The contribution of nuclear medicine to haematology

Clément Bailly, Thomas Carlier, Caroline Bodet-Milin,
Françoise Kraeber-Bodéré

PRISMAP 2024 Nantes

Long history between Nuclear Medicine and Haematology

1996

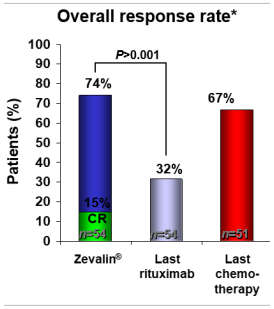
J Clin Oncol by the group of Michigan
Iodine-131-anti-B1 radioimmunotherapy for B-cell lymphoma

2002 2003

FDA approval
Iodine-131 Tositumomab (brand as **Bexxar**)

FDA approval
Zevalin

90Y-antiCD20 Zevalin radioimmunotherapy vs rituximab
for refractory B-cell lymphoma

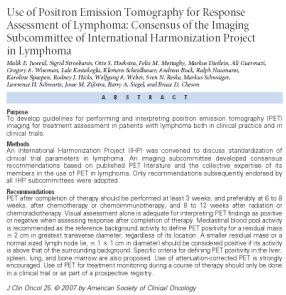


Witzig TE, J Clin Oncol 2002;20:3262–3269.

2007

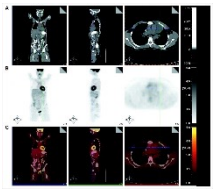
FDG PET recommendations and standardization for lymphoma

Use of Positron Emission Tomography for Response Assessment of Lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma



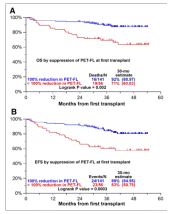
J Clin Oncol 25. © 2007 by American Society of Clinical Oncology

FDG PET for B-cell lymphoma
J Clin Oncol by Juweid



2009

FDG PET for myeloma
By Little rock group



2014

Marketing approval of Bexxar was withdrawn

2017

FDG PET recommendations for MM

International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders

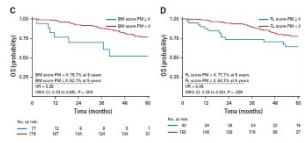
Role of ^{18}F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group

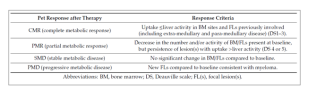
2019

2021

FDG PET standardization for MM

Standardization of ^{18}F-FDG–PET/CT According to Deauville Criteria for Metabolic Complete Response Definition in Newly Diagnosed Multiple Myeloma





Role of nuclear medicine in haematological tumors

- FDG-PET is used for **pre-therapy staging** with prognostic value in lymphoma and MM : **risk classification**
- FDG-PET confirms **complete response** after therapy (**prognostic value**) in lymphoma and MM
- FDG-PET allows to early evaluate the response and **guide therapy** in agressive lymphoma and hodgkin disease
- Major interest of **whole body metabolic imaging** to assess disseminated disease (medullary and extra-medullary)
- International recommendations and standardization use **Deauville scale**
- Strong potential of **radiomics and AI**, althought too immature for clinical practice use
- Radiotherapeutics (Zevalin) has not become a standard in lymphoma but can be used as an option
- Other radiopharmaceuticals (PET or therapy) are only at the stage of research

European Association of Nuclear Medicine (EANM) Focus 4 consensus recommendations: molecular imaging and therapy in haematological tumours

Cristina Nanni, Carsten Kobe*, Bettina Baeßler, Christian Baues, Ronald Boellaard, Peter Borchmann, Andreas Buck, Irène Buvat, Björn Chapuy, Bruce D Cheson, Robert Chzran, Ann-Segolene Cottereau, Ulrich Dührsen, Live Eikenes, Martin Hutchings, Wojciech Jurczak, Françoise Kraeber-Bodéré, Egesta Lopci, Stefano Luminari, Steven MacLennan, N George Mikhaeel, Marcel Nijland, Paula Rodríguez-Otero, Giorgio Treglia, Nadia Withofs, Elena Zamagni, Pier Luigi Zinzani, Josée M Zijlstra, Ken Herrmann*, Jolanta Kunikowska**

www.thelancet.com/haematology Vol 10 May 2023

“Nuclear haematology group” at Nantes University Hospital

Expertises in:

- Lymphoma, Myeloma, Acute leukemia
- Clinical trials and cohorts
- PET/CT and PET/MR
- Radiotheranostics and innovative radiopharmaceuticals
- IA and radiomics

Collaborations with

- IFM and LYSA cooperative groups
- CRCI2NA, Arronax, Centrale
- Academic and industrial partners

Long history between Nuclear Medicine and Haematology

FDA approval
Iodine-131
Tositumomab (branded as **Bexxar**)
(lymphomes)

FDA approval
Zevalin
for refractory B-cell lymphoma

FDG PET recommendations and standardization for lymphoma

Use of Positron Emission Tomography for Response Assessment of Lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma

Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification

FDG PET recommendations for MM

International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders

Role of ^{18}F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group

FDG PET standardization for MM

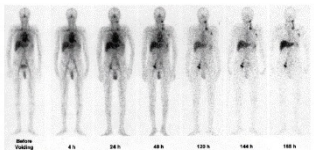
Standardization of ^{18}F-FDG–PET/CT According to Deauville Criteria for Metabolic Complete Response Definition in Newly Diagnosed Multiple Myeloma

2002 2003 | **2007** | **2008** | **2009** | **2014** | **2015** | **2016** | **2017** | **2019** | **2020** | **2021** | **2023**

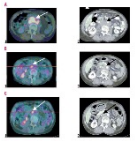
Radioimmunotherapy of Non-Hodgkin's Lymphoma with ^{90}Y-DOTA Humanized Anti-CD22 IgG (^{90}Y-Epratuzumab): Do Tumor Targeting and Dosimetry Predict Therapeutic Response?

The Journal of Nuclear Medicine • Vol. 44 • No. 12 • December 2003

90Y antiCD22 RIT
for refractory B-cell lymphoma
Collaboration with D. Goldenberg and B Sharley



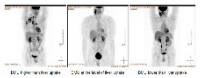
FDG PET
To assess efficay of RIT in B-cell lymphoma
Heamatologica by Bodet-Milin



FDG PET
for Richter detection
Heamatologica by Bodet-Milin

Investigation of FDG-PET/CT imaging to guide biopsies in the detection of histological transformation of indolent lymphoma

FDG PET
for Hodgkin staging
EJNM



Zevalin RIT in lymphoma

Fractionated ^{90}Y-ibritumomab Tiuxetan Radioimmunotherapy As an Initial Therapy of Follicular Lymphoma: An International Phase II Study in Patients Requiring Treatment According to GELF/BNLI Criteria

90Y antiCD22 RIT
for consolidation in DLBCL

Consolidation anti-CD22 fractionated radioimmunotherapy with ^{90}Y-epratuzumab tetraxetan following R-CHOP in elderly patients with diffuse large B-cell lymphoma: a prospective, single group, phase 2 trial

90Y antiCD22 RIT
for leukemia

^{90}Y-labelled anti-CD22 epratuzumab tetraxetan in adults with refractory or relapsed CD22-positive B-cell acute lymphoblastic leukaemia: a phase 1 dose-escalation study

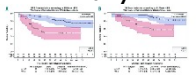
Lancet Haematol 2015; 2: e108–17

FDG PET vs MRI
for MM: Imajem study

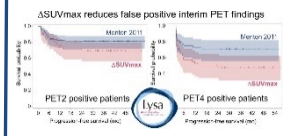
Journal of Clinical Oncology — Original Report

Prospective Evaluation of Magnetic Resonance Imaging and [^{18}F]Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography at Diagnosis and Before Maintenance Therapy in Symptomatic Patients With Multiple Myeloma Included in the IFM/DFCI 2009 Trial: Results of the IMAJEM Study

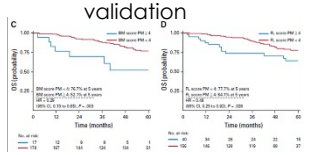
FDG PET
In mantle cell lymphoma
Heamatologica by Bailly



FDG PET
Delta-SUV in DLBCL
JNM



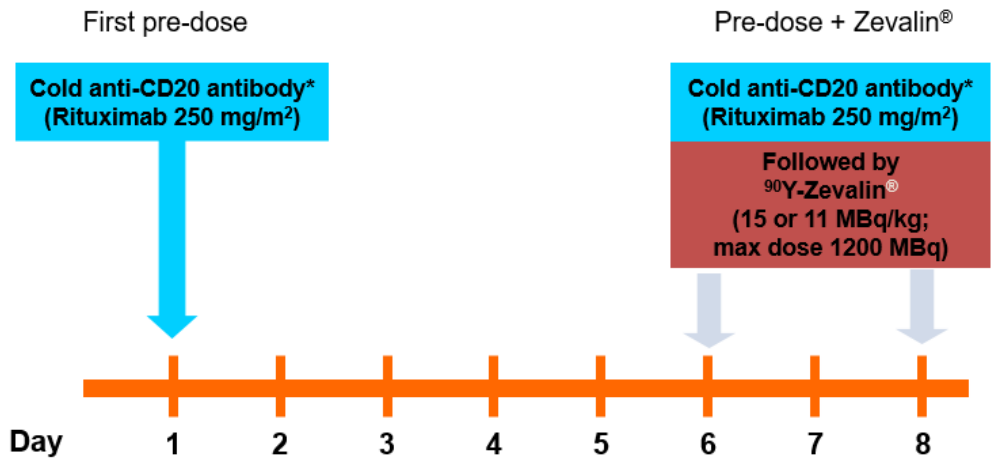
FDG PET
for MM: Deauville scale validation



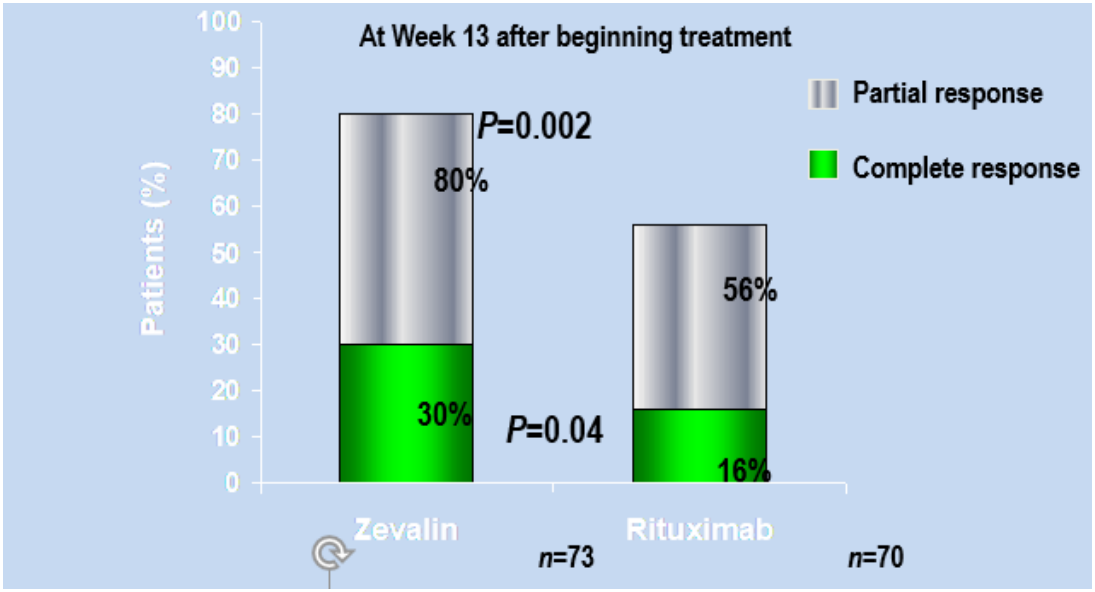
Clinical research axis

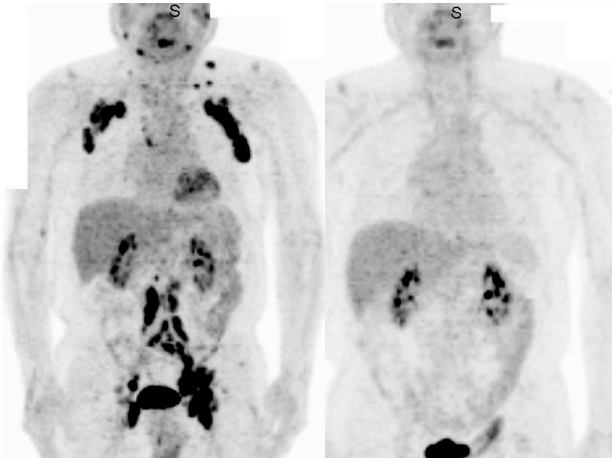
- Numerous clinical trials of **radionuclide therapies**, industrial and academic, anti-CD20 and anti-CD22 RIT with the Goelams group and Immunomedics and anti-CXCR4 RLT with PentixaPharm (PI F. Kraeber-Bodéré and C. Bodet-Milin)
- Numerous clinical trials and cohorts of **FDG-PET in lymphoma**, in particular with the LYSA cooperative group (PI C. Bodet-Milin and C. Bailly)
- Clinical trials and cohorts of **MM patients** using FDG-PET, other tracers and PET-MRI, in collaboration with the IFM cooperative group, the group of Bologna and PentixaPharm (PI F. Kraeber-Bodéré, C. Bodet-Milin, B. Jamet and C. Bailly)
- **Radiomics and IA** developments in collaboration with Centrale Nantes (T. Carlier and D. Mateus)

Zevalin® approved for CD20+ follicular lymphoma in relapse or consolidation



*Dose of cold anti-CD20 monoclonal antibody to optimize biodistribution of Zevalin®





Before and after 1 injection of Zevalin

Wagner *et al. J Nucl Med* 2002;43:267–272

Anti-CD22 hLL2-90Y (epratuzumab)

- Developed by Immunomedics (Morris Plains, New Jersey)
- Humanized mAB used without loading dose of cold antibody, at variance with anti-CD20 Zevalin® and Bexxar®

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

High Rates of Durable Responses With Anti-CD22 Fractionated Radioimmunotherapy: Results of a Multicenter, Phase I/II Study in Non-Hodgkin's Lymphoma

Franck Morschhauser, Françoise Kraeber-Bodéré, William A. Wegener, Jean-Luc Harousseau, Marie-Odile Petillon, Damien Huglo, Lorenz H. Trümper, Johannes Meller, Michael Pfreundschuh, Carl-Martin Kirsch, Ralph Naumann, Joachim Kropp, Heather Horne, Nick Teoh, Steven Le Gouill, Caroline Bodet-Milin, Jean-Francois Chatal, and David M. Goldenberg

Table 2. Treatment Responses

Characteristic	OR			CR/CRu		
	No.	Total Patients	%	No.	Total Patients	%
Overall (n = 61)*	38	61	62	29	61	48
No prior ASCT (n = 44)	31	44	71	24	44	55
Follicular lymphoma	20	25	80	18	25	72
Total ^{90}Y dose, mCi/m^2						
≤ 30	7	12	58	6	12	50
> 30	13	13	100	12	13	92
Nonfollicular	11	19	58	6	19	32
Histology						
Marginal-zone lymphoma†	2	2	100	2	2	100
Diffuse large B-cell lymphoma‡	3	6	50	2	6	33
Mantle-cell lymphoma§	6	11	55	2	11	18
Poor-risk patients						
Bulky disease (> 5 cm)	10	14	71	6	14	43
Elevated LDH	7	13	54	5	13	39
Positive bone marrow involvement	6	10	60	4	10	40
Refractory to:						
Last therapy	12	17	71	9	17	53
Last anti-CD20–containing regimen	11	15	73	9	15	60
Prior ASCT (n = 17)	7	17	41	5	17	29
Follicular lymphoma	5	9	56	3	9	33
Nonfollicular‖	2	8	25	2	8	25

Abbreviations: OR, objective response; CR, complete response; CRu, complete response unconfirmed; ASCT, autologous stem-cell transplantation; LDH, lactate dehydrogenase.

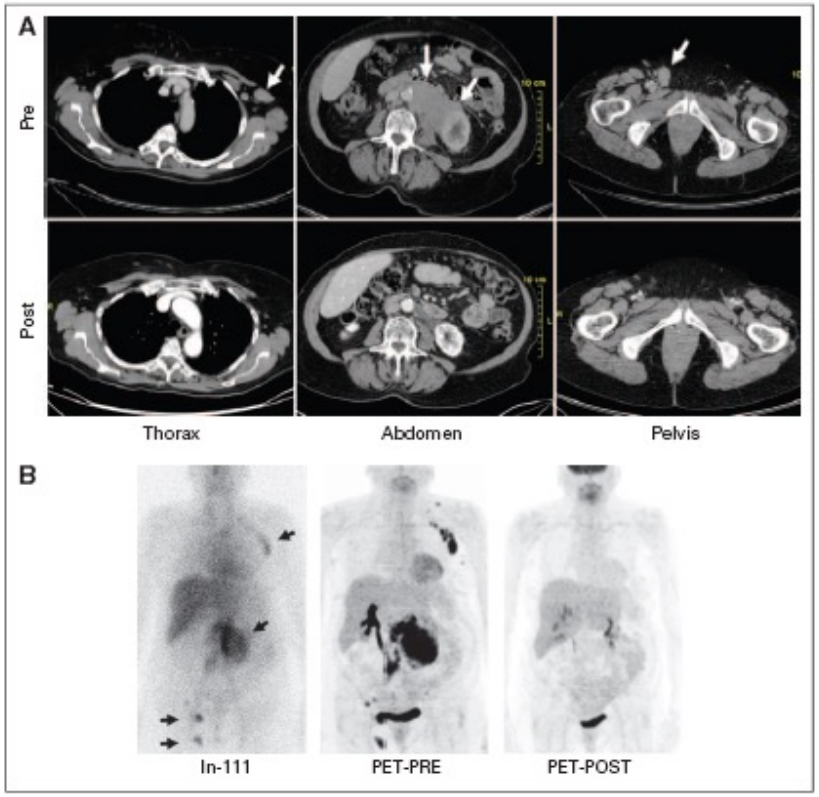
*Sixty-one evaluable patients with best objective response based on International Working Group criteria[21] (OR = CR + CRu + partial response). There were 22 CRs, seven CRus, and nine partial responses.

†Two CR/CRus (at 25 and 30 mCi/m^2 total dose).

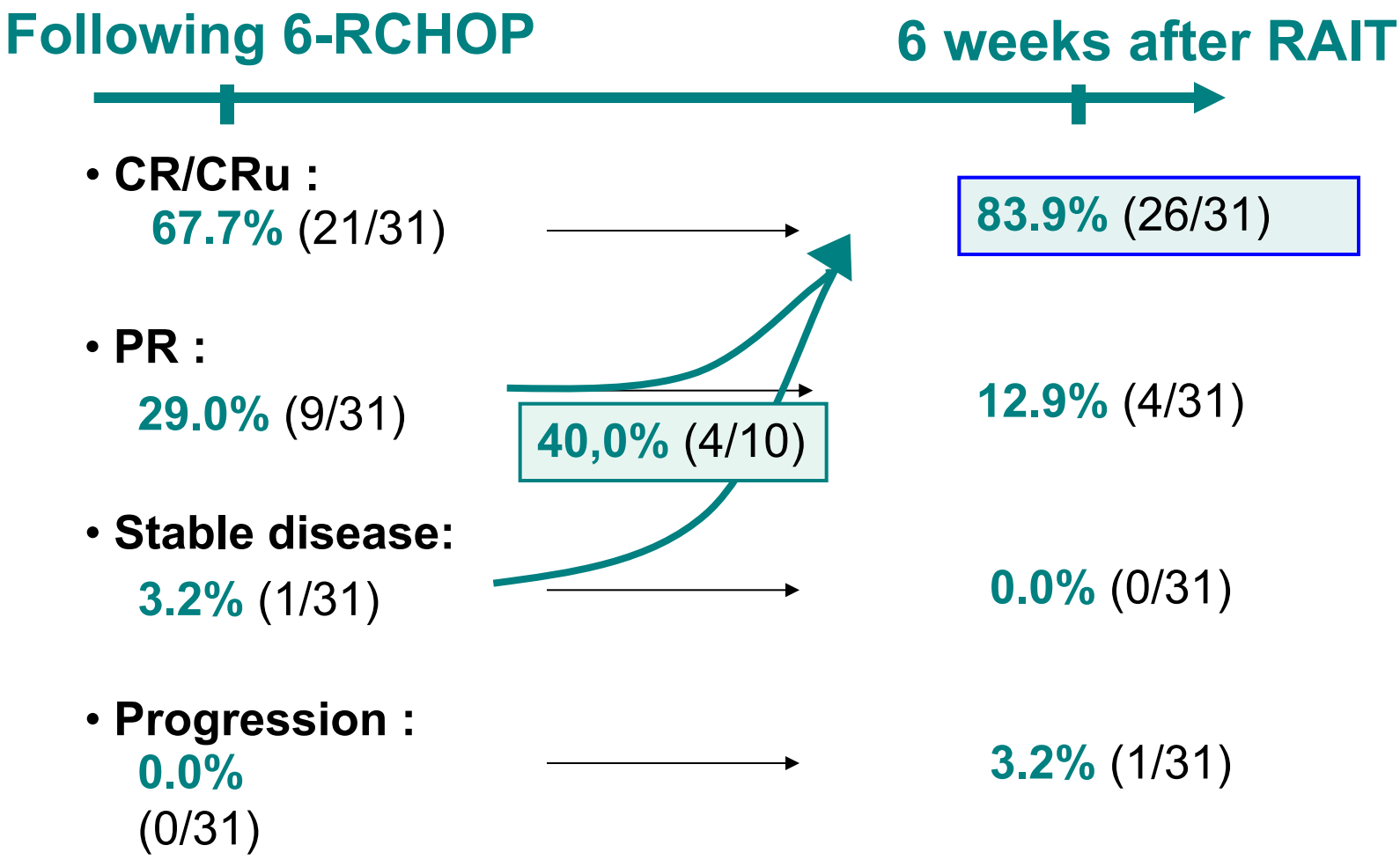
‡Two CR/CRus (both at 30 mCi/m^2 total dose) and one partial response (45 mCi/m^2 total dose).

§Two CR/CRus (at 20 and 30 mCi/m^2 total dose) and four partial responses (one at 15 and 30 and two at 37.5 mCi/m^2 total dose).

‖Marginal-zone lymphoma and mantle-cell lymphoma: one CR/Cru each (both at 7.5 mCi/m^2 total dose).



A Phase II trial of fractionated ^{90}Y-epratuzumab, as consolidation after R-CHOP induction,in patients with DLBCL
Sponsor: French group Goelams, 75 patients



Kraeber-Bodéré, et al. Lancet Heamatol, 2017

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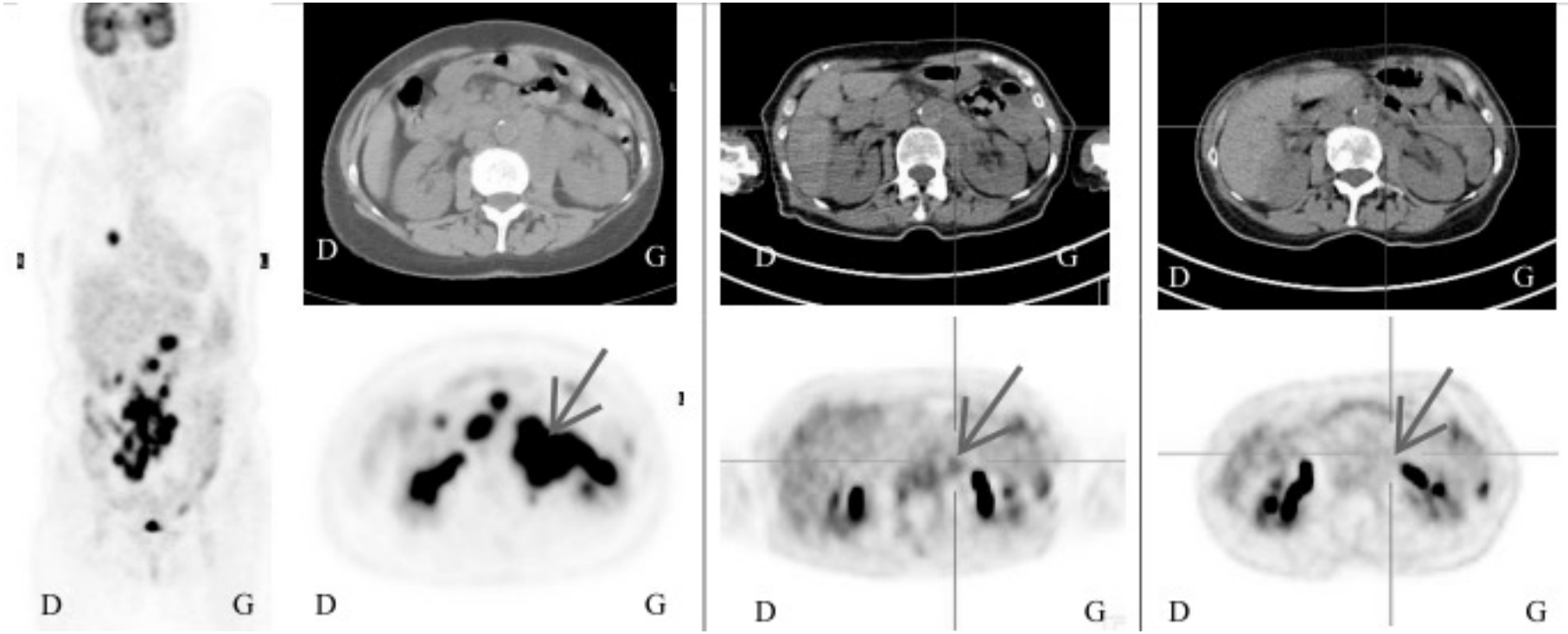


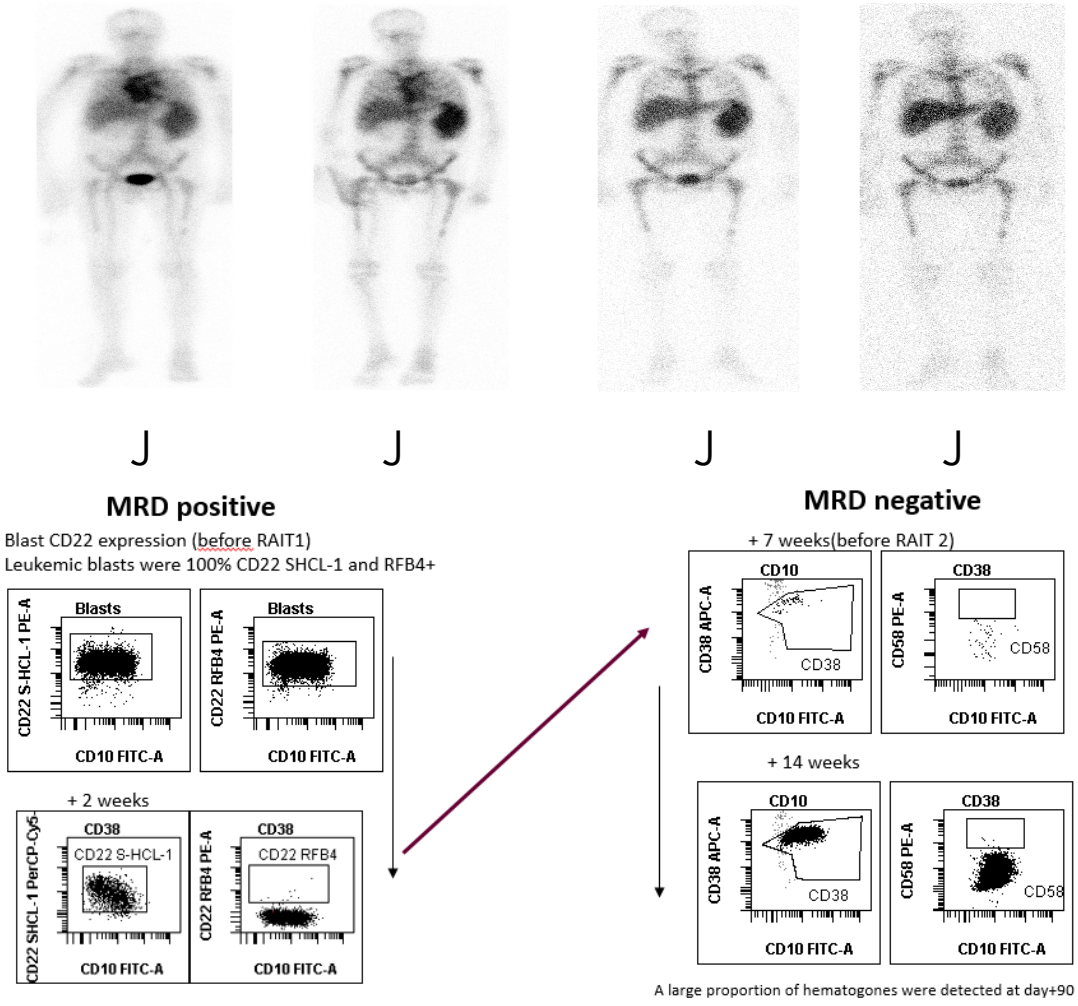
Baseline | Following 6-RCHOP | 6 wks after RIT

Kraeber-Bodéré, et al. Lancet Heamatol, 2017

Phase I using anti-CD22 ^{90}Y-epratuzumab in patients with refractory LAL
Sponsor Nantes: **A molecular complete response**

Chevallier, 2015; Bodet-Milin, 2016

- Different approaches of a and β RIT targeting CD33, CD45, CD66 or CD22 have been already evaluated with encouraging results.



CXCR4 RLT in Acute leukemia

- CXCR4 overexpression could be demonstrated in more than **30 different types of cancer** including acute leukemia (AL), lymphoma and multiple myeloma (MM), associated **with adverse prognosis**.

- Promising results have been reported with **CXCR4-directed PET** imaging with the human-specific CXCR4-binding peptide **^{68}Ga-Pentixafor** in several tumors including AML and MM.

- A modified version of Pentixafor, **Pentixather**, allows labeling with β-emitting radionuclides (**^{177}Lu; ^{90}Y**) for radionuclide therapy/**theranostics approaches**.

ARRONAX

Project **PENTILULA**: PHRC-K 2019

Phase ½ study assessing radio-ligand therapy (RLT) using 177Lu-pentixather for relapsed/refractory CXCR4+ acute leukemia. *PI: Pr P. Chevallier*

Main objective

Safety and tolerance of RLT with one injection of ^{177}Lu-pentixather.

Primary endpoint (in relation with the main objective)

Safety and tolerance of RLT using one injection of ^{177}Lu-pentixather.

The primary endpoint is to evaluate the incidence of DLT in order to determine the MTD from a standard dose escalating 3+3 study design.

The DLT is defined as any of the following events:
-non-reversible grade 3 or 4 non-hematological toxicity lasting for >7 days
-a grade 4 pancytopenia with hypocellular bone marrow (no disease detection) lasting for >6 weeks
-a cumulative kidney dose exceeding 23 Gy evaluated by dosimetry study
-a cumulative bone marrow dose exceeding 2 Gy evaluated by dosimetry study
-a cumulative liver dose exceeding 30 Gy, evaluated by dosimetry study

If no DLT is observed at one level, the escalade can go on with the next upper level.

First 3 patients: 2.5 GBq of 177Lu-pentixather (+ 3 patients if DLT)
Patients 4 to 6: 5 GBq of 177Lu-pentixather (+ 3 patients if DLT)
Patients 7 to 9: 7.5 GBq of 177Lu-pentixather (+ 3 patients if DLT)
Patients 10 to 12: 10 GBq of 177Lu-pentixather (+ 3 patients if DLT)

Secondary objectives

- Overall response rate (ORR) (CR, CRp and PR) after the ^{177}Lu-pentixather infusion
- Complete response rate (CR + CRp) after ^{177}Lu-pentixather infusion
- Rate of CR/CRp according to CXCR4 MFI intensity
- Minimal residual disease
- Whole body bio-distribution, pharmacokinetics and dosimetry (organ exposure to radiation) of ^{177}Lu-pentixather infusion
- Renal safety.

PENTALLO: grant obtained by PHRC-IR 2018

Phase1 study assessing radioligand therapy (RLT) using 177lu-pentixather associated with a reduced intensity conditioning regimen for allogeneic transplantation in patients with AML/ALL CXCR4+ in second remission *PI: Pr P. Chevallier*

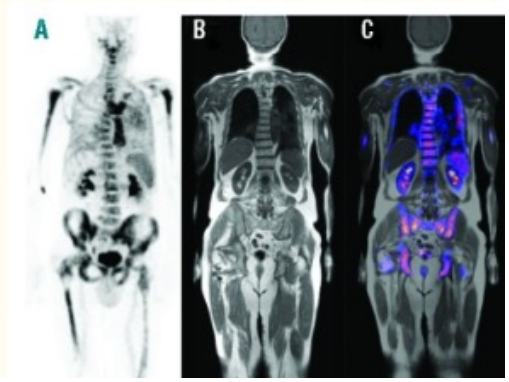
- Prospective open-label oligocentric phase 1 dose escalation study
- Administration of a single dose of 177Lu-pentixather before the administration of a standard reduced conditionning regimen for allogeneic SCT
- 177Lu-pentixather RLT will be tested at three dose levels with the aim to document the maximum tolerated dose of the RLT tested according to a traditional escalation design (3+3).
  - Level 1: 7.5 GBq
  - Level 2: 15 GBq
  - Level 3: 20 GBq
- Only patients identified (at relapse) by cytometry as CXCR4+ expression >=20% of the blast population will receive the Investigational Medicinal Product administration.
- A standard reduced conditioning regimen will be administered in the sterile unit of each participating center, as follows:
  - Fludarabine IV (Fludara®) : 30 mg/m² IV, days -6, -5, -4, -3 a
  - Busulfan IV (Busilvex®): 3.2 mg/kg/day at day -5 and -4
  - Thymoglobuline®: 2.5 mg/kg/day IV at days -2 and -1
- Allograft at Day 0

Main objective

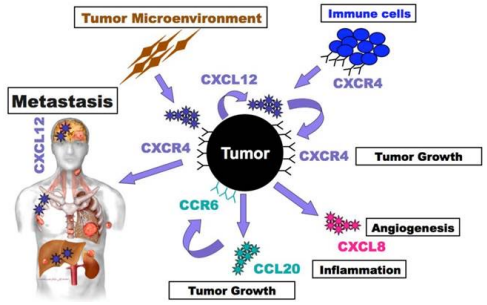
To determine the maximum tolerated dose (MTD) of one infusion of increasing doses of 177Lu-pentixather in combination with a standard reduced intensity conditioning regimen before allogeneic stem cell transplantation.

Secondary objectives

Engraftment, Primary and secondary graft failure
Neutrophils and platelet recoveries
Overall survival (OS)
Leukemia free survival (LFS)
Non-relapse mortality (NRM)
Relapse incidence (RI)
Acute and chronic GVHD
Graft-free relapse free survival (GRFS)
Minimal residual disease (MRD): CXCR4 expression on leukemic cells at 4/6 weeks and 3 months post-transplant
Whole body biodistribution and pharmacokinetics of 177Lu-pentixather
Dosimetry of 177Lu-pentixather (organ exposure to radiation)
Immune reconstitution: CD4, CD8, B, NK, EPP at 3 , 6, 9 and 12 months post-transplant
Chimerism at days +30, +60, +90 and one year post-transplant.
Infections after transplant: bacterial, viral, parasitic and fungal
Quality of life: before RLT, at D-7,D30, D90, D180, D365 post-transplant
Renal and hepatic safety.

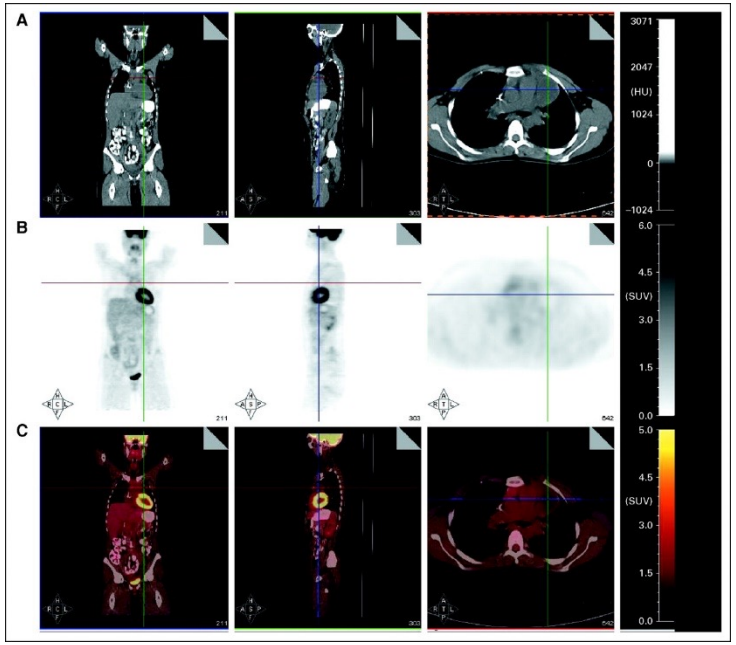


Herhaus, Haematologica 2016



Wald et al. Theranostics 2013

FDG PET in lymphoma: characterization of residual masses and first recommandations



Juweid, M. E. et al. J Clin Oncol; 25:571-578 2007

Revised Response Criteria for Malignant Lymphoma

Bruce D. Cheson, Beate Pfistner, Malik E. Juweid, Randy D. Gascoyne, Lena Specht, Sandra J. Horning, Bertrand Coiffier, Richard I. Fisher, Anton Hagenbeek, Emanuele Zucca, Steven T. Rosen, Sigrid Stroobants, T. Andrew Lister, Richard T. Hoppe, Martin Dreyling, Kensei Tobinai, Julie M. Vose, Joseph M. Connors, Massimo Federico, and Volker Diehl

A B S T R A C T

Purpose
Standardized response criteria are needed to interpret and compare clinical trials and for approval of new therapeutic agents by regulatory agencies.

Methods
The International Working Group response criteria (Cheson et al, J Clin Oncol 17:1244, 1999) were widely adopted, but required reassessment because of identified limitations and the increased use of [18F]fluorodeoxyglucose-positron emission tomography (PET), immunohistochemistry (IHC), and flow cytometry. The International Harmonization Project was convened to provide updated recommendations.

Results
New guidelines are presented incorporating PET, IHC, and flow cytometry for definitions of response in non-Hodgkin's and Hodgkin's lymphoma. Standardized definitions of end points are provided.

Conclusion
We hope that these guidelines will be adopted widely by study groups, pharmaceutical and biotechnology companies, and regulatory agencies to facilitate the development of new and more effective therapies to improve the outcome of patients with lymphoma.

J Clin Oncol 25:579-586. © 2007 by American Society of Clinical Oncology

2007

Use of Positron Emission Tomography for Response Assessment of Lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma

Malik E. Juweid, Sigrid Stroobants, Otto S. Hoekstra, Felix M. Mottaghy, Markus Dietlein, Ali Guermazi, Gregory A. Wiseman, Lale Kostakoglu, Klemens Scheidhauer, Andreas Buck, Ralph Naumann, Karoline Spaepen, Rodney J. Hicks, Wolfgang A. Weber, Sven N. Reske, Markus Schwaiger, Lawrence H. Schwartz, Josee M. Zijlstra, Barry A. Siegel, and Bruce D. Cheson

A B S T R A C T

Purpose
To develop guidelines for performing and interpreting positron emission tomography (PET) imaging for treatment assessment in patients with lymphoma both in clinical practice and in clinical trials.

Methods
An International Harmonization Project (IHP) was convened to discuss standardization of clinical trial parameters in lymphoma. An imaging subcommittee developed consensus recommendations based on published PET literature and the collective expertise of its members in the use of PET in lymphoma. Only recommendations subsequently endorsed by all IHP subcommittees were adopted.

Recommendations
PET after completion of therapy should be performed at least 3 weeks, and preferably at 6 to 8 weeks, after chemotherapy or chemoimmunotherapy, and 8 to 12 weeks after radiation or chemoradiotherapy. Visual assessment alone is adequate for interpreting PET findings as positive or negative when assessing response after completion of therapy. Mediastinal blood pool activity is recommended as the reference background activity to define PET positivity for a residual mass ≥ 2 cm in greatest transverse diameter, regardless of its location. A smaller residual mass or a normal sized lymph node (ie, ≤ 1 × 1 cm in diameter) should be considered positive if its activity is above that of the surrounding background. Specific criteria for defining PET positivity in the liver, spleen, lung, and bone marrow are also proposed. Use of attenuation-corrected PET is strongly encouraged. Use of PET for treatment monitoring during a course of therapy should only be done in a clinical trial or as part of a prospective registry.

J Clin Oncol 25. © 2007 by American Society of Clinical Oncology

Published Ahead of Print on February 11, 2008, as doi:10.3324/haematol.10591.

Original Article

Evaluation of response to fractionated radioimmunotherapy with ^{90}Y-epratuzumab in non-Hodgkin's lymphoma by ^{18}F-fluorodeoxyglucose positron emission tomography

Caroline Bodet-Milin,[1] Françoise Kraeber-Bodéré,[1,2,3] Benoît Dupas,[4] Franck Morschhauser,[5] Thomas Gastinne,[6] Steven Le Gouill,[6] Loïc Campion,[7] Jean-Luc Harousseau,[6] William A. Wegener,[8] David M. Goldenberg,[8] and Damien Huglo[10]

FDG PET was more accurate than CT to assess RIT.
FDG PET allowed characterization of the residual masses classified as uCR by CT

PET positive-uCR

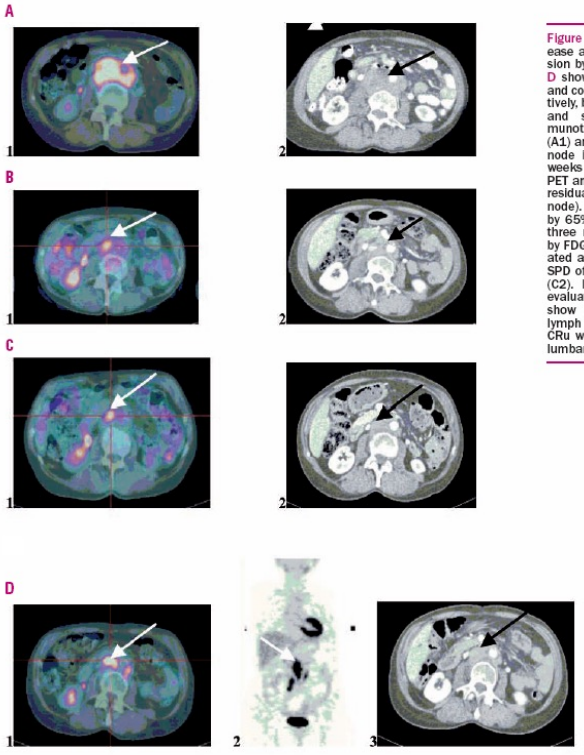


Figure 1. Detection of residual disease and early detection of progression by FDG-PET. Images A, B, C and D show FDG-PET and CT transverse and coronal images recorded, respectively, before RIT and six weeks, three and six months after radioimmunotherapy. Pre-treatment FDG-PET (A1) and CT (A2) show lumbar lymph node involvement. Response at six weeks was evaluated as PR by FDG-PET and CT (B1 and B2 arrows show residual masses in lumbar lymph node). The lesion has been reduced by 65% on CT images. Response at three months was evaluated as PR by FDG-PET (C1), while CT was evaluated as CRu with a reduction of the SPD of 80% compared with baseline (C2). FDG-PET at six months was evaluated as PD (D1 and D2: arrows show increase of size of lumbar lymph nodes), while CT confirmed CRu with a reduction of 84% of the lumbar mass (D3).

PET negative-uCR

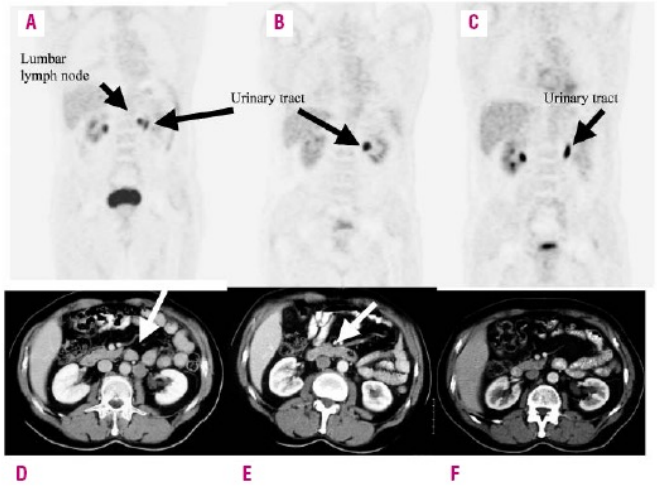


Figure 2. Early detection of complete response by FDG-PET. A, B, and C show FDG-PET coronal images recorded, respectively, before radioimmunotherapy and six weeks and three months after radioimmunotherapy. D, E, and F show CT transverse images performed, respectively, before radioimmunotherapy and six weeks and 18 months after radioimmunotherapy. Pre-treatment imaging shows one lumbar lymph node (A: black arrows show lumbar abnormal focus and normal urinary tract, D: white arrow shows lumbar lymph node). Response at six weeks was evaluated as CRu by CT (E: white arrow shows lumbar lymph node with 80% decrease) and CR by FDG-PET (B: black arrow shows normal urinary tract). CT three months later confirmed the CR, and successive serial CT and PET imaging documented continuing CR, including the negative image obtained at 18 months (F).

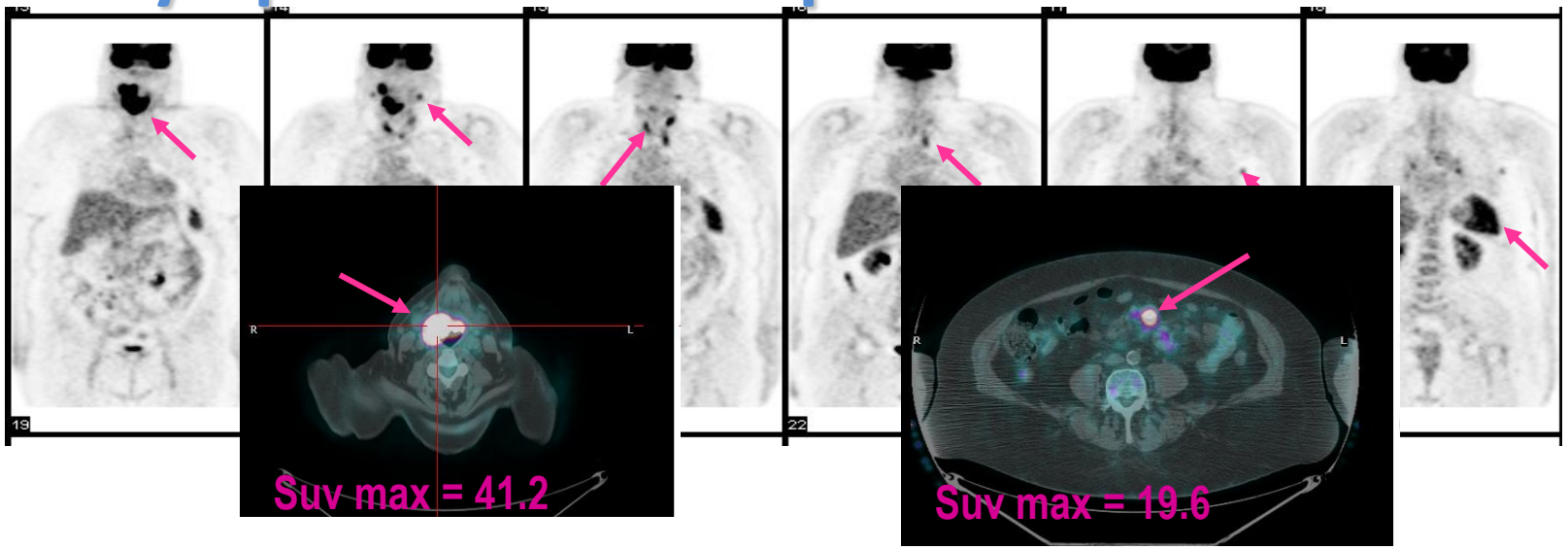
Bodet-Milin et al. Haematologica 2008

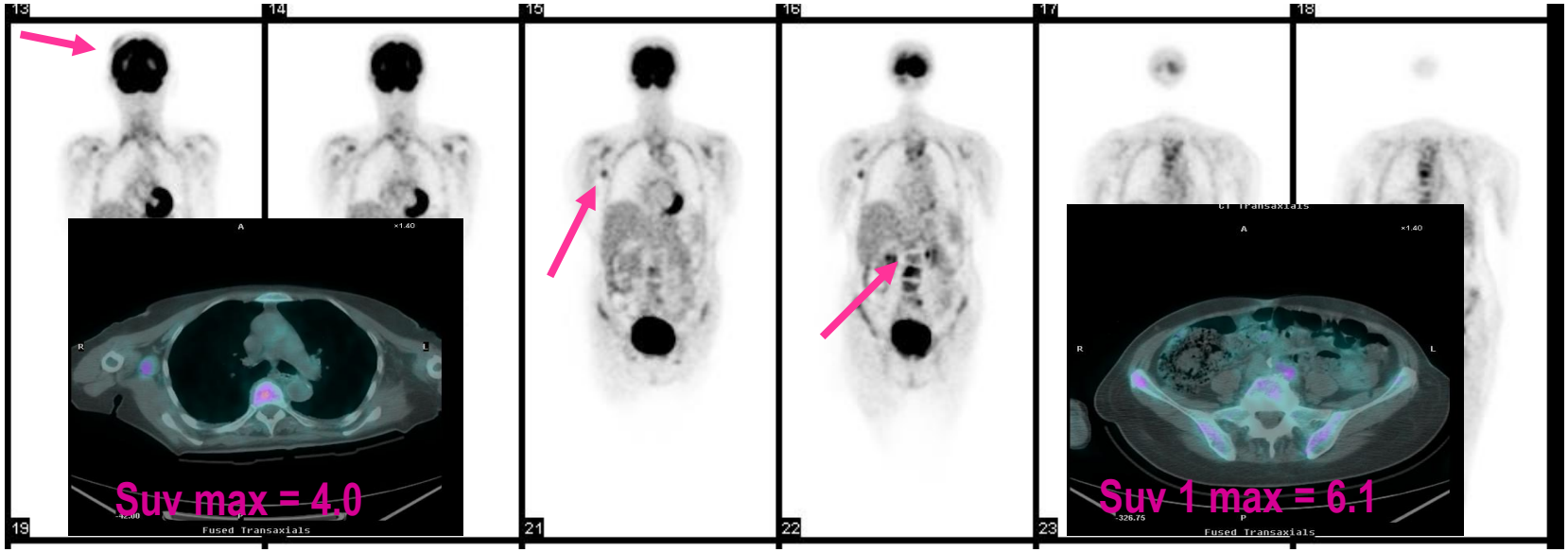
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

High Rates of Durable Responses With Anti-CD22 Fractionated Radioimmunotherapy: Results of a Multicenter, Phase I/II Study in Non-Hodgkin's Lymphoma

Franck Morschhauser, Françoise Kraeber-Bodéré, William A. Wegener, Jean-Luc Harousseau, Marie-Odile Petillon, Damien Huglo, Lorenz H. Trümper, Johannes Meller, Michael Pfreundschuh, Carl-Martin Kirsch, Ralph Naumann, Joachim Kropp, Heather Horne, Nick Teoh, Steven Le Gouill, Caroline Bodet-Milin, Jean-Francois Chatal, and David M. Goldenberg

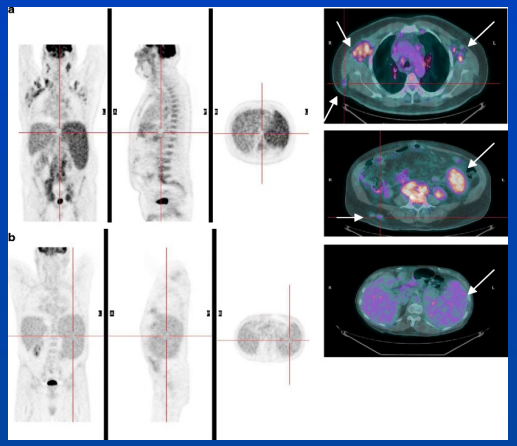
FDG-PET to guide biopsy in low grade lymphoma with suspected transformation

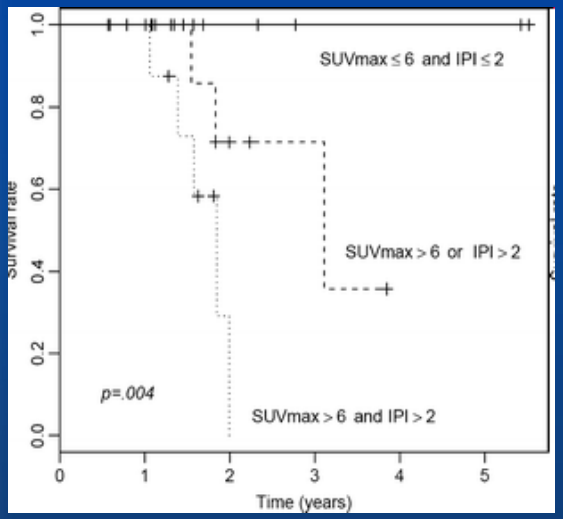




Bodet-Milin et al. Haematologica 2008

FDG-PET for mantle cell lymphoma in LYMA trials: prognostic value at baseline





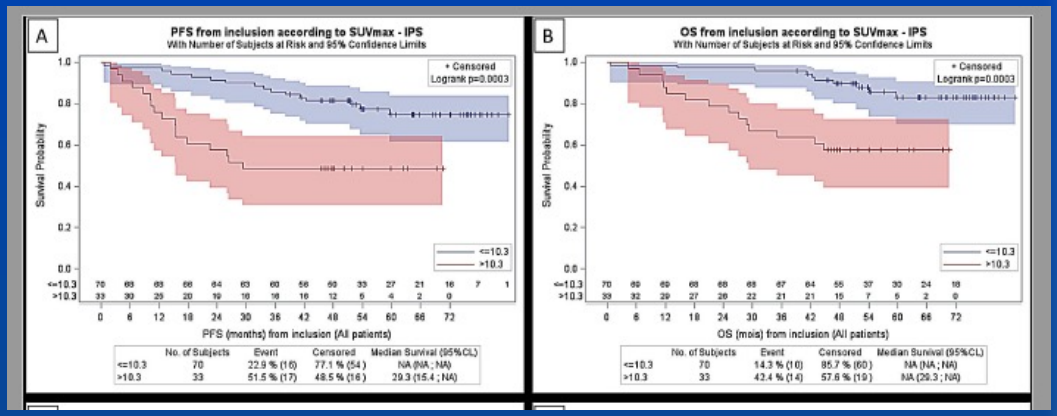
Bodet-Milin, EJNM, 2010

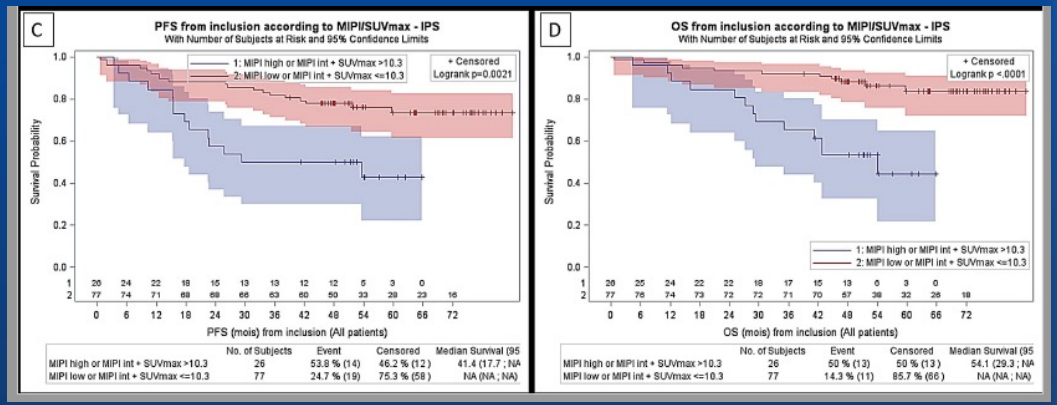
haematologica

Journal of The Ferrata Storti Foundation

Prognostic value of FDG-PET in patients with mantle cell lymphoma: results from the LyMa-PET Project

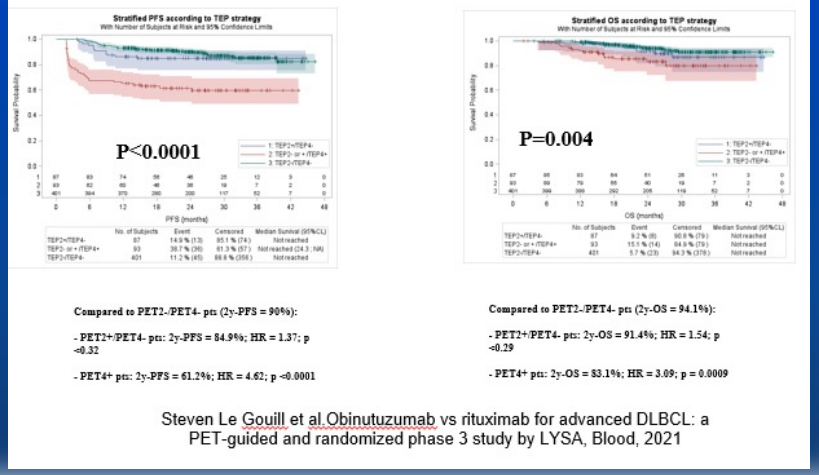
by Clément Bailly, Thomas Carlier, Alina Berriolo-Riedinger, Olivier Casasnovas, Emmanuel Gyan, Michel Meignan, Anne Moreau, Barbara Burroni, Loic Djaileb, Remy Gressin, Anne Devillers, Thierry Lamy, Catherine Thieblemont, Olivier Hermine, Françoise Kraeber-Bodéré, Steven Le Gouill, and Caroline Bodet-Milin





Bailly, Haematologica, 2019

FDG-PET for DLBCL in the GAINED trial: Survival using the PET-driven strategy



Compared to PET2-/PET4- pts (2y-PFS = 90%):

- PET2+/PET4- pts: 2y-PFS = 84.9%; HR = 1.37; p =0.32
- PET4+ pts: 2y-PFS = 61.2%; HR = 4.62; p <0.0001

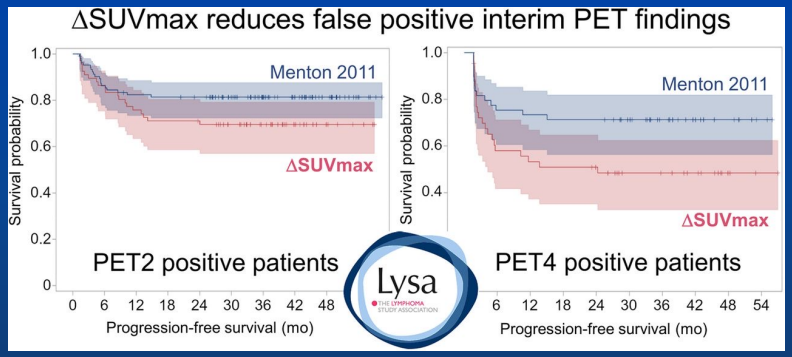
Compared to PET2-/PET4- pts (2y-OS = 94.1%):

- PET2+/PET4- pts: 2y-OS = 91.4%; HR = 1.54; p =0.29
- PET4+ pts: 2y-OS = 83.1%; HR = 3.09; p = 0.0009

Steven Le Gouill et al.Obinutuzumab vs rituximab for advanced DLBCL: a PET-guided and randomized phase 3 study by LYSA, Blood, 2021

Validation of the ΔSUV_{max} for Interim PET Interpretation in Diffuse Large B-Cell Lymphoma on the Basis of the GAINED Clinical Trial

Emmanuel Itti[1], Paul Blanc-Durand[1], Alina Berriolo-Riedinger[2], Salim Kanoun[2], Françoise Kraeber-Bodéré[3], Michel Meignan[†1], Elodie Gat[4], Steven Le Gouill[5], René-Olivier Casasnovas[6], and Caroline Bodet-Milin[3]

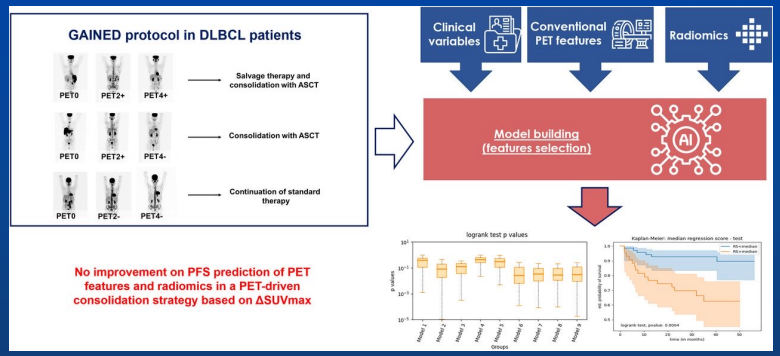


Journal of Nuclear Medicine, published on September 21, 2023 as doi:10.2967/jnumed.123.265871

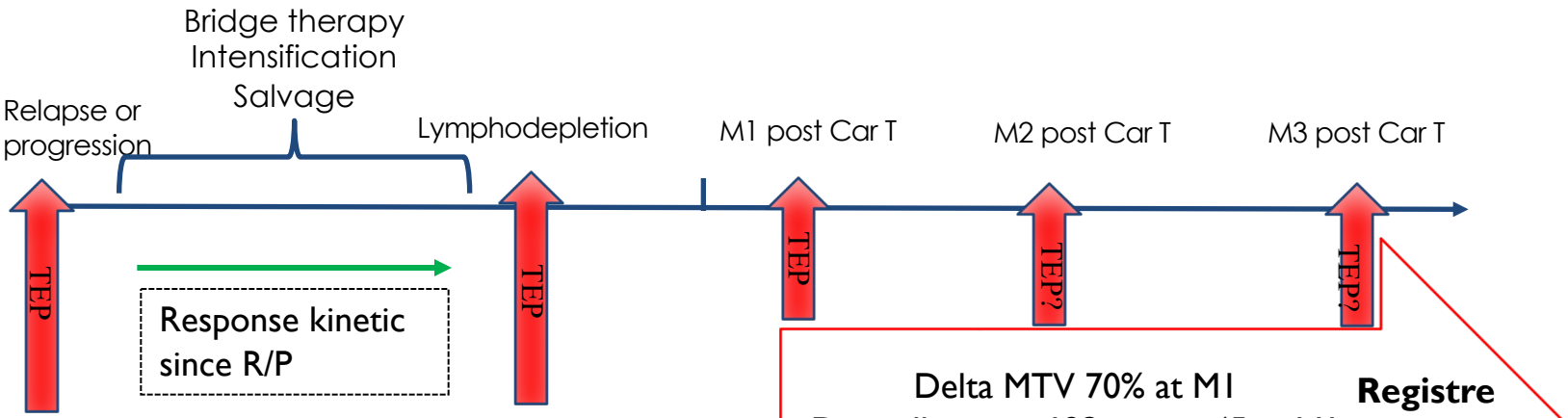
Prognostic Value of ^{18}F-FDG PET Radiomics Features at Baseline in PET-Guided Consolidation Strategy in Diffuse Large B-Cell Lymphoma: A Machine-Learning Analysis from the GAINED Study

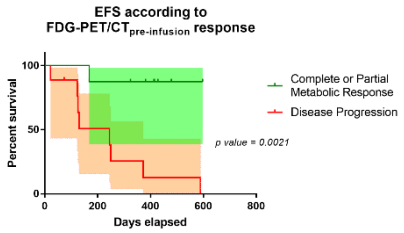
Thomas Carlier[1,2], Gauthier Frécon[1,2], Diana Mateus[3], Mira Rizkallah[3], Françoise Kraeber-Bodéré[1,2], Salim Kanoun[4], Paul Blanc-Durand[5], Emmanuel Itti[5], Steven Le Gouill[6], René-Olivier Casasnovas[7], Caroline Bodet-Milin[1,2], and Clément Bailly[1,2]

J Nucl Med 2024; 65:156–162



On going studies in lymphoma: Prediction of efficacy/evaluation of Car T Cells





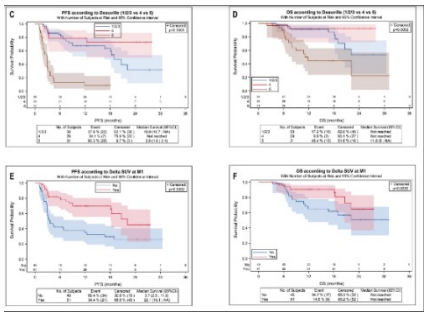
Bailly et al, Hematol Oncol, 2022

MTV>80ml
Number of extranodals sites>2

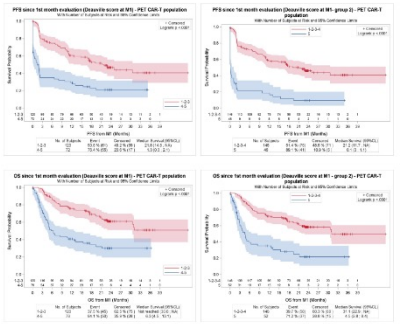
Vercellino et al.2020

MTV<30cm^3 in 212 R/R DLBCL patient included in the DescarT register

Al Tabaa et al. ASH 2023

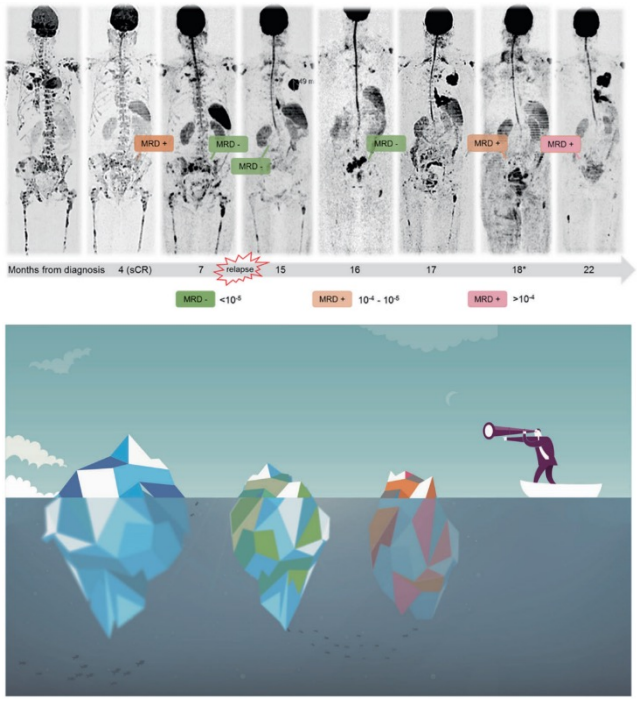


Galtier at et al.2022



Al Tabaa et al. ASH 2023

FDG PET in MM: characterization of heterogeneous disease



Rasche, L. et al. *Combination of flow cytometry and functional imaging for monitoring of residual disease in myeloma.* Leukemia (2019).

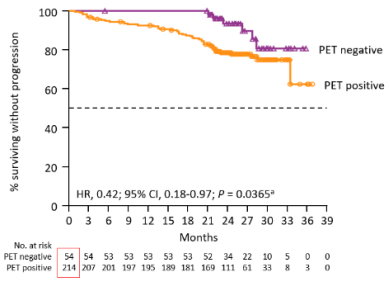
- MM is a highly **heterogeneous disease** with patchy bone marrow infiltration but also extra-medullary disease and variable clinical course and treatment response due to **molecular variation.**
- Accurate early identification of **high risk** patients and evaluation of **intra and extra-medullary residual disease** is needed to guide therapy.
- The International Myeloma Working Group (IMWG) included minimal residual disease (**MRD**) as a standard criterion in the evaluation of treatment response.
- Modern imaging techniques are also recommended, including **whole-body low-dose CT, FDG PET/CT or WB-MRI**.

blood
2011 118: 5984-5985
doi:10.1182/blood-2011-09-379818

PET-CT in MM: a new definition of CR

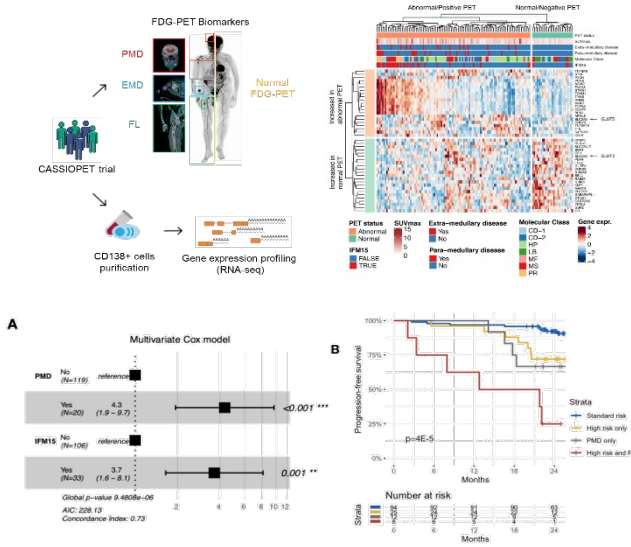
Philippe Moreau

FDG PET at baseline in NDMM: prognostic biomarkers



PFS was improved in patients who were PET negative vs PET positive at baseline

Kraeber-Bodéré et al, Haematologica 2023



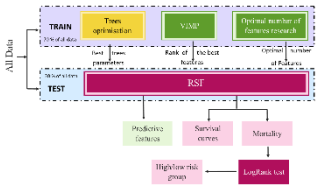
Alberge et al, JNM, 2021

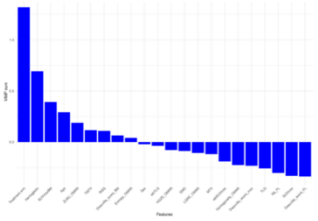
European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-020-05049-6

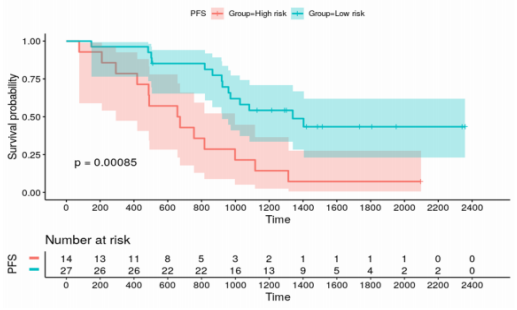
ORIGINAL ARTICLE

Random survival forest to predict transplant-eligible newly diagnosed multiple myeloma outcome including FDG-PET radiomics a combined analysis of two independent prospective European trial

Bastien Jamet[1] · Ludivine Morvan[2,3] · Cristina Nanni[4] · Anne-Victoire Michaud[1] · Clément Bailly[1,2] · Stéphane Chauvie[5] · Philippe Moreau[6] · Cyrille Touzeau[6] · Elena Zamagni[7] · Caroline Bodet-Milin[1,2] · Françoise Kraeber-Bodéré[1,2,8] · Diana Mateus[3] · Thomas Carlier[1,2]







FDG-PET/CT for response to therapy assessment in MM: How to define complete metabolic response ?

Multicenter Study > J Clin Oncol. 2021 Jan 10;39(2):116-125. doi: 10.1200/JCO.20.00386.
Epub 2020 Nov 5.

Standardization of ^{18}F-FDG-PET/CT According to Deauville Criteria for Metabolic Complete Response Definition in Newly Diagnosed Multiple Myeloma

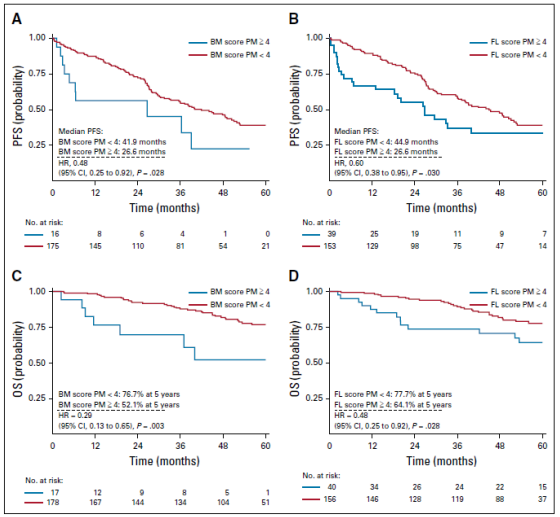
Elena Zamagni [1], Cristina Nanni [2], Luca Dozza [1], Thomas Carlier [3], Clément Bailly [3], Paola Tacchetti [1], Annibale Versari [4], Stephane Chauvie [5], Andrea Gallamini [6], Barbara Gamberi [7], Denis Caillot [8], Francesca Patriarca [9], Margaret Macro [10], Mario Boccadoro [11], Laurent Garderet [12], Simona Barbato [1], Stefano Fanti [2], Aurore Perrot [13], Francesca Gay [11], Peter Sonneveld [14], Lionel Karlin [15], Michele Cavo [1], Caroline Bodet-Milin [3], Philippe Moreau [16], Françoise Kraeber-Bodéré [3]

Affiliations + expand

PMID: 33151787 DOI: 10.1200/JCO.20.00386

TABLE 7. Proposed Refinement of PET Response Criteria After Therapy

PET Response After Therapy	Response Criteria
Complete metabolic response	Uptake ≤ liver activity in BM sites and FLs previously involved (including extramedullary and paramedullary disease [DS score 1-3])
Partial metabolic response	Decrease in number and/or activity of BM/FLs present at baseline, but persistence of lesion(s) with uptake > liver activity (DS score 4 or 5)
Stable metabolic disease	No significant change in BM/FLs compared with baseline
Progressive metabolic disease	New FLs compared with baseline consistent with myeloma



PENTIMYELO: Relevance of [^{68}Ga]Ga-PentixaFor for initial staging and therapeutic evaluation of symptomatic multiple myeloma patients **in first line treatment or in first relapse**

PI: Pr Bodet-Milin

45 Adults with symptomatic MM in first line or in first relapse

↓

Inclusion criteria met
Consent and inclusion

↓

Initial diagnostic
Clinical and biological Evaluations
FDG-PET
First [^{68}Ga]Ga--PentixaFor-PET

↓

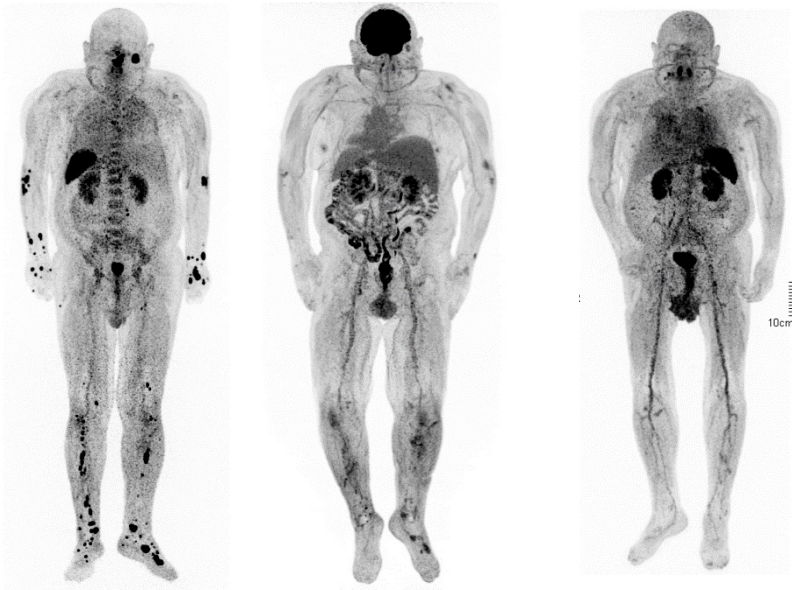
Start of treatment

↓

Therapeutic evaluation [≈D100 if stem cell transplantation or ≈ M6 if no stem cell transplantation (after cycle 6)]
Clinical and biological Evaluations
Myelogram
FDG-PET
Second [^{68}Ga]Ga-PentixaFor-PET

↓

Follow-up every 6 months until relapse



PENTIXAFOR-PET Before therapy | FDG-PET | PENTIXAFOR-PET After therapy

RESULTS: PER LESION ANALYSIS

- FOCAL LESION:

Patients	1	2	3	4	5	6	7	8	9	Total
CXCR4	0	0	>20	5	0	0	>40	0	0	> 65
FDG	0	0	4	2	0	0	9	0	0	15

- PARAMEDULLARY DISEASE:

Patients	1	2	3	4	5	6	7	8	9	Total
CXCR4	0	1	>45	0	0	0	0	0	0	>46
FDG	0	1	>20	0	0	0	0	0	0	>21

- EXTRA-MEDULLARY DISEASE:

Patients	1	2	3	4	5	6	7	8	9	Total
CXCR4	0	0	2	0	0	0	0	0	0	2
FDG	0	0	0	0	0	0	0	0	0	0

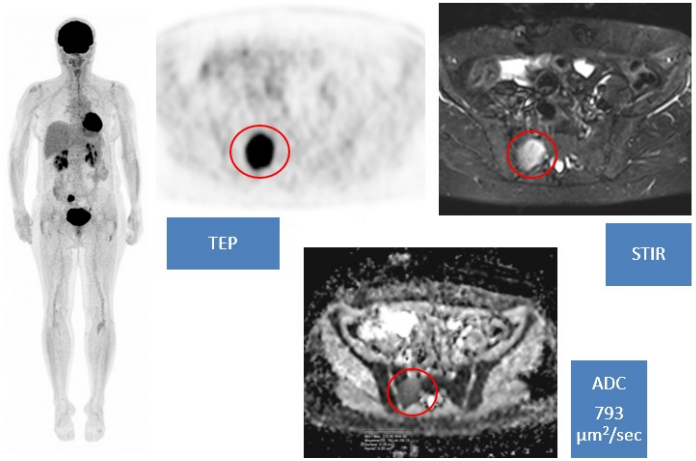
CENTRE HOSPITALIER UNIVERSITAIRE DE NANTES

ILIAD

Hybrid simultaneous whole-body 2-[^{18}F]FDG-PET/MRI imaging in newly diagnosed multiple myeloma: first diagnostic performance and clinical added value results

Oncology | Published: 06 April 2023
Volume 33, pages 6438–6447, (2023) Cite this article

Bastien Jamet, Thomas Carlier, Clément Bailly, Caroline Bodet-Milin, Aurélien Monnet, Eric Frampas, Cyrille Touzeau, Philippe Moreau & Francoise Kraeber-Bodere



RESEARCH ARTICLE Open Access

DCE-MRI to distinguish all monoclonal plasma cell disease stages and correlation with diffusion-weighted MRI/PET-based biomarkers in a hybrid simultaneous whole body-2-[18F]FDG-PET/MRI imaging approach

Bastien Jamet[1,5*], Hatem Necib[1], Thomas Carlier[1], Eric Frampas[2], Juliette Bazin[2], Paul-Henri Desfontis[2], Aurélien Monnet[3], Caroline Bodet-Milin[1], Philippe Moreau[4], Cyrille Touzeau[4] and Francoise Kraeber-Bodere[1]

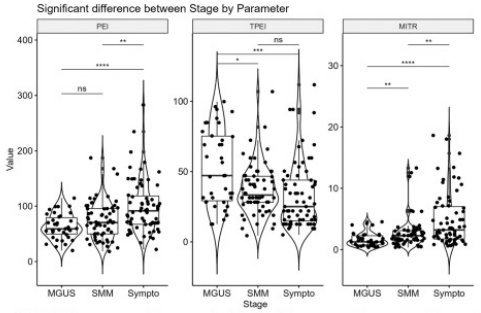


Fig. 3 DCE-MRI-based PEI,TPEI,MITR parameters in different monoclonal plasma cell disease stages. *NS: no significant;* "*": $p < 0,05$; "**": $p < 10^{-2}$; "***": $p < 10^{-3}$; "****": $p < 10^{-4}$) PEI: Peak Enhancement Intensity; TPEI: Time to PEI; MITR: Maximum Intensity Time ratio (PEI/TPEI) MGUS: monoclonal gammapathy of undetermined significance; SMM: smoldering multiple myeloma; Sympto: symptomatic multiple myeloma

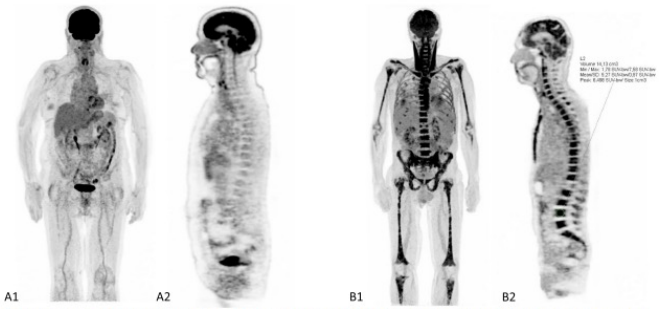


Fig. 6 Patient with monoclonal gammapathy of undetermined significance (**A**) without diffuse bone marrow involvement (no significant uptake) on maximum intensity projection (MIP, A1) and sagittal (A2) positron emission tomography (PET) images. Patient with symptomatic multiple myeloma (**B**) and diffuse bone marrow involvement (diffuse uptake higher than liver background uptake) on MIP (B1) and sagittal (B2) PET images with maximum standardized uptake value (SUV_{max}): 7.58 inside L4 vertebral body

Conclusion

- Dynamic clinical research in haematology
- Large cohorts of patients for radiomics and AI developments as well as combined analysis including PET and biology
- Clinical cohorts/studies for evaluation of new immunotherapeutics including Car T cells evaluation in lymphoma and myeloma
- New radiopharmaceuticals for PET in MM and radionuclide therapy in acute leukemia
- Interest for PET-MRI in myeloma