

Cancer du sein avancé traitement de la maladie ολιγο- métastatique

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ESME

1^{ère} évolution métastatique

	N=16703	RH+ N=9914	HER2+ N=2830	TNBC N=2318
Nombre de sites Médian (min-max)	1 (1-8)	1 (1-8)	1 (1-7)	1 (1-8)
Os	9891 (59,2%)	6559 (66,2%)	1425 (50,5%)	865 (37,3%)
Viscères	10073 (60,3%)	5589 (56,4%)	1960 (69,2%)	1674 (71,1%)
Autres	6120 (36,6%)	3318 (33,5%)	1079 (38,1%)	1211 (52,2%)

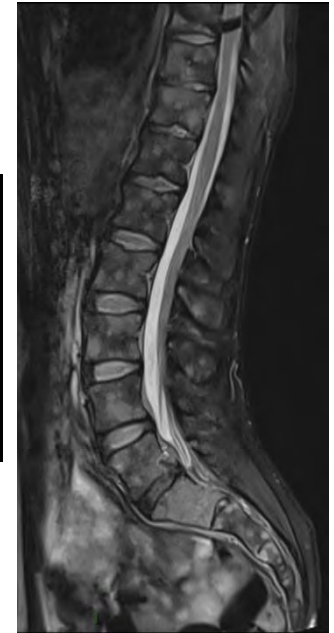
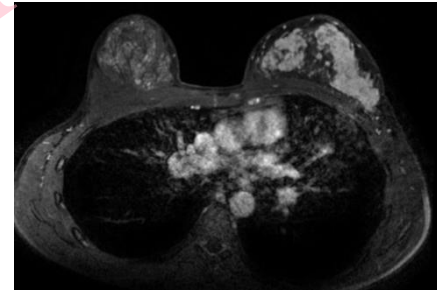
50% des patientes n'ont qu'**UN SEUL SITE** métastatique à la première évolution métastatique

Un seul site, mais... oligo métastatique ?

HER2 +



RE+



Quelques histoires cliniques

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Cancers RE+

Née en 1956

1995 T2-N0-M0, 1N+/6, RE 80% ++, RP 20% +++, de grade I. Tumorectomie, irradiation, FEC

1998 : métastases osseuses rachidiennes. CA 15.3 à 54.
ENDOXAN-TAXOTERE 6 cycles. Rémission complète.
TAMOXIFENE depuis février 1999 avec rémission complète plusieurs fois confirmée.

Juin 2008 : évolution osseuse isolée en L3:
cimentoplastie L3 et LETROZOLE.

Novembre 2011 : progression de L3 : radiothérapie et complément de cimentoplastie. CAPECITABINE.

05/2017 : réponse complète confirmée, pause thérapeutique.



Cancers RE+

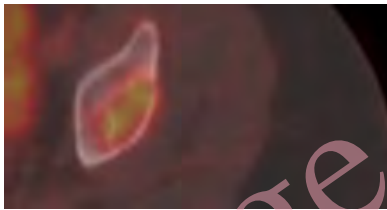
Née en 1968

2007: Carcinome canalaire infiltrant grade II, index mitotique faible, 18 mm +, 9 N-/9, RO +, pas de surexpression de cerb B2, irradiation, TAMOXIFENE 2007-2012

06/2017 : progression osseuse et pulmonaire, RO+ (80%), RP+ (60%), HER2-, Ki67 20%

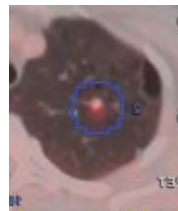
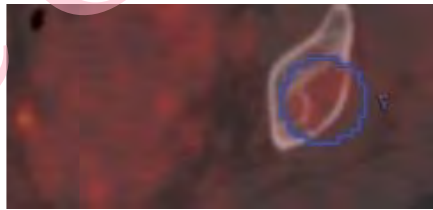
GOSERELINE, LETROZOLE et CDKi débutés le 03/07/2017

juillet

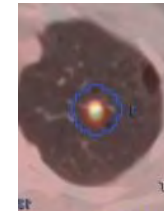
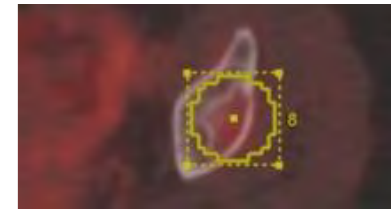


MAIS:

janvier

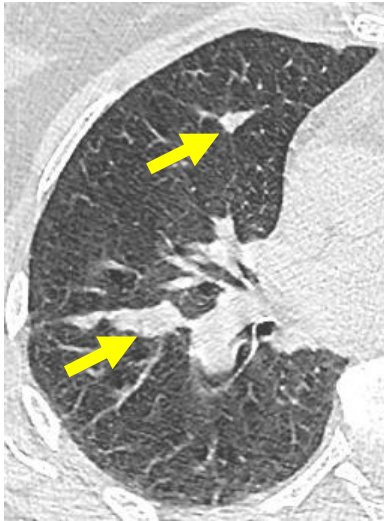


juillet



**Poursuite CDKi
RADIOFREQUENCE !**

Cancers RE+

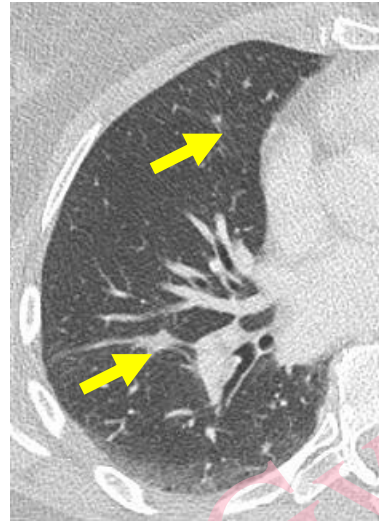


Née en 1958

Mai 2017

Métastatique de novo

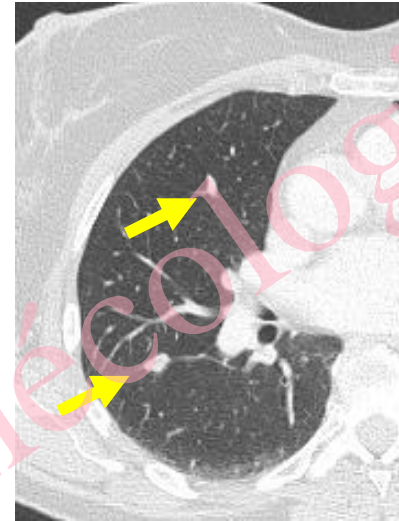
Letrozole + CDKi



Sept 2017

Réponse majeure

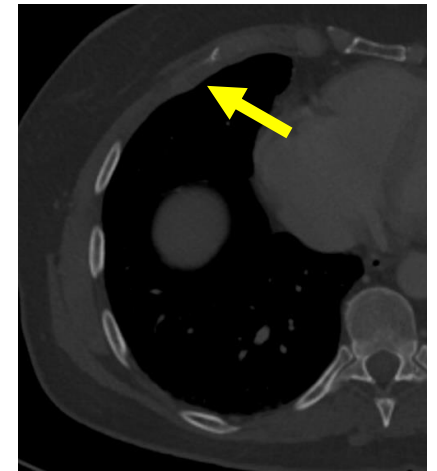
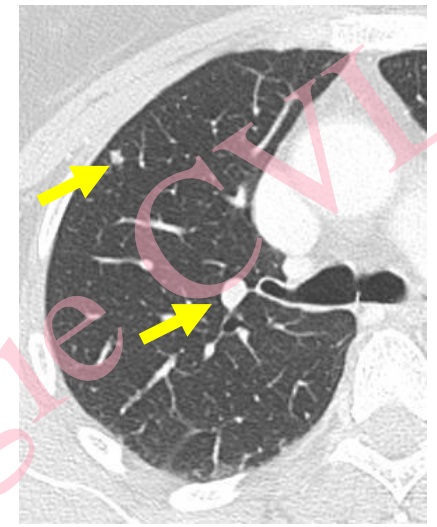
Sein et poumon



Janvier 2018

Progression pulmonaire et costale

Sein en réponse majeure



- **Changement de traitement systémique**
- **RT costale**

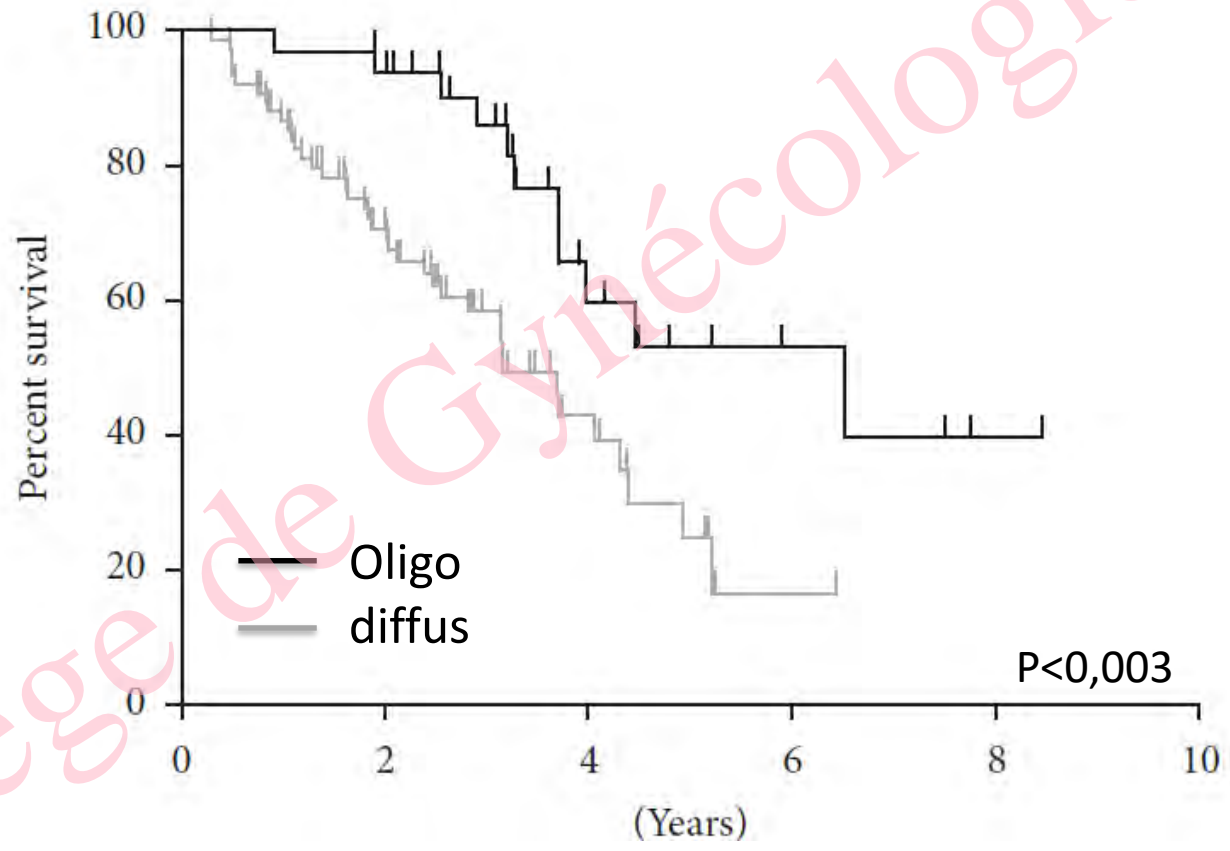
Cancers RE+

traitement systémique

		Progression diffuse ≥ 3 organes/tissus	Progression Oligométastatique
		74	34
Nb de <i>localisations</i>			
	≤6	15 (22%)	15 (44%)
	>6	52 (78%)	19 (56%)
Sites			
	Os	53 (72%)	16 (47%)
	locorégional	34 (46%)	7 (21%)
	Poumon/médiastin	27 (36%)	10 (29%)
	Foie	22 (30%)	12 (35%)
Traitements			
	≥3 L Hormonothérapie	17 (23%)	12 (35%)
	Ttt local	-	14 (41%)

Cancers RE+

traitement systémique



Cancers HER2+

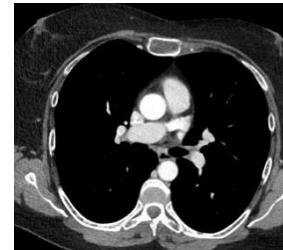
- Née en 1966
- **Mai 2004** : carcinome canalaire infiltrant du sein droit bifocal, 50+16 mm, RH-, HER2+ découvert à l'arrêt de l'allaitement.
Bilan d'extension : métastases osseuses et hépatiques.
Juin 2004 à septembre 2004 : TAXOTERE + EPIRUBICINE : 6 cycles
- **Novembre 2004 : TAXOTERE + HERCEPTIN.** Rémission complète puis radiothérapie mammaire + HERCEPTIN.

• **Février 2012 : persistance de la rémission complète, arrêt des traitements**



- Née en 1964
- **1993** : T2 N0 du sein G, SBR III, RH+, HER2+ (FISH) traitée par tumorectomie curage, chimiothérapie et radiothérapie.
- **Avril 2002** : métastases osseuses + masse rétro et présternale.
- Chimiothérapie TAXOTERE ADRIBLASTINE x 6 puis FUN.
- **Mars 2003 : FEMARA HERCEPTIN** jusqu'en novembre (FEV gauche abaissée); poursuite par Femara-Décapeptyl
- **Février 2006** : rechute sternale (cytologie positive).
- NAVELBINE HERCEPTIN x 6 avec rémission complète.
- Relais par XELODA HERCEPTIN août 2006 - Janvier 2007
- **Janvier 2007** : DECAPEPTYL FEMARA et HERCEPTIN.

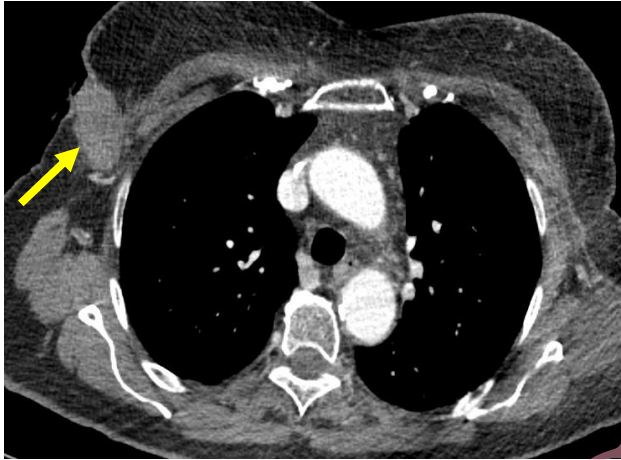
• **Janvier 2012 : persistance de la rémission complète, poursuite par DECAPEPTYL - FEMARA. Arrêt de l'HERCEPTIN.**



Cancers triples négatifs

Née en 1931

2007

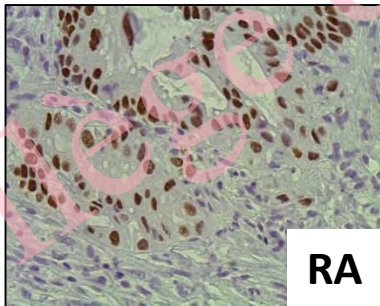


03/2001: T2N1 du QIE du sein *gauche* (CCI peu différencié SBR II, RE -, RP -, N1b) traité par
- chimiothérapie néo-adjuvante 4 FEC 75 puis 2 FEC 50
- tumorectomie curage le 14/09/01 (persistance d'une tumeur, 25mm, 1N+R+/14)
- radiothérapie (sein, CMI, susclav)

10/2007 : Rechute ganglionnaire axillaire *droite isolée* (cyto+)

Refus de la chirurgie. XELODA par périodes.

2014



06/2014 : progression ganglionnaire, RE -, RP -, HER2 -, RA+ 100 % : **inclusion étude AMA (ABIRATERONE).**

Octobre 2014 : progression ganglionnaire axillaire droite. **Chirurgie récusée. Diverses lignes de chimiothérapie**

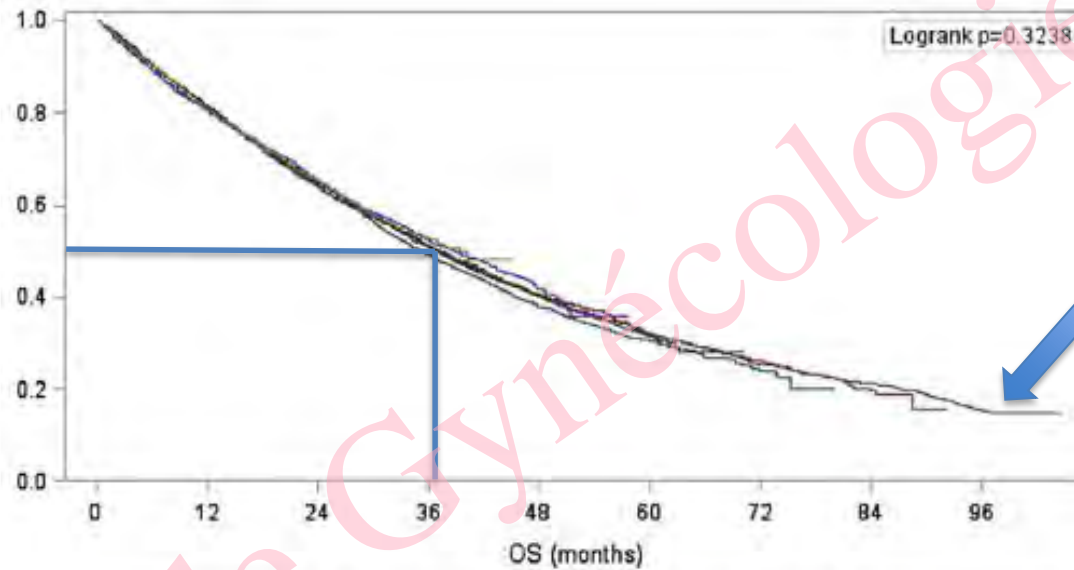
Avril 2018 : décès par progression

Données générales

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Survie globale



Period-Subgroups based on the metastatic diagnosis

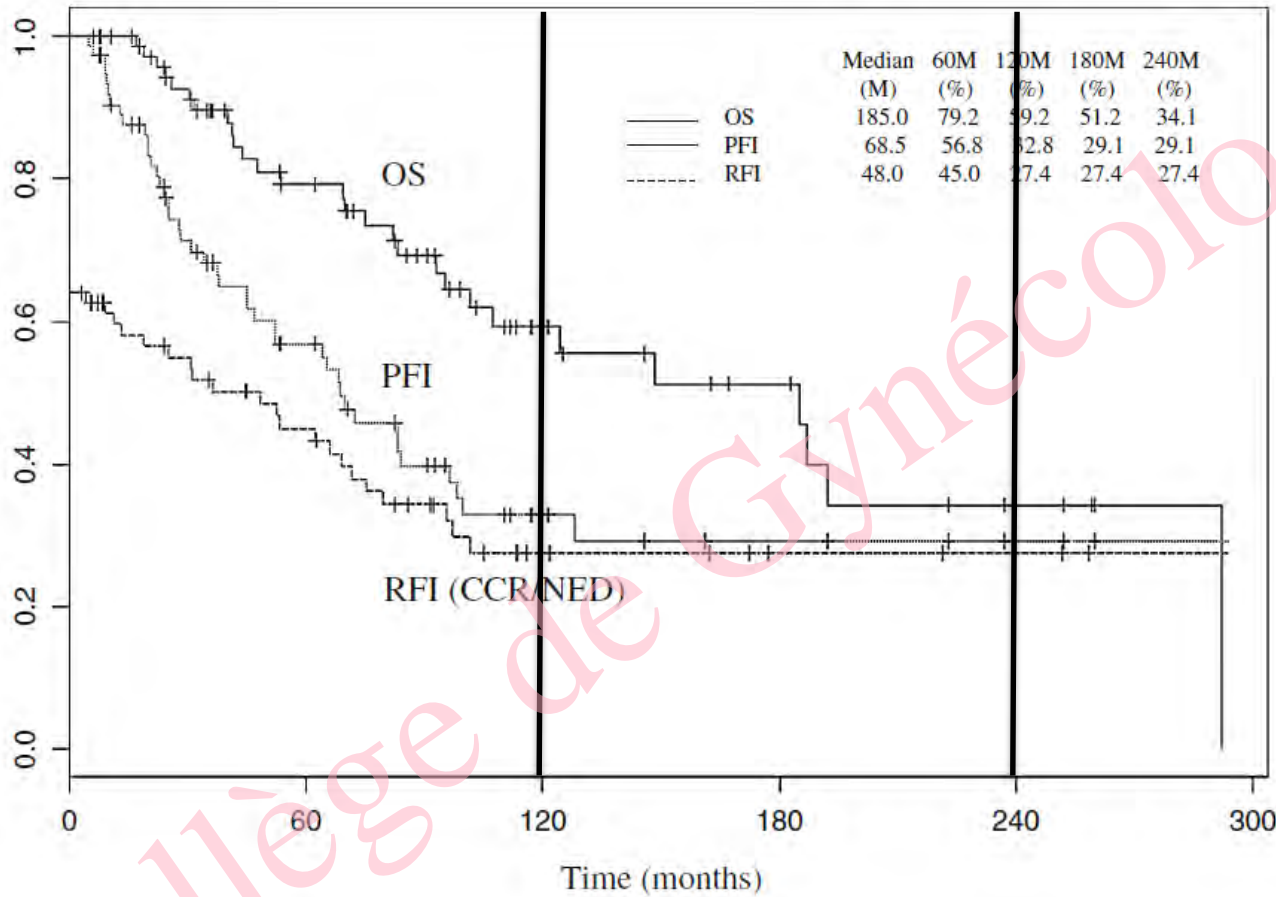
	1: inferior or equal to 2006	2: in 2009	3: in 2010	4: in 2011	5: in 2012	6: superior or equal to 2013
1	2508	1943	1480	1123	862	637
2	2431	1893	1450	1084	818	618
3	2441	1888	1435	1056	765	542
4	2483	1926	1487	1089	804	126
5	2520	1918	1474	1071	178	0
6	4316	3253	1775	240	0	0

Expérience japonaise

n=75 sur 30 ans

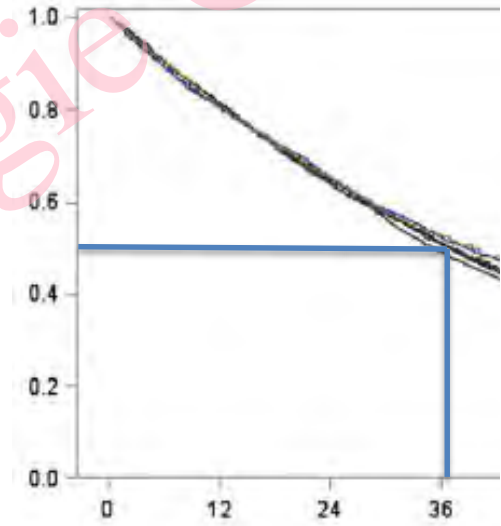
	N (%)
DFI	25 (0-168)
Nb sites	
1	44 (59%)
2	31 (41%)
Atteinte viscérale	36 (48%)
RH+	48 (64%)
HER2+	13 (17%)
Basal like	18 (24%)
Traitements	
local seul	0
Combiné	75 (100%)
Systémique seul	68 (91%)

Expérience japonaise



10 ans

20 ans



ESME

Données historiques

Auteur	Années	N	Traitements	Survie médiane (mois)	Survie à 5 ans (%)
Borner	1982-1991	167	Ttt local	-	74
			Ttt systémique	-	76
Blumenschein	1986-1996	59	Combiné	132	85
Nieto	1991-1998	60	Combiné	80	62
Hanrahan	1974-2004	285	Combiné	87	36-59
Rahman	1973-1982	1581	chimiothérapie	49 patientes en RC à 5 ans	

Traitements locaux

- **Chirurgie**

- Hépatique : SG à 5 ans 18-65%
- Pulmonaire: SG à 5 ans 14-54%
- Cérébrale, etc
- Et cimentoplastie

- **Radiothérapie**

- Conventionnelle
- stéréotaxique

Scorsetti, The Breast 2016

Wong, Cancer 2016

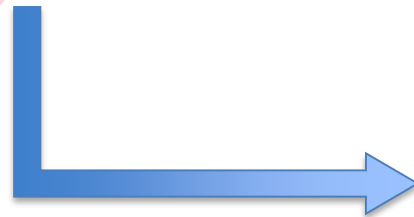
Klement, Radiot Oncol 2017

Trovo, Radiot Oncol 2017

Pagani, JNCI 2010

Résection hépatique

Raab et al. 1998 [6]	34	5-year survival: 22	Negative margins (R0), no prior local recurrence
Pocard et al. 2000 [7]	52	3-year survival: 49	Long DFI
Yoshimoto et al. 2000 [8]	25	5-year survival: 27	Not reported
Pocard et al. 2001 [9]	65	4-year survival: 46	Long DFI
Elias et al. 2003 [11]	54	5-year survival: 34	Positive hormone receptor status
Vlastos et al. 2004 [14]	31	5-year survival: 61	Not reported
Sakamoto Y et al. 2005 [15]	35	5-year survival: 31	No extrahepatic disease
Adam et al. 2006 [16]	85	5-year survival: 37	Response to preoperative chemotherapy, no R2 resection, possibility of rehepatectomy in the further course of disease
Zegarac M et al. 2013 [20]	32	Median OS 37 months	Positive hormone receptor status, negative lymph nodes, long DFI, single metastases
Weinreich 2014 [12]	21	5-year survival: 33	Negative margin (R0), low primary tumor size, negative lymph nodes, low-grade histopathology, low number of liver metastases, long DFI
Ye et al. 2015 [18]	28	5-year survival: 53 10-year survival: 33	DFI >36 months, negative margins, no tumor recurrence before metastectomy
Margonis et al. 2016 [17]	131	3-year survival: 75.2	Negative margin (R0), small diameter of the liver metastasis
Kobryn et al. 2016 [19]	30	3-year survival: 36.4	Not reported
Ercolani et al. 2005 [13] and 2018 [10]	51	5-year survival: 36 10-year survival: 16	Small tumor diameter, positive progesterone receptor status, and triple negative status

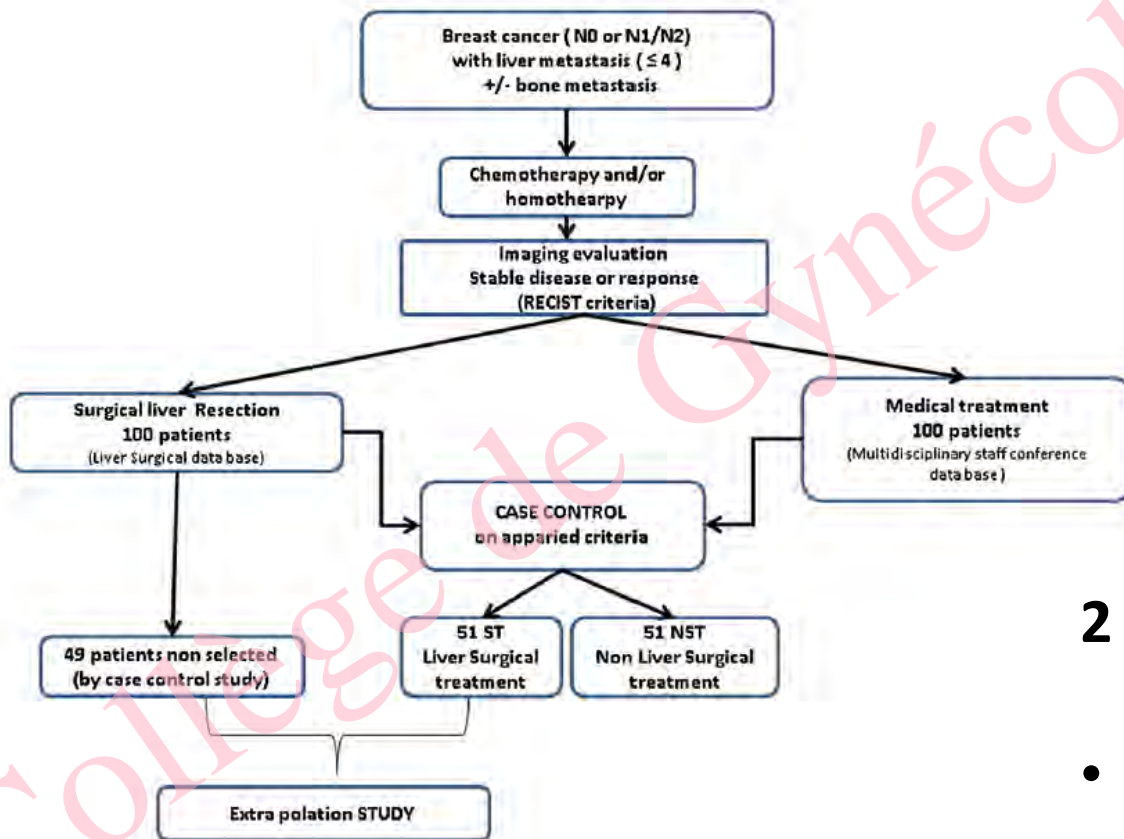


- **Rechute tardive**
- **RH+**
- **Sensible**
- **Résection complète**

Liver metastases from breast cancer: Surgical resection or not? A case-matched control study in highly selected patients

P. Mariani ^{a,*}, V. Servois ^b, Y. De Rycke ^c, S.P. Bennett ^a, J.G. Feron ^a, M.M. Almubarak ^a,
F. Reyal ^a, B. Baranger ^a, J.Y. Pierga ^d, R.J. Salmon ^a

EJSO 2013



2 facteurs indépendants

- Résection hépatique
- 0 Métastase osseuse

Métastases cérébrales

traitement systémique

Protocoles	Nombre de patients	Taux de réponse (%)
CFP/CFP-MTX-vincristine/MTX-vincristine-prednisolone/CA	100	50
Cisplatine + VP16	22	55
CMF/CAF	22	59
Paclitaxel	152	35
Cisplatine + étoposide	56	38
Épirubicine/docétaxel	92	68
Topotécan	16	38
TMZ + cisplatine	15	40
MTX IVHD	32	28
TMZ + capécitabine	24	18
Capécitabine	7	43

International Guidelines for Management of Metastatic Breast Cancer: Can Metastatic Breast Cancer Be Cured?

Olivia Pagani, Elzbieta Senkus, William Wood, Marco Colleoni, Tanja Cufer, Stella Kyriakides, Alberto Costa, Eric P. Winer, Fatima Cardoso, on behalf of the ESO-MBC Task Force

JNCI 2010

- **Définition: « solitary or few detectable metastases »**
- **N: 1-10%**
- **« more aggressive and multidisciplinary approach »**
- **Données rétrospectives uniquement**
 - **identification des patientes : TEP ?**
 - **concept de guérison en situation métastatique**
 - **définition de la guérison**
 - **Objectifs et critères de jugement « appropriés »**
 - **Quelle définition pour le « Long terme » ?**

International Guidelines for Management of Metastatic Breast Cancer: Can Metastatic Breast Cancer Be Cured?

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JNCI 2010



- **Rôles du traitement systémique**
 - Réponse complète
 - Réponse durable
 - « adjuvant » après traitement local
 - 36-52% NED à 5 ans
 - Innovation
 - Chimiothérapie locale
 - Intrahépatique
 - intrathécale

Littérature récente

Review
Stereotactic radiotherapy in metastatic breast cancer
Marco Paganini, Carlo Greco
Journal homepage: www.breastjournal.com

ARTICLE INFO

ISSN: 1744-7612
DOI: 10.1007/s12282-012-0212-1
Received: 12 June 2012
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Breast Care

Oligometastatic Breast Cancer: A Shift from Palliative to Potentially Curative Treatment?
Santina Di Lauro, Olivia Pagani
Structure of oligometastatic disease: Treatment: Multi

ABSTRACT

The development of novel systemic therapies has improved the prognosis of breast cancer patients with oligometastatic disease. A shift in the paradigm of oligometastatic breast cancer is being observed, with the potential for curative treatment. This review discusses the current evidence for the use of systemic therapies in oligometastatic breast cancer, and the potential for curative treatment. The review also discusses the use of local therapies, such as stereotactic radiotherapy, in the treatment of oligometastatic breast cancer.

KEYWORDS

Breast cancer; Oligometastatic disease; Treatment; Multi

Surgery or Ablative Radiotherapy for Breast Cancer Oligometastases
Joseph A. Sparano, MD and Steven J. Chinnai, MD, PhD

OVERVIEW

Precisely defined selection of breast cancer patients with oligometastatic disease is being identified. The use of local therapies, such as surgery or ablative radiotherapy, may be curative in these patients. This review discusses the current evidence for the use of local therapies in the treatment of breast cancer oligometastases, and the potential for curative treatment.

INTRODUCTION

The term oligometastatic disease (OMD) has been used to describe a subset of breast cancer patients with a limited number of metastases. The use of local therapies, such as surgery or ablative radiotherapy, may be curative in these patients. This review discusses the current evidence for the use of local therapies in the treatment of breast cancer oligometastases, and the potential for curative treatment.

PLOS ONE

Classification for long-term survival in oligometastatic patients treated with ablative radiotherapy: A multi-institutional pooled analysis
Julien C. Hong, Diandra N. Ayala-Peacock, Joseph Lee, A. William Blackwell, Paul D. Chung, Max W. Sung, Phillip B. Wenzel, Anthony K. Rex, James J. Grunberg, Michael T. Milano, Steven J. Chinnai, Joseph A. Sparano

RESEARCH ARTICLE

This study aims to define a classification for long-term survival in oligometastatic patients treated with ablative radiotherapy. The study includes a multi-institutional pooled analysis of patients with oligometastatic breast cancer treated with ablative radiotherapy. The study results show that a classification based on the number of metastases and the response to treatment can predict long-term survival.

memo
Journal of Metastatic Breast Cancer

Cure in metastatic breast cancer
Theresa Westphal, Simon Peter, Christopher Galardi, Dimosthenis Richard Drex

Short review

Journal: *memo* | Volume: 1 | Issue: 1 | Page: 1-10 | Published online: 17 August 2012

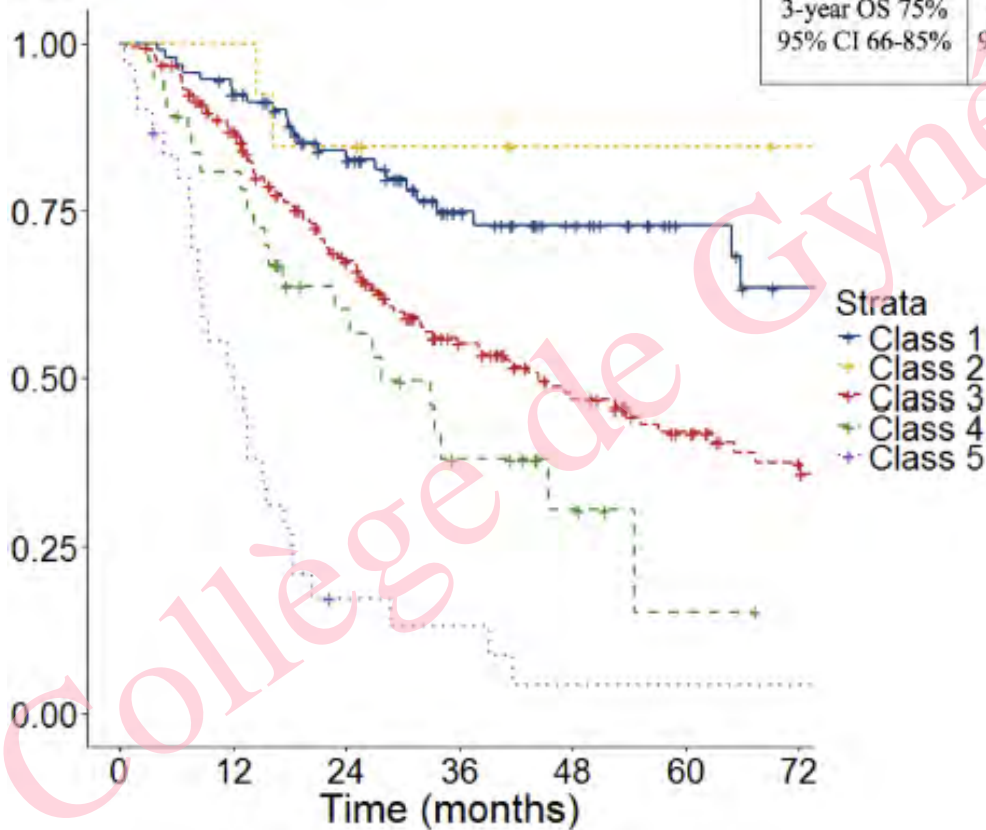
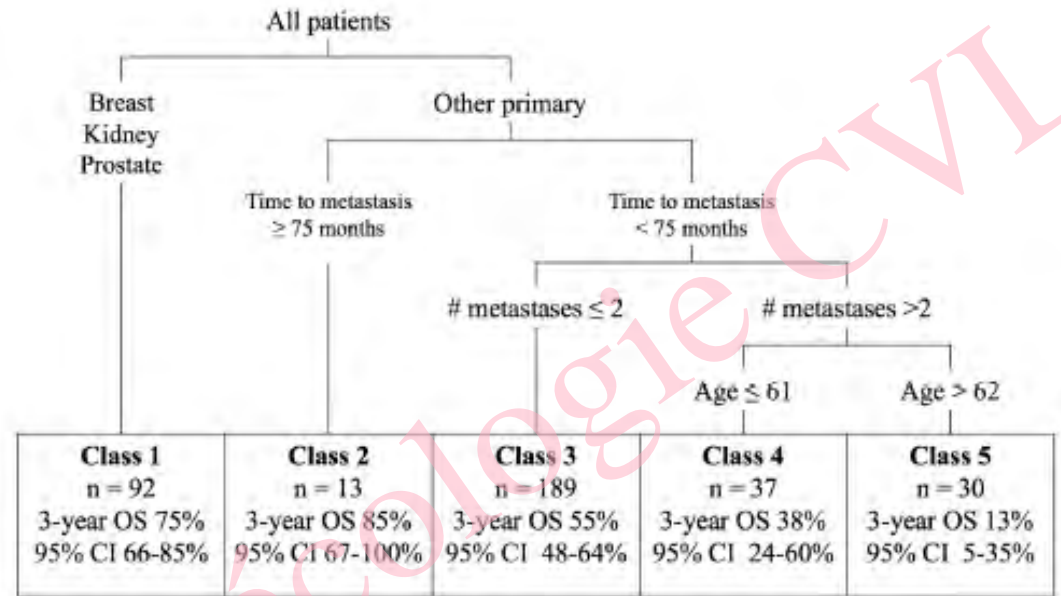
ABSTRACT

This review discusses the current evidence for the use of local therapies in the treatment of breast cancer oligometastases, and the potential for curative treatment. The review also discusses the use of systemic therapies in oligometastatic breast cancer.

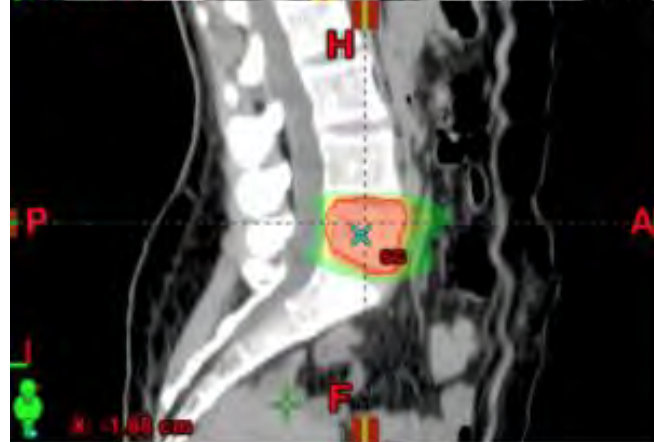
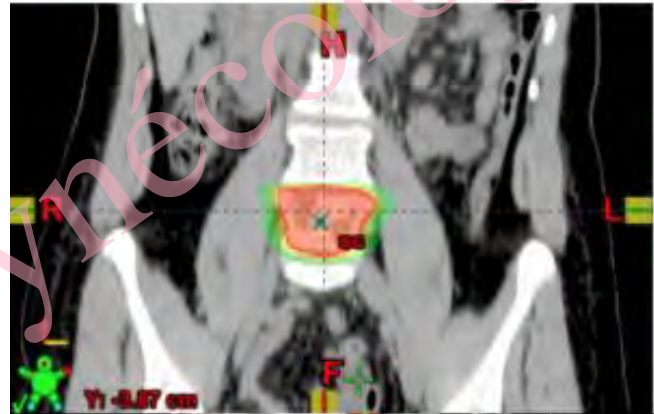
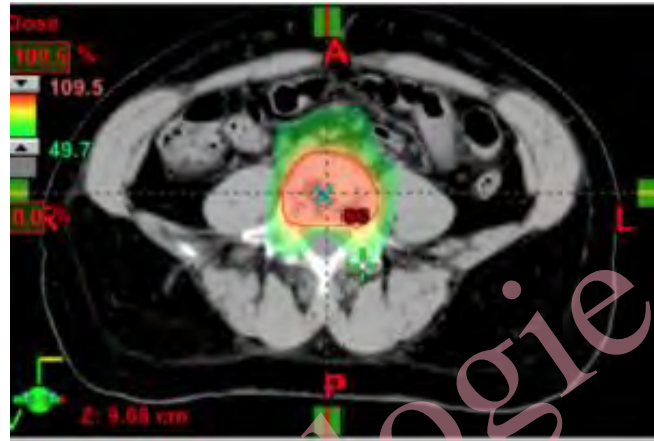
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Classification

≤ 5 métas



Stéréotaxie



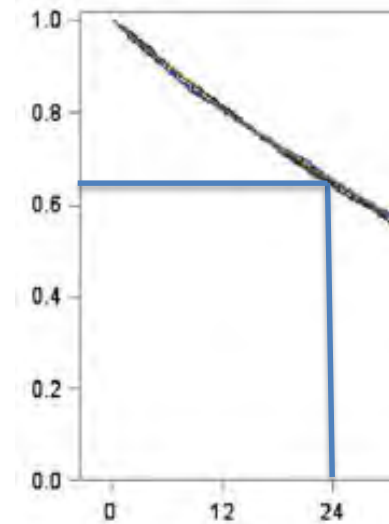
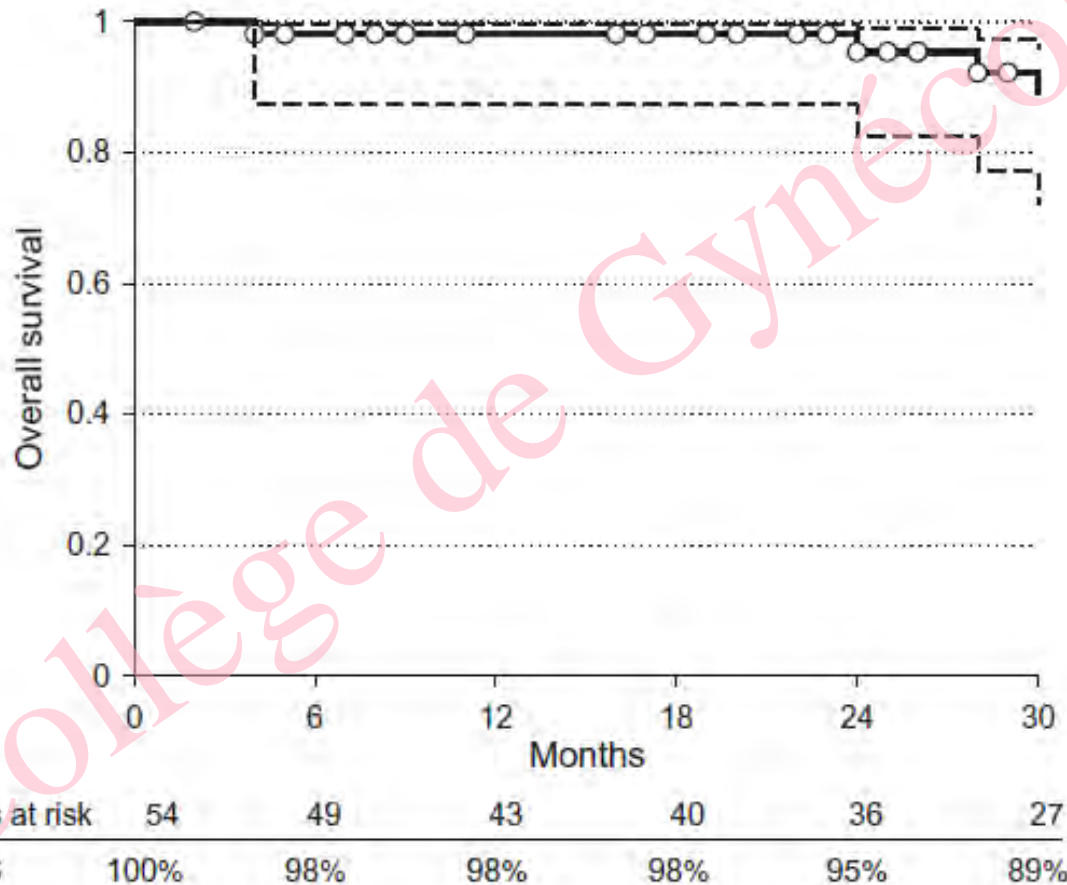
Radical radiation therapy for oligometastatic breast cancer: Results of a prospective phase II trial



Marco Trovo^{a,*}, Carlo Furlan^a, Jerry Polesel^b, Francesco Fiorica^c, Stefano Arcangeli^d, Niccolò Gaj-Levra^e, Filippo Alongi^e, Alessandro Del Conte^f, Loredana Militello^f, Elena Muraro^g, Debora Martorelli^g, Simon Spazzapan^{e,f}, Massimiliano Berretta^f

Radioth Oncol 2018

- ≤ 5 métastases
- Pas de méta cérébrale



ESME

ABC 3

SECTION 2. ABC IMPORTANT DEFINITIONS

GUIDELINE STATEMENT

OLIGO-METASTATIC DISEASE is defined as low volume metastatic disease with limited number and size of metastatic lesions (up to five and not necessarily in the same organ), potentially amenable for local treatment, aimed at achieving a complete remission status.

LoE

Expert opinion

Consensus

Voters: 36

Yes: 78% (28)

Abstain: 6% (2)

Recommandation:

- **Bilan : TEP TDM ou TDM Scinti os**
- **Approche multi-modale**
- **Intention curatrice**

4th ESO–ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4)[†]

F. Cardoso^{1*}, E. Senkus², A. Costa³, E. Papadopoulos⁴, M. Aapro⁵, F. André⁶, N. Harbeck⁷

- Oligometastatic disease is defined as low volume metastatic disease with limited number and size of metastatic lesions (**up to 5 and not necessarily in the same organ**), potentially amenable for local treatment, **aimed at achieving a complete remission status**. Expert opinion 78%
- A small but very important subset of patients with ABC, for example those with oligometastatic disease or low volume metastatic disease that is highly sensitive to systemic therapy, can achieve complete remission and a long survival. A **multimodal approach**, including locoregional treatments with **curative intent**, should be considered for these selected patients. A prospective clinical trial addressing this specific situation is needed. Expert opinion 91%

Synthèse

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De quoi avons-nous parlé ?

oligos (« peu abondant »)

sanscrit *liç*, être petit, avec o prosthétique



Niveau

diagnostic

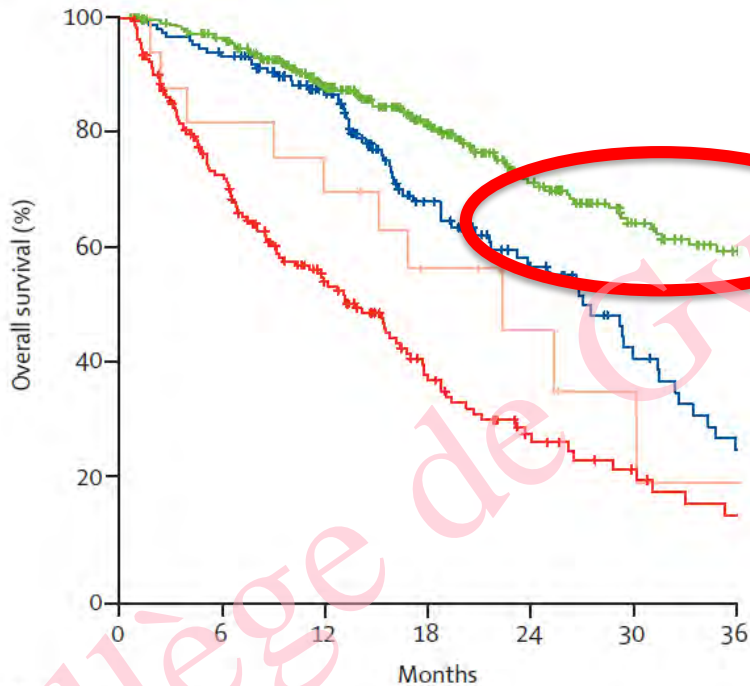
« oligo »

Lésions « peu »
nombreuses/solitaire
+/- un seul organe
Ttt local curatif envisageable

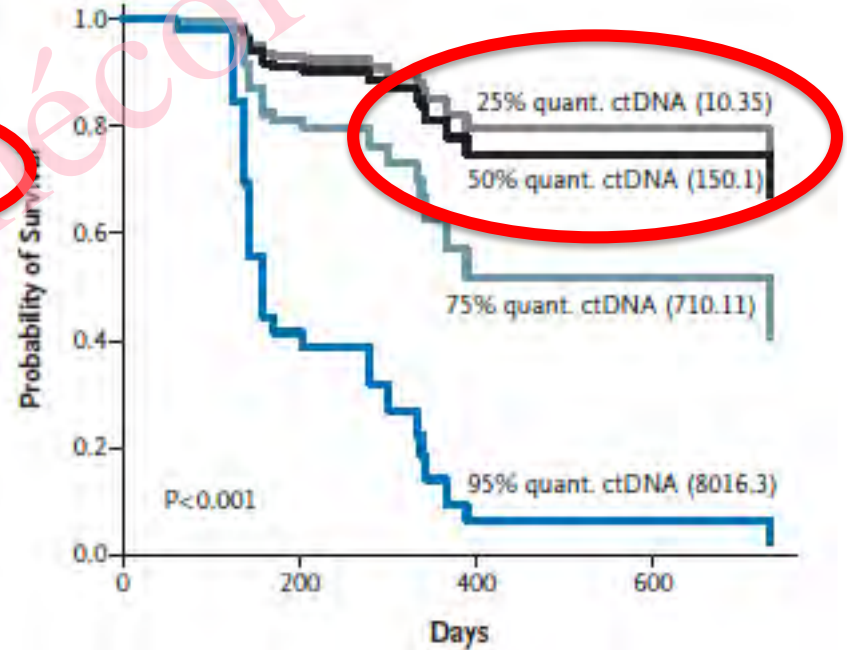


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Micro et Nano



Number at risk	0	6	12	18	24	30	36
Decrease	149	135	104	59	36	20	11
Increase	17	13	11	7	4	2	1
Stable negative	327	296	231	160	102	68	50
Stable positive	179	116	68	36	18	10	5

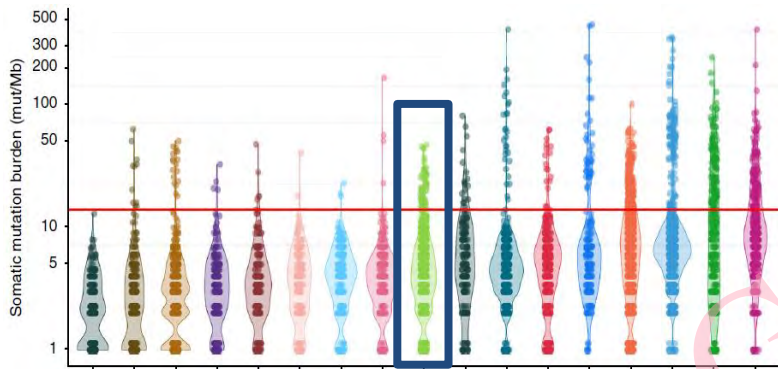


Maladie métastatique

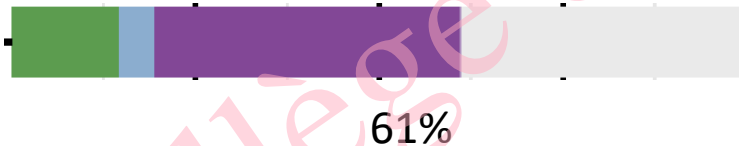
biologie 1ère rechute



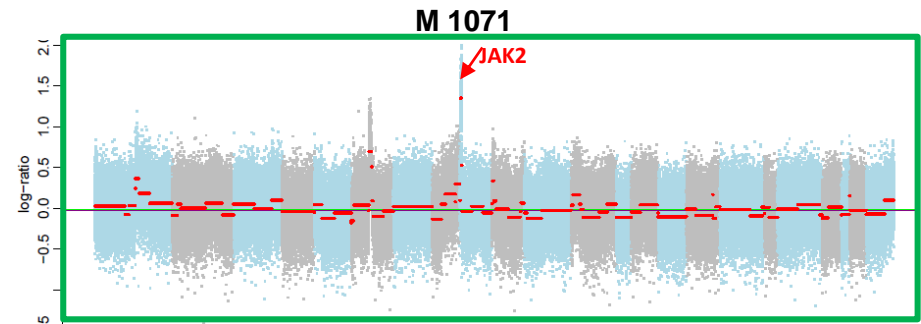
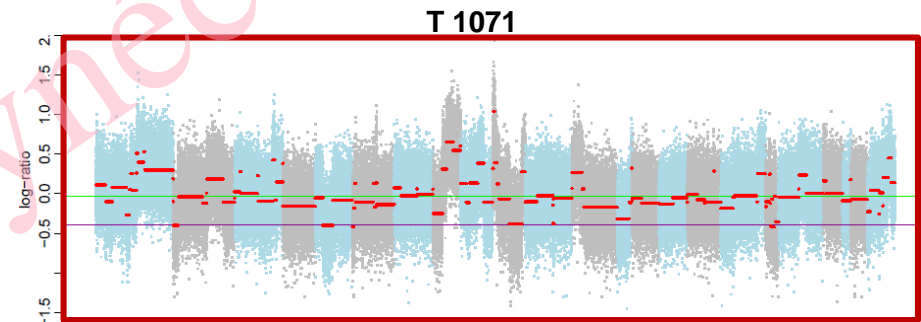
Violin plot : TMB



Actionable mutations



CNAs



Messages

- **Oligométastatique ?**
 - Definition pragmatique
 - Aucune étude prospective évaluant la stratégie globale
 - Quelques cas « guéris »
- **Combiner local ET systémique**
 - Accord d'experts
- **La biologie de la métastase est potentiellement informative dès la maladie métastatique « précoce »**
 - Bénin ou autre cancer = 10% !
 - Biologie circulante en devenir