



8<sup>a</sup> edizione

Progetto **CANOA**

# **CARCINOMA MAMMARIO:**

QUALI NOVITA' PER IL 2018?

*"Saper leggere" uno studio clinico per migliorare la pratica clinica*

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Ospedaletto di Pescantina (VR) 23/24 Marzo 2018  
Villa Quaranta Park Hotel

# Quale impatto nella pratica clinica?

Chiara Saggia

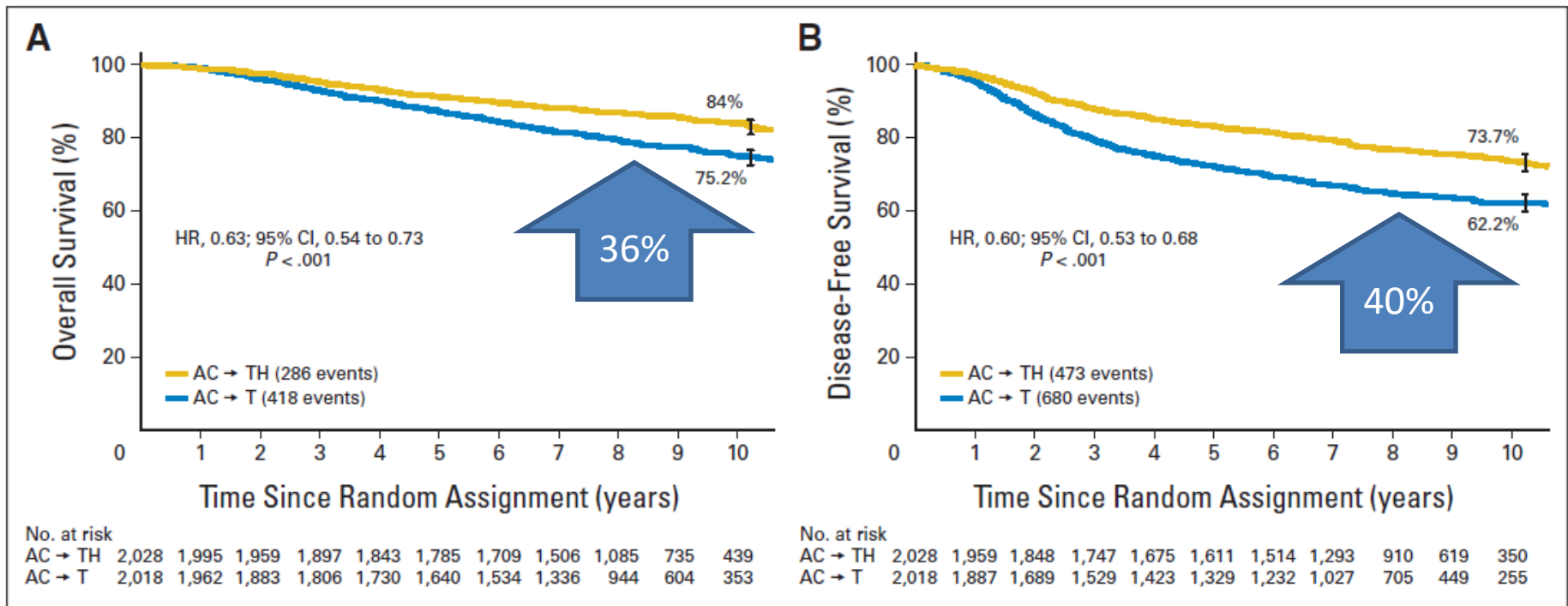
Oncologia

AOU "Maggiore della carità",  
Novara

# The standard

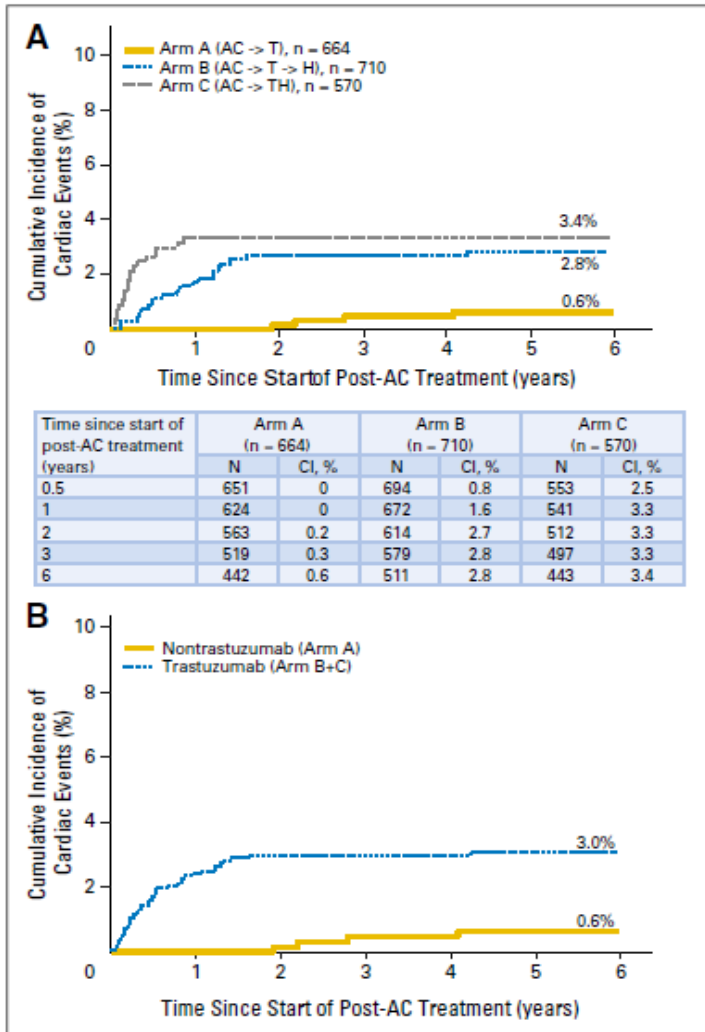
Trastuzumab Plus Adjuvant Chemotherapy for Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer: Planned Joint Analysis of Overall Survival From NSABP B-31 and NCCTG N9831

Median follow-up 8.4 years

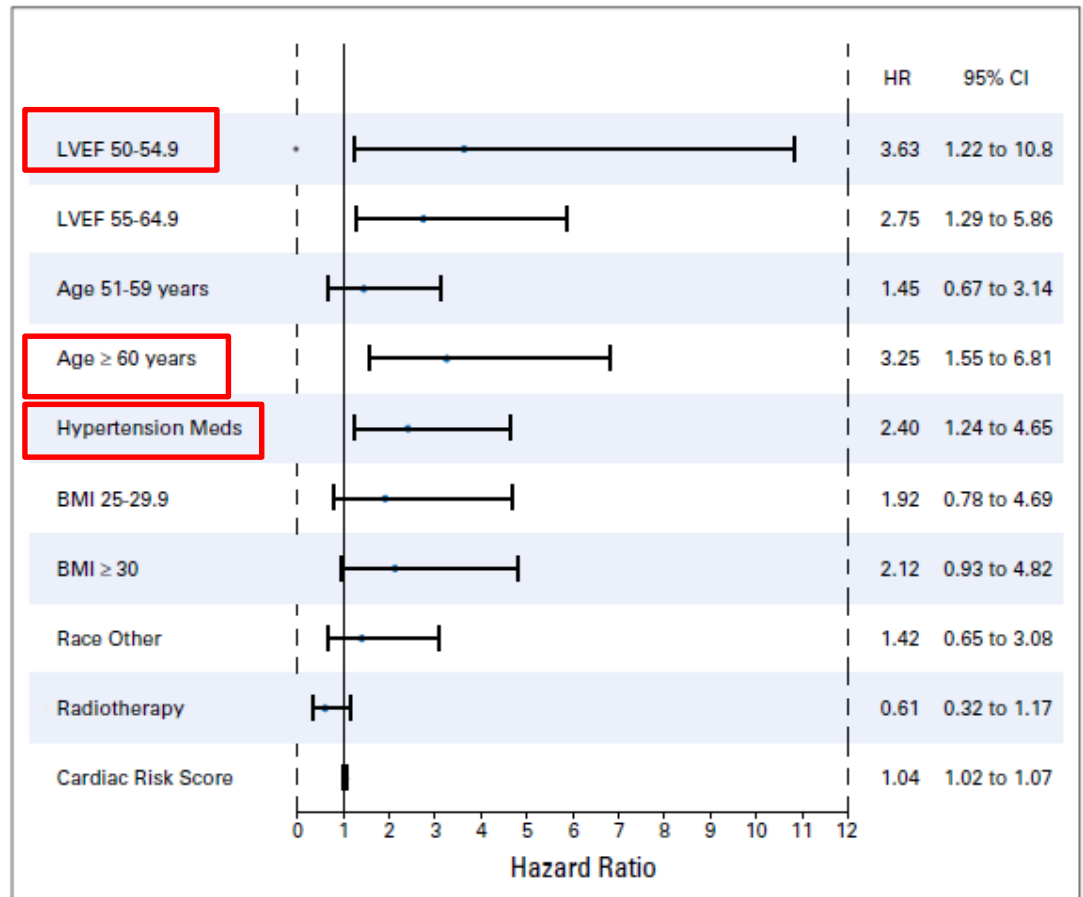


# The standard

## Long-Term Cardiac Safety Analysis of NCCTG N9831 (Alliance) Adjuvant Trastuzumab Trial



### Median follow-up 6 years



# The standard: Without anthracyclines...

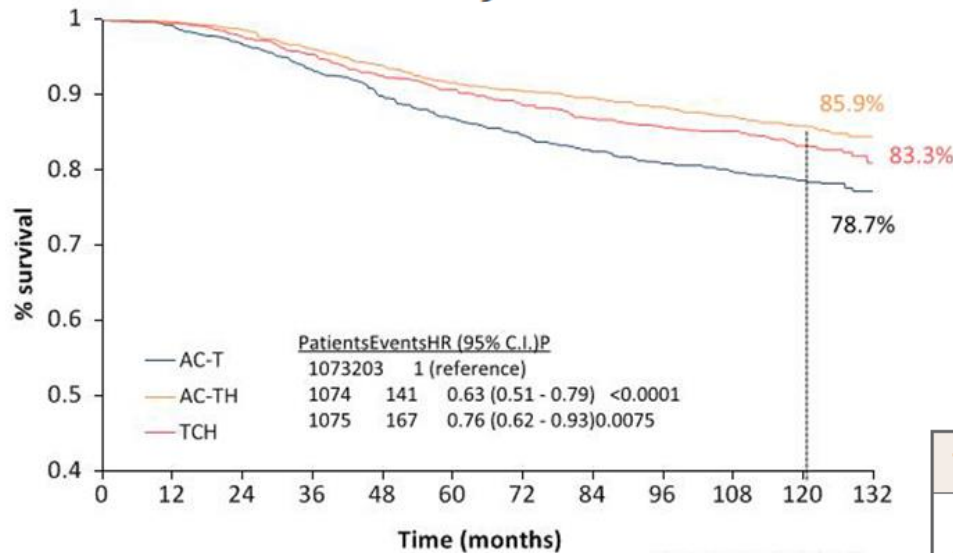
## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

OCTOBER 6, 2011

VOL. 365 NO. 14

### Adjuvant Trastuzumab in HER2-Positive Breast Cancer



**Table 2. Therapeutic Index for Critical Clinical Events.\***

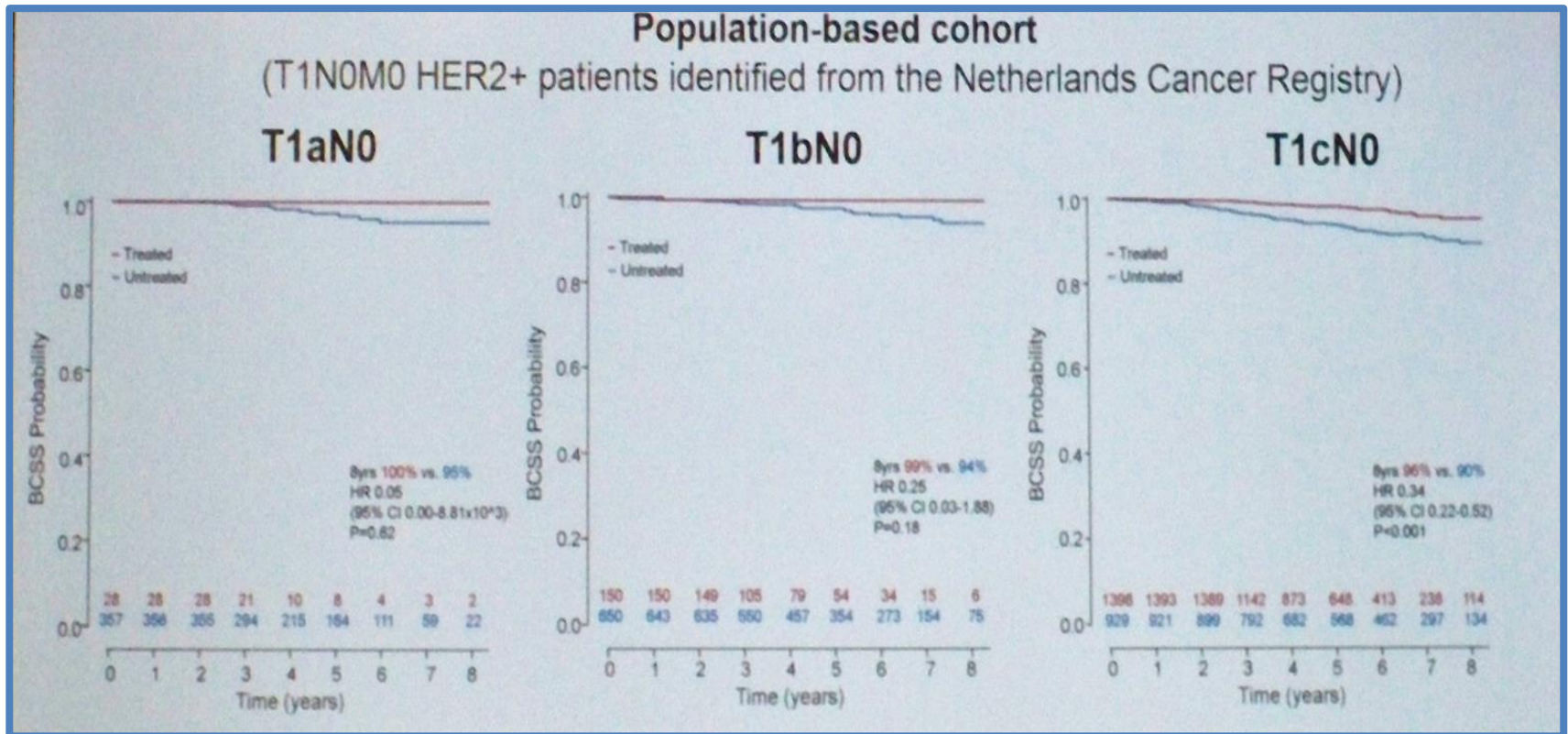
Clinical Event	AC-T	AC-T plus Trastuzumab	
		TCH	TCH
<i>number of events</i>			
Total events	201	146	149
Distant breast-cancer recurrence	188	124	144
Grade 3 or 4 congestive heart failure	7	21	4
Acute leukemia	6	1	1†

# Less is sufficient?

Breast Cancer Research and Treatment

July 2016, Volume 158, Issue 2, pp 361–371 | [Cite as](#)

## The effect of trastuzumab-based chemotherapy in small node-negative HER2-positive breast cancer



3512 patients

# Less is sufficient?

[Breast Cancer Research and Treatment](#)

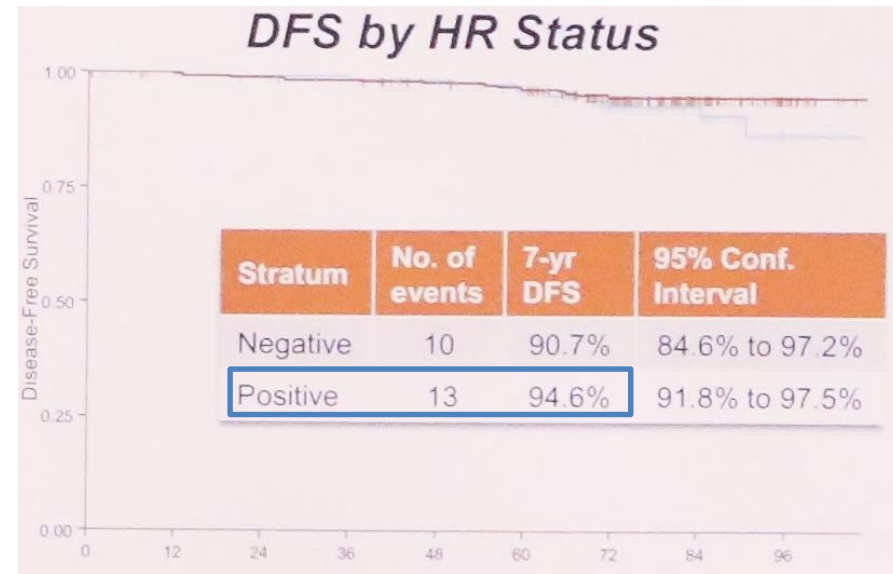
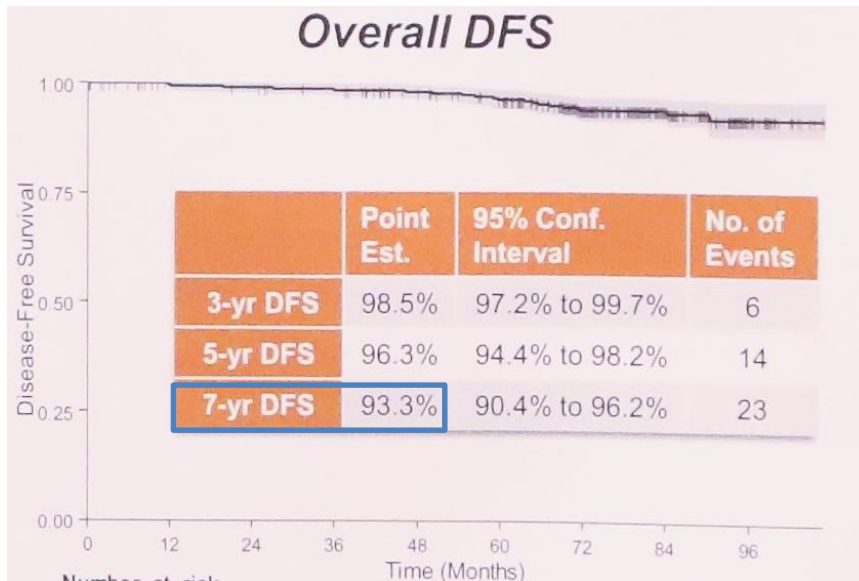
July 2016, Volume 158, [Issue 2](#), pp 361–371 | [Cite as](#)

## The effect of trastuzumab-based chemotherapy in small node-negative HER2-positive breast cancer

1. **T1N0 HER2 + EBC** have a good prognosis but still a sizeable risk of *relapse e death*
2. Adjuvant CT and/or Trastuzumab seem to provide a clinical meaningfully decrease of this risk ( $\geq 5\%$  ↓ death)
3. *Residual risk to trastuzumab-based therapy seems too small to justify to “add-on” therapy (regardless their potential benefit)*
4. *“De-escalation” should be instead considered*

# Less is sufficient: De-escalation

## Seven-year Follow-up of Adjuvant Paclitaxel and Trastuzumab (APT Trial) for Node-Negative, HER2+ Breast Cancer

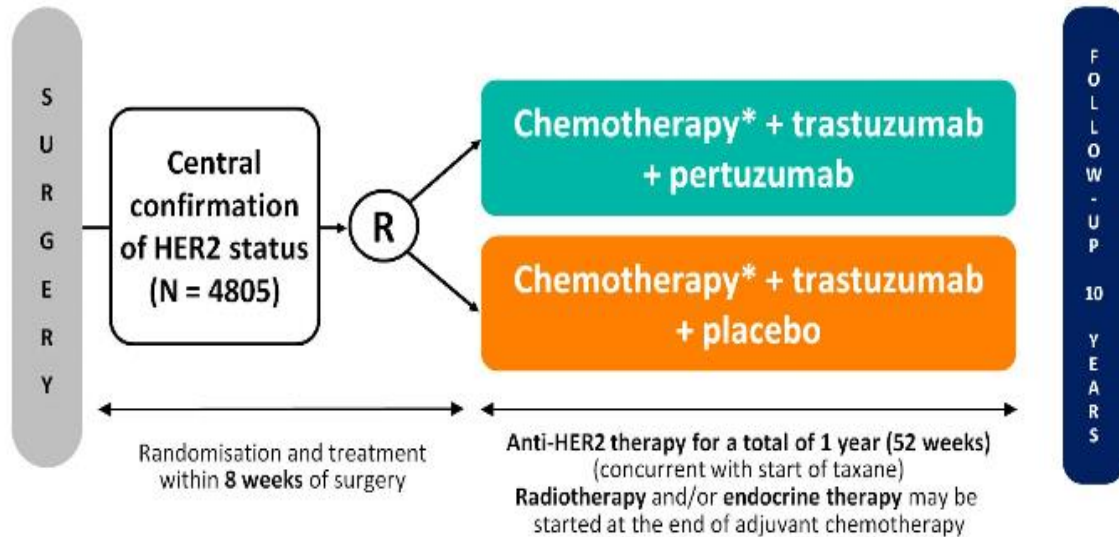


# APHINITY: More is better?

ORIGINAL ARTICLE

Adjuvant Pertuzumab and Trastuzumab  
in Early HER2-Positive Breast Cancer

## APHINITY: Trial Design



\*A number of standard anthracycline-taxane-sequences or a non-anthracycline (TCH) regimen were allowed

	EXPECTED 3-year IDFS rate Placebo vs. Pertuzumab
HR=0.75	89.2% vs. 91.8% ( $\Delta=2.6\%$ )



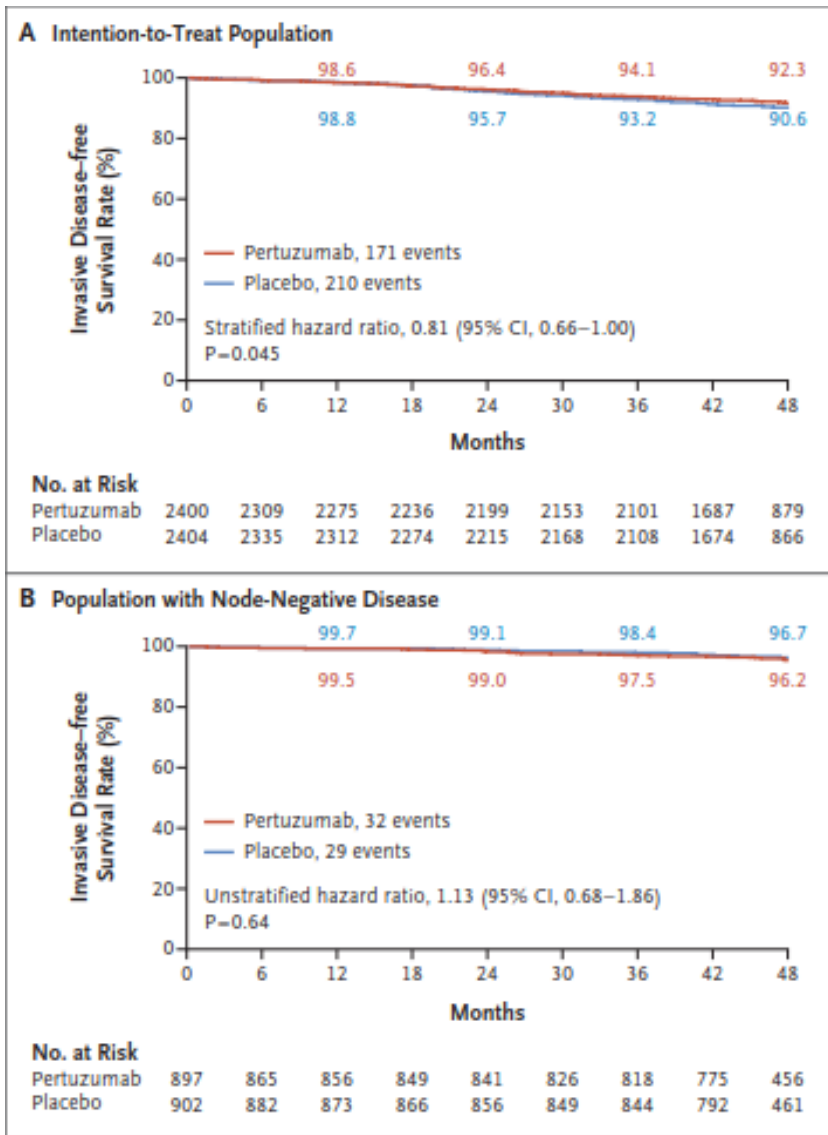
# APHINITY: More is better?

## APHINITY: IDFS Forest Plot by Subgroups

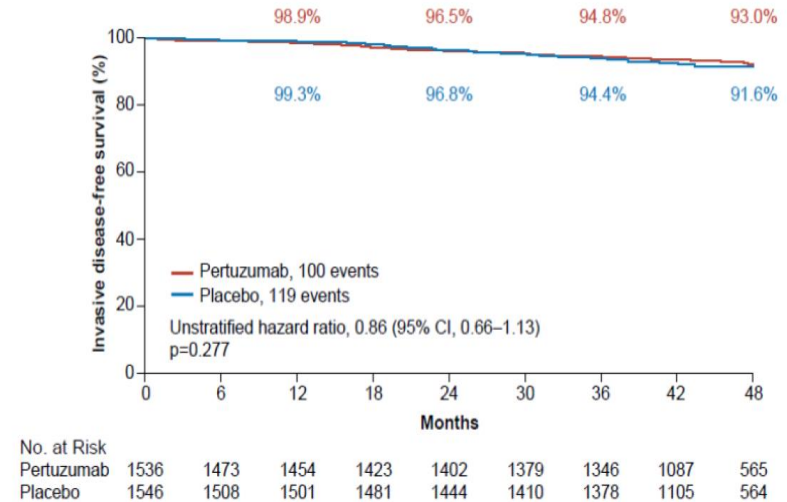
Subgroup	No. of Events / No. of Patients		Unstratified Hazard Ratio (95%CI)	3-year IDFS Rate, %		Interaction test p-value
	Pertuzumab	Placebo		Pertuzumab	Placebo	
All patients	171 / 2400	210 / 2404	0.82 (0.67-1.00)	94.1	93.2	NA
<b>Nodal status</b>						
0 positive nodes, tumor ≤ 2 cm					97.5	
0 positive nodes, tumor > 2 cm					98.5	0.374
1-3 positive nodes					93.8	
≥4 positive nodes					84.7	
<b>Adjuvant chemotherapy received</b>						
0 positive nodes					98.4	0.169
≥1 positive nodes					90.2	
Anthracycline					93.0	0.996
Non-anthracycline					94.0	
<b>Central hormone receptor status</b>						
Positive (ER- and/or PgR-positive)					94.4	0.543
Negative (ER- and PgR-negative)					91.2	

**RISULTATO INCONCLUSIVO E QUINDI...NON CONSIDERABILE RILEVANTE DAL PUNTO DI VISTA CLINICO**

# APHINITY: ITT

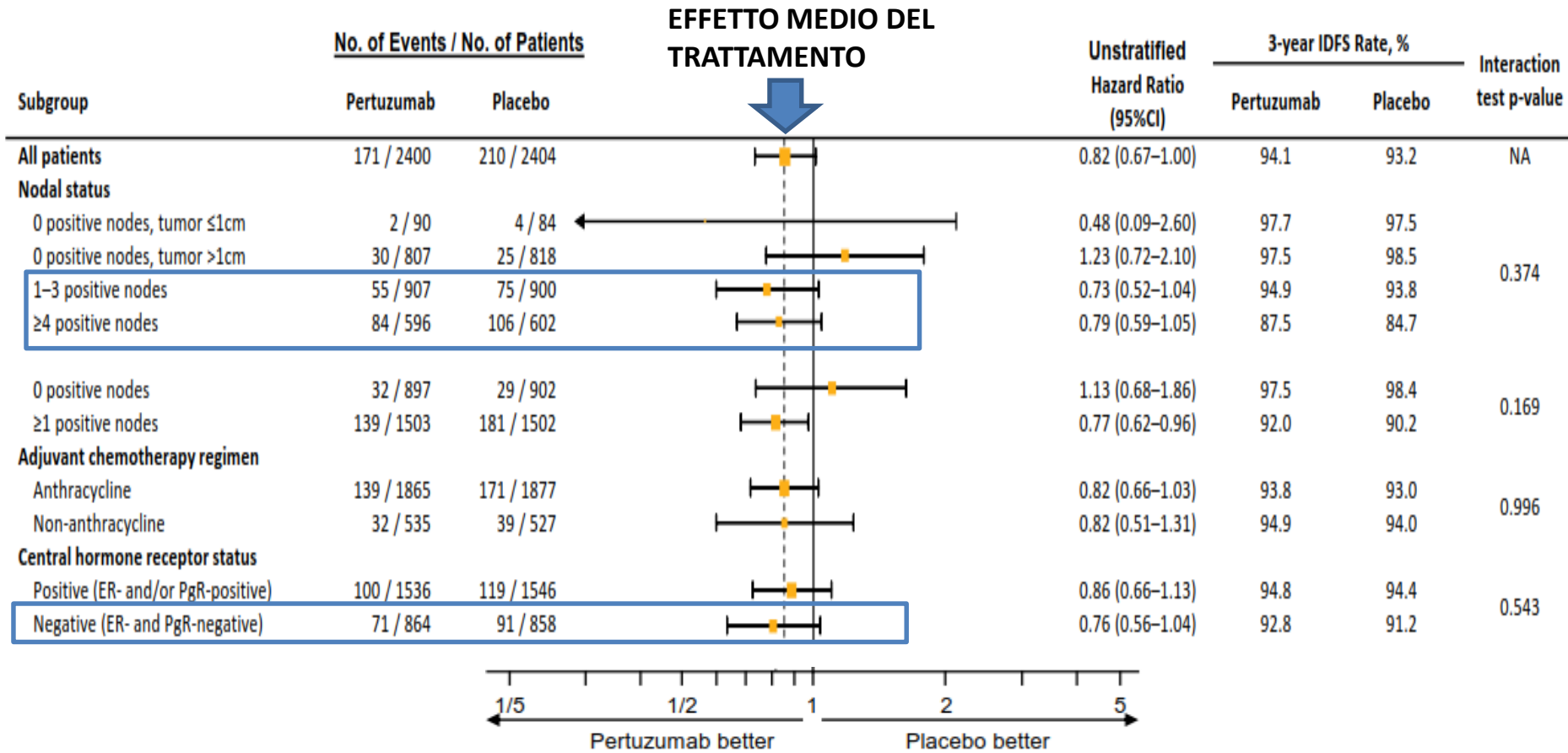


## APHINITY: Hormone Receptor-positive Subgroup



**ITT: devo trattare 112 paz per evitare un evento**

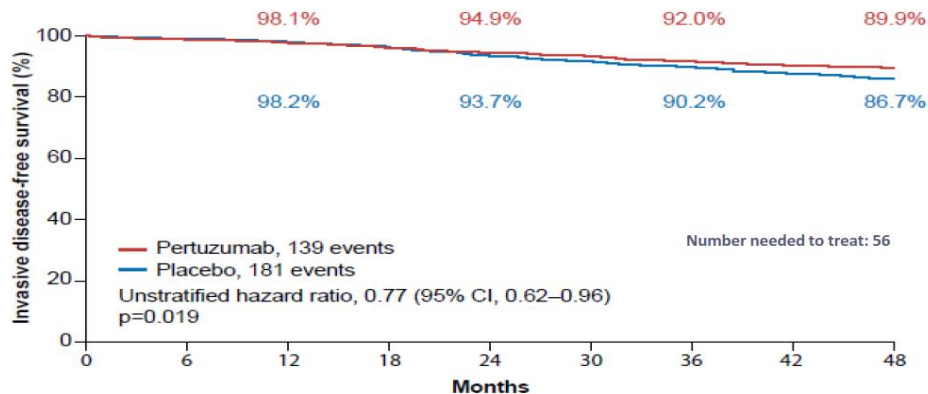
# APHINITY: IDFS Forest Plot by Subgroups



# APHINITY: SOTTOGRUPPI

## APHINITY: Node-positive Subgroup

$\Delta=3.2\%$

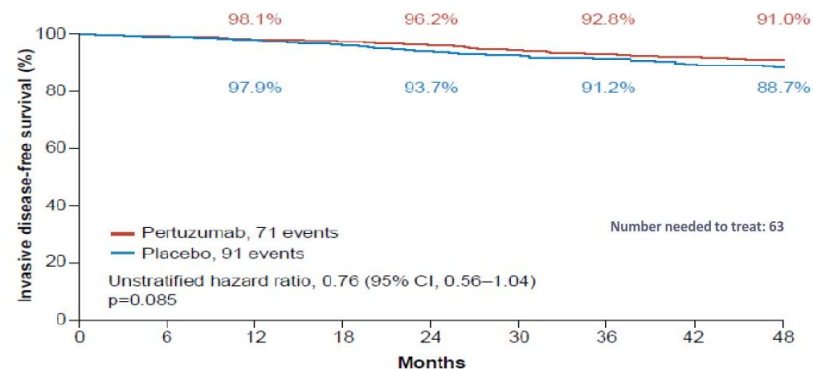


**N + : devo trattare 56 paz per evitare un evento**

No. at Risk	0	6	12	18	24	30	36	42	48
Pertuzumab	1503	1444	1419	1387	1358	1327	1283	912	423
Placebo	1502	1453	1439	1408	1359	1319	1264	882	405

## APHINITY: Hormone Receptor-negative Subgroup

$\Delta=2.3\%$



**ER- : devo trattare 63 pazienti per evitare un evento**

No. at Risk	0	6	12	18	24	30	36	42	48
Pertuzumab	864	836	821	813	797	774	755	600	314
Placebo	858	827	811	793	771	758	730	569	302

# DISCUSSIONE

- Le pazienti dello studio sono quelle del quesito quindi **la trasferibilità del dato alla clinica è possibile**
- Tuttavia dal punto di vista clinico rispetto IDFS **avremmo preferito come obiettivo primario OS per cui non è assolutamente sufficiente il follow-up di 3 anni presentato** e la DFS di cui mancano completamente i dati

# DISCUSSIONE

CLINICO-PATHOLOGICAL FEATURES (T AND N) SHOULD BE FINE-TUNED TO DEFINE A CONTINUOUS RISK OF RELAPSE

