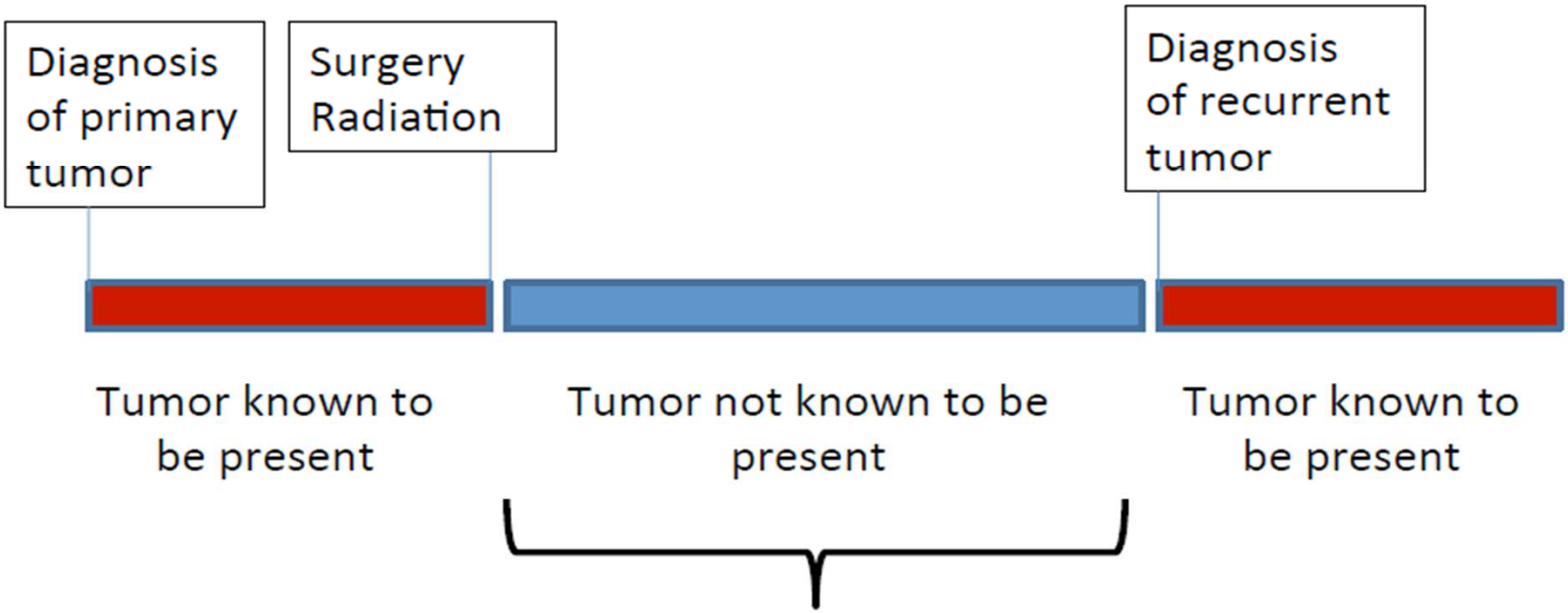
Definition of Clinical Tumor Dormancy



NO implication of mechanisms or state of cancer cells in this interval

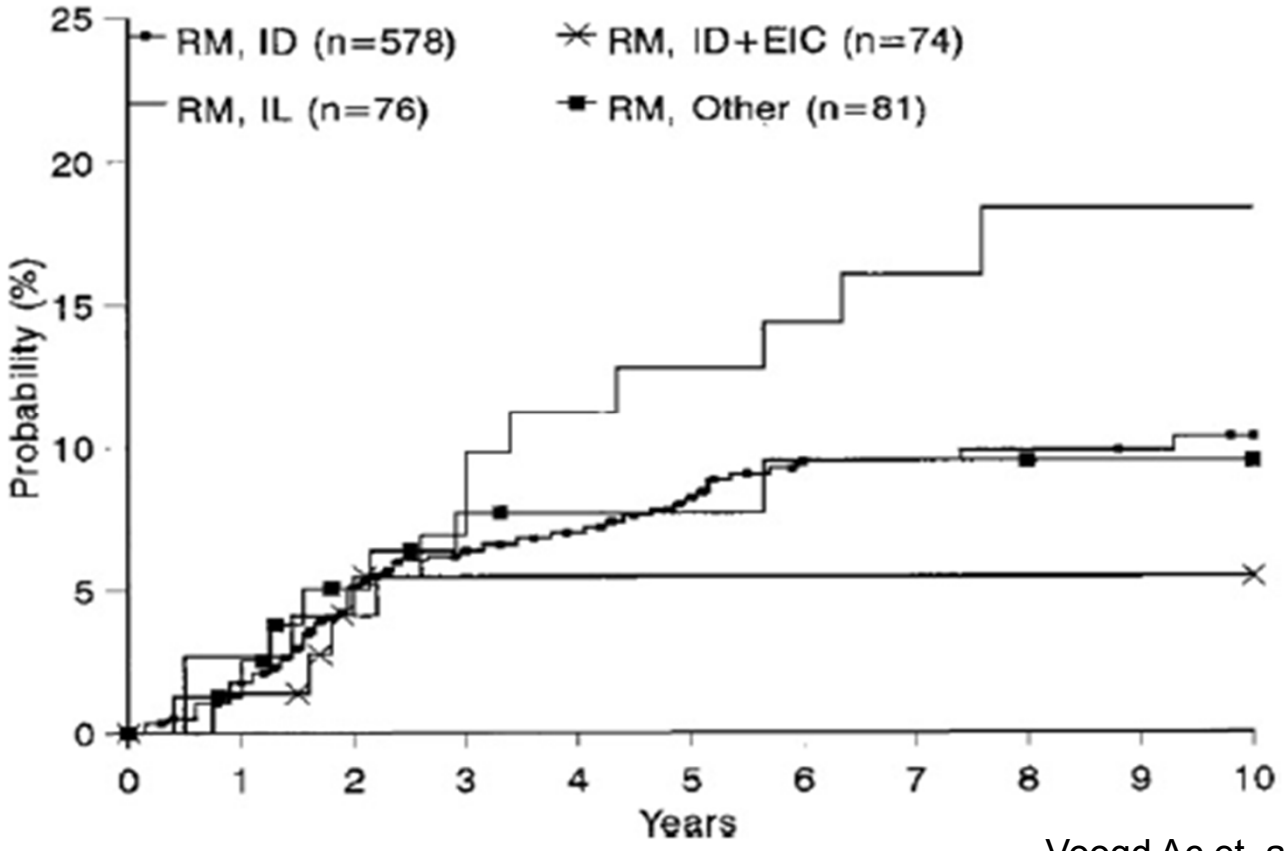
Surveillance loco-régionale personnalisée

= évaluation du risque de récidive locorégionale personnalisée

Histologie : les carcinomes Lobulaires

Taux de récidives locales après mastectomie

Differences in risk factors for local and distant recurrence after breast-conserving therapy or mastectomy for stage I and II breast cancer: pooled results of two large European randomized trials.



Voogd Ac et al. J Clin Oncol 2001;19:1688–97.

Histologie : les carcinomes Lobulaires

Taux de récidives locales après traitement conservateur

Author	FUP	ILC		IDC	
		LR	TR/MM	LR	TR/MM
Sastre-Garau [8]	10	20	NR	22	NR
Peiro [9]	10	15	86	13	78
Warneke [22]	5	3	NR	–	–
Weiss [23]	5	9	100	7	71
Schnitt [20]	6.25	14	100	12	80
Fodor [15]	15	13	93	–	–
Silverstein [21]	6.6	5	NR	5	NR
All studies	5–15	3–20	86–100	5–22	71–80

Polgár C, Radiother Oncol 2010;94:264–73..

Selon l'atteinte ganglionnaire

Prognostic factors of young women (≤35 years) with node positive breast cancer: possible influence on post- therapeutic follow-up

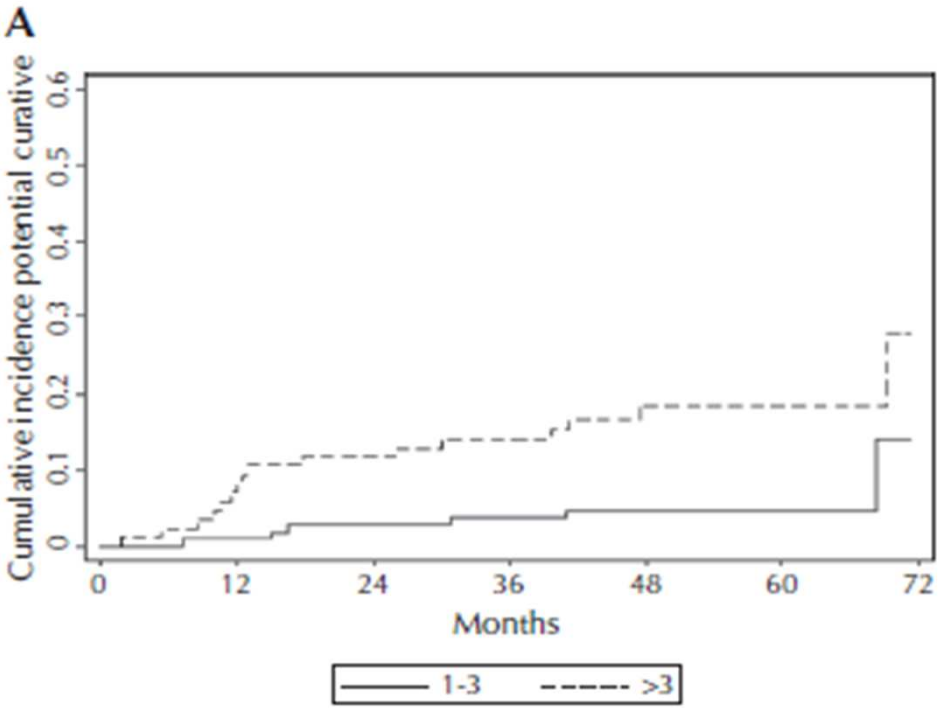


Table 3. Multivariate analysis Fine & Gray – potential curative ($n = 183$).

sHR	95 %CI	*P*
Number of positive lymph node		
1-3	1	
>3	3.38 [1.36; 8.40]	<0.01
Vascular invasion		
Absence	1	
Presence	2.14 [0.96; 4.78]	0.06

Filleron T *Bull Cancer* 2013 ; 100 : E22-E29.

Association de la récidive locale et densité mammaire

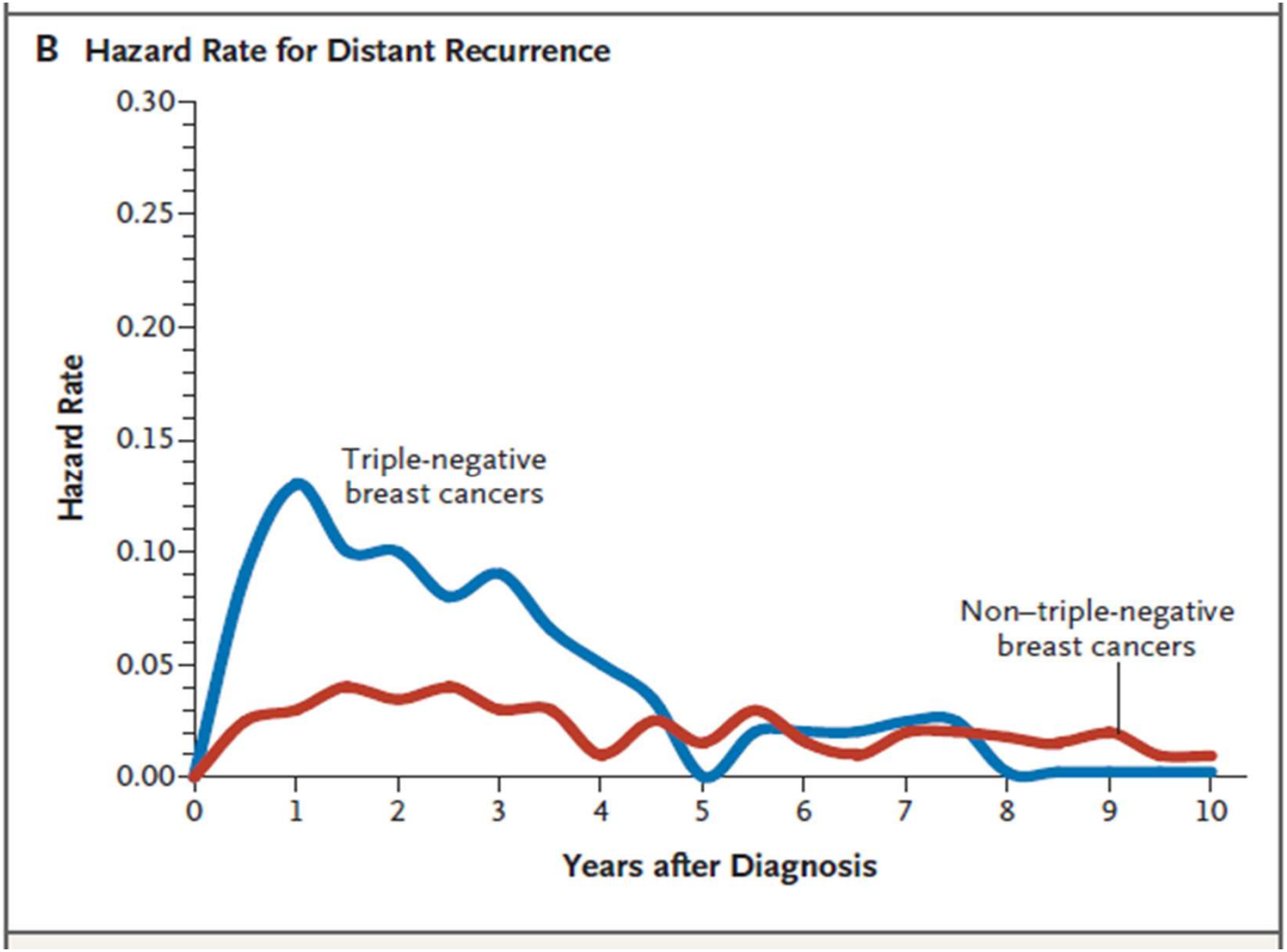
Table 4 Association between mammographic density categorized into quartiles and local and locoregional recurrence

	Local recurrence			Locoregional recurrence		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Model 1[a]			0.008			0.012
PD, 1st quartile[b]	1.00 (Ref)			1.00 (Ref)		
PD, 2nd quartile[c]	1.72	0.78-3.78		1.43	0.79-2.60	
PD, 3rd quartile[d]	1.91	0.86-4.24		1.34	0.72-2.50	
PD, 4th quartile[e]	3.14	1.38-7.16		2.36	1.27-4.39	
Model 2[f]			0.017			0.035
PD, 1st quartile[b]	1.00 (Ref)			1.00 (Ref)		
PD, 2nd quartile[c]	1.80	0.80-4.05		1.38	0.75-2.53	
PD, 3rd quartile[d]	1.78	0.77-4.11		1.29	0.68-2.45	
PD, 4th quartile[e]	3.03	1.28-7.17		2.10	1.11-3.97	

Eriksson et al. Breast Cancer Research 2013, 15:R56

Sous-type histologique

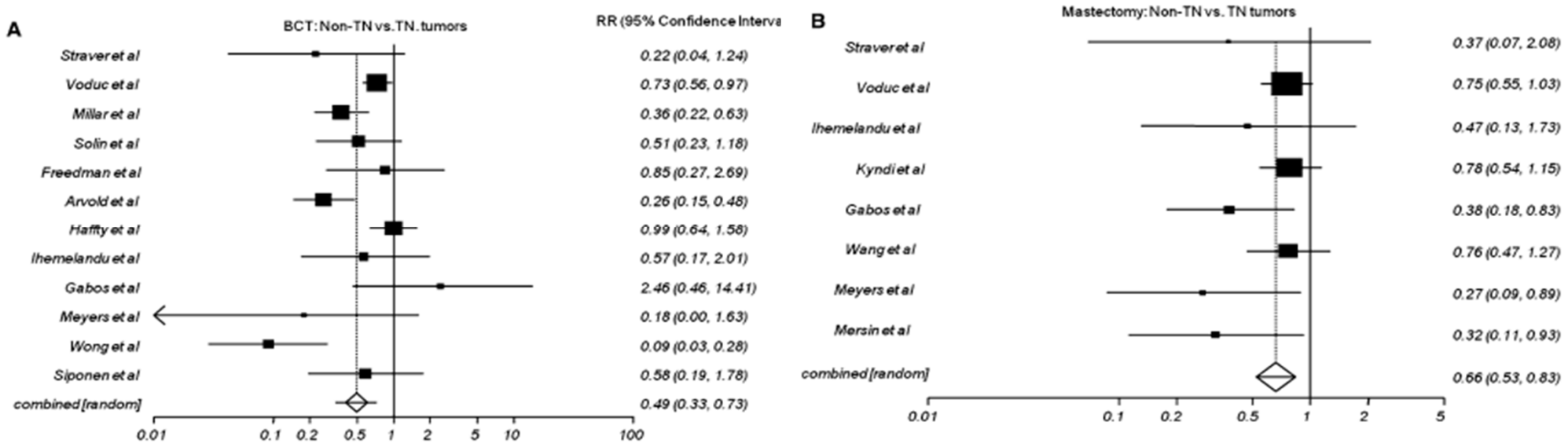
Survie sans métastase des triple négatifs comparée aux non triple-négatifs.



Dent et al, adapted by Foulkes et al NEJM 2010

Locoregional recurrence after breast cancer surgery: a systematic review by receptor phenotype

Tumeurs triple négatives

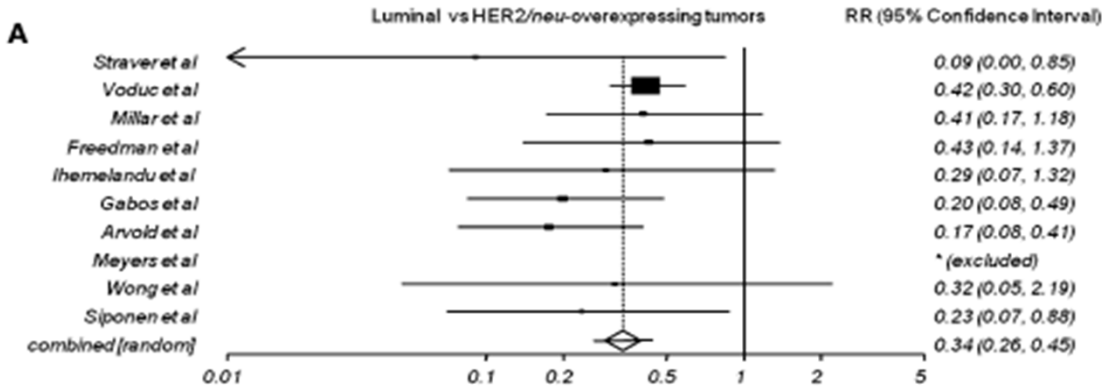


N= 12 592 patientes

Lowery Breast Cancer Res Treat (2012) 133:831–841

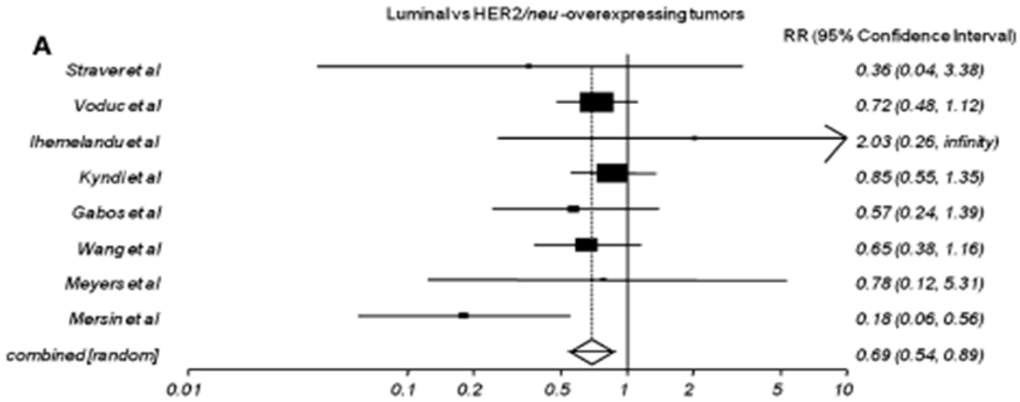
Méta analyse récidive loco-régionale

Après traitement conservateur



Tumeurs HER2+

AprèsMastectomie

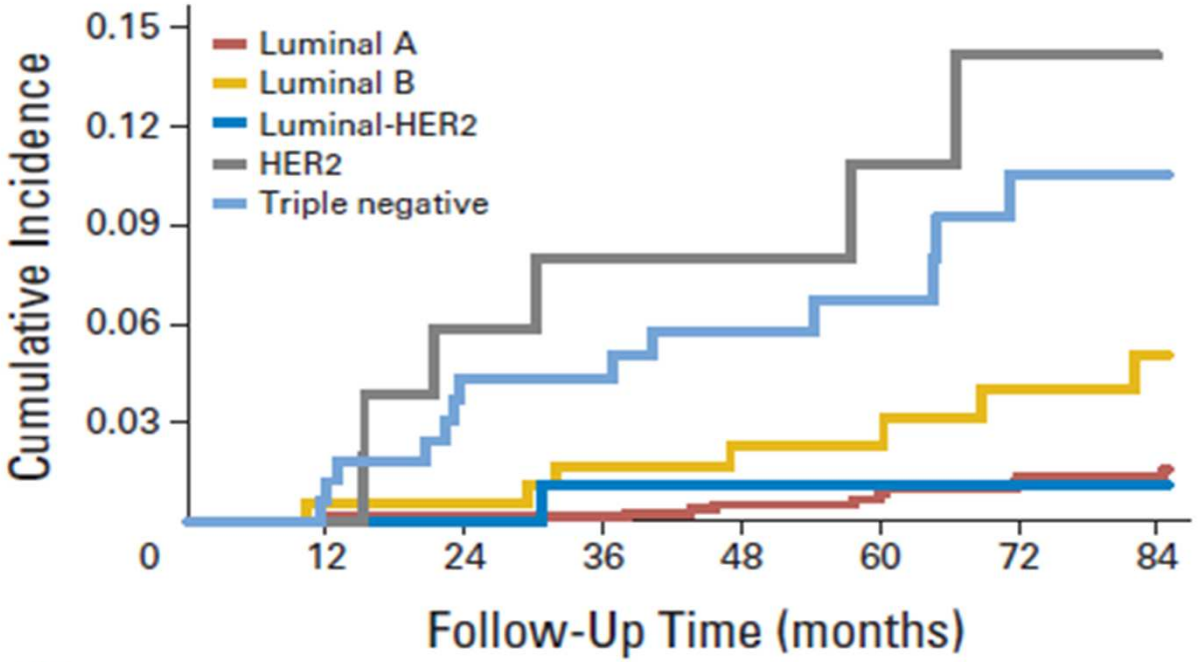


Patients with triple-negative and HER2/neu-overexpressing breast tumors are at increased risk of developing LRR following BCT or mastectomy.

Breast cancer subtype should be taken into account when considering local control and identifies those at increased risk of LRR, who may benefit from more aggressive local treatment.

Lowery Breast Cancer Res Treat (2012) 133:831–841

Risque cumulatif de récidive locale selon le sous-type de cancer du sein



No. at risk								
Luminal A	905	891	872	850	749	582	522	441
Luminal B	198	191	181	170	157	116	105	87
Luminal-HER2	105	104	95	90	83	71	69	65
HER2	55	53	47	43	39	30	26	20
Triple negative	171	164	150	139	116	79	70	65

ND Arvold *J Clin Oncol 29:3885-3891. © 2011*

Triple Negative Breast Cancer Is Associated With an Increased Risk of Residual Invasive Carcinoma After Lumpectomy

Table 4. Multivariate Analysis

Variable	OR (95% CI)	*P*
TN (vs non-TN)	3.28 (1.56-6.89)	.002
Positive lymph node	3.06 (1.77-5.30)	<.0001
Tumor size 1.1-2.0 cm vs <1.0 cm	1.89 (0.94-3.82)	.076
Tumor size >2.0 cm vs <1.0 cm	3.49 (1.65-7.38)	.001

CI indicates confidence interval; OR, odds ratio; TN, triple negative.

A review of pathologic specimens was performed for women with invasive breast cancer treated with lumpectomy followed by reexcision. N=369

Sioshansi Cancer 2012;118:3893-8.

Récidive locale selon le sous-type moléculaire

Impact of molecular subtype on local control.

Author	Follow-up (years)	Number of patients	(%Local recurrence)			
			Luminal A	Luminal B	HER2[a]	Basal
Breast-conserving therapy						
Millar [8]	5	498	1.0	4.3	7.7	9.6
Voduc [9]	10	1461	8.0	10.0	21.0	14.0
Arvold [6]	5	1434	0.8	2.3	10.9	8.8
Mastectomy						
Voduc [9]	10	2985	8	14	17	19
Kyndi [7]	5	489	2	3	13	21

[a] No adjuvant trastuzumab.

Morrow M. Oncologist 2013

Signature biologique

Recurrence score ONCOTYPE Dx

Association Between the 21-Gene Recurrence Score Assay and Risk of Locoregional Recurrence in Node-Negative, Estrogen Receptor–Positive Breast Cancer: Results From NSABP B-14 and NSABP B-20

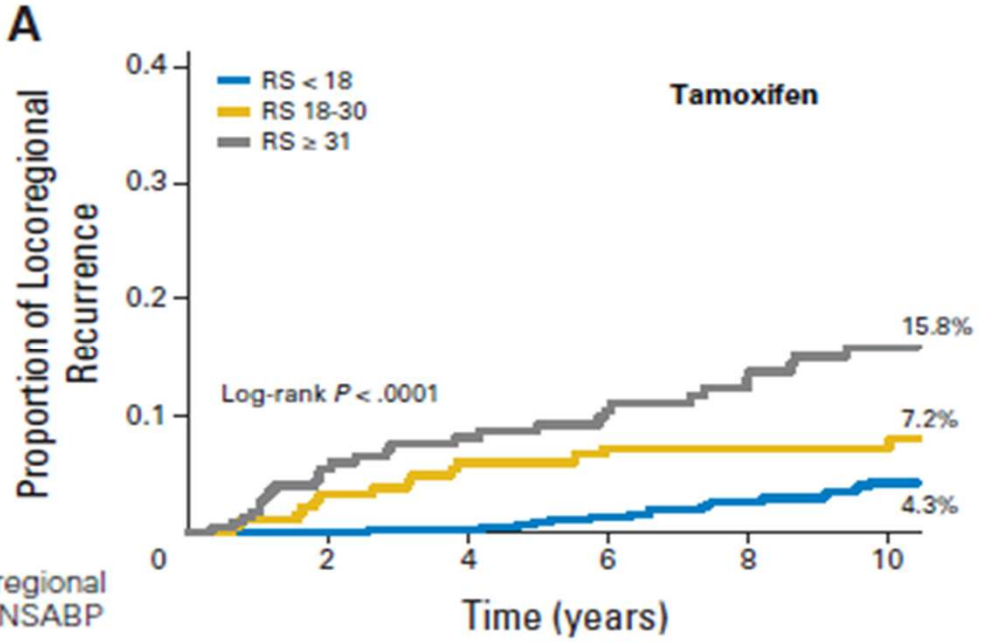
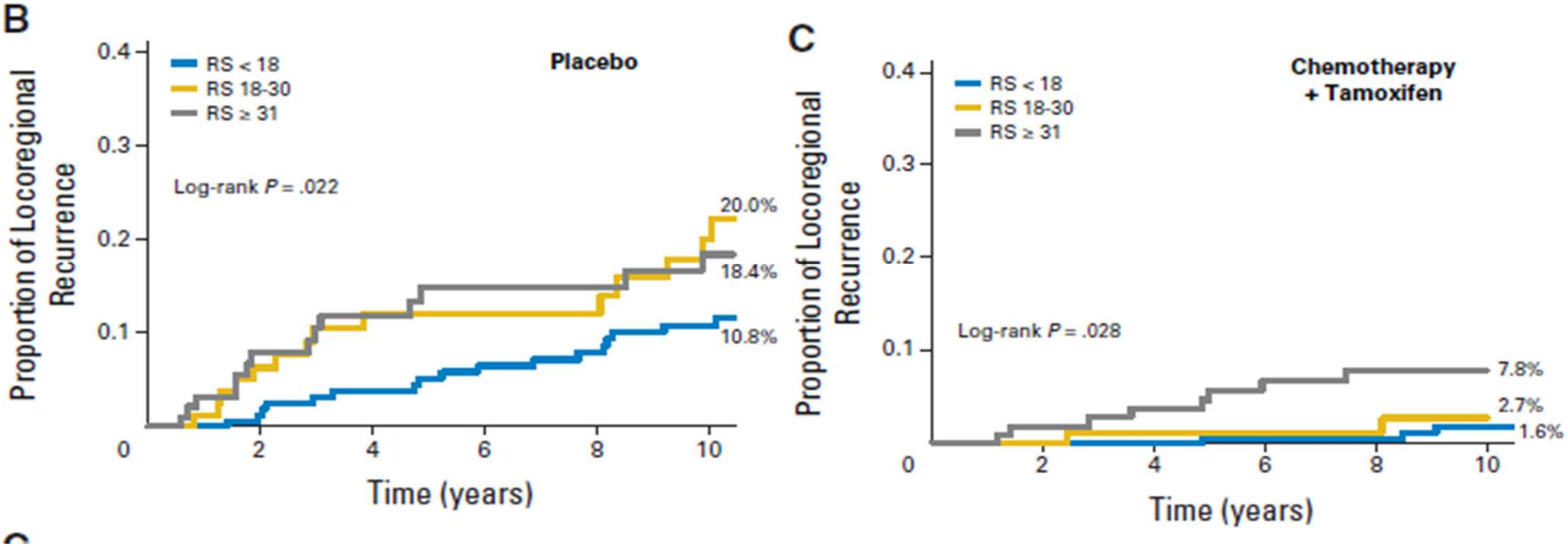


Table 3. Multivariate Cox Regression Analysis of Predictors of Locoregional Recurrence in the Cohort of 895 Tamoxifen-Treated Patients From NSABP Trials B-14 and B-20

Variable	Hazard Ratio	95% CI	Wald Test *P*
Age (≥ 50 *v* < 50)	0.40	0.25 to 0.65	.0002
Mastectomy *v* L + XRT	0.62	0.39 to 0.99	.047
Clinical tumor size (> 2 *v* ≤ 2 cm)	0.98	0.61 to 1.59	.933
Tumor grade (moderate *v* well)	1.10	0.54 to 1.92	.113
Tumor grade (poor *v* well)	1.76	0.89 to 3.48	
Recurrence score*	2.16	1.26 to 3.68	.005

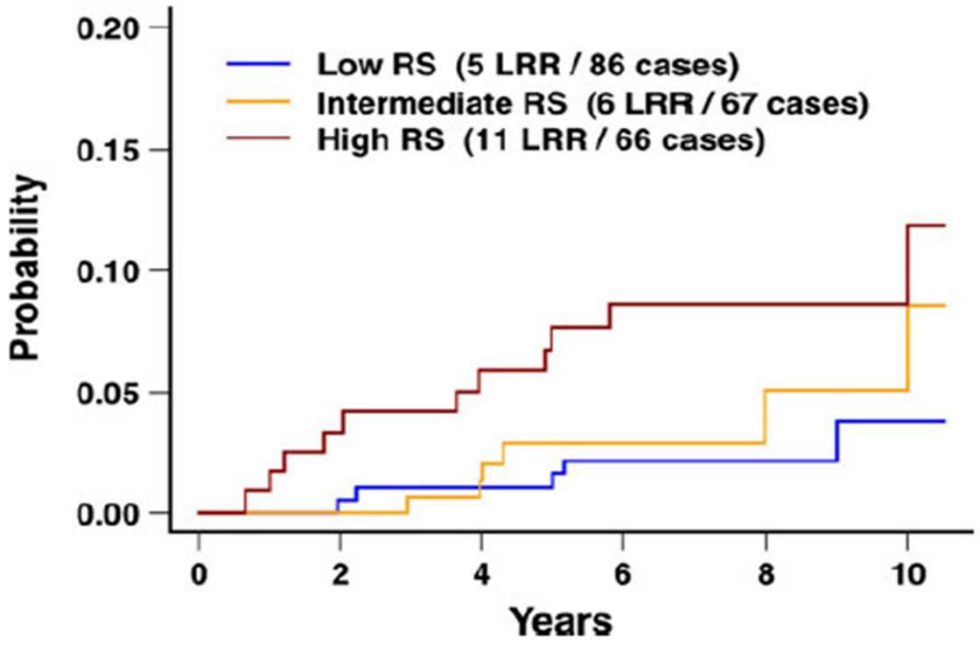
Mamounas et al *J Clin Oncol 28:1677-1683. © 2010*

Association Between the 21-Gene Recurrence Score Assay and Risk of Locoregional Recurrence in Node-Negative, Estrogen Receptor–Positive Breast Cancer: Results From NSABP B-14 and NSABP B-20



Mamounas et al *J Clin Oncol 28:1677-1683. © 2010*

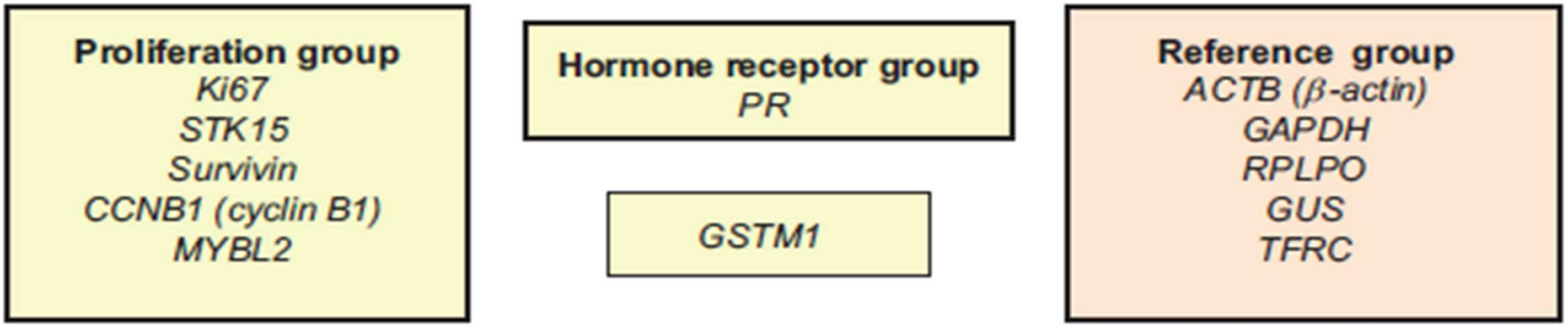
Prognostic value of biologic subtype and the 21-gene recurrence score relative to local recurrence after breast conservation treatment with radiation for early stage breast carcinoma: results from the Eastern Cooperative Oncology Group E2197 study



The difference between the three curves was not statistically different (P = 0.12).

LJ Solin Breast Cancer Res Treat (2012) 134:683–692

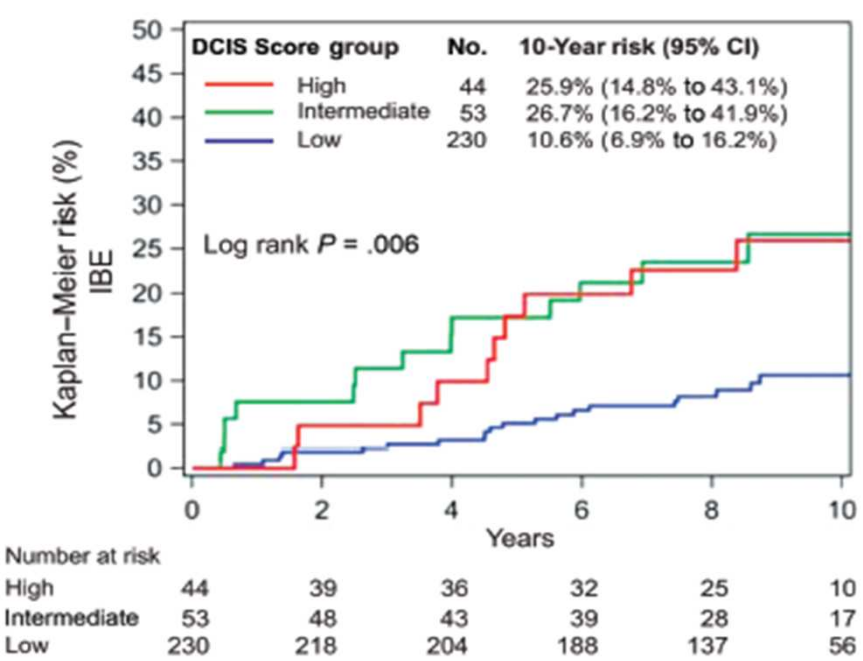
A Multigene Expression Assay to Predict Local Recurrence Risk for Ductal Carcinoma In Situ of the Breast

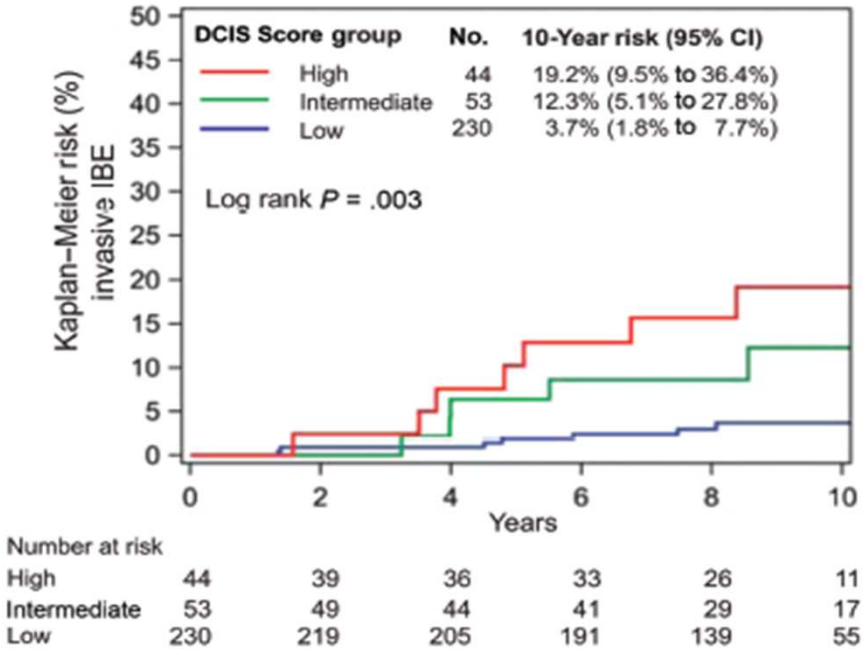


12 genes

LJ Solin J Natl Cancer Inst;2013;105:701–710

A Multigene Expression Assay to Predict Local Recurrence Risk for Ductal Carcinoma In Situ of the Breast





(ECOG) E5194 study N=327

LJ Solin J Natl Cancer Inst;2013;105:701–710

A Multigene Expression Assay to Predict Local Recurrence Risk for Ductal Carcinoma In Situ of the Breast

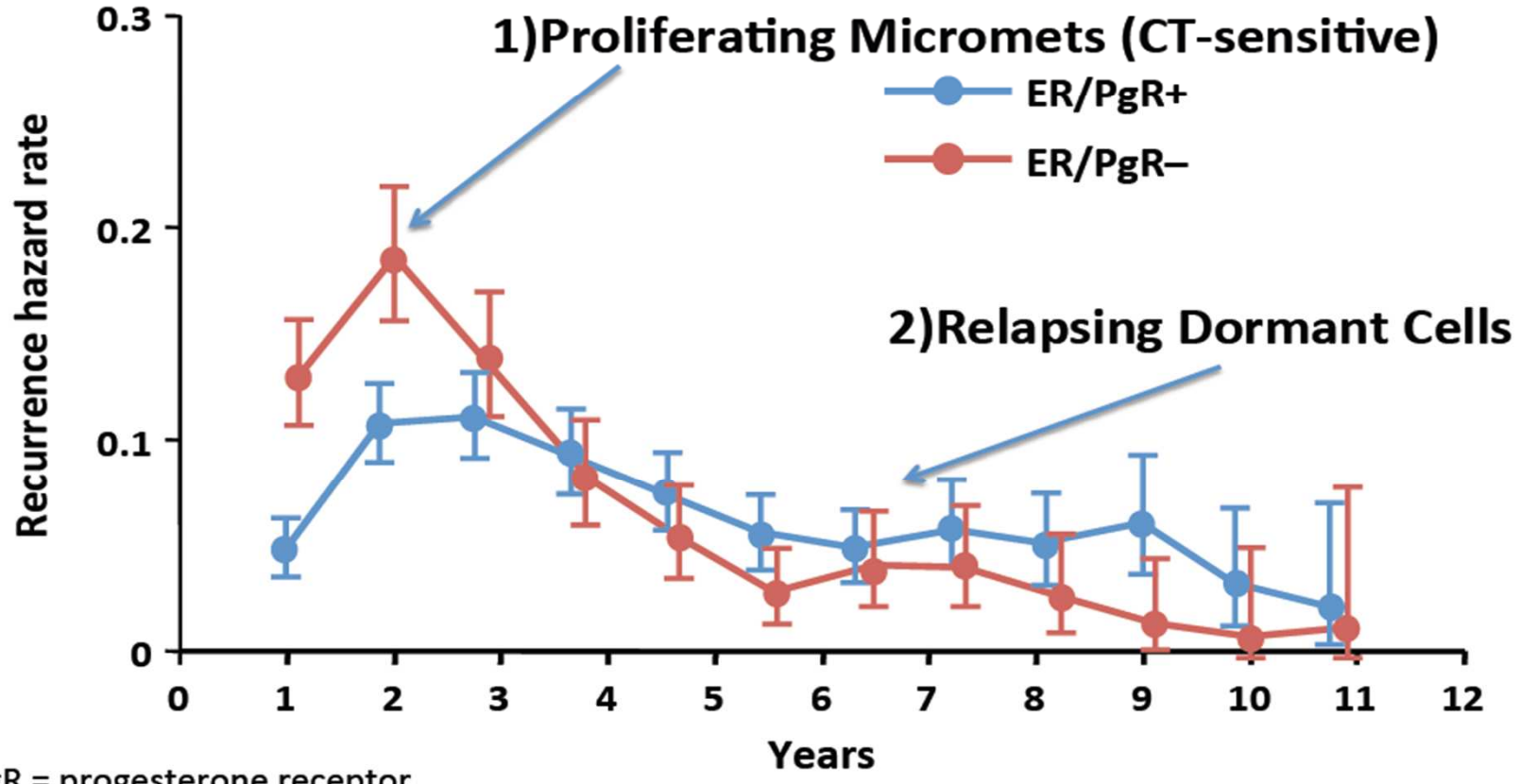
Table 4. Multivariable Cox proportional hazards models for the risk of an ipsilateral breast event

Analyses and variables	Hazard ratio (95% CI)*	P†
Multivariable analysis of significant clinical and pathologic factors, excluding the DCIS Score		
Menopausal status		.02
Premenopausal	1.00 (referent)	
Postmenopausal	0.49 (0.27 to 0.90)	
Tumor size‡	1.54 (1.14 to 2.02)	.006
Multivariable analysis of significant clinical and pathologic factors, including the DCIS Score		
Menopausal status		.02
Premenopausal	1.00 (referent)	
Postmenopausal	0.49 (0.27 to 0.90)	
Tumor size‡	1.52 (1.11 to 2.01)	.01
DCIS Score‡	2.37 (1.14 to 4.76)	.02

(ECOG) E5194 study N=327

LJ Solin J Natl Cancer Inst;2013;105:701–710

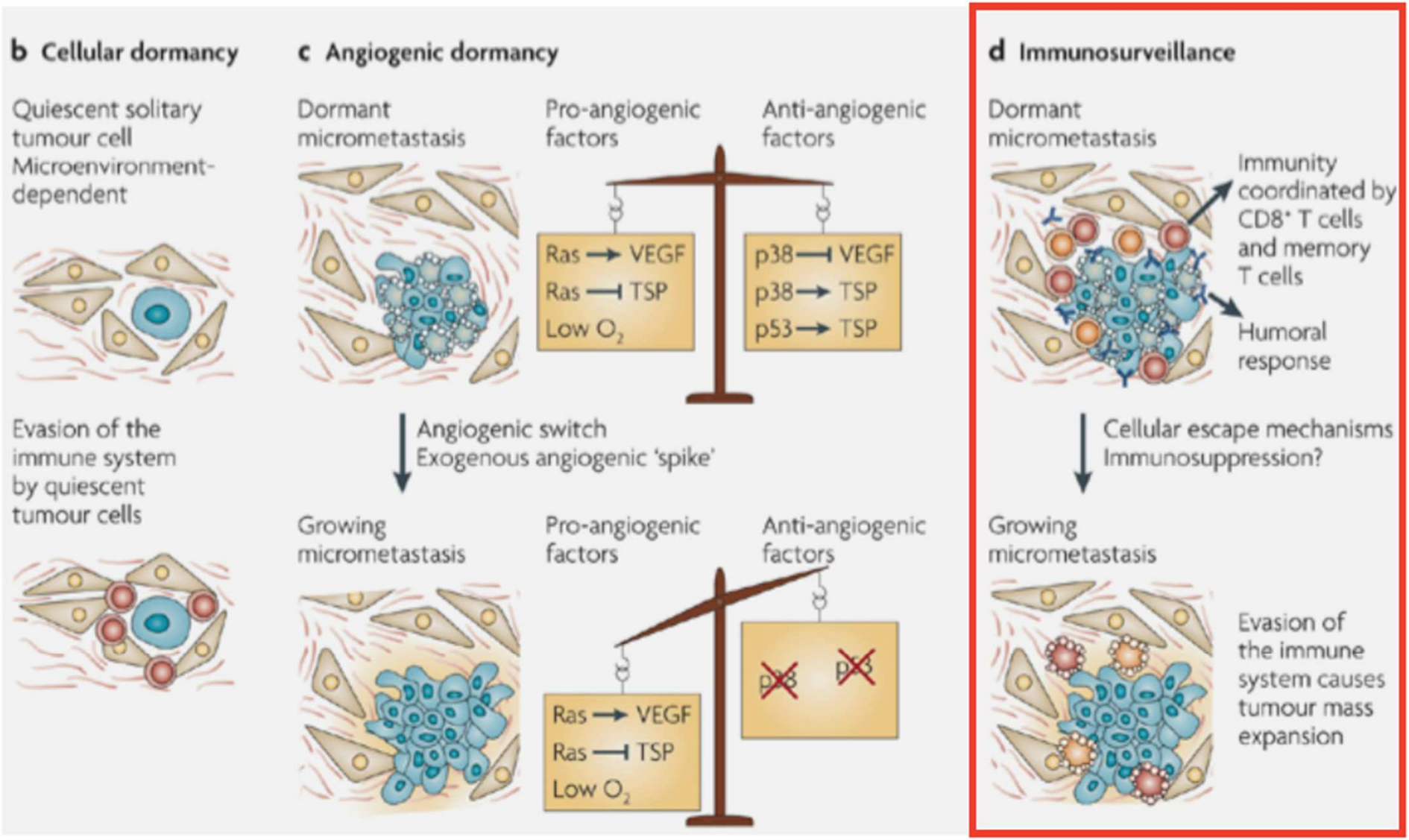
Risk of Breast Cancer Recurrence:
Two Cell Populations



PgR = progesterone receptor.

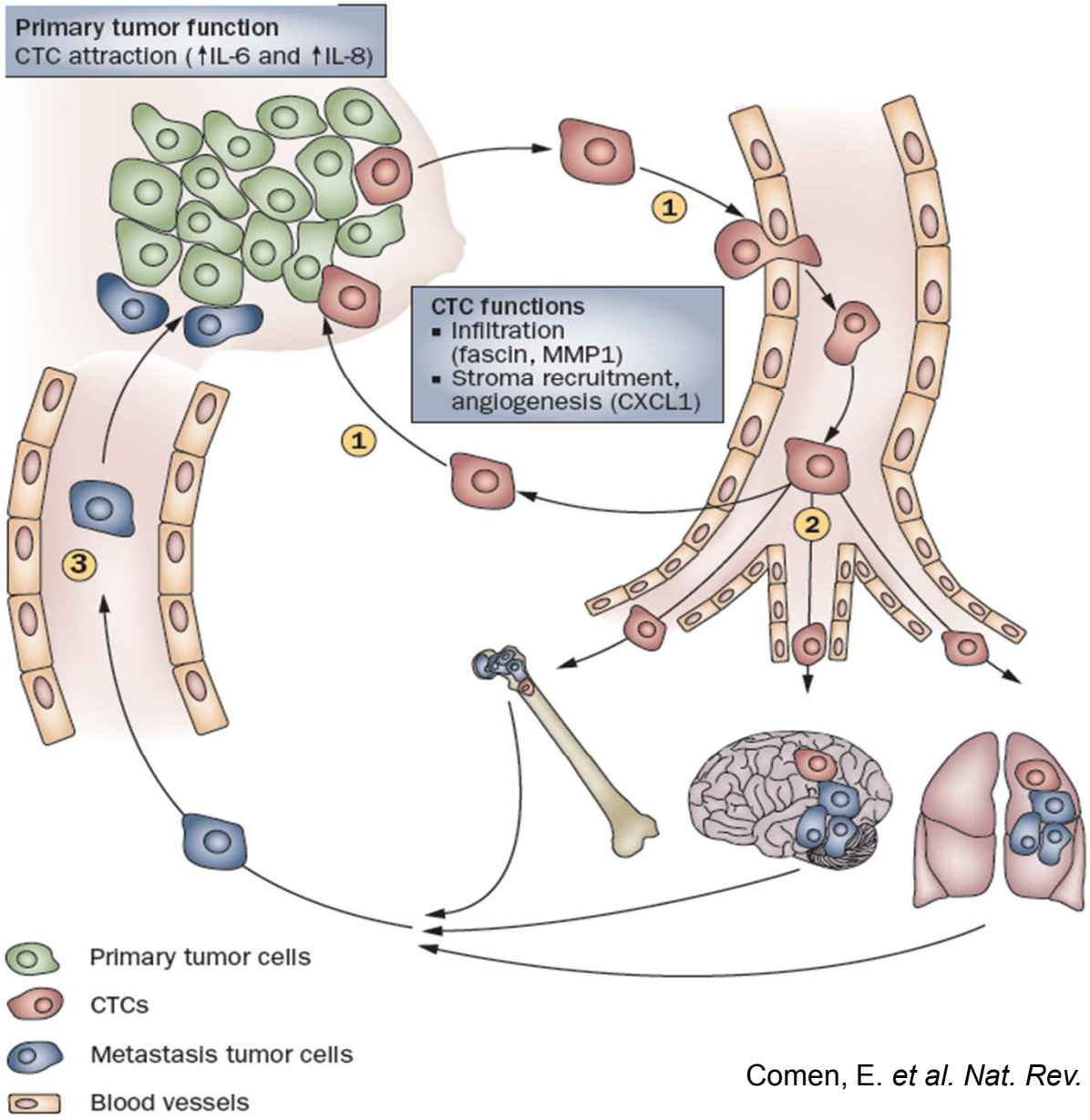
Saphner et al. *J Clin Oncol*. 1996;14:2738.

Which Dormant Cells Do We Attack?



Julio A. Aguirre-Ghiso, Nature Cancer Reviews, 2007

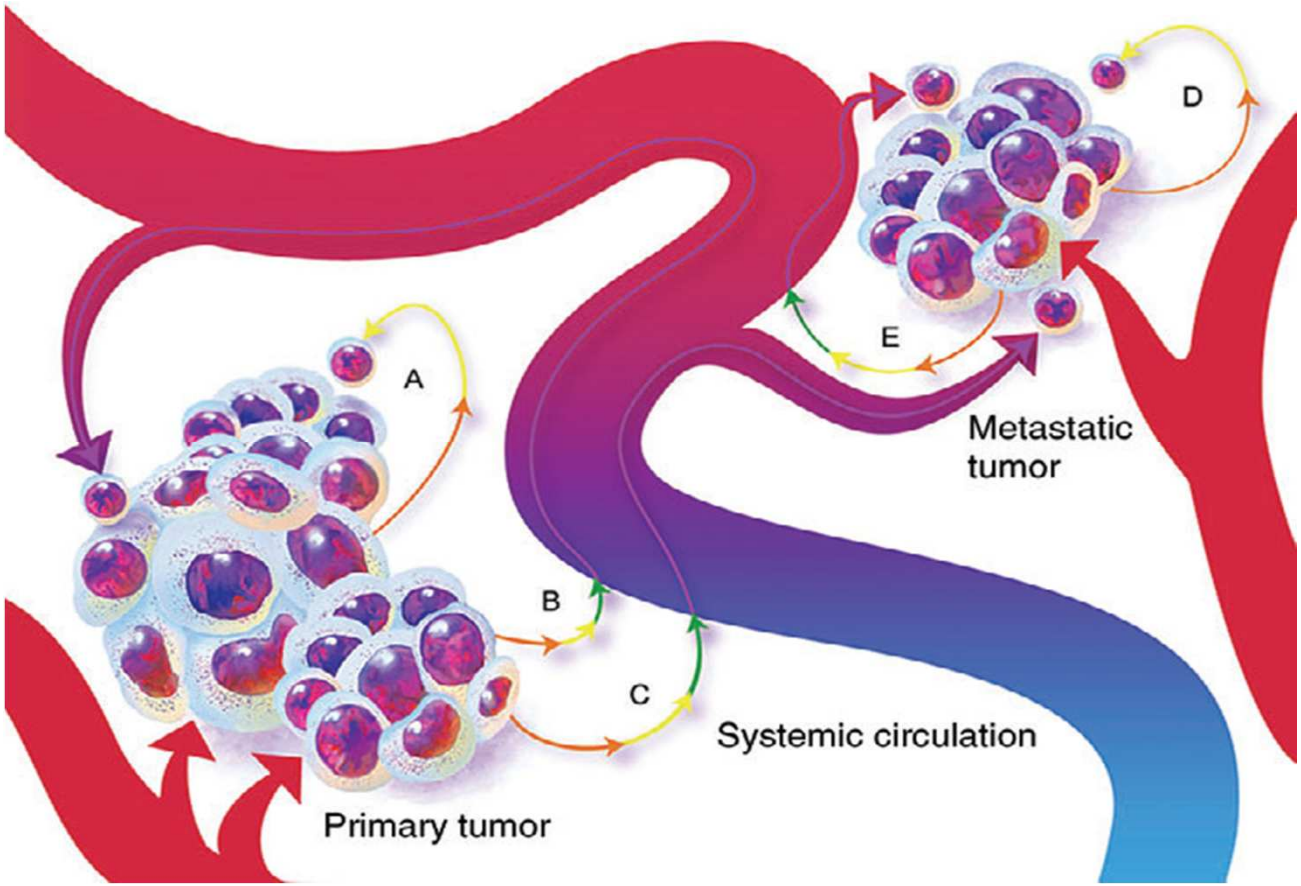
Self-Seeding: auto-ensemencement?



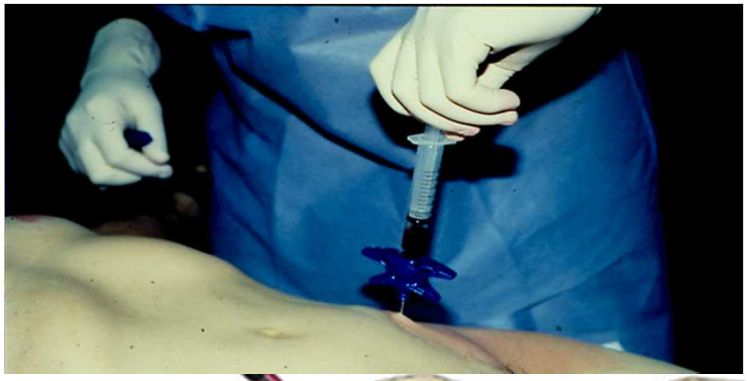
Comen, E. *et al. Nat. Rev. Clin. Oncol. 8, 369–377 (2011)*

Is cancer a disease of self-seeding?

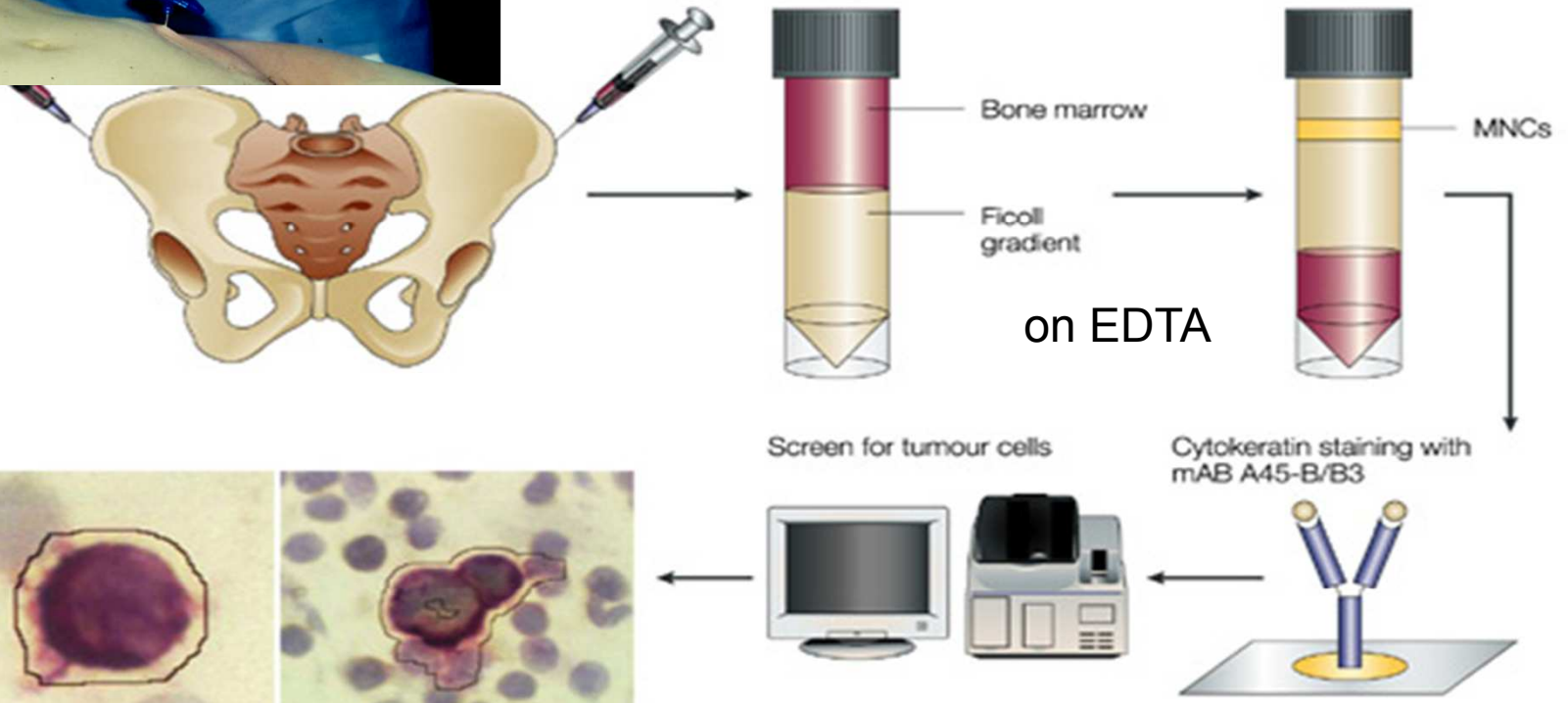
Larry Norton & Joan Massagué Nature Medicine, 12, 2006



Méthodes de détection des DTC au niveau médullaire

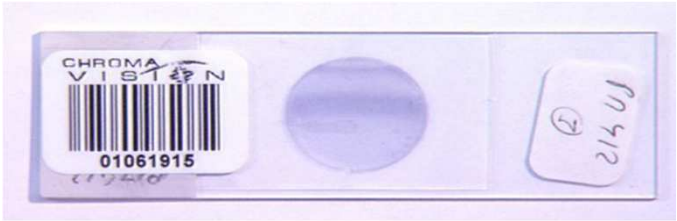


Preoperative bilateral bone marrow aspirations from both anterior iliac crests (3 to 5 ml per sample)
Or one bone marrow aspiration under local anesthesia from posterior iliac crest or sternum (3 to 5 ml per sample)



1x10 ^{6} CMN/cytospot X 3 slides

Same number of control slides

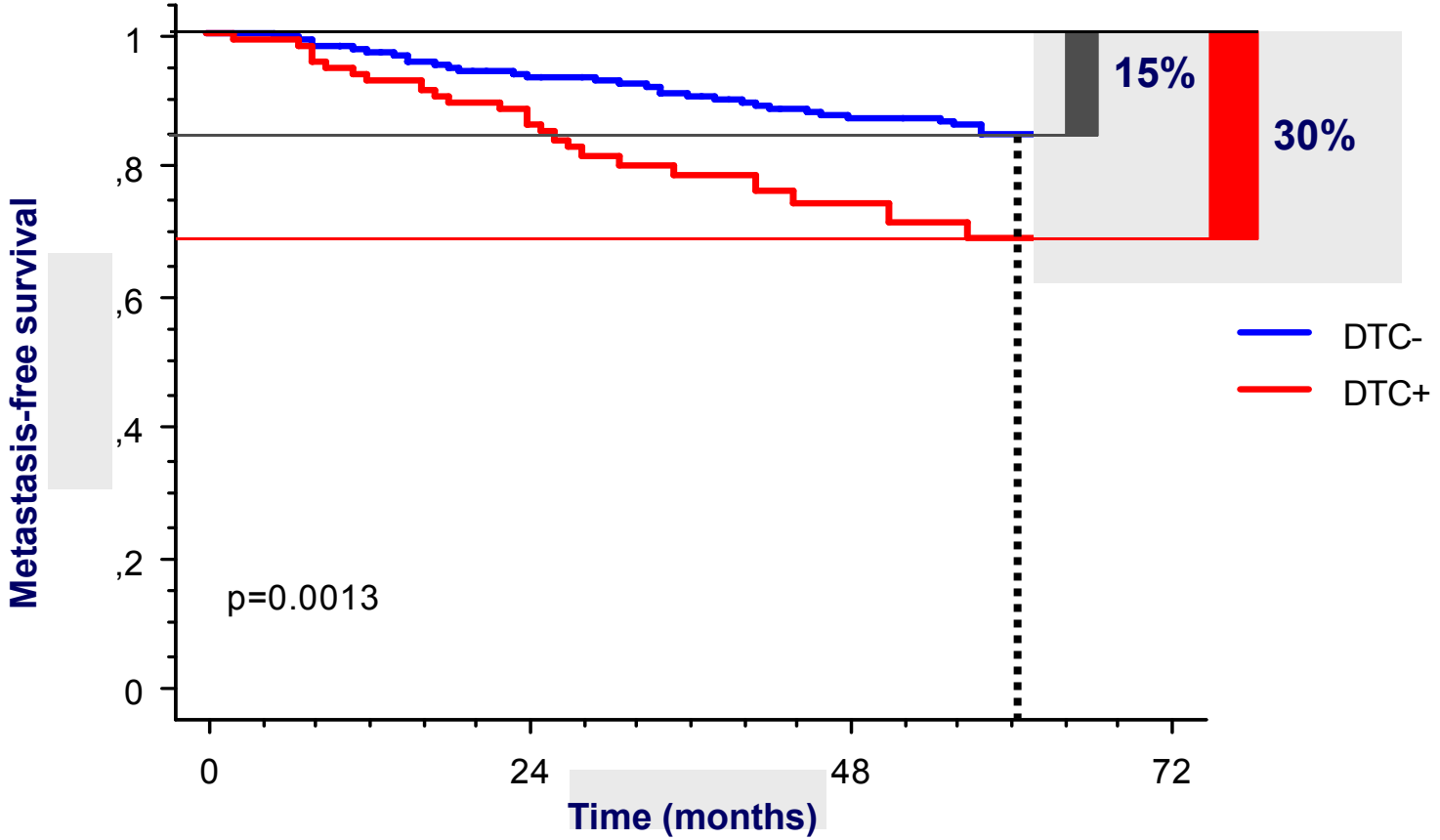


Adapted from Pantel K, Nature Cancer Reviews, 2004, **4**, 448

Disseminated Tumor Cells: Distant Metastase Free Survival

Adjuvant

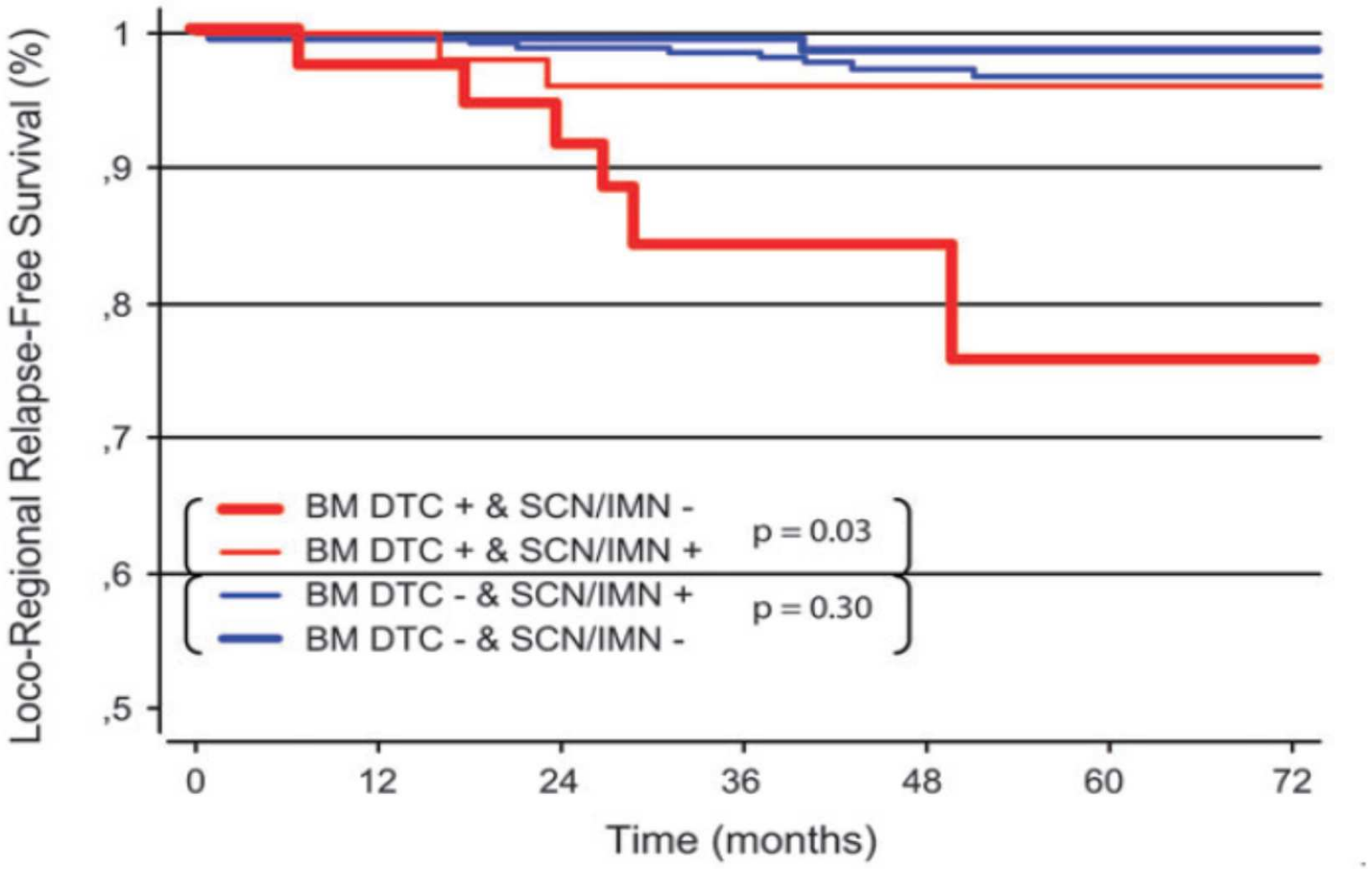
N 621 pts



15.1% positivity rate

Bidard FC (…) Pierga JY, Clin cancer Res 2008

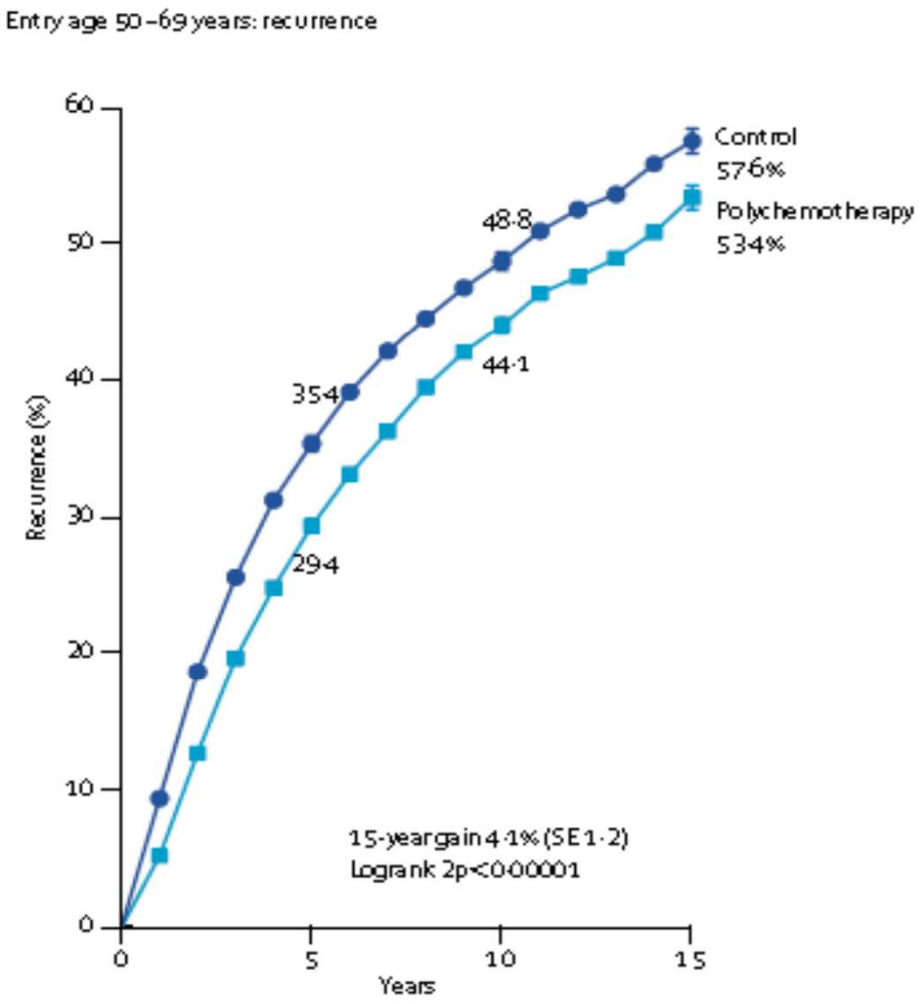
DTC and Local Relapse Free Survival

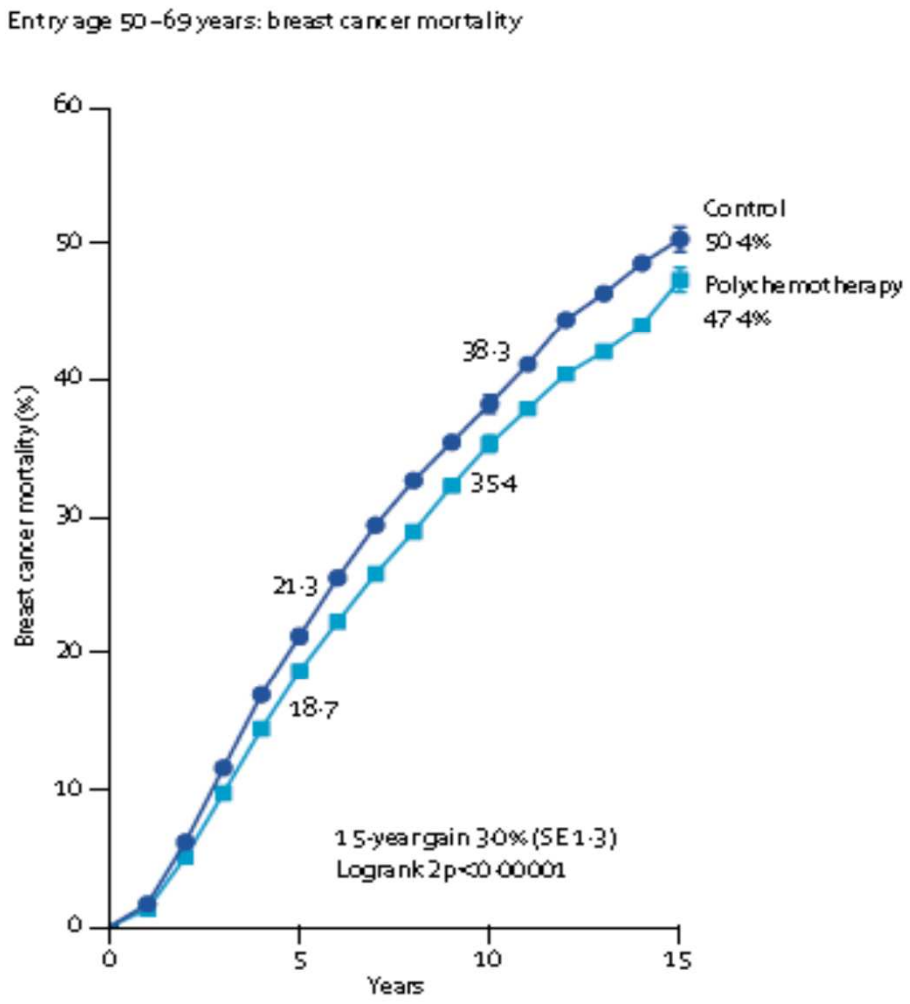


Recolonization by CTC?

Bidard FC, Kirova Y et al, Ann Oncol, 2009

Combien de temps surveiller ?





EBCTCG Lancet 2011

Reco HAS

5.4. Examens paracliniques

La mammographie annuelle bilatérale (après chirurgie partielle) ou unilatérale (après mastectomie totale) constitue l'examen de référence de la surveillance paraclinique. Elle peut être associée à une échographie mammaire (bilatérale ou controlatérale selon la chirurgie).

La première mammographie de surveillance doit être réalisée 1 an après la mammographie initiale et au moins 6 mois après la fin de la radiothérapie.

Pour les patientes traitées par tamoxifène, une échographie pelvienne annuelle est nécessaire du fait du risque de cancer de l'endomètre.

Il n'y a pas d'indication à la réalisation systématique d'autres examens d'imagerie (en particulier hépatique ou thoracique). Les autres examens complémentaires sont discutés en présence de signes d'appel.

D'autre part, aucun dosage de marqueurs tumoraux sériques n'est recommandé dans le suivi.

RECOMMENDATION

Mammography

- Post-treatment mammograms should be performed adhering to the following schedule:

Post-Treatment Mammogram Schedule	
First	No earlier than 6 months after definitive radiation therapy
Subsequent	Every 6 to 12 months for surveillance of abnormalities
Subsequent (Conditional)	Yearly if stability of mammographic findings is achieved after completion of locoregional therapy

Summary

RECOMMENDED MODES OF BREAST CANCER SURVEILLANCE	
History/Physical Exam	Every 3 to 6 months for the first 3 years after primary therapy; every 6 to 12 months for years 4 and 5, then annually.
Patient Education	Counsel patients about the symptoms of recurrence including new lumps, bone pain, chest pain, abdominal pain, dyspnea or persistent headaches.
Referral for Genetic Counseling	Criteria to recommend referral include Ashkenazi Jewish heritage; history of ovarian cancer in patient or any first- or second-degree relative; any first degree relative with a history of breast cancer diagnosed before age 50; two or more first- or second-degree relatives diagnosed with breast cancer; patient or relative with diagnosis of bilateral breast cancer; or, history of breast cancer in a male relative.
Breast Self-Exam	All women should be counseled to perform monthly breast self-examination.
Mammography	First post-treatment mammogram 1 year after the initial mammogram that leads to diagnosis, but no earlier than 6 months after definitive radiation therapy. Subsequent mammograms should be obtained as indicated for surveillance of abnormalities.
Pelvic Examination	Regular gynecologic follow-up is recommended for all women. Patients who receive tamoxifen should be advised to report any vaginal bleeding to their physicians.
Coordination of Care	Continuity of care for breast cancer patients is encouraged and should be performed by a physician experienced in the surveillance of cancer patients and in breast examination, including the examination of irradiated breasts. If follow-up is transferred to a PCP, the PCP and the patient should be informed of the long-term options regarding adjuvant hormonal therapy for the particular patient. This may necessitate re-referral for oncology assessment at an interval consistent with guidelines for adjuvant hormonal therapy.
BREAST CANCER SURVEILLANCE TESTING - NOT RECOMMENDED	
Routine blood tests	CBCs and liver function tests are not recommended
Imaging Studies	Chest x-ray, bone scans, liver ultrasound, CT scans, FDG-PET scans, and breast MRI are not recommended
Tumor markers	CA 15-3, CA 27.29 and CEA are not recommended.

ASCO GUIDELINES
Clinical Tools and Resources

Conclusions

Pas de recommandations particulière sur la surveillance locorégionale personnalisée (HAS, ASCO, etc…°)

Tenir compte de l'histologie, du sous-type moléculaire

Le niveau de preuve est-il suffisant?