

Radiothérapie des cancers du sein de la « femme âgée »

Inter-régionales de cancérologie

Mai 2014 Nantes

Gérard Ganem

Le Mans

Objectifs

- En cas de traitement conservateur selon préférences des malades?
- Si mastectomie?
- Aires ganglionnaires?
- Quelles indications?
- Quels schémas?

Faut-il irradier systématiquement le sein après traitement conservateur ?

Population: Pts > 70 ans, T < 2 cm, N0, RE positifs

Etude CALGB 9343, puis RTOG et ECOG
De 1994 à 1999

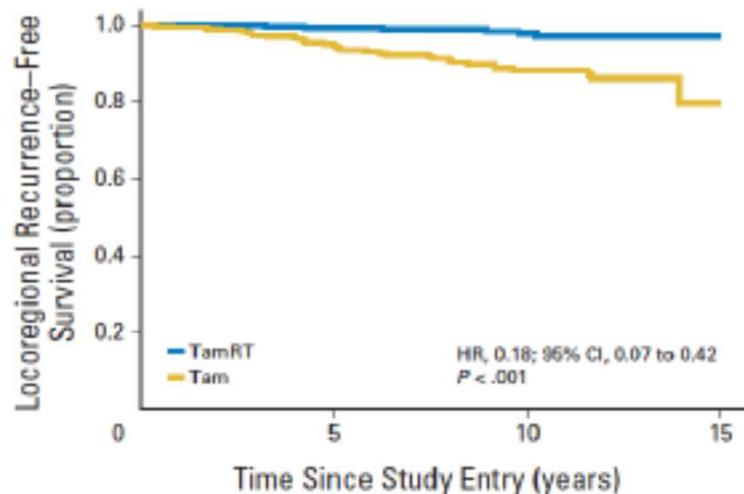
Tumorectomie, Tamoxifene



Pas de RT (n=317)

RT sein seul (n=319)

(45 Gy + Boost: 14 Gy e-)



No. at risk				
TamRT	317	261	162	7
Tam	319	243	144	2

Fig 2. Time to local or regional recurrence. HR, hazard ratio; Tam, tamoxifen alone; TamRT, tamoxifen plus radiation therapy.

A 10 ans :

- RLR : 2% vs 10%

- Sans ≠ mastectomie, survie, survie spécifique

Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

Kevin S. Hughes, Lauren A. Schnaper, Jennifer R. Bellon, Constance T. Cirrincione, Donald A. Berry,

- Pas de RTE axillaire (tangentiels +/- boost)
- Curage encouragé
- Stratif selon curage ou non, et âge < ou > 75 ans
- Suivi médian 12,6 ans

JCO 2013

Characteristic	Tamoxifen + Irradiation (N=317)	Tamoxifen (N=319)
	<i>no. of women (%)</i>	
Stratification		
Age		
70-74 yr	139 (44)	146 (46)
≥75 yr	178 (56)	173 (54)
Axillary dissection		
No	200 (63)	204 (64)
Yes	117 (37)	115 (36)
Demographic		
Race or ethnic group*		
White	287 (91)	287 (90)
Hispanic	5 (2)	8 (2)
Black	23 (7)	22 (7)
Asian	0	2 (1)
Other	1 (<1)	0
Unknown	1 (<1)	0
Estrogen-receptor status		
Negative	6 (2)	4 (1)
Positive	308 (97)	310 (97)
Unknown	3 (1)	5 (2)
Progesterone-receptor status		
Negative	56 (18)	67 (21)
Positive	251 (79)	245 (77)
Unknown	10 (3)	7 (2)
Size of primary tumor		
≤2 cm	312 (98)	310 (97)
>2 cm	5 (2)	9 (3)

Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

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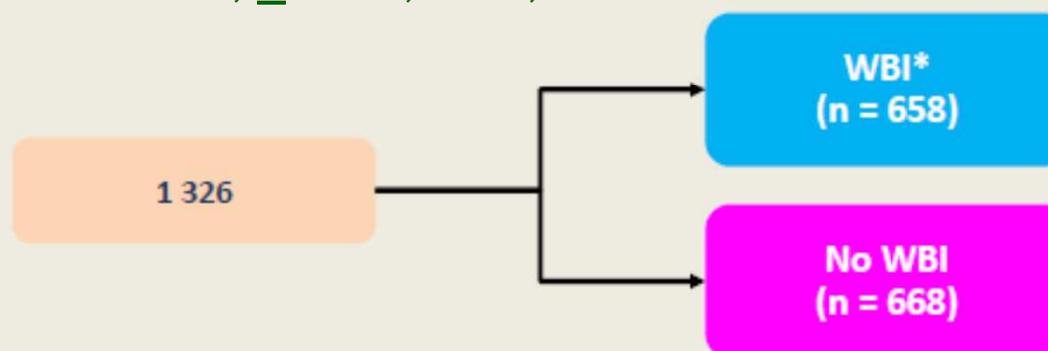
Pas de résultats selon
-âge < ou > 75 ans
-modalités de RTE
-RH

Treated Patients	TamRT Arm	Tam Arm	Total
Total	317	319	636
Recurrence	23	42	65
Local or regional ± distant	6	32	38
IBTR alone	2	20	22
Axilla alone	0	5	5
IBTR with axilla	0	1	1
IBTR with distant	4	6	10
Distant alone	17	10	27
Death			
All cause	166	168	334
Breast cancer specific	13	8	21

Abbreviations: IBTR, ipsilateral breast recurrence; Tam, tamoxifen alone; TamRT, tamoxifen plus radiation therapy.

Schéma de l'étude PRIME-2

> 65 ans; \leq 3 cm, RH+, N0

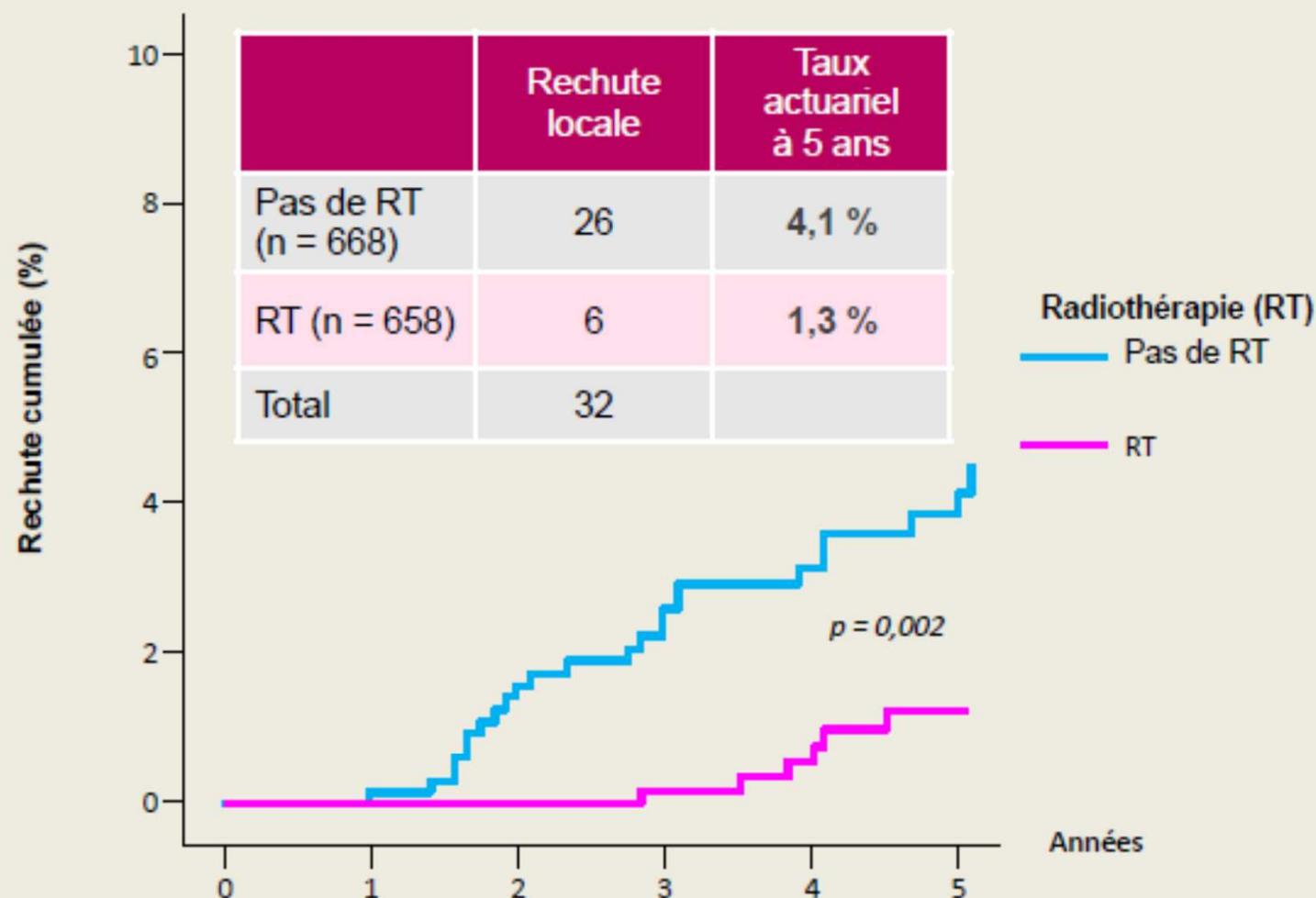


- Taille de la population calculée : 1 300 patientes sur la base d'un taux de rechute locale de 2% à 5 ans avec la radiothérapie (RT) vs 5% sans RT
- 98 centres dans 6 pays
- Suivi médian de 5 ans
- Gel de la base de données le 9 Décembre 2013

*Irradiation totale du sein (WBI) : 40 – 50 Gy in 15 – 25 fractions

D'après Kunkler IH *et al.* SABC5 2013
oral presentation S2-1; Abst.

Résultats d'efficacité : contrôle local

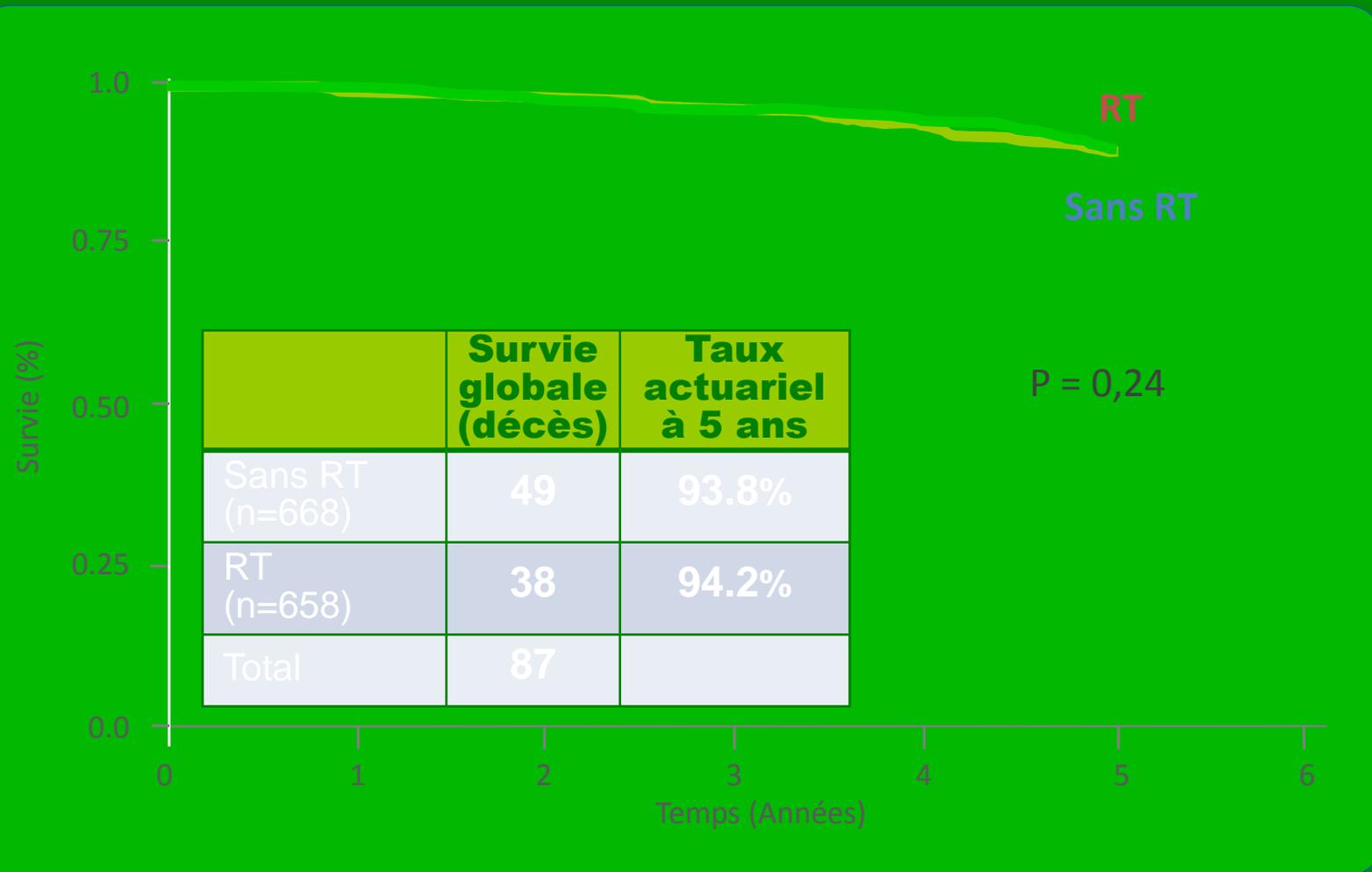


Pas de différence en survie

PRIME II - Effet de la RT en fonction du niveau d'expression des RE

Récidive locale /N (%)			
RE*	RT -	RT +	p-value
Elevée (7-8)	19/594 (3.2%)	5/602 (0.8%)	0.003
Faible (2-6)	7/63 (11.1%)	0/54 (0%)	0.015

PRIME II – SG



Effectiveness of Radiation Therapy for Older Women With Early Breast Cancer

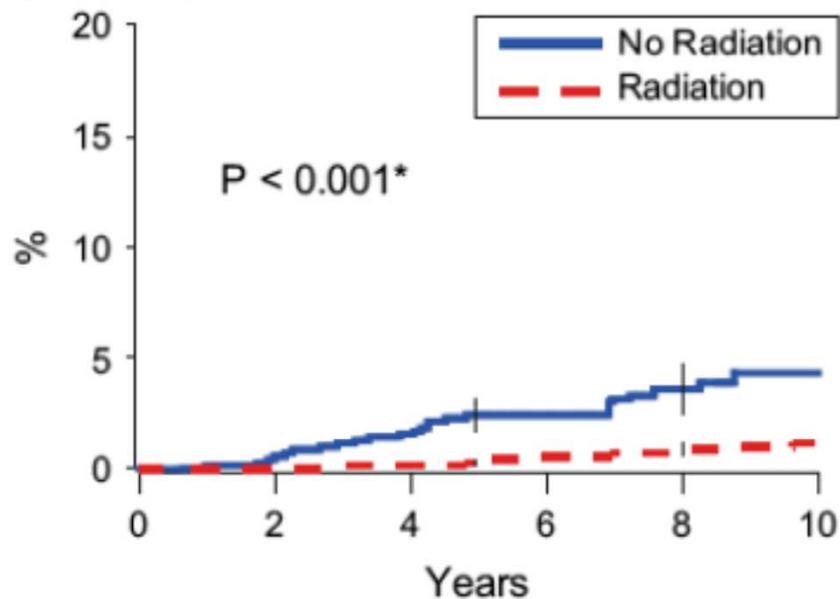
Benjamin D. Smith, Cary P. Gross, Grace L. Smith, Deron H. Galusha, Justin E. Bekelman, Bruce G. Haffty **J Natl Cancer Inst 2006;98:681–90**

and End Results (SEER)–Medicare database from January 1, 1992, through December 31, 1999, to identify 8724 women aged 70 years or older treated with conservative surgery for small, lymph node–negative, estrogen receptor–positive (or unknown receptor status) breast cancer. We used a propor-

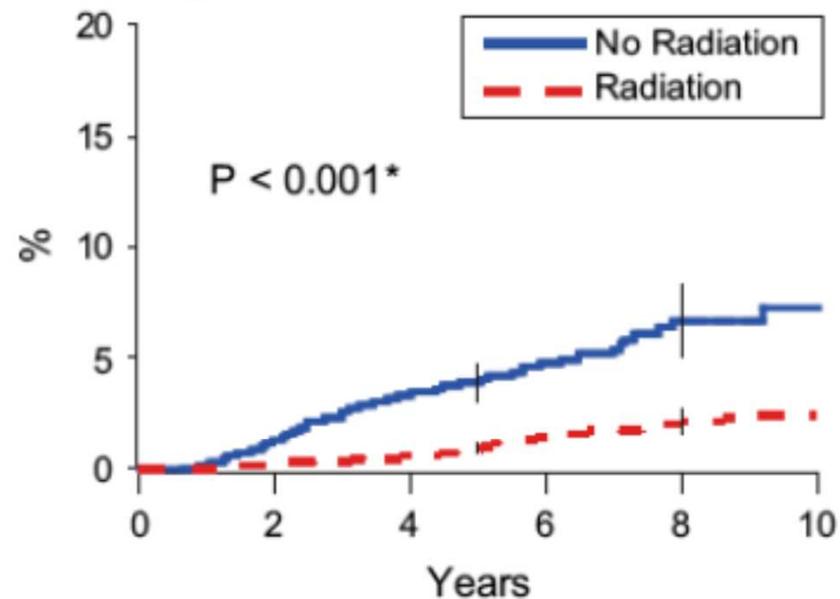
All statistical tests were two-sided. *Results:* Radiation therapy, compared with no radiation therapy, was associated with a lower risk of the combined outcome (hazard ratio = 0.19, 95% confidence interval = 0.14 to 0.28). Radiation therapy was associated with an absolute risk reduction of 4.0 events per 100 women at 5 years (i.e., from 5.1 events without radiation therapy to 1.1 with radiation therapy) and 5.7 events per 100 persons at 8 years (i.e., from 8.0 events without radiation therapy to 2.3 with radiation therapy) ($P < .001$, log-rank test).

- Etude SEER
- 8724 pts - 1992-1999

A. Second ipsilateral breast cancer reported by SEER



B. Subsequent mastectomy reported by Medicare claims



Number at Risk:

No RT	2,364	2,078	1,455	780	334	102
RT	6,360	6,179	4,820	2,832	1,328	368

No RT	2,364	2,011	1,327	687	270	81
RT	6,360	6,009	4,496	2,503	1,100	308

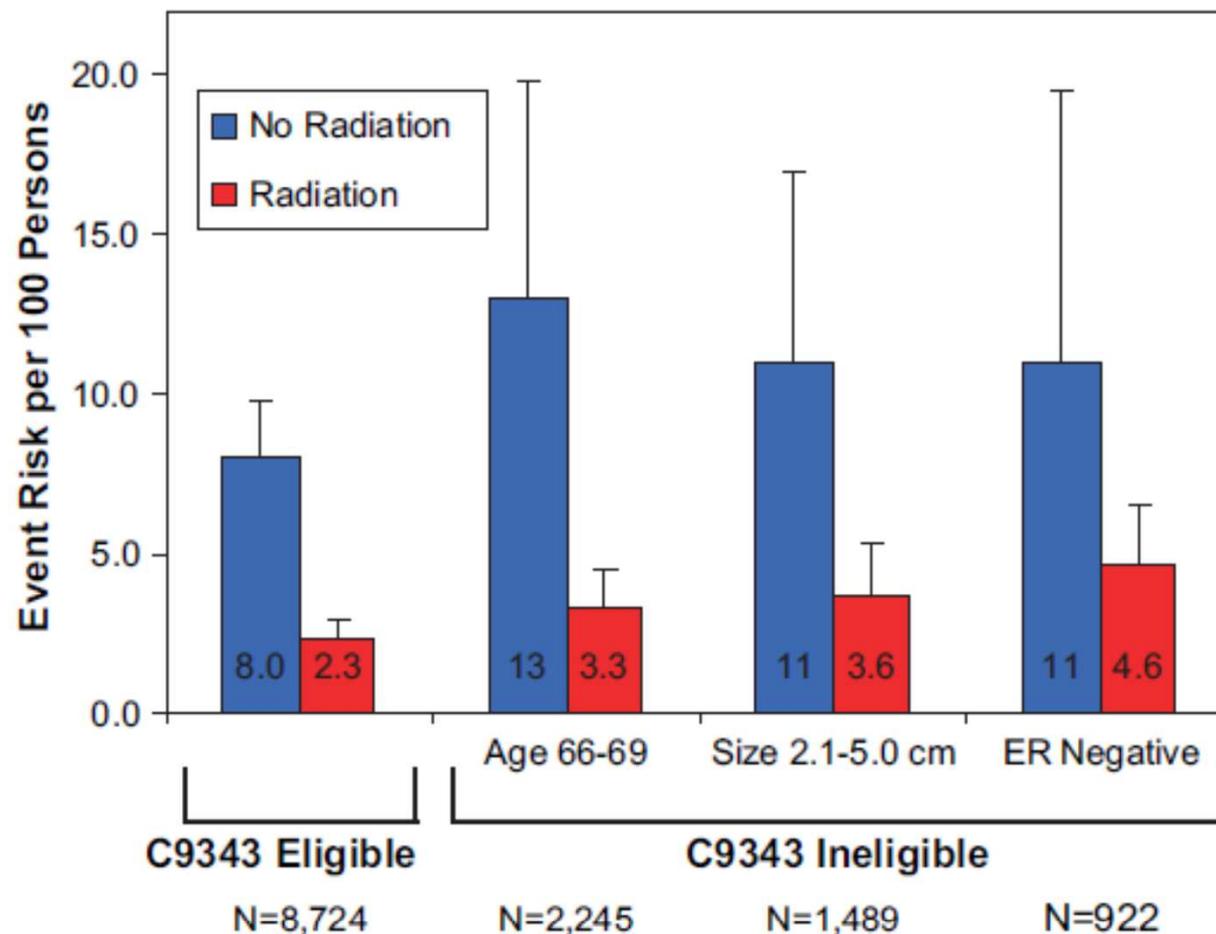


Fig. 2. Risk of a second breast cancer event among patients eligible and ineligible for trial C9343. Eight-year event risk without and with radiation therapy is reported for the four mutually exclusive patient groups, including patients eligible for trial C9343, patients ineligible for trial C9343 because of age 66–69 years, patients ineligible for trial C9343 because of tumor size 2.1–5.0 cm, and patients ineligible for trial C9343 because of estrogen receptor (ER)–negative status. Patients in each of the ineligible groups, including age 66–69 years, tumor size 2.1–5.0 cm, and ER-negative status, meet all the other criteria for trial C9343. Error bars = 95% confidence intervals. All risks are

Radiation therapy was most likely to benefit those aged 70–79 years without comorbidity (number needed to treat [NNT] to prevent one event = 21 to 22 patients) and was least likely to benefit those aged 80 years or older with moderate to severe comorbidity (NNT = 61 to 125 patients). *Conclusion:* For

Table 5. Number needed to treat (NNT) to prevent one second breast cancer event*

Age	Comorbidity score	No.	8-year survival (95% CI), %†	Adjusted NNT (95% CI)‡
70–74 y	0	2188	84 (83 to 86)	21 (16 to 31)
	1	640	72 (68 to 76)	24 (18 to 33)
	2–9	226	47 (40 to 53)	37 (28 to 55)
75–79 y	0	1721	79 (76 to 81)	22 (17 to 33)
	1	572	62 (58 to 67)	28 (21 to 42)
	2–9	262	43 (36 to 51)	41 (31 to 60)
80–84 y	0	1096	61 (57 to 64)	29 (22 to 43)
	1	388	47 (40 to 53)	38 (28 to 56)
	2–9	218	29 (21 to 36)	61 (46 to 90)
≥85 y	0	661	33 (29 to 38)	53 (40 to 78)
	1	316	18 (13 to 24)	97 (73 to 143)
	2–9	178	14 (7.2 to 21)	125 (94 to 185)

RTE « à la carte »: plus l'espérance de vie est longue et les Fc pronostiques défavorables (RH+/-)

Postmastectomy Radiation and Survival in Older Women With Breast Cancer

Benjamin D. Smith, Bruce G. Haffty, Arti Hurria, Deron H. Galusha, and Cary P. Gross

JCO 2006

-SEER 1992-99

- Parmi 60717 femmes \geq 70 ans atteintes de cancer du sein (hormono non rapportée)

Risk Group

Low (T1/2, N0)	n=7416
Intermediate (T1/2, N1)	n=2125
High (T3/4 and/or N2/3)	n=2053

Characteristic	Total No.	PMRT* (%)	P†	Chemotherapy‡ (%)	P†
Entire cohort	11,594	13		13	
Age, years					
70-74	4,204	16	< .0001	20	< .0001
75-79	3,690	15		13	
80-84	2,435	10		6	
85 or older	1,265	7		2	
Race/ethnicity					
White	10,227	13	.008	13	.06
Black	565	17		15	
Asian/Pacific Islander	358	15		15	
White Hispanic	350	16		16	
Other	94	18		10	
Comorbidity index					
0	7,178	14	< .0001	13	.32
1	2,493	11		12	
2 to 9	1,255	11		12	
Unknown	668	18		14	

Postmastectomy Radiation and Survival in Older Women With Breast Cancer

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JCO 2006

Risk Group
Low (T1/2, N0)
Intermediate (T1/2, N1)
High (T3/4 and/or N2/3)

	Total No.	PMRT* (%)	P†	Chemotherapy‡ (%)	P†
Median tumor size, cm					
0-2.0	6,682	9	< .0001	9	< .0001
2.1-5.0	4,232	16		17	
> 5.0	680	39		25	
Clinical stage T4	287	42	< .0001	20	.0006
Tumor grade					
Low	1,481	8	< .0001	6	< .0001
Medium	4,243	12		10	
High/undifferentiated	3,733	17		20	
Unknown	2,157	13		11	
Histology					
Ductal	8,297	12	< .0001	13	.03
Lobular	1,336	19		12	
Other	1,961	12		11	
Estrogen receptor					
Positive	9,565	13	.0009	10	< .0001
Borderline	92	14		17	
Negative	1,937	16		28	
Progesterone receptor					
Positive	8,035	12	< .0001	10	< .0001
Borderline	138	14		17	
Negative	3,421	16		20	
No. of involved regional nodes					
0	7,685	8	< .0001	5	< .0001
1 to 3	2,361	13		20	
4 to 6	670	33		34	
7 to 9	323	41		39	
10 or more	555	50		44	

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JCO 2006

Risk Group

Low (T1/2, N0)

Intermediate (T1/2, N1)

High (T3/4 and/or N2/3)

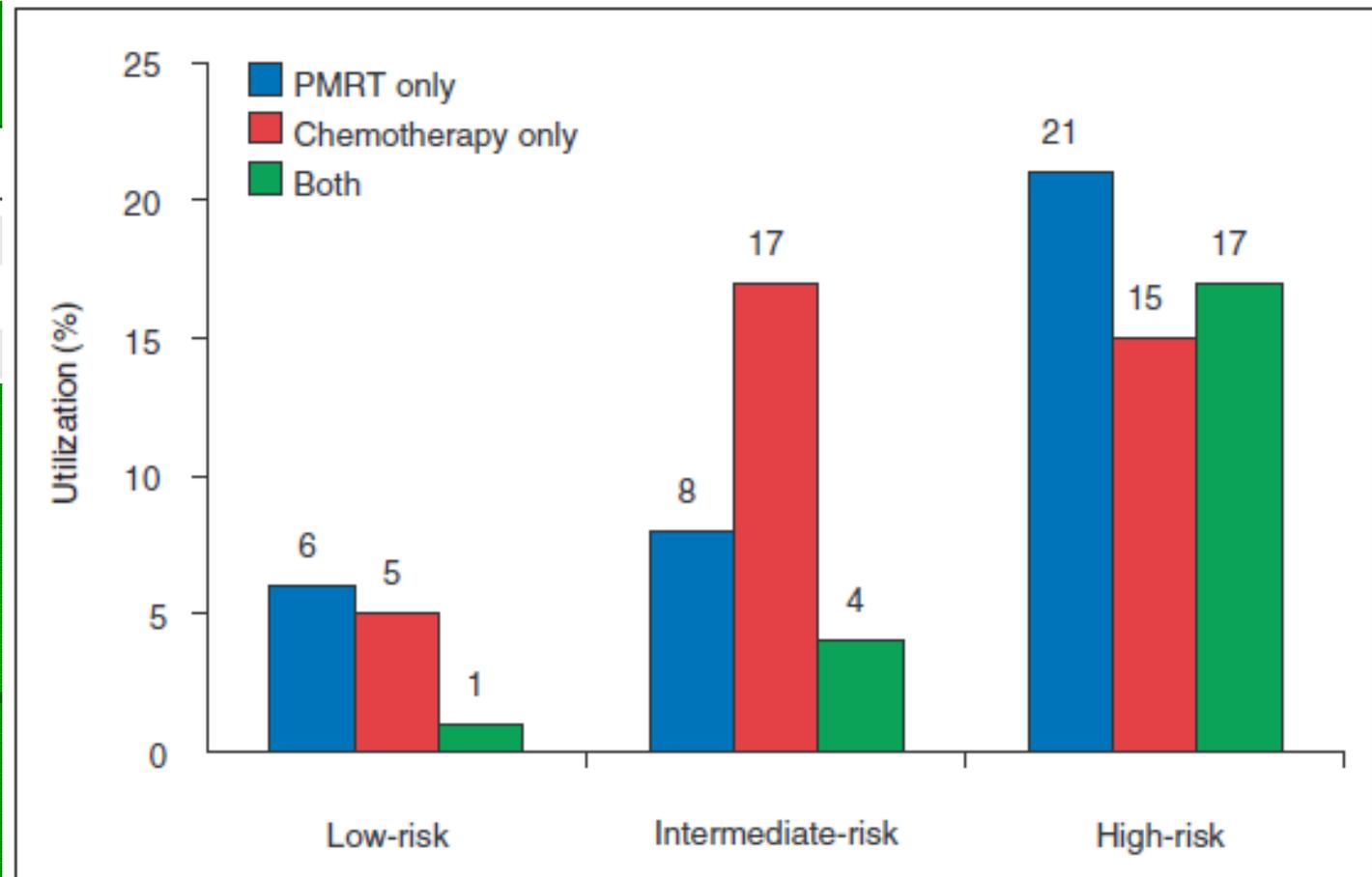


Fig 1. Utilization of postmastectomy radiation therapy (PMRT) and chemotherapy by risk group. The percentage of patients treated with PMRT only, chemotherapy only, or both PMRT and chemotherapy stratified by risk group. Low risk (T1/2 N0); intermediate risk (T1/2 N1); high risk (T3/4 and/or N2/3); PMRT (postmastectomy radiation therapy).

Postmastectomy Radiation and Survival in Older Women With Breast Cancer

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JCO 2006

Risque relatif de décès

Tumor characteristics

Size, cm	1.11	1.10 to 1.13	< .0001
Clinical stage T4	1.17	1.00 to 1.37	.05
Grade			
Low	1.0		
Intermediate	1.22	1.10 to 1.35	.0002
High/undifferentiated	1.43	1.28 to 1.59	< .0001
No. of involved regional nodes	1.06	1.05 to 1.07	< .0001
Histology			
Ductal	1.0		
Lobular	0.80	0.72 to 0.88	< .0001
Other	0.98	0.91 to 1.06	.60
Estrogen receptor			
Positive	1.0		
Borderline	1.05	0.78 to 1.40	.76
Negative	1.17	1.08 to 1.28	.0003
Progesterone receptor			
Positive	1.0		
Borderline	1.18	0.93 to 1.50	.17
Negative	1.19	1.11 to 1.28	< .0001

Postmastectomy Radiation and Survival in Older Women With Breast Cancer

Benjamin D. Smith, Bruce G. Haffty, Arti Hurria, Deron H. Galusha, and Cary P. Gross

JCO 2006

Risque relatif de décès

Age, years	1.073	1.067 to 1.078	< .0001
Charlson comorbidity score			
0	1.0		
1	1.50	1.40 to 1.61	< .0001
2-9	2.12	1.94 to 2.31	< .0001

Impact de la radiothérapie

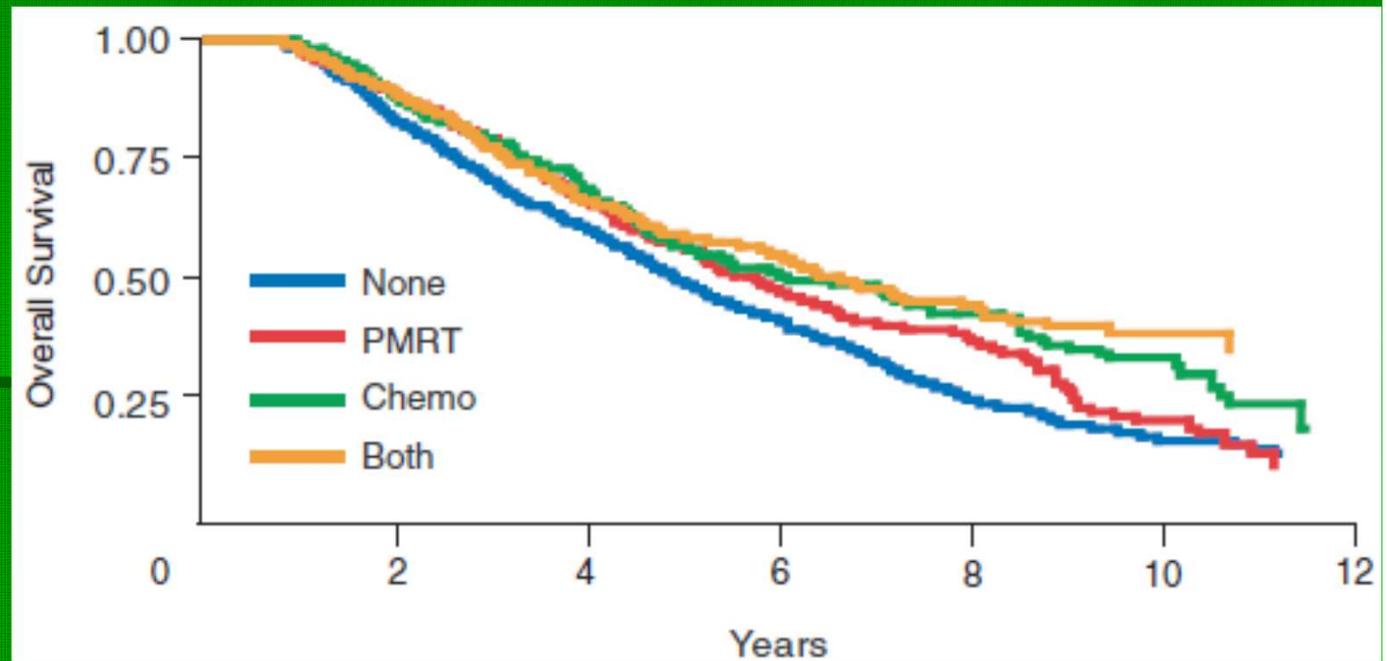
Risk Group	Untreated HR	PMRT		
		HR	95% CI	P
Low (T1/2, N0)	1.0	1.06	0.90 to 1.24	.48
Intermediate (T1/2, N1)	1.0	1.23	0.99 to 1.52	.06
High (T3/4 and/or N2/3)	1.0	0.85	0.75 to 0.97	.02
All risk groups	1.0	1.03	0.95 to 1.13	.49

Postmastectomy Radiation and Survival in Older Women With Breast Cancer

Benjamin D. Smith, Bruce G. Haffty, Arti Hurria, Deron H. Galusha, and Cary P. Gross

JCO 2006

Groupe « haut risque »



Annals of Oncology Advance Access published March 13, 2014

Review of current best practice and priorities for research in radiation oncology for elderly patients with cancer: the International Society of Geriatric Oncology (SIOG) task force

I.H. Kunkler¹, R. Audisio², Y. Belkacemi³, M. Betz⁴, E. Gore⁵, S. Hoffe⁶, Y. Kirova⁷, P. Koper⁸, J-L Lagrange³, A. Markouizou⁹, R. Pfeffer¹⁰, S. Villa¹¹, On behalf of the SIOG Radiotherapy Task Force

¹Edinburgh Cancer Research Centre, University of Edinburgh, Edinburgh, Scotland

²Department of Surgical Oncology, University of Liverpool, St Helens, England

³Service de Radiothérapie, APHP-GH Henri Mondor, and UPEC (Université Paris Est Créteil), France

Key Message: "There is limited Level 1 evidence for the role in curative radiotherapy in older patients. The evidence base for commonly treated solid tumours is reviewed. Best practice and research priorities are presented."

Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)

Laura Biganzoli, Hans Wildiers, Catherine Oakman, Lorenza Marotti, Sibylle Loibl, Ian Kunkler, Malcolm Reed, Stefano Ciatto, Adri C Voogd, Etienne Brain, Bruno Cutuli, Catherine Terret, Margot Gosney, Matti Aapro, Riccardo Audisio

- Actualisation des recos de 2007
- 100 à 350/an /100000 habitants en Europe
- Manque de données de niveau 1
- Présentation différente/femme jeune:
 - RH+ (50-60% vs 75-85%)
 - HER2+ (22% vs 10%)
 - N+ un peu plus fréquent à tumeur de taille égale
- Risque de mortalité spécifique vs autres causes: âge non suffisant pour décider
- Evaluation gériatrique? ADLs et IADLs mais de toute façon pas facile à décider
- Préférences des malades ?

Lancet Oncol 2012

Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)

Laura Biganzoli, Hans Wildiers, Catherine Oakman, Lorenza Marotti, Sibylle Loibl, Ian Kunkler, Malcolm Reed, Stefano Ciatto, Adri C Voogd, Etienne Brain, Bruno Cutuli, Catherine Terret, Margot Gosney, Matti Aapro, Riccardo Audisio

Lancet Oncol 2012

	2007 recommendations (SIOG)	Current recommendations (SIOG/EUSOMA)
General recommendations for all aspects of management	..	All management decisions for an older individual with breast cancer should consider: Physiological age Life expectancy Potential risks vs absolute benefits Treatment tolerance Patient preference Potential barriers to treatment
Radiotherapy	WBRT after BCS, with a boost to the tumour bed, should be considered in all elderly patients since it decreases risk of local relapse (there is no evidence for an overall survival advantage in analyses restricted to elderly patients) Post-mastectomy chest-wall radiation should be considered for elderly patients with at least four nodes or a pT3/4 tumour The role of omission of postoperative WBRT, partial breast irradiation, and hypofractionation are undefined	WBRT after BCS, with a boost to the tumour bed, should be considered in all elderly patients since it decreases risk of local relapse. There is no subgroup of fit older patients in whom post-BCS WBRT can be systematically omitted (see text) Post-mastectomy chest-wall radiation should be considered for elderly patients with at least four nodes or a pT3/4 tumour Hypofractionated radiation schedules offer similar local-regional control and adverse effects as standard WBRT The evidence for PBI in older patients is not sufficiently robust to recommend it as standard therapy

Conclusions Recos 2012

WBRT after BCS, with a boost to the tumour bed, should be considered in all elderly patients since it decreases risk of local relapse. There is no subgroup of fit older patients in whom post-BCS WBRT can be systematically omitted (see text)

Post-mastectomy chest-wall radiation should be considered for elderly patients with at least four nodes or a pT3/4 tumour

Hypofractionated radiation schedules offer similar local-regional control and adverse effects as standard WBRT

The evidence for PBI in older patients is not sufficiently robust to recommend it as standard therapy

Essais START

The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials

Joanne S Haviland, J Roger Owen, John A Dewar, Rajiv K Agrawal, Jane Barrett, Peter J Barrett-Lee, H Jane Dobbs, Penelope Hopwood, Pat A Lawton, Brian J Magee, Judith Mills, Sandra Simmons, Mark A Sydenham, Karen Venables, Judith M Bliss, John R Yarnold*, on behalf of the START Trialists' Group†*

Lancet Oncol 10 2013

Méthodes

- entre 1999 et 2002. Après exérèse chirurgicale complète pour carcinome infiltrant de stades pT1-3a, pN0-N1, M0, les malades ont été randomisées dans plusieurs schémas de RT :
- **START-A : n=2236 malades**
- Soit 50 Gy en 25 fractions de 2 Gy sur 5 semaines (bras contrôle)
- Soit 41,6 Gy en 13 fractions sur 5 semaines
- Soit 39 Gy en 13 fractions sur 5 semaines
- **START-B : n=2215 malades**
- Soit 50 Gy classique
- Soit 40 Gy en 15 fractions et 3 semaines
- Un boost éventuel de 10 Gy en 5 fractions était autorisé mais décidé avant randomisation pour ne pas déséquilibrer les bras.
- Les études étaient stratifiées par centre investigateur, type de chirurgie et boost éventuel.

- START-A :
- Patientes : âge médian 57 ans, chirurgie conservatrice (85%), pT1 (51%), pN1 (29%), chimio adjuvante (35%), radiothérapie ganglionnaire (14%) et boost (61%) en cas de traitement conservateur
- Le suivi médian est de 9,3 ans : 1700 malades sont en vie et sans rechute (76%).
- Les taux de rechute locale sont respectivement de 6,7% pour 50 Gy, 5,6% pour 41,6 Gy et 8,1% pour 39 Gy sans différence significative.
- Il n'est pas observé de différence en termes de survie sans récurrence et de survie globale entre les 3 bras

	Events (n/patients; %)	Estimated proportion of patients with event by 5 years (%; 95% CI)	Estimated proportion of patients with event by 10 years (%; 95% CI)	Crude hazard ratio (95% CI)	p value*
Local relapse					
50 Gy	40/749 (5.3%)	3.4% (2.3-5.1)	6.7% (4.9-9.2)	1.00	-
41.6 Gy	37/750 (4.9%)	3.1% (2.0-4.7)	5.6% (4.1-7.8)	0.90 (0.57-1.40)	0.63
39 Gy	47/737 (6.4%)	4.4% (3.1-6.2)	8.1% (6.1-10.7)	1.20 (0.79-1.83)	0.39
Local-regional relapse					
50 Gy	45/749 (6.0%)	4.0% (2.8-5.7)	7.4% (5.5-10.0)	1.00	-
41.6 Gy	42/750 (5.6%)	3.8% (2.6-5.5)	6.3% (4.7-8.5)	0.91 (0.59-1.38)	0.65
39 Gy	52/737 (7.1%)	5.1% (3.7-7.1)	8.8% (6.7-11.4)	1.18 (0.79-1.76)	0.41
Distant relapse					
50 Gy	100/749 (13.3%)	9.8% (7.9-12.3)	14.7% (12.2-17.7)	1.00	-
41.6 Gy	110/750 (14.7%)	9.5% (7.6-11.9)	16.8% (14.0-20.0)	1.08 (0.82-1.41)	0.58
39 Gy	121/737 (16.4%)	11.8% (9.7-14.4)	18.0% (15.1-21.2)	1.24 (0.95-1.61)	0.11

- START-B : n=2215 malades incluses : âge médian 57 ans, 92% de chirurgie conservatrice, 64% de pT1, 23% pN+, 22% de chimio adjuvante, 7% de radiothérapie ganglionnaire et 43% de boost. Par rapport à START-A, la population semble sélectionnée à un stade plus précoce.
- Le suivi médian est de 9,9 ans. La survie sans rechute est de 78,2%.
- Les taux de rechute locale sont respectivement de 5,2% à 50 Gy et 3,8% à 40 Gy. Les taux de rechute locorégionale sont de 5,5% à 50 Gy et de 4,3% à 40 Gy.
- Il n'est pas observé non plus de différence en

	Events (n/patients; %)	Estimated proportion of patients with event by 5 years (%; 95% CI)	Estimated proportion of patients with event by 10 years (%; 95% CI)	Crude hazard ratio (95% CI)	p value ^a
Local relapse					
50 Gy	50/1105 (4.5%)	3.3% (2.4-4.6)	5.2% (3.9-6.9)	1.00	-
40 Gy	36/1110 (3.2%)	1.9% (1.2-3.0)	3.8% (2.7-5.2)	0.70 (0.46-1.07)	0.10
Local-regional relapse					
50 Gy	53/1105 (4.8%)	3.5% (2.5-4.8)	5.5% (4.2-7.2)	1.00	-
40 Gy	42/1110 (3.8%)	2.3% (1.5-3.4)	4.3% (3.2-5.9)	0.77 (0.51-1.16)	0.21
Distant relapse					
50 Gy	158/1105 (14.3%)	10.5% (8.8-12.5)	16.0% (13.8-18.5)	1.00	-
40 Gy	121/1110 (10.9%)	7.5% (6.0-9.2)	12.3% (10.3-14.6)	0.74 (0.59-0.94)	0.014

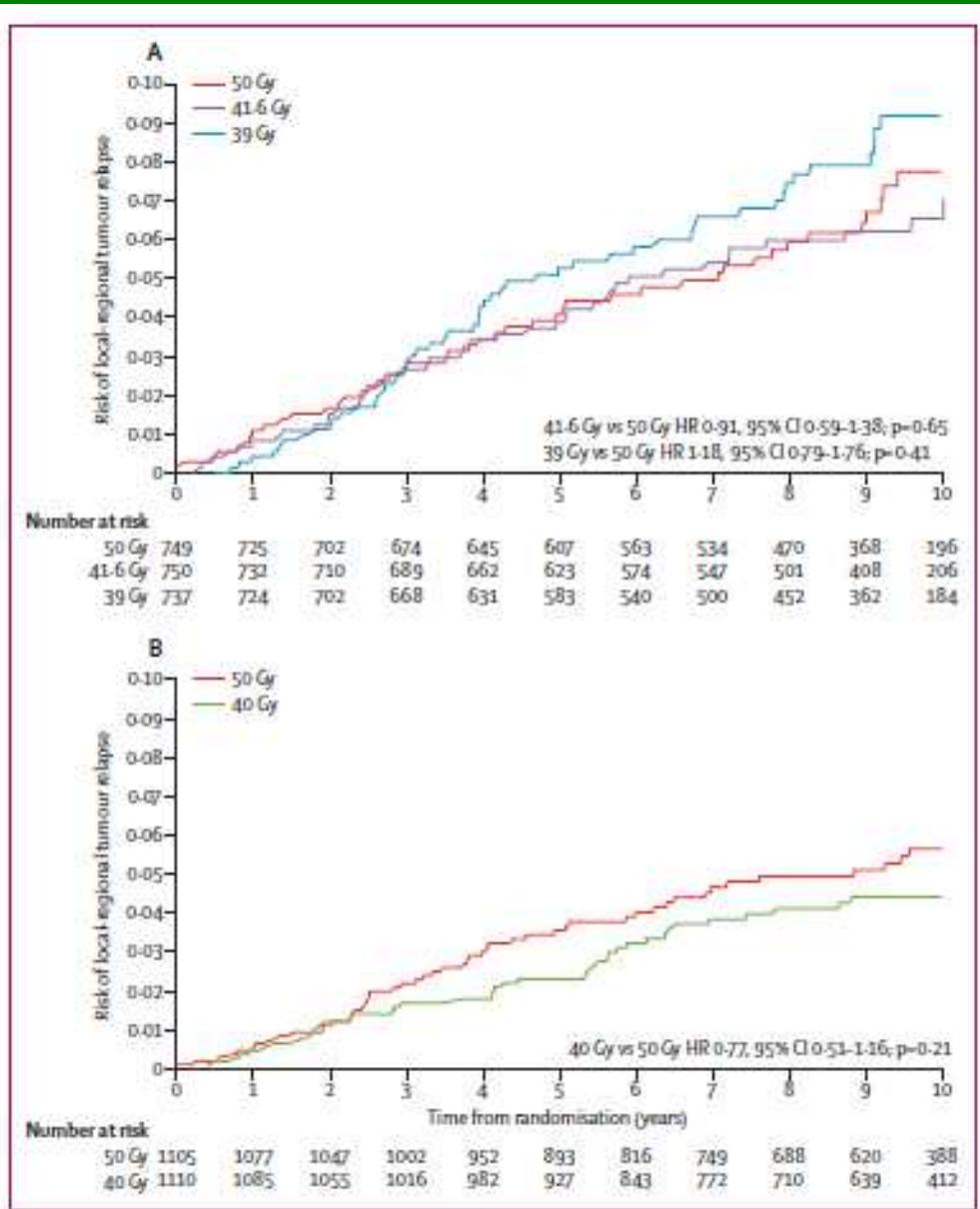


Figure 1: Cumulative risk of local-regional tumour relapse
In START-A (A) and START-B (B).

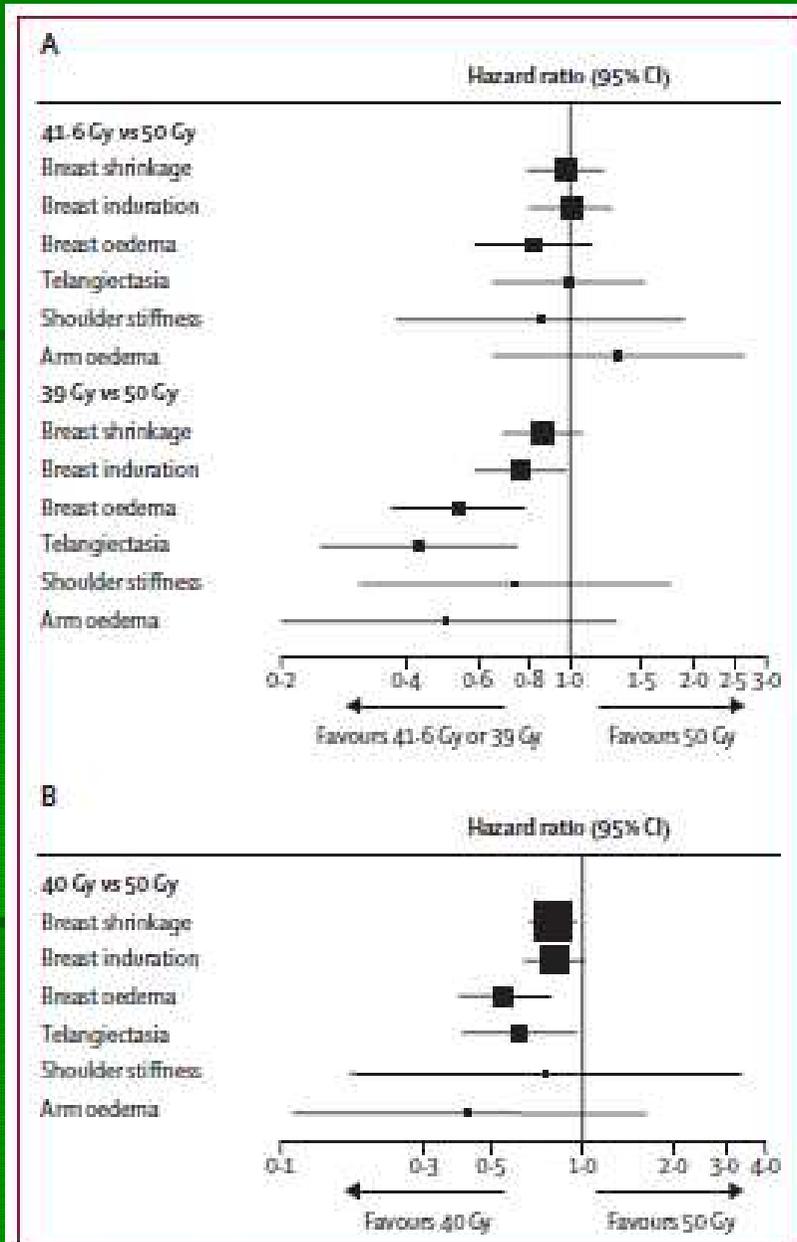


Figure 3: Late normal tissue effects in START-A (A) and START-B (B). Assessed as moderate or marked by physicians.

Une méta-analyse rassemblant les 2 essais ne retrouve pas d'influence de l'âge, du type de chirurgie, de l'atteinte ganglionnaire du grade histologique, du boost et de la chimiothérapie sur les résultats, aussi bien que pour les complications tardives

Supportent largement l'utilisation considérée « standard » du schéma 40 Gy en 15 fractions et 3 semaines, comme recommandé par le NICE (National Institute for health and Cancer Excellence).

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

NEJM 2010

Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D.,

We conducted a study to determine whether a hypofractionated 3-week schedule of whole-breast irradiation is as effective as a 5-week schedule. Women with invasive breast cancer who had undergone breast-conserving surgery and in whom resection margins were clear and axillary lymph nodes were negative were randomly assigned to receive whole-breast irradiation either at a standard dose of 50.0 Gy in 25 fractions over a period of 35 days (the control group) or at a dose of 42.5 Gy in 16 fractions over a period of 22 days (the hypofractionated-radiation group).

RESULTS

The risk of local recurrence at 10 years was 6.7% among the 612 women assigned to standard irradiation as compared with 6.2% among the 622 women assigned to the hypofractionated regimen (absolute difference, 0.5 percentage points; 95% confidence interval [CI], -2.5 to 3.5). At 10 years, 71.3% of women in the control group as compared with 69.8% of the women in the hypofractionated-radiation group had a good or excellent cosmetic outcome (absolute difference, 1.5 percentage points; 95% CI, -6.9 to 9.8).

CONCLUSIONS

Ten years after treatment, accelerated, hypofractionated whole-breast irradiation was not inferior to standard radiation treatment in women who had undergone breast-conserving surgery for invasive breast cancer with clear surgical margins and negative axillary nodes. (ClinicalTrials.gov number, NCT00156052.)

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

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- N= 612 dans bras 50 Gy
- 622 dans bras 42,5 Gy
- N- et pas de boost
- 25% < 50 ans
- 31% T > 2cm
- 26% RH-
- 42% TMX adjuvant
- 11% chimio adjuvante

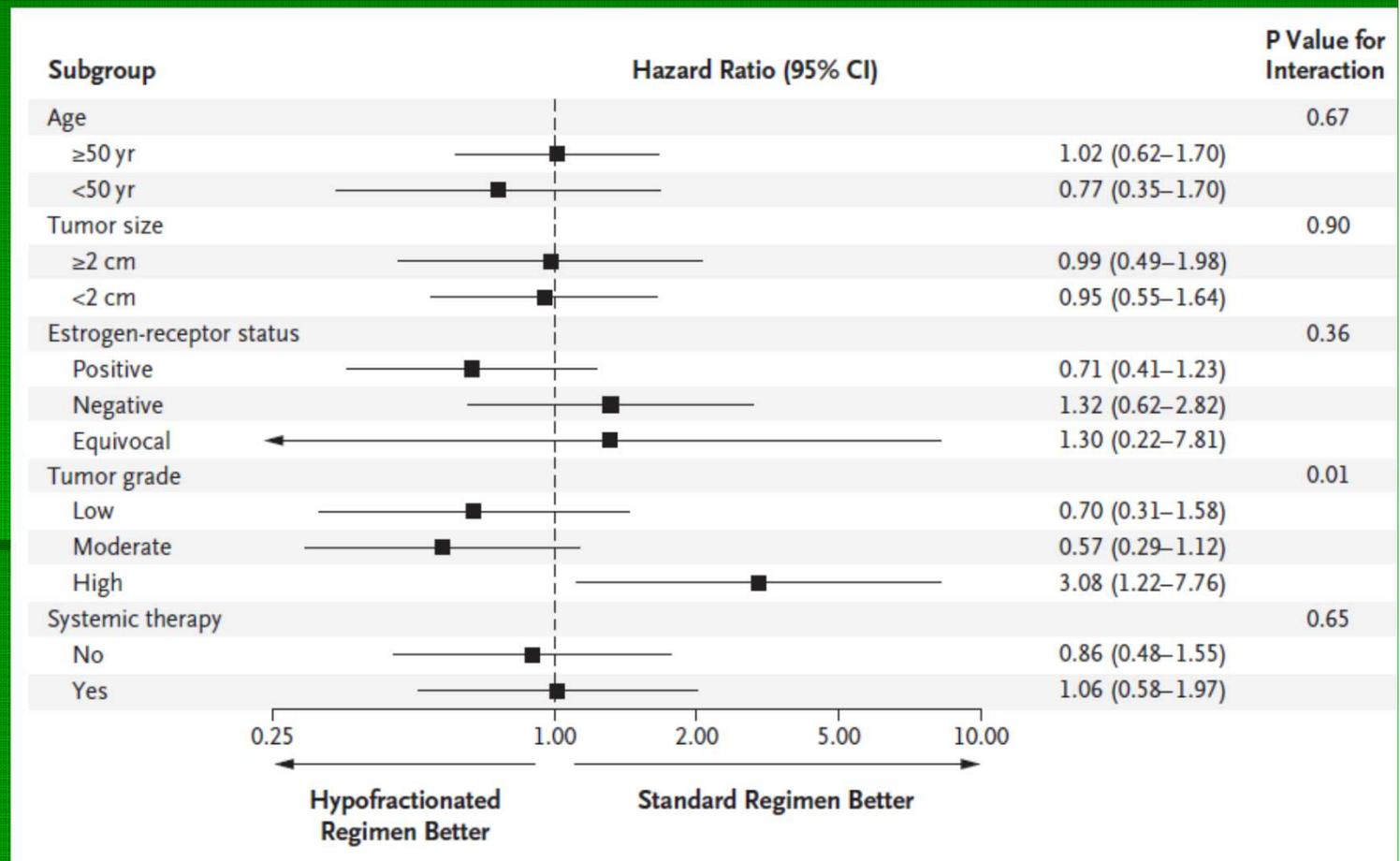
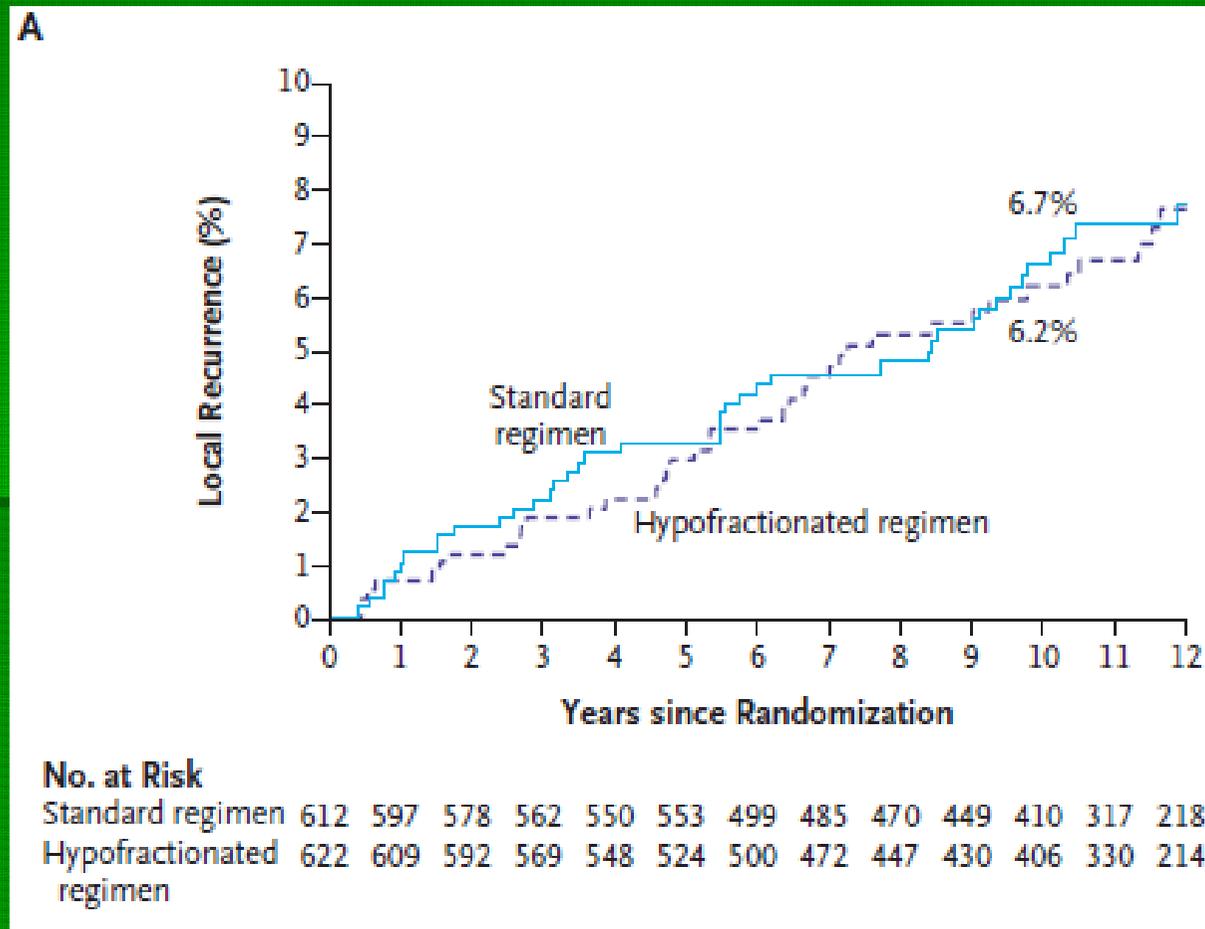


Figure 2. Hazard Ratios for Ipsilateral Recurrence of Breast Cancer in Subgroups of Patients.

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Table 1. Late Toxic Effects of Radiation, Assessed According to the RTOG–EORTC Late Radiation Morbidity Scoring Scheme.*

Site and Grade	5 Yr		10 Yr	
	Standard Regimen (N=424)	Hypofractionated Regimen (N=449)	Standard Regimen (N=220)	Hypofractionated Regimen (N=235)
	<i>percent of patients</i>			
Skin				
0†	82.3	86.1	70.5	66.8
1	14.4	10.7	21.8	24.3
2	2.6	2.5	5.0	6.4
3	0.7	0.7	2.7	2.5
Subcutaneous tissue				
0‡	61.4	66.8	45.3	48.1
1	32.5	29.5	44.3	40.0
2	5.2	3.8	6.8	9.4
3	0.9	0.9	3.6	2.5

*Effects of radiation therapy on skin and subcutaneous tissue were graded on a scale of 0 to 4 (with 0 indicating no toxic effects and grade 4 indicating skin ulceration or soft-tissue necrosis). RTOG–EORTC denotes the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer.

Tumor Factors Predictive of Response to Hypofractionated Radiotherapy in a Randomized Trial Following Breast Conserving Therapy

A. L. Bane^{1,2}, T. J. Whelan², G. R. Pond², S. Parpia², G. Gohla¹, A. W. Fyles³, J-P. Pignol³, K. I. Pritchard⁴, S. Chambers², M. N. Levine²

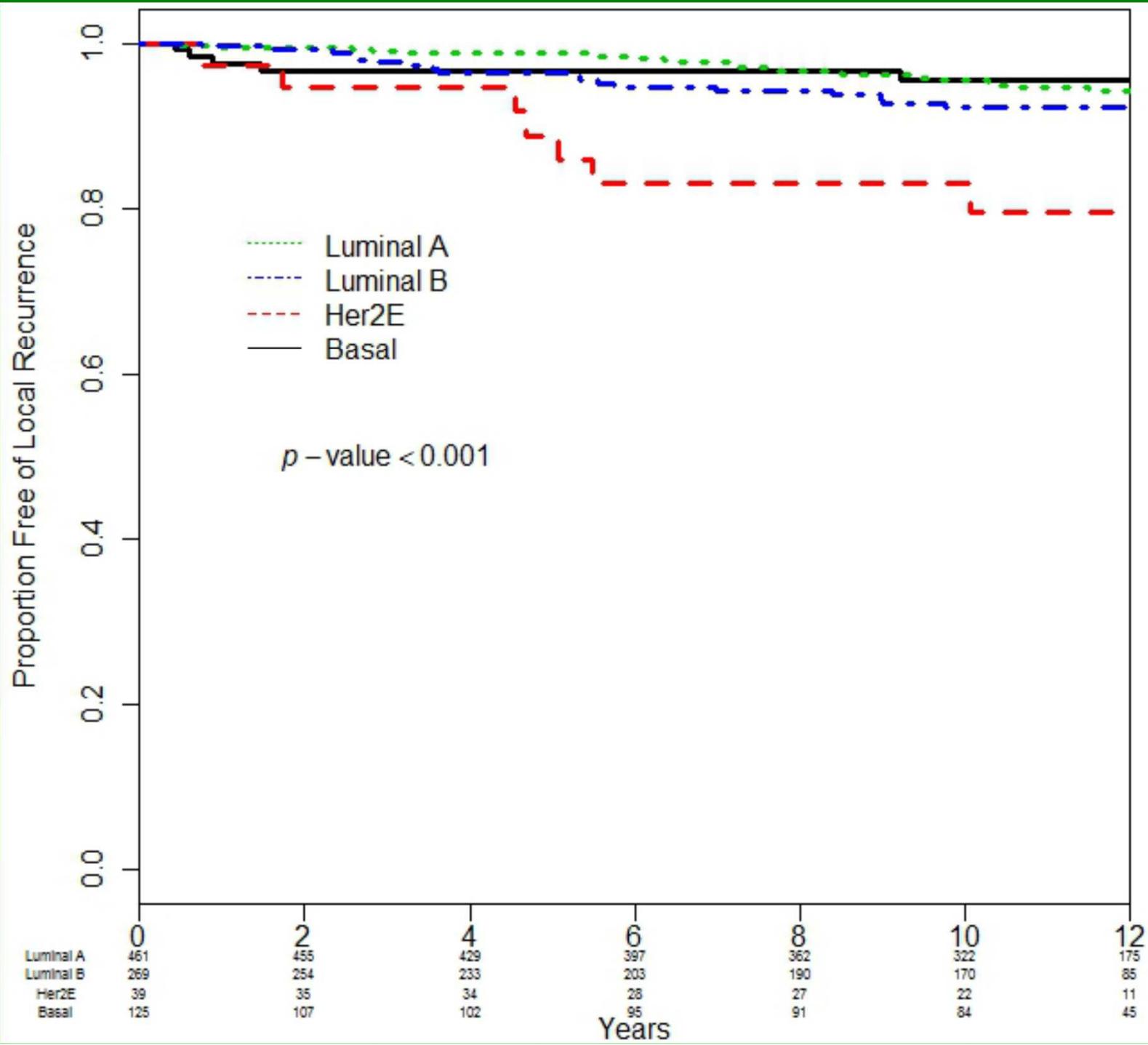
Key Message: "Using tumor blocks from 989 patients enrolled in a randomised controlled trial of hypofractionated radiotherapy vs. standard radiotherapy following breast conserving surgery we demonstrate that tumor molecular subtype is predictive of local recurrence and that breast tumors of all grades and molecular subtypes may be safely treated with hypofractionated radiotherapy."

Purpose. To determine whether tumor grade, molecular subtype and hypoxia predict response to hypofractionated vs. standard radiotherapy (RT) following breast conserving surgery (BCS) for node negative breast cancer in a randomised controlled trial (RCT).

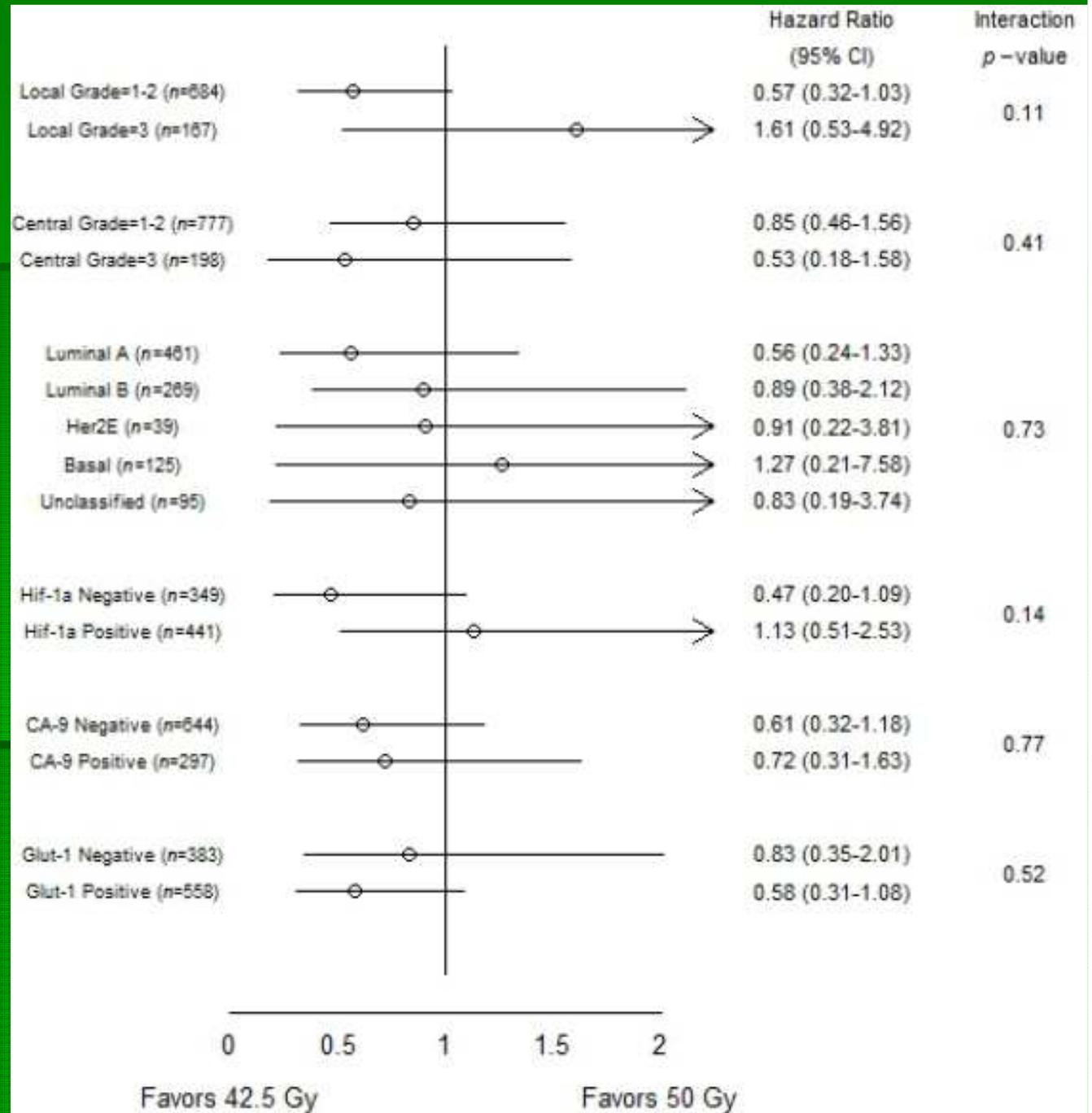
Patients and Methods. Formalin fixed paraffin embedded (FFPE) tumor blocks were available on 989 of 1234 patients enrolled in the Hypofractionation Whole Breast Irradiation (HWBI) Trial. A central pathology review and assessment of tumor grade using the Nottingham grading system was performed. Tumors were classified by molecular subtype as luminal A, luminal B, HER2 enriched, basal-like or unclassified using a six-biomarker panel; ER, PR, HER-2, Ki67, CK5/6 and EGFR. Tumors were also classified as hypoxic based on the expression of HIF1 α , CAIX or GLUT-1. The primary end point was local recurrence (LR).

Results. Median follow-up was 12 years. In the multivariable Cox model molecular subtype was the only factor predictive of LR, the 10 year cumulative incidence was 4.5% for luminal A and basal-like, 7.9% for luminal B and 16.9% for HER-2 enriched tumors ($p < 0.01$). Tumor grade, molecular subtype or hypoxia did not predict response to hypofractionation.

Conclusions. In women enrolled in the HWBI trial following BCS tumor molecular subtype predicted LR. However tumor grade, molecular subtype and hypoxia did not predict response to hypofractionation suggesting that patients with node negative breast tumors of all grades and molecular subtypes may be safely treated with hypofractionated RT regimens.



Contrôle local



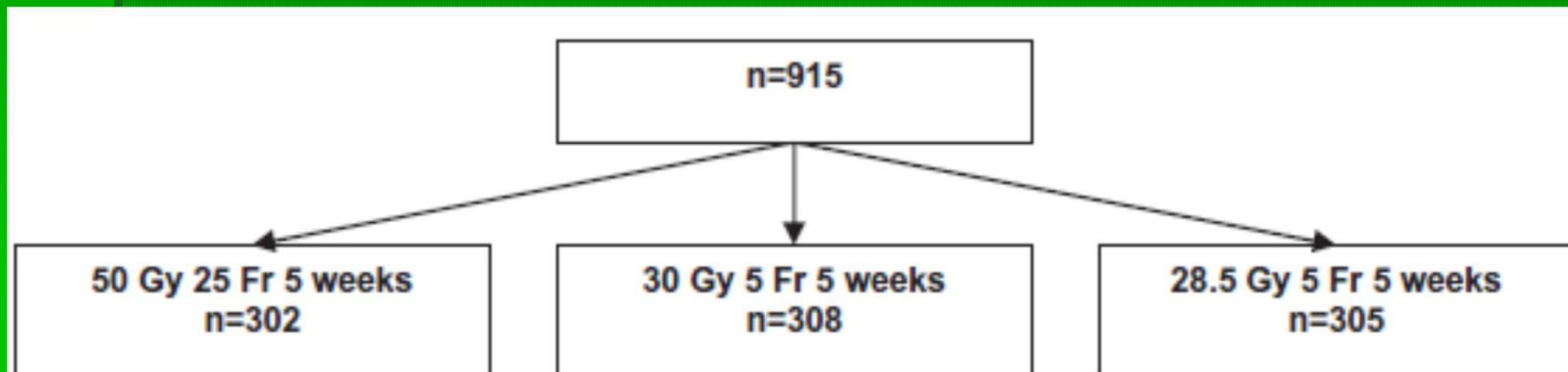
« Ultra » Hypofractionnement

First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015)

The FAST Trialists group¹

Radiotherapy and Oncology 100 (2011) 93–100

Age > 50 ans, T ≤ 3 cm, marges OK et N- (environ 16% ≥ 70 ans)



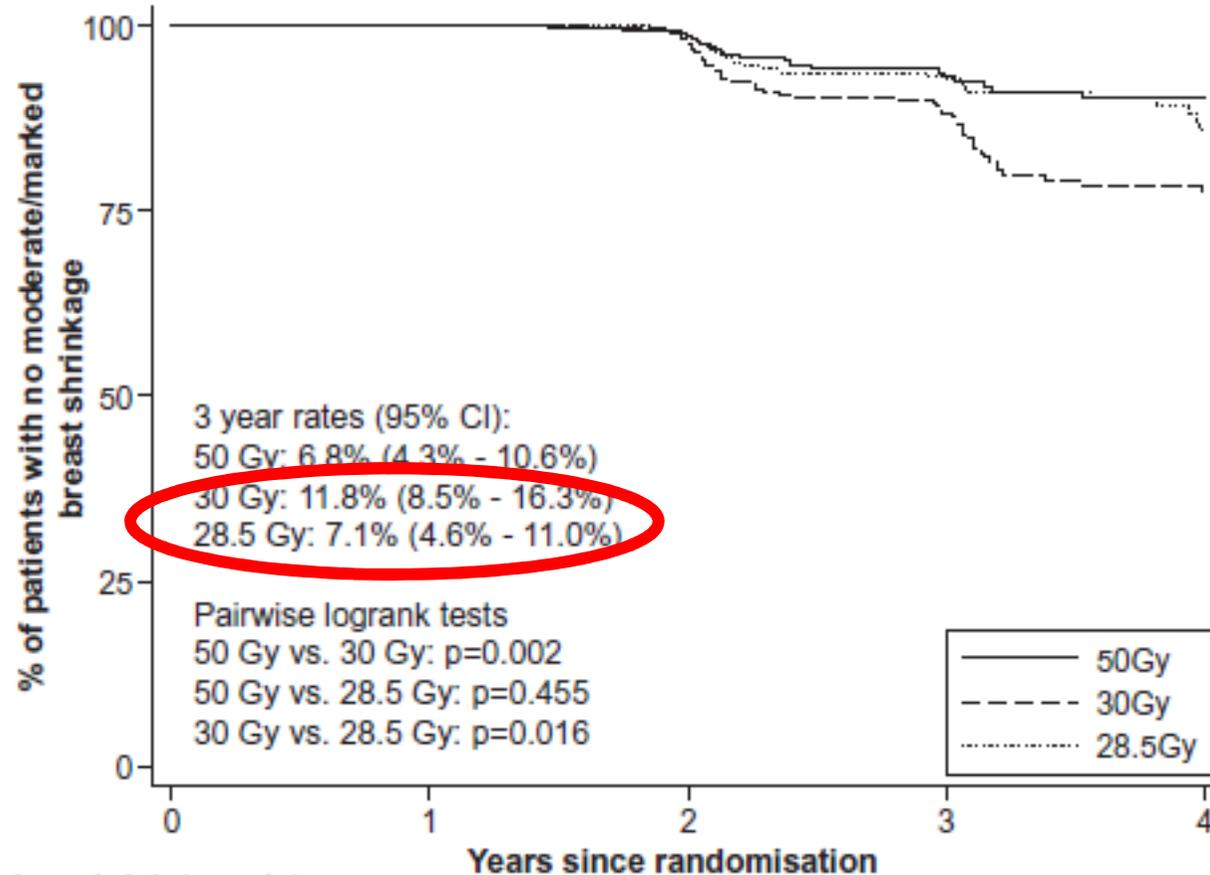
Critère majeur: aspect esthétique par photographie (RTOG)

Médiane de suivi: 3 ans

First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015)

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Number at risk (events)

	0	1	2	3	4
50 Gy	302	299	273 (4)	185 (14)	72 (4)
30 Gy	308	301	281 (7)	183 (25)	63 (16)
28.5 Gy	305	298	279 (4)	191 (15)	64 (8)

First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015)

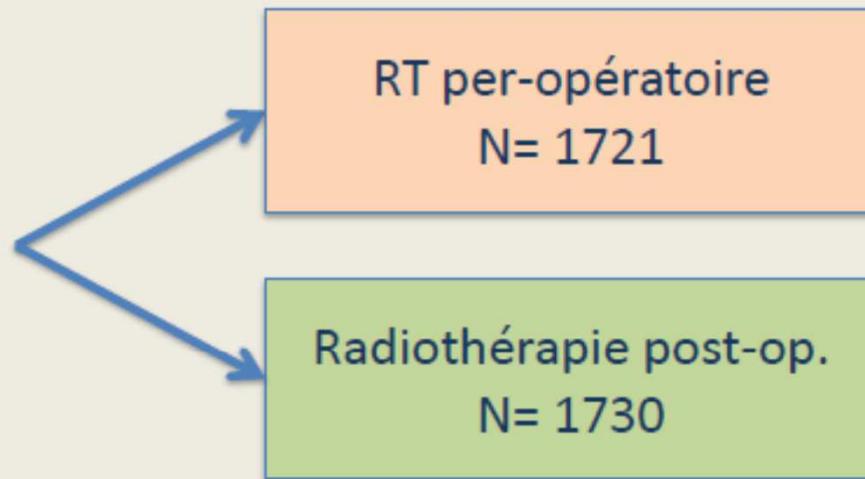
The FAST Trialists group¹

Relapses, second primary cancers and deaths by fractionation schedule.

	Fractionation schedule			Total
	50 Gy	30 Gy	28.5 Gy	
Relapses				
Local (breast skin or parenchyma)	2	0	0	2
Regional (axilla or supraclavicular fossa)	1	0	2	3
Distant	5	2	10	17

Radiothérapie intra-opératoire

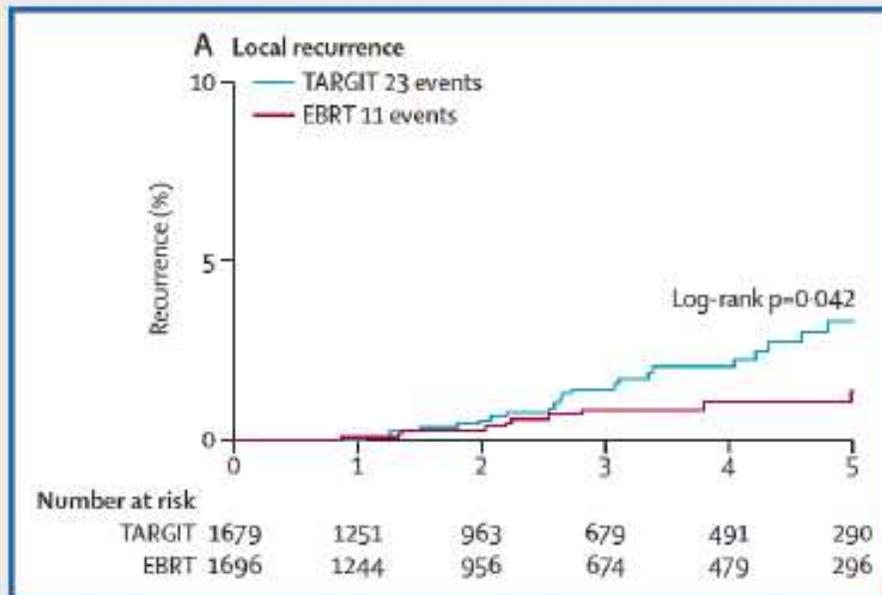
Actualisation de l'essai Targit



- Entre 2000 et 2012 (33 centres dans 11 pays)
- 50 kv 20 Gy: 5-7 Gy à 1 cm
- 85% < 2 cm
- 83% N0
- 90% RH+
- 95 % canalaire

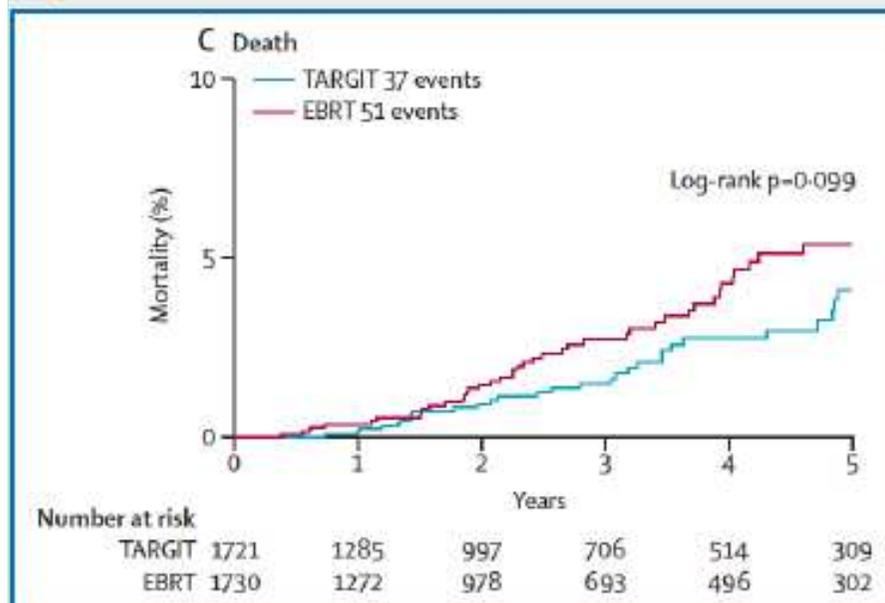


Actualisation du Targit A

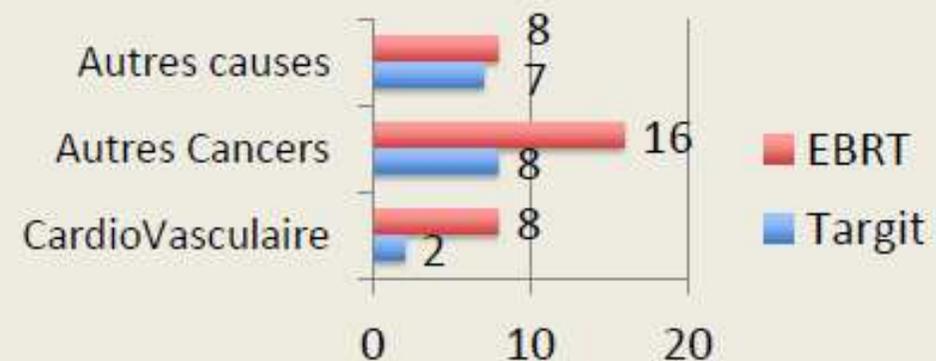


Récidives locales

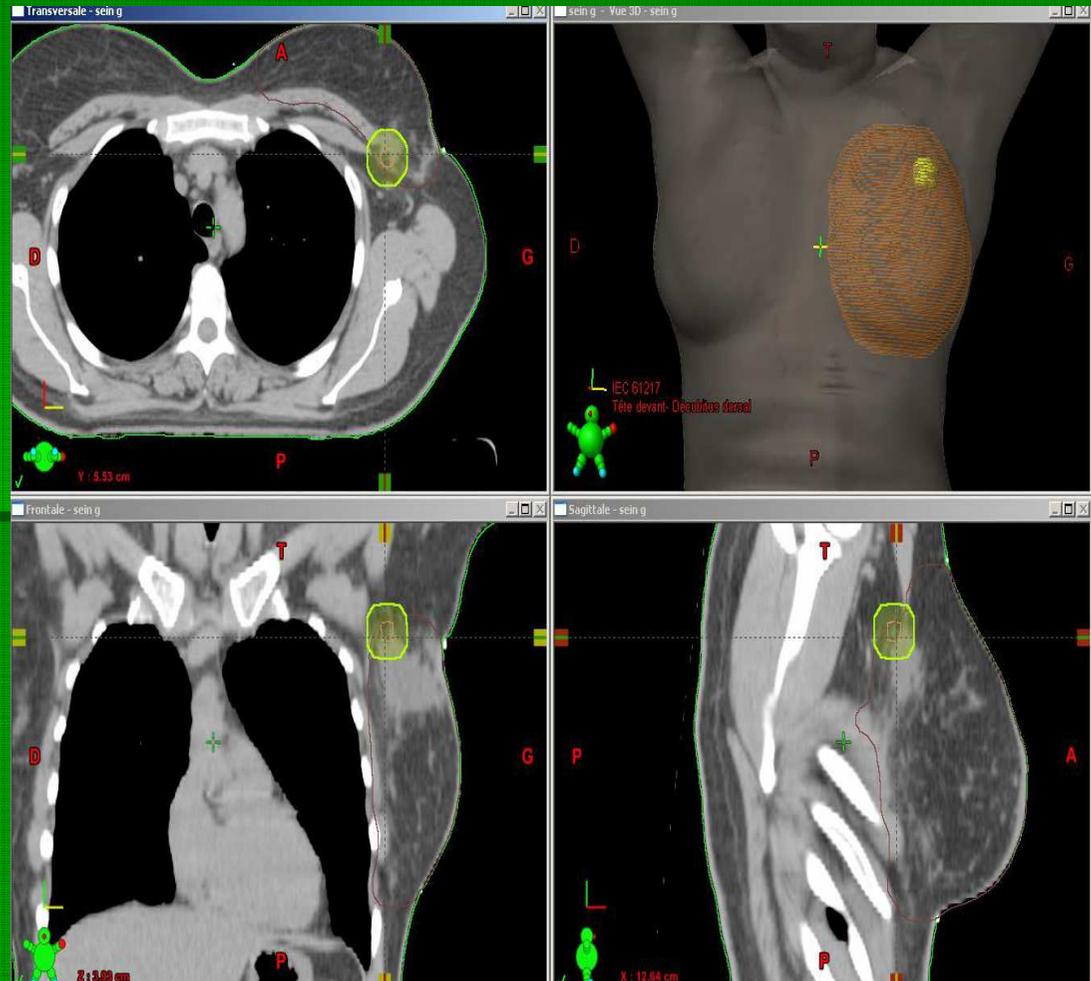
	EBRT	Targit
Toutes	1,3	3,3
1° chir.	1,1	2,1
2° Chir.	1,7	5,4



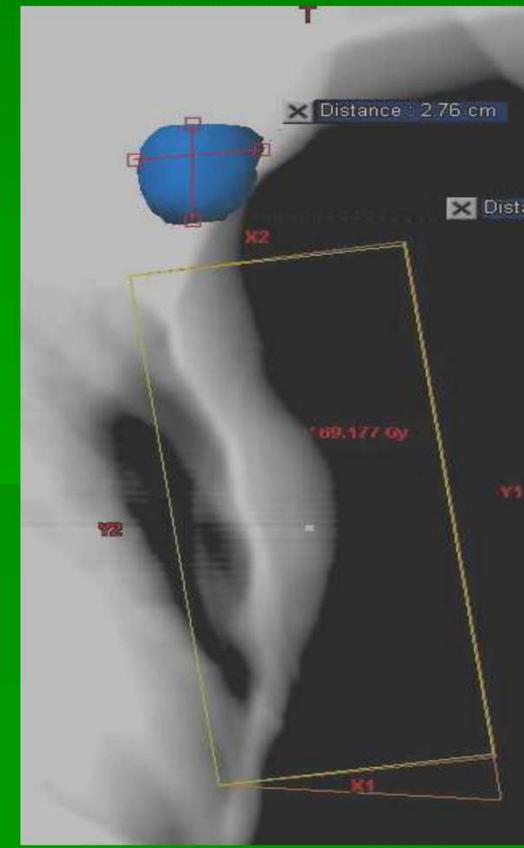
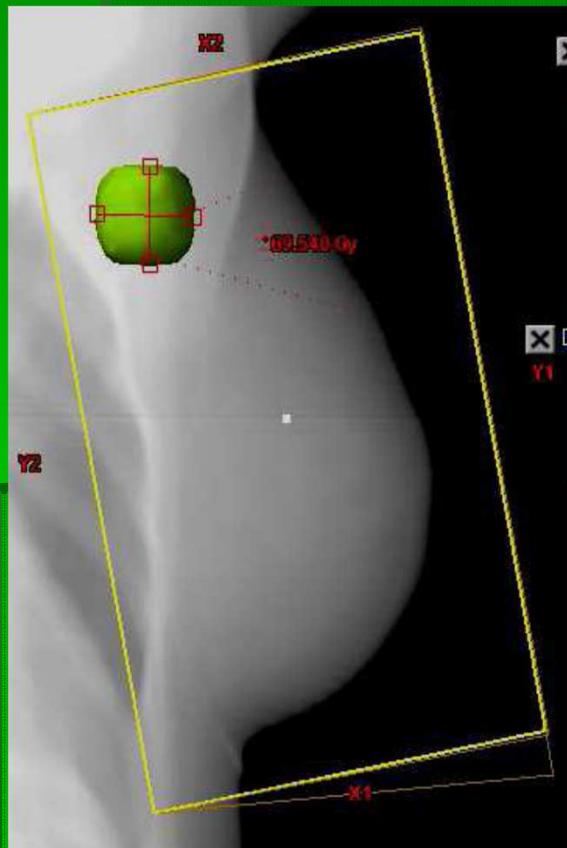
Mortalité



Aires ganglionnaires axillaires basses et volumes irradiés par les tangentiels



Aires ganglionnaires axillaires basses et volumes irradiés par les tangentiels



Conclusion: « à la carte »

