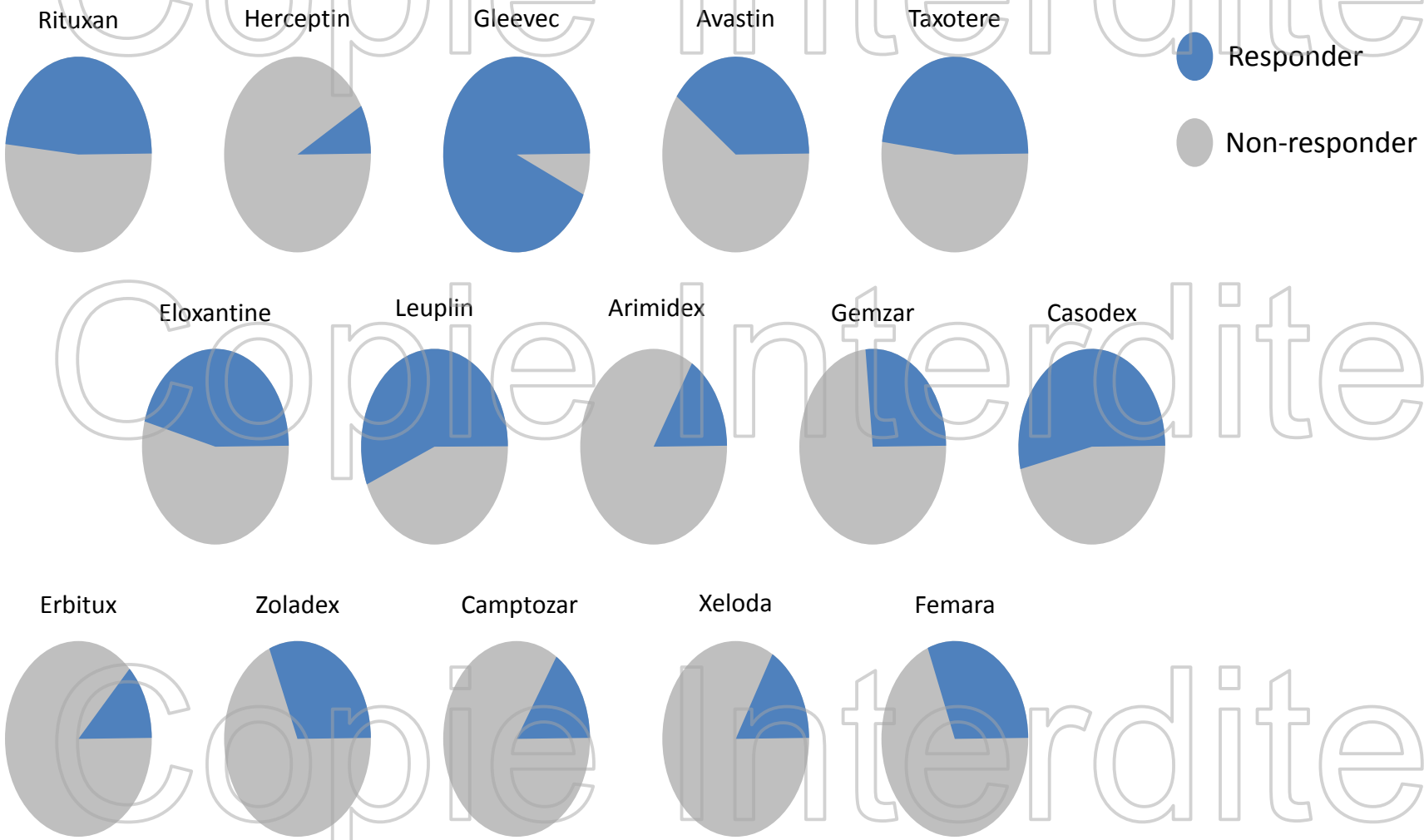
ONCOLOGIE NUCLEAIRE THERANOSTIQUE

F . COURBON , M BAURIAUD, C FONTAN , E. GABIACHE, S BRILLOUET

La cancérologie et ses échecs



Jackson DB, Clinical and economic impact of the non-responder problem; Drug Discovery Today, April 2009; Analysis of FDA label data for top 15 drugs

THERANOSTIC

LE CONCEPT :

CIBLE + → TRAITEMENT +

CIBLE – → TRAITEMENT -

Rôle de l'imagerie

Taxonomie :

expression de cible,

pronostic cTNM > vascularisation> nécrose> signal biologique

Réponse

Critère de substitution/ précoce d'efficacité

PK Phase R0

Vous avez dit : « Théranostique »

On en fait depuis longtemps

tout ce qui n'est pas prose est vers et tout ce qui n'est point vers est prose !

RADIOTHERAPIE INTERNE VECTORISEE

NIS :131I Kc de la thyroïde

NA :131ImIBG Neuroblastomes, T endocrines

CD20 : 90Y-MoAb LMNH

SSTr :177Lu ou 90Y ou 111In -peptide T endocrines

Annals of Oncology Advance Access published April 13, 2007

review

Annals of Oncology
doi:10.1093/annonc/mdm111

Targeted therapy in nuclear medicine—current status and future prospects

W. J. G. Oyen[1,2*], L. Bodei[1,3], F. Giammarile[1,4], H. R. Maecke[1,5], J. Tennvall[1,6], M. Luster[1,7] & B. Brans[1,8]

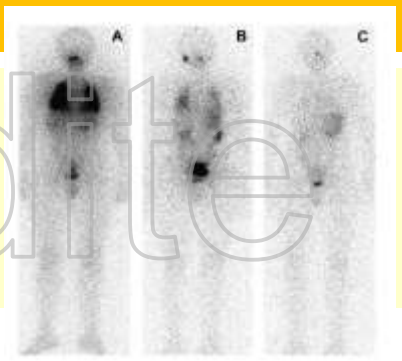
TEP ^{18}FDG…

CIBLE + ➔ TRAITEMENT +

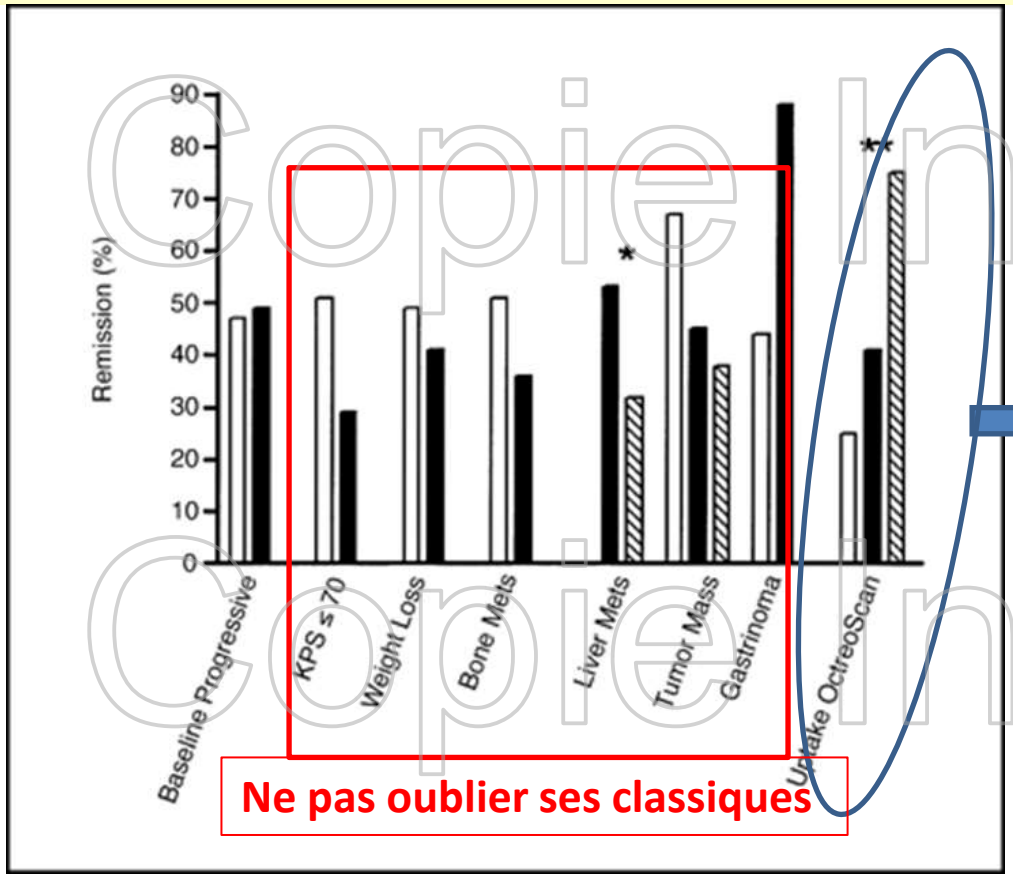
131-I et Cancer de la thyroïde

En général I131 + ➔ REPONSE +

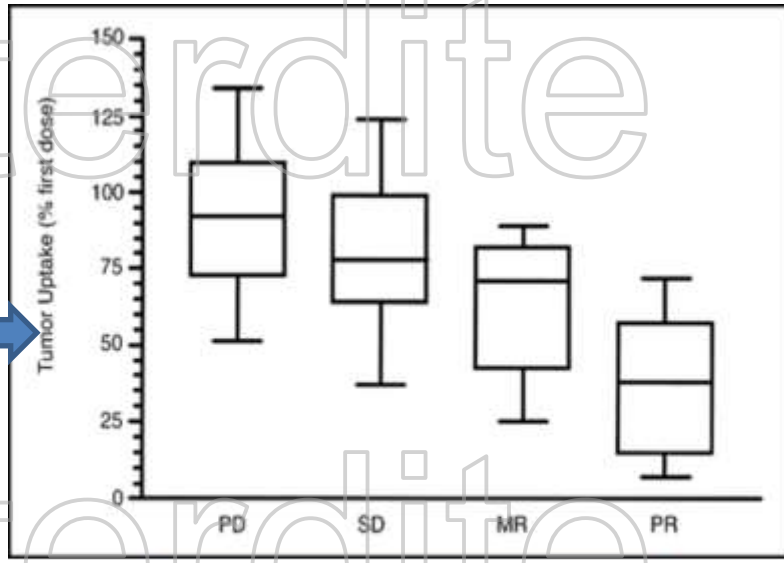
Oyen et al 2007



90Y, 177 Lu – SMS analogues T Endocrines



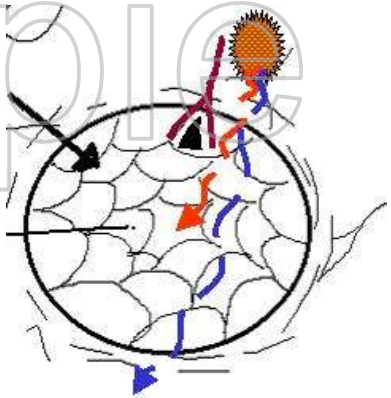
Ne pas oublier ses classiques



Les répondeurs fixent de moins en moins

CIBLE + ➔ TRAITEMENT + SOUS CONDITION

1° La taille



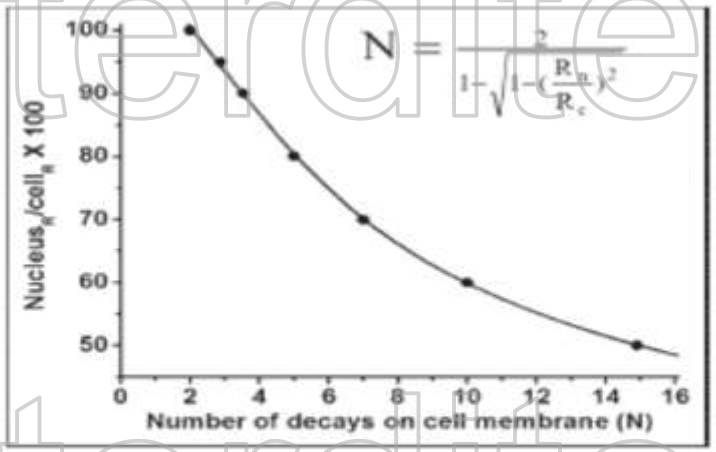


FIGURE 1. Number of radioactive atoms needed to assure traversal of cell nucleus by a single energetic particle as function of distance from nuclear membrane. Nuclear-to-cell radius (percentage) plotted as function of number of decays in cell membrane.

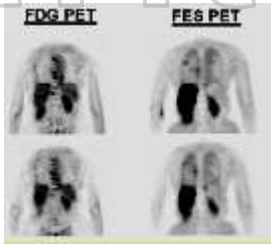
Zevalin (0.4mCi/Kg) vs Rituximab Witzig et al JCO 2002
ORR 80% vs 56 %
CR 30% vs 16%
TTP 17.8 m vs 11.2 **LF**

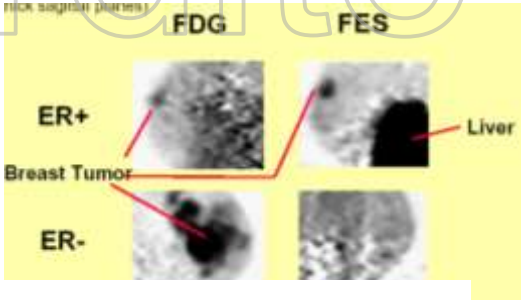
2° le nombre de cibles

Pas d'antigène spécifique d'une prolifération tumorale
Par défaut:
100 fois plus par les cellules tumorales,
> 500000 sites par cellules,
constante d'affinité > 10^8 M.

CIBLE + ➔ TRAITEMENT + : Pas systématique

Caractérisation fonctionnelle et Réponse tumorale *16-α-[18F]fluoro-17-estradiol* Kc du sein





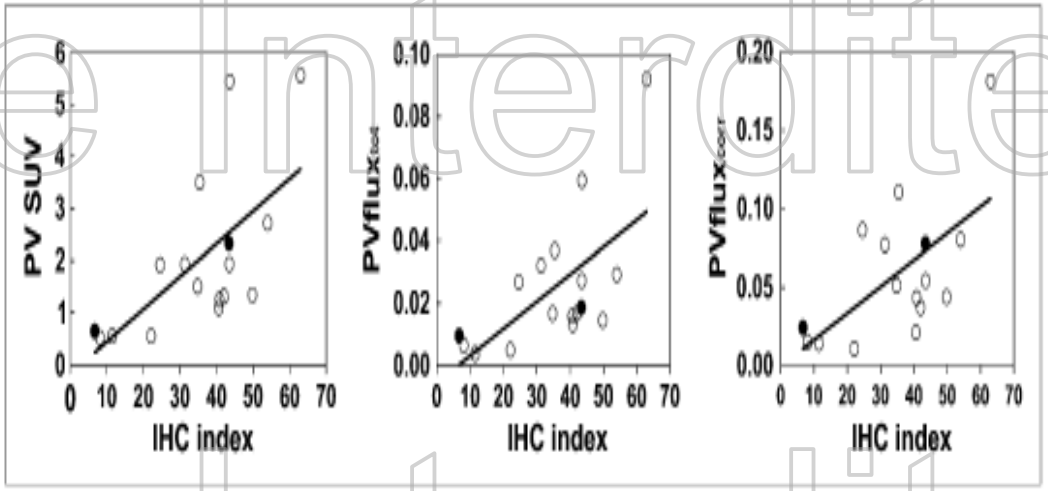
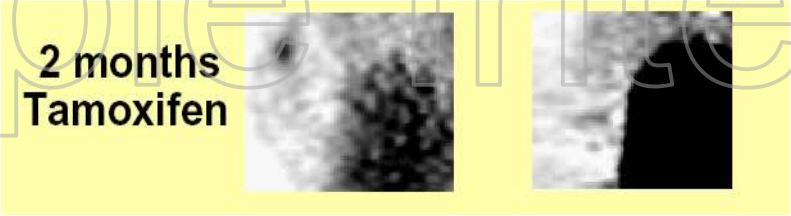


FIGURE 5. Comparison of ^{18}F-FES uptake measures with IHC index (Photoshop analysis). Treated patients are identified by closed circles.

Quantitative Imaging of Estrogen Receptor Expression in Breast Cancer with PET and ^{18}F-Fluoroestradiol

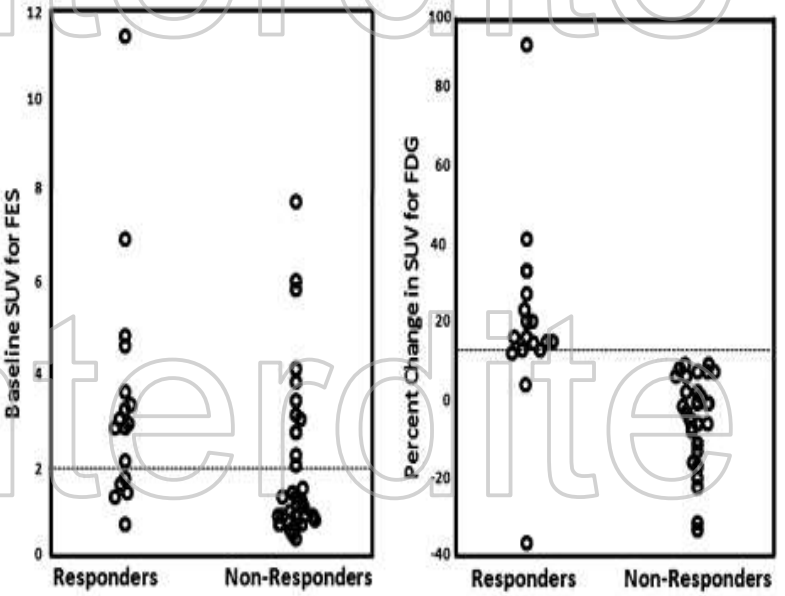
☞Différence entre voir une cible et tester une cible :



FGD FES

Test de stimulation par œstrogènes

Fig. 2 The baseline tumor FES (left) and percent change in tumor FDG (right) uptake after estradiol challenge in patients who responded and who did not respond to endocrine therapy



Breast Cancer Res Treat (2009) 113:509–517
DOI 10.1007/s10549-008-9953-0

CLINICAL TRIAL

PET-based estradiol challenge as a predictive biomarker of response to endocrine therapy in women with estrogen-receptor-positive breast cancer

FDG Flair up

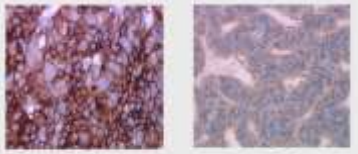
•CIBLE – ➔ PAS DE CIBLE

Outcome of Differentiated Thyroid Cancer with Detectable Serum Tg and Negative Diagnostic ^{131}I Whole Body Scan: Comparison of Patients Treated with High ^{131}I Activities *Versus* Untreated Patients 2001

Treatment of iodine-negative thyroglobulin-positive thyroid cancer: differences in outcome in patients with macrometastases and patients with micrometastases EJNM 20004

Immunostaining vs octreoscan®

Asnacios et al JCO 2008



sst2 sst5

(n = 82 patients)		Octreo -	Octreo +
anti-sst2	0	28	5
	+	12	36

p < 0.001

68Ga-DOTA-Tyr3-Octreotide PET in Neuroendocrine Tumors: Comparison with Somatostatin Receptor Scintigraphy and CT Virgolini et al **JNM 2007**

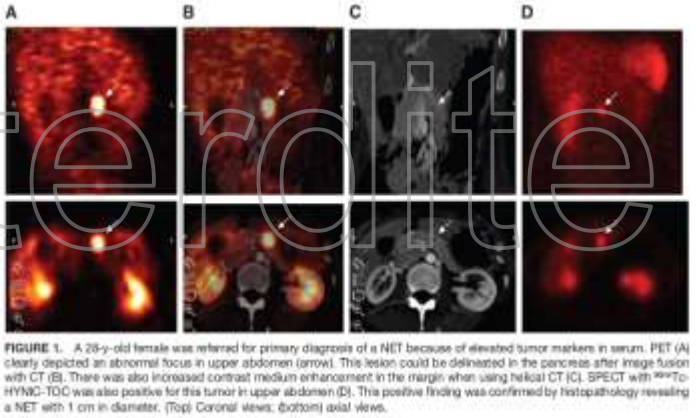


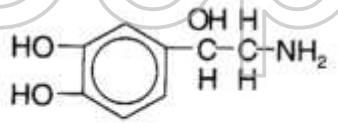
FIGURE 1. A 28-y-old female was referred for primary diagnosis of a NET because of elevated tumor markers in serum. PET (A) clearly depicted an abnormal focus in upper abdomen (arrow). This lesion could be delineated in the pancreas after image fusion with CT (B). There was also increased contrast medium enhancement in the margin when using helical CT (C). SPECT with ^{99m}Tc-HYNIC-TOC was also positive for this tumor in upper abdomen (D). This positive finding was confirmed by histopathology revealing a NET with 1 cm in diameter. (Top) Coronal views; (bottom) axial views.

68Ga-DOTA-Tyr3-Octreotide PET > CT

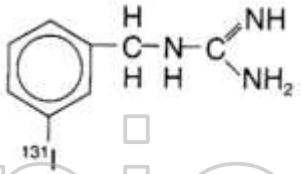
68Ga-DOTA-Tyr3-Octreotide PET > SRS

•CIBLE – → PAS DE CIBLE

Interférences médicamenteuses



Noradrenaline



^{131}I-m-Iodobenzylguanidine

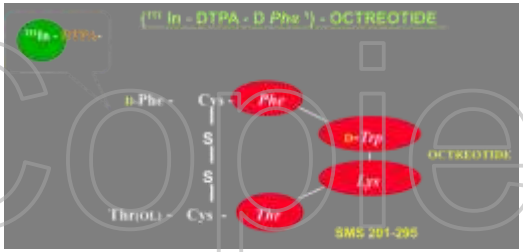
Interférences médicamenteuses (liste non exhaustive).

Antidépresseurs :

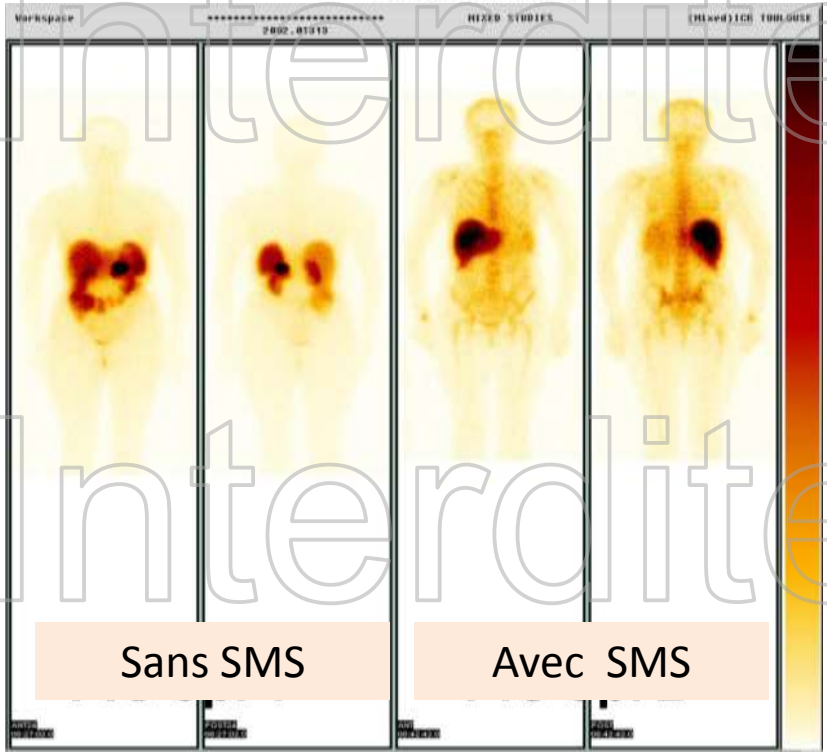
– médicaments qui contiennent Amitriptyline (Elavil®, Laroxil®), Amoxapine (Defanyl®), Clomipramine (Anafranil®), Désipramine (Pertrofan®), Dosulépine (Prothiaden®), Doxépine (Sinequan®), Maprotiline (Ludiomil®), Opiridamol (Insidon®), Quinupramine (Kinupril®), Trimipramine (Surmontil®).

Antihypertenseurs, béta-bloquants ou autres :

– médicaments qui contiennent Coedarone®, Digitoxine (Digitaline®, Digoxine®), Israpidine (Icaz®), Labelatol (Trandate®), Nicardipine (Loxen®), Nifédipine (Adalate®), Réserpine (Tensionorme®)



Analogue froids de la SMS



Sans SMS

Avec SMS

CIBLE - → PAS DE TRAITEMENT -

SRS pas de Valeur prédictive de l'efficacité de thérapeutique

Vezzozi et al European Journal of Endocrinology, 2005

Mieux vaut faire un test thérapeutique

Clinical Endocrinology (2008) 68, 904–911 doi: 10.1111/j.1365-2265.2007.03136.x

ORIGINAL ARTICLE

Short- and long-term somatostatin analogue treatment in patients with hypoglycaemia related to endogenous hyperinsulinism

D. Vezzosi*, A. Bennet*, F. Courbont and P. Caron*

*Department of Endocrinology and †Department of Nuclear Medicine, Centre Hospitalier Universitaire, Toulouse, France

Cible fonctionnelle → imagerie Fonctionnelle :

Restauration de fonction

Ex permeabilité péritonéale / Carcinose P

Comparison of peritoneal equilibration test with ^{99m}Tc-DTPA excretion in the assessment of peritoneal permeability

B. K. Das[1], M. S. Senthilnathan[1], P. K. Pradhan[1], S. Nagabhushan[1], T. K. Jeloka[2], R. K. Sharma[2]

[1] Department of Nuclear Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India
[2] Department of Nephrology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Received: 28 August 2003 / Accepted: 31 December 2003 / Published online: 18 February 2004

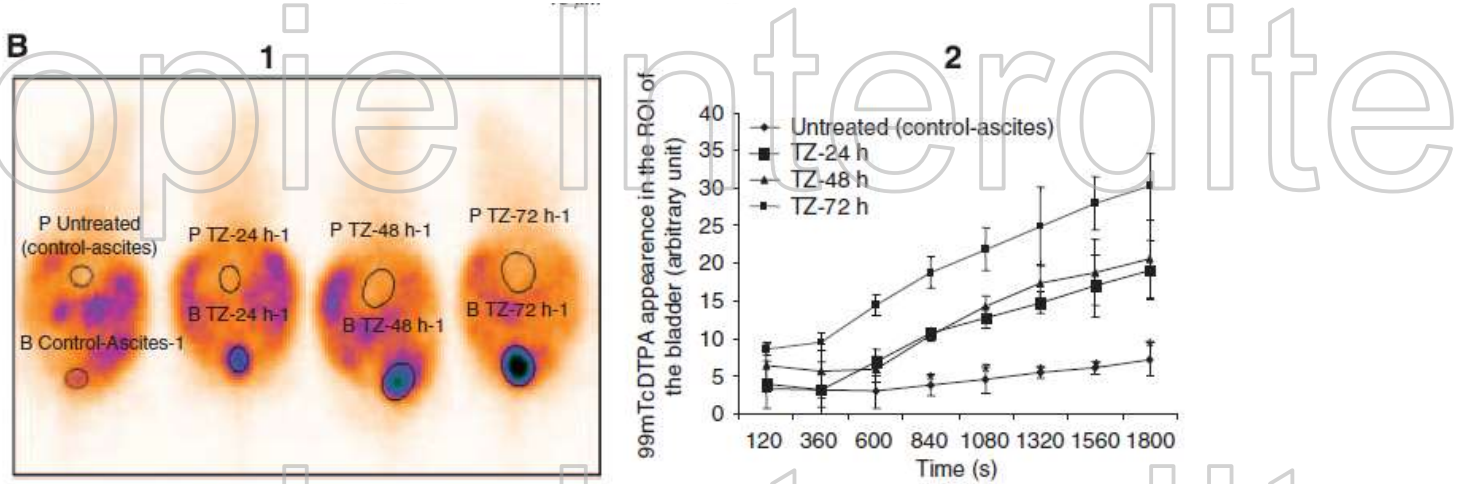


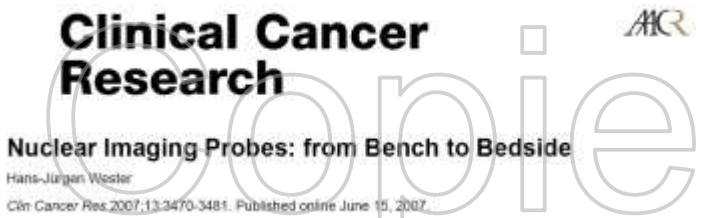
Figure 1 (**A**) Pathological pattern of the peritoneum 20 days after OVCAR-3WT implantation. Nude mice bearing OVCAR-3 macroscopic ascites were treated with vehicle (**A1**) or trastuzumab at a dose of 150 μg ml per day (**A2**) administered by i.p. route for 72 h. Naive nude mice were i.p. injected once a day for 3 days with 1 ml of either RPMI-1640 (**A3** control group) or the 24 h serum-free cleared supernatant collected from OVCAR-3 cells in culture (**A4**). Mice were killed and the peritonea were collected and formalin fixed. Microscopic examination was performed and pictures were taken. (**B**) Concentrations of ^{99m}Tc-DTPA over time in the bladder: peritoneal permeability. ^{99m}Tc-DTPA appeared in the bladder more intensively in treated animals compared with the untreated group. Arbitrary units express the ^{99m}Tc-DTPA intensity detection in the region of interest (ROI) of the bladder (shortened by 'B' and by 'P' for the peritoneum:). *$P<0.05$. Student's *t*-test compared untreated group (control-ascites) with trastuzumab (TZ) treatment groups.

Delord et al . Br J Cancer. 2010

innovations thérapeutiques

Théranostique : quelle méthode choisir ?

- Identifier une cible
- Evaluer précocement une altération métabolique

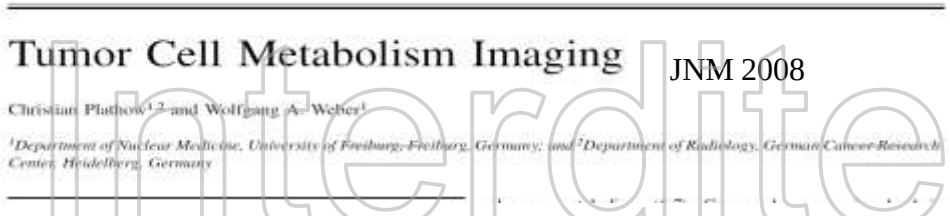

Clinical Cancer Research

AACR

Nuclear Imaging Probes: from Bench to Bedside

Hans-Jurgen Wester

Clin Cancer Res 2007;13:3470-3481. Published online June 15, 2007.

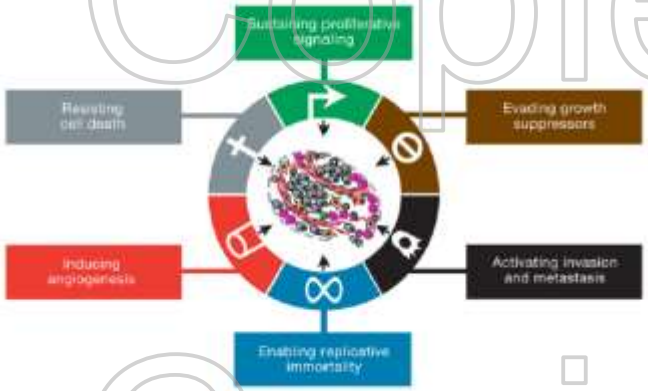

Tumor Cell Metabolism Imaging

JNM 2008

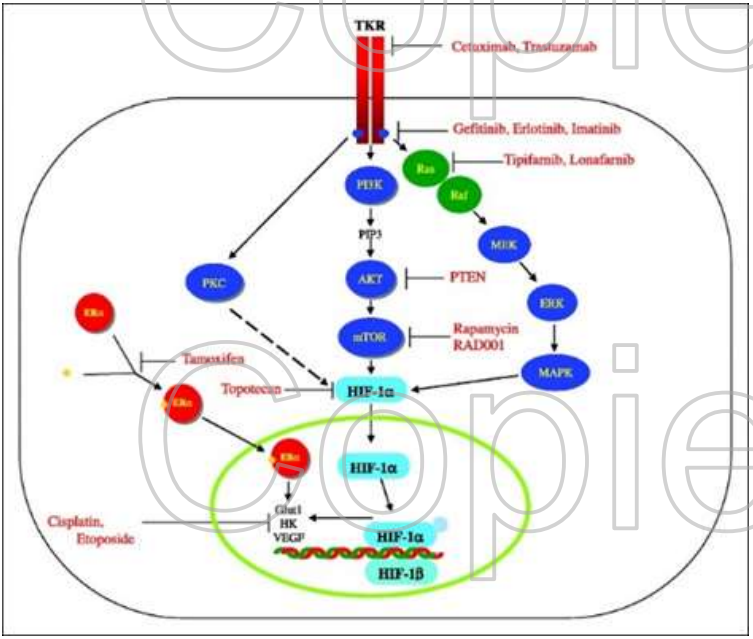
Christian Plathow[1,2] and Wolfgang A. Weber[1]

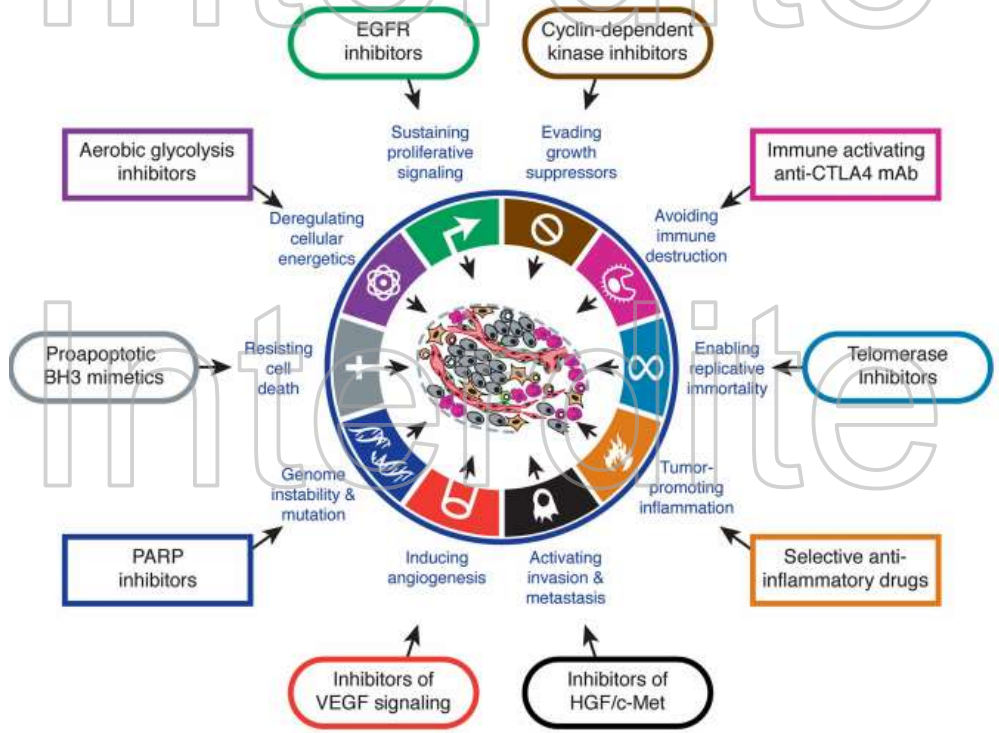
[1]Department of Nuclear Medicine, University of Freiburg, Freiburg, Germany; and [2]Department of Radiology, German Cancer Research Center, Heidelberg, Germany

Métabolisme



Années 2000



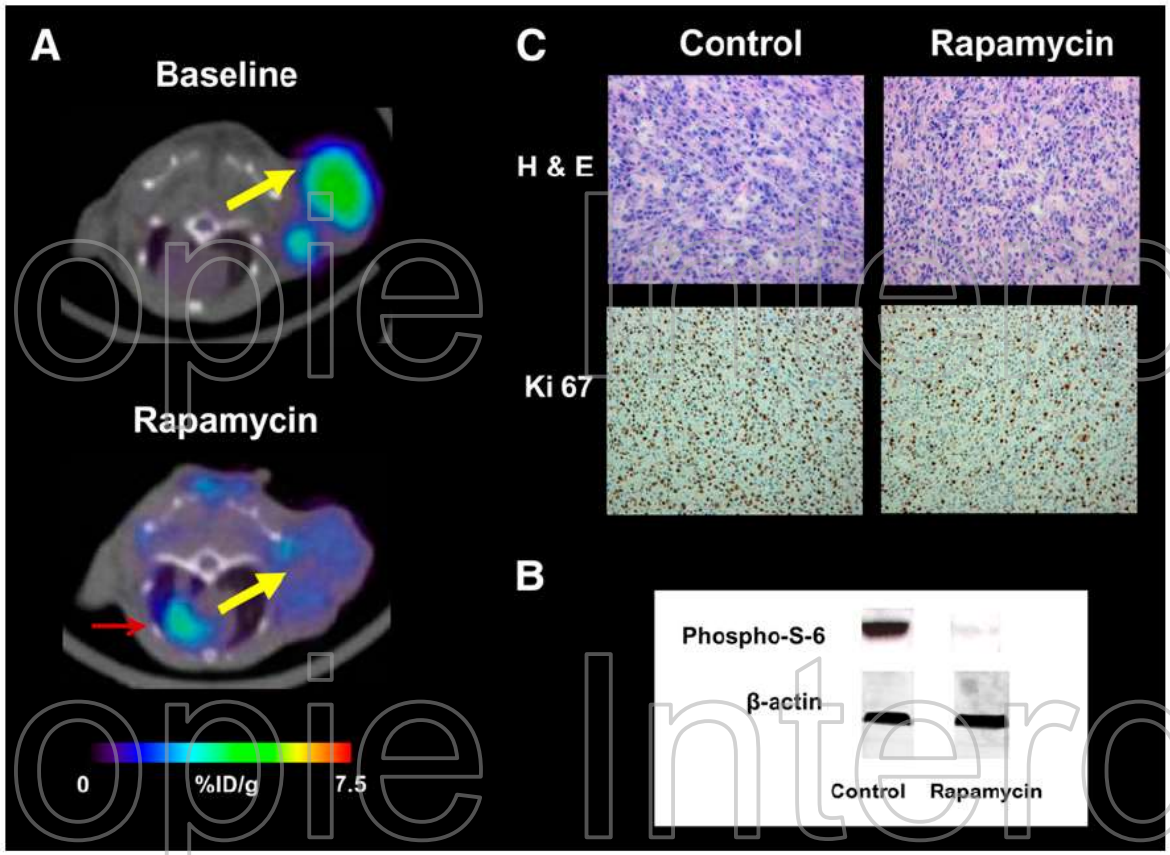


Hanahan D, Cell, 2011; 144:646-74

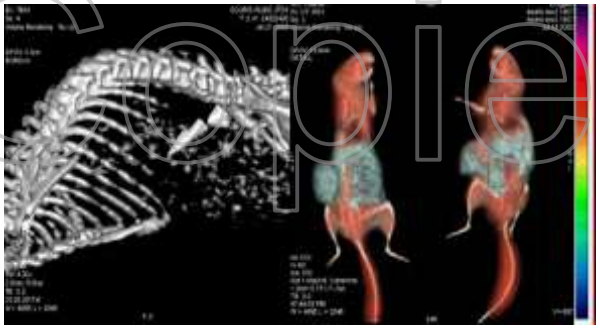
D Sullivan. Clinical Cancer Research Vol. 11, 2785-2808, April 15, 2005

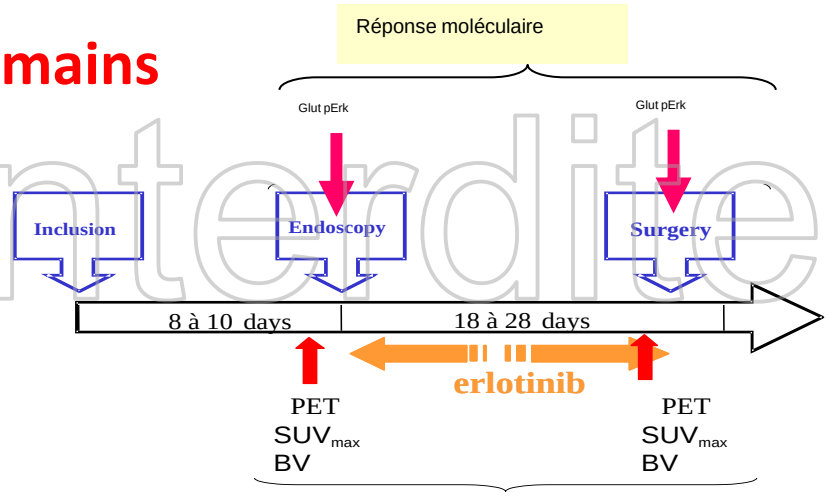
FDG un traceur spécifique !

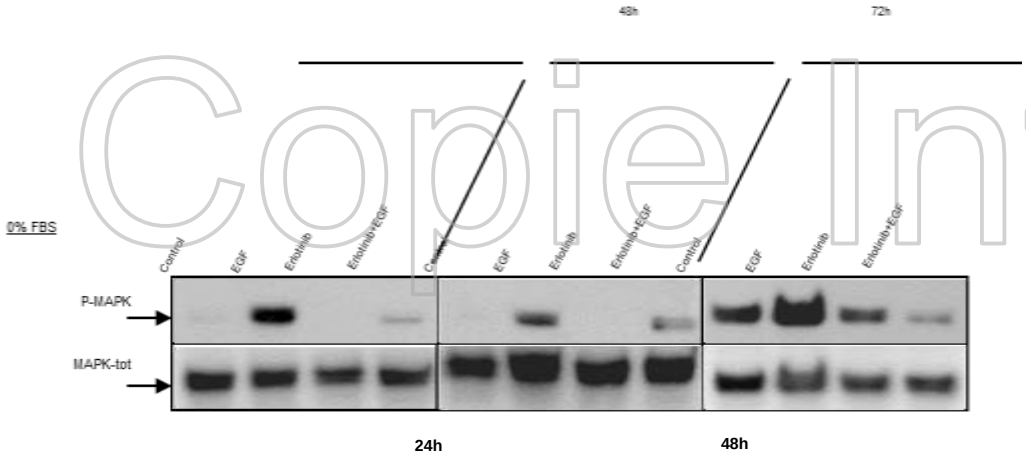
mTORi et TEP FGD

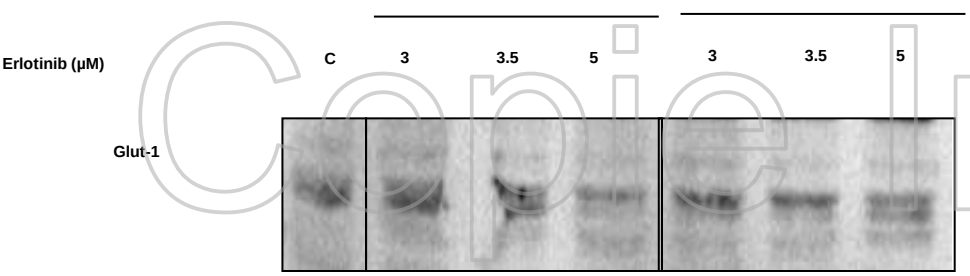


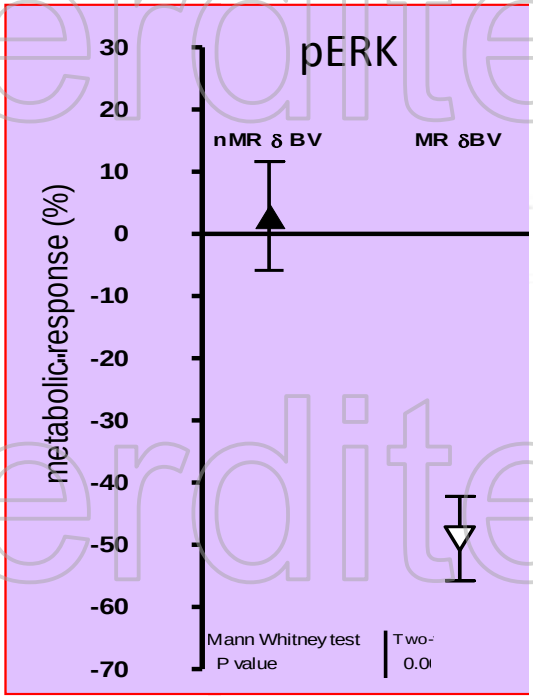
Tk_i Confirmation des souris aux humains







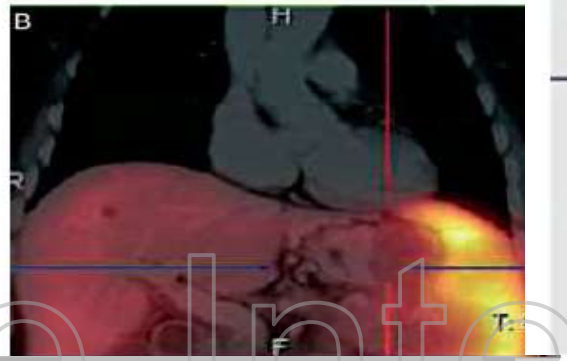




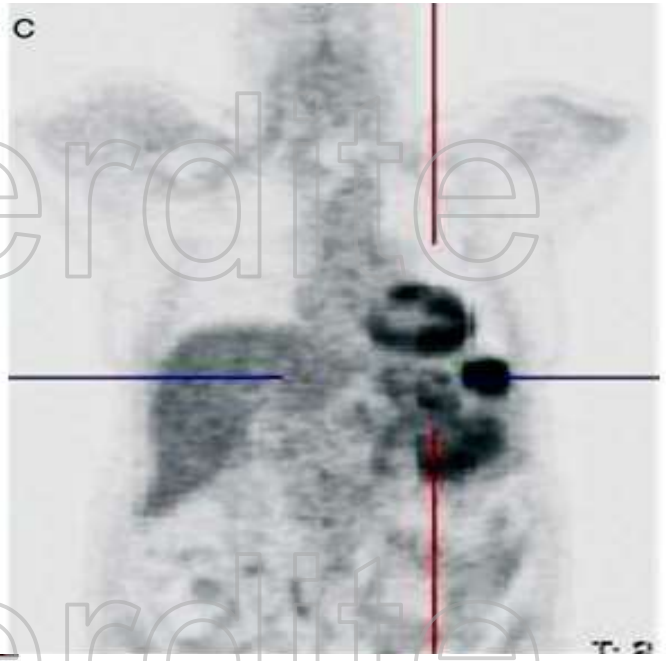
Vergez et al Clin Can Res 2007 -2010

^{18} FDG TEP : le paraddigme

1. Pronostic (ex Garin et al. pour les TE)
2. Evaluation de la response



SST neg



FDG pos.

G. Cadiot et al 2015

Théranostic et MoAb marqués

Eur J Nucl Med Mol Imaging (2012) 39:512–520
DOI 10.1007/s00259-011-2008-5

ORIGINAL ARTICLE

Biodistribution, radiation dosimetry and scouting of ^{90}Y-ibritumomab tiuxetan therapy in patients with relapsed B-cell non-Hodgkin's lymphoma using ^{89}Zr-ibritumomab tiuxetan and PET

Saiyada N. F. Rizvi · Otto J. Visser ·

The dose-limiting organ in patients undergoing stem cell transplantation is the liver.

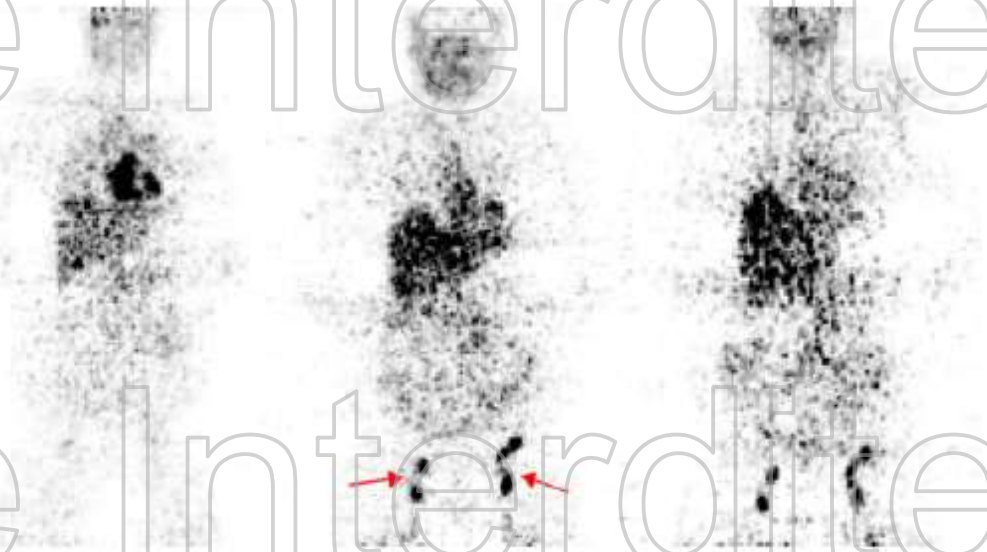


Fig. 1 Typical coronal section ^{89}Zr-ibritumomab tiuxetan images at 1, 72 and 144 h p.i. *Arrows* indicate tumour localizations

Le foie vous dis-je!

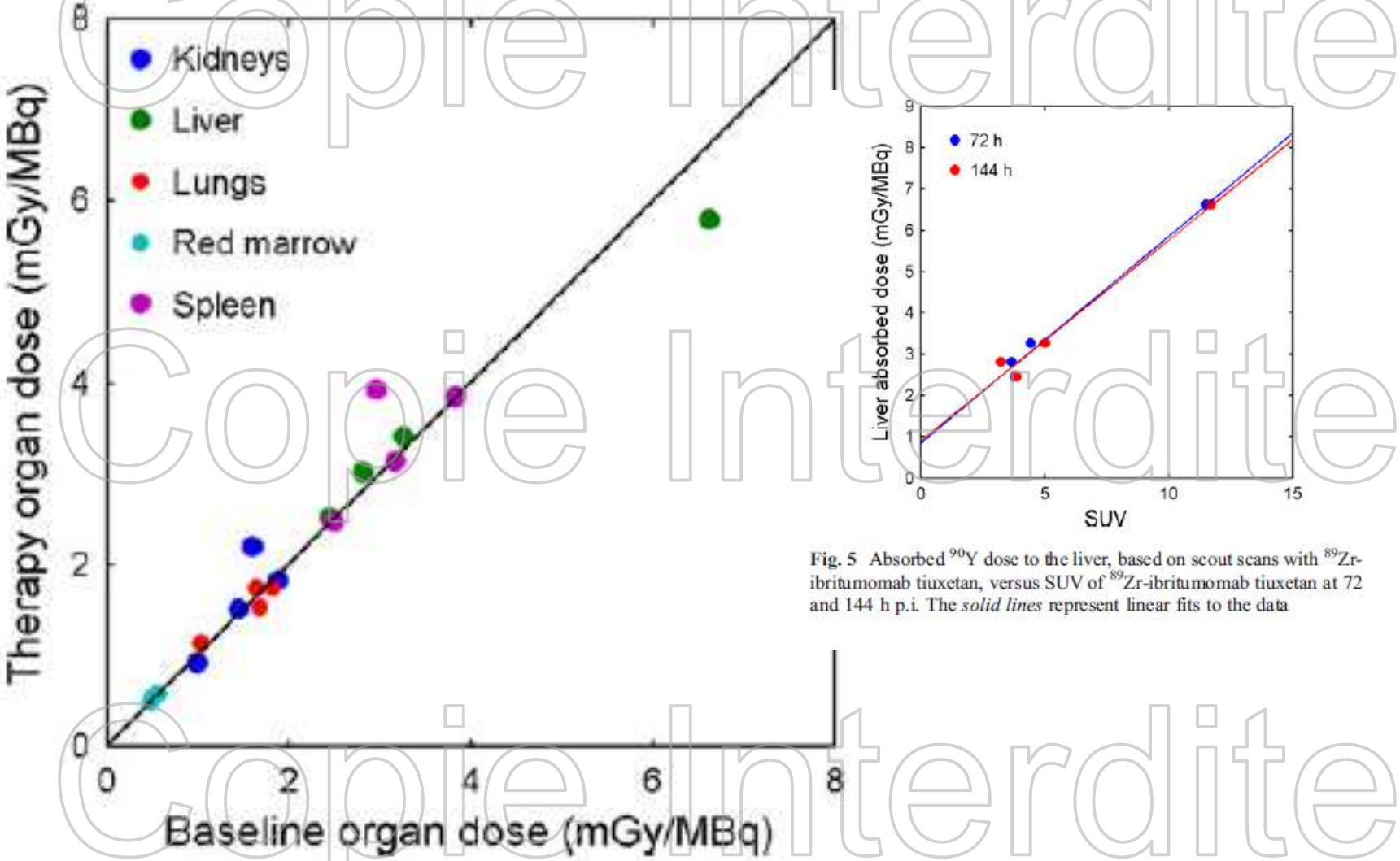


Fig. 5 Absorbed ^{90}Y dose to the liver, based on scout scans with ^{89}Zr-ibritumomab tiuxetan, versus SUV of ^{89}Zr-ibritumomab tiuxetan at 72 and 144 h p.i. The *solid lines* represent linear fits to the data

Apres le SUV … la texture :

Mais que diable allait-il faire dans cette galère?

Hanaoka *et al. EJNMMI Research* (2015) 5:10
DOI 10.1186/s13550-015-0093-3

EJNMMI Research
a SpringerOpen Journal

ORIGINAL RESEARCH **Open Access**

Heterogeneity of intratumoral ^{111}In-ibritumomab tiuxetan and ^{18}F-FDG distribution in association with therapeutic response in radioimmunotherapy for B-cell non-Hodgkin's lymphoma

Kohei Hanaoka[1], Makoto Hosono[2*], Yoichi Tatsumi[3], Kazunari Ishii[4], Sung-Woon Im[1], Norio Tsuchiya[2], Kenta Sakaguchi[2] and Itaru Matsumura[3]

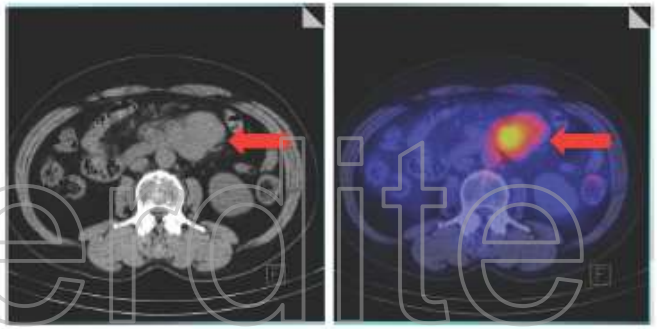


Figure 4 Representative CT and fused image of the markedly accumulation of ^{111}In-ibritumomab tiuxetan in the para-aortic lymph node (arrow). A male patient with B-cell non-Hodgkin's lymphoma had a standardized uptake value of para-aortic lymph node of 3.81, skewness of 0.813, kurtosis of 2.95, and AUC-CSH of 0.344.

Du SUV à la texture, Vicini et al 1997, Baek et al 2012 !

quantification of the spatial heterogeneity of voxel-based activities

$$\text{Skewness} = \frac{1}{n}\sum_{i=1}^{n}(x_i-\bar{x})^3/s^3$$

$$\text{Kurtosis} = \frac{1}{n}\sum_{i=1}^{n}(x_i-\bar{x})^4/s^4$$

where n is the number of voxels in the

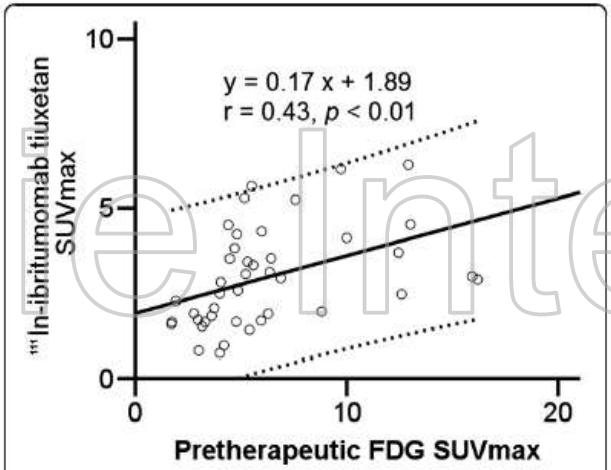


Figure 2 Correlation between pretherapeutic FDG SUVmax and ^{111}In-ibritumomab tiuxetan SUVmax in all lesions. The solid line is the progression line. Dotted lines represent 95% confidence intervals of the progression line.

PREDICTION
FDG > RX

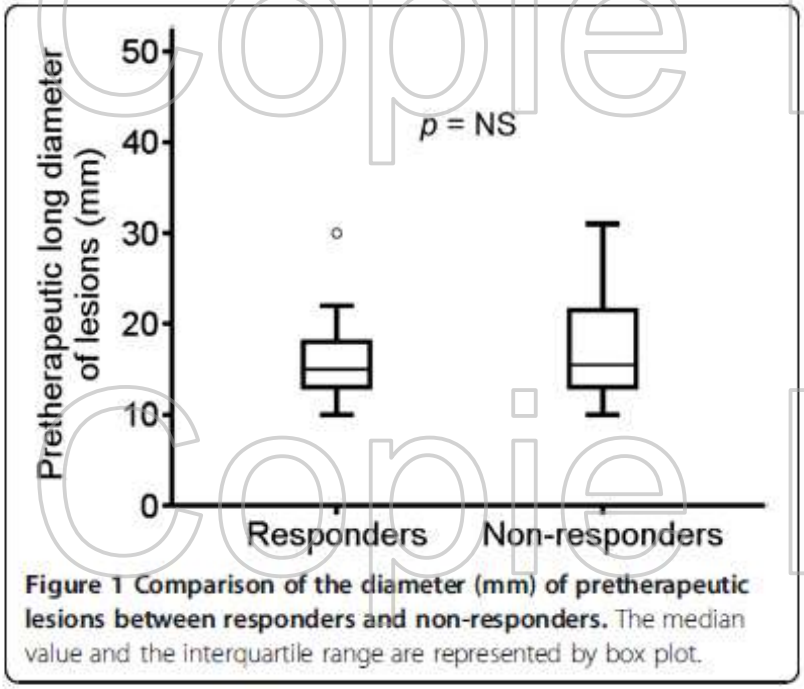


Figure 1 Comparison of the diameter (mm) of pretherapeutic lesions between responders and non-responders. The median value and the interquartile range are represented by box plot.

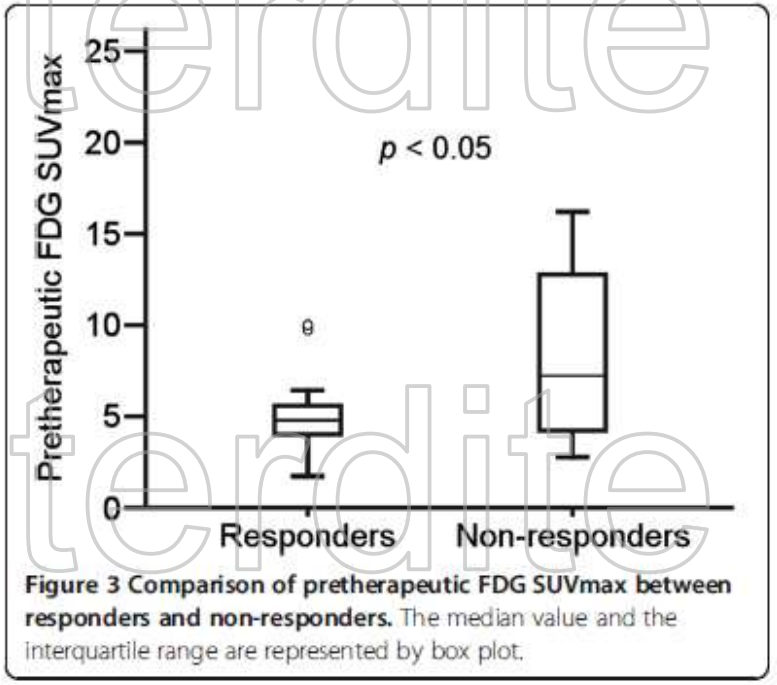


Figure 3 Comparison of pretherapeutic FDG SUVmax between responders and non-responders. The median value and the interquartile range are represented by box plot.

Table 2 Comparison of FDG accumulation and intratumoral distribution between responders and non-responders

	Responder ($n = 26$)	Non-responder ($n = 16$)	p value
SUVmax	4.8 ± 2.0	8.5 ± 4.7	<0.05
Skewness	1.07 ± 0.29	1.17 ± 0.40	n. s.
Kurtosis	3.56 ± 0.91	3.99 ± 1.34	n. s.
AUC-CSH	0.30 ± 0.05	0.30 ± 0.06	n. s.

n. s., not significant.

Table 3 Comparison of ^{111}In-ibritumomab tiuxetan accumulation and intratumoral distribution between responders and non-responders

	Responder ($n = 26$)	Non-responder ($n = 16$)	p value
SUVmax	2.74 ± 1.43	3.29 ± 1.47	n. s.
%ID/g	0.0022 ± 0.0009	0.0024 ± 0.0008	n. s.
Skewness	0.58 ± 0.16	0.73 ± 0.24	<0.05
Kurtosis	2.39 ± 0.32	2.78 ± 0.53	<0.02
AUC-CSH	0.37 ± 0.04	0.34 ± 0.05	<0.05

n. s., not significant.

Indium-111–Labeled Trastuzumab Scintigraphy in Patients With Human Epidermal Growth Factor Receptor 2–Positive Metastatic Breast Cancer

Patrick J. Perik, Marjolijn N. Lub-De Hooge, Jourik A. Gietema, Winette T.A. van der Graaf, M. Alexander de Korte, Sharon Jonkman, Jos G.W. Kosterink, Dirk J. van Veldhuisen, Dirk T. Sleijfer, Pieter L. Jager, and Elisabeth G.E. de Vries

JCO 2006

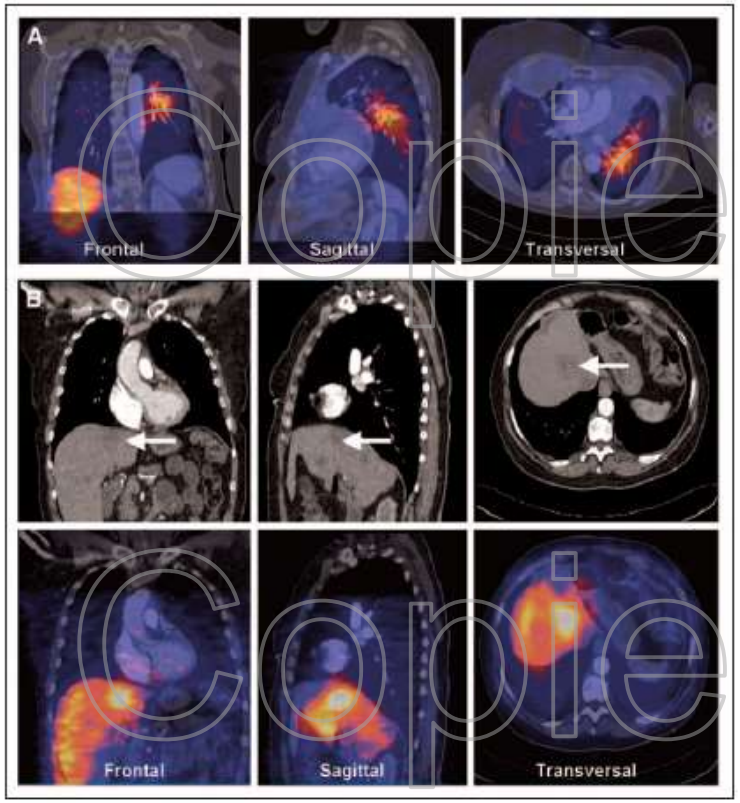


Fig 2. (A) Fused computed tomography (CT) with indium-111–diethylenetriamine penta-acetic acid anhydride (^{111}In-DTPA)–trastuzumab single-photon emission tomography (SPECT) image 196 hours after tracer injection). (B) CT images (top) of a patient with a large liver metastasis (↔). Fusion with ^{111}In-DTPA-trastuzumab SPECT (bottom) shows correspondence of liver metastases and SPECT hot spot.

Associations between the uptake of ^{111}In-DTPA-trastuzumab, HER2 density and response to trastuzumab (Herceptin) in athymic mice bearing subcutaneous human tumour xenografts

Kristin McLarty · Bart Cornelissen · Deborah A. Scollard · Susan J. Done · Kathy Chun · Raymond M. Reilly

EJNM 2009

Conclusions

1.HER2 expression : Semi quantification : vers un SUV_{SPECT}?

2. Fixation non Spécifique : LE FOIE

3.Fixation tumorale de 111In-DTPA-trastuzumab associée à T réponse

Evaluation of [^{18}F]gefitinib as a molecular imaging probe for the assessment of the epidermal growth factor receptor status in malignant tumors

Helen Su · Yann Seimbille · Gregory Z. Ferl · Claudia Bodenstein · Barbara Fueger · Kevin J. Kim · Yu-Tien Hsu · Steven M. Dubinett · Michael E. Phelps · Johannes Czernin · Wolfgang A. Weber

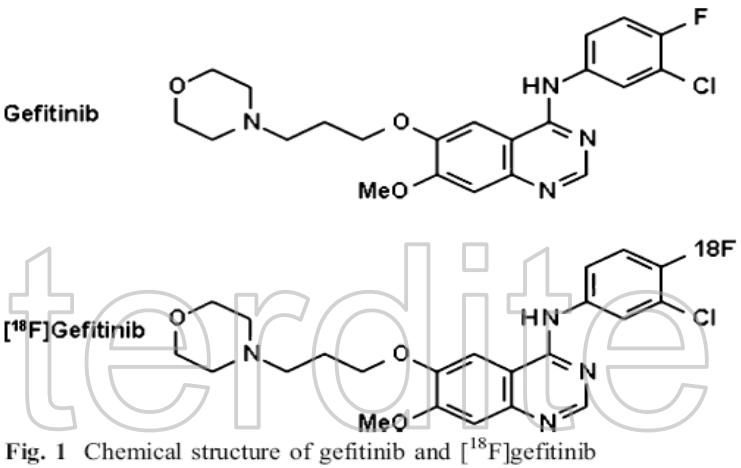


Fig. 1 Chemical structure of gefitinib and [^{18}F]gefitinib

Conclusions

1.[18F]- gefitinib = PK .

2.Pb, fixation non spécifique

Clinical Cancer Research

^{89}Zr-trastuzumab and ^{89}Zr-bevacizumab PET to Evaluate the Effect of the HSP90 Inhibitor NVP-AUY922 in Metastatic Breast Cancer Patients

Sietske B.M. Gaykema[1], Carolien P. Schröder[1], Joanna Vitfell-Rasmussen[5], Sue Chua[5], Thijs H. Oude Munnink[1], Adrienne H. Brouwers[2], Alfons H.H. Bongaerts[3], Mikhail Akimov[6,7], Cristina Fernandez-Ibarra[6,7], Marjolijn N. Lub-de Hooge[2,4], Elisabeth G.E. de Vries[1], Charles Swanton[5], and Udai Banerji[5]

DEUX CIBLES
ErbB2,
VEGF

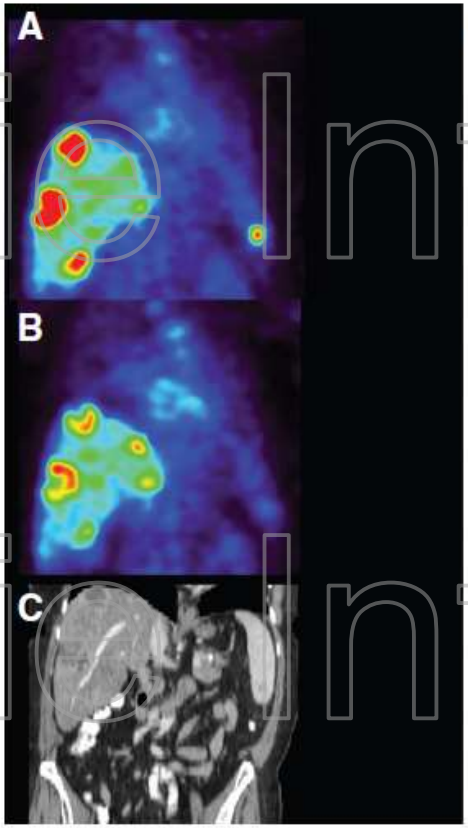


Figure 2. Representative coronal ^{89}Zr-trastuzumab PET images of a patient scanned before (A) and after (B) 3 weeks of treatment. Multiple liver lesions and one splenic lesion are shown. ^{89}Zr-trastuzumab PET could be performed in 6 of 10 HER2-positive patients, of which 5 underwent repeated scan procedures. The CT scan pretreatment is shown in C. D, a heterogeneous response in individual tumor lesions ($n = 29$) between baseline and follow-up, with an average decrease in SUV_{max} of 18%.

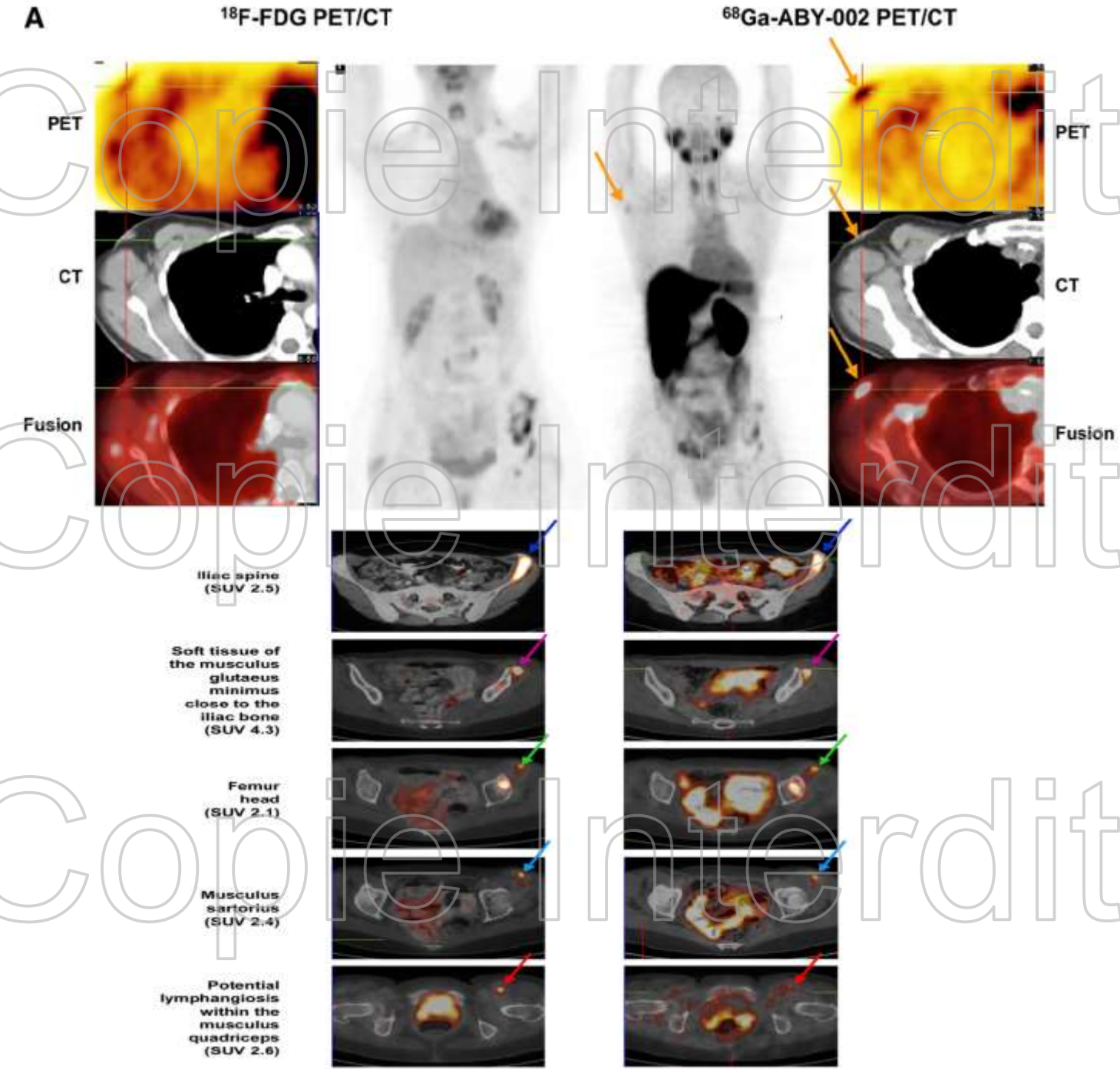
The smaller the better ?

On the Selection of a Tracer for PET Imaging of HER2-Expressing Tumors: Direct Comparison of a ^{124}I-Labeled Affibody Molecule and Trastuzumab in a Murine Xenograft Model

Anna Orlova[1,2], Helena Wållberg[1], Sharon Stone-Elander[3], and Vladimir Tolmachev[1,2,4]

Molecular Imaging of *HER2*-Expressing Malignant Tumors in Breast Cancer Patients Using Synthetic ^{111}In- or ^{68}Ga-Labeled Affibody Molecules

Richard P. Baum[1], Vikas Prasad[1], Dirk Müller[1], Christiane Schuchardt[1], Anna Orlova[2,3], Anders Wennborg[2], Vladimir Tolmachev[2,3], and Joachim Feldwisch[2,3]



Perspectives

Quand l'imagerie sert à la pharmacocinétique !

Advanced Drug Delivery Reviews 63 (2011) 539–546

Contents lists available at ScienceDirect

Advanced Drug Delivery Reviews

journal homepage: www.elsevier.com/locate/addr

Approaches using molecular imaging technology — use of PET in clinical microdose studies ☆

Claudia C. Wagner [a], Oliver Langer [a,b,*]

[a] Department of Clinical Pharmacology, Medical University of Vienna, Währinger-Gürtel 18-20, A-1090, Vienna, Austria
[b] Health & Environment Department, Molecular Medicine, AIT Austrian Institute of Technology GmbH, A-2444 Seibersdorf, Austria

The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

London, 23 January 2003
CPMP/SWP/2599/02

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

POSITION PAPER ON NON-CLINICAL SAFETY STUDIES TO SUPPORT CLINICAL TRIALS WITH A SINGLE MICRODOSE

DATA MINING

No patient selection

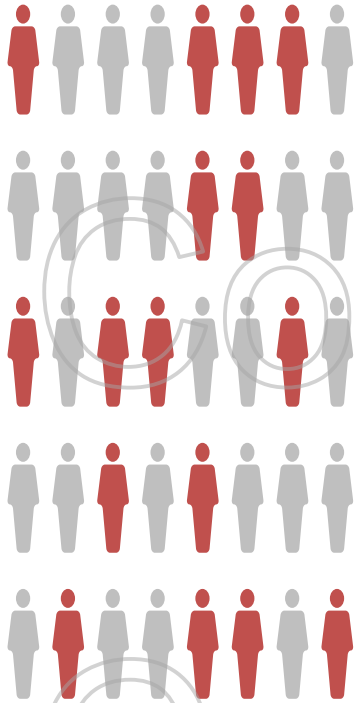
Test*

Patient selection

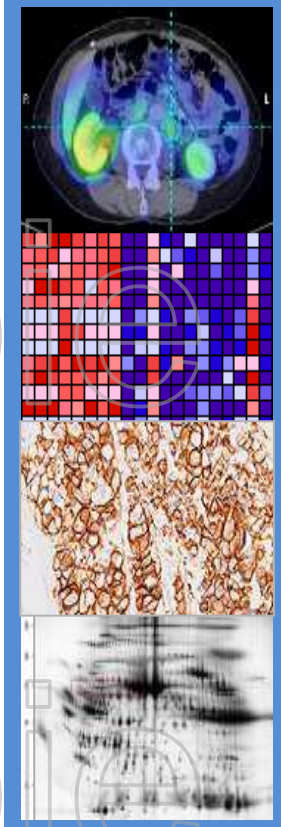
Response to therapy

High

Low



40% benefit from therapy



Treat

94% benefit from therapy

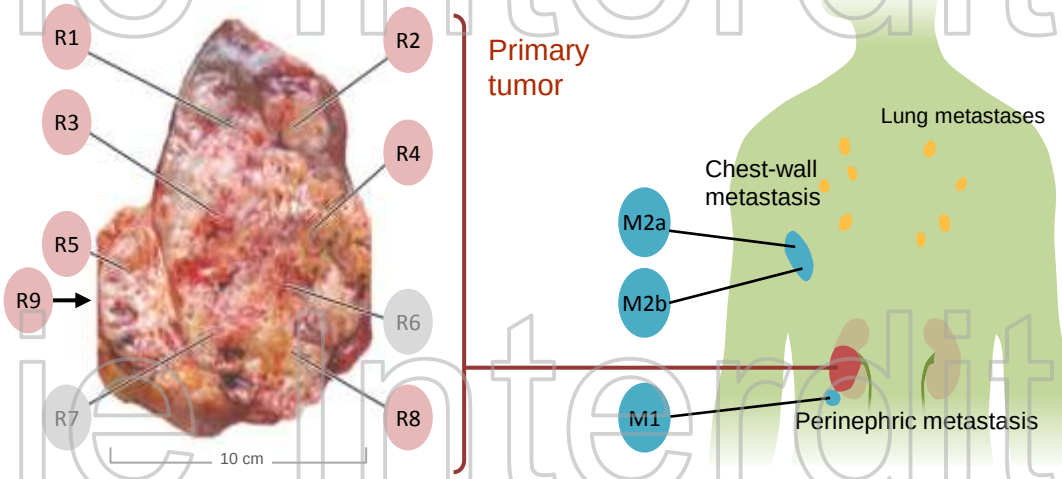
Don't treat

Try alternate therapy

* Blood, tissue or imaging marker that can be used to prospectively identify patients

Pénétrer dans la cible

Intra and inter-tumor heterogeneity

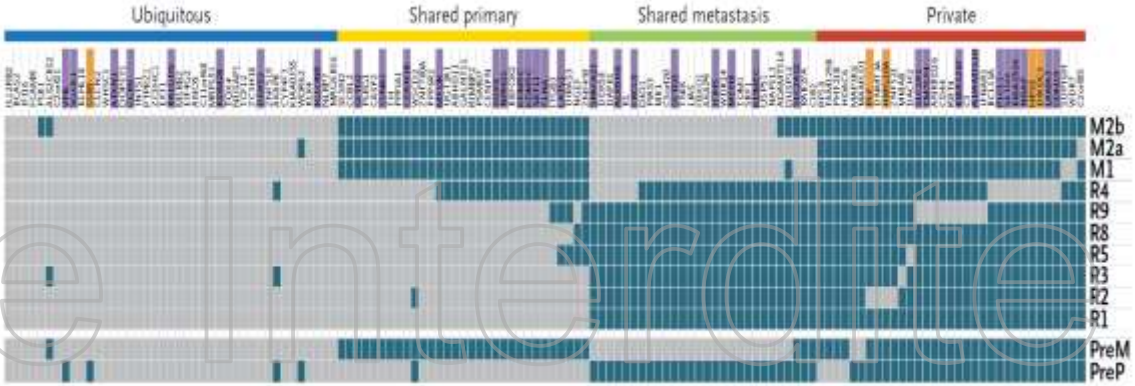


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 8, 2012 VOL. 366 NO. 10

Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing

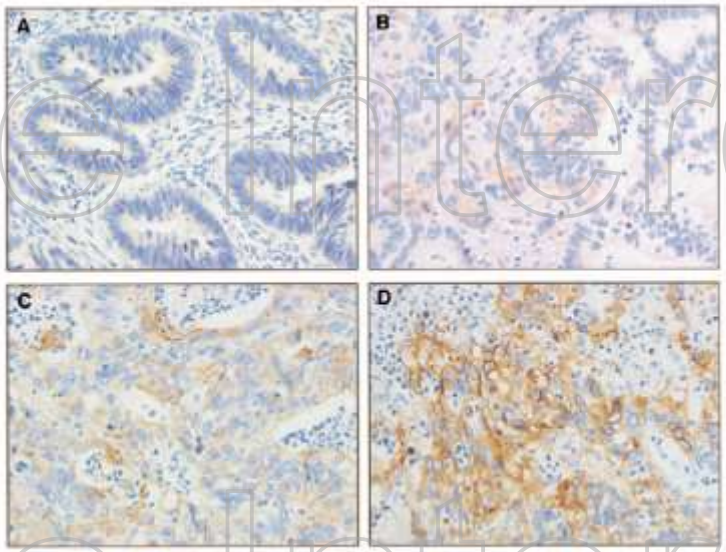
Gerlinger et al. N Engl J Med 2012



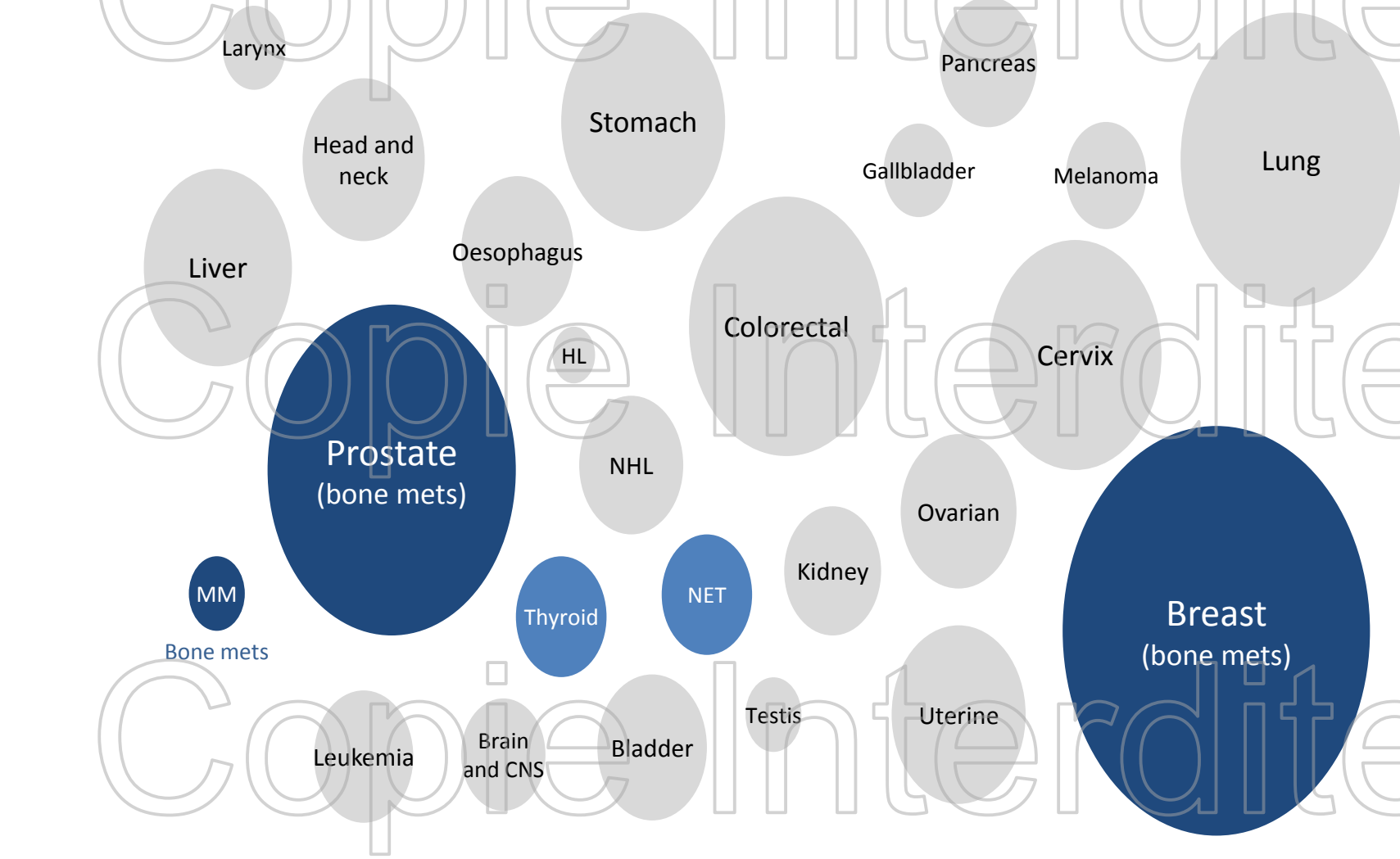
Cetuximab Shows Activity in Colorectal Cancer Patients With Tumors That Do Not Express the Epidermal Growth Factor Receptor by Immunohistochemistry

Ki Young Chung, Jinru Shia, Nancy E. Kemeny, Manish Shah, Gary K. Schwartz, Archie Tse, Audrey Hamilton, Dorothy Pan, Deborah Schrag, Lawrence Schwartz, David S. Klimstra, Daniel Fridman, David P. Kelsen, and Leonard B. Saltz

JCO 2005

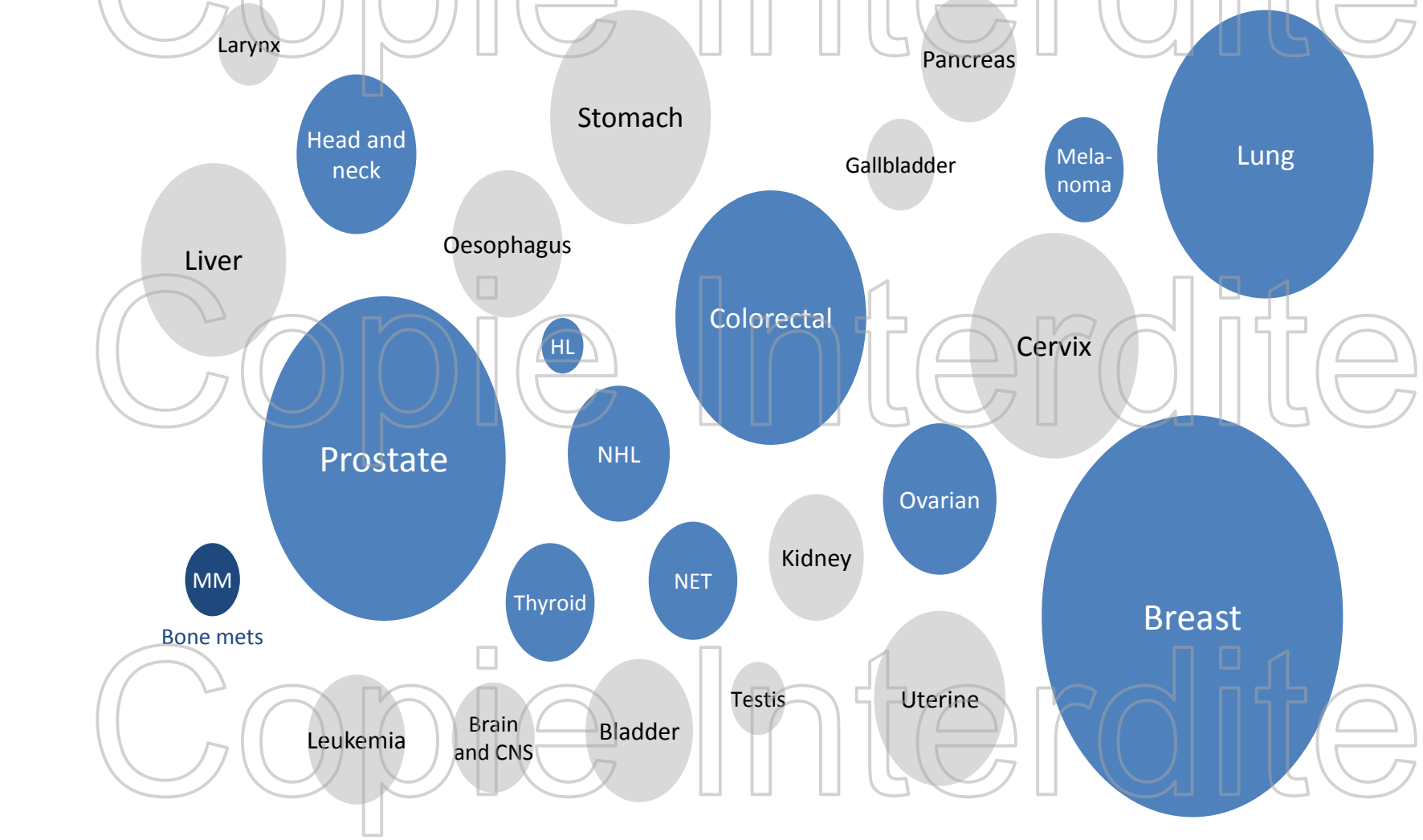


Imaging and the cancer landscape in the 1990s



Size of bubble proportional to incidence, Globocan 2012
http://globocan.iarc.fr, estimated cancer incidence world

Imaging and the cancer landscape is changing rapidly



Size of bubble proportional to incidence, Globocan 2012
http://globocan.iarc.fr, estimated cancer incidence world

QUELLE APPROCHE THERANOSTIQUE POUR LE RADIUM . MDP. F Na, F CHOLINE

^{99m}Tc-MDP ⟶ ? ⟶ Samarium/ strontium/ radium

diphosphonates

Médecine Nucléaire - Imagerie fonctionnelle et métabolique - 2006 - vol.30 - n°3

Dans le doute

Recent bisphosphonate therapy may reduce ^{89}Sr, ^{153}Sm-lexidronam or ^{186}Re-etidronate uptake by bone metastases and reduce the effectiveness of pain palliation. An interval of at least 48 h is recommended between bisphosphonate administration and ^{89}Sr, ^{153}Sm-lexidronam or ^{186}Re-etidronate treatment.

EJNM guidelines 2002

4.5 Interactions avec d'autres médicaments et autres formes d'interactions

Aucune étude clinique d'interaction n'a été réalisée.

Des interactions avec le calcium et le phosphate ne pouvant être exclues, il doit être envisagé de suspendre une supplémentation à base de ces traitements et/ou la prise de Vitamine D quelques jours avant le début du traitement par Xofigo.

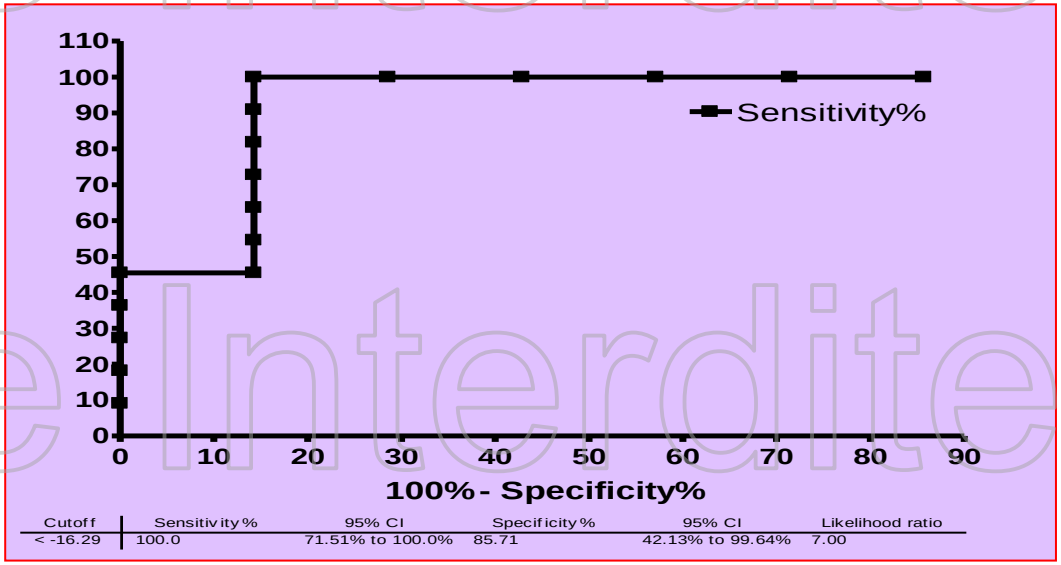
L'administration concomitante d'une chimiothérapie et de Xofigo peut produire des effets additifs en ce qui concerne la myélosuppression (voir rubrique 4.4). La sécurité d'emploi et l'efficacité de l'administration concomitante d'une chimiothérapie et de Xofigo n'ont pas été établies.

Xofigo® RCP

http://www.ema.europa.eu/docs/f

MR
Molecular response
nMR
No molecular response

FDG vs pERK



Cutoff	Sensitivity %	95% CI	Specificity %	95% CI	Likelihood ratio
< -16.29	100.0	71.51% to 100.0%	85.71	42.13% to 99.64%	7.00

(F Thomas Clin Can Res 2007, Delord *et al* – Courbon *et al* Abs 2005-2006)
SNM 2009
Soumis A Clin Cancer Res
2éme rev

Evolution de l ‘imagerie

structure

Bilan d’extension

Fonction

Diagnostic bilan d’extension

- Enriched tumor localisation
- Cancer metabolism
- Tumor staging

Intervention optimisée

- Track treatment response
- PERCIST
- Guides radiotherapy
- Guides surgery

Nomograme thérapeutique/ taxonomie

- Patient matching
- Disease matching

Imagerie de phénotye

Métabolisme

- Glucose
- Choline
- Acetate

Expression de cible

- Tyrosine analogues
- VEGF
- RET/RTK
- Folate receptor

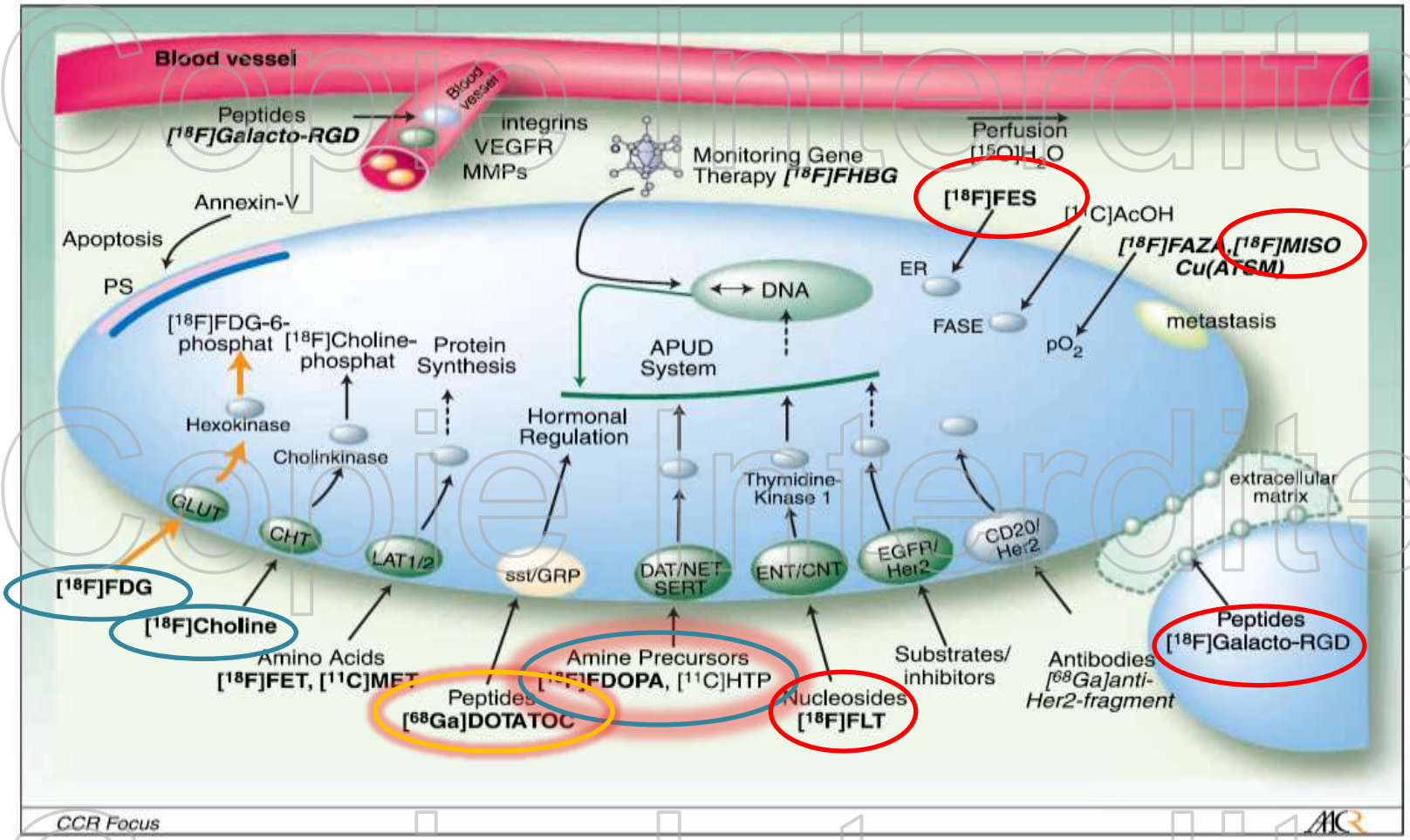


Fig. 2. Selected targets and corresponding nuclear imaging probes already established for nuclear molecular imaging in the clinic (*bold*) or currently under assessment in clinical studies (*italic*).

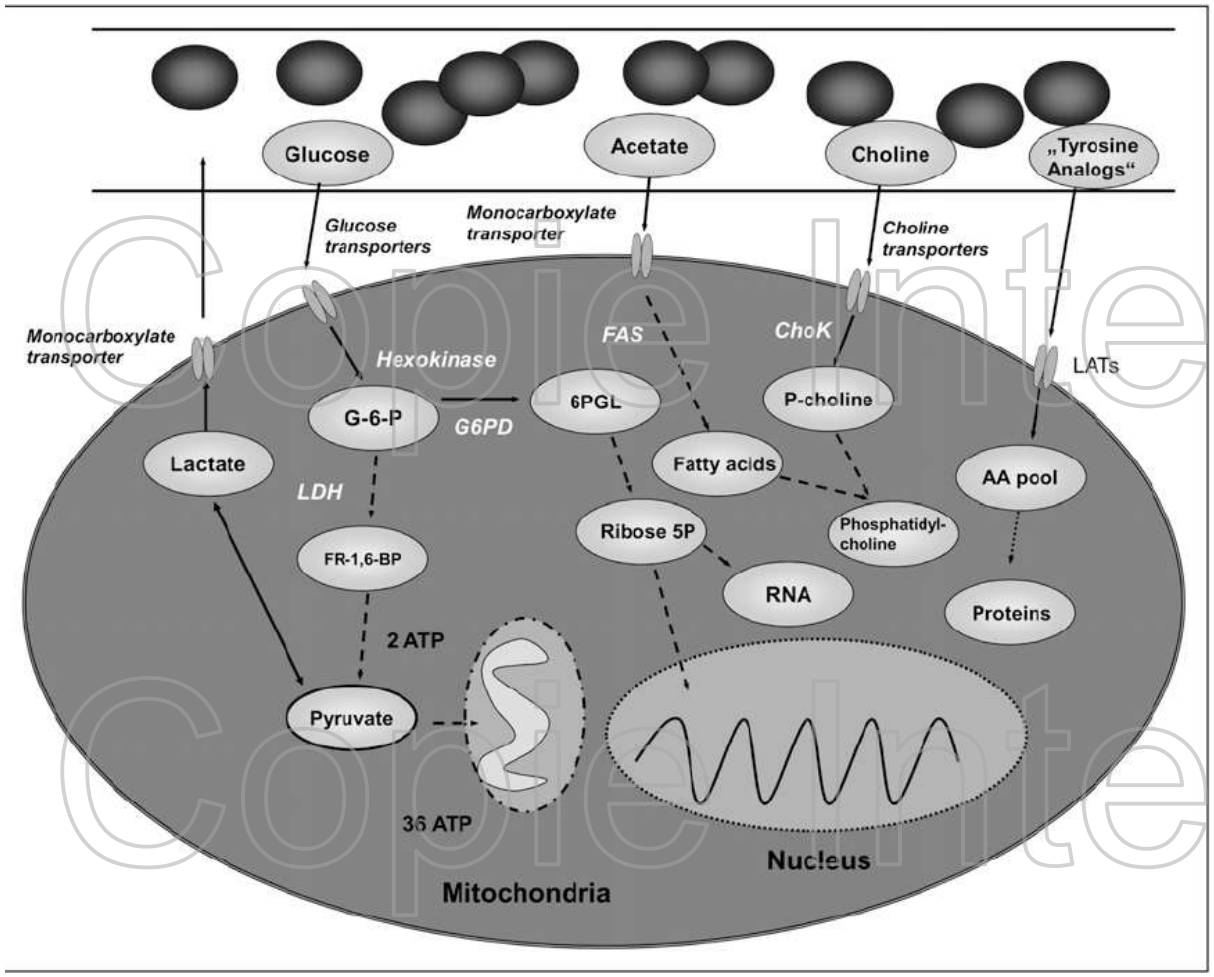


FIGURE 1. Simplified overview of metabolic processes targeted by PET and MRI. AA pool = amino acid pool; ChoK = choline kinase; FAS = fatty acid synthase; FR-1,6-BP = fructose-1,6-bisphosphate; G-6-P = glucose-6-phosphate; LAT = L-type amino acid transporter; LDH = lactate dehydrogenase; P-choline = phosphocholine; Ribose 5P = ribose-5-phosphate.