

# Het lobulair carcinoom: Chemogevoelig?



Rudi Roumen

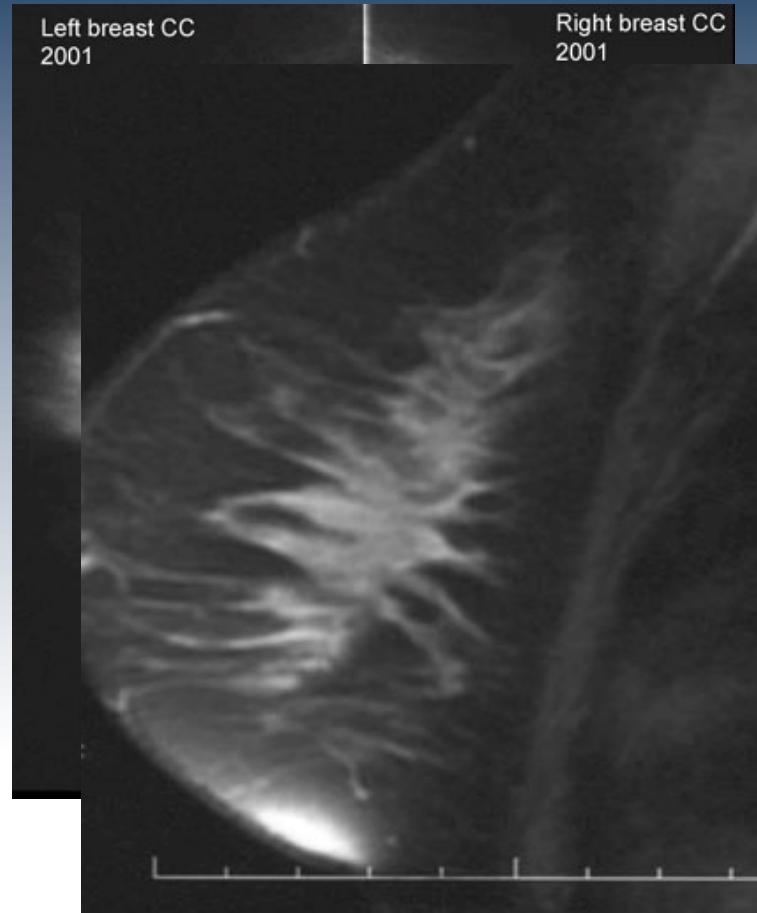
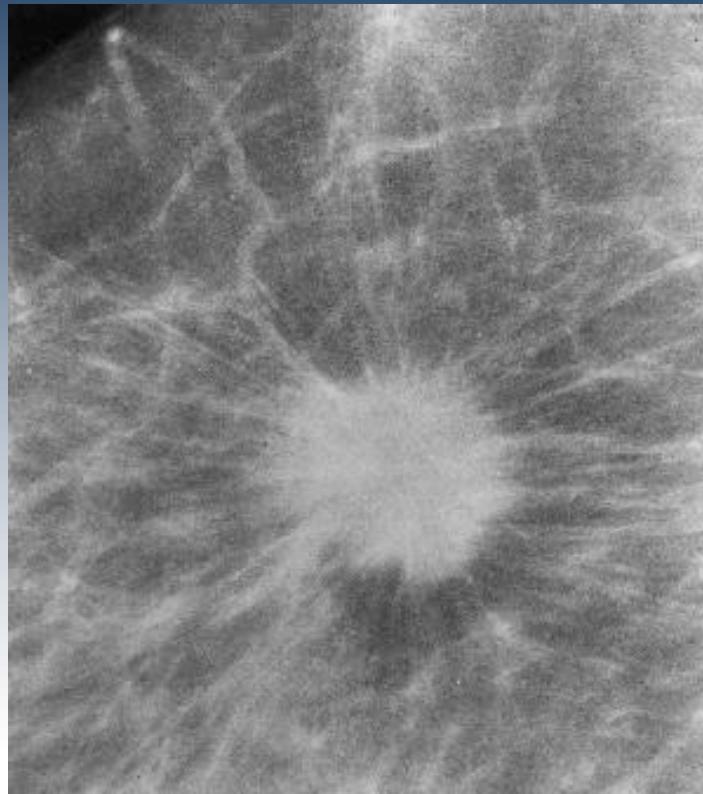
&



**A. Voogd** – G. Vreugdenhil – M. vdr Heiden-vdr Loo – S. Siesling – **W. Truin**



# Klinisch probleem



Jafri, 2007

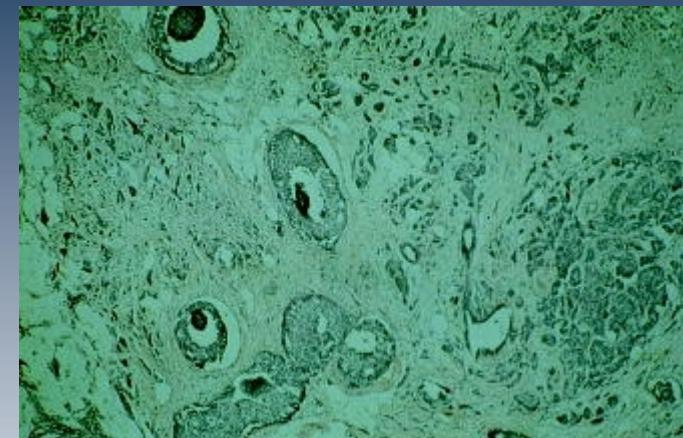


máxima  
medisch centrum  
gewoon goed

# Introductie

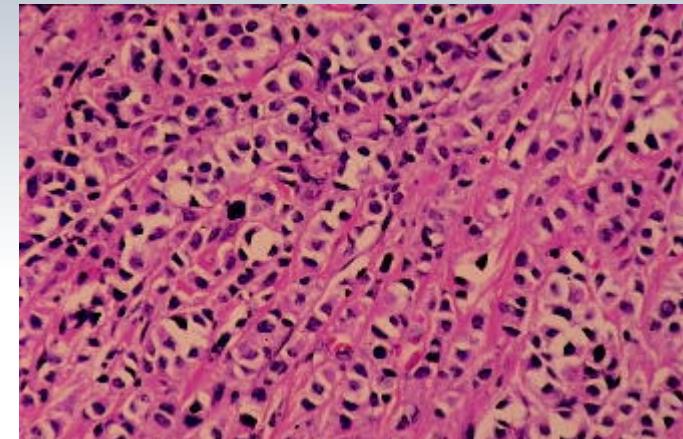
## Invasief mammacarcinoom

- 85% ductaal
- 15% lobulair



## Verschillen

- histologisch
- moleculair
- klinisch

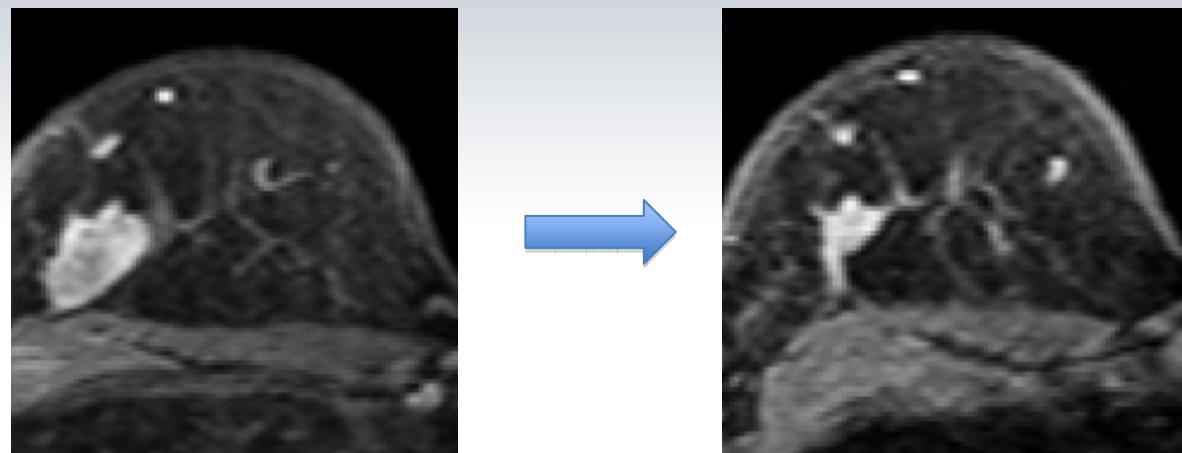


máxima  
medisch centrum  
gewoon goed

Pestalozzi, 2008  
Katz, 2007

# Neo-adjuvante therapie

- Doel
  - tumoren converteren naar operabel
  - in vivo respons meting
    - geen respons
    - partiële respons
    - complete respons (klinisch en histologisch)



máxima  
medisch centrum  
gewoon goed

# Respons

- Pathologische Complete Respons
  - ductaal: 10%
  - lobulair: < 2%
- Lagere chemosensitiviteit lobulair mamma carcinoom?



# Borstsparende therapie

- BST minder succesvol in ILC
- Surgical Margin Involvement bij BST
  - ILC 43% !!
  - IDC 16%
- Neo-adjuvante chemotherapie
  - geen toename van BST in ILC door neo-adjuvante chemotherapie

# Chemo en histologie

*"at present, our studies of adjuvant and neoadjuvant chemotherapy do not take histological distinction into account for stratification and treatment allocation"*

Katz, JCO 2005

*"frequently used guidelines still do not consider the potential differences in the natural history and treatment effectiveness between ILC and IDC, potentially exposing ILC patients to ineffective treatment"*

Katz, Lancet Oncology 2007

*"Even in the adjuvant setting, there is a lack of evidence regarding the degree of benefit of systemic chemotherapy for patients with classic ILC"*

Purushotham, JCO 2010

# Adjuvante therapie

Geen data over verschil in effect van  
*adjuvante* chemotherapie bij lobulair en ductaal  
carcinoom!!



máxima  
medisch centrum  
gewoon goed

Farese, 2009  
Purushotham, 2010

# Regionale data

## The Breast

Original article

Influence of histology on the effectiveness of adjuvant chemotherapy in patients with hormone receptor positive invasive breast cancer

Wilfred Truin <sup>a,\*</sup>, Adri C. Voogd <sup>b,e</sup>, Gerard Vreugdenhil <sup>c</sup>, Maurice J.C. van der Sangen <sup>d</sup>, Mike W.P.M. van Beek <sup>f</sup>, Rudi M.H. Roumen <sup>a</sup>

- IDC 1617 patiënten, ILC 498 patiënten
- Betere overall survival in IDC tov ILC
- In multivariate analyse geen significante verschillen
- Wel: trend naar beperkte waarde van adjuvante chemotherapie in ILC
- Te kleine aantallen?

# Dan dus naar de Landelijke Data-base

- 1995 tot 2008
- 25.000 pt. hormonaal adj behandeld + / - chemo
- Geen gemitastaseerde ziekte, 50 tot 70 jr
- Follow up > 10 jr (med 6jr)

Characteristic	Ductal (n = 19,609)	Pure Lobular (n = 3,685)
Age at diagnosis		
50-59	10,750	1,700
60-70	8,750	1,700
Period of diagnosis		

### Tumor size

T1	9,948	51	1,164	32
T2	8,251	42	1,836	50
T3	545	3	454	12
T4	452	2	101	3
Unknown	413	2	130	4

Unknown  
Tumor size  
T1

1,051      5      135      4

### Grade

1	2,218	11	394	11
2	7,551	39	1,550	42
3	7,076	36	418	11
Unknown	2,764	14	1,323	36

UNKNOWN  
Type of surgery  
Breast-conserving

2,764      14      1,323

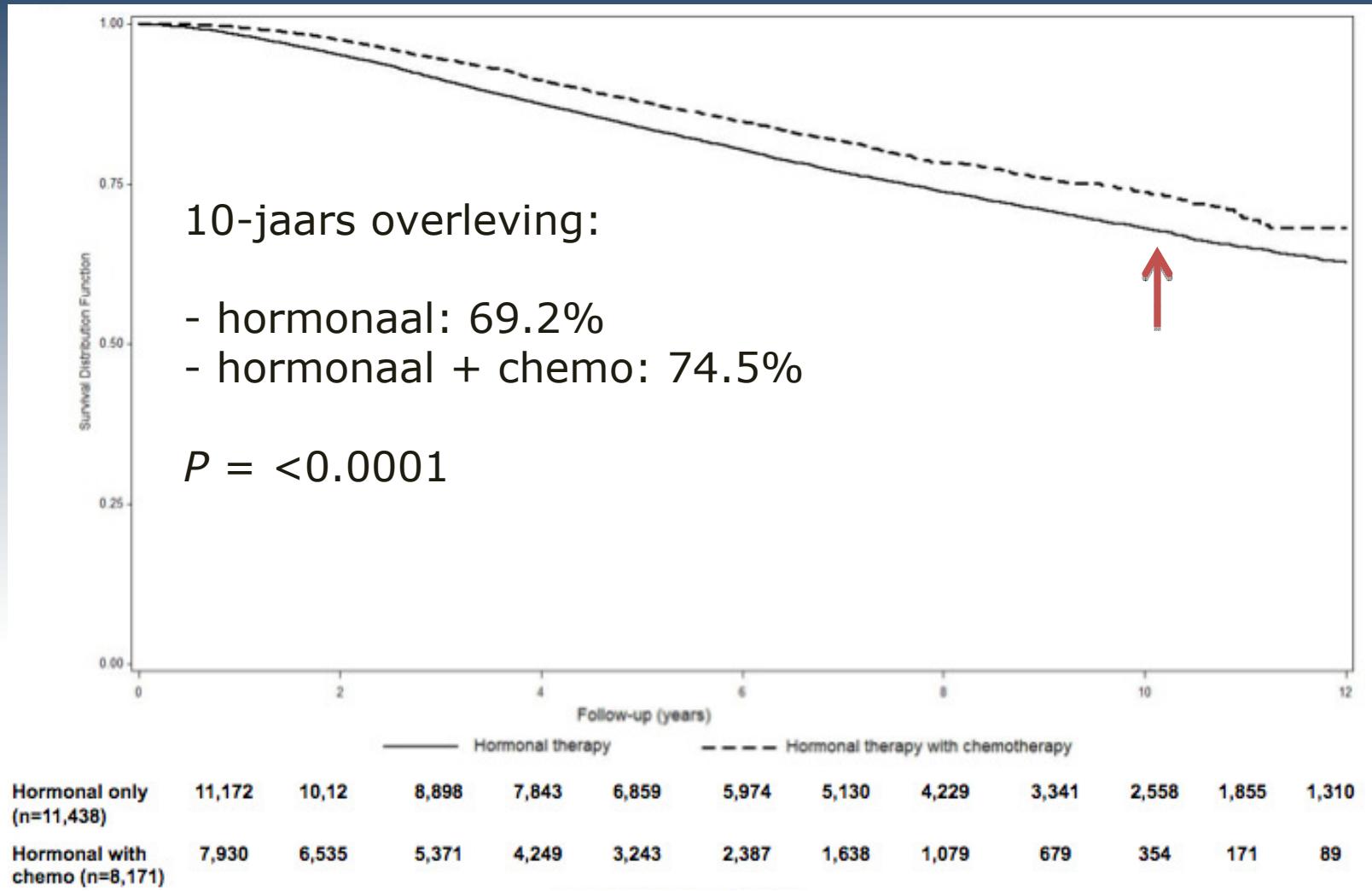
### Systemic treatment

Hormonal alone	11,438	58	2,170	59
Hormonal + Chemotherapy	8,171	42	1,515	41

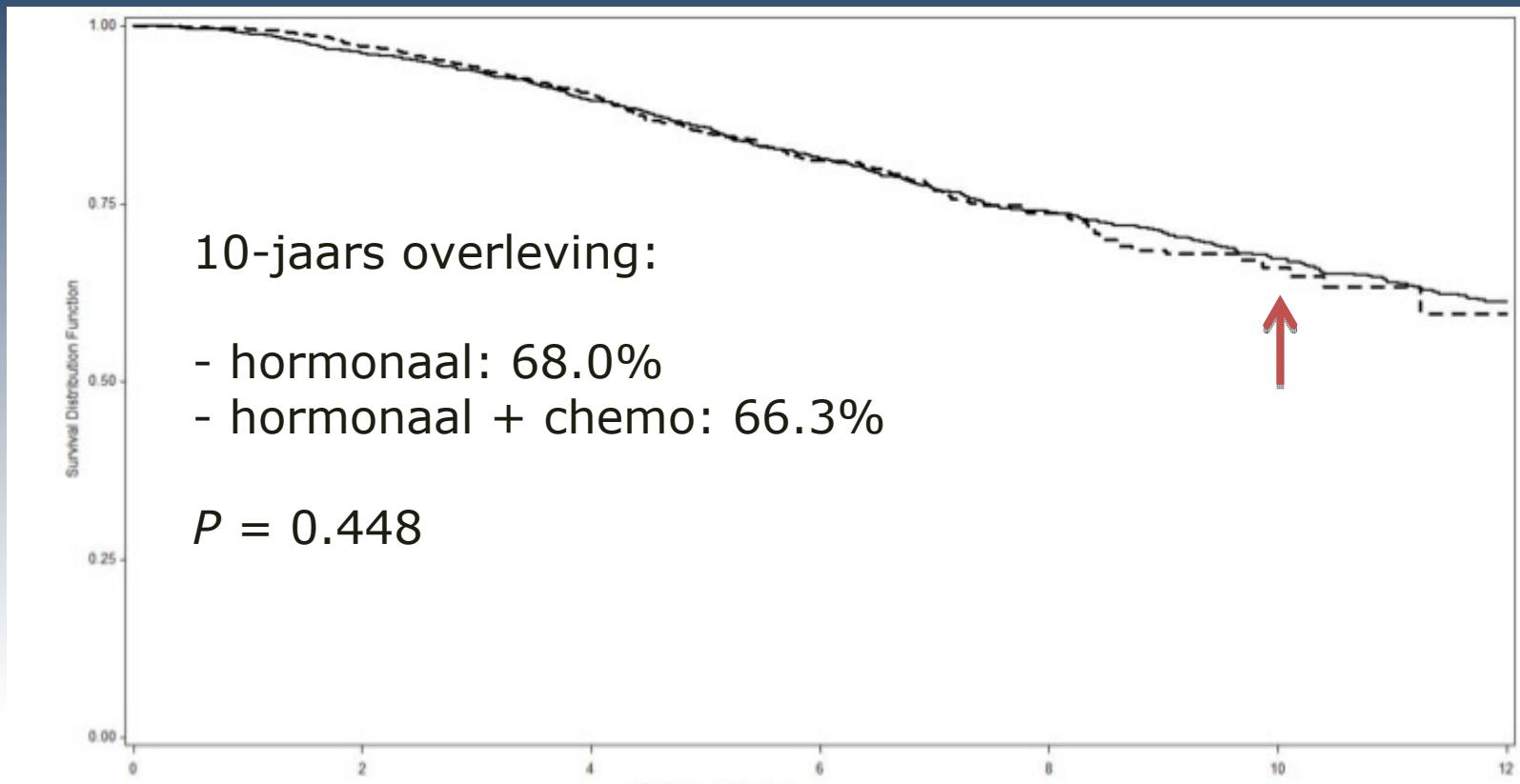
Systemic treatment  
Hormonal alone  
Hormonal + Chemotherapy

11,438      58      2,170      59  
8,171      42      1,515      41

# Ductaal carcinoom



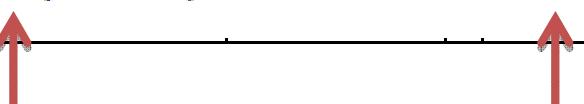
# Lobulair carcinoom



	2,124	1,897	1,701	1,495	1,305	1,128	988	823	656	490	352	242
Hormonal only (n=2,170)												
Hormonal with chemo (n=1,515)	1,469	1,214	979	756	547	404	284	190	115	54	22	13

# Multivariate analyse

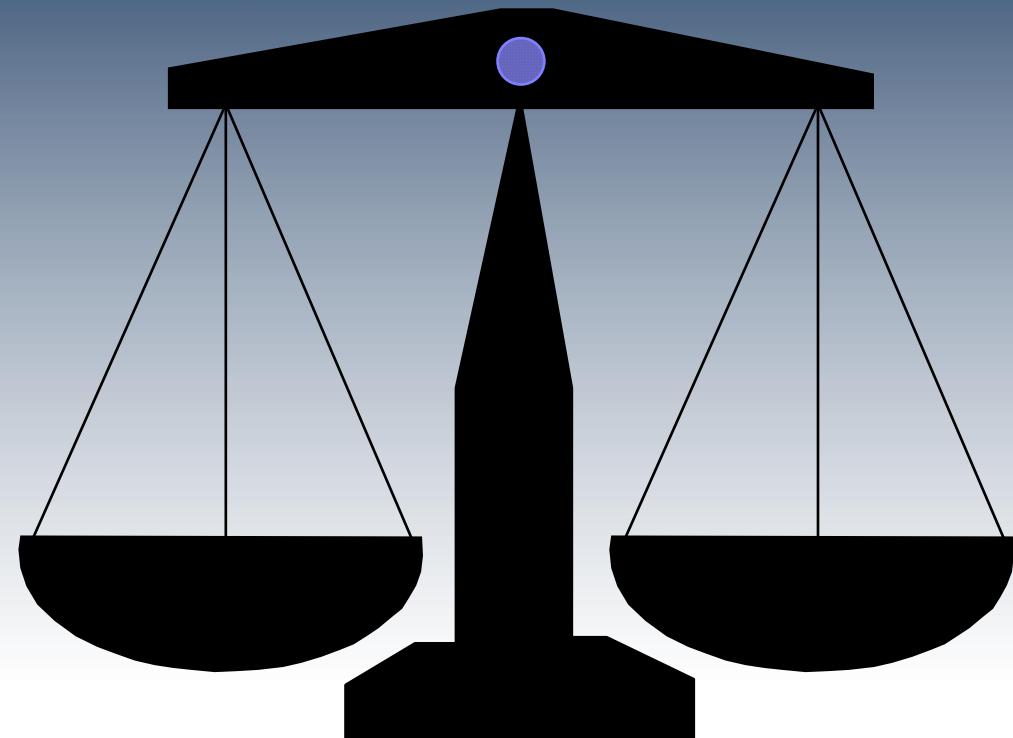
Variable	Ductal (n = 18,185)		Pure Lobular (n = 3,426)	
	Hazard Ratio for Events (95% CI)	P	Hazard Ratio for Events (95% CI)	P
<b>Age</b>				
Per year increase	1.03 (1.02-1.03)	<.00001	1.04 (1.03-1.06)	<.00001
<b>Nodal status</b>				
pN1mi versus pN0	1.04 (0.86-1.27)	.686	1.27 (0.81-1.97)	.297
pN1a versus pN0	2.10 (1.90-2.33)	<.00001	2.39 (1.86-3.07)	<.00001
pN>1a versus pN0	2.79 (2.44-3.20)	<.00001	3.39 (2.52-4.56)	<.00001
<b>Tumor size</b>				
T2 versus T1	1.68 (1.56-1.81)	<.00001	1.59 (1.32-1.92)	<.00001
T3-4 versus T1	2.88 (2.57-3.22)	<.00001	1.94 (1.55-2.43)	<.00001
<b>Grade</b>				
2 versus 1	1.61 (1.36-1.91)	<.00001	1.14 (0.82-1.58)	.433
3 versus 1	2.71 (2.30-3.20)	<.00001	1.54 (1.07-2.22)	.021
x versus 1	2.38 (2.00-2.82)	<.00001	1.42 (1.04-1.95)	.027
<b>Systemic adjuvant treatment</b>				
Hormonal + Chemotherapy versus Hormonal alone	0.70 (0.64-0.76)	<.00001	1.00 (0.82-1.21)	.965



# Conclusie

- Lobulair carcinoom is specifieke entiteit met eigen biologische, histologische, klinische en prognostische kenmerken
- Postmenopausale vrouwen met ER/PR+ lobulaire carcinomen hebben waarschijnlijk nauwelijks (geen?) baat bij adjuvante chemotherapie
- De rol van adjuvante chemotherapie in ILC moet opnieuw beoordeeld worden

# Bedankt voor uw aandacht!



máxima  
medisch centrum  
gewoon goed