

**bjcclub** breast  
Journal  
Club

***L'IMPORTANZA DELLA RICERCA IN ONCOLOGIA***

**20 - 21 APRILE  
2023 ROMA**

**THE HIVE HOTEL**

Via Torino, 6

**THE  
OXFORD DEBATE  
EDITION**

La linfadenectomia **NON** è un intervento  
imprescindibile per le decisioni terapeutiche

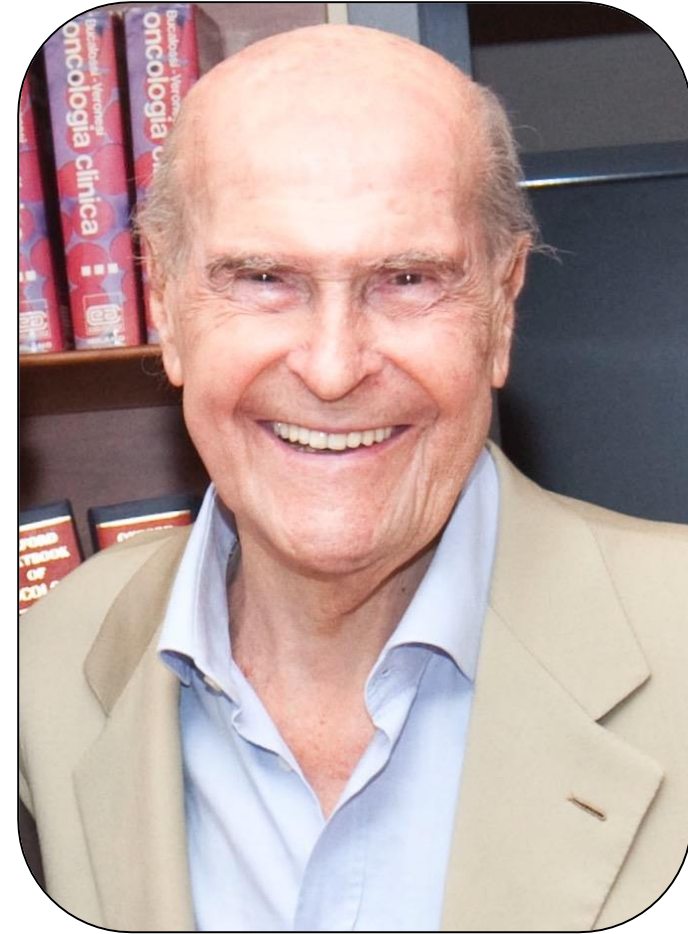
# Chapter #1

## Never Forget The Milestones

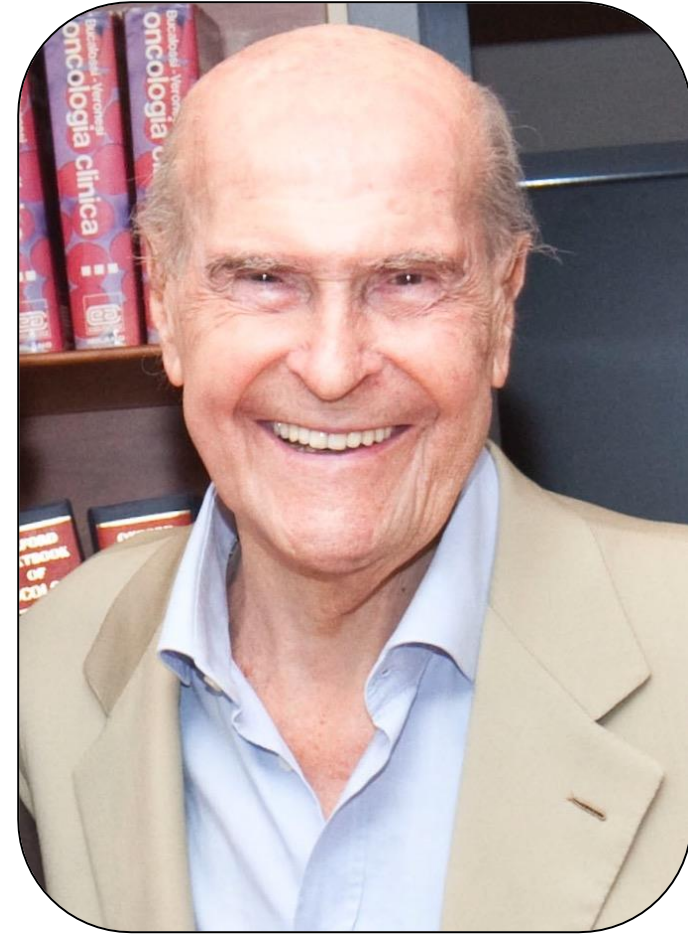




Ludwing Mies van der Rohe  
Architect; 1886-1969

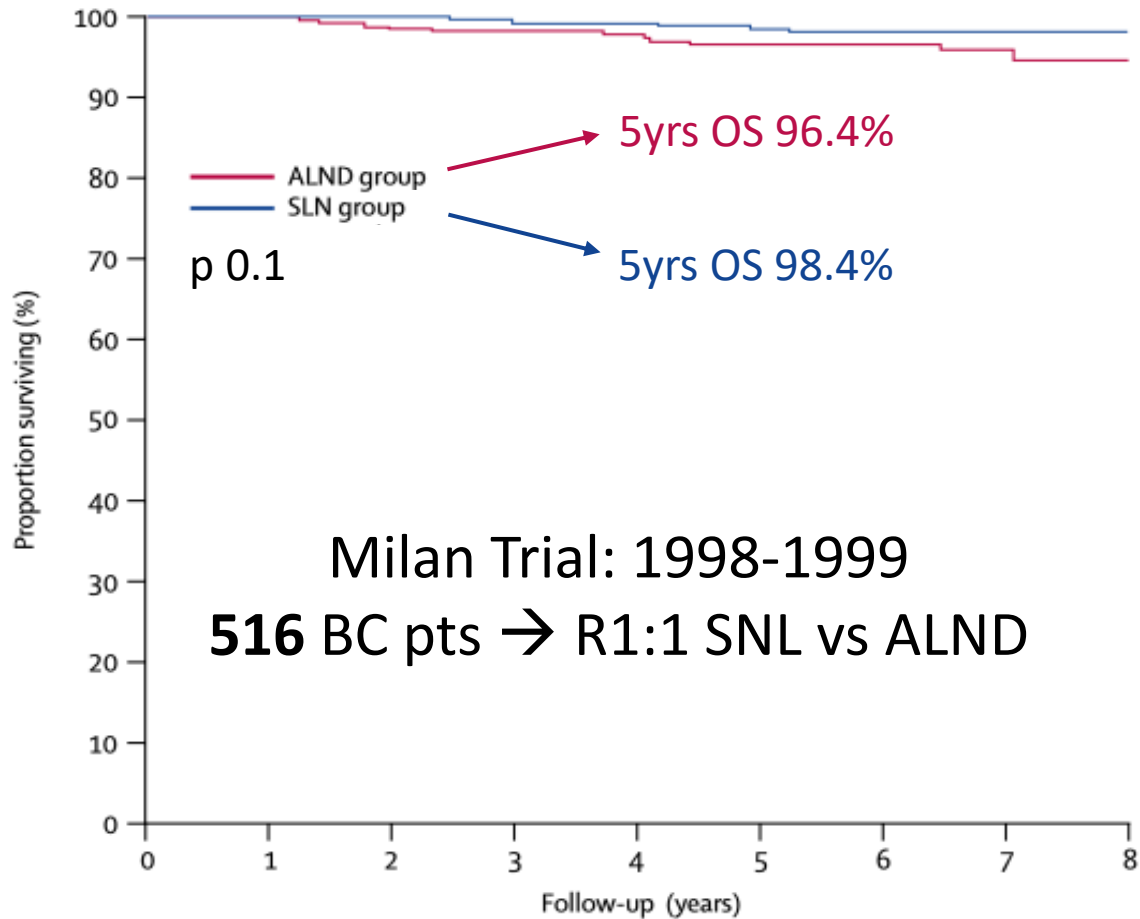


Umberto Veronesi  
Doctor; 1925-2016

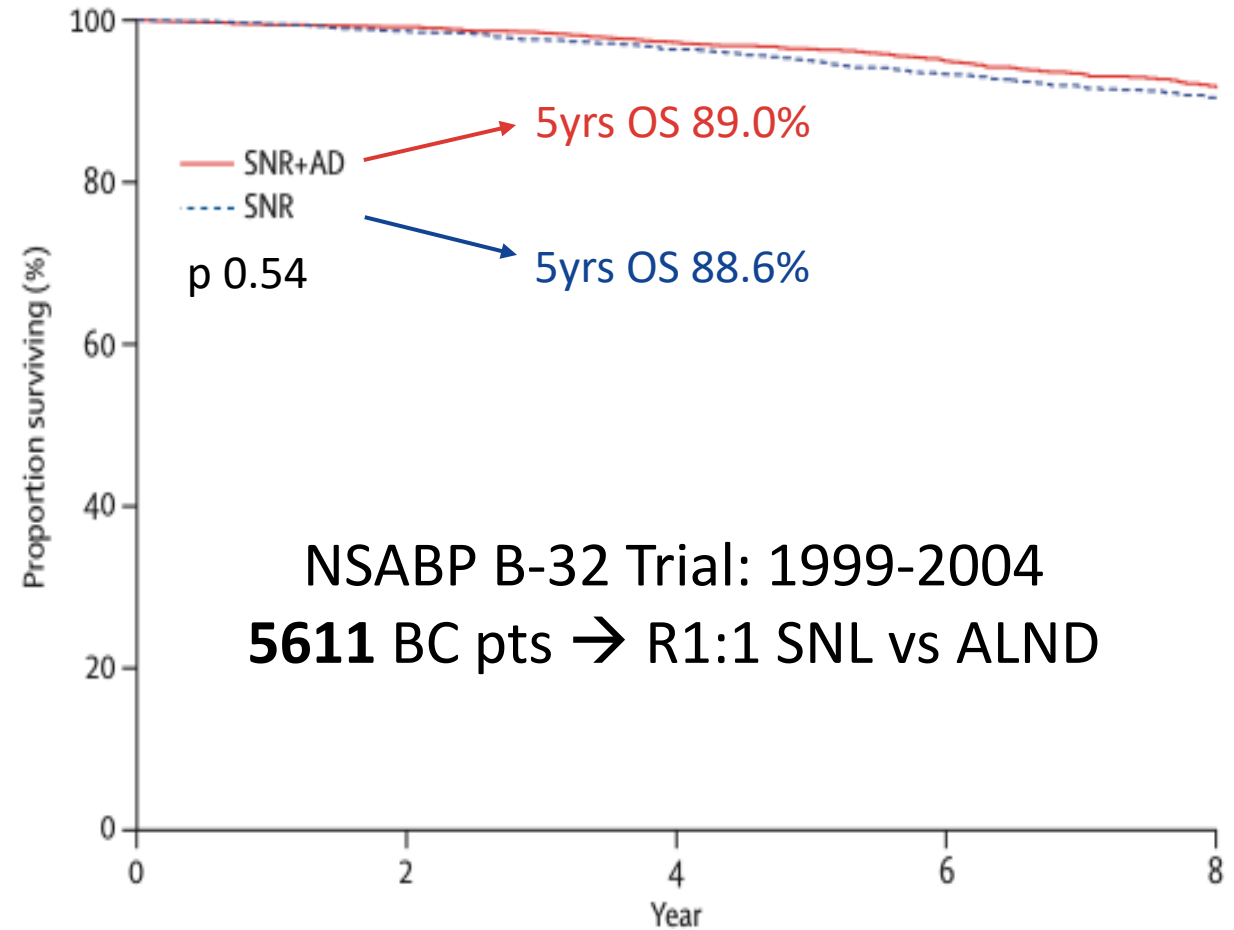
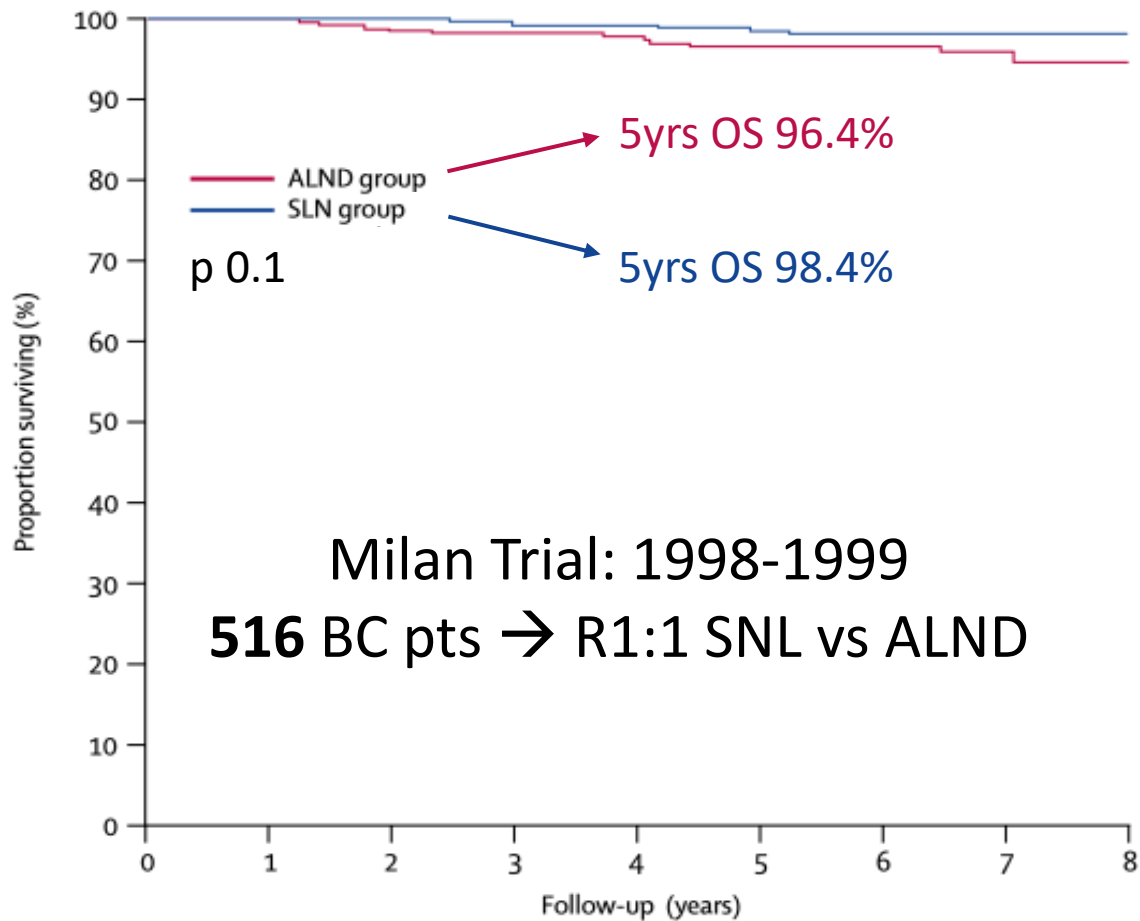


**LESS IS MORE**

# Where Everything Started From...



# Where Everything Started From...





**Less ALND**

**=**

**Less Lymphedema**

**Less Movement Impairment**

**Less Numbness**

**=**

**Better QoL**



# Chapter #2

## Trials That Left a Mark

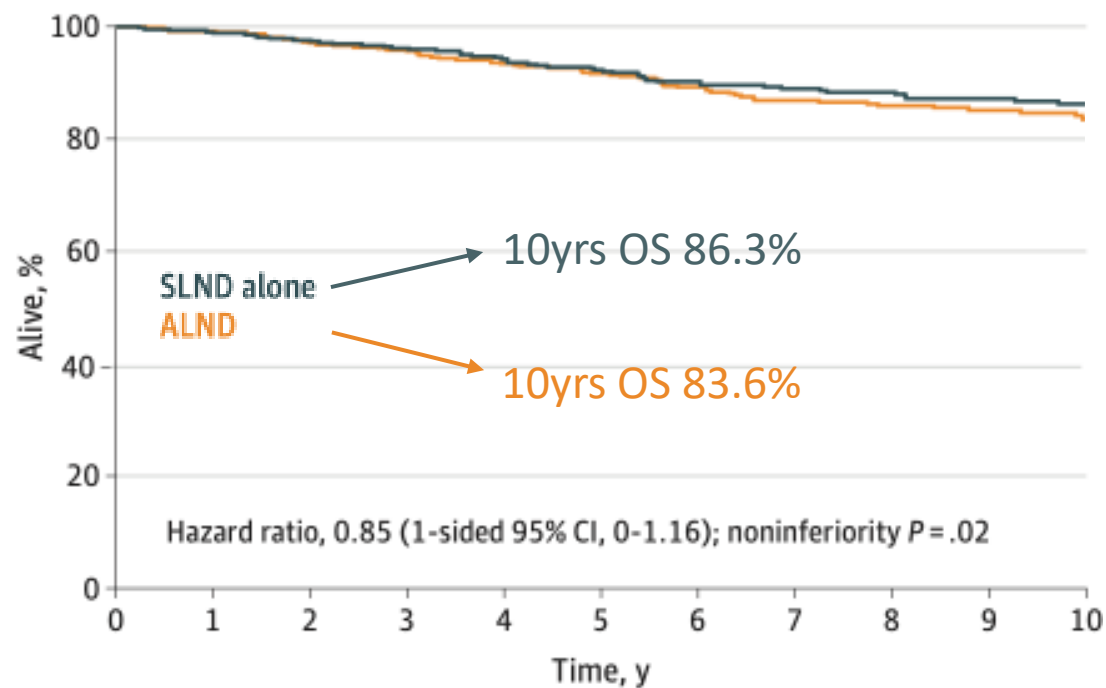


# ACOSOG Z0011

1999-2004

856 cT1-2 cN0 BC pts - BCS

1/2 N+ → R1:1 SLND alone vs ALND

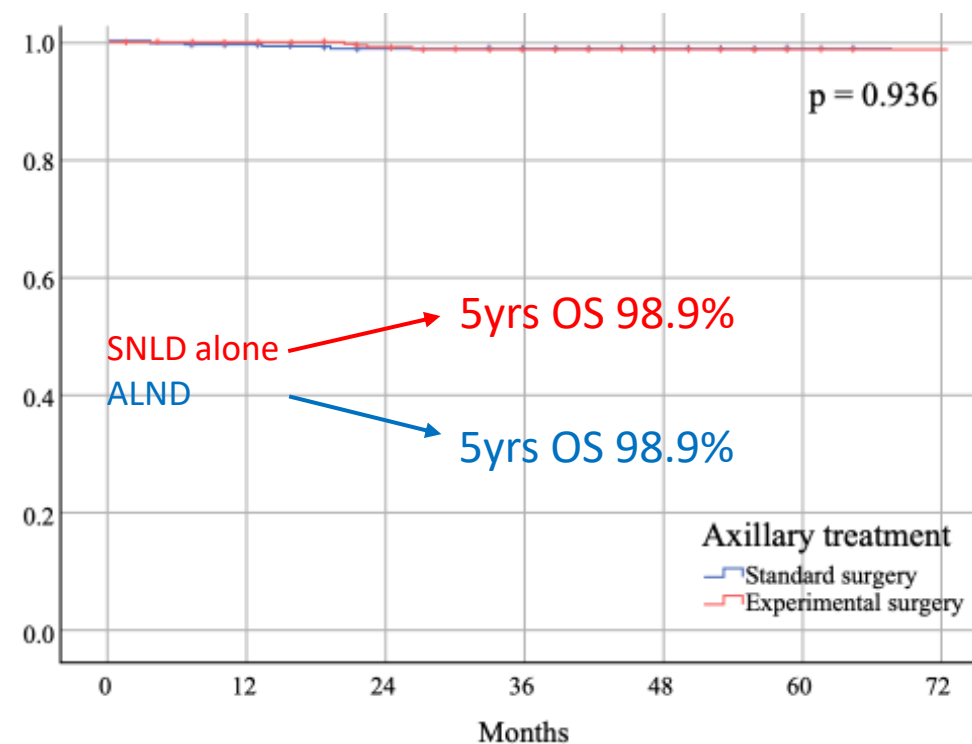


# SINODAR ONE

2015-2020

889 cT1-2 cN0 BC pts - BCS/Mastectomy

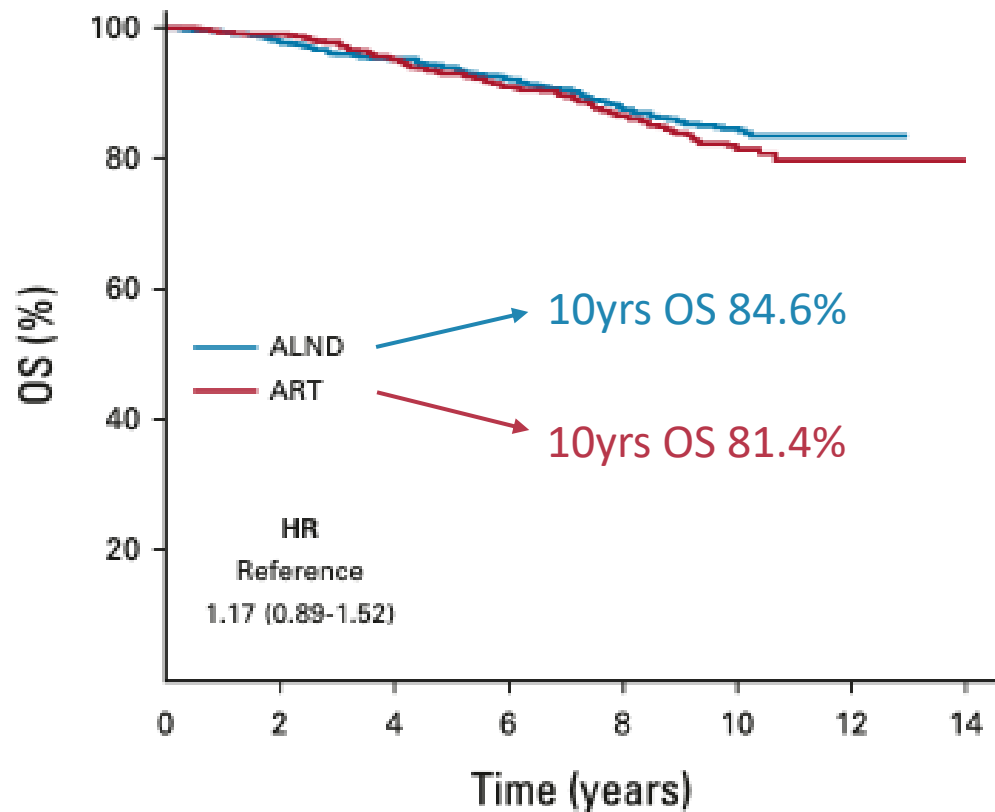
1/2 N+ → R1:1 SLND alone vs ALND



# AMAROS

2001-2010

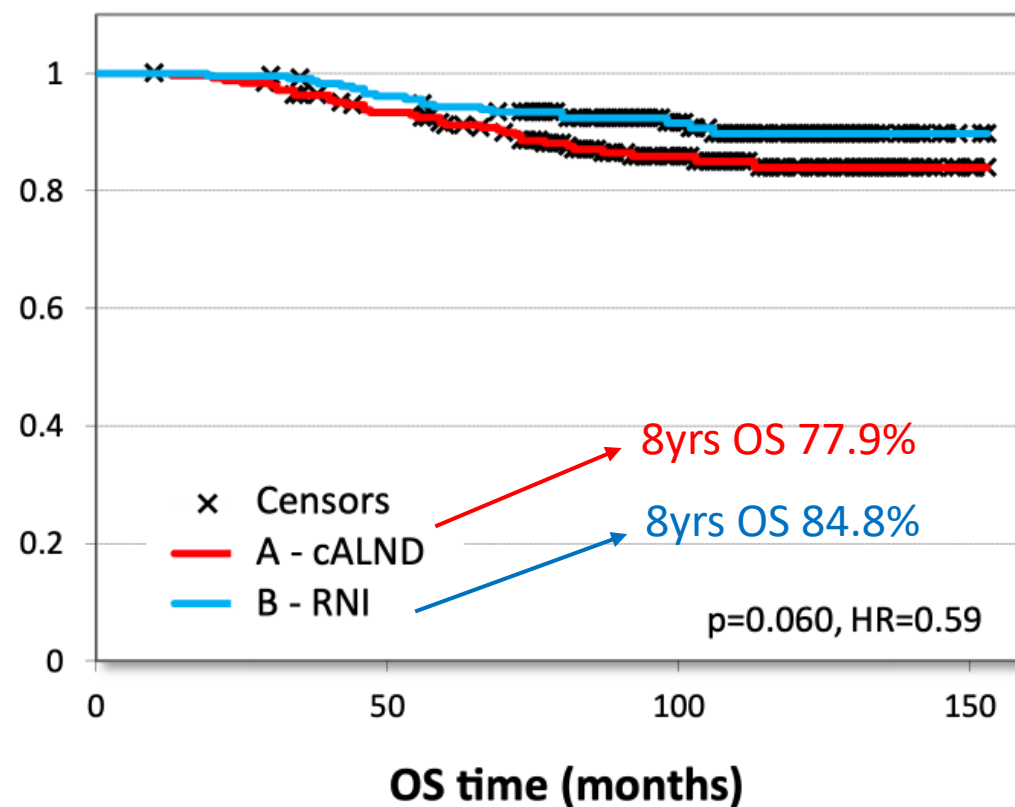
1425 cT1-2 cN0 BC pts  
SLN+ → R1:1 ALND vs ART



# OTOASOR

2002-2009

2106 cT< 3 cm cN0 BC pts  
1/2 N+ → R1:1 SLND vs RNI



# Chapter #3

## The Times They Are A-Changin'\*



# RxPONDER Trial Design

## Key Inclusion Criteria

- Women age  $\geq 18$  yrs
- HR+/HER2- BC with 1-3 N+; M0
- Able to receive adjuvant CHT
- Axillary staging by SNLB or ALND

Recurrence Score  
0-25

1:1

**Arm 1**  
CHT followed by ET

**Arm 2**  
ET alone

N 5000

**Stratified by:**  
RS 0-13 vs 14-25  
Pre vs postmenopausal  
SLNB vs ALND

Recurrence Score  
>25

Off study  
CHT followed by ET  
recommended

# monarchE Trial Design

## HR+, HER2-, node positive high-risk EBC

- Women or men
- Pre-/postmenopausal
- With or without prior neo- and/or adjuvant chemotherapy
- No metastatic disease
- Maximum of 16 months from surgery to randomization and 12 weeks of ET following the last non-ET

## Cohort 1: High risk based on clinical pathological features

- $\geq 4$  ALN OR
- 1-3 ALN and at least 1 of the below:
  - Grade 3 disease
  - Tumor size  $\geq 5$  cm

## Cohort 2: High risk based on Ki-67

- 1-3 ALN and
- Ki-67  $\geq 20\%$  and
- Grade 1-2 and tumor size  $< 5$  cm

### Stratified for:

- Prior chemotherapy
- Menopausal status
- Region

On-study treatment period  
2 years

**Abemaciclib**  
(150mg twice daily)  
+  
**Endocrine Therapy: AI or tamoxifen**

R 1:1  
N = 5637

**Endocrine Therapy: AI or tamoxifen**

**Follow-up period**  
Endocrine Therapy  
3-8 years as clinically indicated

**Primary Objective: IDFS**

**Secondary Objectives: IDFS in high Ki-67 populations, DRFS, OS, Safety, PK, PRO**

# Chapter #4

## The Times They Are A-Changin'...

# ...OR NOT?

# Likelihood of pN<sub>≥</sub> 2 according to HR/HER2 status

MSKCC Cohort 1998-2010, N=11596 BC

	<b>HR+/HER2-</b>	<b>HR+/HER2+</b>	<b>HR-/HER2+</b>	<b>HR-/HER2+</b>	p-value
Number	8526 (74%)	928 (8%)	625 (5%)	1517 (13%)	
≥1 N+	40%	49%	53%	41%	<0.0001
<b>≥4 N+</b>	<b>9%</b>	16%	22%	15%	<0.0001

**HORMONE RECEPTOR STATUS MATTERS!**



# Likelihood of additional N+ at ALND in pts with SLN+

MSKCC Cohort 2006-2011, N= 5262 cN0 BC → 1314 (25%) SLN+\*

ALND	1146 (87%)
1-2 N+	996 (76%)
3 N+	102 (8%)
<b>≥4 N+</b>	<b>216 (16%)</b>

\* Includes N1mi

# Prediction of 1-2 pN+ by pre-operative US

## German Cohort 2015-2020

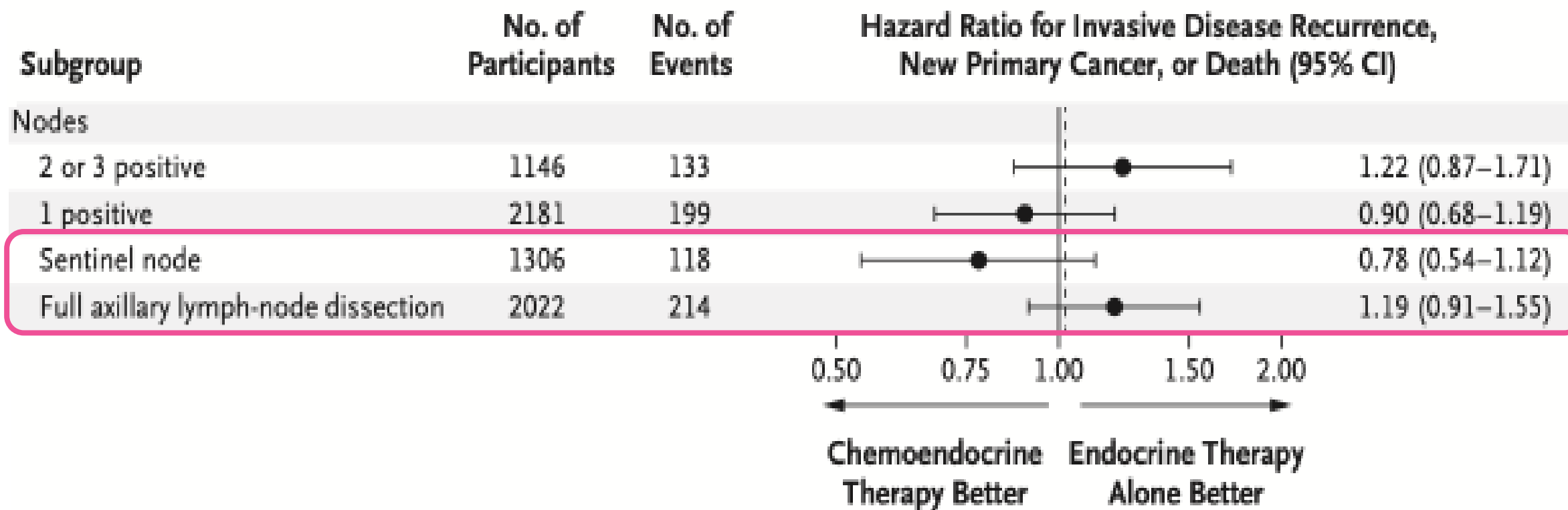
N=2095 → 79% cN0, 21% cN+ - 74% pN0, 26% pN+

US performance	Accuracy	Sensitivity	Specificity	FNR
N0	94%	79%	100%	21%
<b>1 cN+</b>	94%	<b>92%</b>	96%	<b>8%</b>
2 cN+	89%	89%	89%	11%

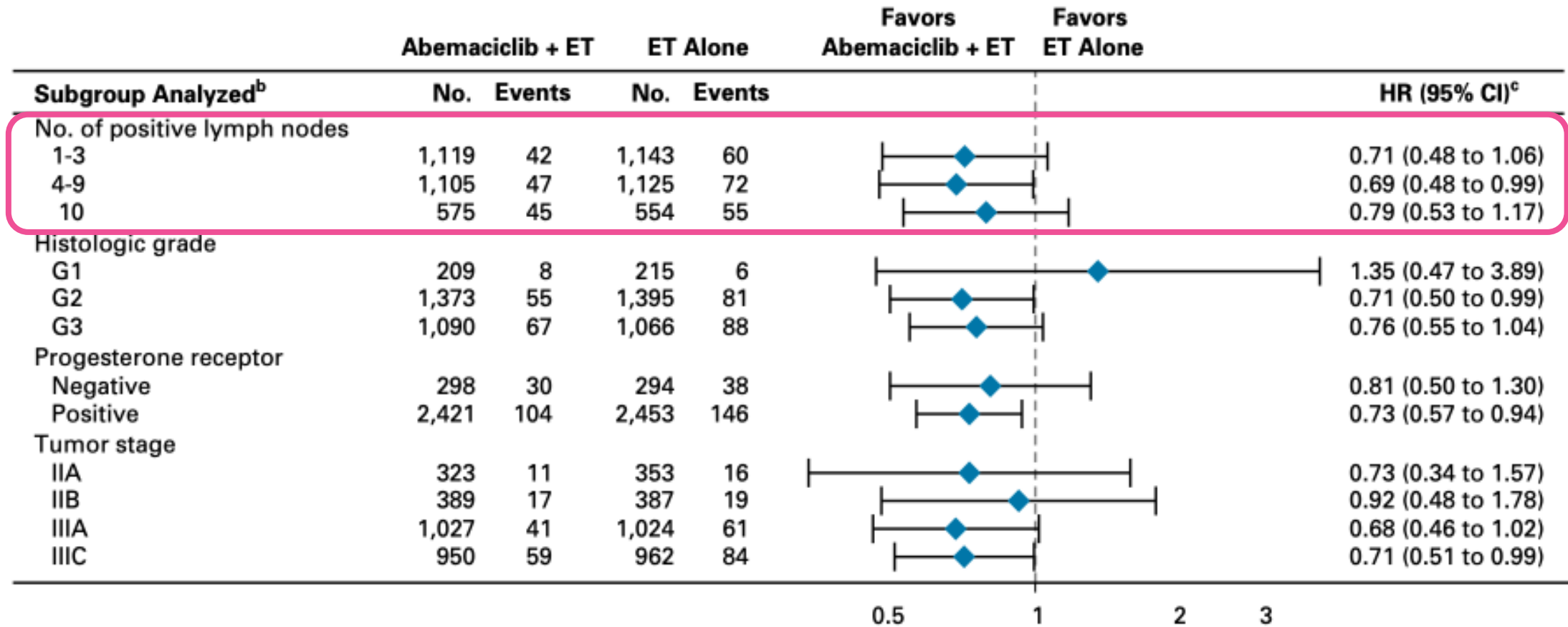
**15/179** pts with 1cN+ at pre-op. US had pN<sub>≥</sub>2 disease

# RxPONDER Trial (Postmenopausal Cohort)

## Outcomes According to Axillary Surgery and Nodal Involvement



# monarchE Trial



**NO DATA ABOUT THE TYPE OF AXILLARY SURGERY!**

«...RxPONDER and monarchE are **systemic therapy trials**,  
not surgical trials and should be interpreted  
in the context of nodal burden as determined  
by current surgical management of the axilla  
that has been defined by prospective randomized studies  
addressing that specific question»

# (My) Moral of The Story: If Biology Wins Over Anatomy...



...then lymphadenectomy is **NOT** essential  
for clinical decision-making

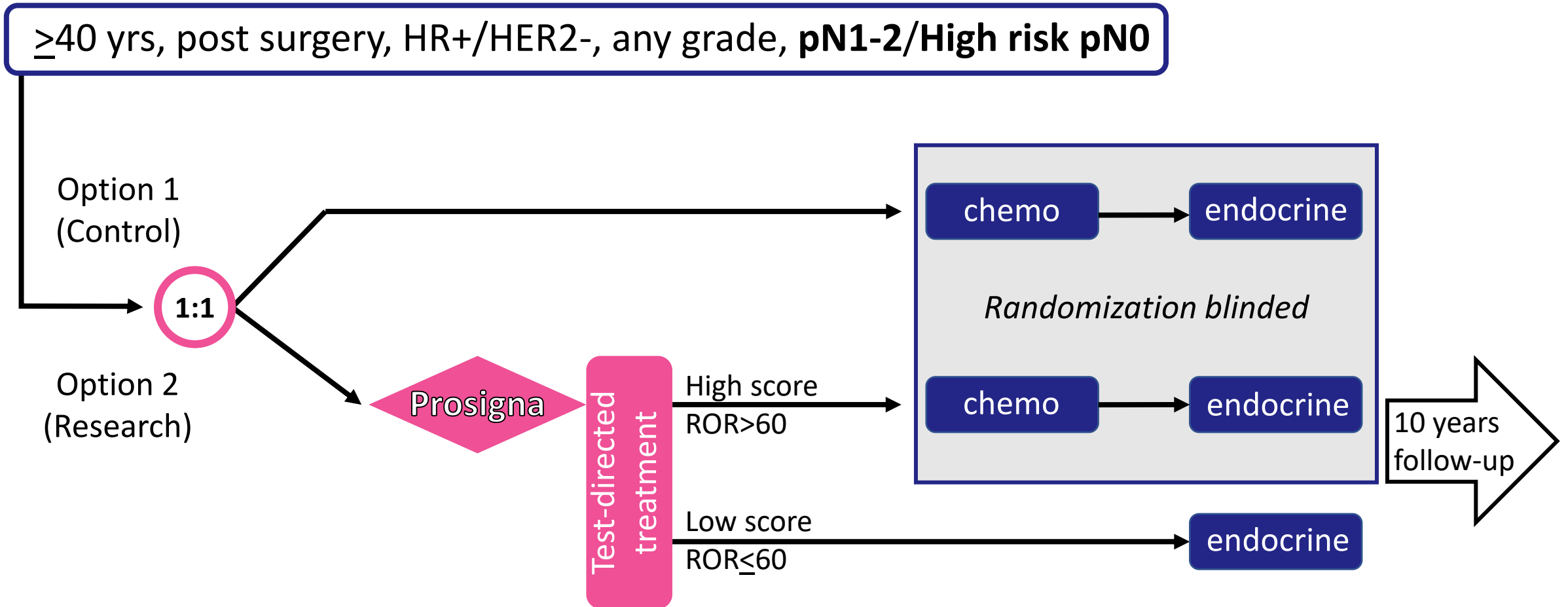
# Prologue

## This Is Not The End Of The Story





# OPTIMA Trial Design



# NATALee Trial Design

## Key Inclusion Criteria

- Women/men with HR+/HER- EBC
- Stage III OR  
Stage II with N1 OR  
Stage II with T3 N0 OR  
Stage II with T2 N0 and G3 OR  
G2 and Ki67 $\geq$ 20% and/or RS>25
- Completion of surgery, CT, RT

R  
1:1

Ribociclib (400 mg) for up to 36m  
+ NSAI +/- LHRHa (for up to 60m)

NSAI +/- LHRHa (for up to 60m)

**Stratified for:**  
Menopausal status  
Prior CT  
Region



KEEP  
CALM  
AND  
SLN ON