

Radiothérapie après traitement néo-adjuvant

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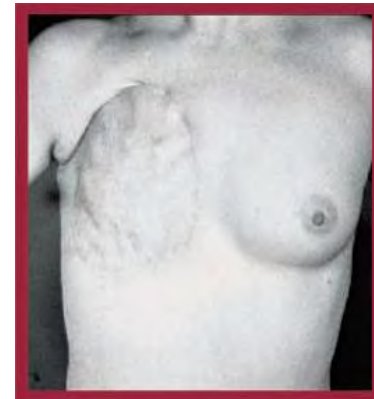
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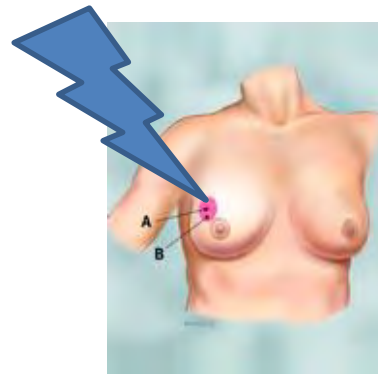
Traitement multimodal



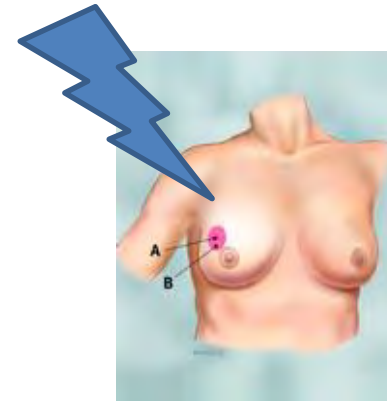
La maladie doit être réséquée à n'importe quel prix



Une chirurgie peut être moins invalidante si on y associe une modalité adjuvante



On améliore la survie des patientes en associant plus de modalités adjuvantes



On définit les traitements adjuvants sur la base des facteurs pronostics

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COMBINATION **CHEMOTHERAPY** AS AN ADJUVANT TREATMENT IN OPERABLE BREAST CANCER

GIANNI BONADONNA, M.D., ERCOLE BRUSAMOLINO, M.D., PINUCCIA VALAGUSSA, B.S.,
ANNA ROSSI, M.D., LUISA BRUGNATELLI, M.D., CRISTINA BRAMBILLA, M.D.,
MARIO DE LENA, M.D., GABRIELE TANCINI, M.D., EMILIO BAJETTA, M.D.,
RENATO MUSUMECI, M.D., AND UMBERTO VERONESI, M.D.

Abstract Prolonged cyclic combination chemotherapy with cyclophosphamide, methotrexate and fluorouracil was evaluated as adjuvant treatment to radical mastectomy in primary breast cancer with positive axillary lymph nodes.

After 27 months of study, treatment failure occurred in 24 per cent of 179 control patients and in 5.3 per cent of 207 women given combination chemotherapy ($P < 10^{-6}$), the advantage appearing statistically significant in all subgroups of patients. Patients with four or

more positive axillary nodes had a higher per cent of relapses than those with fewer nodes. The initial new clinical manifestations occurred in distant sites in 81.5 per cent of relapsed patients. Long-term chemotherapy produced an acceptable toxicity, thus allowing the administration of a high percentage of drug dosage. These results should be considered with caution, since, at present, the effect of this therapy on survival and possible long-term side effects remain unknown. (N Engl J Med 294:405-410, 1976)

La chirurgie apportait les informations pronostiques

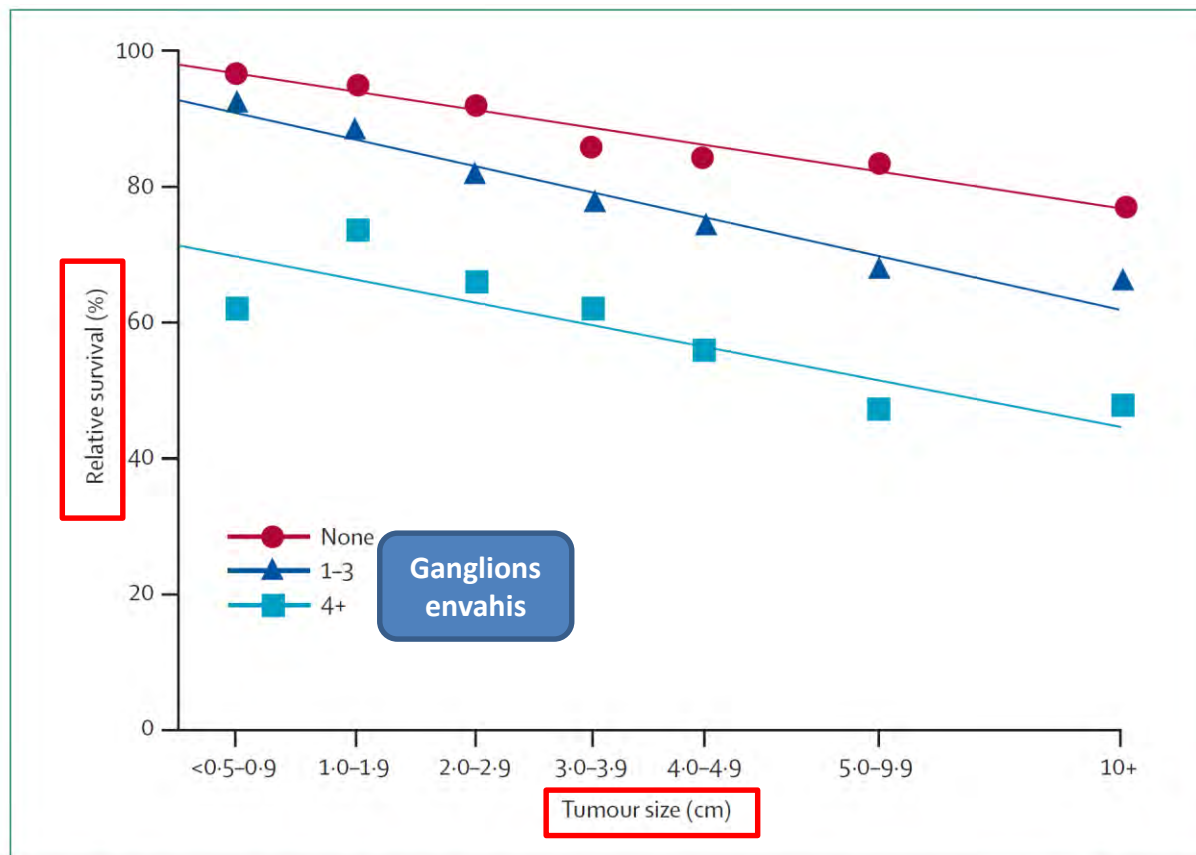
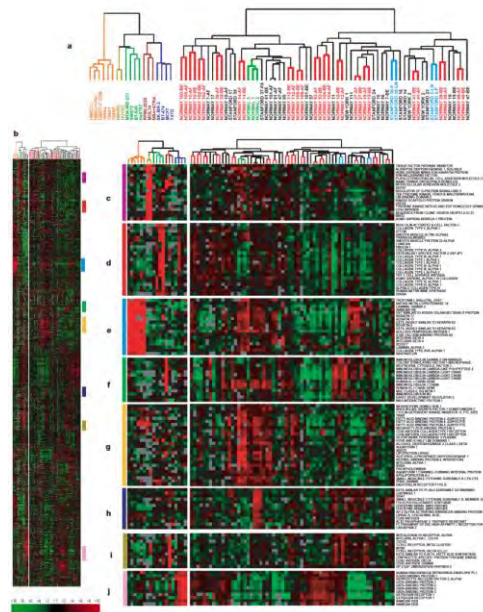


Figure 2: Relative rates of 5-year survival in relation to tumour size and number of positive regional lymph nodes (SEER database 1977-198²³).

La biologie apporte plus d'information pronostique et thérapeutique

Nature Reviews Clinical Oncology | Published online 13 Sep 2016; doi:10.1038/nrclinonc.2016.150

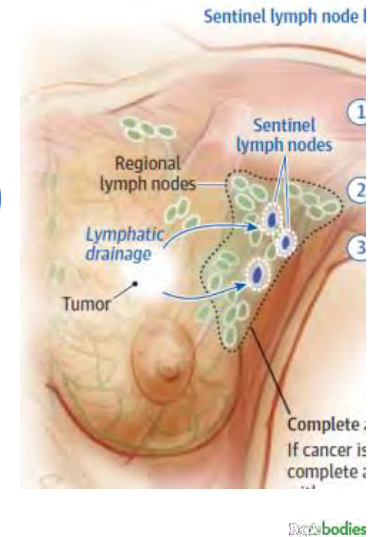
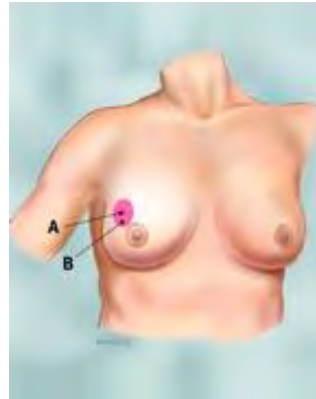


NATURE | VOL 406 | 17 AUGUST 2000 | www.nature.com



Un traitement préopératoire nous permet

De diminuer la maladie à réséquer

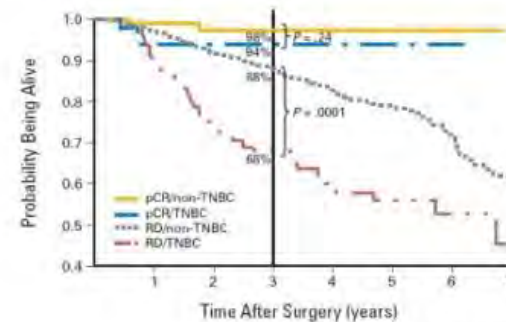


... mais la chirurgie n'apporte plus les mêmes informations quant à l'extension de la maladie

Un traitement préopératoire nous permet

- D'avoir l'information pronostique

Importance of Pathologic CR Overall Survival



Liedtke et al, JCO 2008; 26(8): 1275-81

Guidance for Industry

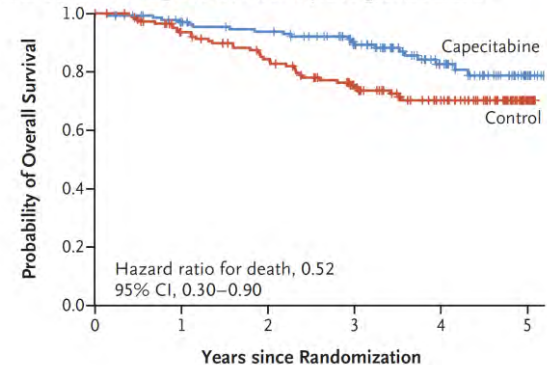
Pathological Complete Response in
Neoadjuvant Treatment of High-Risk
Early-Stage Breast Cancer: Use as an
Endpoint to Support Accelerated
Approval

- D'apprendre et faire évoluer plus vite le traitement

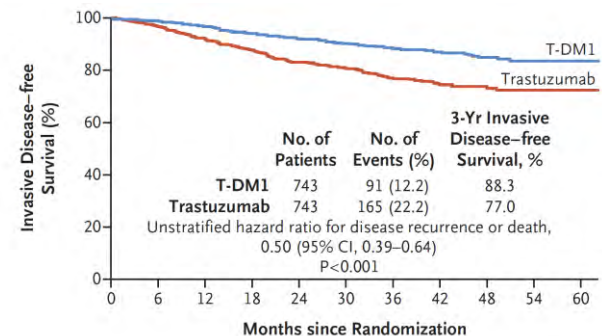
Un traitement préopératoire nous permet

- De sélectionner les patientes qui ne répondent pas au traitement systémique appliqué
- Pour compléter avec d'autres traitements systémiques

D Overall Survival among Patients with Triple-Negative Disease



N Engl J Med 2017;376:2147-59.



N Engl J Med 2019;380:617-28.

Donc, le traitement néo-adjuvant prend de plus en plus de place

Table 4. Systemic therapy for HER2-positive or triple-negative breast cancers

Stage		Tumor Subtype	
		HER2+	TNBC
Stage 1	T1a	TH – case by case	Chemotherapy – case by case
Typically as adjuvant therapy	T1b	TH	TC chemo
	T1c	TH	AC/T chemo
Stages 2 and 3		AC TH (± P) or TCH (± P) Consider neratinib in N2, ER+ tumors not receiving P	AC/T chemotherapy ± platinum ^a
Residual invasive cancer after NST		Trastuzumab emtansine	capecitabine

N2 = 4+ positive lymph nodes.

^aSome panelist prefer including platinum-based chemotherapy in women with BRCA1/2 associated breast cancers though data for this are inconsistent.

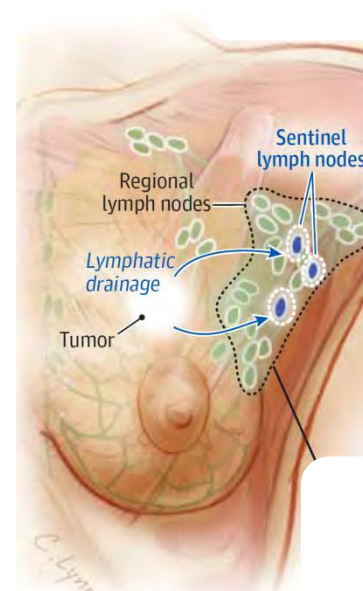
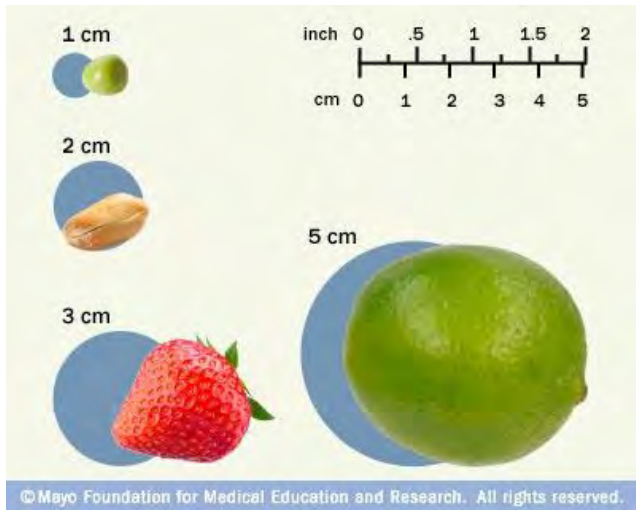
H, trastuzumab; P, pertuzumab; A, anthracycline chemotherapy; Cb, carboplatin chemotherapy; C, cyclophosphamide chemotherapy; T, taxane chemotherapy.

...mais, qu'en est-il de la radiothérapie dans ce contexte ?

Comment sont définies les indications de la RT ?



Facteurs pronostiques sur l'histologie définitive



JAMA October 9, 2013 Volume 310, Number 14

Mais qui viennent tous de l'expérience de chirurgie primaire.....

Quelle RT après NACT ?

RT selon le stade clinique ou pathologique ?



Standard actuel de RT après chimiothérapie néo adjuvante



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 3.2019
Invasive Breast Cancer

[NCC](#)

POTENTIALLY OPERABLE DISEASE: ADJUVANT THERAPY AFTER PREOPERATIVE SYSTEMIC THERAPY

- Complete planned chemotherapy regimen course if not completed preoperatively.
 - Consider adjuvant capecitabine in patients with triple-negative breast cancer and residual invasive cancer following standard neoadjuvant treatment with taxane-, alkylator-, and anthracycline-based chemotherapy.
- and
- Adjuvant radiation therapy^s is based on maximal disease stage from prechemotherapy tumor characteristics at diagnosis and post-chemotherapy pathology results.
 - ▶ Post mastectomy:^s
 - ◇ Strongly consider radiation to the chest wall + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk for clinical N1, ypN0.
 - ◇ For ANY positive axillary nodes after chemotherapy, radiation therapy as indicated to the chest wall + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk.
 - ▶ Post lumpectomy:^s
 - ◇ Adjuvant radiation post-lumpectomy is indicated to the whole breast with or without boost to the tumor bed.
 - ◇ Strongly consider radiation to the whole breast + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk for clinical N1, ypN0.
 - ◇ For ANY positive axillary nodes after chemotherapy, radiation therapy as indicated to the whole breast + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk.

Pourtant...

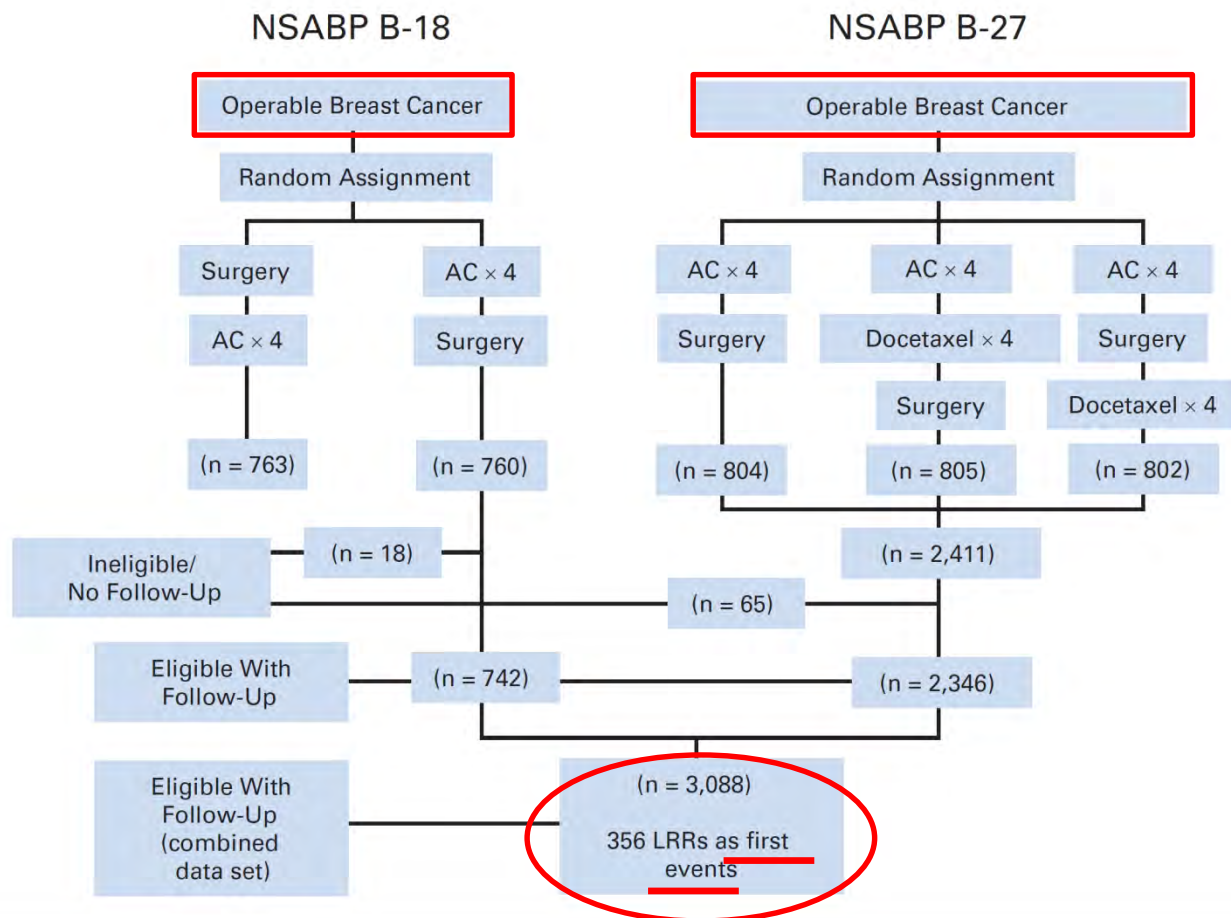
Evidence préliminaire

- La NACT *peut* changer le risque de récidence locorégionale en fonction de la réponse
- *Peut-être* il y a la place pour moins de RT aux bonnes répondeuses
- et pour plus de RT aux mauvaises répondeuses?

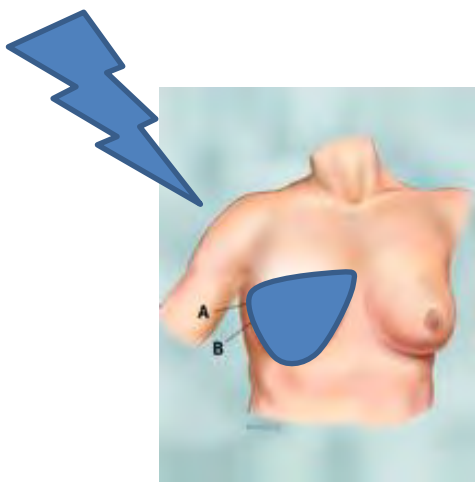
Quelle est l'évidence ?

Predictors of Locoregional Recurrence After Neoadjuvant Chemotherapy: Results From Combined Analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27

Eleftherios P. Mamounas, Stewart J. Anderson, James J. Dignam, Harry D. Bear, Thomas B. Julian,
Charles E. Geyer Jr, Alphonse Taghian, D. Lawrence Wickerham, and Norman Wolmark



RT standard dans les études NSABP B18 et 28



**RT du
sein**



**Pas de
RT**

Facteurs pronostics de la récurrence locorégionale

Table 2. Multivariate Analysis of Independent Predictors of 10-Year LRR in the Combined Data Set*

Variable	HR	95% CI	P
Age ≥ 50 v < 50 year†	0.78	0.63 to 0.98	.03
Clinical tumor size > 5 v ≤ 5 cm†	1.51	1.19 to 1.91	$< .001$
Clinical nodal status cN(+) v cN(-)†	1.61	1.28 to 2.02	$< .001$
Nodal/breast pathologic status			$< .001$
ypN(-)/no <u>breast pCR</u> v ypN(-)/breast pCR†	1.55	1.01 to 2.39	
ypN(+) <u> v ypN(-)/breast pCR†</u>	2.71	1.79 to 4.09	

Clinique

Réponse

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ORIGINAL REPORT

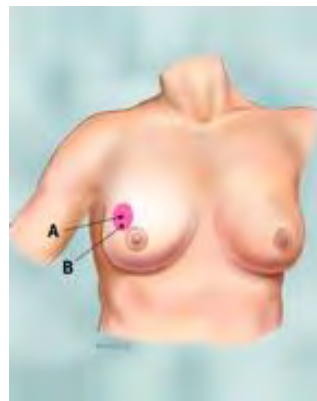
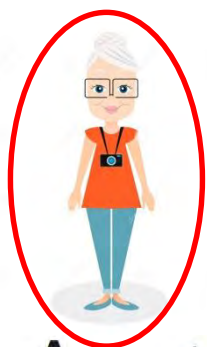
Predictors of Locoregional Recurrence After Neoadjuvant Chemotherapy: Results From Combined Analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27

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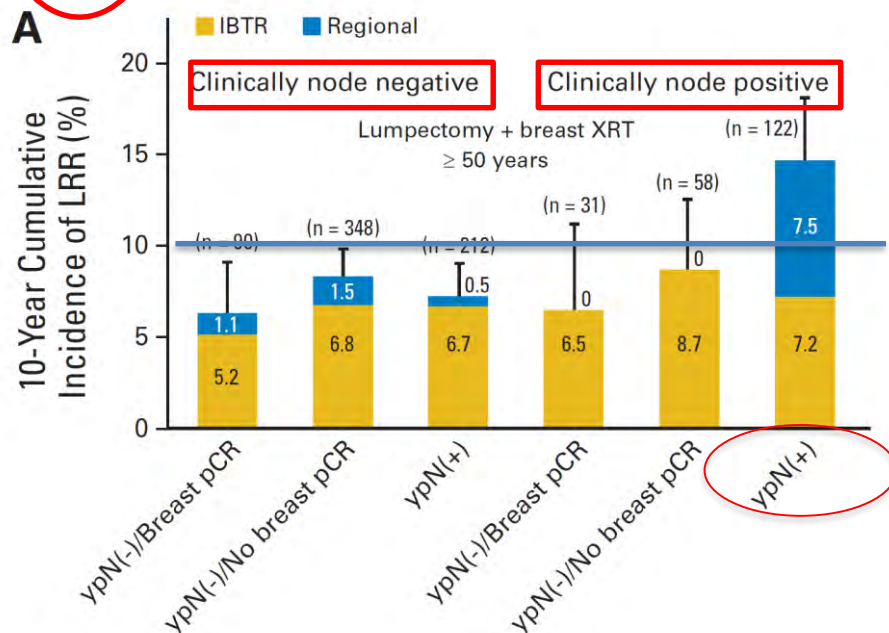
En fonction de la chirurgie effectuée

Table 3. Multivariate Analysis of Independent Predictors of 10-Year LRR According to Type of Surgery

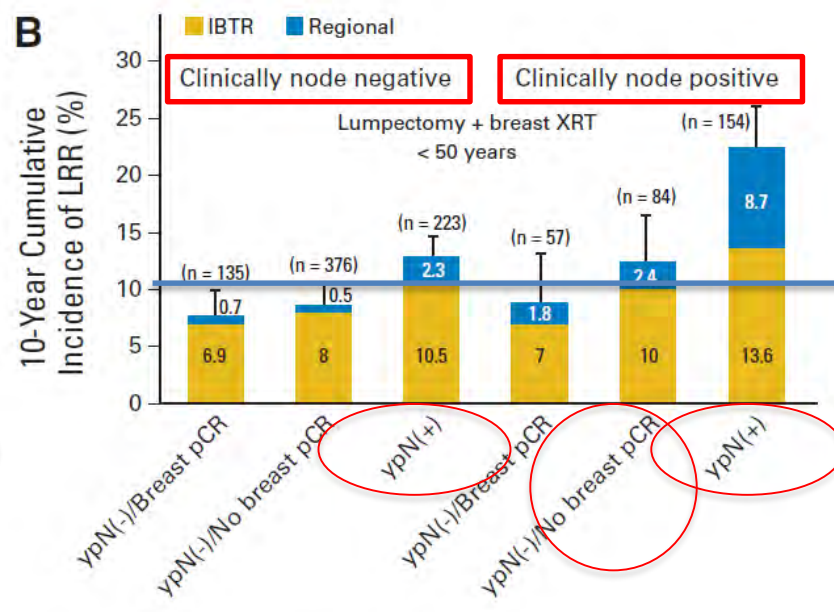
Variable	No. of Patients	LRR Events	HR	95% CI	P
Patients treated with mastectomy*	1,071	131			
Clinical tumor size > 5 v ≤ 5 cm†			1.58	1.12 to 2.23	.0095
Clinical nodal status cN(+) v cN(-)†			1.53	1.08 to 2.18	.017
Nodal/breast pathologic status					< .001
ypN(-)/no breast pCR v ypN(-)/breast pCR†			2.21	0.77 to 6.30	
ypN(+) v ypN(-)/breast pCR†			4.48	1.64 to 12.21	
Patients treated with lumpectomy plus breast XRT*	1,890	189			
Age ≥ 50 v < 50 years			0.71	0.53 to 0.96	.025
Clinical nodal status cN(+) v cN(-)†			1.70	1.26 to 2.31	< .001
Nodal/breast pathologic status					< .001
ypN(-)/no breast pCR v ypN(-)/breast pCR†			1.44	0.90 to 2.33	
ypN(+) v ypN(-)/breast pCR†			2.25	1.41 to 3.59	



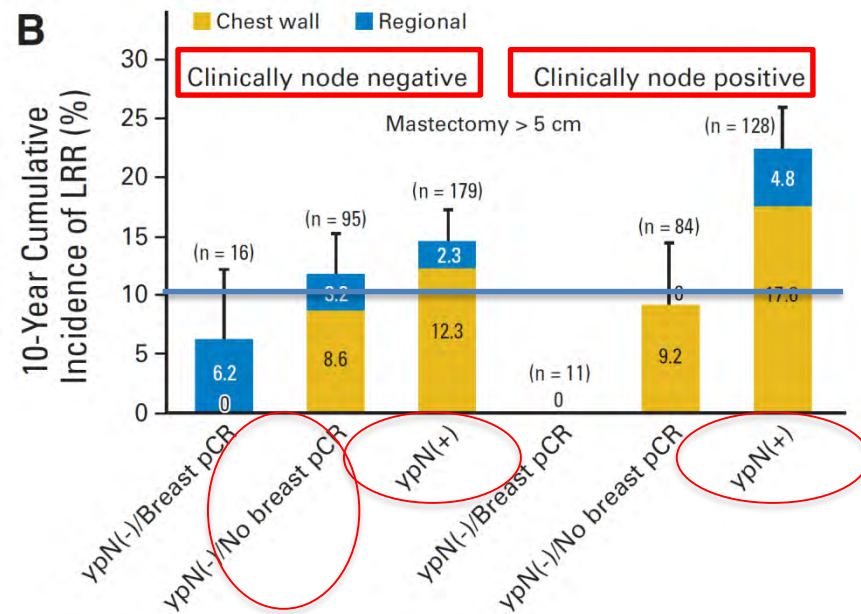
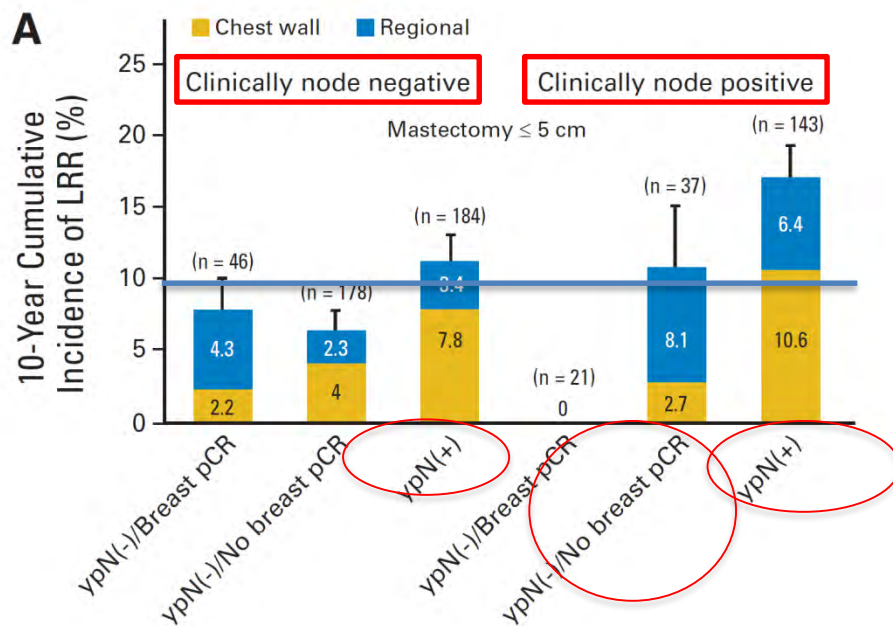
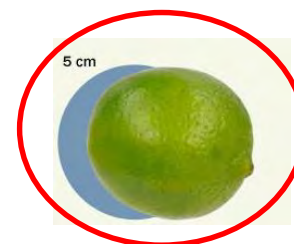
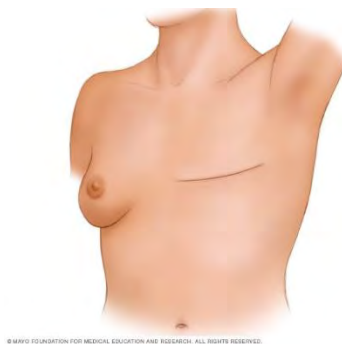
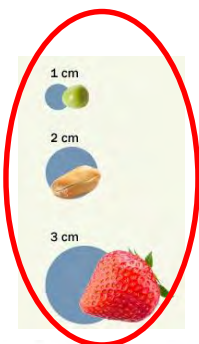
A



B

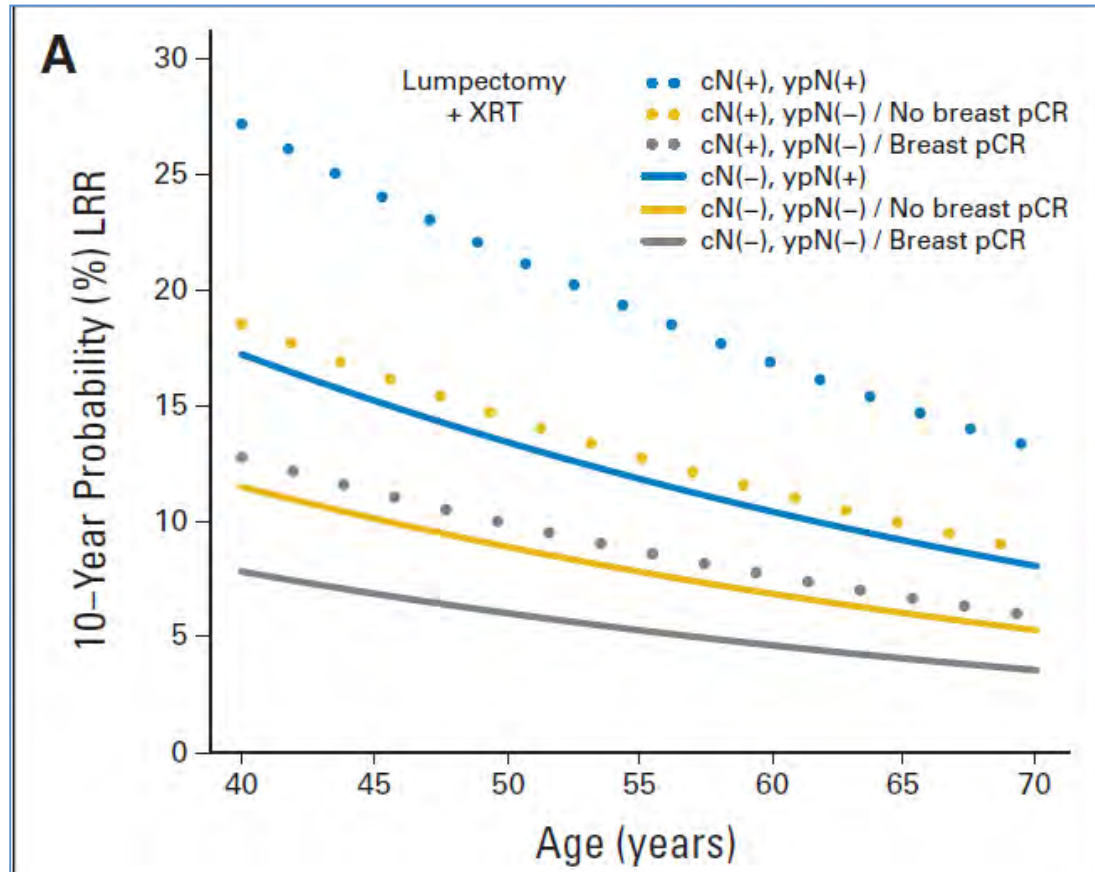


Attention: que RT locale !

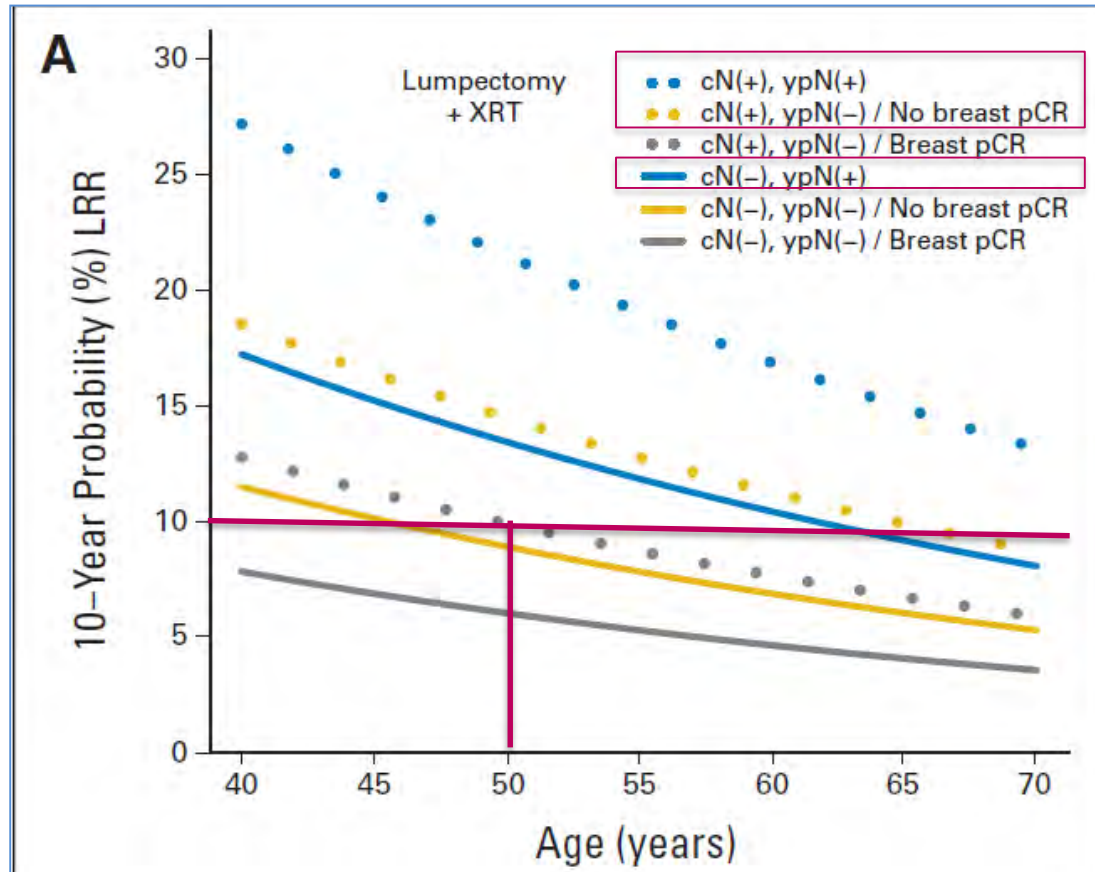


Attention: pas de RT!

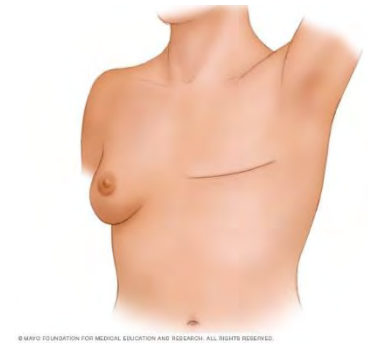
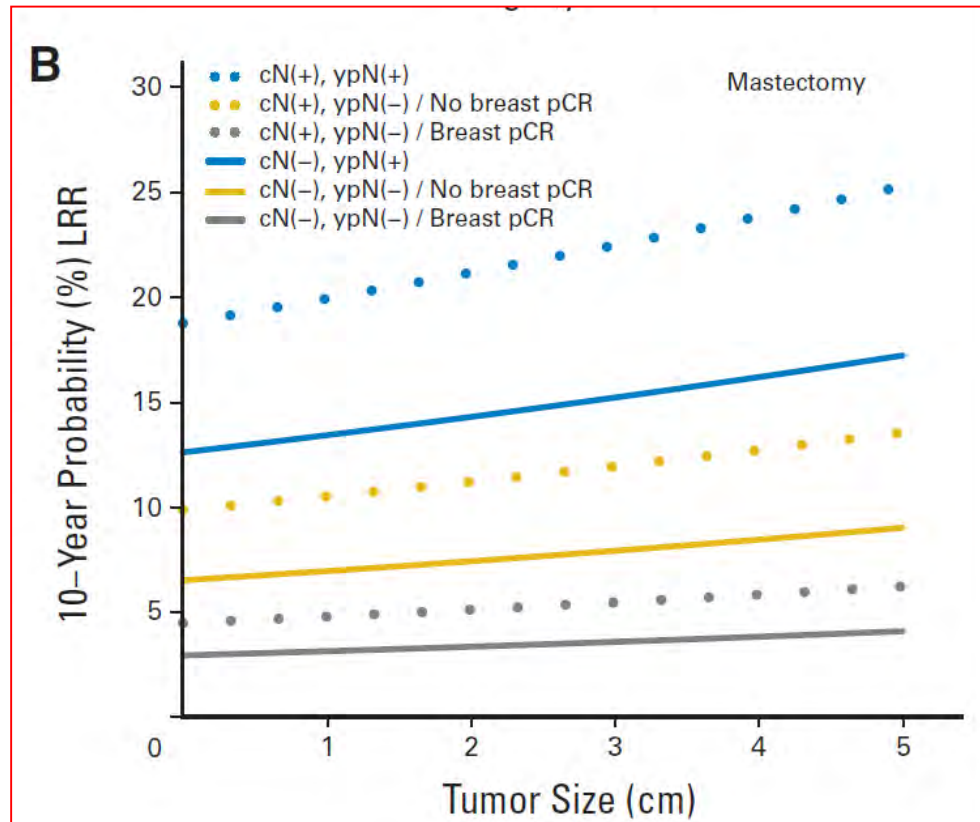
Nomogramme pour la prédiction du risque de la récurrence locorégionale à 10 ans après Chirurgie conservatrice et RT locale



Nomogramme pour la prédiction du risque de la récurrence locorégionale à 10 ans après Chirurgie conservatrice et RT locale

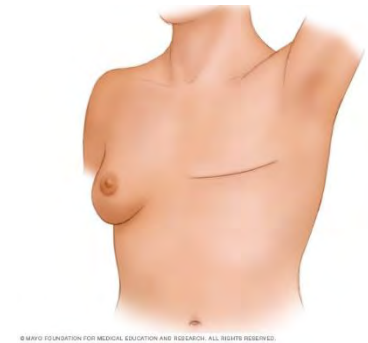
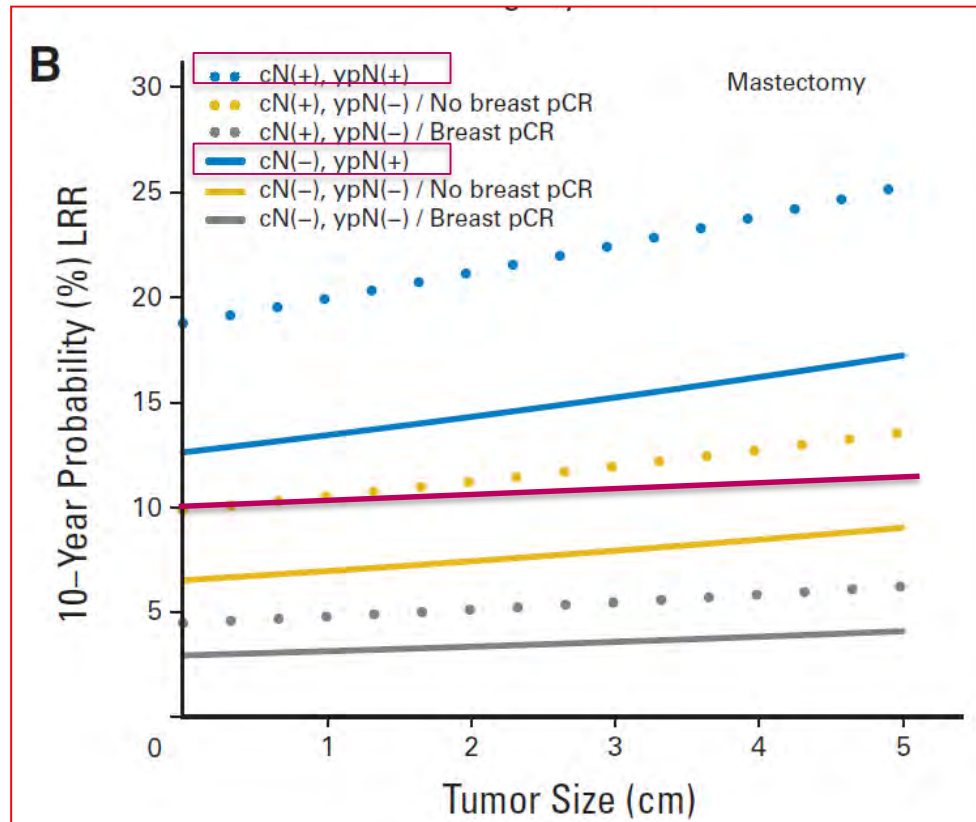


Nomogramme pour la prédiction du risque de la récidive locorégionale à 10 ans après Mastectomie sans RT



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Nomogramme pour la prédiction du risque de la récurrence locorégionale à 10 ans après Mastectomie sans RT



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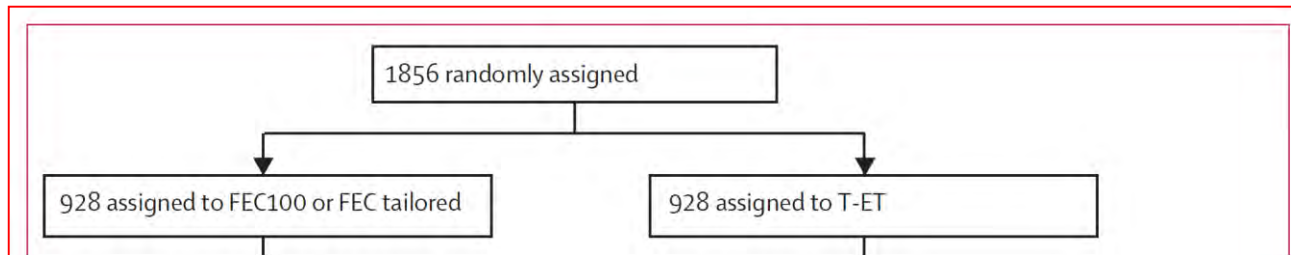
Qu'est ce qu' on a appris ?

- La **réponse pathologique**, surtout **nodale**, prédomine au risque de récurrence locorégionale
- Les **facteurs de récurrence classiques**: âge, taille tumorale, stade clinique gardent une certaine importance
- Le **risque** de récurrence locorégionale en cas de **bonne réponse** reste **bas**

TP53 status for prediction of sensitivity to taxane versus non-taxane neoadjuvant chemotherapy in breast cancer (EORTC 10994/BIG 1-00): a randomised phase 3 trial



Hervé Bonnefoi, Martine Piccart, Jan Bogaerts, Louis Mauriac, Pierre Fumoleau, Etienne Brain, Thierry Petit, Philippe Rouanet, Jacek Jassem, Emmanuel Blot, Khalil Zaman, Tanja Cufer, Alain Lortholary, Elisabet Lidbrink, Sylvie André, Saskia Litière, Lissandra Dal Lago, Véronique Becette, David A Cameron, Jonas Bergh, Richard Iggo, on behalf of the EORTC 10994/BIG 1-00 Study Investigators*



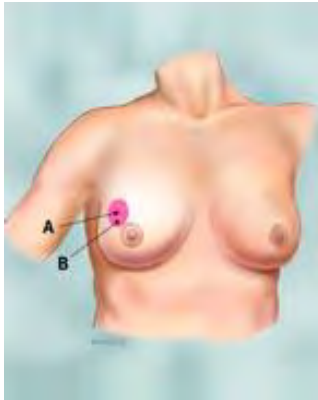
Tumour category

Ineligible	3 (<1%)	3 (<1%)
Locally advanced or inflammatory tumour	213 (23%)	208 (22%)
Large operable tumour	712 (77%)	717 (77%)

Traitements reçus

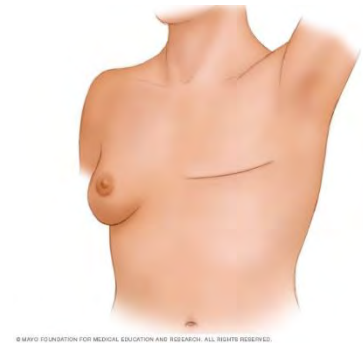
Type of surgery		
Lumpectomy or quadrantectomy	378 (42%)	386 (43%)
Mastectomy	524 (58%)	521 (57%)
Adjuvant treatment for ER-positive or PR-positive tumours§		
Any adjuvant endocrine treatment		
No	21 (3%)	7 (1%)
Yes	595 (95%)	597 (97%)
Not known	12 (2%)	9 (1%)
Adjuvant aromatase inhibitor		
No	261 (42%)	267 (44%)
Yes	350 (56%)	331 (54%)
Not known	17 (3%)	15 (2%)
Adjuvant trastuzumab for HER2-positive patients		
No	147 (64%)	154 (70%)
Yes	78 (34%)	64 (29%)
Not known	5 (2%)	3 (1%)

RT standard dans l' étude EORTC 10994/BIG 1-00



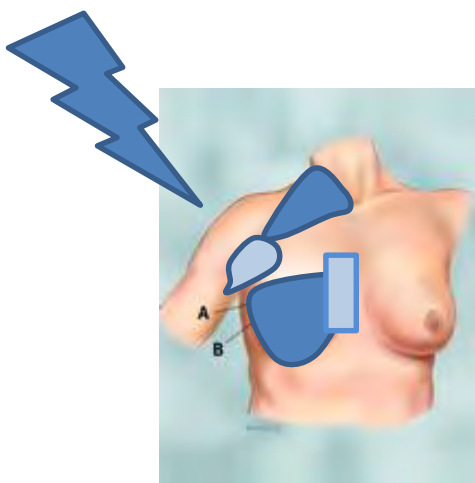
RT du
sein

- Sus et sousclaviculaire:
à **toutes les patientes**
- CMI optionnelle
- Axillaire:
si pas de chirurgie axillaire ou
chirurgie axillaire limitée



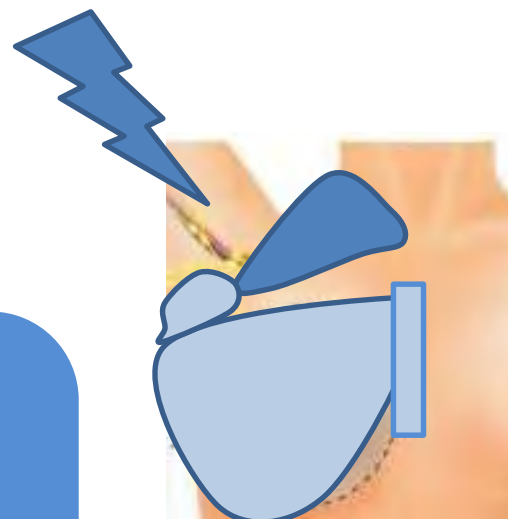
RT de la paroi
si tumeurs localement
avancées

RT standard dans l' étude EORTC 10994/BIG 1-00



RT du
sein

- Sus et sousclaviculaire:
à **toutes les patientes**
- CMI optionnelle
- Axillaire:
si pas de chirurgie axillaire ou
chirurgie axillaire limitée



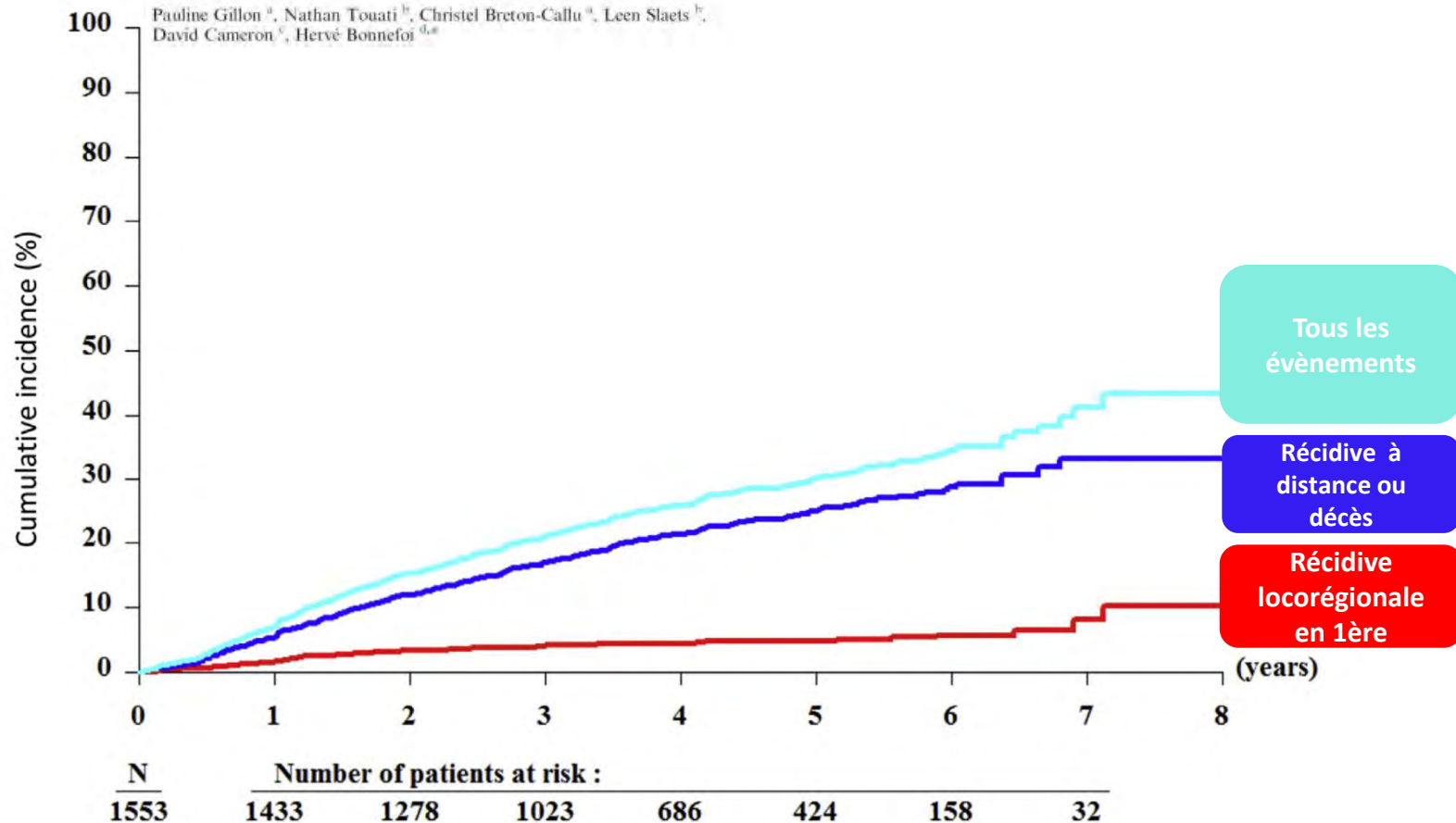
RT de la paroi
si tumeurs localement
avancées

Original Research

Factors predictive of locoregional recurrence following neoadjuvant chemotherapy in patients with large operable or locally advanced breast cancer: An analysis of the EORTC 10994/BIG 1-00 study



Pauline Gillon ^a, Nathan Touati ^b, Christel Breton-Callu ^a, Leen Slaets ^b, David Cameron ^c, Hervé Bonnefoi ^{d,*}



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Table 2

Patterns of locoregional recurrences as first event, number of involved sites per patient and time to LRR from date of surgery by site of relapse.

Site of LRR as first event	Total number of involved sites N (%)	Number of involved sites per patient		Time to LRR from date of surgery (years)	
		1 site (N = 65), N (%)	≥2 sites (N = 11), N (%)	Median in years (95% CI)	Min–Max (years)
Local	31 (40.8)	27 (41.5)	4 (36.4)	1.72 (1.16–2.35)	0.44–7.13
Chest wall	28 (36.8)	23 (35.4)	5 (45.5)	0.98 (0.53–1.10)	0.12–6.90
Axillary nodes	11 (14.5)	4 (6.2)	7 (63.6)	2.44 (0.26–4.17)	0.25–6.46
Internal mammary nodes	3 (3.9)	1 (1.5)	2 (18.2)	1.15 (0.88–2.27)	0.88–2.27
Infraclavicular nodes	6 (7.9)	4 (6.2)	2 (18.2)	2.00 (0.65–4.30)	0.64–4.31
Supraclavicular nodes	8 (10.5)	6 (9.2)	2 (18.2)	1.72 (0.06–4.12)	0.06–4.31

LRR, locoregional recurrence; CI, confidence interval; Min, minimum; Max, maximum.

Multivariate analysis for predictive factors of locoregional recurrence as first event at 5 years.

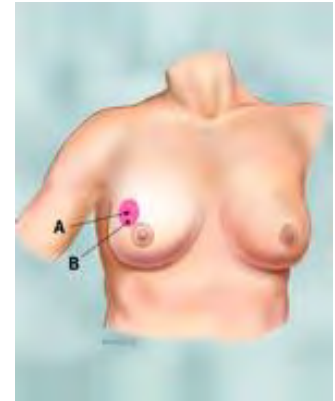
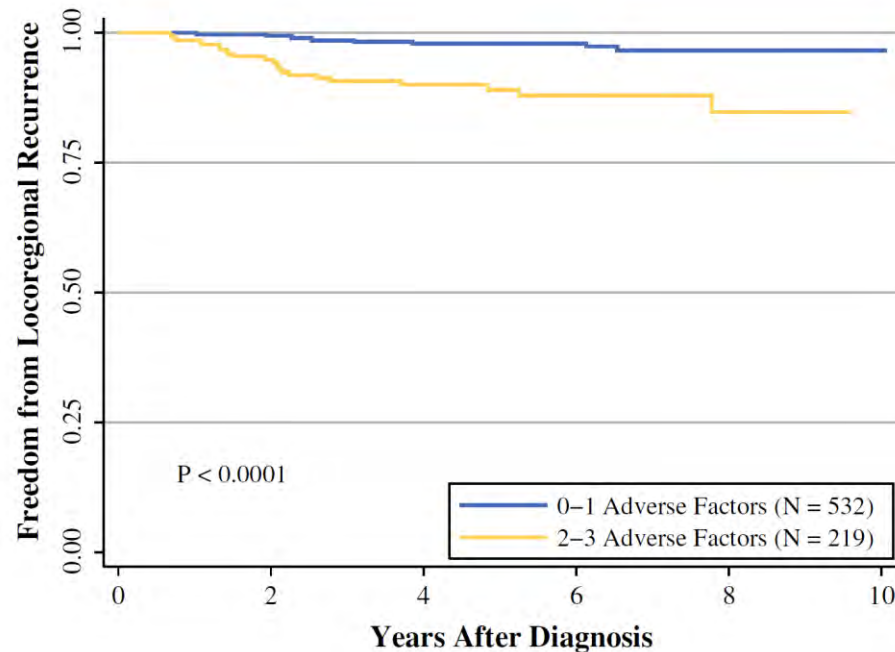
Potential predictive factors	Patients N, % (N = 1505)	LRR as first event N, % (N = 74)	Competing events N, % (N = 341)	Full; Multivariate Fine and Gray model HR (95% CI)	Backward procedure selection Yes/No	Final; Multivariate Fine and Gray model HR (95% CI)	2-sided p-Value (Gray test)
Age at diagnosis (years)							
≤40	303 (20.1)	21 (28.4)	82 (24.0)	1.00	No		
41–50	592 (39.3)	28 (37.8)	116 (34.0)	0.83 (0.45–1.54)			
51–70	610 (40.5)	25 (33.8)	143 (41.9)	0.61 (0.34–1.12)			
Clinical tumour status (cT)							
cT1–2	838 (55.7)	30 (40.5)	128 (37.5)	1.00	No		
cT3	507 (33.7)	29 (39.2)	153 (44.9)	1.50 (0.80–2.78)			
cT4	160 (10.6)	15 (20.3)	60 (17.6)	2.16 (1.01–4.61)			
Clinical nodal status (cN)							
cN0	674 (44.8)	23 (31.1)	101 (29.6)	1.00	No		
cN+	831 (55.2)	51 (68.9)	240 (70.4)	1.27 (0.75–2.13)			
Type of surgery							
Lumpectomy or quadrantectomy	702 (46.6)	33 (44.6)	106 (31.1)	1.00	No		
Mastectomy	803 (53.4)	41 (55.4)	235 (68.9)	0.71 (0.39–1.28)			
Histological type							
Ductal	1256 (83.5)	66 (89.2)	282 (82.7)	1.00	No		
Lobular	176 (11.7)	6 (8.1)	41 (12.0)	0.79 (0.34–1.86)			
Other	73 (4.9)	2 (2.7)	18 (5.3)	0.39 (0.10–1.63)			
Breast cancer subtype/trastuzumab							
Luminal A	491 (32.6)	8 (10.8)	83 (24.3)	1.00	Yes	1.00	< 0.0001
Luminal B (HER2–)	143 (9.5)	5 (6.8)	37 (10.9)	1.99 (0.64–6.17)		2.29 (0.76–6.97)	
HER2+ Trastu–	245 (16.3)	25 (33.8)	84 (24.6)	5.70 (2.57–12.67)		6.26 (2.81–13.93)	
HER2+ Trastu+	105 (7.0)	5 (6.8)	18 (5.3)	3.15 (1.03–9.62)		3.37 (1.10–10.34)	
Triple negative	219 (14.6)	20 (27.0)	50 (14.7)	6.12 (2.67–14.01)		6.44 (2.83–14.69)	
Unknown	302 (20.1)	11 (14.9)	69 (20.2)	2.20 (0.88–5.47)		2.28 (0.93–5.63)	
Pathological response							
ypT0/is ypN0	278 (18.5)	16 (21.6)	24 (7.0)	1.00	Yes	1.00	< 0.0001
ypT + ypN0	420 (27.9)	10 (13.5)	42 (12.3)	0.60 (0.26–1.37)		0.58 (0.26–1.28)	
ypT + ypN+ 1–3 nodes	450 (29.9)	14 (18.9)	121 (35.5)	0.68 (0.33–1.39)		0.74 (0.36–1.52)	
ypT + ypN+ ≥4 nodes	357 (23.7)	34 (45.9)	154 (45.2)	2.16 (1.11–4.02)		2.43 (1.34–4.40)	
Surgical margins							
R0	1398 (92.9)	65 (87.8)	309 (90.6)	1.00	No		
R1	107 (7.1)	9 (12.2)	32 (9.4)	1.68 (0.75–3.75)			

HR, hazard ratio; LRR, locoregional recurrence; HER2, human epidermal growth factor receptor 2.

Qu'est ce qu' on a appris ?

- Les **soustypes moléculaires** prédominent à la prediction du risque de récurrence locorégionale
- La **réponse pathologique**, surtout **nodale**, est très importante quant au risque de récurrence locorégionale
- Le **risque** de récurrence locorégionale (1er évènement) reste **bas** même pour des tumeurs localement avancées
- *...mais la récurrence locorégionale reste pertinente même en cas de rechute à distance*
- Une **RT plus extensive** et l'**utilisation de trastuzumab** a probablement contribué aux taux de rechute bas

Analyse MD Anderson d'une série moderne- chirurgie conservatrice



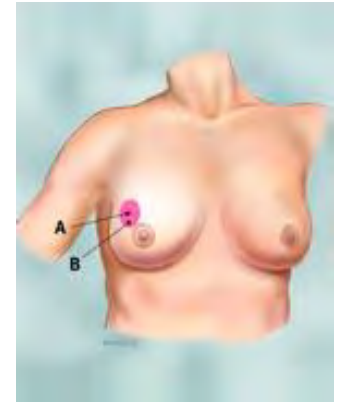
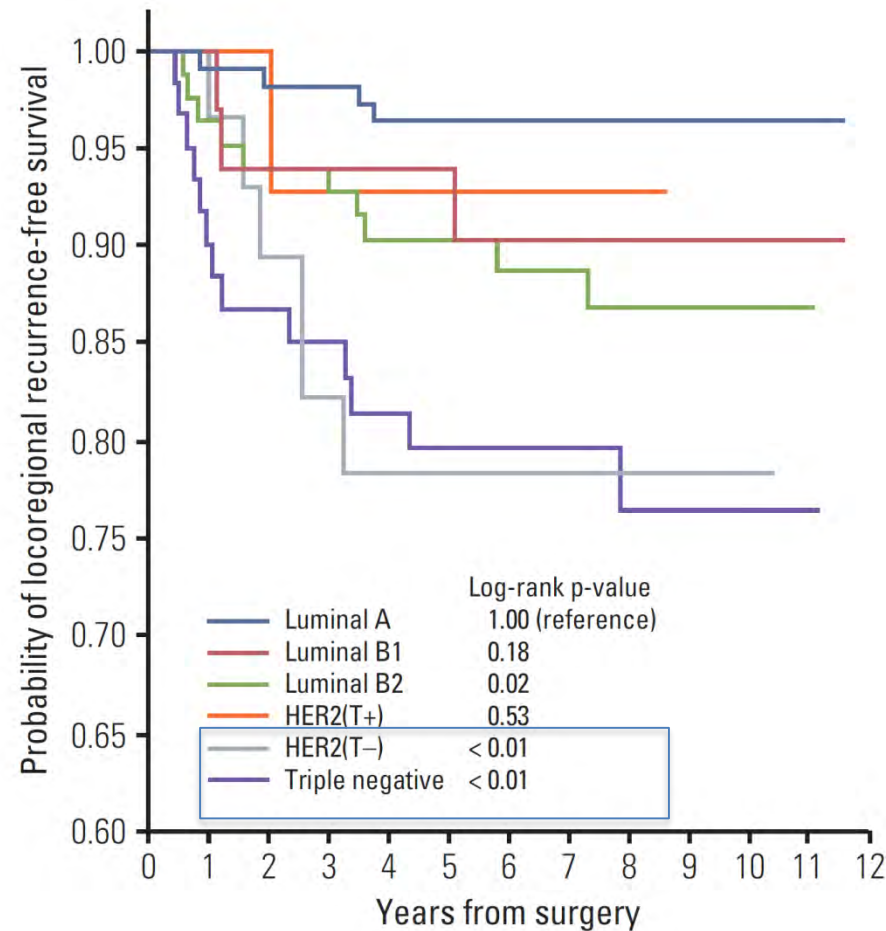
Facteurs adverses:

- Triple négatif
- St III
- Pas de pCR

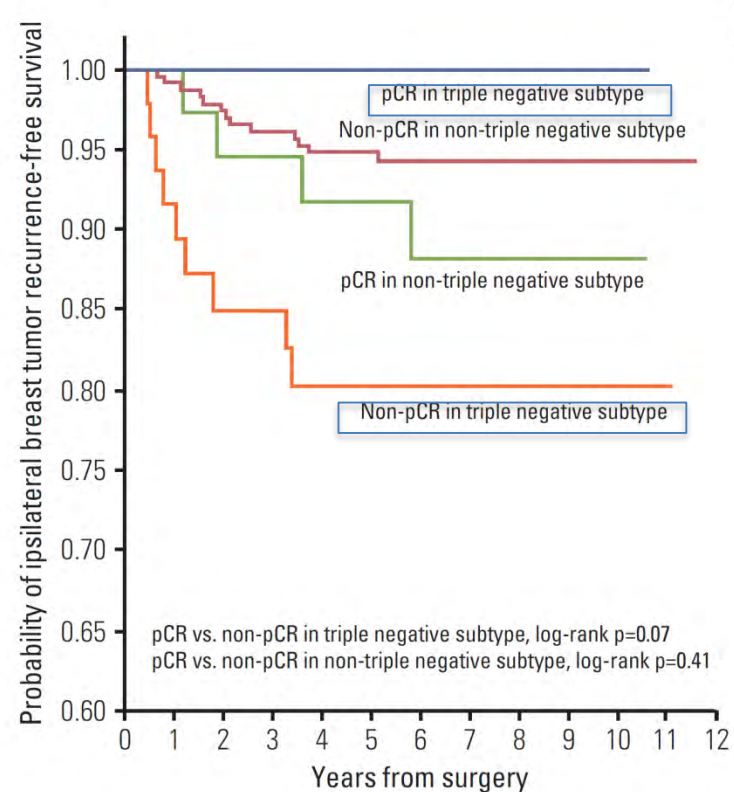
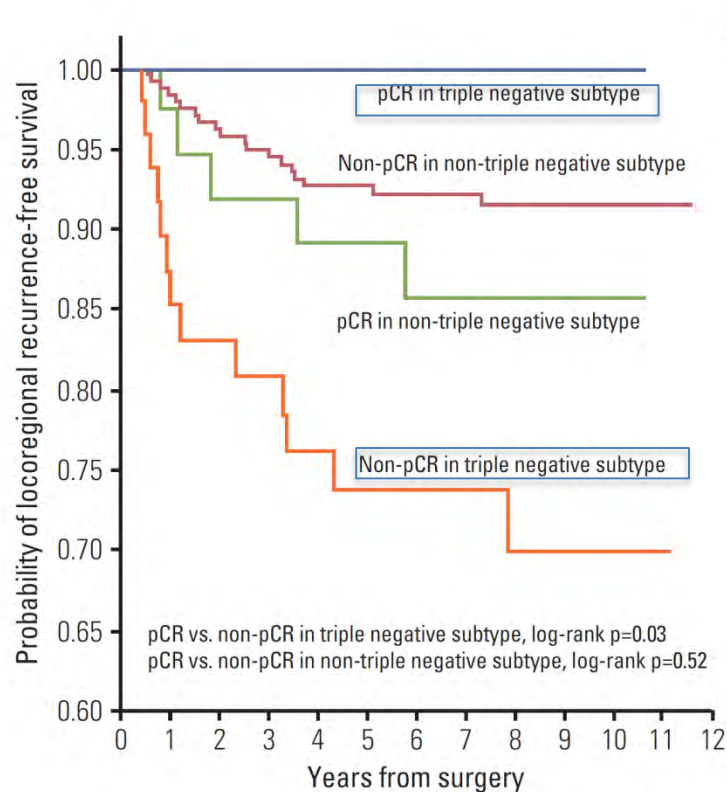
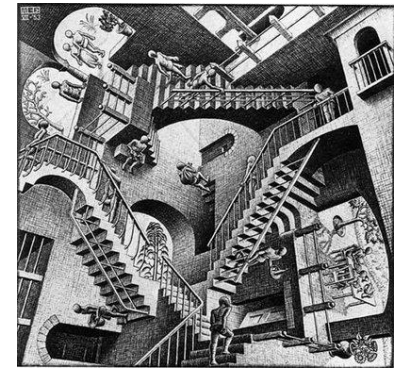
Locoregional Control According to Breast Cancer Subtype and Response to Neoadjuvant Chemotherapy in Breast Cancer Patients Undergoing Breast-conserving Therapy

Shannon K. Swisher¹, Jose Vila, MD¹, Susan L. Tucker, PhD², Isabelle Bedrosian, MD¹, Simona F. Shaitelman, MD, EdM³, Jennifer K. Litton, MD⁴, Benjamin D. Smith, MD⁵, Abigail S. Caudle, MD, MPH¹, Henry M. Kuerer, MD, PhD¹, and Elizabeth A. Mittendorf, MD, PhD¹

Analyse Coréenne: une série moderne avec trastuzumab chirurgie conservatrice



Le soustype triple négatif: le paradoxe triple négatif encore une fois ?

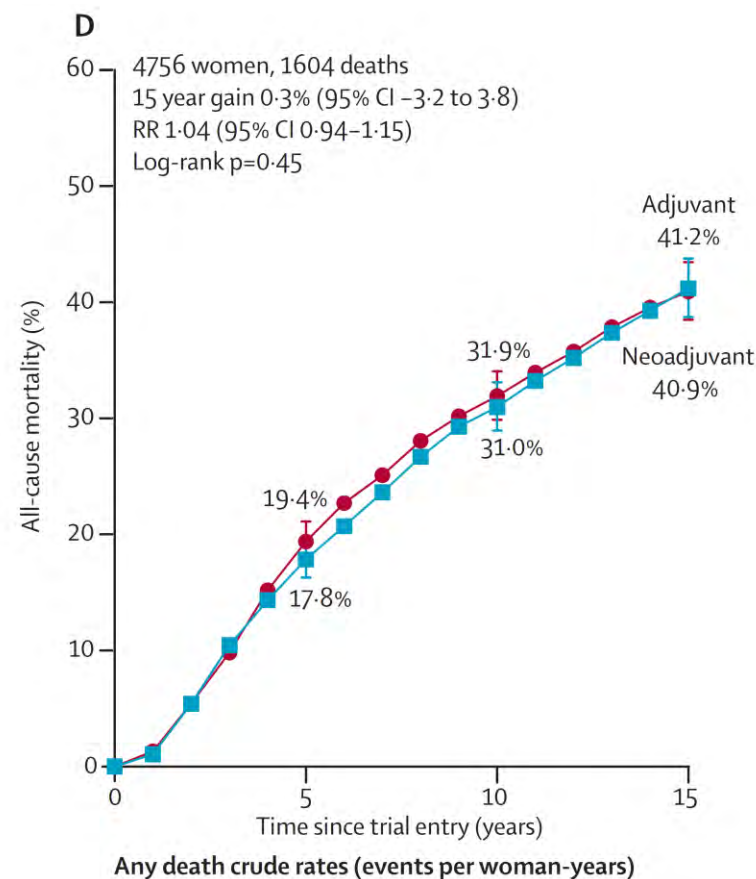
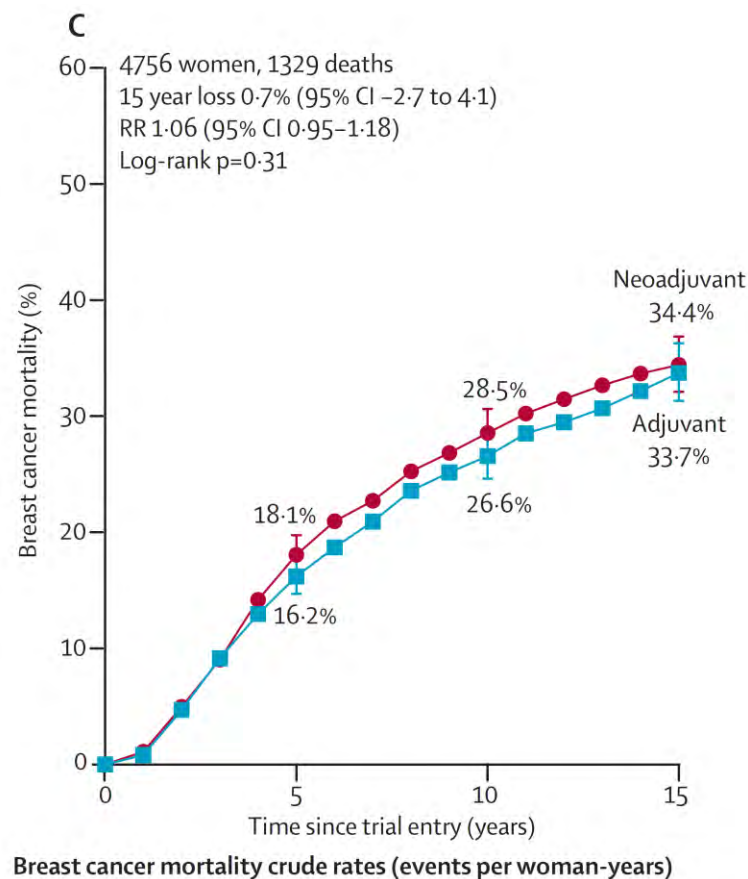


Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*



Lancet Oncol 2018; 19: 27-39

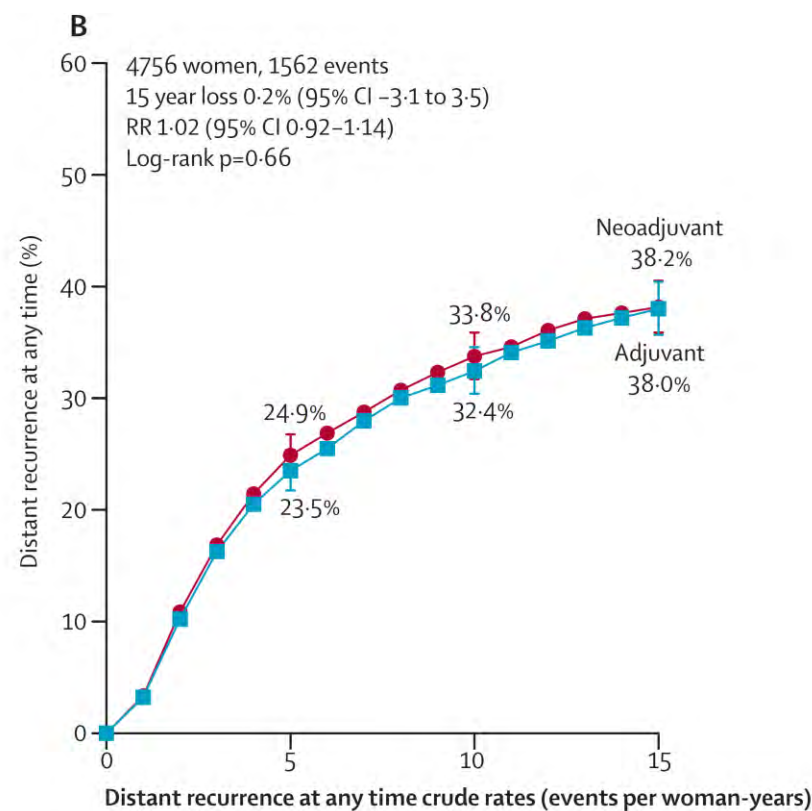
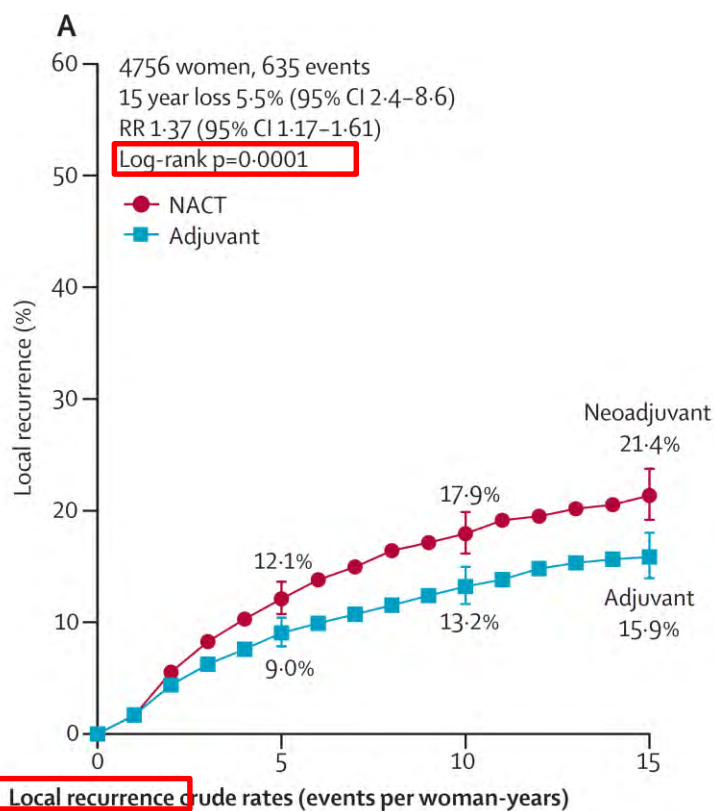


Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials

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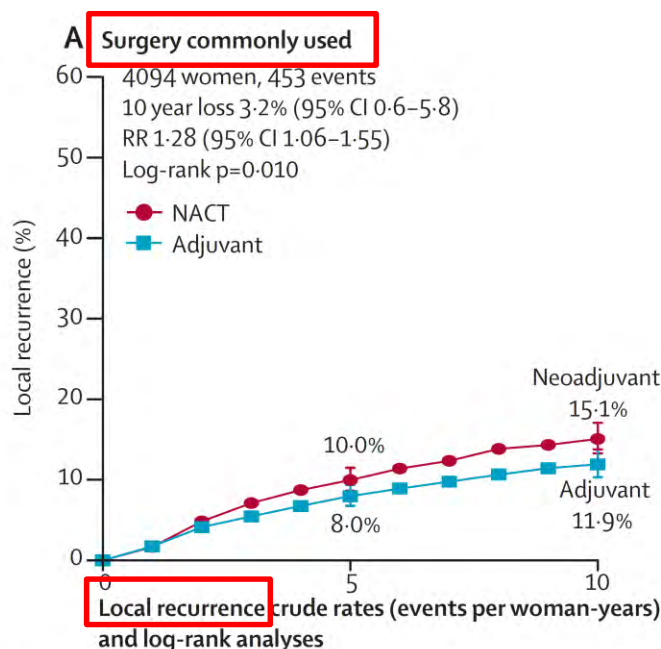
Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials



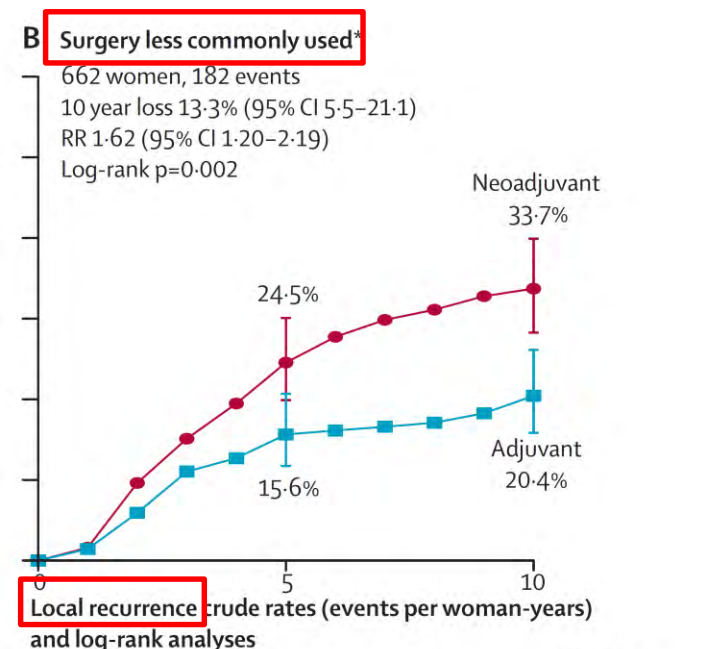
Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*



Lancet Oncol 2018; 19: 27-39



	Years 0-4	Years 5-9	Years ≥10
Neoadjuvant	2.12 (173/8164)	1.21 (57/4721)	0.85 (22/2577)
Adjuvant	1.73 (142/8200)	0.94 (45/4778)	0.55 (14/2547)
Rate ratio (95% CI)	1.26 (1.00-1.58)	1.35 (0.91-2.01)	1.32 (0.65-2.69)
from (O-E)/V	17.3/75.2	7.3/24.3	2.1/7.5



	Years 0-4	Years 5-9	Years ≥10
Neoadjuvant	5.42 (72/1329)	2.73 (22/806)	2.11 (20/947)
Adjuvant	3.37 (43/1277)	1.07 (9/840)	1.61 (16/994)
Rate ratio (95% CI)	1.63 (1.12-2.39)	2.30 (1.13-4.70)	1.15 (0.58-2.27)
from (O-E)/V	13.2/26.8	6.3/7.5	1.1/8.2

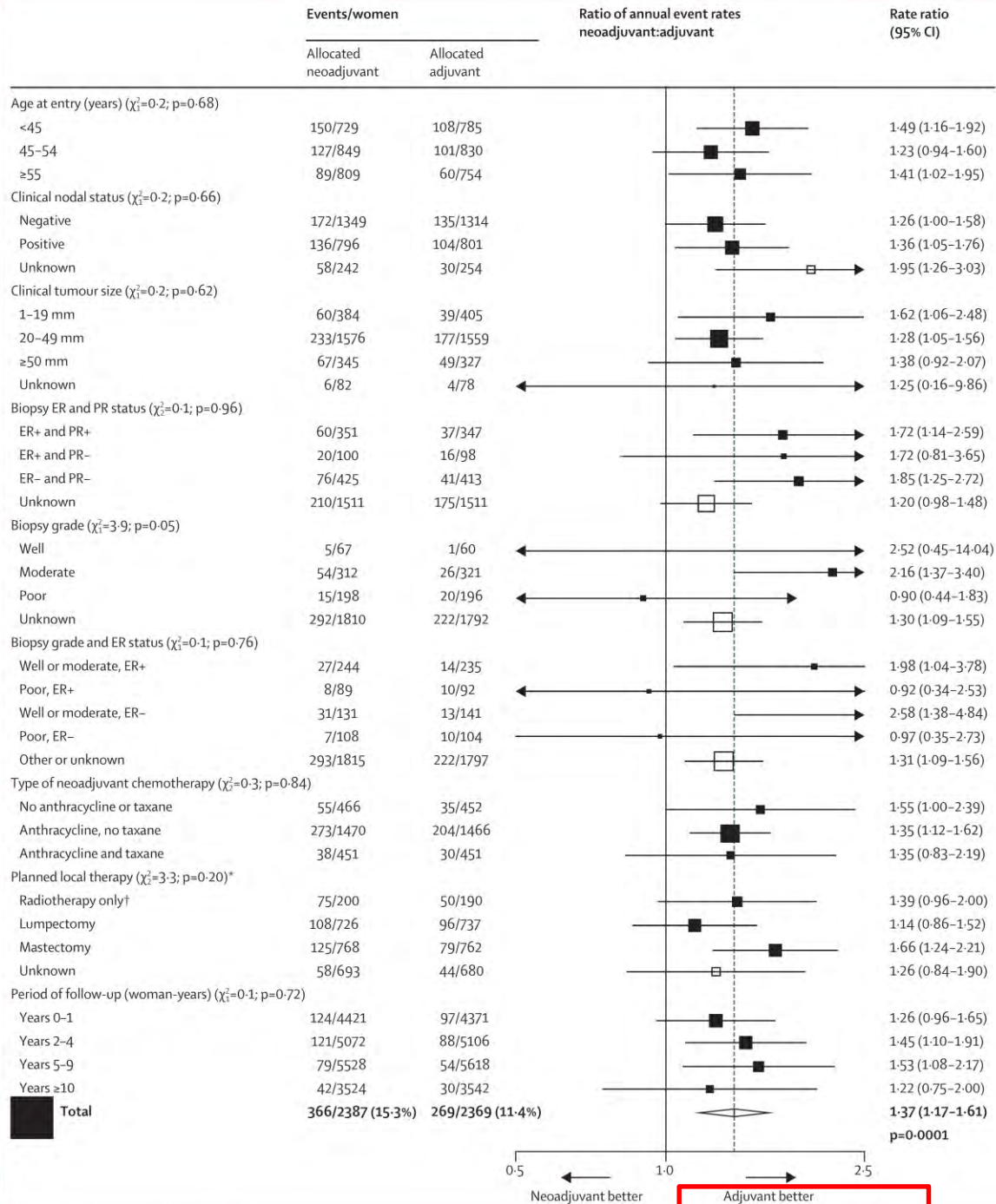
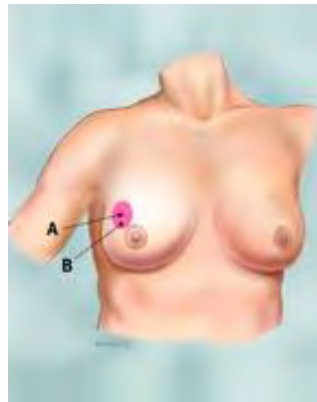


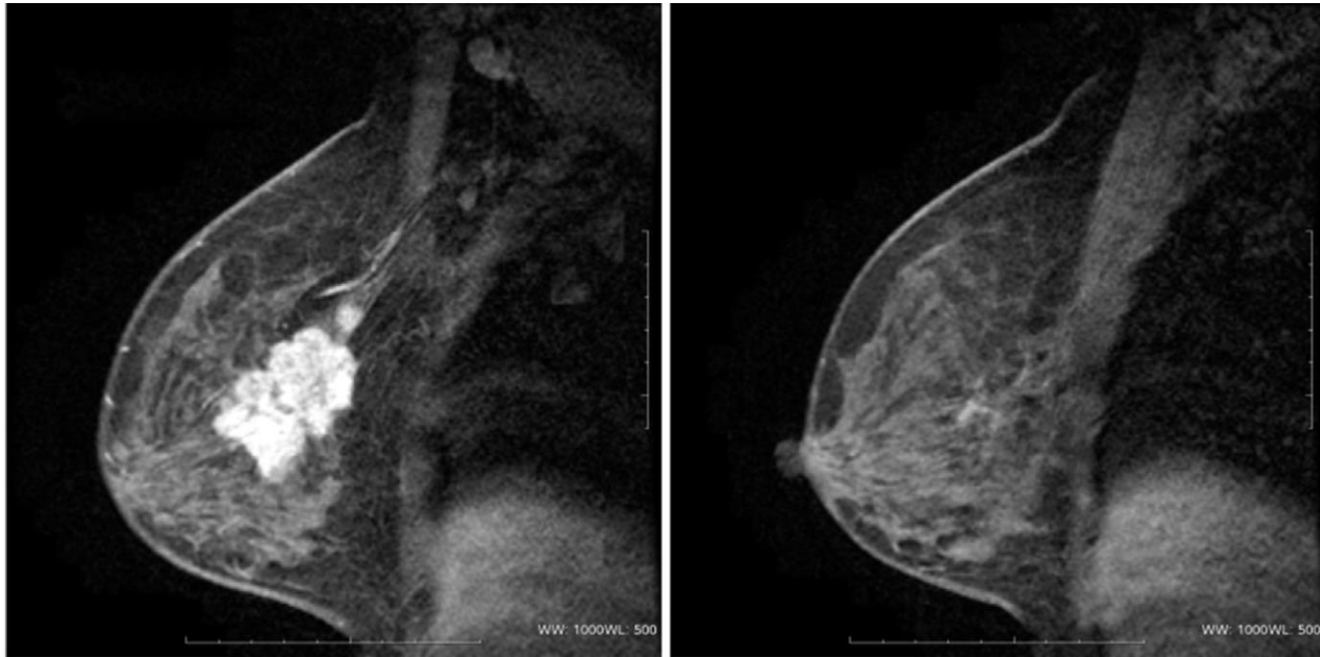
Figure 5: Local recurrence rate ratios

Questions

RT après chirurgie conservatrice suite à une chimiothérapie
néo-adjuvante



Est-il nécessaire d'irradier le sein après une pCR ?



L'irradiation du sein même après une pCR reste le standard

Des études vont définir s'ils existent des groupes des patientes avec pCR qui peuvent éviter la RT après chirurgie conservatrice

**RT après mastectomie suite à une chimiothérapie néo-
adjuvante:
Faut-il irradier ?**



Toute l'évidence est rétrospective

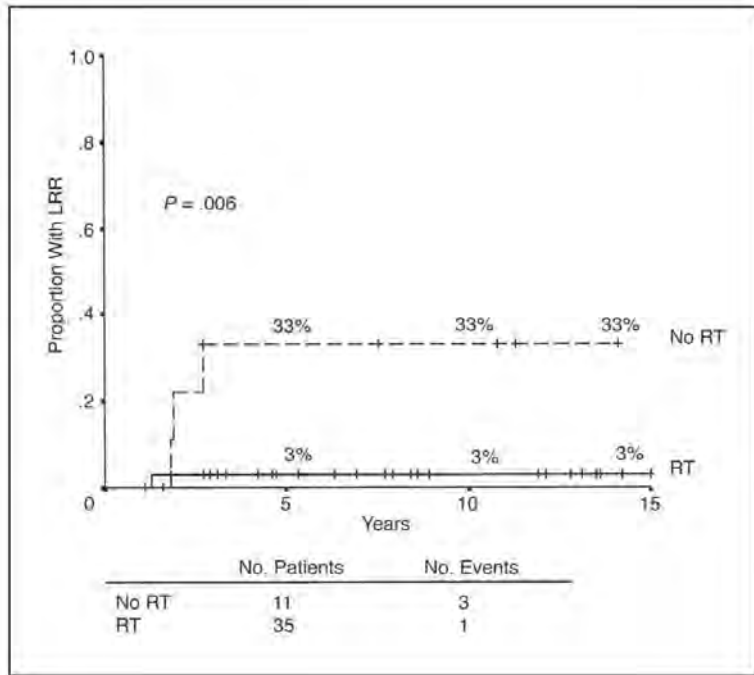
Table 1 Summary of Key Retrospective Studies Evaluating Role of Postmastectomy Radiation Therapy After Neoadjuvant Chemotherapy

	No. of Patients	Follow-up mo	% Clinical Stage	% Complete Response Rate	% LRR		
					PMRT	No PMRT	P
Huang et al, ¹⁹ 1974-2000	676	67	I-II 30 III 70	14.3	11	22	0.0001
McGuire et al, ²⁰ 1985-2004	106	62	I-II 33 III 67	100	5	10	0.40
Garg et al, ²¹ 1975-2005 (younger than 35 years)	107	72	II 27 III 73	17.7	12	37	0.001
Nagar et al, ²² 1985-2004	162	—	cT3N0	8	4	24	<0.001
Le Scodan et al, ²³ 1990-2004	134	91	II 63% III 37%	100% ypN0	4	12	0.12
Shim et al, ²⁴ 1998-2009	151	57	II 60% III 40%	100% ypN0	2	8	0.15

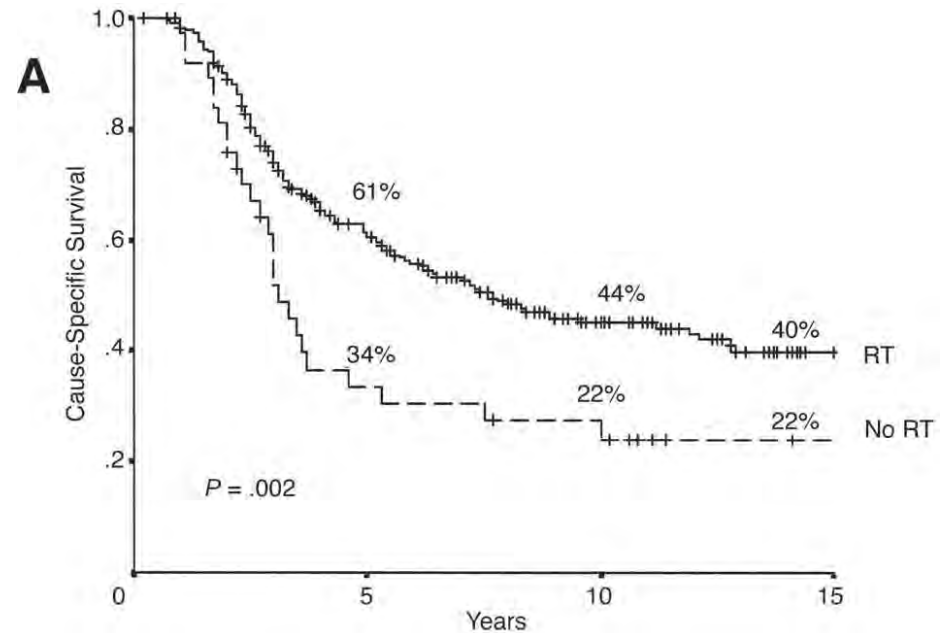
M
DA
CC



La série de MD Anderson

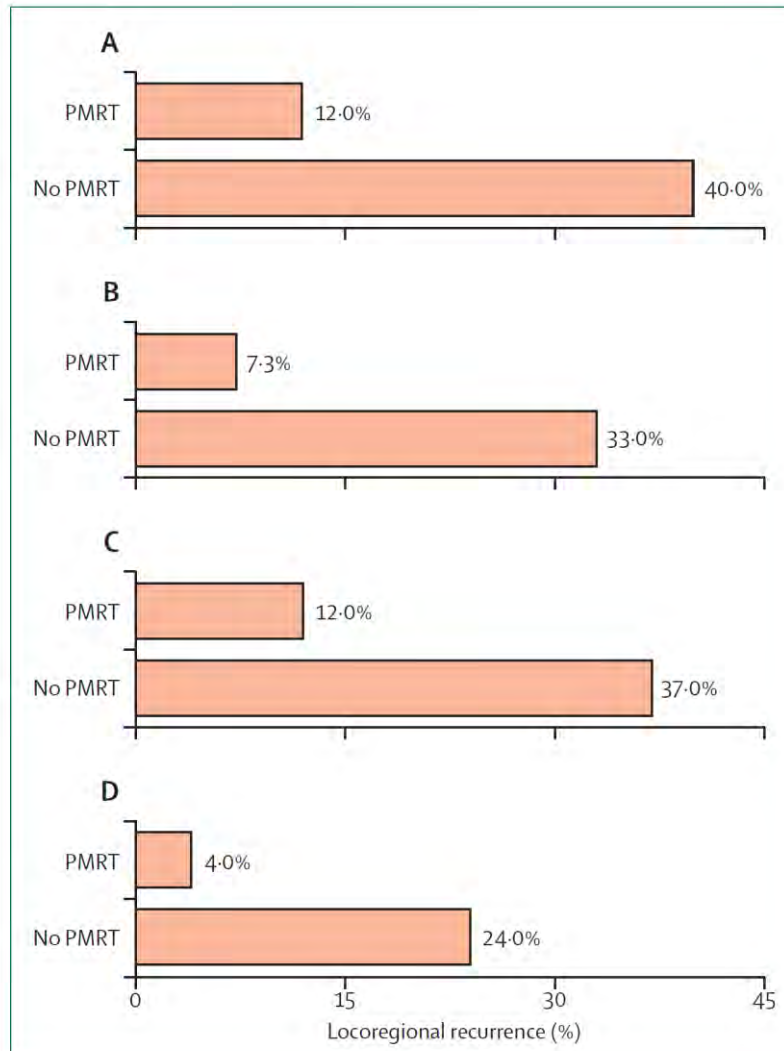


St III- IV et pCR
Rechute locorégionale



St IIIB- IV
Survie spécifique à la maladie

Après mastectomie- données MD Anderson



cN2-3

St III et pCR

<35y
St II-III

cT3N0

Récidive
locorégionale
à 10 ans

Récidive
locorégionale
à 5 ans

Personal View

Optimising radiation treatment decisions for patients who receive neoadjuvant chemotherapy and mastectomy

Konecni, Hoffman, Elsamir, & Mittendorf, Thomas & Buchholz

Whereas randomised clinical trials have established which patients might benefit from postmastectomy radiation

Est-il nécessaire d'irradier les aires ganglionnaires?

Quand ?

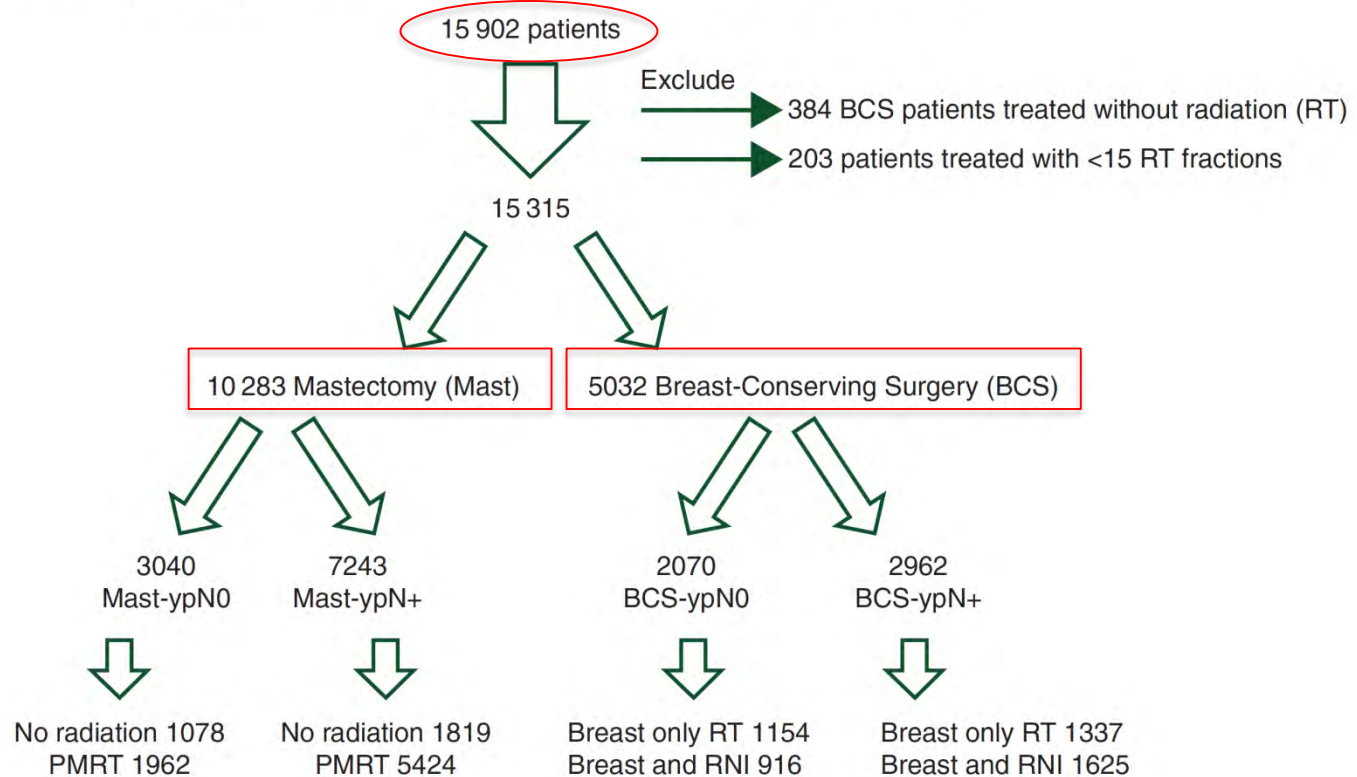
Lesquelles ?

pN1 → ypN0



Les patientes cN1

Women in the NCDB with **cT1–3 cN1 M0 breast cancer**
Receiving Neoadjuvant Chemotherapy (NAC) and definitive surgery from 2003–2011



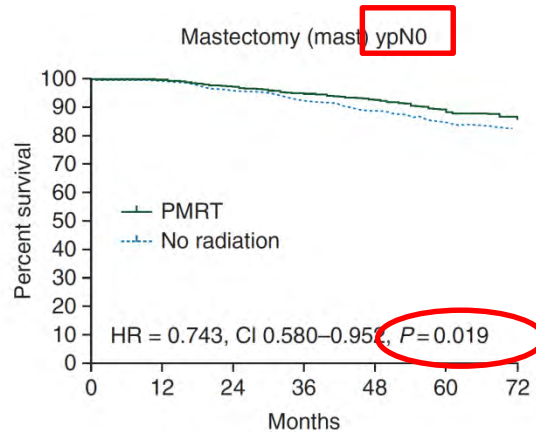
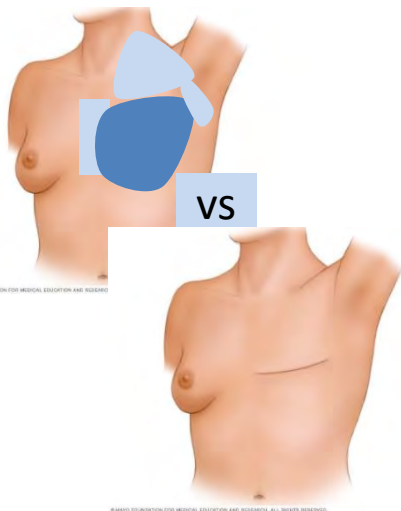
Annals of Oncology 27: 818–827, 2016
doi:10.1093/annonc/mdw046
Published online 9 February 2016

The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis

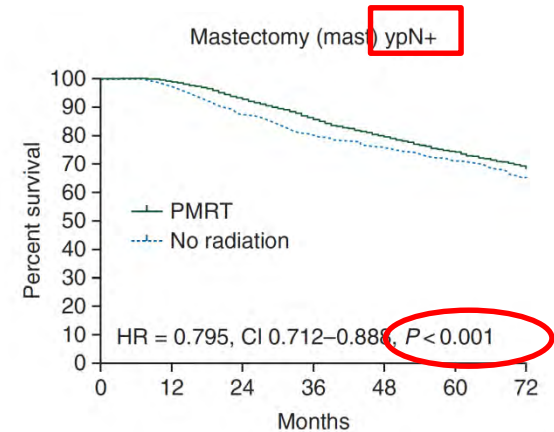
C. G. Rusthoven^{1*}, R. A. Rabinovitch¹, B. L. Jones¹, M. Koshy^{2,3}, A. Amini¹, N. Yeh¹, M. W. Jackson¹ & C. M. Fisher¹

Benefice de la RT

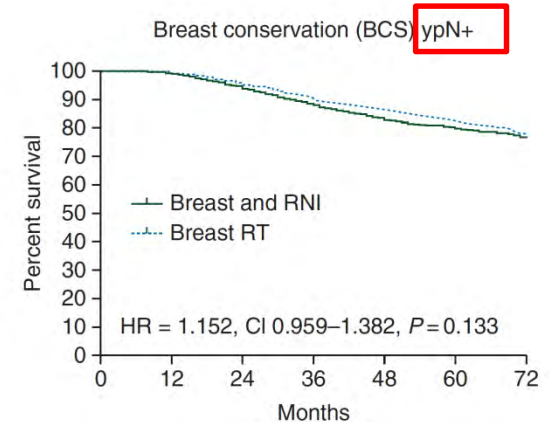
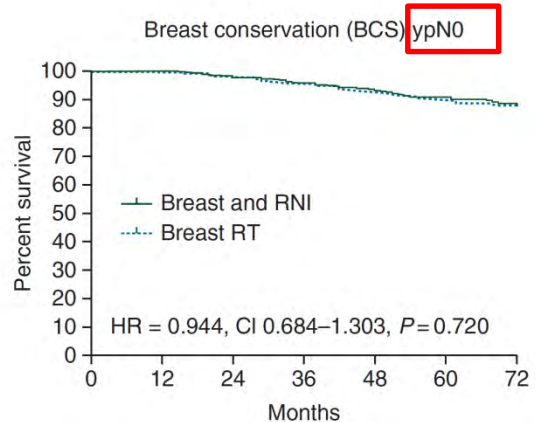
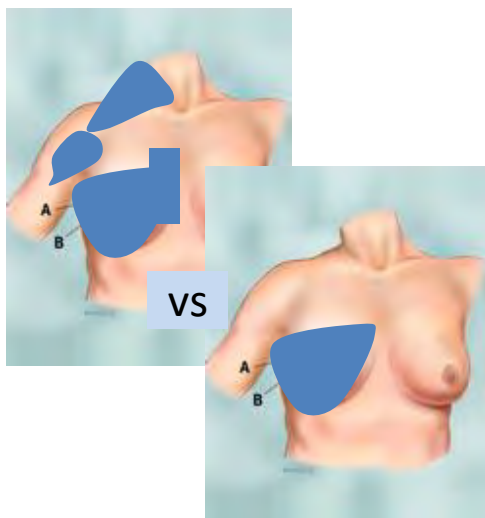
**Mais attention:
curage axillaire**



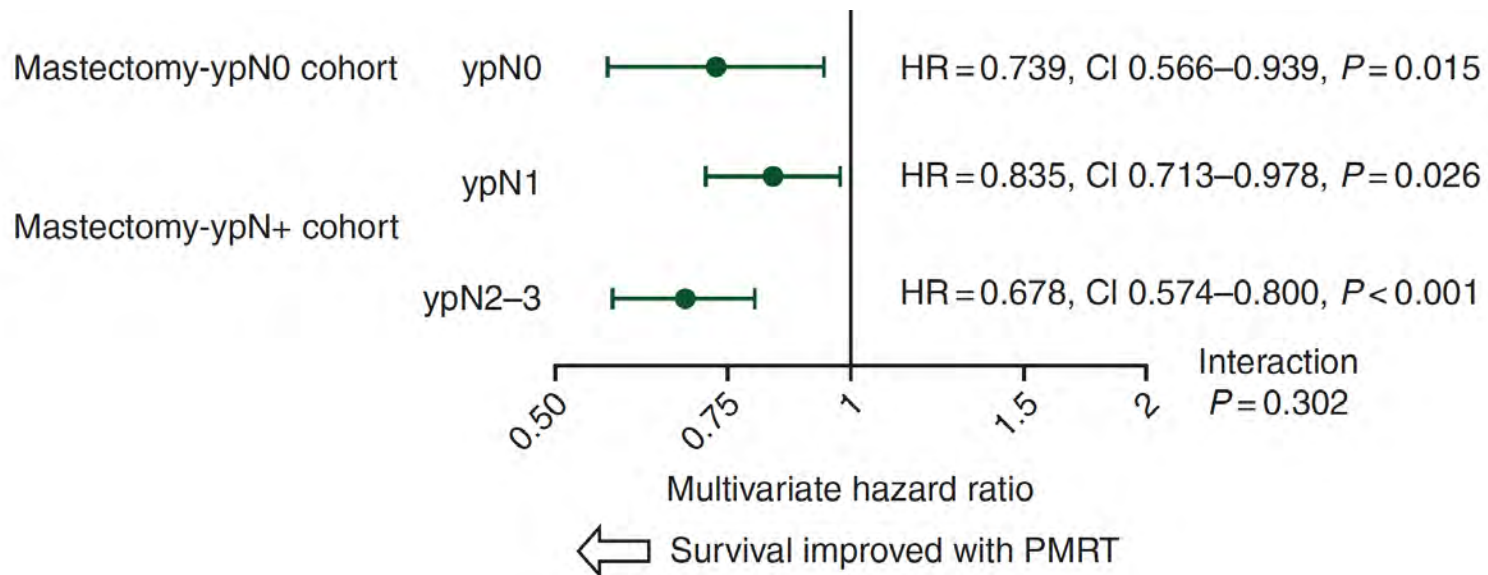
No radiation	1078	1034	841	557	376	241	146
PMRT	1962	1911	1590	1080	723	451	266



1819	1727	1375	948	665	434	250
5424	5294	4382	3034	2058	1360	807



Benefice de la RT après mastectomie en fonction de la réponse

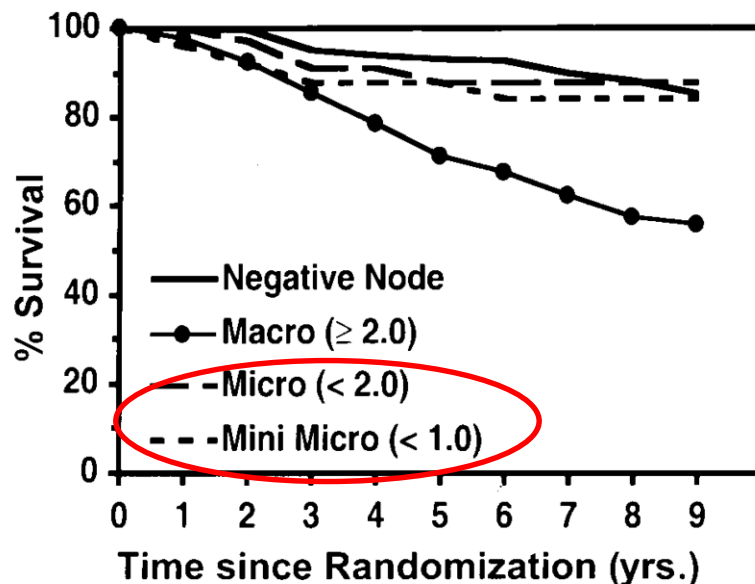


Directions de l'évidence à disposition

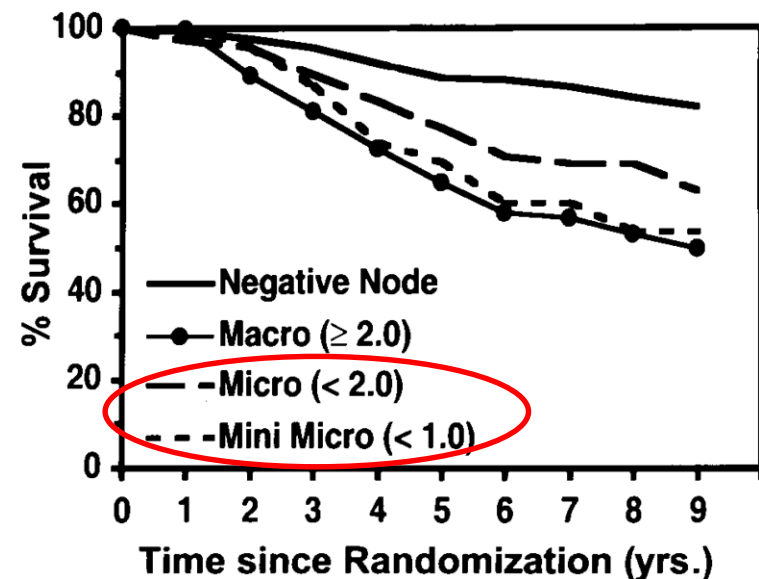
- Évidence de qualité suboptimale: rétrospective/ analyse rétrospective des études prospectives/ analyse des bases des données de patients
- **Après tumorectomie:** RT locale oui, indépendamment de la réponse (mais boost ??)
- **Après mastectomie:** cT3N0, st III (N2 ou T3N1), jeune âge, triple négatif (retrospectifs), cN1 indépendamment de la réponse (analyse NCDB) (mais aussi pour T1/2 cN1 →ypN0 ?)
- **T1/2 cN1→ypN0:** RT locorégionale après chirurgie conservatrice ? Pour le moment standard (NCCN), mais nécessaire? (non, selon NSABP)
- **ypN+:** standard curage, bénéfice après mastectomie (NCDB), bénéfice après chirurgie conservatrice ? Curage+ RT locorégionale ? est-ce que curage peut être remplacé par RT axillaire ?

L'importance de l'atteinte axillaire avant ou après chimiothérapie

Chimio adjuvante



Chimio néo-adjuvante

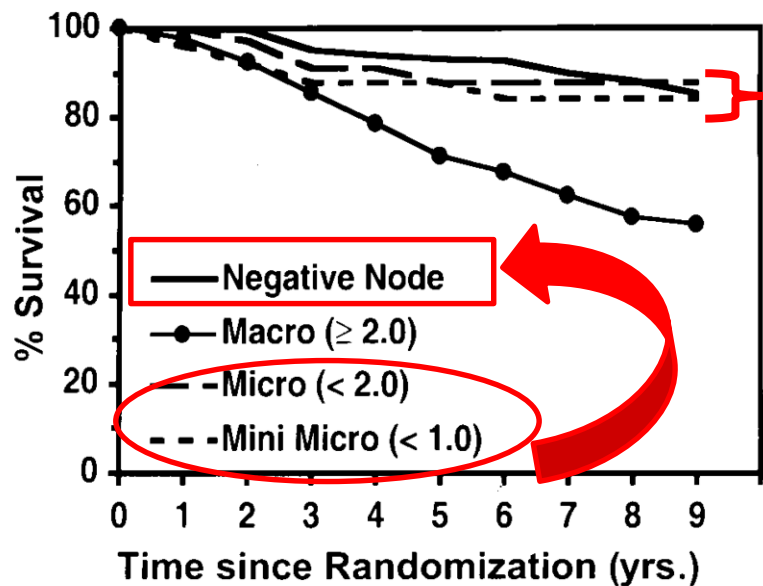


Pathobiology of Preoperative Chemotherapy

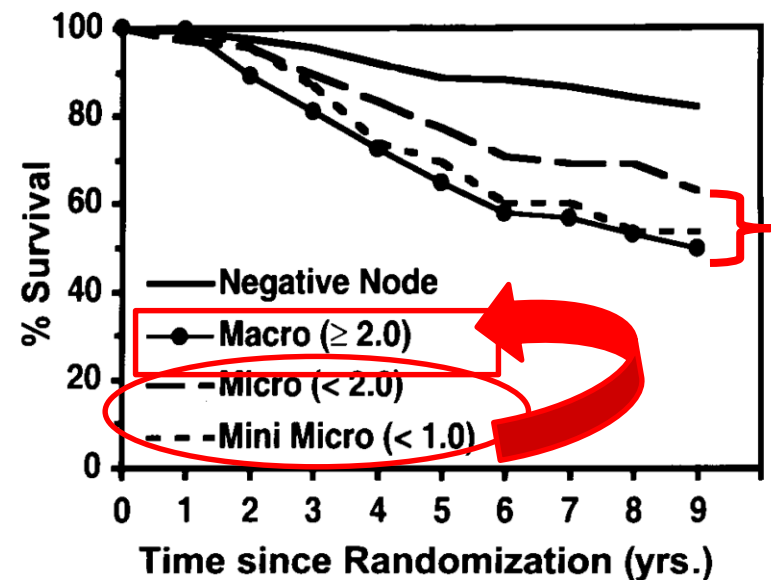
Findings from the National Surgical Adjuvant Breast and Bowel Project (NSABP) Protocol B-18

L'importance de l'atteinte axillaire avant ou après chimiothérapie

Chimio adjuvante



Chimio néo-adjuvante



Pathobiology of Preoperative Chemotherapy

Findings from the National Surgical Adjuvant Breast and Bowel Project (NSABP) Protocol B-18

La signification du ypN+

- Maladie résistante à la chimiothérapie ou maladie partiellement résistant à la chimiothérapie
- Mais, dans les deux cas, pronostic défavorable comparée à la maladie documentée avant tout traitement
- Indique un traitement plus agressif, mais sur traitement à éviter

Et le débat commence...



VOLUME 32 · NUMBER 6 · FEBRUARY 20 2014

JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

Reducing Local Therapy in Patients Responding to Preoperative Systemic Therapy: Are We Outsmarting Ourselves?

Lawrence B. Marks, *University of North Carolina, Chapel Hill, NC*
Leonard R. Prosnitz, *Duke University Medical Center, Durham, NC*

VOLUME 32 · NUMBER 6 · FEBRUARY 20 2014

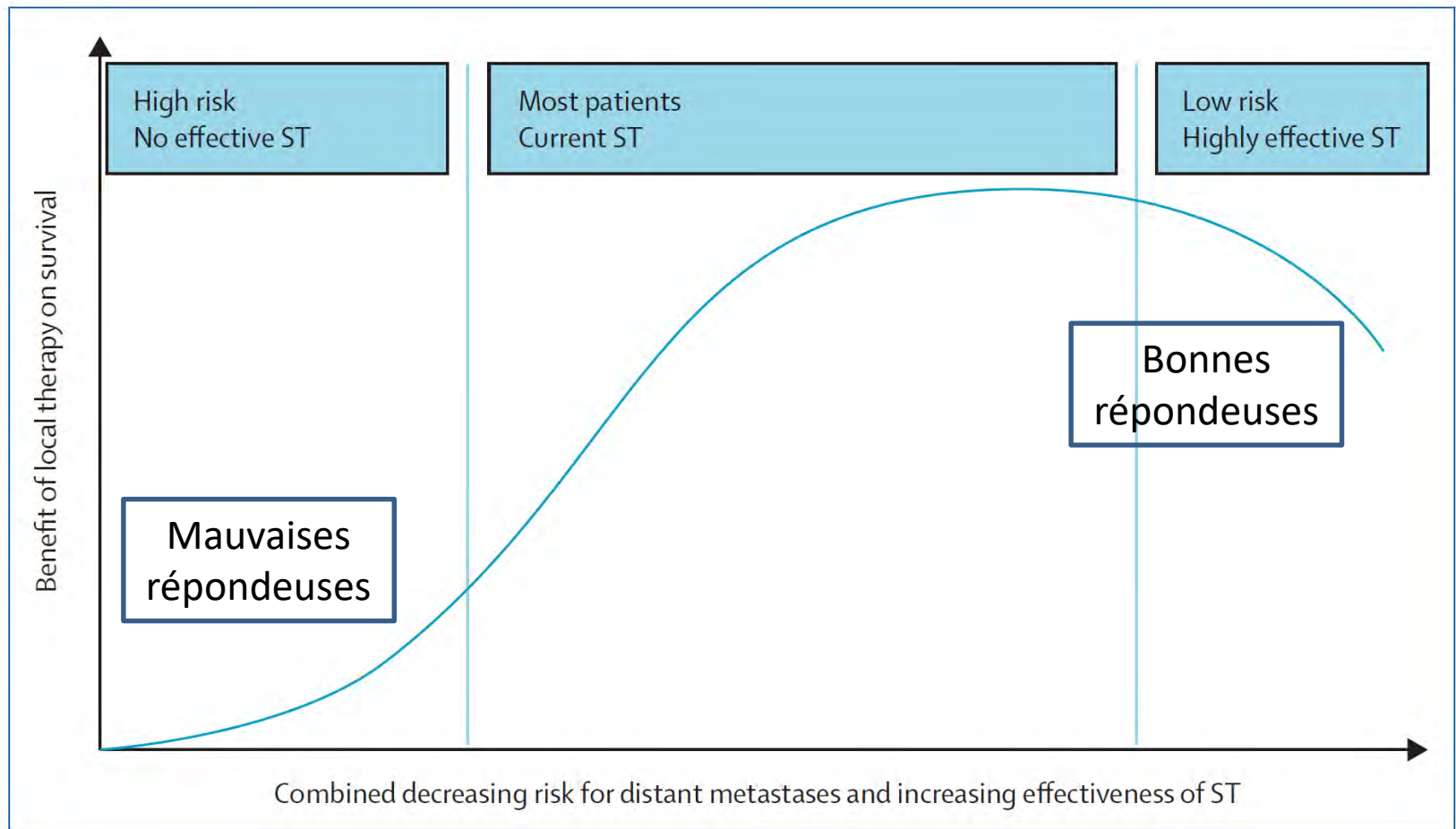
JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

Locoregional Radiotherapy in Patients With Breast Cancer Responding to Neoadjuvant Chemotherapy: A Paradigm for Treatment Individualization

Julia White, *The Ohio State University Comprehensive Cancer Center, Columbus, OH*
Eleftherios Mamounas, *MD Anderson Cancer Center Orlando, Orlando, FL*

Relation entre traitements systémiques et locorégionaux



Quelles sont les réponses à venir ?

Irradiation après NACT chez patientes pN1 et ypN0

- **NSABP B51**

Question:

Est-ce que la RT locorégionale
diminue la rechute locorégionale
chez des patientes pN1 → ypN0?

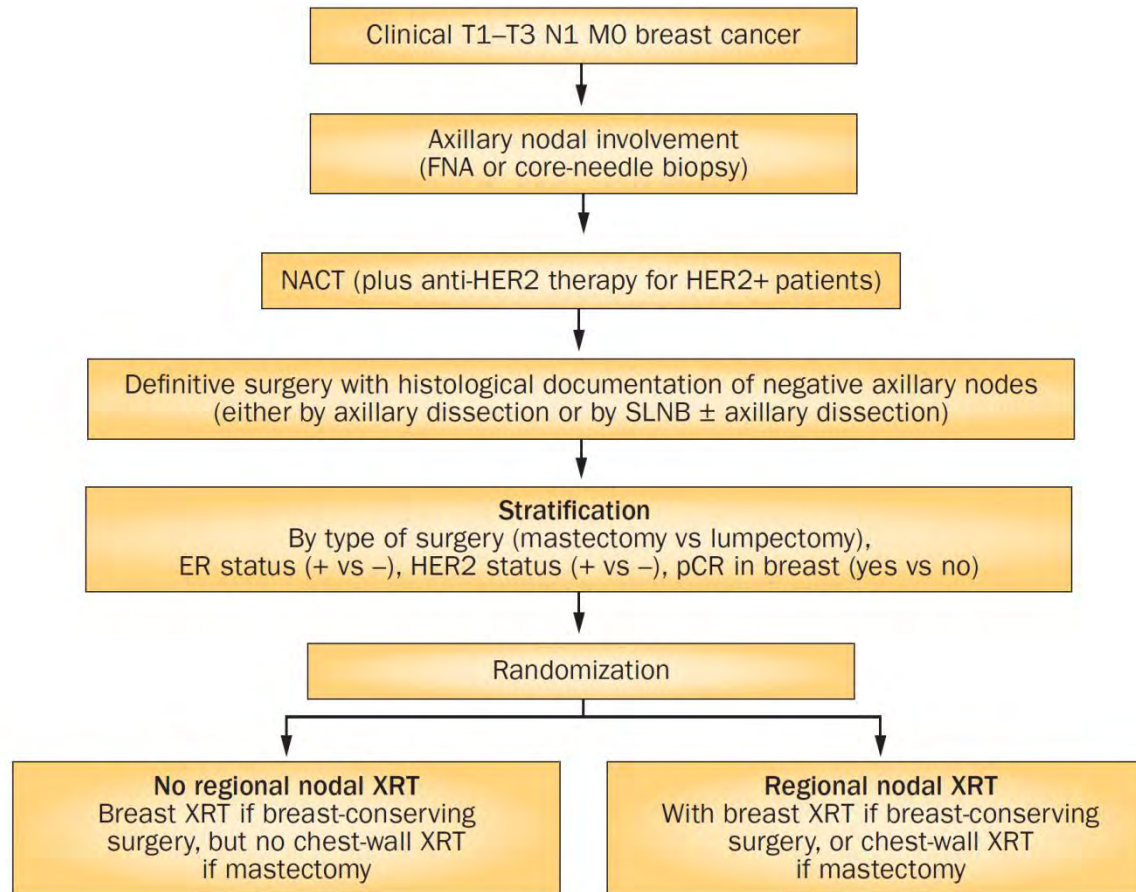
- **ALLIANCE A011202**

Question:

est-ce qu'on peut remplacer le
curage ganglionnaire par une
irradiation axillaire chez les
patientes pN1 → ypN+ ?

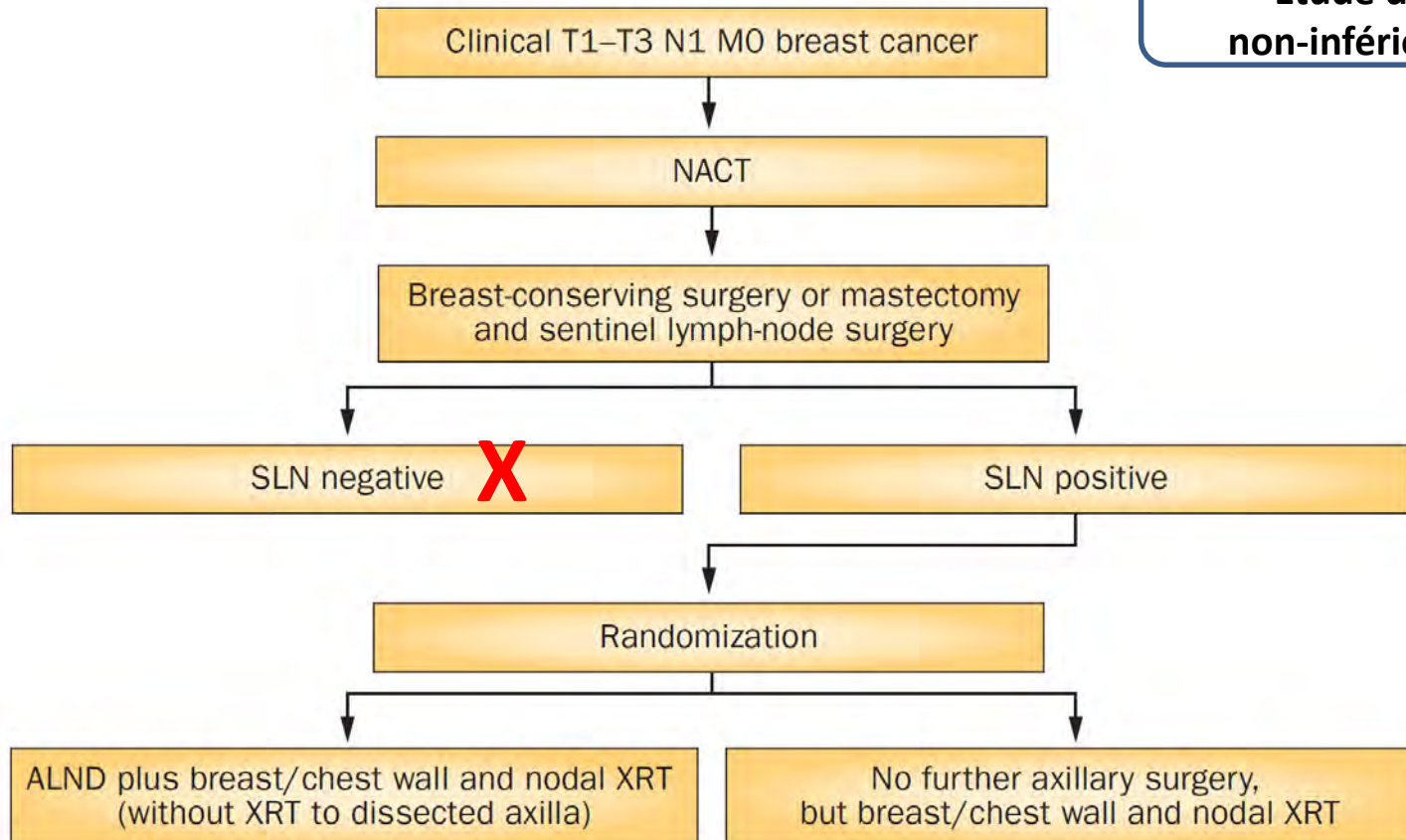
NSABP B51

**Pase III
Étude de
supériorité**



ALLIANCE A011202

Phase III
Étude de
non-infériorité



Étude TAXIS

Phase III
Étude de
non-infériorité

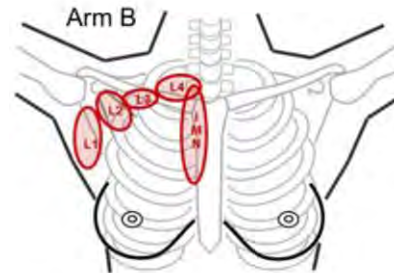
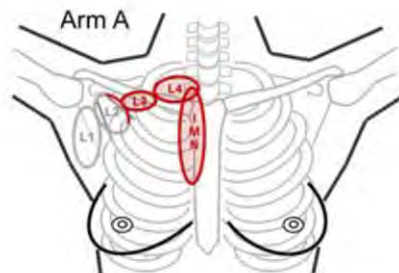
SAKK 23/16 / IBCSG 57-18 / ABCSG-53

TAXIS: Tailored AXillary Surgery with or without axillary lymph node dissection followed by radiotherapy in patients with clinically node-positive breast cancer.

A multicenter randomized phase III trial

Arm A: undissected parts of the axilla (n_L3 and occasionally high n_L2/interpect), supraclavicular (n_L4) and internal mammary (n_IMN) nodes.

Arm B: complete axilla (n_L1, n_L2/interpect, n_L3), supraclavicular (n_L4) and internal mammary nodes (n_IMN).



Étude RAPCHEM

Radiotherapy After Primary Chemotherapy for Breast cancer (RAPCHEM)

- **Completed recrutement**
- **Sponsor:** Maastricht **Radiation** Oncology
- **Collaborators:** The Netherlands Cancer Institute

Étude
observationnelle

Current Primary Outcome Measures

Locoregional recurrence rate [Time Frame: 5 Yr] in **cT1-2cN0-1**

The radiation treatment guidelines for the subsequent three risk groups consist of:

1. Group I - low risk (N = 237):

- a. after MRM: no radiotherapy
- b. after BCT: radiation treatment of the breast with boost (optional)

ypN0/ypNmi

2. Group II - intermediate risk (N = 237):

- a. after MRM: radiation treatment of the thoracic wall
- b. after BCT: radiation treatment of the breast with boost (optional)
- c. if no full ALND is performed: add radiation treatment to level 1 and 2

ypN1/ypNmi+RF

3. Group III - high risk group (N = 237):

- a. after MRM: radiation treatment of the thoracic wall and supraclavicular nodes
 - b. after BCT: radiation treatment of the breast with boost (optional), and supraclavicular nodes
 - c. if no full ALND is performed (not recommended): add radiation treatment to the axilla level 1 and 2 RT of the axillary (after ALND) and internal mammary chain nodes is optional for group III, based on the local protocol. In case of a positive sentinel node in the internal mammary chain prior to chemotherapy, internal mammary chain irradiation is strongly recommended
- Main study parameters/endpoints: The primary endpoint is the 5 yr locoregional recurrence rate (LRR). Secondary endpoints are 10 year LRR, 5, 10, and 15 yr relapse free survival rates (all events except lost to follow-up, invasive contralateral cancer, and secondary primary (non-breast) invasive cancer) and overall survival rates. In addition, analyses will be performed to investigate whether pre-radiotherapy factors (e.g. like age < 40 yr, response to chemotherapy, tumour size) can be identified that correlate with a high LRR.

ypN2/ypN1+RF

Réponses attendues

- T1/2 cN1→ypN0: RT locorégionale ? NSABP B51
- ypN+: est-ce que le curage peut être remplacé par RT axillaire ? ALLIANCE A011202
- est-ce que curage peut-être remplacé par chirurgie ciblée et RT ? TAXIS

En attendant, on suit les guidelines sans oublier de communiquer
et on essaye d'inclure les patientes dans les études (TAXIS)

