

**JOVENS  
NA ONCOLOGIA**

SIMPÓSIO NACIONAL



# **Oncotype DX® no cancro da mama em fase inicial**

**uma experiência num centro do Reino Unido**

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# Conflito de interesses

- O autores não reportam conflitos de interesse subordinados ao tema ou teste genético utilizado

# Contextualização

- **Oncotype Dx<sup>®</sup>**

- Ensaio de expressão genética, recorrendo a análise por RT-PCR
  - Fornece um prognóstico adicional sobre risco de recidiva de doença à distância, independentemente da clínica e/ou patologia do tumor
  - Capacidade preditiva do benefício da quimioterapia adjuvante

## 16 BREAST CANCER RELATED GENES

Estrogen	Proliferation	HER2	Invasion	Others
ER PR Bcl2 SCUBE2	Ki-67 STK15 Survivin Cyclin B1 MYBL2	GRB7 HER2	Stromelysin 3 Cathepsin L2	CD68 GSTM1 BAG1

## 5 REFERENCE GENES

Beta-actin	GAPDH	RPLPO	GUS	TFRC
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# Contextualização

- **Oncotype Dx<sup>®</sup>**

## 2004: NSABP B-14

Valor prognóstico para recidiva à distância em doentes sob Tamoxifeno adjuvante

Taxa de recidiva aos 10 anos de 30,5% para alto risco vs. 6.8% baixo risco

## 2006: NSABP B-20

Valor preditivo sobre o benefício de QT adjuvante

Doentes com score de alto risco obtiveram um benefício absoluto 28% com associação QT+HT adjuvante

## 2008: ATAC results (SABCS)

Independentemente do score, a taxa de recidiva aumentou com o número de gânglios axilares envolvidos

## 2010: SWOG 8814

Sem impacto na sobrevida livre de doença com a adição de QT adjuvante no grupo de baixo risco, apesar de gânglios positivos

# Contextualização

- **Oncotype Dx<sup>®</sup>**

- **2014: Aprovação da NICE**

- “It predicts the likelihood of recurrence in women of **all ages** with newly diagnosed **stage I or II, ER+, LN– or LN+ (up to 3 nodes positive)** breast cancer treated with tamoxifen”

**NCCN Guidelines<sup>®</sup>**

> 0.5 cm, node negative, N1mi

Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy<sup>1</sup>

**ASCO<sup>®</sup> Guidelines**

Node negative

Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy<sup>2</sup>

**St Gallen Consensus**

Node negative, node positive

Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy<sup>3</sup>

**NICE**

Node negative

Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk\* of distant recurrence<sup>4</sup>



# Objetivo

- Exposição de 3 casos clínicos onde o ODX apresentou um impacto clínico na decisão terapêutica.
- Revisão bibliográfica enfatizando a utilidade clínica do ODX

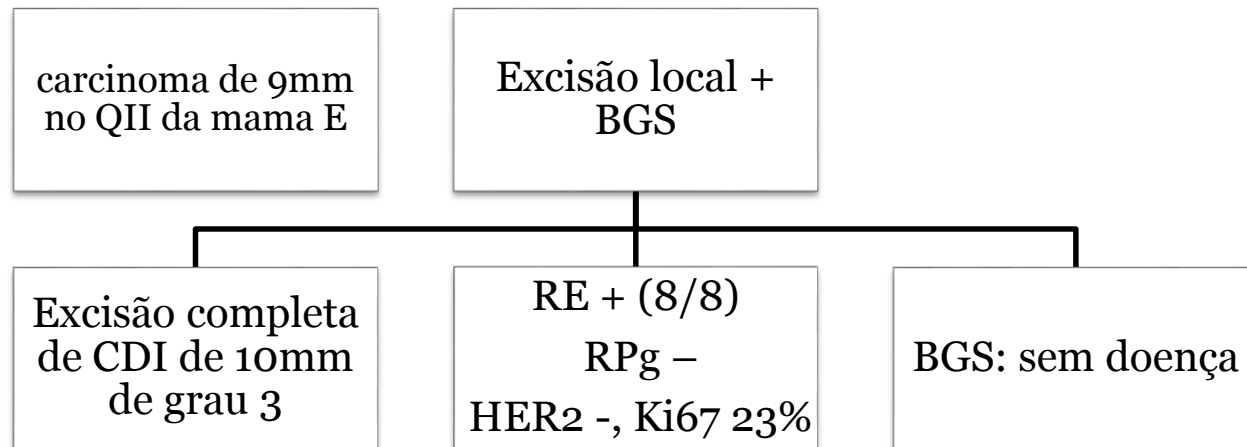
# Métodos

- Seleção de 3 doentes que submeteram ao ODX como método de decisão terapêutica
  - Departamento de Oncologia Médica, Unidade da Mama
  - The Royal Marsden Hospital NHS Foundation Trust, Sutton, Surrey, UK
  - Outubro de 2015
- *Cut-off* de scores de ODX usados na estimativa de risco de recorrência
  - **Baixo risco: 0-17**
  - **Intermédio: 18-30**
  - **Alto:  $\geq 31$**
- Revisão bibliográfica - últimos 10 anos

# Resultados

- **Caso 1**

- Mulher de 52 anos de idade
- agosto 2014: Autodeteção de nódulo mama E





# Resultados

## Prognosis: 10-Year Risk of Distant Recurrence after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-14)

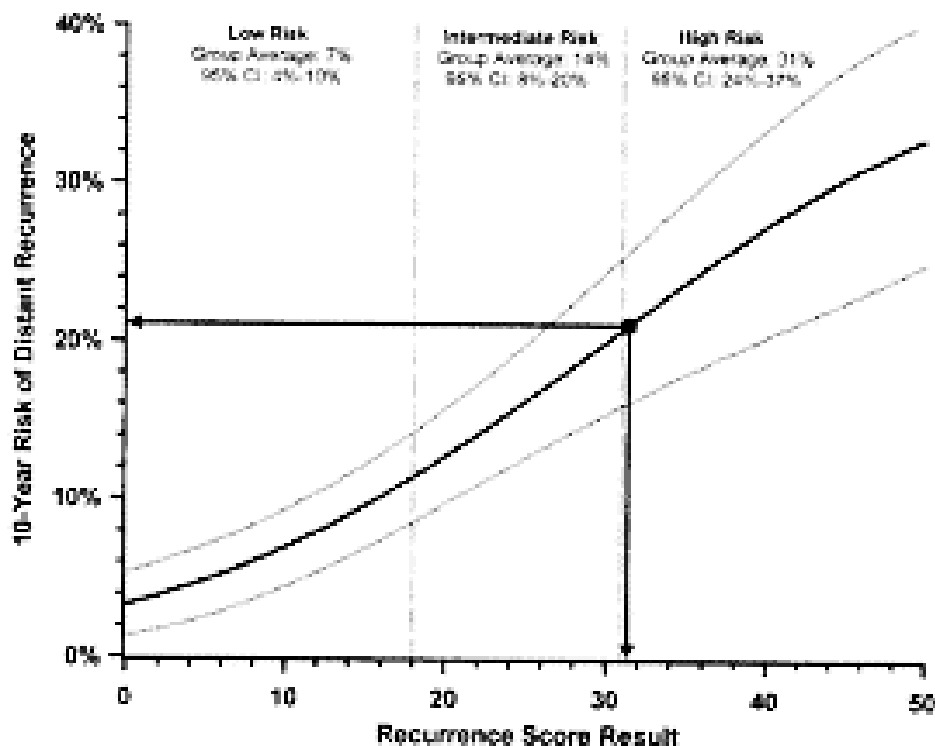
### 10-Year Risk of Distant Recurrence

Tam Alone

**21%** —

[95% CI: 16%-26%]

Score de  
recorrência:  
**31**



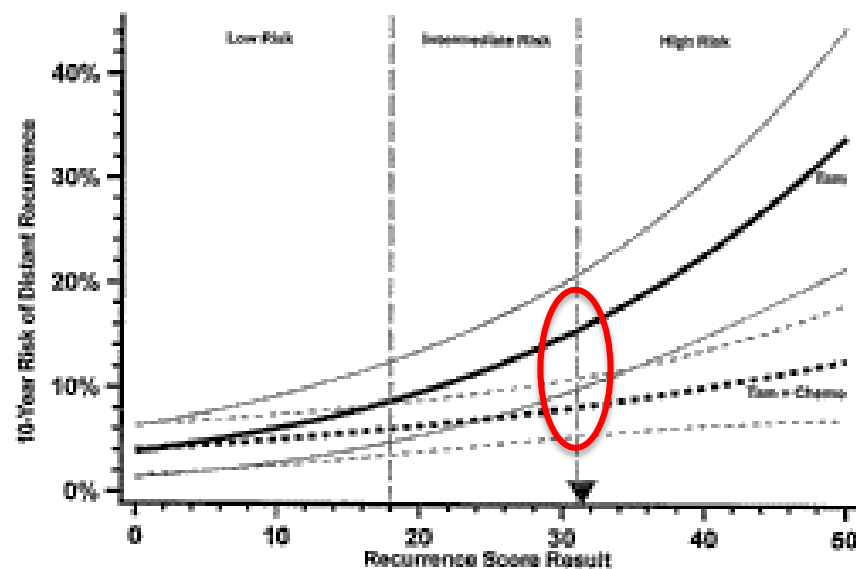
# Resultados

## Prediction of Chemotherapy Benefit after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-20)

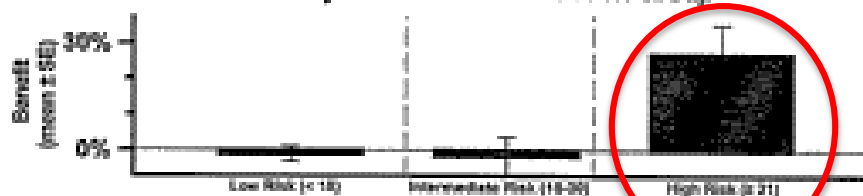
Tam Alone ———

Tam + Chemo - - - - -

Score de  
recorrência:  
**31**



### Absolute Benefit of Chemotherapy at 10 Years by Recurrence Score Risk Group





# Resultados

## **Decisão**

- QT + RT + HT

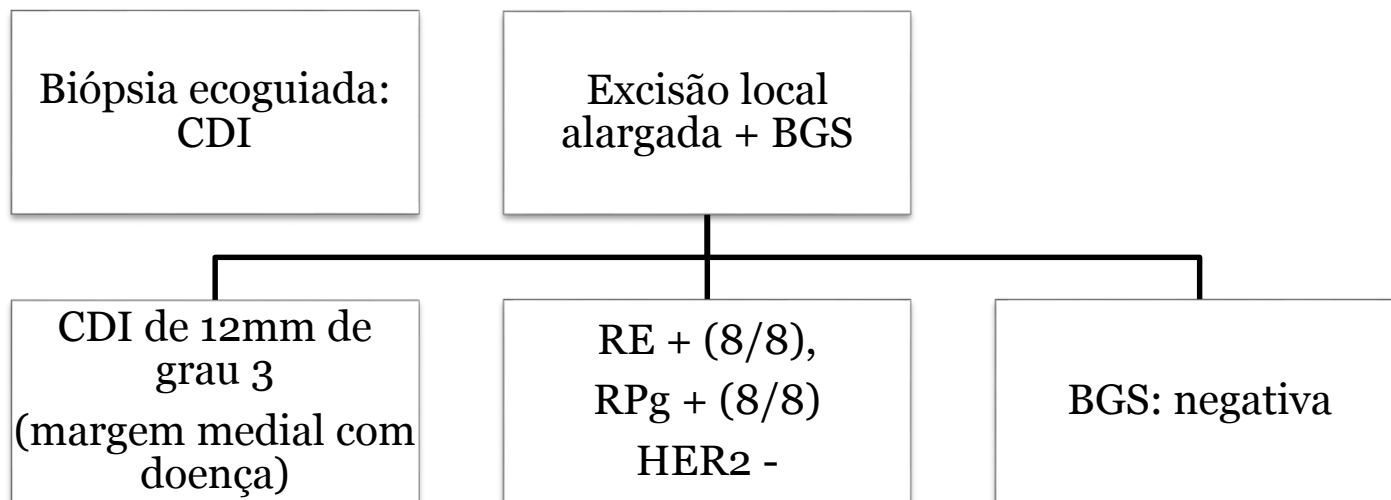
## **Follow-up**

- 1 ano: sem recidiva

# Resultados

- **Caso 2**

- Mulher de 45 anos de idade
- julho 2015: alteração cutânea sintomática peri-areolar E



# Resultados

**Prognosis: 10-Year Risk of Distant Recurrence after 5 Years of Tam,  
Based on the Recurrence Score Result (from NSABP B-14)**

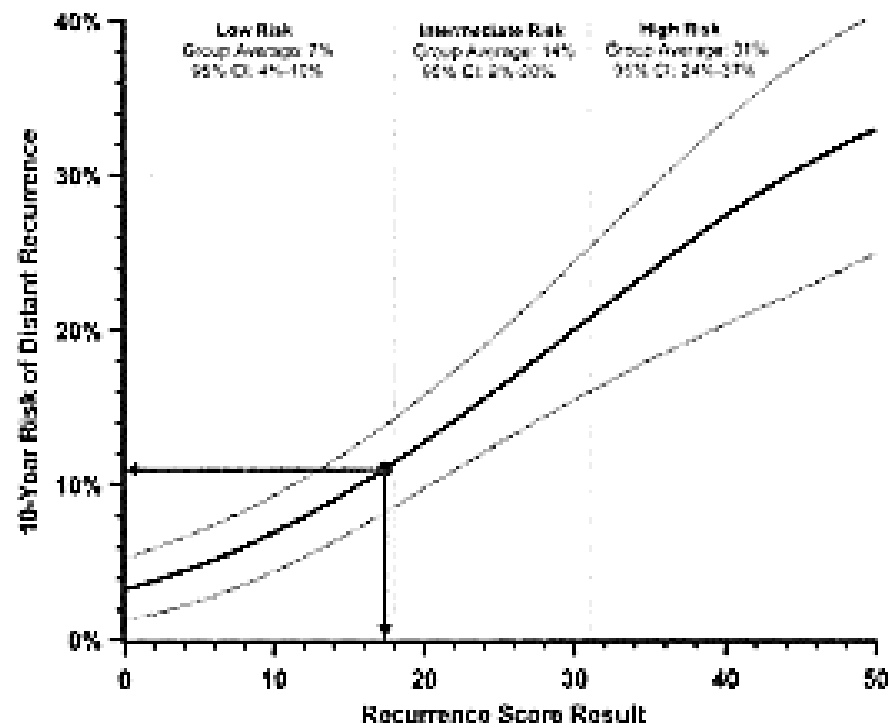
**10-Year Risk of  
Distant Recurrence**

**Tam Alone**

**11% —**

(95% CI: 9%-14%)

Score de  
recorrência:  
**17**



# Resultados

## Prediction of Chemotherapy Benefit after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-20)

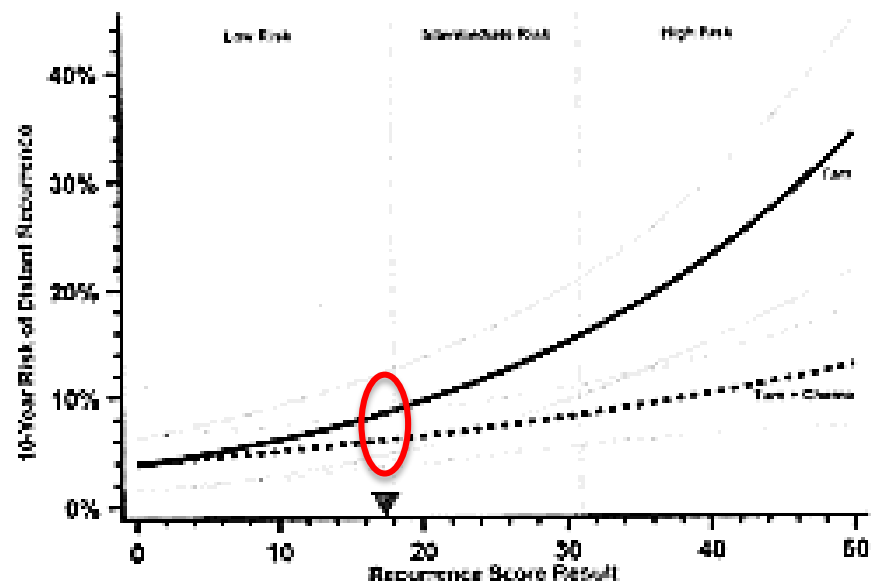
Tam Alone

—

Tam + Chemo

- - - -

Score de  
recorrência:  
**17**



### Absolute Benefit of Chemotherapy at 10 Years by Recurrence Score Risk Group





# Resultados

## **Decisão**

- RT + HT (+ cirurgia da margem medial)

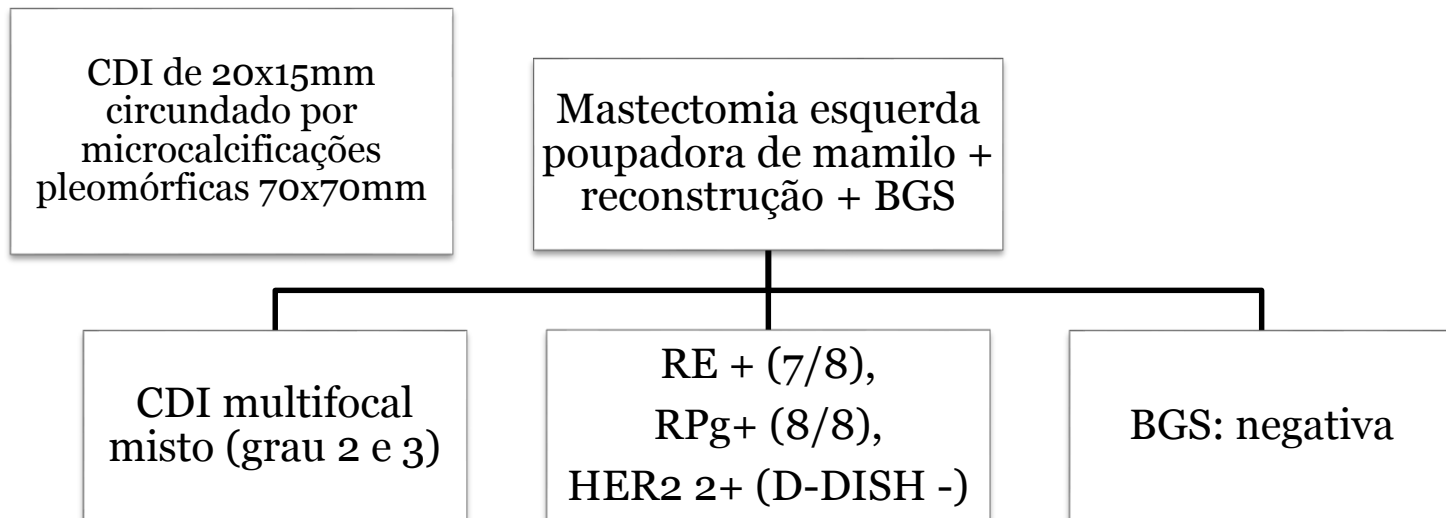
## **Follow-up**

- Sem recidiva

# Resultados

- **Caso 3**

- Mulher de 47 anos de idade
- julho 2015: autodeteção de massa na mama E





# Resultados

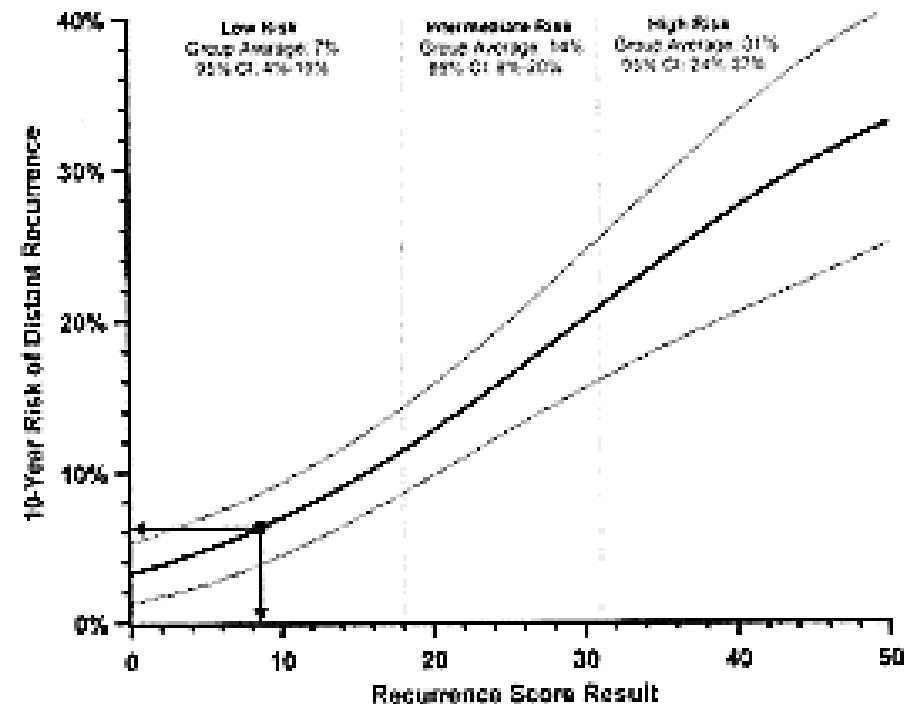
## Prognosis: 10-Year Risk of Distant Recurrence after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-14)

### 10-Year Risk of Distant Recurrence

Tam Alone

**6%** ———  
(95% CI: 4%-8%)

Score de  
recorrência:  
**9**



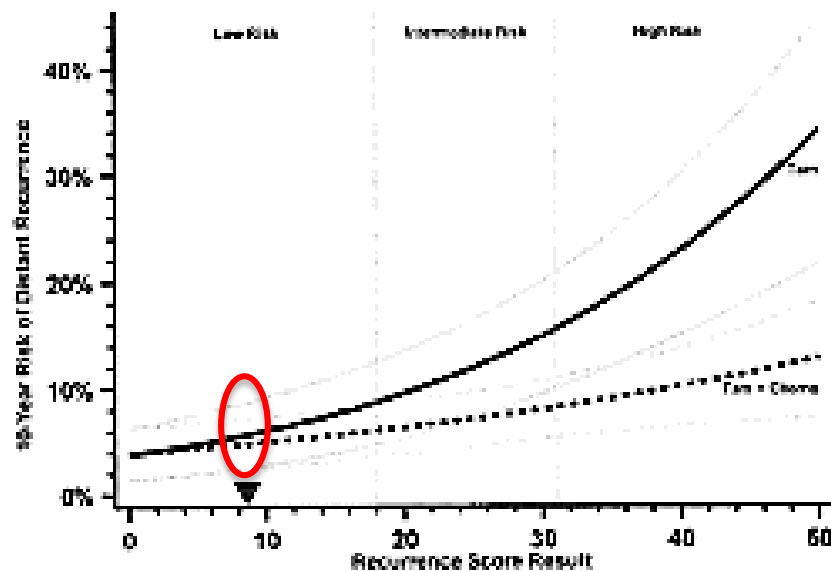
# Resultados

## Prediction of Chemotherapy Benefit after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-20)

Tam Alone ———

Tam + Chemo - - - - -

Score de  
recorrência:  
**9**



### Absolute Benefit of Chemotherapy at 10 Years by Recurrence Score Risk Group





# Resultados

## Decisão

- HT

## Follow-up

- Sem recidiva



# Discussão

*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

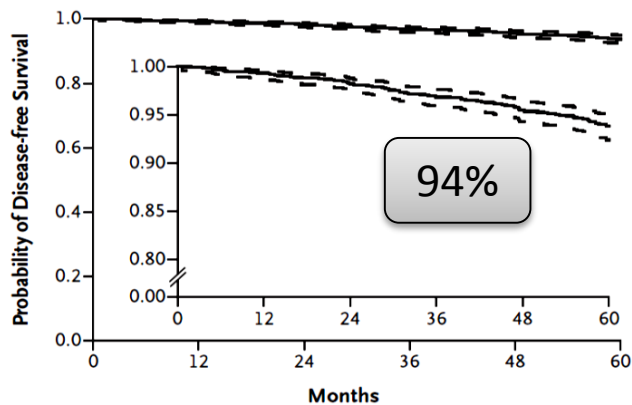
## Prospective Validation of a 21-Gene Expression Assay in Breast Cancer



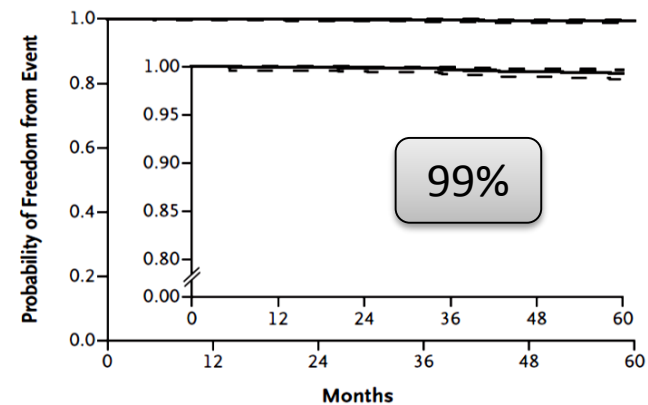
# Discussão

- 1600 mulheres com *score* de baixo risco de recidiva, sob tamoxifeno 5 anos

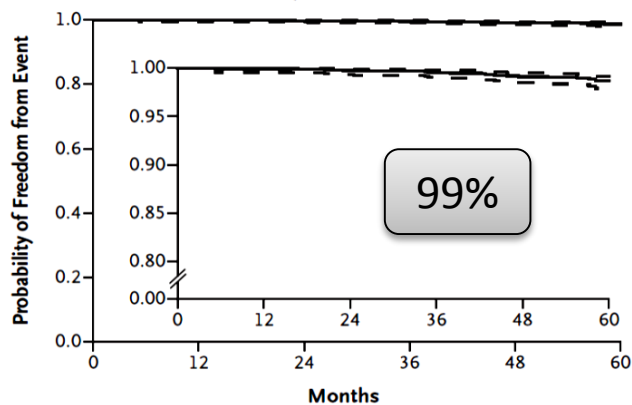
**A Invasive Disease-free Survival**



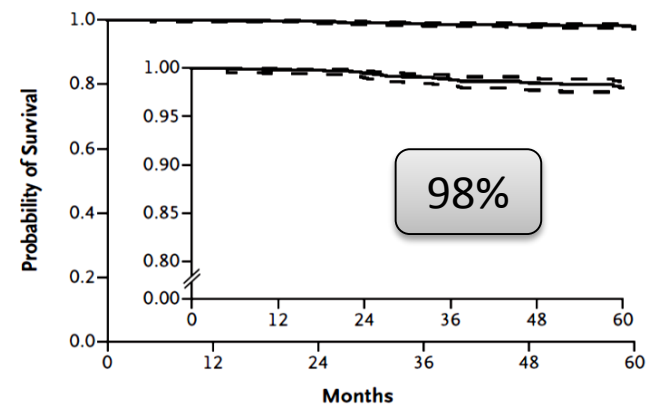
**B Freedom from Recurrence of Breast Cancer at Distant Site**



**C Freedom from Recurrence at Any Site**



**D Overall Survival**





# Discussão

Breast Cancer Res Treat (2015) 152:611–625

DOI 10.1007/s10549-015-3483-3



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## EPIDEMIOLOGY

### **Decision-making impact on adjuvant chemotherapy allocation in early node-negative breast cancer with a 21-gene assay: systematic review and meta-analysis**

- 15 estudos analisados (n= 2229)
- Alteração da decisão de tratamento: 29,5% (IC 95%: 26,29 - 32,86)
- Redução global do uso de QT: 12%

# Discussão

- Bom perfil custo-efetividade

Publication	Reported Findings (ICER in Cost per QALY gained with Oncotype DX)	Country Threshold (Willingness to pay for 1 QALY(\$))	Country	Comment
<i>Lacey L et al. 2011</i>	EUR 9,462	EUR 20,000	Ireland	Cost Effective
<i>Holt et al. 2011</i>	GBP 6,232	GBP 20,000	UK	Cost Effective
<i>Klang et al. 2010</i>	USD 10,700	USD 35,000	Israel	Cost Effective
<i>Tsoi et al. 2010</i>	USD 63,421	USD 75,000	Canada	Cost Effective
<i>Paulden et al. 2011</i>	> USD 29,000	USD 75,000	Canada	Cost Effective
<i>Kondo et al. 2010</i>	USD 3,848	USD 50,000	Japan	Cost Effective
<i>Madaras et al. 2011</i>	USD 14,110	USD 20,000	Hungary	Cost Effective
<i>O'Leary et al. 2010</i>	AUS 9,986	AUS 18,000	Australia	Cost Effective
<i>de Lima Lopez et al. 2011</i>	Improved outcomes (QALYs), reduced costs		Singapore	Cost Savings
<i>Chereau et al, SABC 2011</i>			France	Cost Savings
<i>Hornberger et al. 2005</i>			USA	Cost Savings
<i>Lyman et al. 2007</i>			USA	Cost Savings



# Considerações finais

- Perspetivas futuras:
  - Resultados do TAILORx trial: para os subgrupos de intermédio e alto risco
  - Southwest Oncology Group S1007 RxPONDER trial: avaliar papel do ODX nos casos de envolvimento ganglionar axilar