



MAYO CLINIC
Cancer Center

Updates in Breast Cancer

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Overview

- Operable (Stage I, II or III) Breast Cancer
 - Can some patients forego chemotherapy?
 - Is “more” better?
 - Are 2 HER2-directed drugs better than 1?
 - Are 4 chemotherapy drugs better than 3?
 - Is 10 years of endocrine therapy better than 5?
- Concerns Regarding the Model of Cancer Survivor Care

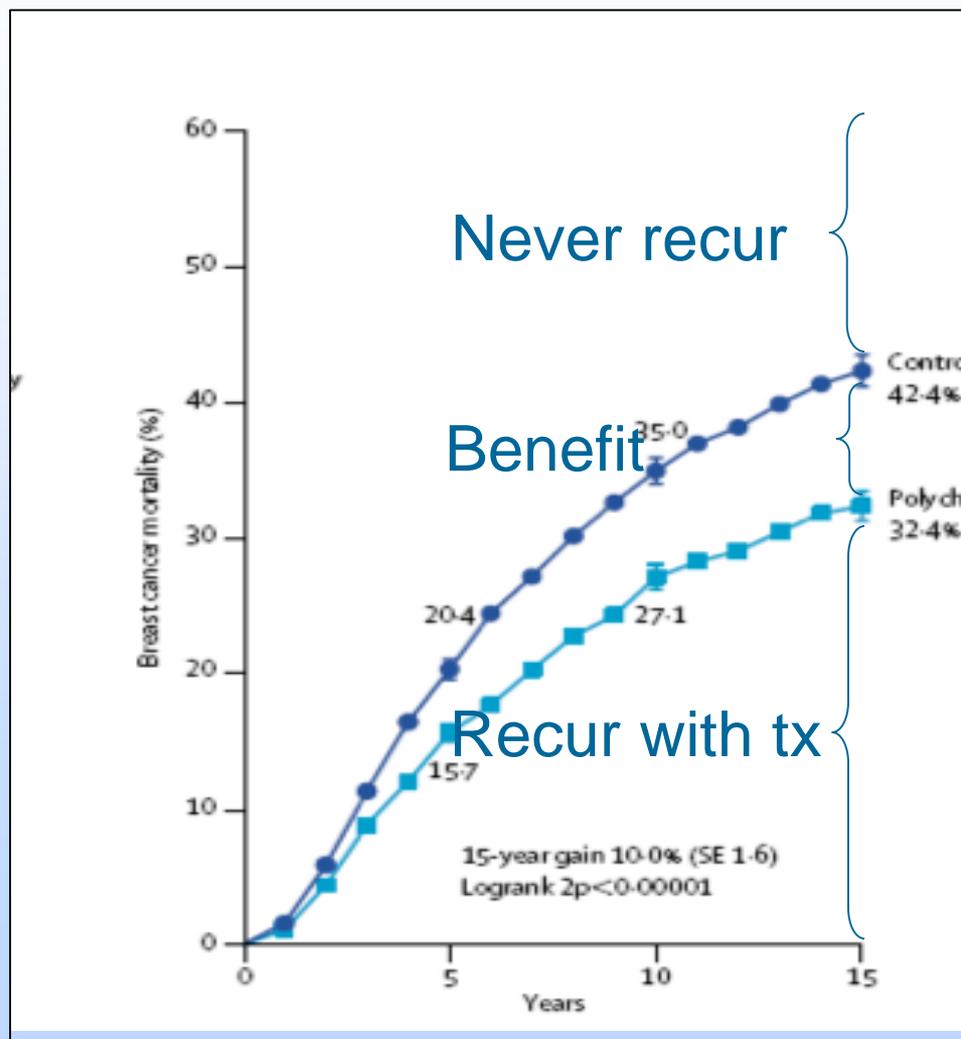


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Operable (Stage I - III) Breast Cancer

Can some patients forego chemotherapy?

Effect of Adjuvant Chemotherapy Therapy on Survival



Individualizing Patient Care for Early-Stage Breast Cancer

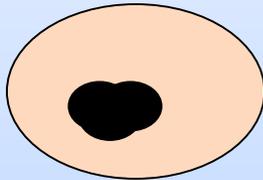
Patient A

63 years old, good health

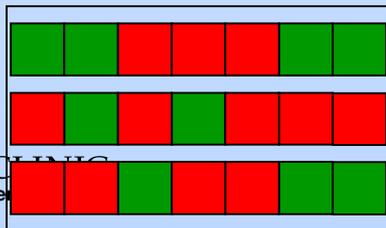
2.0 cm tumor

0 positive lymph nodes

Estrogen receptor positive



Low
Risk



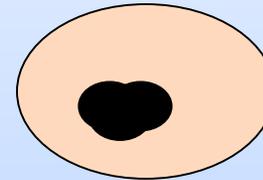
Patient B

63 years old, good health

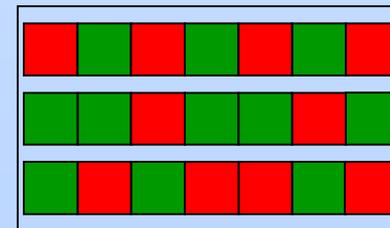
2.0 cm tumor

0 positive lymph nodes

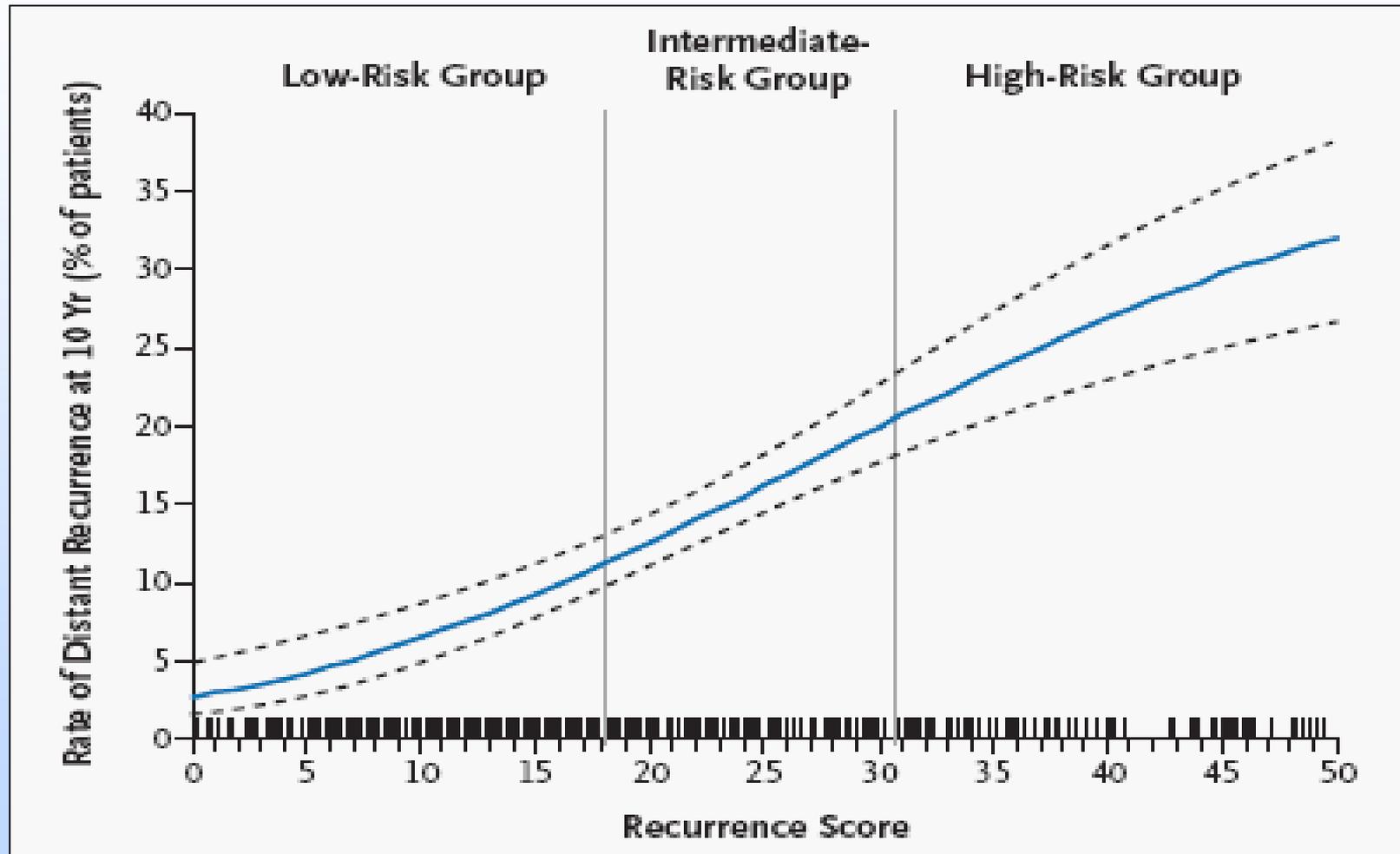
Estrogen receptor positive



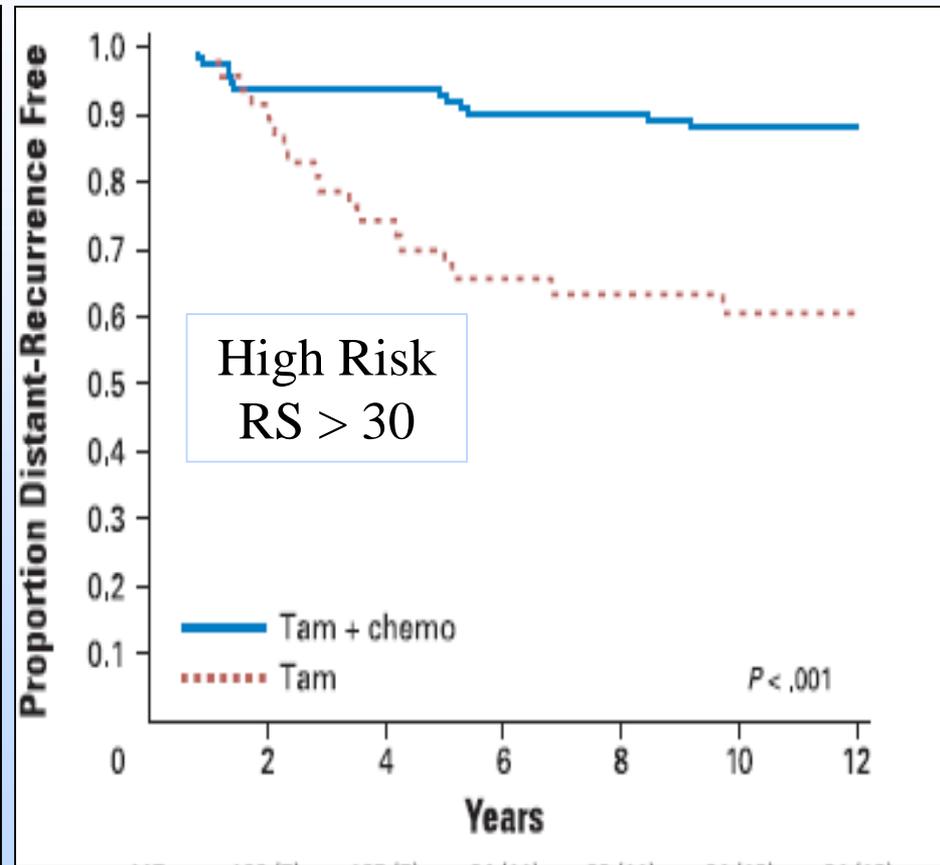
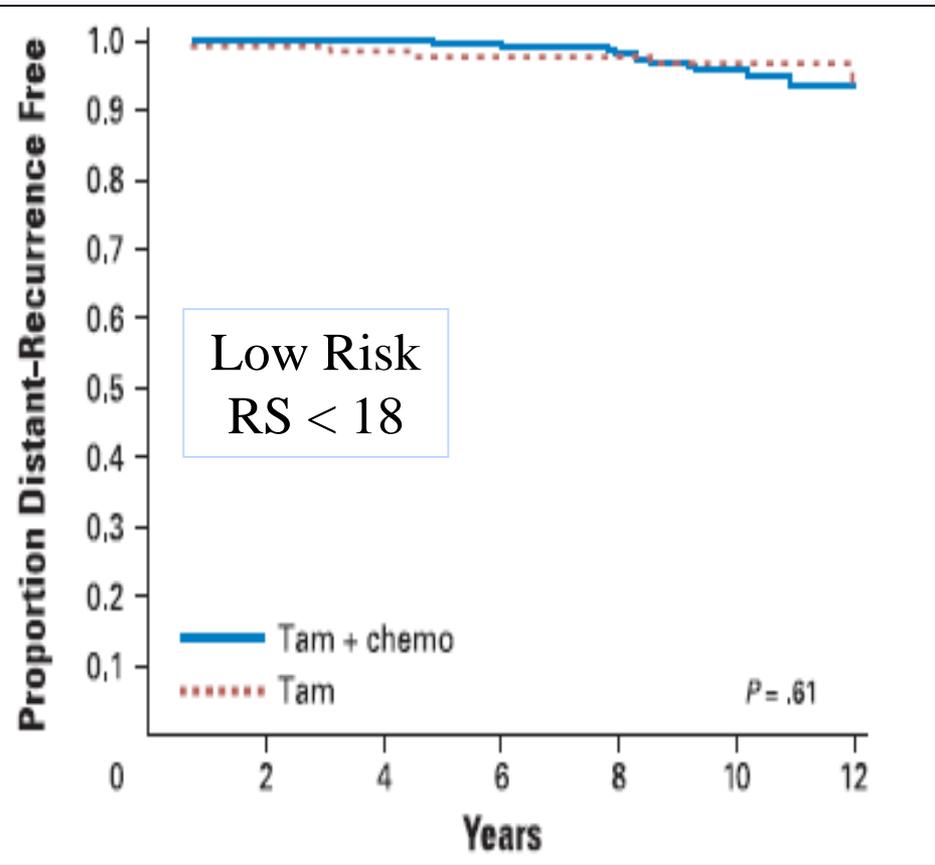
High
Risk



Oncotype Dx® Recurrence Score is Prognostic



Oncotype DX® Predicts Chemotherapy Benefit



Study Schema the TAILORx Trial

Node-Neg, ER-Pos Breast Cancer

Oncotype DX[®] Assay

RS \leq 10
Hormone
Therapy

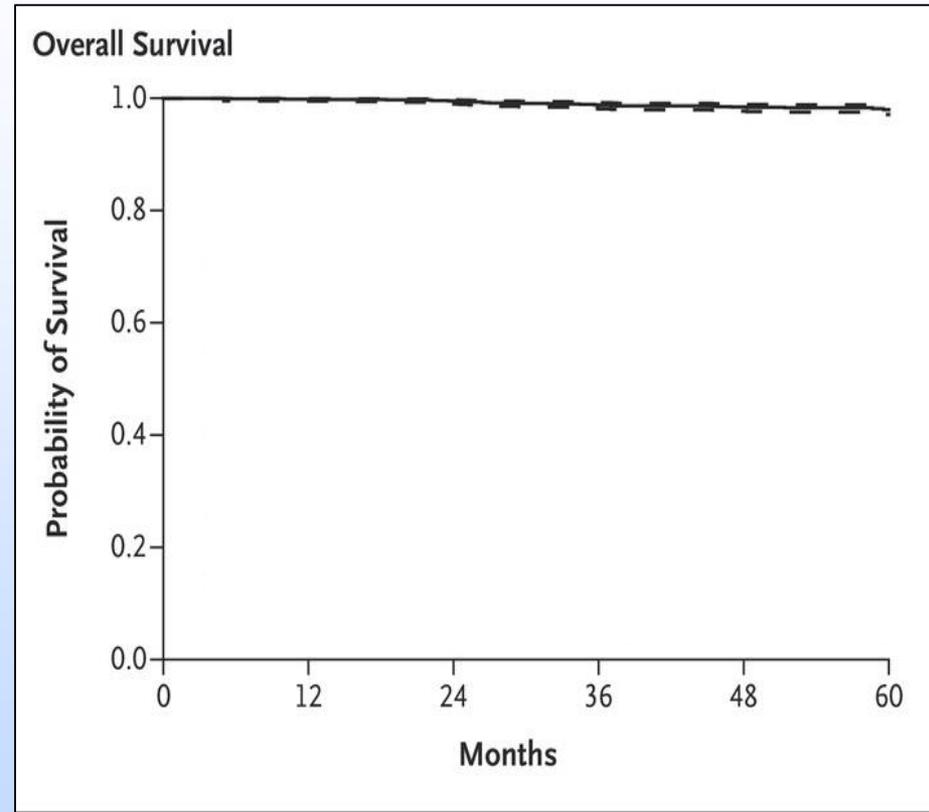
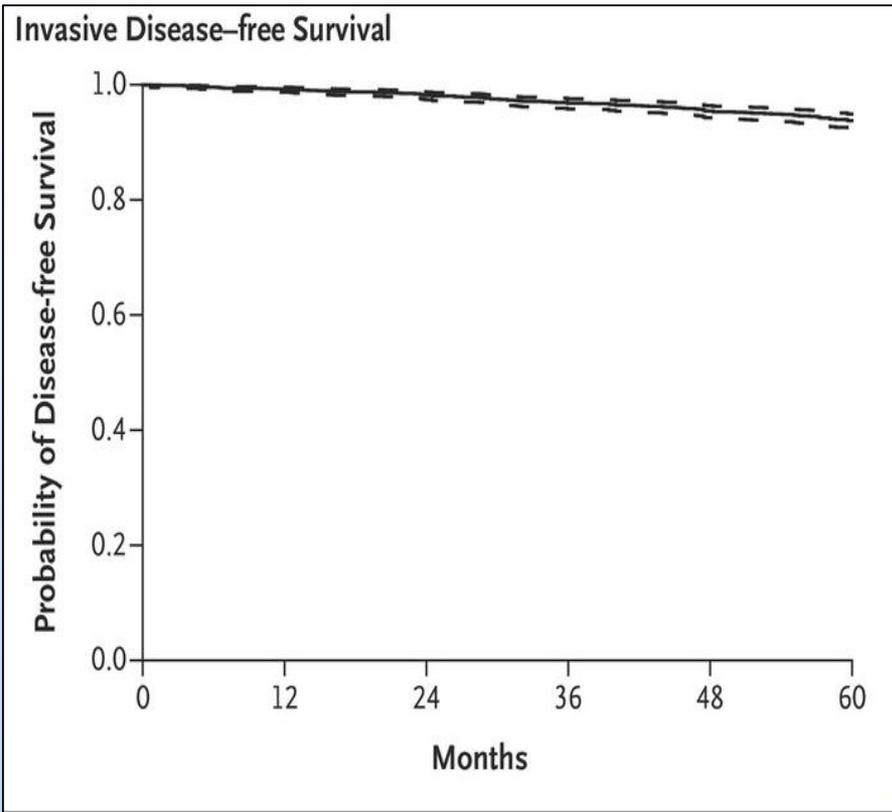
RS 11-25
Randomize
Hormone
vs
Chemotherapy +
Hormone

RS >25
Chemotherapy
+
Hormone

Primary study group

To determine whether adjuvant hormonal therapy is *not inferior* to adjuvant chemohormonal for patients in the "primary study group"

Low Risk Patients Can Forego Chemotherapy



**Prospective Validation of the 21 Gene Recurrence Score:
1626 patients with a recurrence score of 0 to 10.**

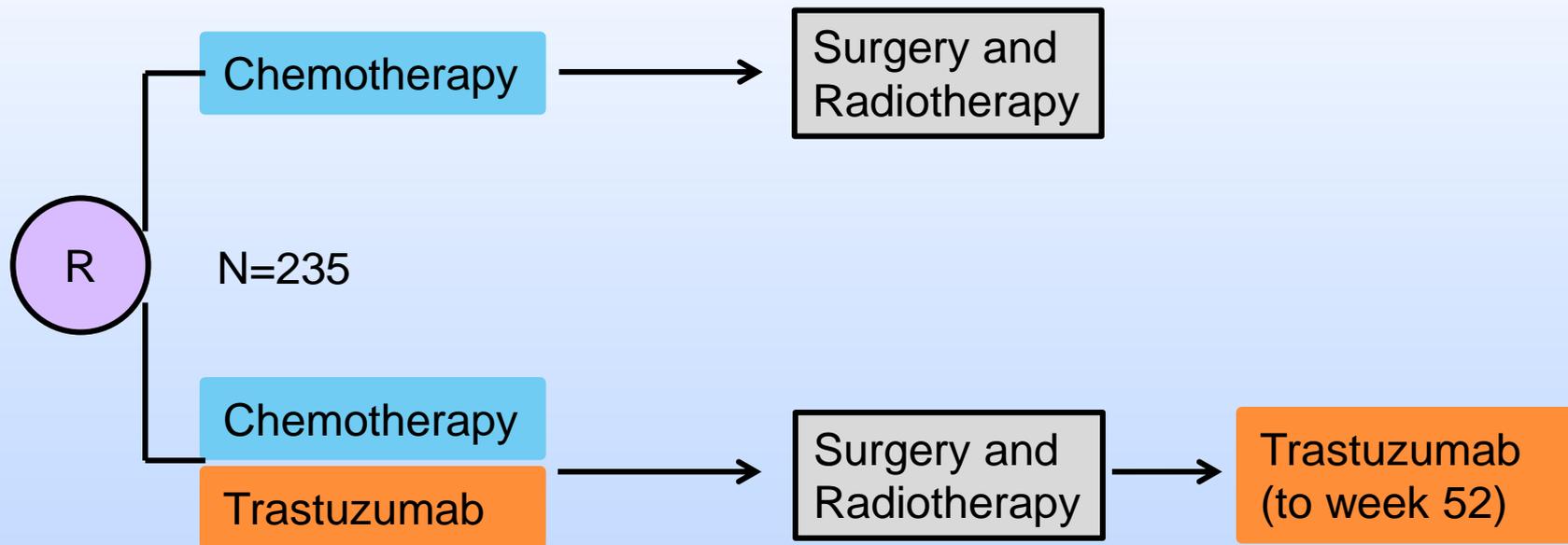


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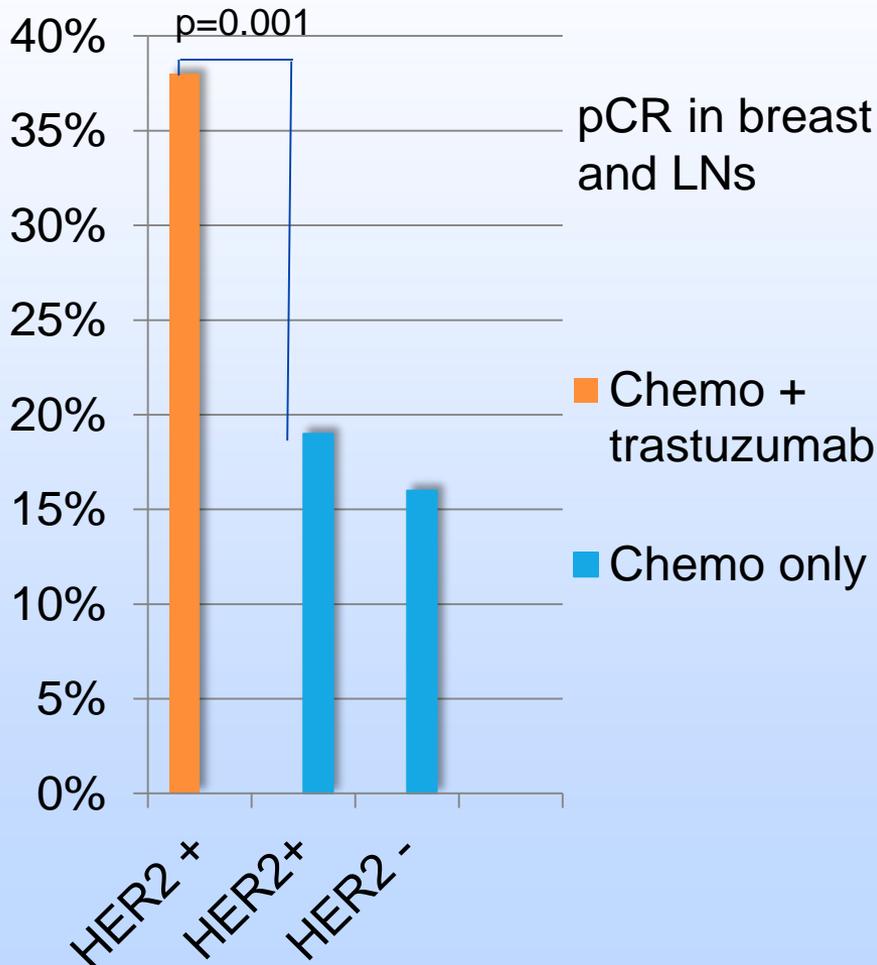
Operable (Stage I - III) Breast Cancer
Is “more” HER2-directed therapy better for
HER2+ disease?

NeOAdjuvant Herceptin (NOAH) Study

- Locally advanced breast cancer, HER2+, n=235



The Addition of Herceptin to Chemotherapy Improves pCR and Survival

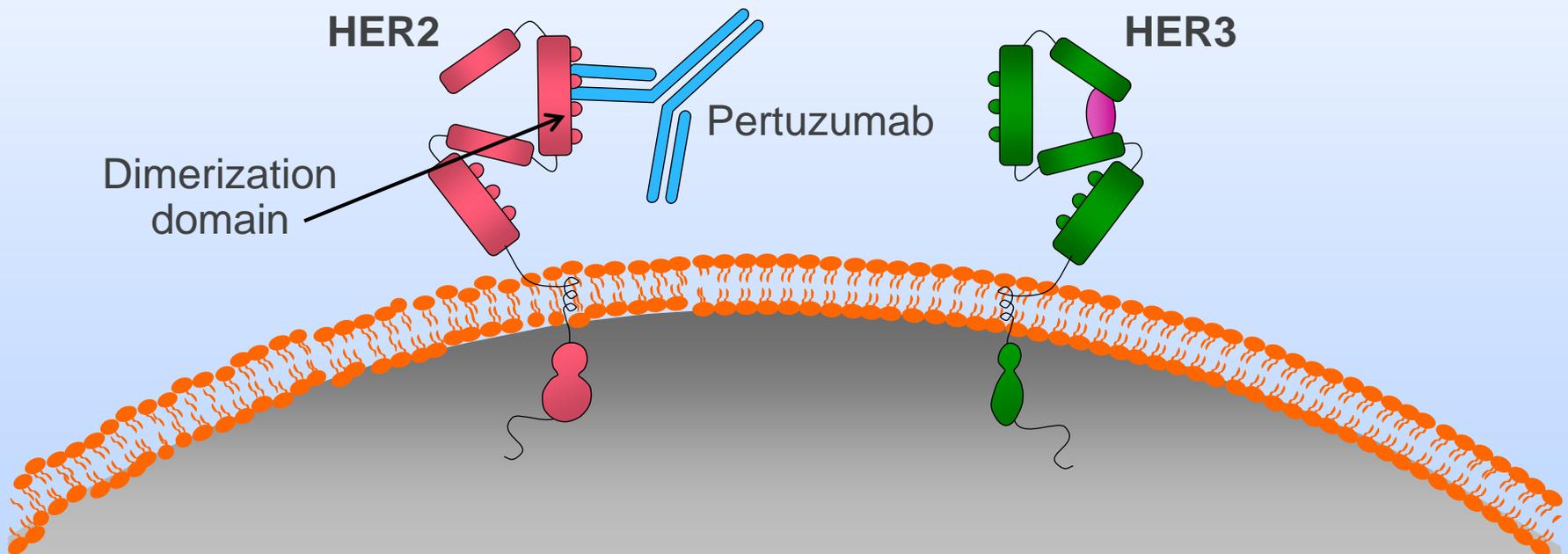


Breast cancer event free survival and overall survival were significantly improved by the addition of Herceptin to Chemotherapy

Pertuzumab Mechanism of Action

By blocking HER2 dimerization, pertuzumab inhibits key HER signaling pathways that mediate cancer cell proliferation and survival¹⁻⁴

Pertuzumab prevents the formation of HER2:HER3 receptor pairs^{1,5}



1. Agus, et al. Cancer Cell 2002;2:127-137.
2. Baselga. Cancer Cell 2002;2:93-95.
3. Citri, et al. Exp Cell Res 2003;284:54-65.
4. Franklin, et al. Cancer Cell 2004;5:317-328.
5. Hughes, et al. Mol Cancer Ther 2009;8:1885-1892.

Slide provided courtesy of Genentech, Inc.

Dual HER2-directed Neoadjuvant Therapy

- Herceptin (H) alone or combined with Perjeta (P)

	Chemotherapy + HER2-directed Therapy		pCR Rate Breast and LNs
NeoSphere ¹ N = 417			
	T _{doc}	H	22%
	T _{doc}	P	18%
	T _{doc}	H+P	39%
	None	H+P	11%

Dual HER2-directed Therapy

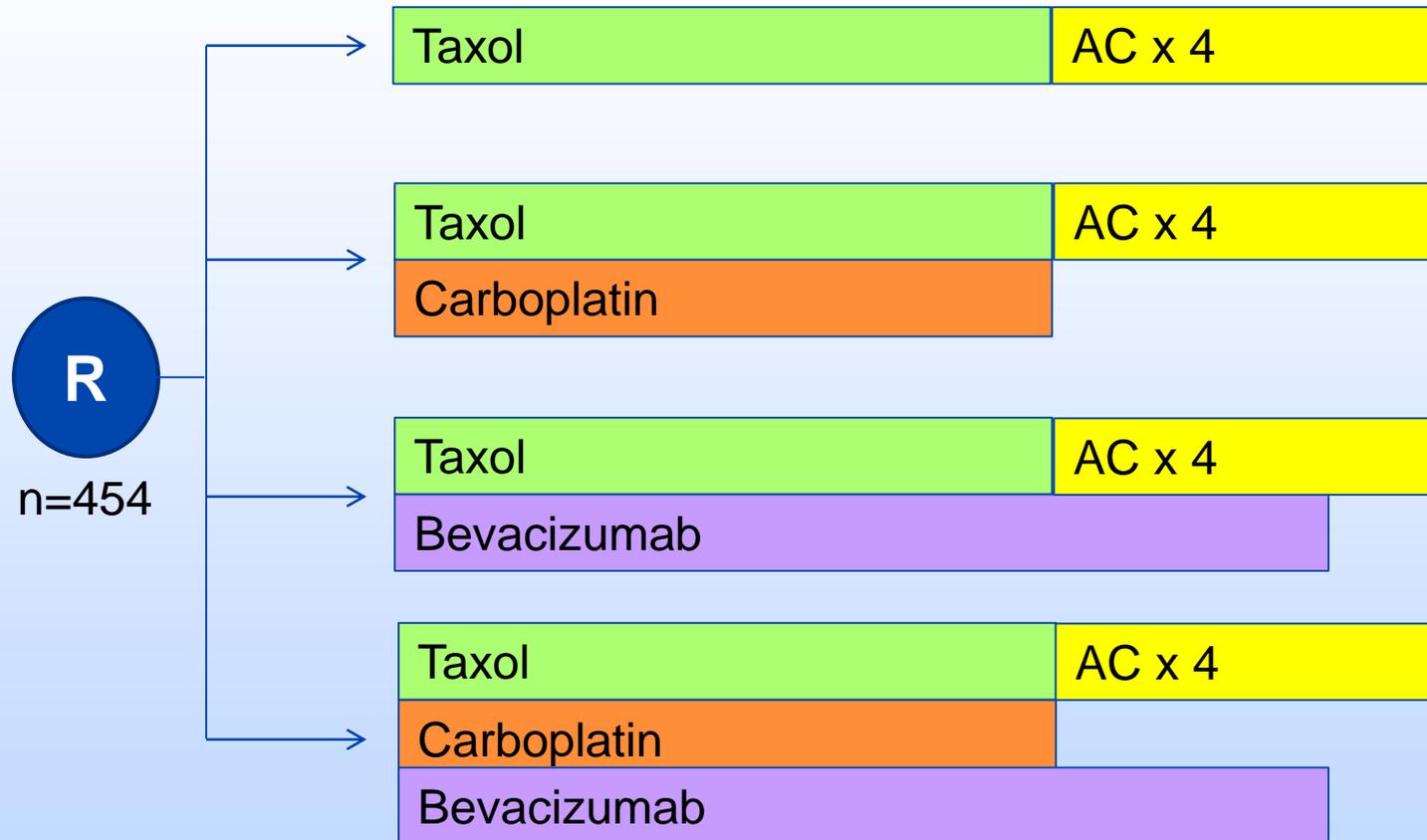
- We await the results of the APHINITY trial to evaluate the benefit of *adjuvant* pertuzumab in combination with trastuzumab
- In the interim...
 - Pertuzumab granted accelerated FDA-approval on 30 Sept 2013



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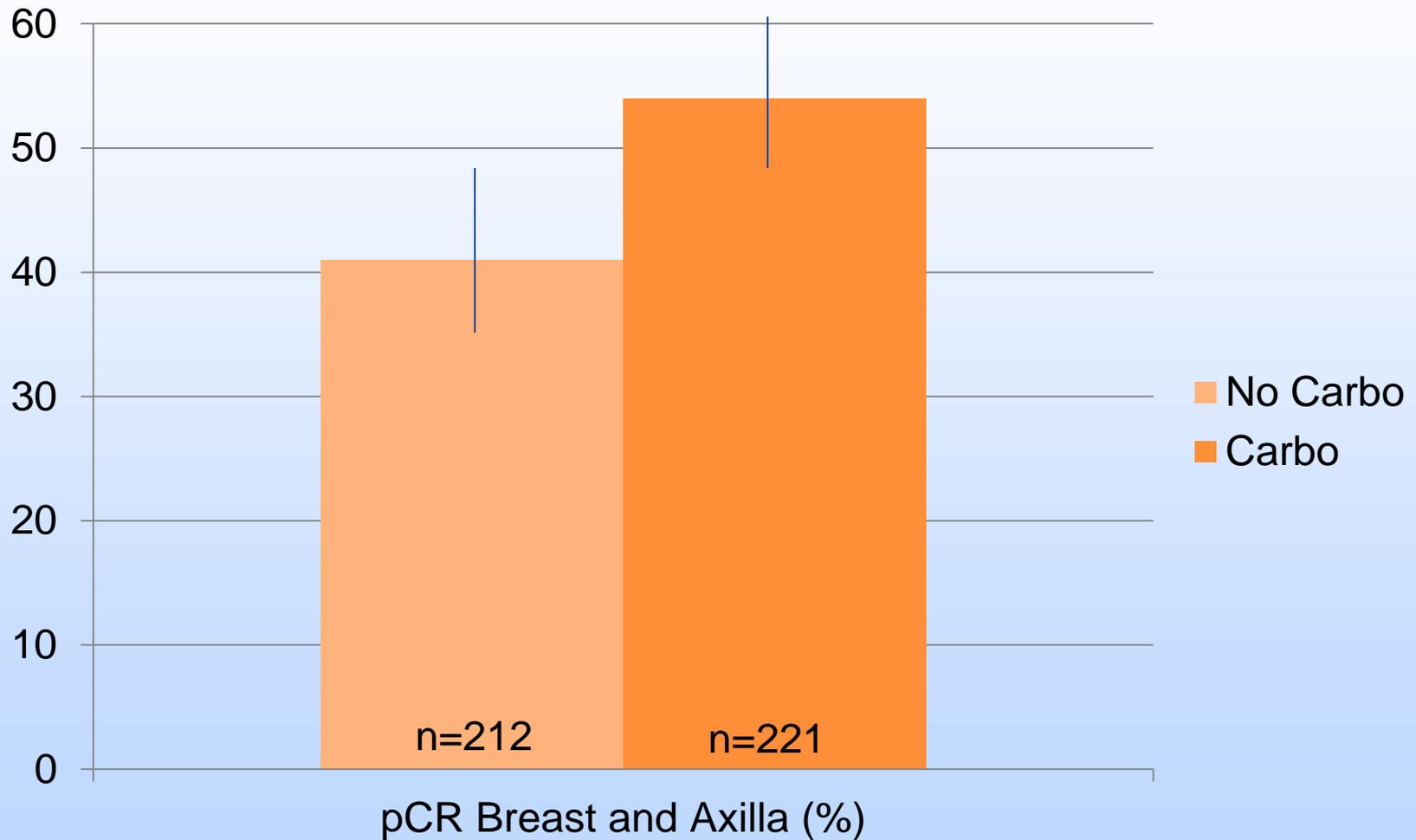
Operable (Stage I - III) Breast Cancer Is “more” chemotherapy better for ER/HER2- disease?

Does the Addition Carboplatin to Standard AC-Taxol Chemotherapy Improve Outcomes?



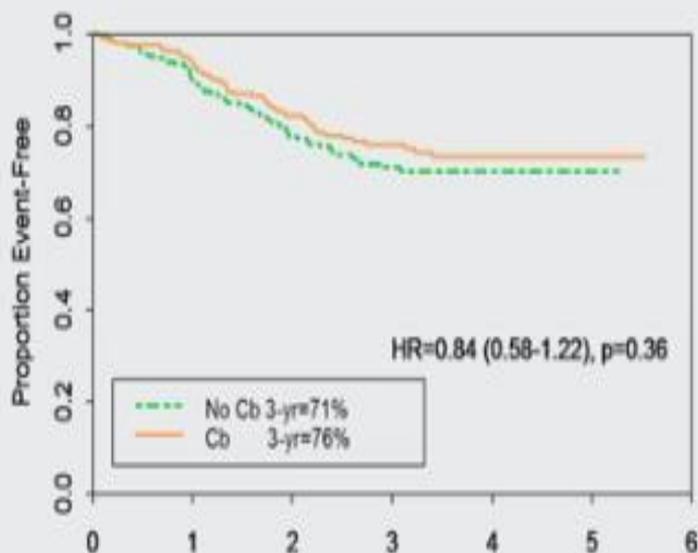
Key Eligibility: Clinical stage II or III breast cancer, ER and PR \leq 10%

Carboplatin Increases the pCR

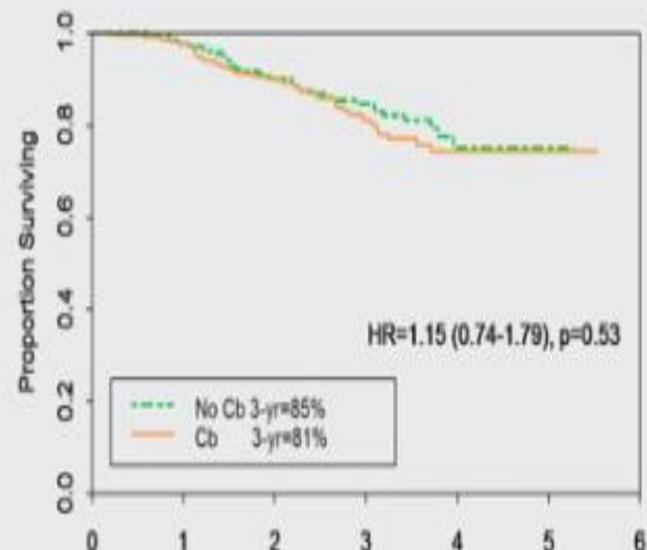


Impact of Carboplatin on EFS and OS is Marginal

CALGB 40603 – EFS for carboplatin vs. not



CALGB 40603 – OS for carboplatin vs. not



Carboplatin for TNBC: *Unanswered Questions*

- A similar German study did show that the addition of Carboplatin increased pCR, as well as EFS and OS
- Should all patients with TNBC get Carbo as part of their treatment plan?
- How can we avoid overtreating the ~40% of patients destined to have a pCR without Carbo?

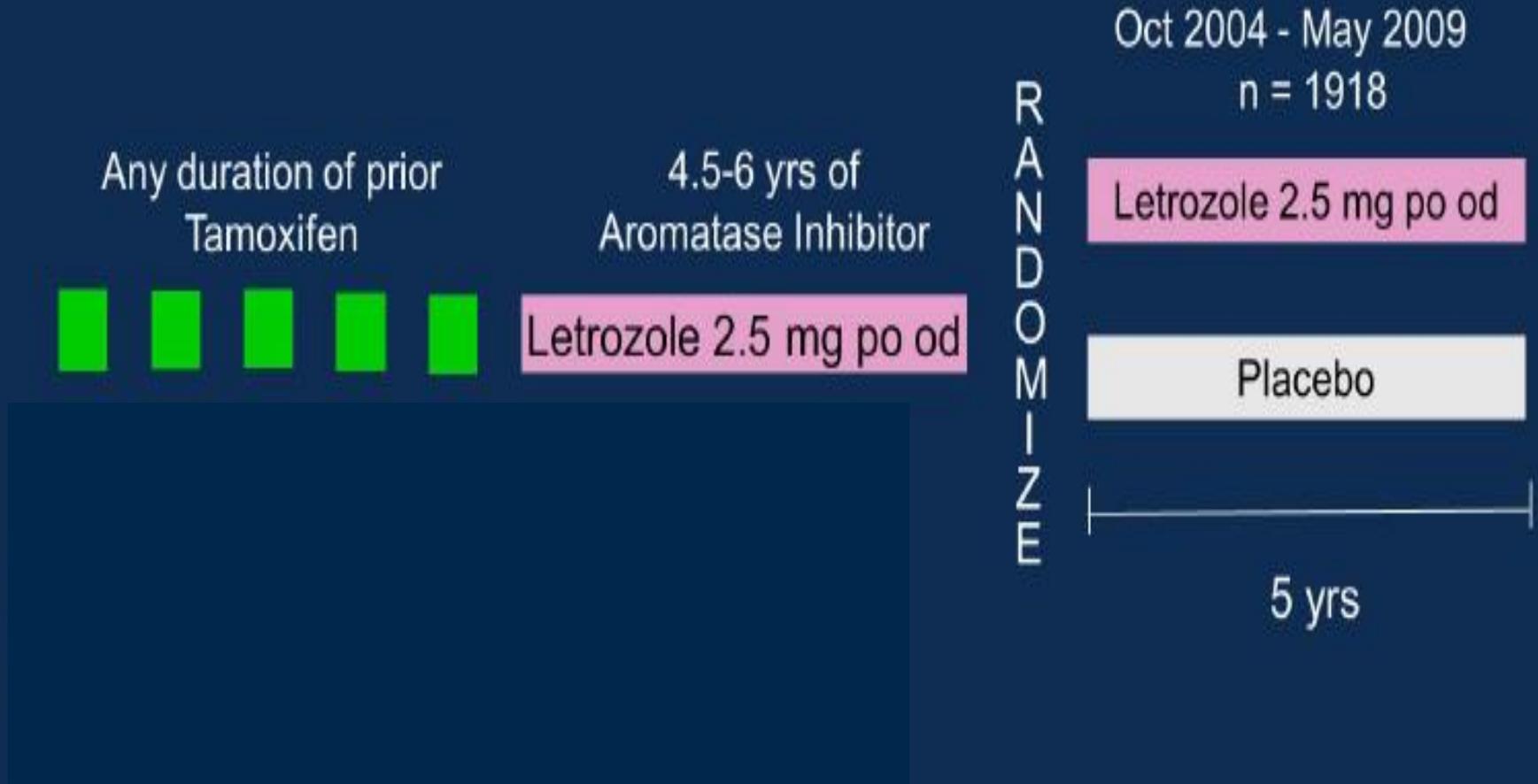


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Operable (Stage I - III) Breast Cancer
Is “more” endocrine therapy better for
ER+/HER2- postmenopausal disease?

MA.17R Trial Schema and Design

AI x 5 yrs - Following Prior 5 years of AI - preceded or not by Tamoxifen

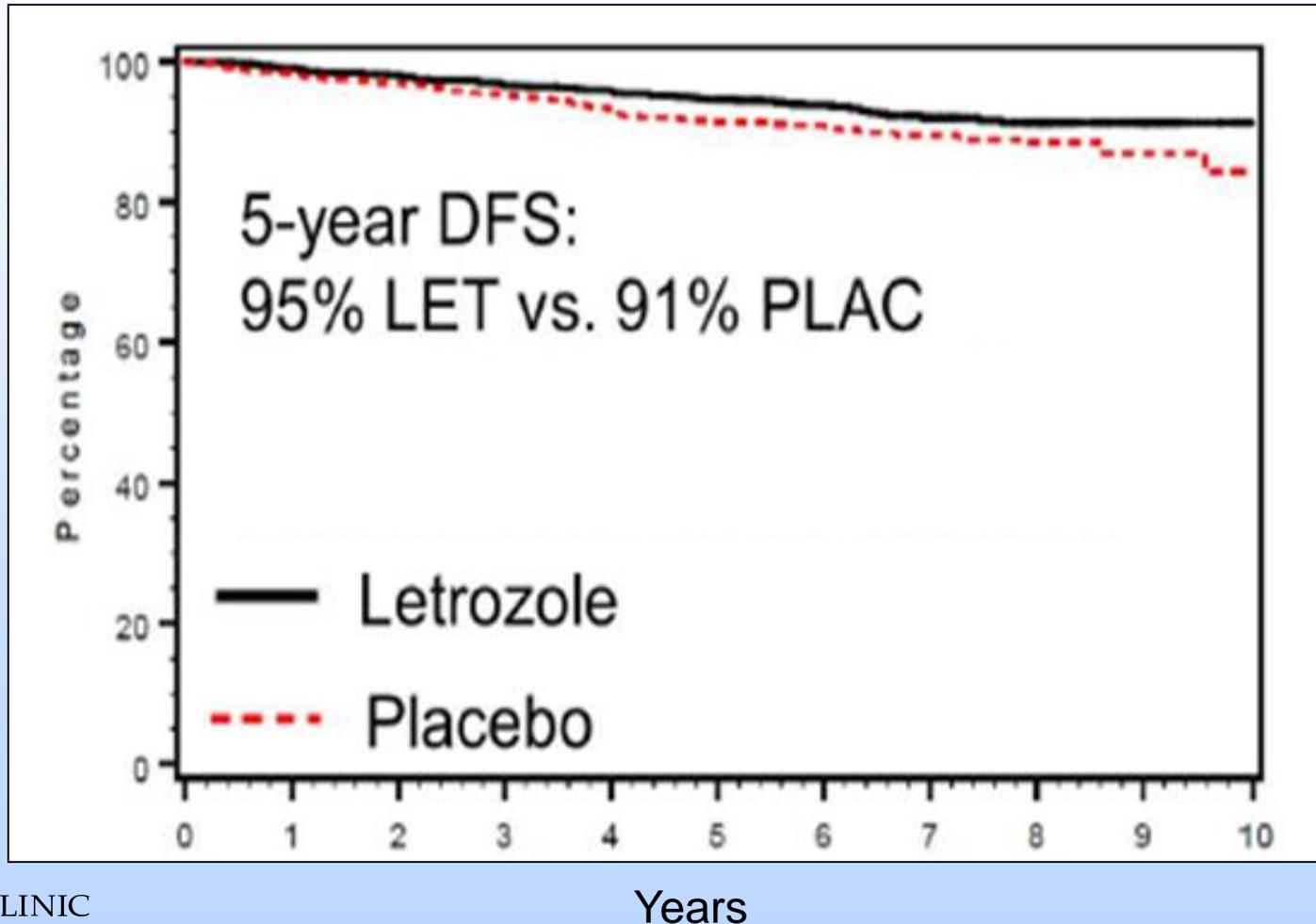


MA.17R Primary Question and Results

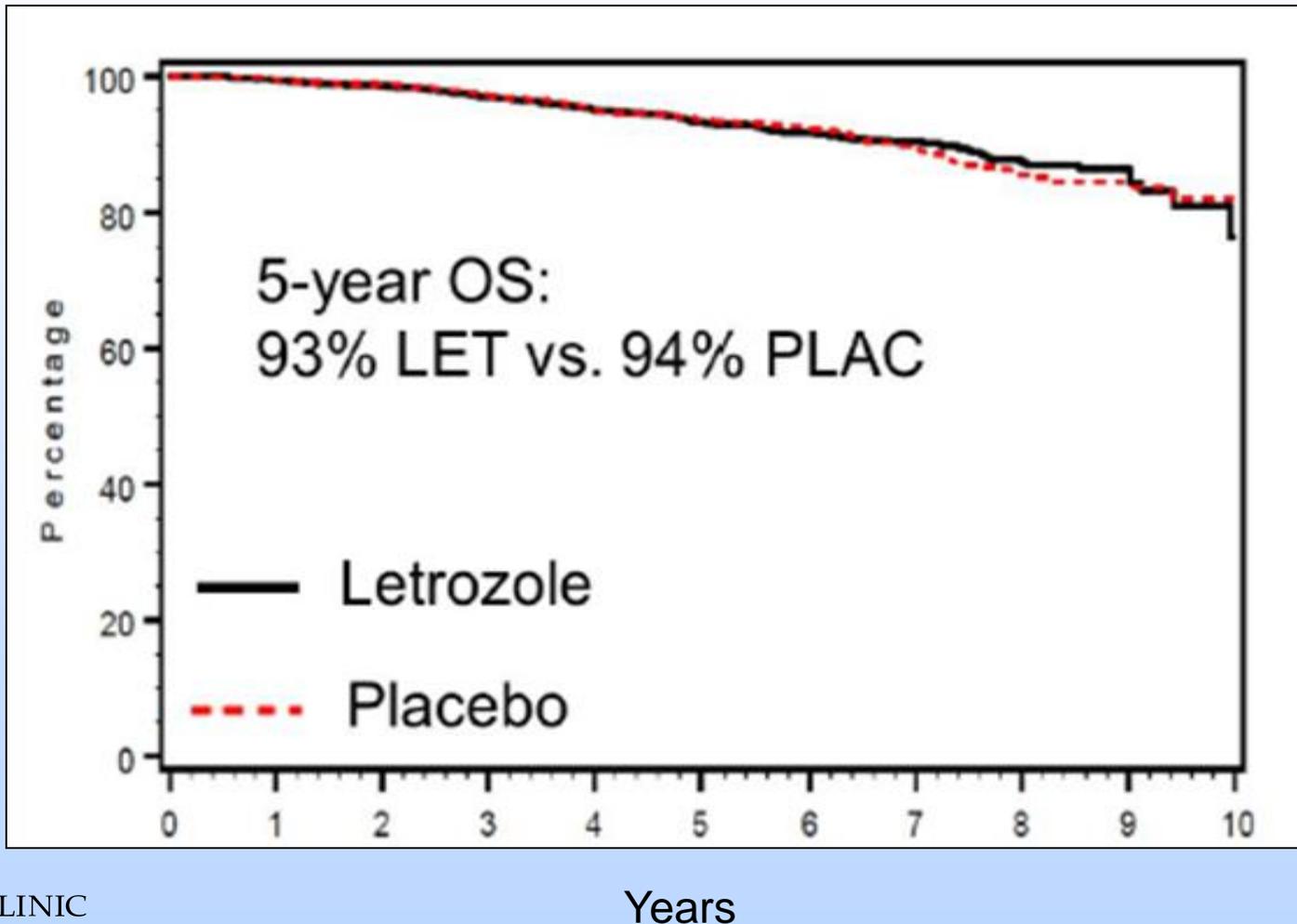
Does extending aromatase inhibitor therapy from 5 to 10 years improve patient outcomes?

As compared to the standard of 5 years of letrozole (Femara), **10 years reduces the risk of breast cancer relapse or a new breast cancer in the opposite breast by 34%**

10 Years is More Effective than 5 Years of Endocrine Therapy for DFS



Patient Survival at 5 Years Follow-up is the Same



Impact on Breast Cancer Events

	Letrozole N = 959	Placebo N = 959	Absolute Benefit
Any relapse or new breast cancer	67 (7.0%)	98 (10.2%)	3.2%
Local relapse in breast or lymph nodes	19	30	1.1%
New breast cancer (opposite breast)	13	31	1.8%
Distant (metastatic) relapse	42	53	1.1%

Toxicities

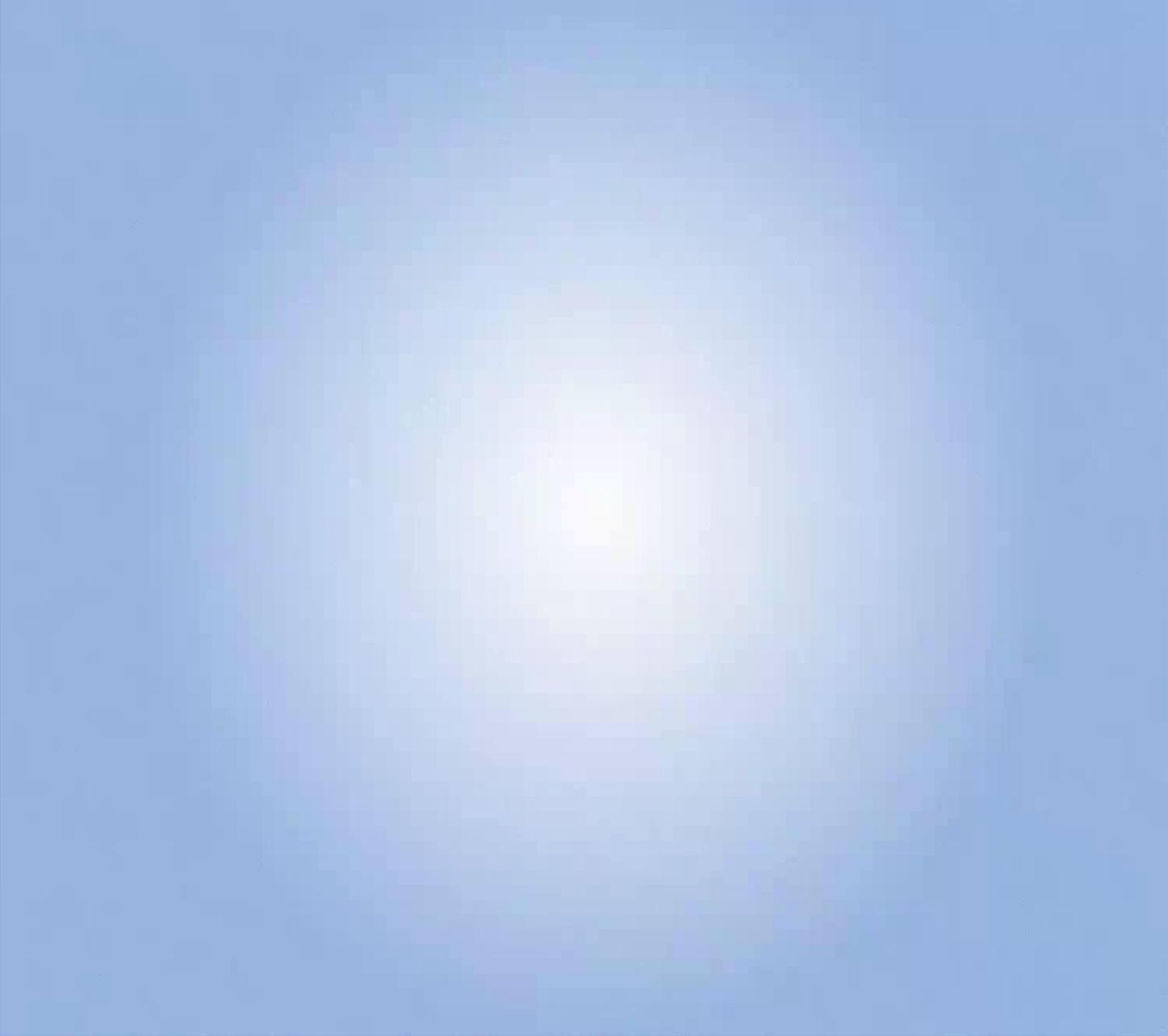
- Patients taking the letrozole (compared to placebo) experienced
 - More musculoskeletal pain
 - 18% v. 14% in placebo
 - More bone fractures
 - 14% v. 9% in placebo
 - More new diagnoses of osteoporosis
 - 11% v. 6% in placebo
 - No compromise to quality of life measures
 - Menopausal symptoms
 - Physical function
 - Mental function



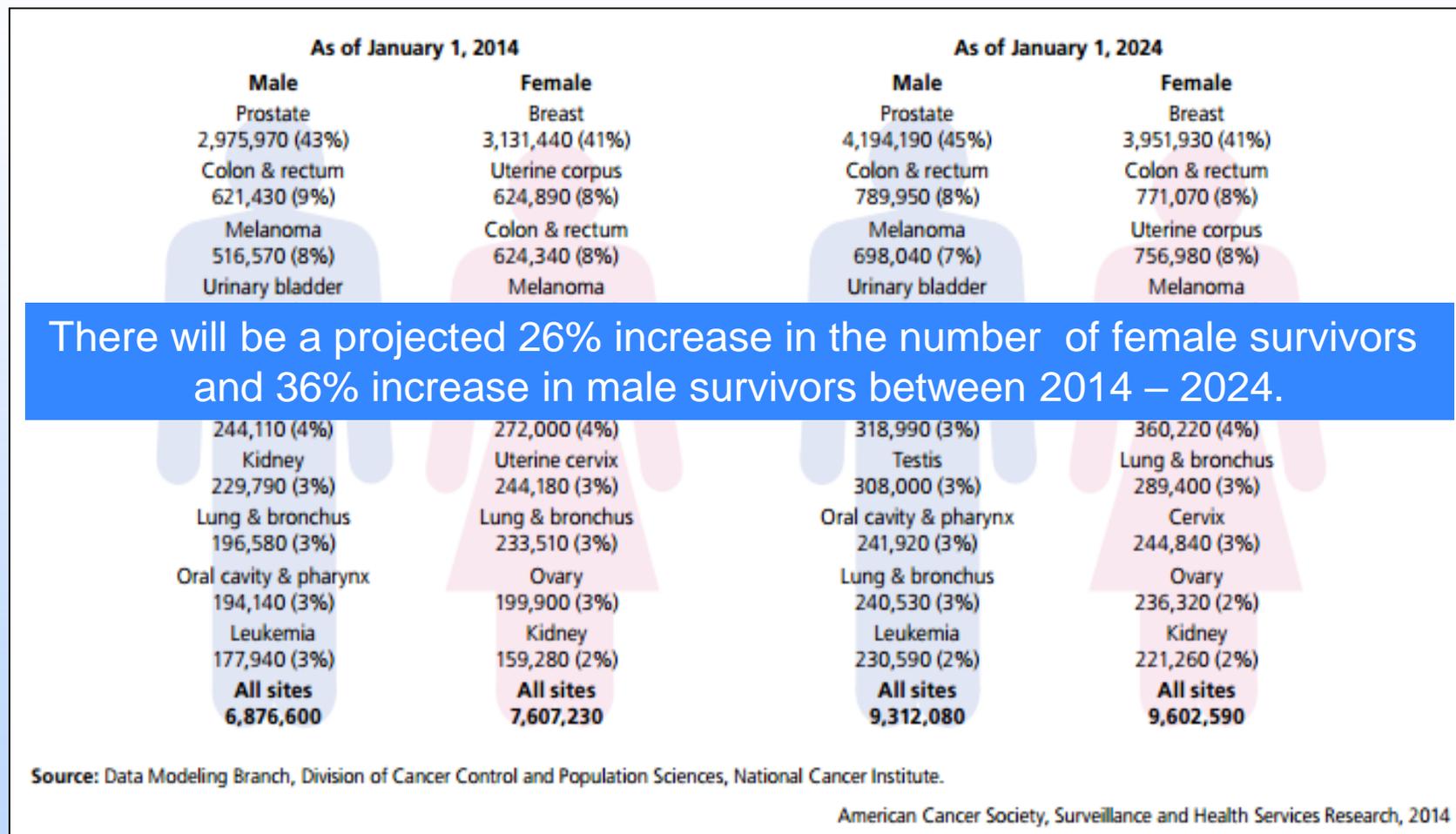
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Concerns Regarding the Model of Cancer Survivor Care

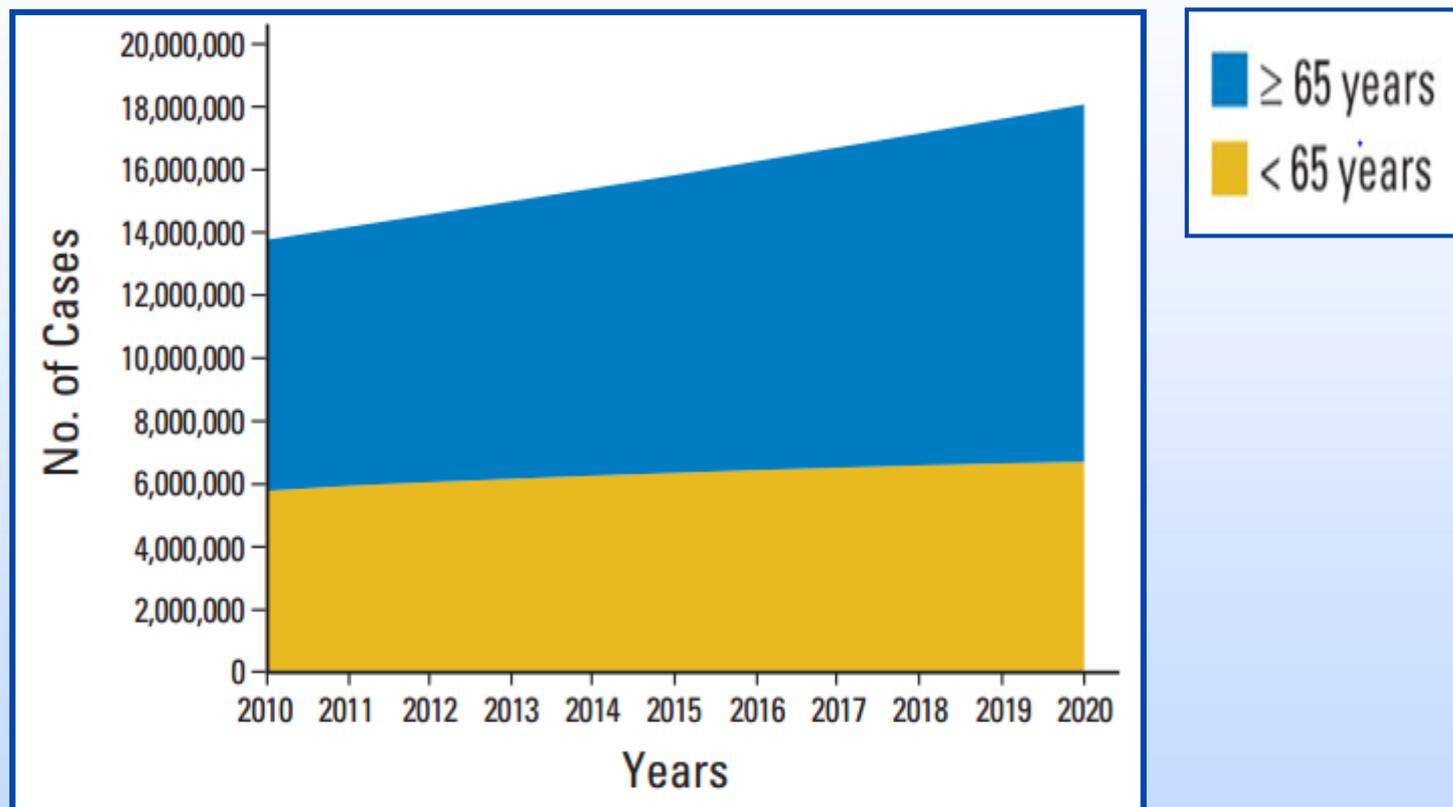
Why should you care about the model by which healthcare is delivered to cancer survivors?



Estimated Numbers of U.S. Cancer Survivors by Site



Cancer Survivor Prevalence by Age



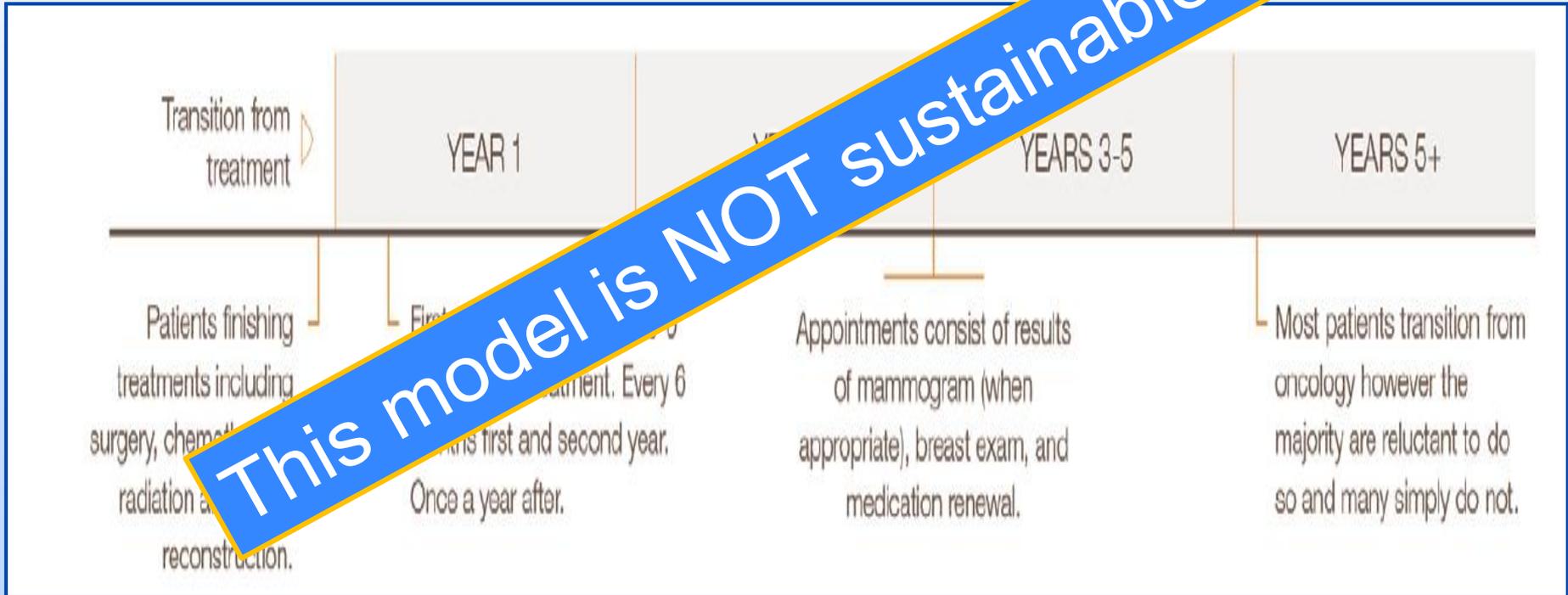
There is a booming population of cancer survivors ≥ 65 years of age

Our Challenges

- Aging population
 - Breast cancer incidence projected to increase by ~45% by 2030
- Survival rates improving
 - Across all stages of disease, ~90% of women alive at 5 years
- Projected shortage of oncologists by 2025

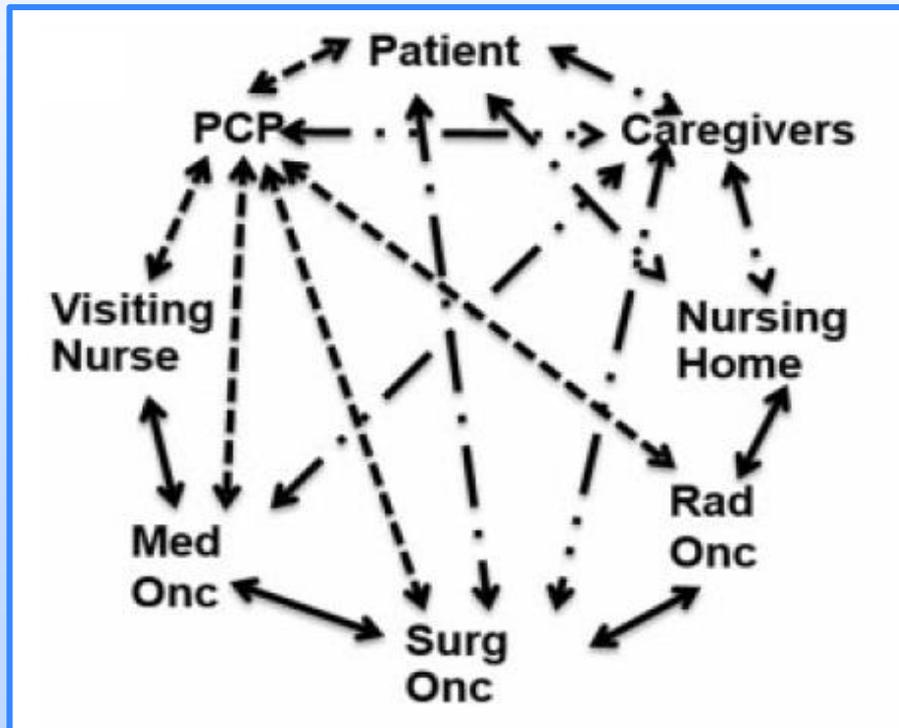
The Current Breast Cancer Survivor Care Model

- Patient completes definitive locoregional therapy +/- chemotherapy/HER2-directed therapy and endocrine therapy (if appropriate)



Issues with the Current Survivor Care Model

- Care is **fragmented** and **duplicated**, leading to a poor patient experience and unnecessary cost



Other Care Teams

- Plastics
- Lymphedema/PT
- Medical Genetics
- Fertility
- Women's Health
- Integrative Medicine

Conclusions

- Up to 1/3 of patients with ER+/HER2-, node-negative breast cancer do not derive benefit from chemotherapy
 - They can be identified by Oncotype DX® evaluation
- For HER2+ breast cancer, dual HER2-directed therapy (Herceptin and Perjeta) combined with chemotherapy can nearly double the pCR rate compared to Herceptin-chemo alone
 - Impact on relapse risk and survival rate are yet to be defined.
- For ER-/HER2- breast cancer, the addition of Carboplatin to standard AC-Taxol increases pCR rates; however, results are mixed as to whether it reduces risk of relapse and improves survival

Conclusions

- For postmenopausal ER+ breast cancer, as compared to 5 years of an aromatase inhibitor, 10 years reduces the risk of a breast cancer event by 34% though absolute gains may be small
 - Nearly as many new breast cancers in the opposite breast were prevented as were relapses in the same breast or elsewhere in the body
- The current model of cancer survivor care is unsustainable and we need to start the conversation and work together for creative solutions to transform the model