

**Adaptando tratamento do Câncer de
Mama através de assinaturas
gênicas:
Oncotype Dx®**

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DECLARAÇÃO

SOBRE CONFLITOS DE INTERESSE

De Acordo Com a Resolução RDC 96/2008 da Agência de Vigilância Sanitária declaro que:



Desempenhei o papel de **SPEAKER** para as seguintes empresas: Roche, Fleury, MSD, Novartis



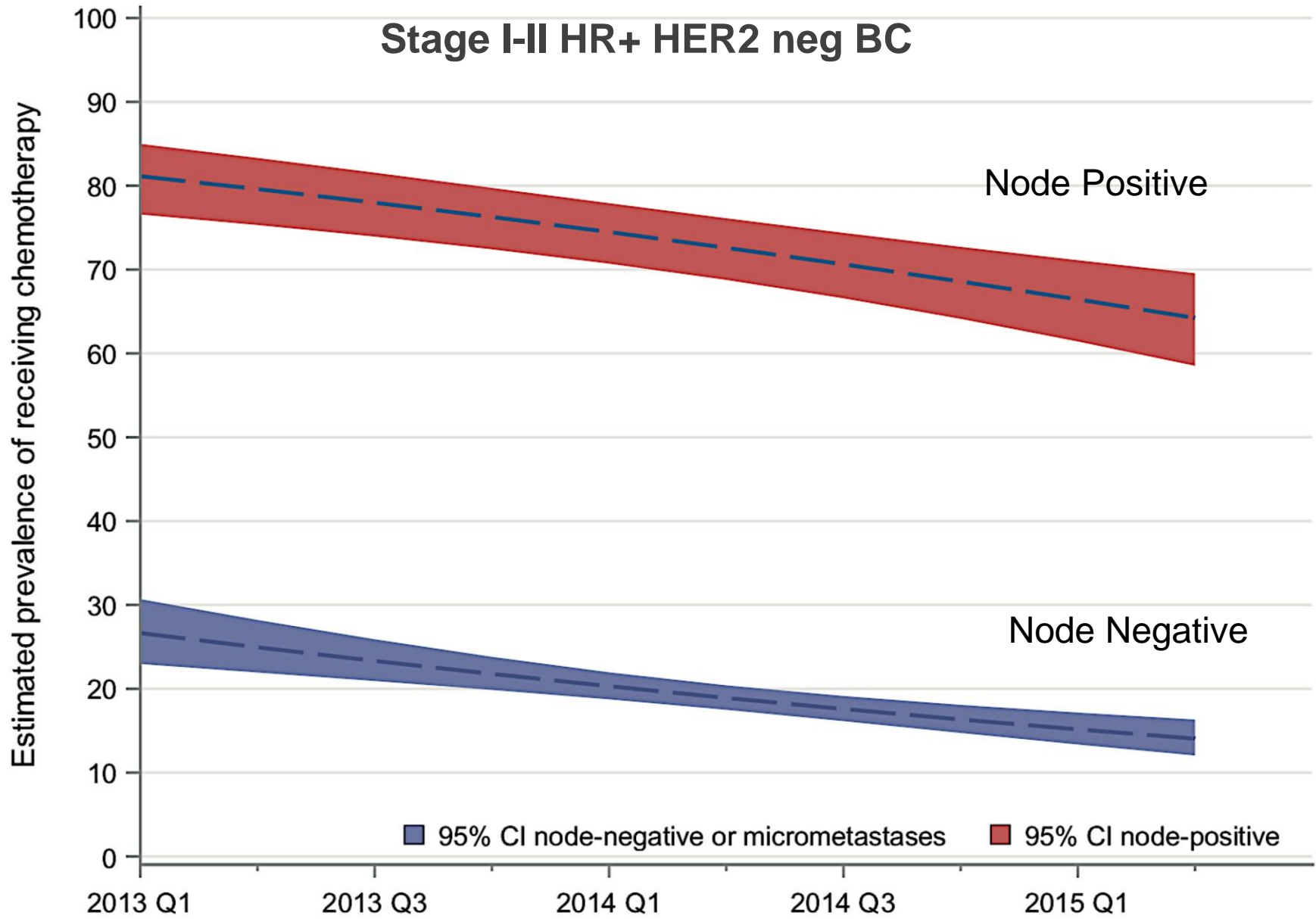
Trabalho como **ONCOLOGISTA** no: Hospital Sírio Libanês



ADVISORY BOARD: Roche, Eisai

Os meus pré-requisitos para participar destas atividades são a autonomia do pensamento científico, a independência de opiniões e a liberdade de expressão, aspectos que esta

Over-treatment is being avoided: Adjuvant Chemotherapy use is declining in early stage BC



THE WALL STREET JOURNAL.



HEALTH

Chemotherapy, a Trusty Weapon Against Cancer, Falls Out of Favor

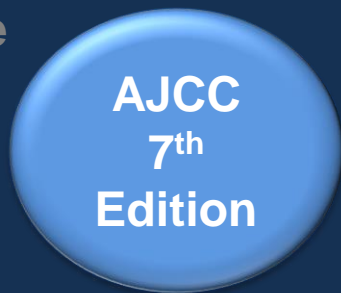
The Wall St Journal, By Lucette Lagnado. January 29, 2018

Chairs: Gabriel N. Hortobagyi and **AJCC 8th Edition**
Armando Giuliano

Started on January 1st, 2018

Tumor
Size

Metastasis
Status



AJCC
7th
Edition

Nodal
Status

Tumor
Size

Metastasis
Status



AJCC
8th
Edition

Nodal
Status

ER PR
HER2
Status

Grade

Molecular
Signature
Oncotype Dx®

When T is...	And N is...	And M is...	And G is...	And HER2 is	And ER is...	And PR is...	Rx Score	Prognosis Stage is...
T1/2	N0	M0	1-3	neg	pos	pos	<11	IA

The Oncotype DX® -> Genomic approach to predict recurrence risk and response to adjuvant therapy

16 Cancer and 5 Reference Genes From 3 Studies

PROLIFERATION

Ki-67
STK15
Survivin
Cyclin B1
MYBL2

ESTROGEN

ER
PR
Bcl2
SCUBE2

$$RS = + 0.47 \times \text{HER2 Group Score} \\ - 0.34 \times \text{ER Group Score} \\ + 1.04 \times \text{Proliferation Group Score} \\ + 0.10 \times \text{Invasion Group Score} \\ + 0.05 \times \text{CD68} \\ - 0.08 \times \text{GSTM1} \\ - 0.07 \times \text{BAG1}$$

GSTM1

BAG1

INVASION

Stromelysin 3
Cathepsin L2

CD68

Reference
Beta-actin
GAPDH
RPLPO
GUS
TFRC

HER2

GRB7
HER2

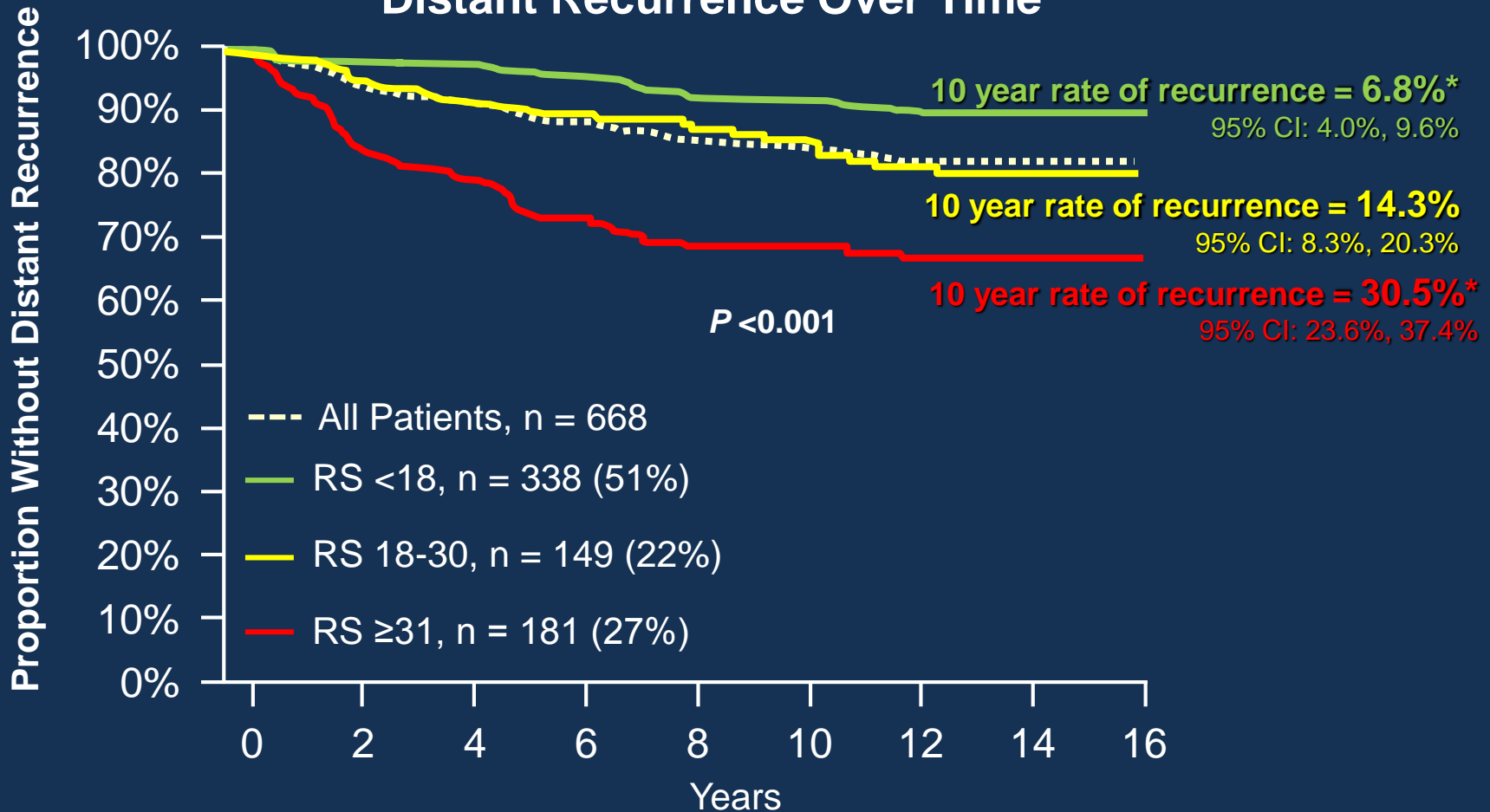
Category	RS (0 -100)
Low risk	RS <18
Int risk	RS 18 - 30
High risk	RS ≥ 31

NSABP B14

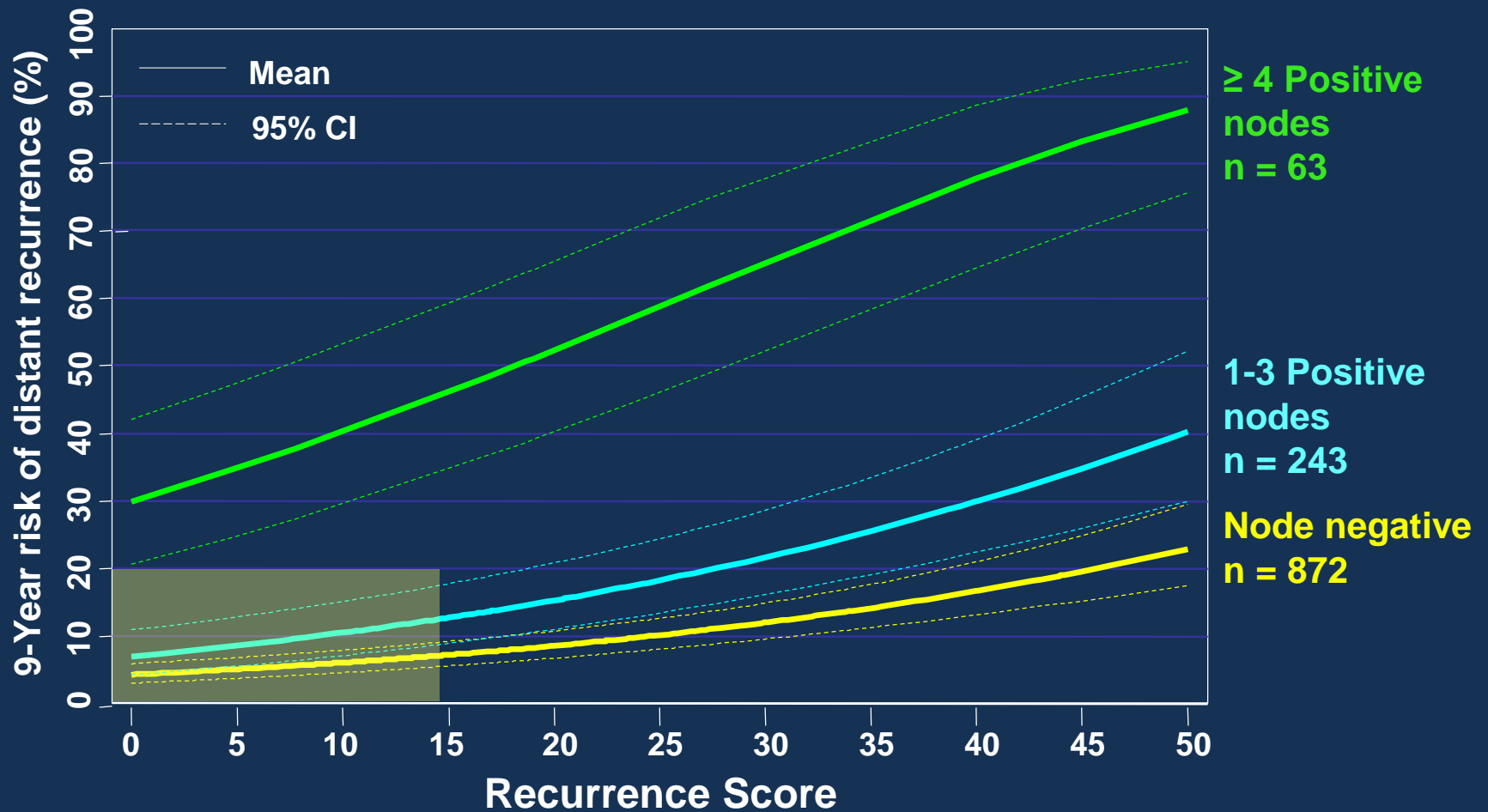
Node Negative BC patients Ranzomized to tamoxi vs placebo

Recurrence Score Validation

Distant Recurrence Over Time



Recurrence Score evaluated at TransATAC Validated in the Node Positive Cohort of Patients

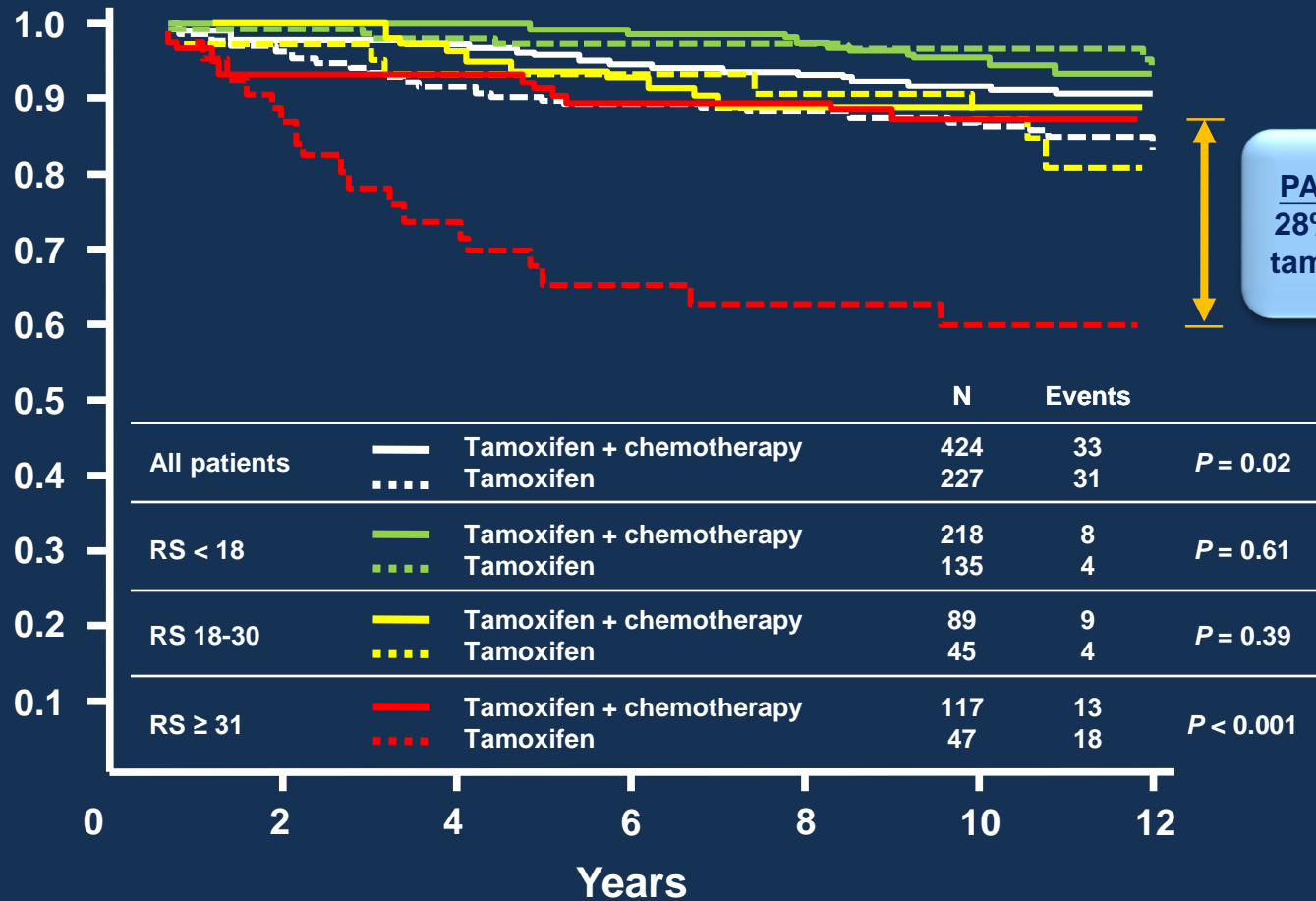


Low Recurrence Score suggests a low risk of recurrence for patients with 1-3 positive nodes

Predicting Benefit from Adjuvant Chemotherapy- NSABP B20

Node Negative Cohort of Patients Randomized to Tamoxifen +or - CMF or MF

Proportion without distant recurrence



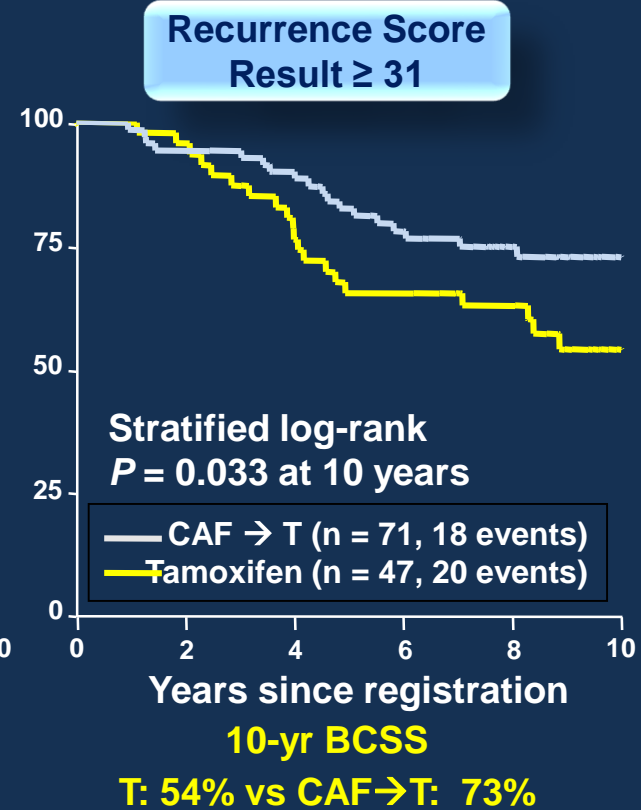
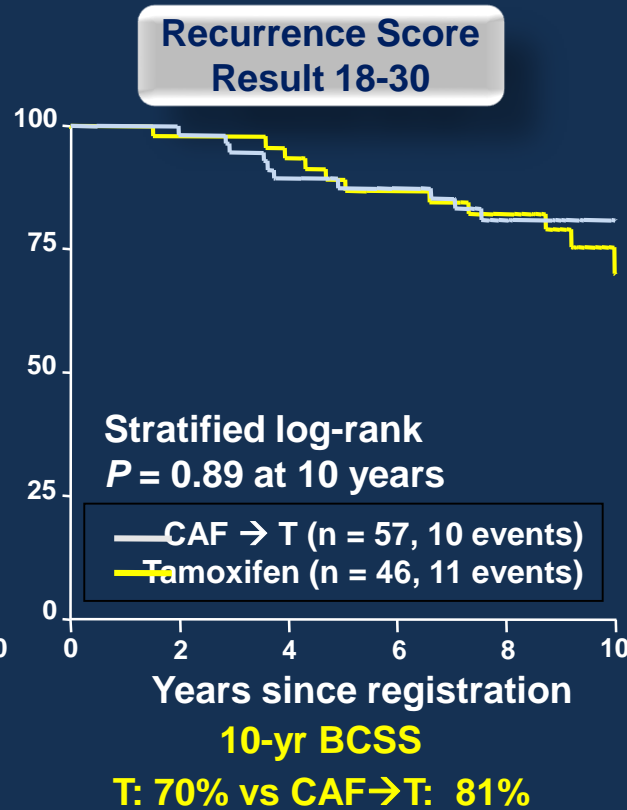
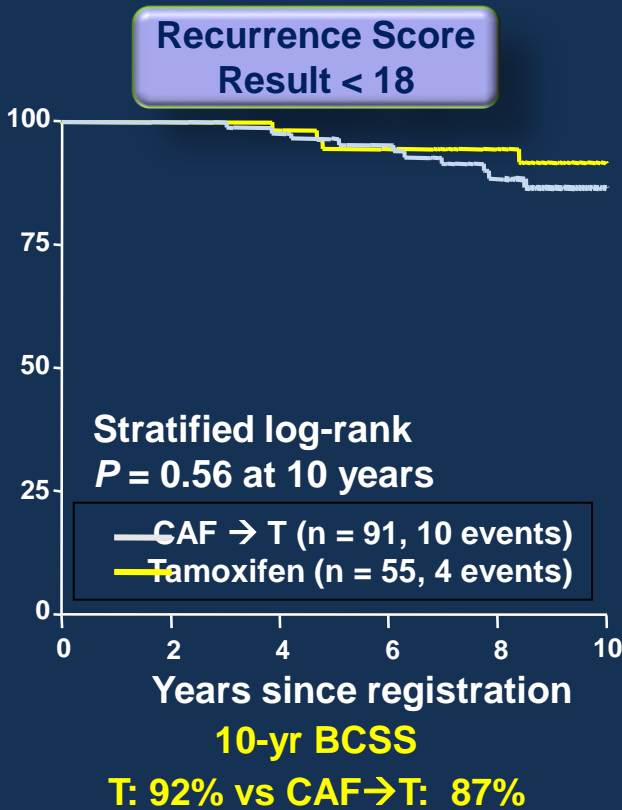
PATIENTS WITH HIGH RS
28% absolute benefit from tamoxifen + chemotherapy

RS, Recurrence Score result

Paik S, et al. *J Clin Oncol.* 2006;24:3726-3734.

SWOG 8814 Benefit from Chemo in Patients with 1-3 Lymph Node Positive Patients Randomized to Tamoxifen +- CAF

BREAST CANCER-SPECIFIC SURVIVAL BY TREATMENT



Interaction $P = 0.021$

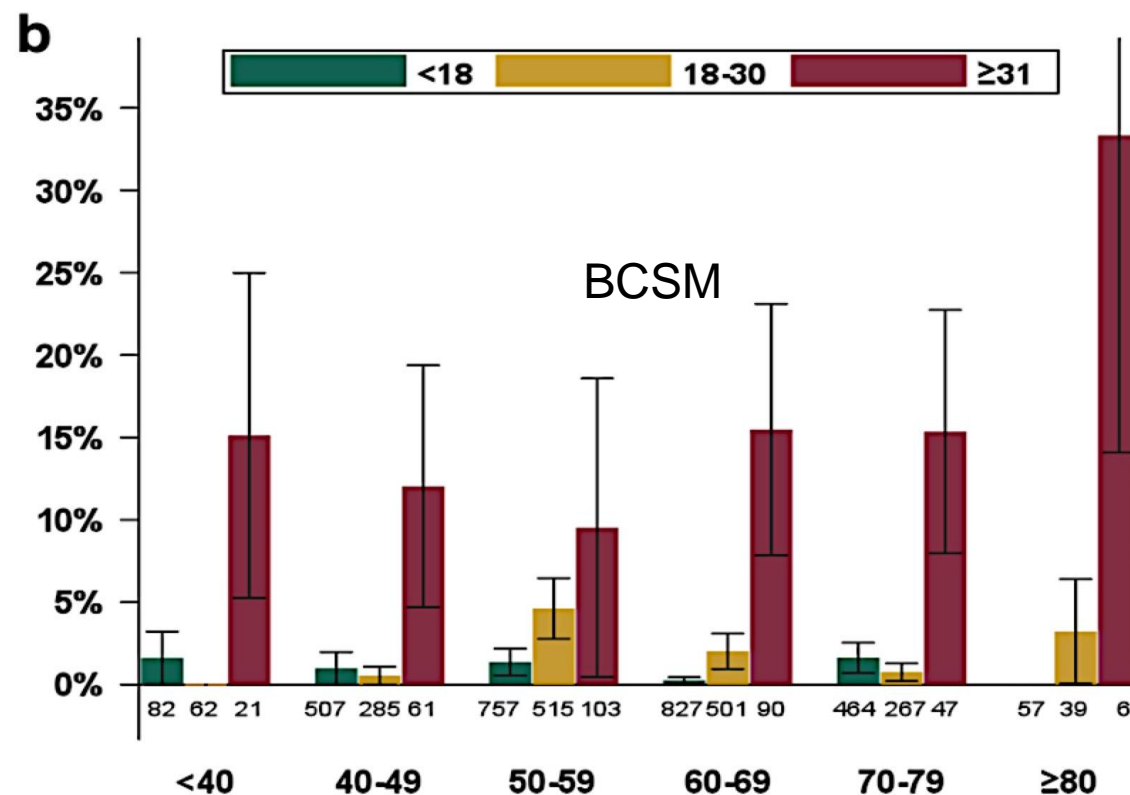
Real World Data – SEER Database

SEER cases from 2004-2011 linked to RS® results

Node Negative N 38568 Node Positive N 4691

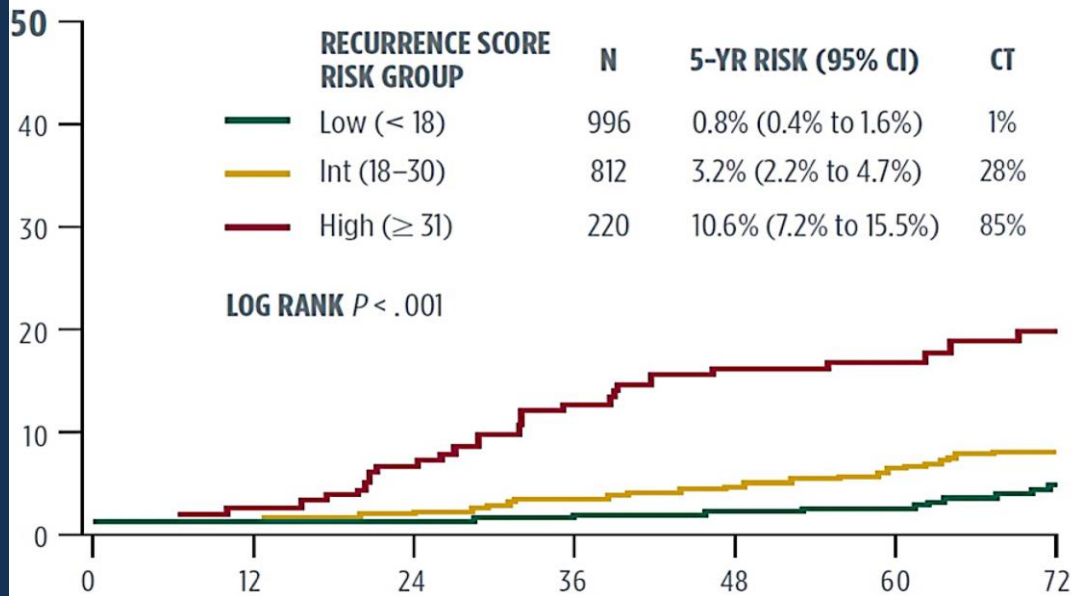
5 y BCSM

	RS<18	RS 18-30	RS>=30
Node Negative	0.4%	1.4%	4.4%
Node Positive	1%	2.3%	14.3%



Shak et al. SABCs 2015; Stemmer et al. SABCs 2015; Valentina I Petkov et al npj Breast Cancer 2016; doi:10.1038/npjbcancer.2016.17

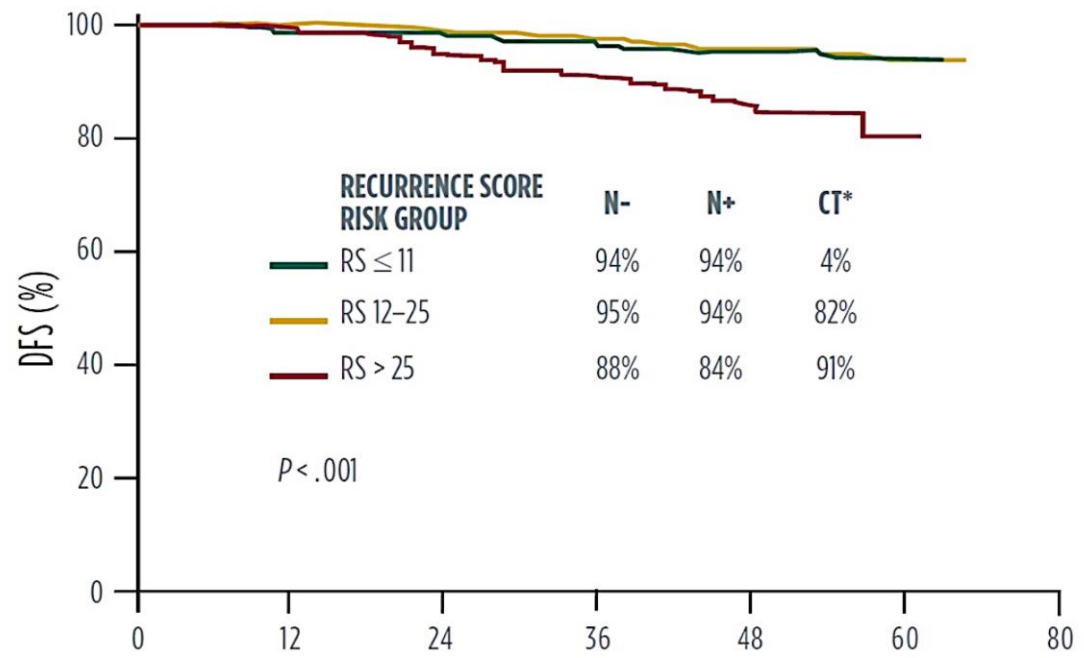
5-Year Distant Recurrence (DR)



CLALIT

PlanB

5-Year Disease-Free Survival (DFS)



TransNEOS: Validation of the Recurrence Score® in Neoadjuvant Setting

Postmenopausal
cT1-2N0 BC
24-18 weeks
Neoadjuvant Letrozol

PR, CR or SD

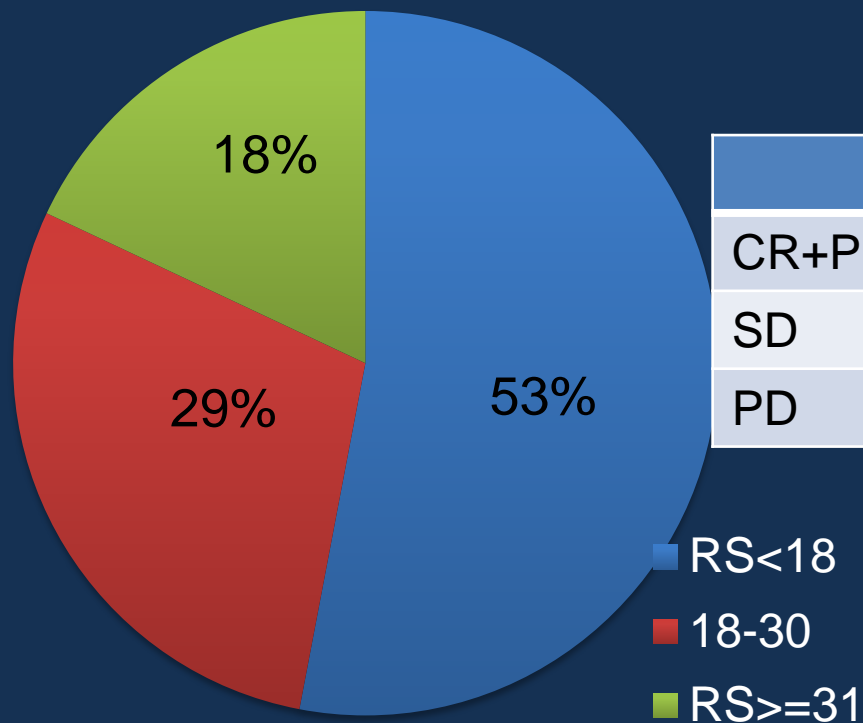


CT + LET 5 y

LET 5 y

PD: Discontinue

RS Distribution



	RS < 18	RS 18-30	RS >= 31
CR+PR	54%	42%	22%
SD	45%	55%	61%
PD	1%	3%	17%

TAILORx: Trial Assigning Individualized Options for Treatment (Rx)

ER+ and/or PR+,
node negative,
HER2-negative
breast cancers
between 1.1 to 5.0
cm (or 5 mm to 1.0
cm with unfavorable
histologic features

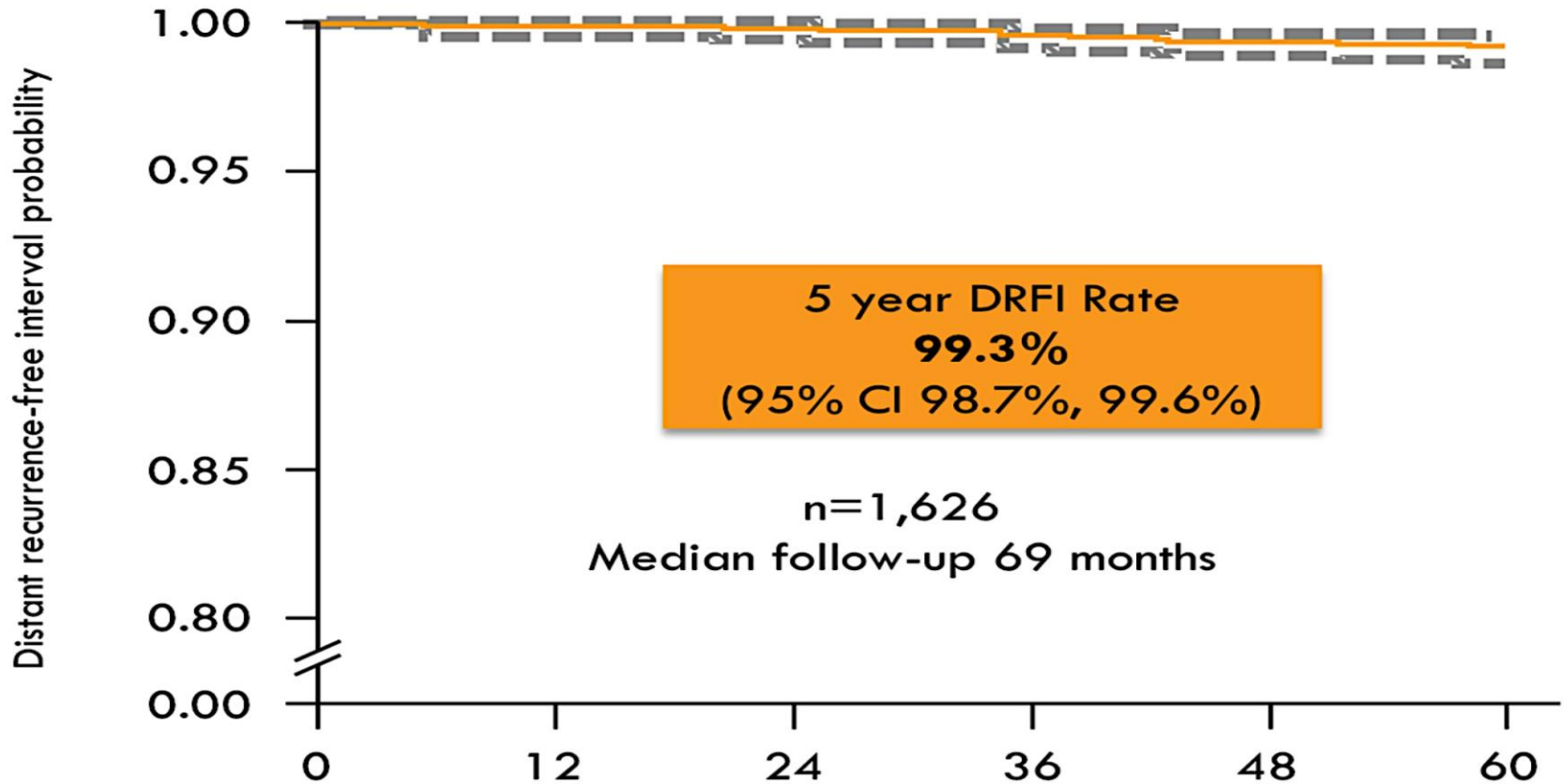


RS<10: Hormone Rx

RS 11-25: Randomized
to hormone Therapy vs
chemotherapy +
hormone therapy

RS>25: chemotherapy +
hormone therapy

Patients with Recurrence Score® Results <11 Have Less than 1% Risk of Distant Recurrence at 5 Years, regardless of grade



	DRFI, % (95% CI)	OS, % (95% CI)
All grades	99.3 (98.7-99.6)	98.0 (97.1-98.6)
Low grade	99.8 (98.3-100)	98.7 (97.0-99.4)
Intermediate grade	99.0 (98.0-99.5)	97.9 (96.8-98.7)
High grade	100 (NC-NC)	97.3 (91.9-99.1)

RxPONDER (SWOG 1007) Trial

Women with HR+, HER2- EBC with 1-3 positive LN

Recurrence Score[®]
≤25



Arm 1:
Chemotherapy and
hormonal therapy

Randomization n=4000

Arm 2: Hormonal
therapy alone

In BC Cancer Patients with ER+ HER2- Localized Node Negative or with 1 to 3 positive lymph nodes

Oncotype Dx® can accurately prognosticate and also identify patients who can safely be spared from adjuvant chemotherapy

The assay is endorsed by ASCO, NCCN, NICE and St Gallen Guidelines

Less cytotoxic chemotherapy is being offered to our patients, sparing them from acute and long term toxicities

It's a new day in BC !!!



OBRIGADA

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