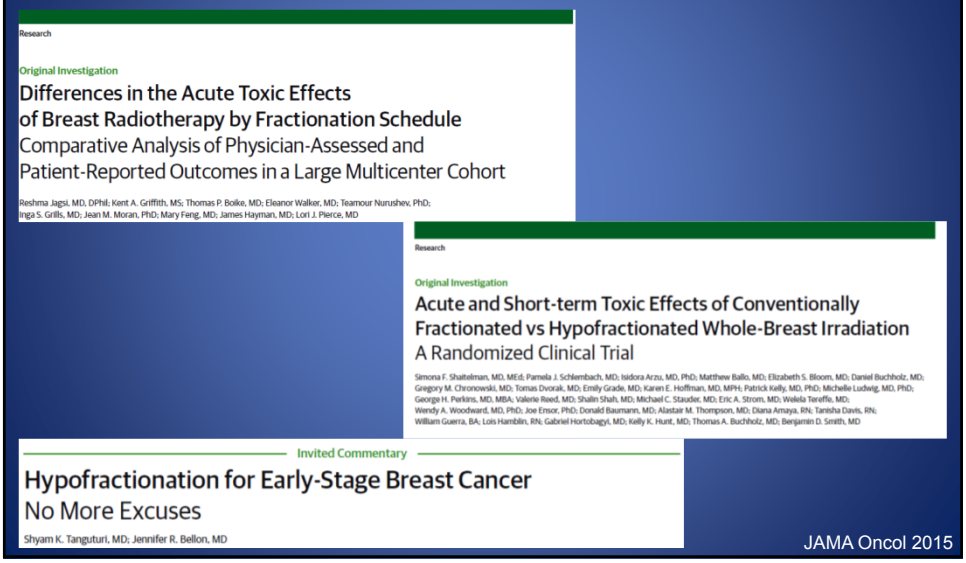
1. Patient is 50 years or older at diagnosis.
2. Pathologic stage is T1–2 N0 and patient has been treated with breast- conserving surgery.
3. Patient has not been treated with systemic chemotherapy.
4. Within the breast along the central axis, the minimum dose is no less than 93% and maximum dose is no greater than 107% of the prescription dose (±7%;) (as calculated with 2-dimensional treatment planning without heterogeneity corrections).

* For patients who do not satisfy all of these criteria, the task force could not reach consensus and therefore chose not to render a recommendation either for or against hypofractionated whole breast irradiation in this setting. Please see the text for a thorough discussion of tumor grade. Patients receiving any type of whole breast irradiation should generally be suitable for breast-conserving therapy with regards to standard selection rules (*e.g.*, not pregnant, no evidence of multicentric disease, no prior radiotherapy to the breast, no history of certain collagen-vascular diseases).

  - I treat more broadly than this since UK results
- ASTRO to update guidelines in 2017
- Not used routinely for nodal irradiation at this time

Smith et al, IJROBP 2011

Recent Publications: Hypofractionation



JAMA Oncol 2015

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Accelerated Partial Breast Irradiation (APBI)

- Different methods for delivery
  - IORT
  - Interstitial
  - Intracavitary
  - EBRT
- Different guidelines/consensus statements
  - ASTRO, ASBS, ABS, ESTRO
  - Inclusion/exclusion criteria for NSABP B39/ RTOG 0413
- ASTRO defines suitable, cautionary, unsuitable groups
- NCCN guidelines based on ASTRO suitable group

Smith et al, IJROBP 2009

ASTRO APBI Consensus Statement

Table 2. Patients "suitable" for APBI if all criteria are present

Factor	Criterion
Patient factors	
Age	≥60 y
BRCA1/2 mutation	Not present
Pathologic factors	
Tumor size	≤2 cm*
T stage	T1
Margins	Negative by at least 2 mm
Grade	Any
LVSI	No†
ER status	Positive
Multicentricity	Unicentric only
Multifocality	Clinically unifocal with total size ≤2.0 cm‡
Histology	Invasive ductal or other favorable subtypes§
Pure DCIS	Not allowed
EIC	Not allowed
Associated LCIS	Allowed
Nodal factors	
N stage	pN0 (i^-, i^+)
Nodal surgery	SN Bx or ALND‖
Treatment factors	
Neoadjuvant therapy	Not allowed

Currently being updated

New draft was open for public comment through March 2016

Smith et al, IJROBP 2009

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Omission of Radiation

- In selected women with lower risk for recurrence
- No survival detriment
- CALGB 9343
  - 70 or older, small cancers, negative nodes, negative margins, ER/PR positive
  - BCS → Tamoxifen ± RT
  - 10% (no RT) vs 2 % (RT) LRR at median 12.6 yrs
- PRIME II, Fyles et al, NSABP B-21

Hughes et al, JCO 2013; Kunkler et al, Lancet Oncol 2015; Fyles et al, NEJM 2004; Fisher et al JCO 2002

Adjuvant Radiation Options Following BCS: Summary

- Hypofractionated Whole Breast Irradiation
  - ***PREFERRED***
- Accelerated Partial Breast Irradiation (APBI)
  - ***ASTRO suitable criteria***
- Omission of RT
  - ***YES in select patients***

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NCCN Guidelines Updates: Breast Cancer

- Post Mastectomy Radiation Therapy (PMRT)
- Regional nodal irradiation (RNI)
  - Either in setting of BCT or PMRT
  - ≥4 LNs +
  - 1-3 LNs +
- Treatment of recurrence

Historical PMRT Indications

Classic Indications

- ≥4 positive axillary lymph nodes
- Positive margins
- Tumor > 5 cm

No radiation

- Tumor < 5 cm
- Negative lymph nodes
- No high risk features

Considerations

- 1-3 positive lymph nodes
- pT3N0
- Close margins
- High risk features
  - Age
  - Extracapsular extension
  - Lymphovascular invasion
  - Certain phenotypes

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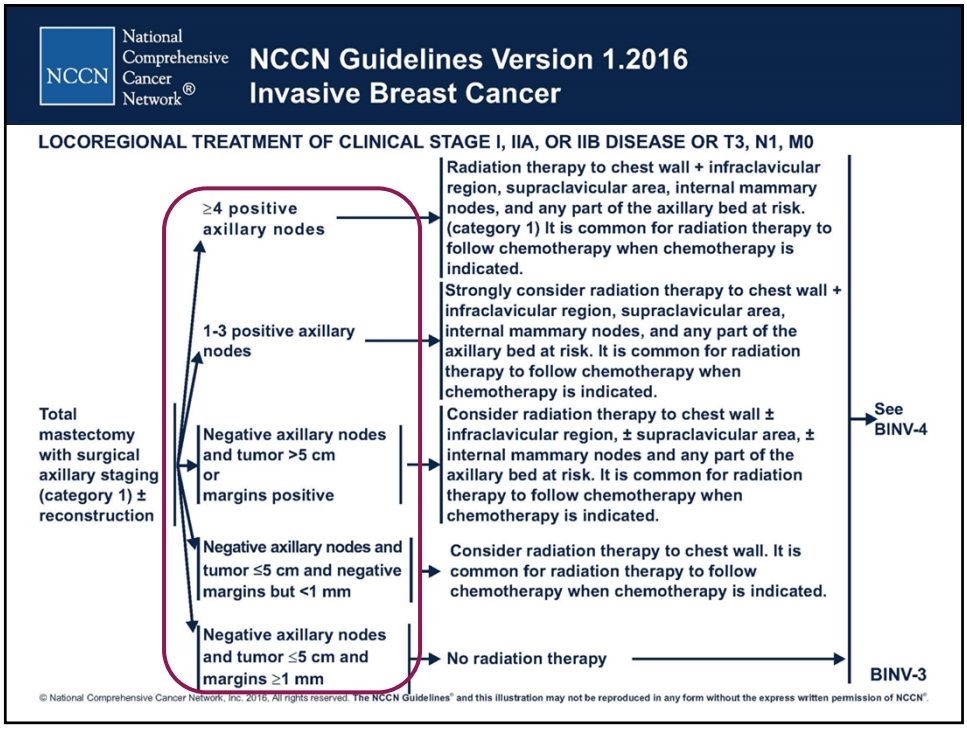

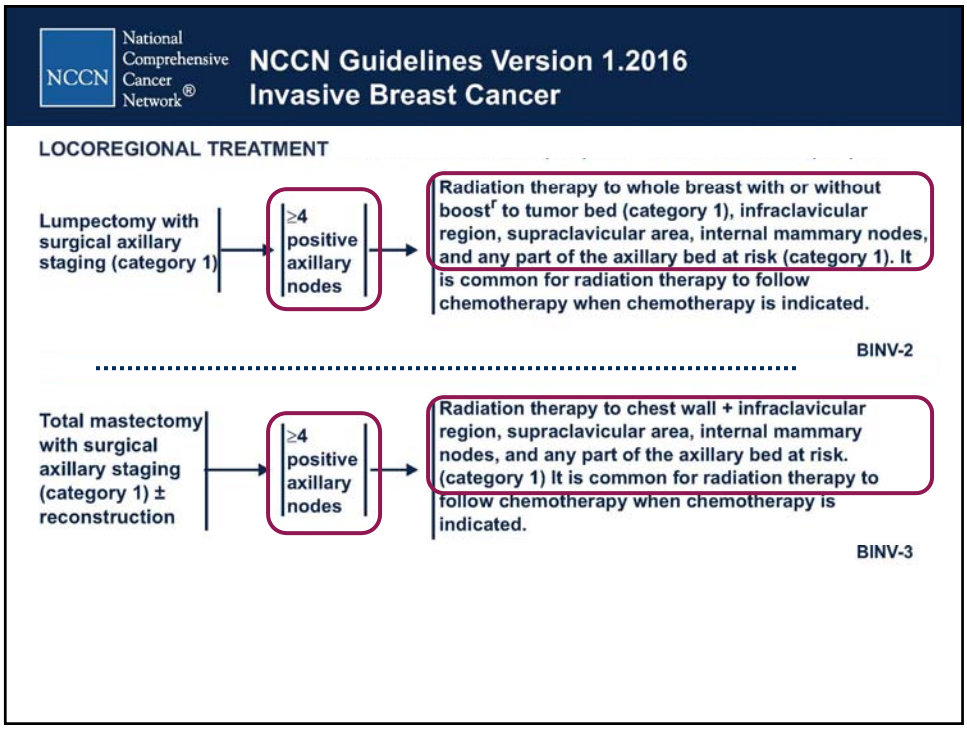

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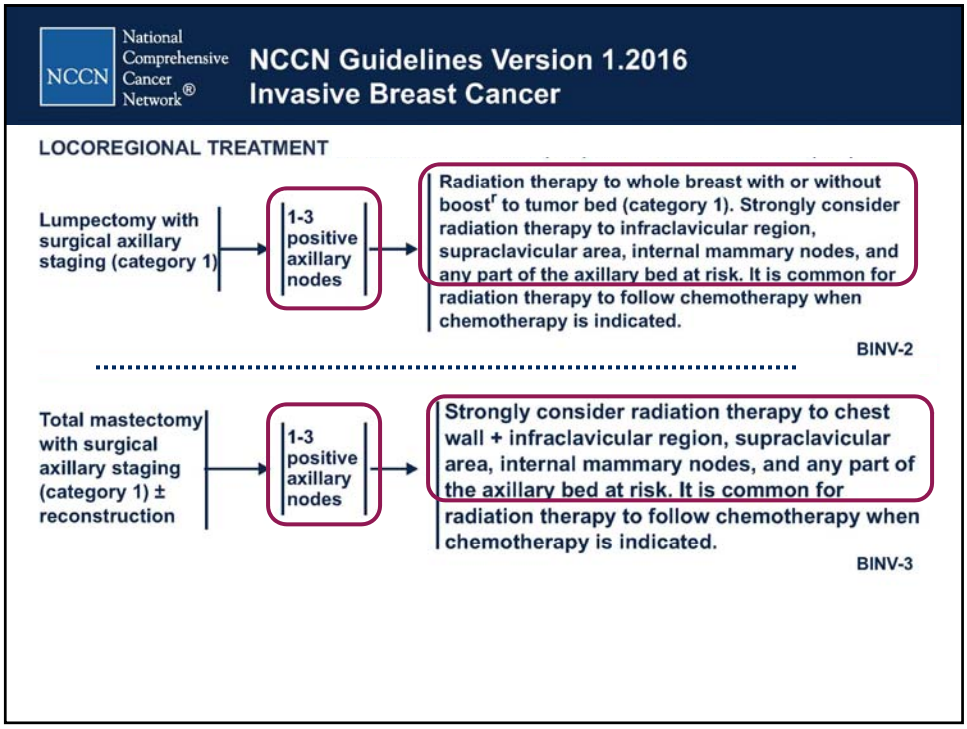
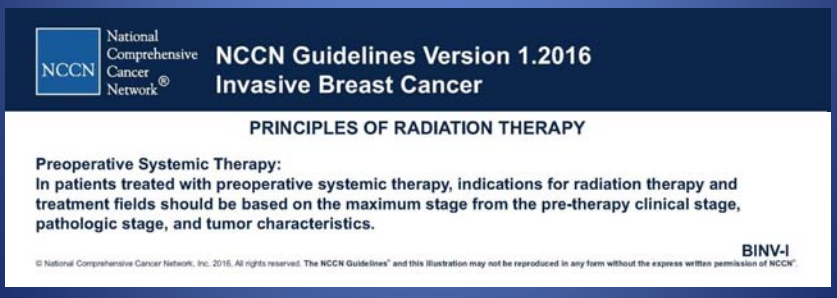


Adjuvant Radiation Recommendations

- After neoadjuvant systemic therapy?
  - *RT recommended as per maximal stage of either clinical staging pre-systemic therapy or pathologic staging*



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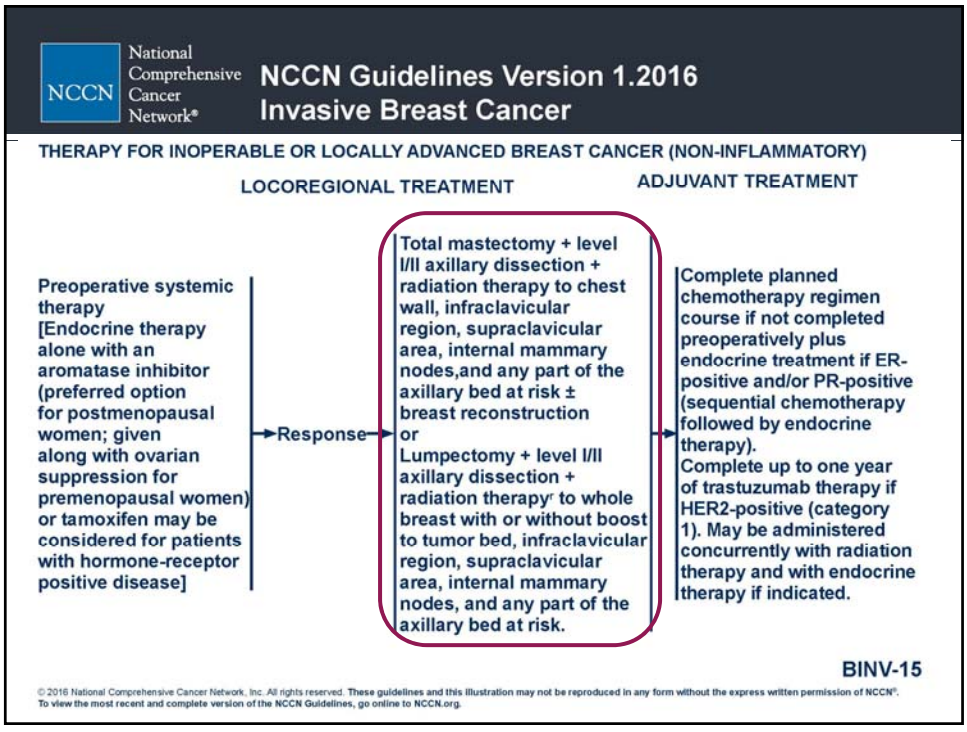
Adjuvant Radiation Recommendations

- Treatment of inoperable or locally advanced breast cancer?
  - Neoadjuvant systemic therapy
  - Either BCT or PMRT with AxLND
  - RT to breast +/- boost or chest wall
  - RNI: SCV, ICV, axillary bed at risk, IMNs



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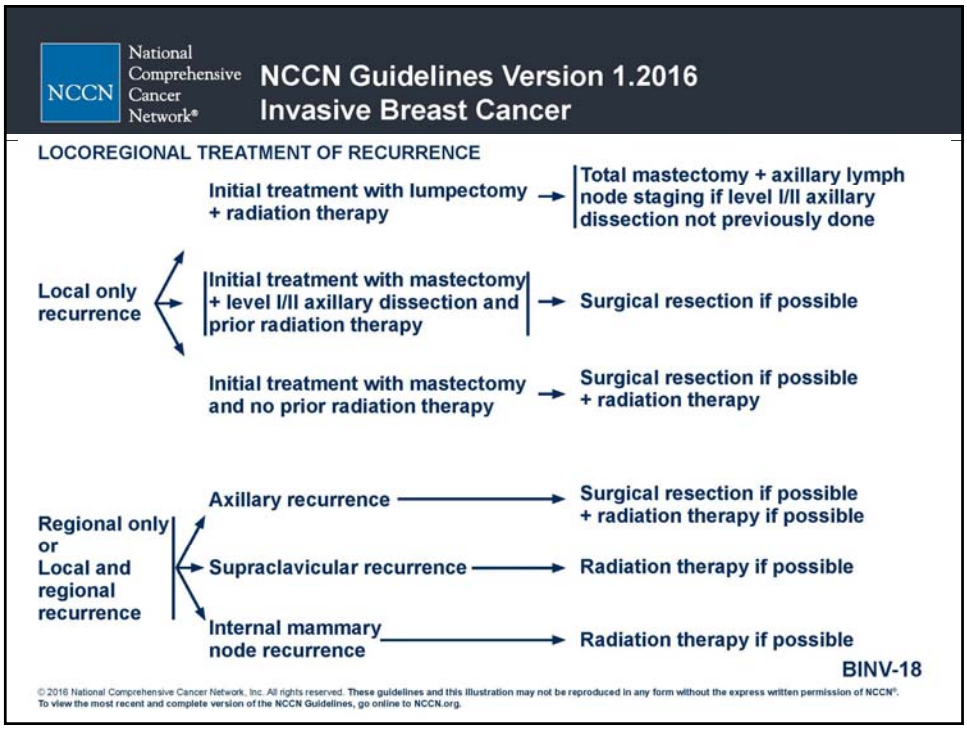
Treatment of Recurrence

- Importance of multi-disciplinary approach for optimal outcomes
- Management of recurrence depends on extent of disease and prior therapies received
  - Prior surgery
  - Prior axillary staging
  - Prior systemic therapy
  - Prior radiation therapy



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Locoregional Updates

- Outline
  - General principles of radiation
  - Guidelines updates
  - Regional nodal irradiation (RNI)
    - Which patients need RNI and to what extent?

NCCN Guidelines Updates: Breast Cancer

- Who needs RNI?
- What influence of surgical resection and axillary surgical staging?
- What about in setting of neoadjuvant chemotherapy?
- What extent of RNI?

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Which patients need regional nodal irradiation (or not)?

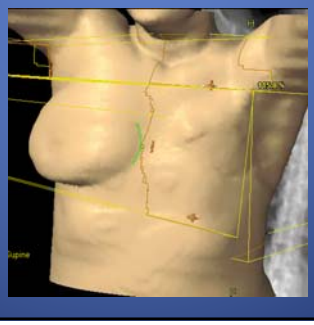
TARGETS:

Whole breast
- Standard Tangents
- High Tangents

Chest wall

±

Regional nodes
- SCV
- ICV
- Axilla at risk
- IMNs



Which patients need regional nodal irradiation (or not)?

- In setting of BCT?
  - ACOSOG Z11: cT1-2N0, 1-2 +SLNs, tangents
  - IBCSG 23-01: N1mic
  - MA 20: higher risk patients
  - EORTC 22922: higher risk patients

Giuliano et al, JAMA 2011; Galimberti et al, Lancet Oncol 2013; Whelan et al, NEJM 2015; Poortmans et al, NEJM 2015;

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Which patients need regional nodal irradiation (or not)?

- In post mastectomy setting?
  - B-04, Danish 82b and 82c, British Columbia
  - ECOG and NSABP pooled analyses
  - Patients on more recent trials?
    - Few on IBCSG and some on EORTC
    - SUPREMO
  - EBCTCG: benefit to RT

Fisher et al, NEJM 2002; Overgaard et al, Radiother Oncol. 2007; Ragaz et al, JNCI 2005; Recht et al, JCO 1999; Taghian et al, JCO 2004; EBCTCG, Lancet, 2014

Which patients need regional nodal irradiation (or not)?

- AxLND vs Axillary RT?
  - AMAROS
  - In setting of neoadjuvant chemo?
  - Currently based on maximal disease stage
  - SENTINA: axillary staging options
  - Current open trials
    - NSABP B51 / RTOG 1304
    - Alliance A011202

Donker et al, Lancet Oncol 2014

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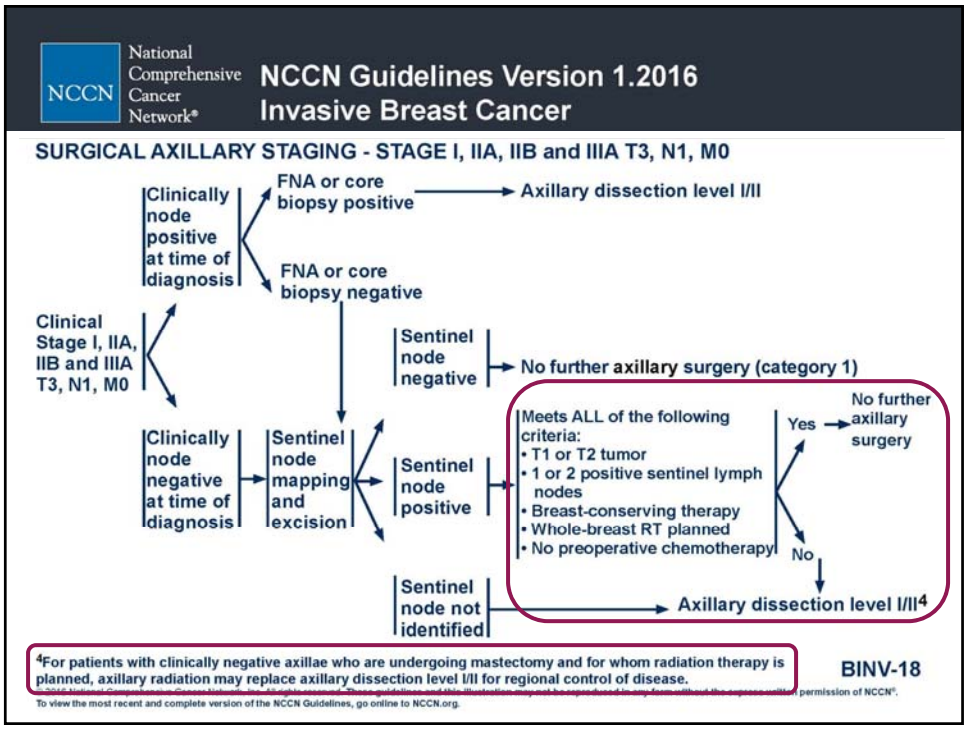
ACOSOG Z11

- RCT of ALND vs observation for women with 1-2 positive SLNs
- 891 pts, cT1-2N0
- ~ 40% of +SLNs were micromets
- On AxLND, 27.4% of patients had additional +LNs
- Whole breast RT via tangents, no nodal
  - QARC analysis showed variation with 3rd field, high tangents use
- Median 6.3 yrs, no difference and low rates of LR / LRR (<5%), less lymphedema with SLN alone

Giuliano et al, JAMA 2011

Jagsi et al, JCO 2014



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EBCTCG Meta-Analysis 2014

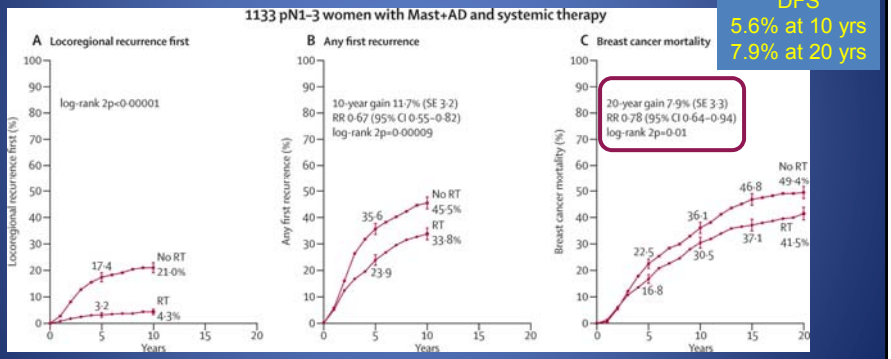
- "Effects of RT after Mastectomy and Axillary Surgery on 10 yr Recurrence and 20 yr Breast Cancer Mortality"
- 8,135 women, 22 randomized trials, 1964-1986
- In women with 1-3 N+ and ≥4 N+ (not N0)
  - RT reduced LRR, OR, and breast cancer mortality
- Are the risks for recurrence the same now?
- Does this mean everyone should be treated?

EBCTCG: Early Breast Cancer Trialists' Collaborative Group

EBCTCG, Lancet 2014

EBCTCG Meta-Analysis 2014

DFS
5.6% at 10 yrs
7.9% at 20 yrs



EBCTCG, Lancet 2014

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EBCTCG Meta-Analysis 2014

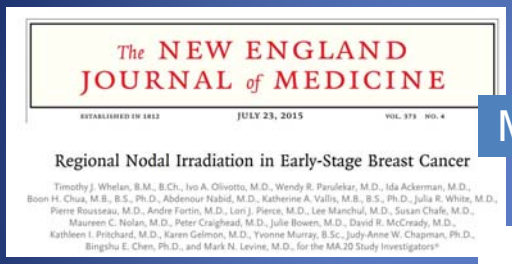
Webtable 1: Randomised trials beginning before the year 2000 and comparing radiotherapy to the chest wall and regional lymph nodes versus not after mastectomy and axillary dissection (Mast+AD) or axillary sampling (Mast+AS) – treatment details.

Year code and study name	Breast surgery	Axillary Surgery* (number of patients)	Chest wall RT	Supraclavicular (SC) and axillary fossa (AF) RT	Internal mammary chain RT	Boost RT to scar	Common systemic chemoendocrine therapy
64B Oslo X-ray	RM	Axillary dissection (552)	25-41 Gy (1.3-2.1 Gy/f) o	36 Gy (1.8 Gy/f) o, SC; 18 Gy (u Gy/f) o, AF	25-41 Gy (1.3-2.1 Gy/f) o	None	Ovarian RT
71B Stockholm A	MRM	Axillary sampling (644)	45 Gy (1.8 Gy/f) e	45 Gy de (1.8 Gy/f) c	45 Gy (1.8 Gy/f) e	None	None
73A Southampton UK	SM	Axillary sampling (151)	46 Gy (2.3 Gy/f) c	55 Gy (2.5 Gy/f) c & b	46 Gy (2.3 Gy/f) c	None	None
74B Edinburgh I	SM	Axillary sampling (348)	42.5-45.0 Gy (4.25-4.5 Gy/f) m	42.5-45.0 Gy (4.25-4.5 Gy/f) m	None	None	F
74D DFCI Boston	MRM or RM	Axillary dissection (218)	45 Gy (2.3 Gy/f) c or m	45 Gy (2.3 Gy/f) c or m	0-45 Gy (0-2.3 Gy/f) c or m	None	Either (AC) 5 cycles or (AC) 10 cycles; or CMF or MF
74Q Piedmont OA (pN4+)	MRM or RM	Axillary dissection (120)	50 Gy (1.5-1.8 Gy/f) c or m	45-50 Gy (1.5-2.8 Gy/f) c or m	45-50 Gy (1.8-2.8 Gy/f) c or m	None	Mel or CMF
76A SECSG 1	MRM or RM	Axillary dissection (257)	50 Gy (2 Gy/f) u	50 Gy (2 Gy/f) u	50 Gy (2 Gy/f) u	None	CMF
76C Glasgow	SM	Axillary dissection (219)	37.8 Gy (2.5 Gy/f) o	37.8 Gy (2.5 Gy/f) o	37.8 Gy (2.5 Gy/f) o	None	CMF
77J MD Ander. 7730B	MRM or SM	Axillary dissection (80) Axillary sampling (17)	45-50 Gy (1.8-2.0 Gy/f) c	45-50 Gy (1.8-2 Gy/f) c	45-50 Gy (1.8-2 Gy/f) c or e	12 Gy (uGy/f) u	bCG+FAC or FAC
78A S Swedish BCG	MRM	Axillary dissection (771)	38 Gy (1.9 Gy/f) e,o,m or c	48-60 Gy (2.4 Gy/f) c or m	48 Gy (2.4 Gy/f) e, c or m	None	Premen: C; Postmen: tam
78G BCCA Vancouver	MRM	Axillary dissection (318)	37.5-40 Gy (2.3 Gy/f) c or m	37.5 Gy de (2.2 Gy/f) c or m	37.5 Gy de (2.3 Gy/f) c or m	None	CMFP+ovarian RT or CMF
78Q Düsseldorf U	Patey	Axillary dissection (88)	40 Gy (2 Gy/f) c	40 Gy (2 Gy/f) c	40 Gy (2 Gy/f) c	None	LMF
79F Coimbra	NS	Axillary sampling (124)	36 Gy (3 Gy/f) o or m	39-45 Gy (3.3-3.8 Gy/f) m	39 Gy (3.3 Gy/f) m	None	AC
79G Metaxas Athens	MRM, Patey MRM, or RM	Axillary dissection (71)	45-60 Gy (2 Gy/f) m	45-60 Gy (2 Gy/f) m	45-60 Gy (2 Gy/f) m	None	CAMF & tam Premen: ovarian RT
80S Helsinki	RM	Axillary dissection (99)	45 Gy (3 Gy/f) c	45 Gy (3 Gy/f) c, SC; 45 Gy (3 Gy/f) c, AF	45 Gy (3 Gy/f) c	None	CAFt
80W NSABC Israel	NS	Unknown (112)	46-50 Gy (2 Gy/f) c or m	46-50 Gy (2 Gy/f) c or m	40 Gy (2 Gy/f) c or m	None	CMF
82B Danish BCG 82b pre	SM	Axillary dissection (418) Axillary sampling (1,386)	36-50 Gy (1.8-2.2 Gy/f) o or e	36-50 Gy (1.8-2.2 Gy/f) o or m	36-50 Gy (1.8-2.2 Gy/f) o or e	None	CMF
82C Danish BCG 82c post	SM	Axillary dissection (344) Axillary sampling (1,119)	36-50 Gy (1.8-2.2 Gy/f) o or e	36-50 Gy (1.8-2.2 Gy/f) o or m	36-50 Gy (1.8-2.2 Gy/f) o or e	None	tam
82Q ECOG EST3181	MRM or RM	Axillary dissection (332)	46 Gy (2 Gy/f) c or m	46-50 Gy (2 Gy/f) c or m	46 Gy (2 Gy/f) c, m or e	None	CAF&H&tam
84A GBSG 03 Germany	Patey	Axillary sampling (199)	50 Gy (2 Gy/f) c or m	50 Gy (2 Gy/f) c or m	44 Gy(1.8 Gy/f) c or m	None	CMF
85F Nottingham	SM	Axillary sampling (77)	45 Gy (3 Gy/f) m	45 Gy (3 Gy/f) m	None	None	Premen; CMF Postmen;tam
86C CRC, UK	NS	Unknown (71)	Various	Various	Various	Various	None

* Based on the description of axillary surgery in the trial protocol or publications or on information on individual women. Women were classified as having axillary dissection if they were in a trial where the protocol required removal of axillary lymph nodes in at least levels I & II or, if individual information was available (MD Ander. 7730B, Danish BCG 82b pre, Danish BCG 82c post), resection of ≥10 nodes. In other trials, women were classified as having axillary dissection if the trial publication indicated that the median number of nodes removed was ≥ 10. Women with less extensive axillary surgery were classified as having axillary sampling. A=doxorubicin (adriamycin), AC=doxorubicin and cyclophosphamide, AF=axillary fossa, b= additional posterior boost to axilla, bCG=bacillus Calmette-Guérin, C=cyclophosphamide, c=cobalt-60, de=dose at depth (of nodes), F=fluorouracil, Ft=Florafur, f=fraction, Gy=Gray (intended dose), H=halotestin, L=chlorambucil, m=megavoltage, M=methotrexate, Mel=melphalan, MRM=modified radical mastectomy, NS=surgery not specified in detail (Patey mastectomy, or modified radical mastectomy), o=orthovoltage, P=prednisone, Patey= Patey mastectomy, RM=radical mastectomy (Halsted), RT=radiotherapy, SC=supraclavicular, SM=simple (total) mastectomy; tam=tamoxifen, u=unknown.

EBCTCG, Lancet 2014

Recent Publications: Regional Nodal Irradiation

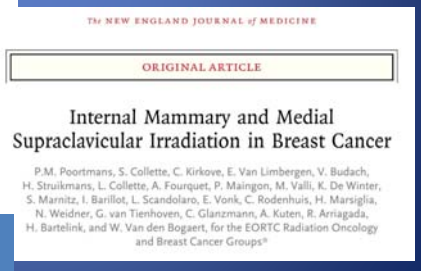

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 23, 2015 VOL. 373 NO. 4

Regional Nodal Irradiation in Early-Stage Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Ivo A. Olivotto, M.D., Wendy R. Parulekar, M.D., Ida Ackerman, M.D., Boon H. Chua, M.B., B.S., Ph.D., Abdenour Nabid, M.D., Katherine A. Vallis, M.B., B.S., Ph.D., Julia R. White, M.D., Pierre Rousseau, M.D., Andre Fortin, M.D., Lori J. Pierce, M.D., Lee Manchul, M.D., Susan Chafe, M.D., Maureen C. Nolan, M.D., Peter Craighead, M.D., Julie Bowen, M.D., David R. McCready, M.D., Kathleen I. Pritchard, M.D., Karen Gelmon, M.D., Yvonne Murray, B.Sc., Judy-Anne W. Chapman, Ph.D., Bingshu E. Chen, Ph.D., and Mark N. Levine, M.D., for the MA.20 Study Investigators*

MA.20


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

P.M. Poortmans, S. Collette, C. Kirkove, E. Van Limbergen, V. Budach, H. Struikmans, L. Collette, A. Fourquet, P. Maingon, M. Valli, K. De Winter, S. Marnitz, I. Barillot, L. Scandolaro, E. Vonk, C. Rodenhuis, H. Marsiglia, N. Weidner, G. van Tienhoven, C. Glanzmann, A. Kuten, R. Arriagada, H. Bartelink, and W. Van den Bogaert, for the EORTC Radiation Oncology and Breast Cancer Groups*

EORTC 22922

Whelan et al, NEJM 2015

Poortmans et al, NEJM 2015

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Regional Nodal Irradiation

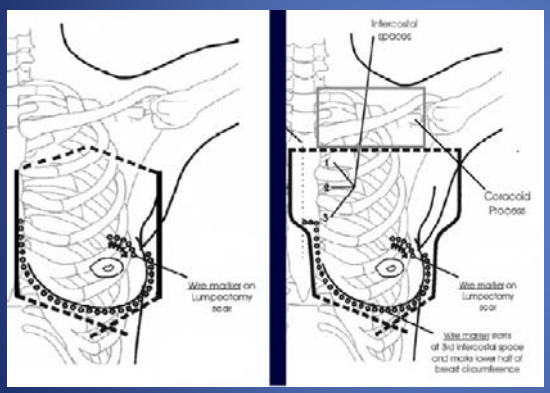
- MA.20:
  - 1832 pN+ (85% N1) or high risk N- pts (10%)
  - BCS and ALND, adjuvant systemic tx
  - WBI ± RNI
    - RNI = IMNs, SCV, ICV, ± Ax
- EORTC 22922:
  - 4000 pN+ (44% N1) or high risk N- pts (43%)
  - BCS (76%) or M and ALND, adjuvant systemic tx
  - WBI or CW ± RNI
    - RNI = IMNs, SCV, ICV, ± Ax

* definitions of high risk N- differed as types did use of chemotherapy/endocrine therapy

Whelan et al, NEJM 2015

Poortmans et al, NEJM 2015

MA.20 Radiation



- WBI
  - 50/25 +/- 10 Gy boost
- WBI + RNI (45/25)
  - IMNs
  - SCV/Level III

Whelan et al, NEJM 2015

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Regional Nodal Irradiation

- Results from MA 20 and EORTC 22922:
  - 10 yr median follow up
  - Primary endpoint was OS
  - RNI improved locoregional DFS, distant DFS, and death from breast cancer, but did not improve OS

Whelan et al, NEJM 2015

Poortmans et al, NEJM 2015

MA.20 Results

OS
82.8% vs 81.8%
p=0.38

ER-
81.3% vs 73.9%
p=0.05

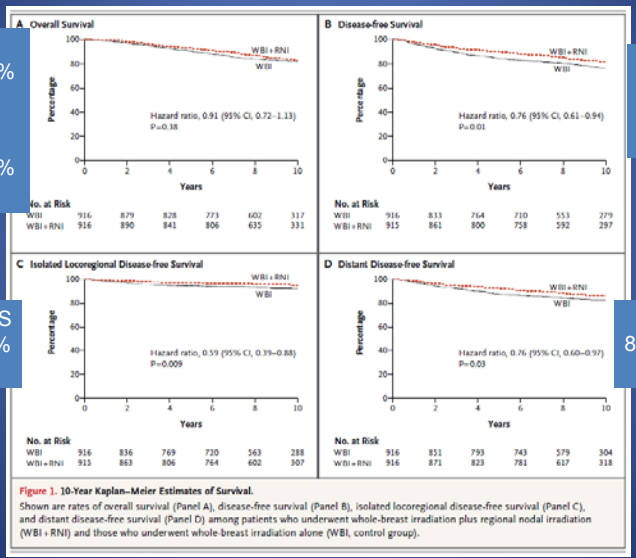

Figure 1. 10-Year Kaplan–Meier Estimates of Survival.
Shown are rates of overall survival (Panel A), disease-free survival (Panel B), isolated locoregional disease-free survival (Panel C), and distant disease-free survival (Panel D) among patients who underwent whole-breast irradiation plus regional nodal irradiation (WBI + RNI) and those who underwent whole-breast irradiation alone (WBI, control group).

DFS
5% at 10 yrs
82% vs 77%
p=0.01

Isolated LR DFS
95.2% vs 92.2%
p=0.009

Distant DFS
86.3% vs 82.1%
p=0.03

Whelan et al, NEJM 2015

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How do we interpret and reconcile the differences between these studies in determining the role for regional nodal irradiation?

Which patients need regional nodal irradiation?

- Consider whether a given study is applicable and whether an individual patient met the study eligibility.
- Assess individual risk for recurrence.
- Nomograms may be helpful.

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Which patients need regional nodal irradiation?

- Questions and answers regarding the extent of lymph node surgery (SLN Bx vs Ax LND) are not the same as question and answers regarding the need for, type of, and extent of regional nodal radiation.

Clinical Case

48 year old premenopausal female with a cT2N1M0 (bx proven N+) left breast invasive carcinoma NST, grade 3, ER/PR negative, Her2 positive receives neoadjuvant chemotherapy with significant clinical response.

She is desirous of BCT and proceeds with WLE and SLN biopsy.

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Clinical Case

Pathology returns ypT1aN1a(sn) with 4 mm residual disease, associated DCIS, negative margins, and 1/2 lymph nodes positive with 3 mm involvement and no ECE.

What are your recommendations for next therapies?

Audience Response Question

1. Axillary LND before any RT recommendation
2. Whole breast RT using high tangents with boost
3. Whole breast RT with boost + RNI to SCV, ICV and axilla, no IMNs
4. Whole breast RT with boost + RNI to SCV, ICV, axilla, and IMNs
5. Clinical trial

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Regional Nodal Irradiation Recommendations: Summary

- ***≥4 LNs +***

  Following either BCT or PMRT

  RT to breast +/- boost or chest wall +RNI

  (category 1)

Regional Nodal Irradiation Recommendations: Summary

- ***1-3 LNs +***

  BCT

  – RT to breast +/- boost (category 1)

  – ***Strongly consider RNI***

  PMRT

  – ***Strongly consider RT to chest wall +/- boost and RNI***

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Regional Nodal Irradiation Recommendations: Summary

- Which nodal volumes treated?
  - SCV
  - ICV
  - Axillary bed at risk
  - IMNs
- Attention to normal tissue dose constraints
  - In particular heart and lung

Areas of Ongoing Study

- Concominant boost with hypofractionation
  - RTOG 1005
- cN+ disease receiving neoadjuvant chemotherapy
  - Extent of axillary surgery and/or radiation
  - SLN bx negative→ NSABP B51 / RTOG 1304
  - SLN bx positive → Alliance A011202
- Hypofractionation for nodal RT / PMRT?
- Use of biologic parameters to guide local therapy options

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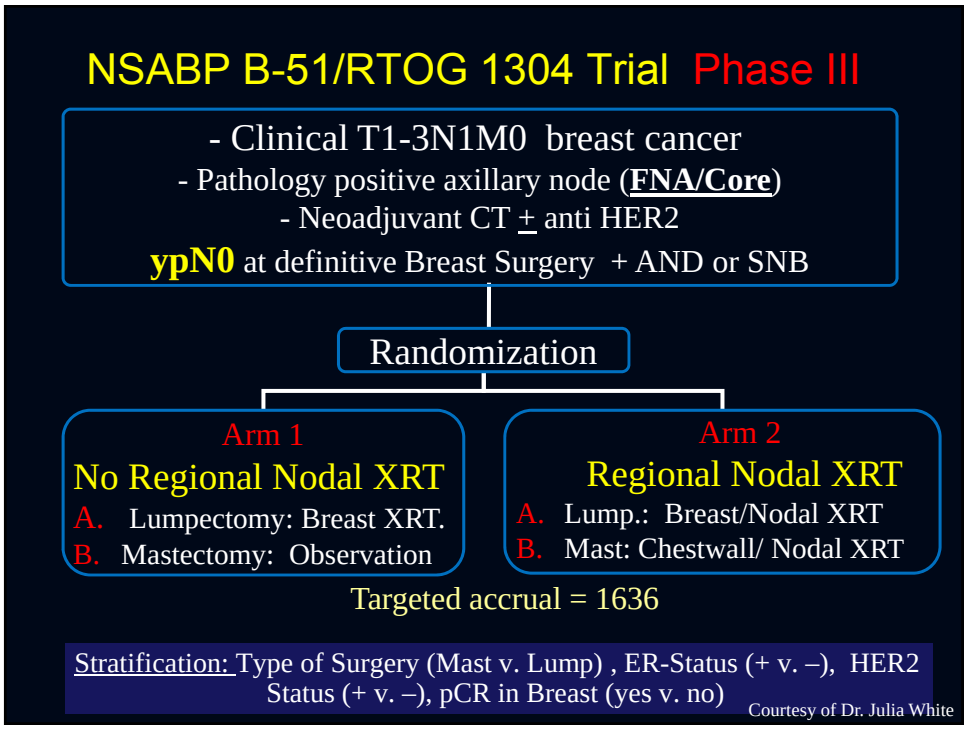
cN1 → ypN0(sn) Extent of RNI: NSABP B51 / RTOG 1304

A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chest Wall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy



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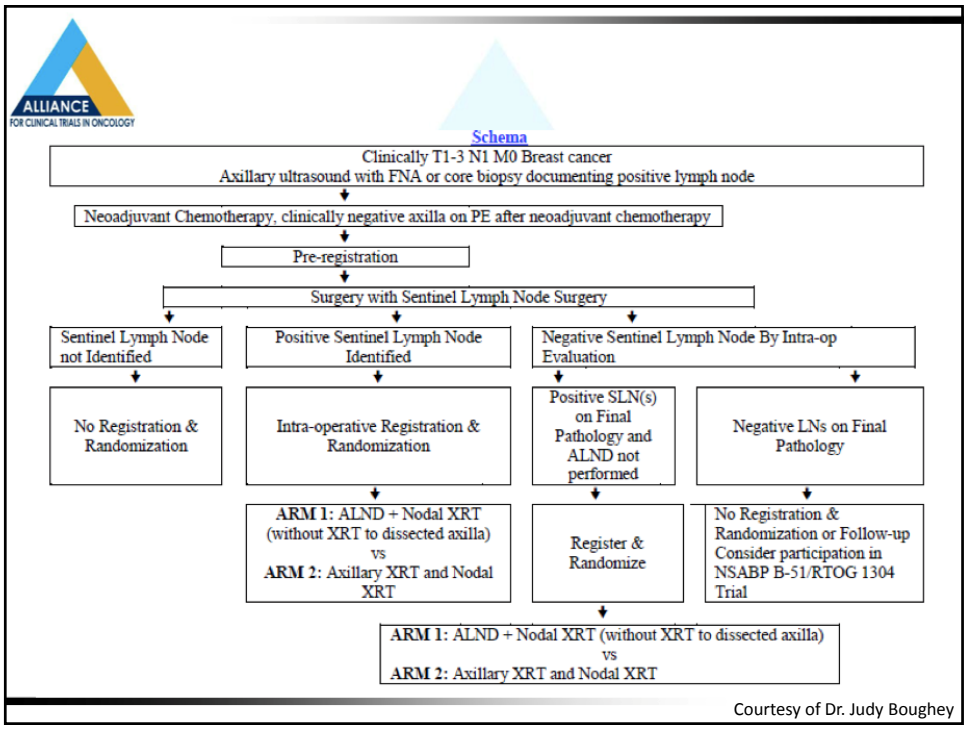
cN1 → ypN+(sn) Extent of Axillary Sx: Alliance A011202

A Randomized Phase III Trial Comparing Axillary Lymph Node Dissection to Axillary Radiation in Breast Cancer Patients (cT1-3 N1) who have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy



Courtesy of Dr. Judy Boughey

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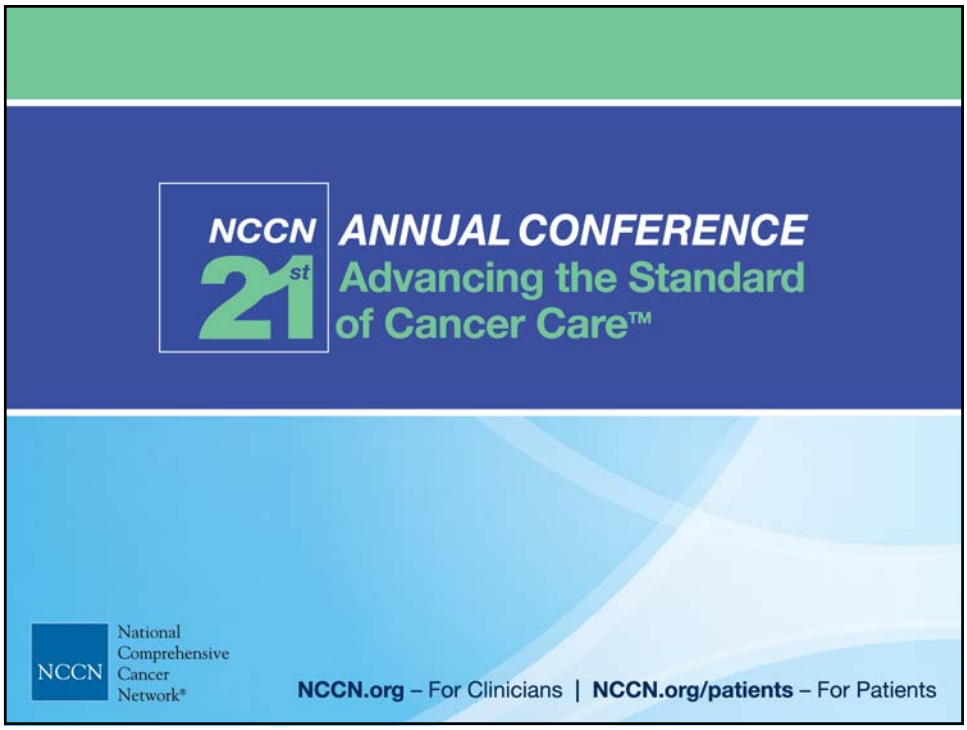

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