Guideline on the use of [^{18}F]FDG PET/CT in multiple myeloma

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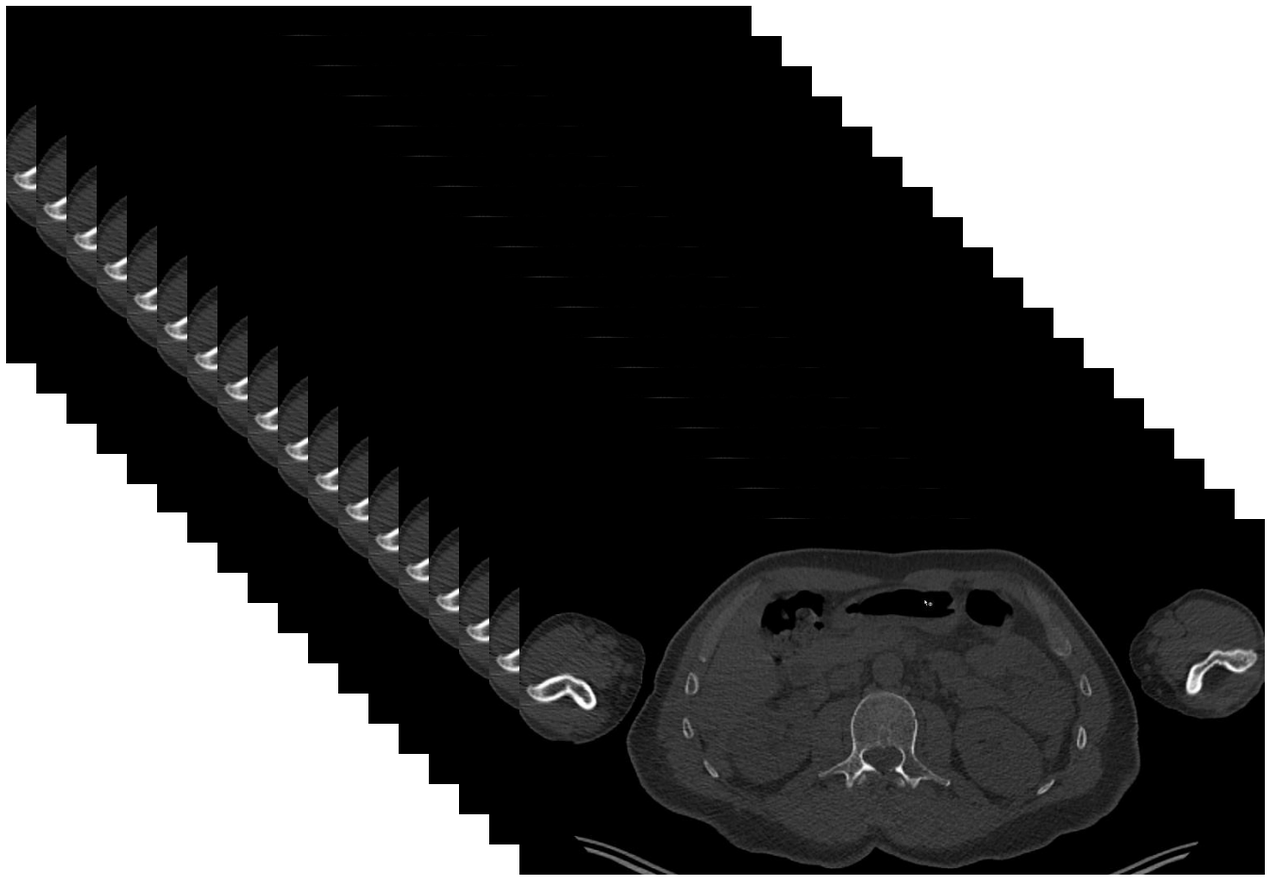
BELNUC seminar
PET in Hemalotogical Malignancies
February 24, 2024

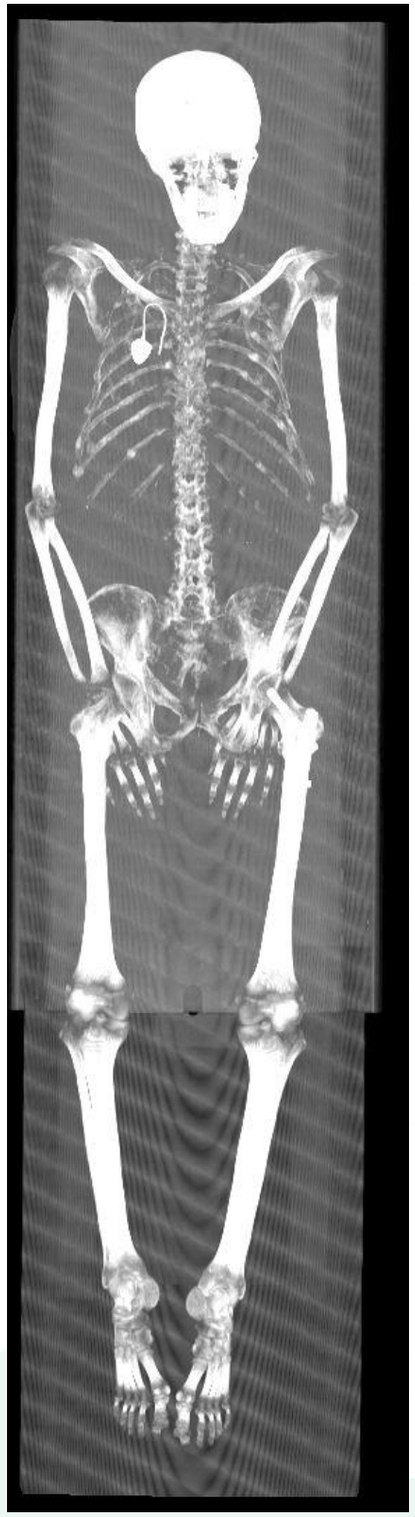
Agenda

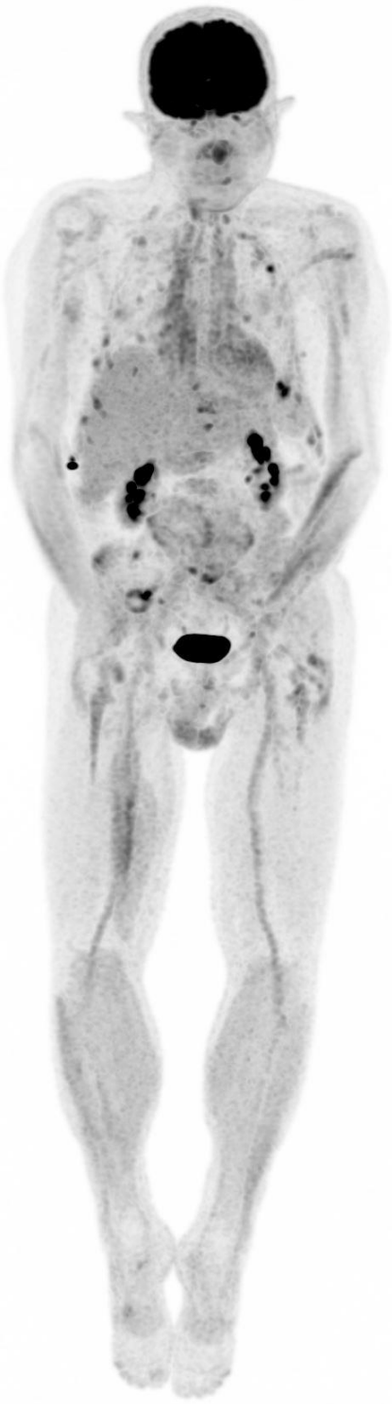
[^{18}F]FDG PET/CT in multiple myeloma

- Diagnostic tool
- Prognostic biomarker
- Treatment assessment

PET/CT in multiple myeloma (MM)







PET/CT in multiple myeloma (MM)

International myeloma working group (IMWG) consensus for diagnosis and imaging

International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma

S Vincent Rajkumar, Meletios A Dimopoulos, Antonio Palumbo, Joan Blade, Giampaolo Merlini, María-Victoria Mateos, Shaji Kumar, Jens Hillengass, Efstathios Kastritis, Paul Richardson, Ola Landgren, Bruno Paiva, Angela Dispenzieri, Brendan Weiss, Xavier LeLeu, Sonja Zweegman, Sagar Lonial, Laura Rosinol, Elena Zamagni, Sundar Jagannath, Orhan Sezer, Sigurdur Y Kristinsson, Jo Caers, Saad Z Usmani, Juan José Lahuerta, Hans Erik Johnsen, Meral Beksac, Michele Cavo, Hartmut Goldschmidt, Evangelos Terpos, Robert A Kyle, Kenneth C Anderson, Brian G M Durie, Jesus F San Miguel

Lancet Oncol 2014; 15: e538–48

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

Michele Cavo, Evangelos Terpos, Cristina Nanni, Philippe Moreau, Suzanne Lentzsch, Sonja Zweegman, Jens Hillengass, Monika Engelhardt, Saad Z Usmani, David H Vesole, Jesus San-Miguel, Shaji K Kumar, David Miguel Gay, Paul G Richardson, Joseph R Mikhael, Fernando Leal da Costa, Meletios-Athanassios Dimopoulos, Chiara Zingaretti, Hartmut Goldschmidt, Robert Z Orlowski, Wee Joo Chng, Hermann Einsele, Sagar Lonial, Bart Barlogie, Kenneth C Anderson, Brian G M Durie, Elena Zamagni

The International Myeloma Working Group has published consensus guidelines ... ned to provide recommendations for the optimal use of ...

Lancet Oncol 2017; 18: e206–17

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

Jens Hillengass, Saad Usmani, S Vincent Rajkumar, Brian G M Durie, María-Victoria Mateos, Sagar Lonial, Cristina Joao, Kenneth C Anderson, Ramón García-Sanz, Eloísa Riva, Juan Du, Niels van de Donk, Jesús G Berdeja, Evangelos Terpos, Elena Zamagni, Robert A Kyle, Jesús San Miguel, Hartmut Goldschmidt, Sergio Giralt, Shaji Kumar, Noopur Raje, Heinz Ludwig, Enrique Ocio, Rik Schots, Hermann Einsele, Fredrik Schjesvold, Wen-Ming Chen, Niels Abildgaard, Brea C Lipe, Dominik Dytfeld, Baldeep Mona Wirk, Matthew Drake, Michele Cavo, Juan José Lahuerta, Suzanne Lentzsch

Recent advances in the treatment of multiple myeloma have increased the need for accurate diagnosis of the disease.

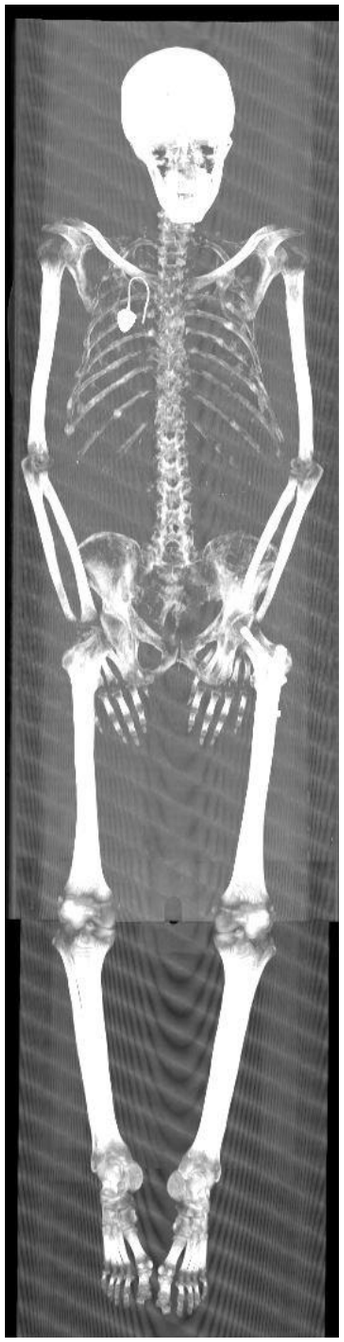
Lancet Oncol 2019; 20: e302–12

→ Guidelines

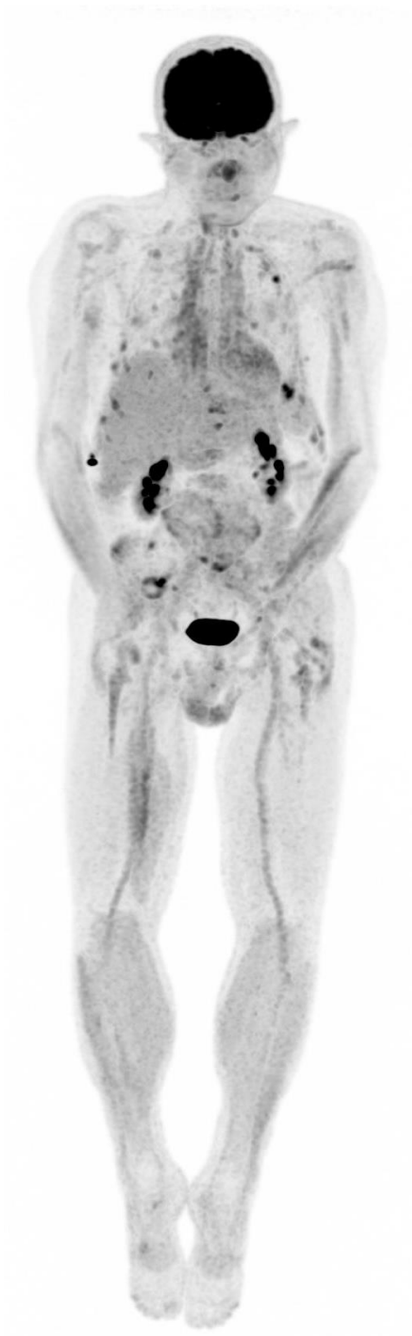
Soon...

Whole-body imaging modalities for MM

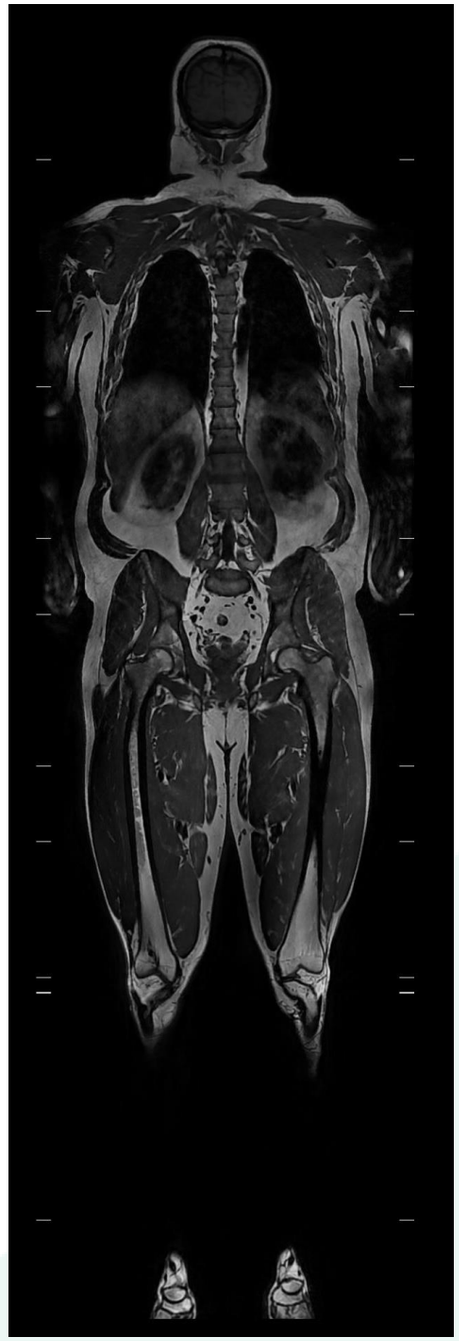
Low dose CT

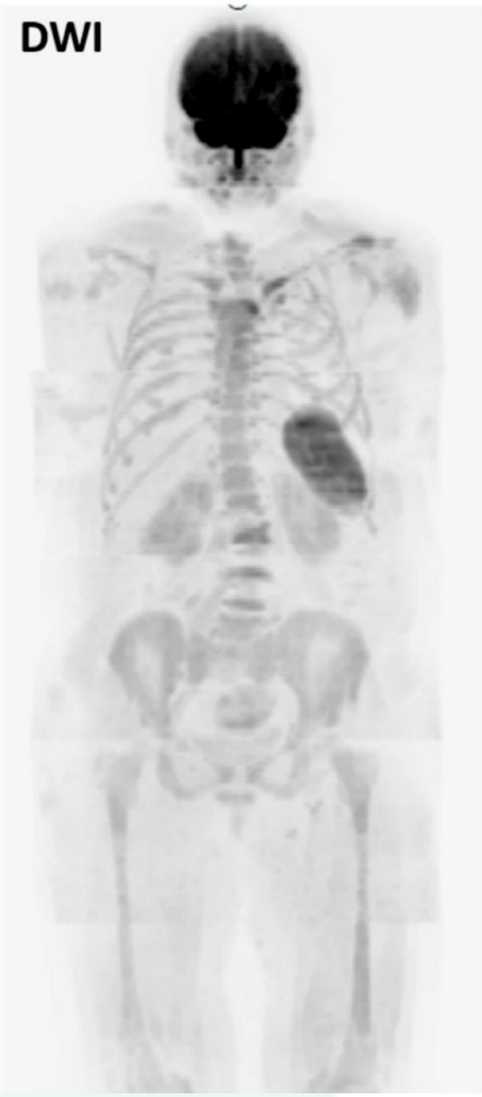


[^{18}F]FDG PET/CT



MRI





Fast

More time
More sensitive

Outline

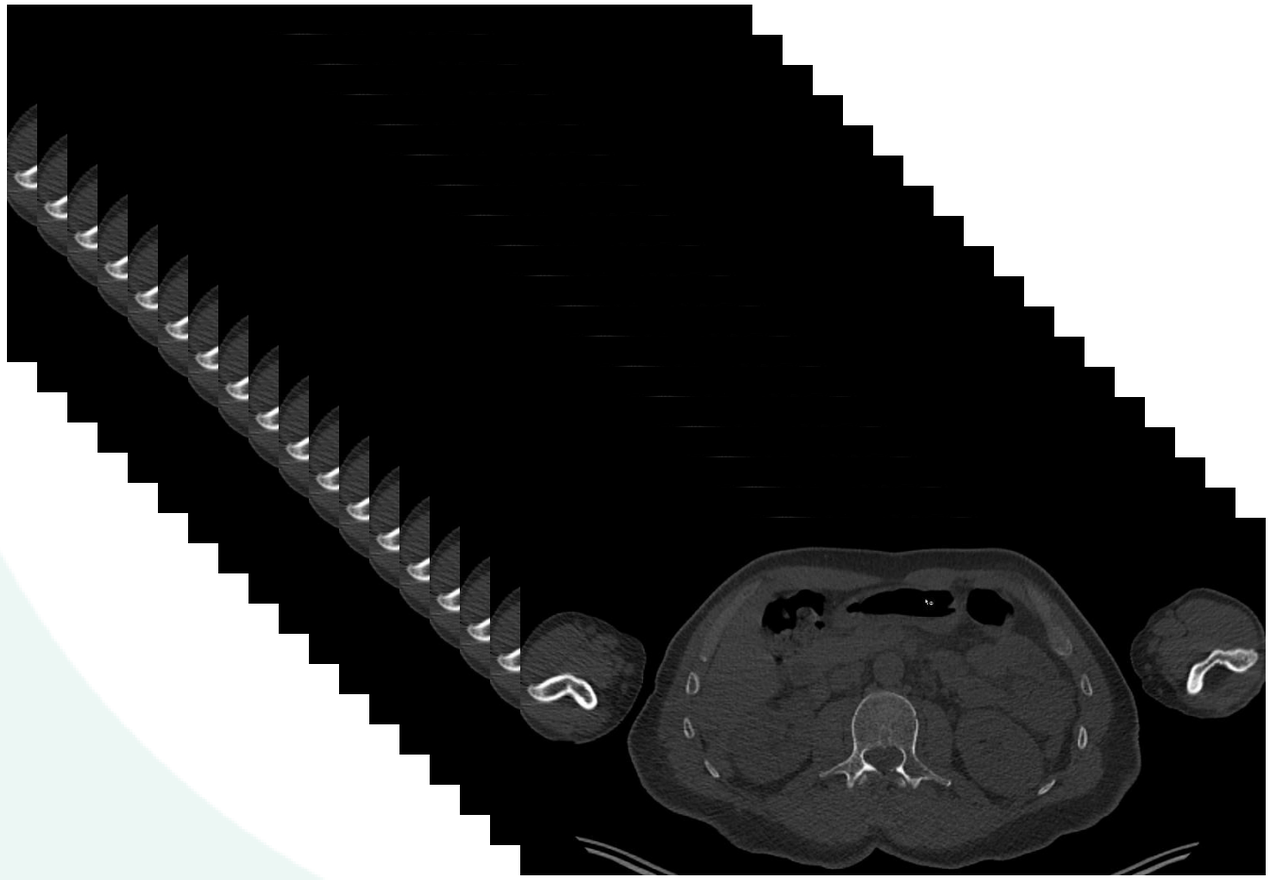
[^{18}F]FDG PET/CT in multiple myeloma

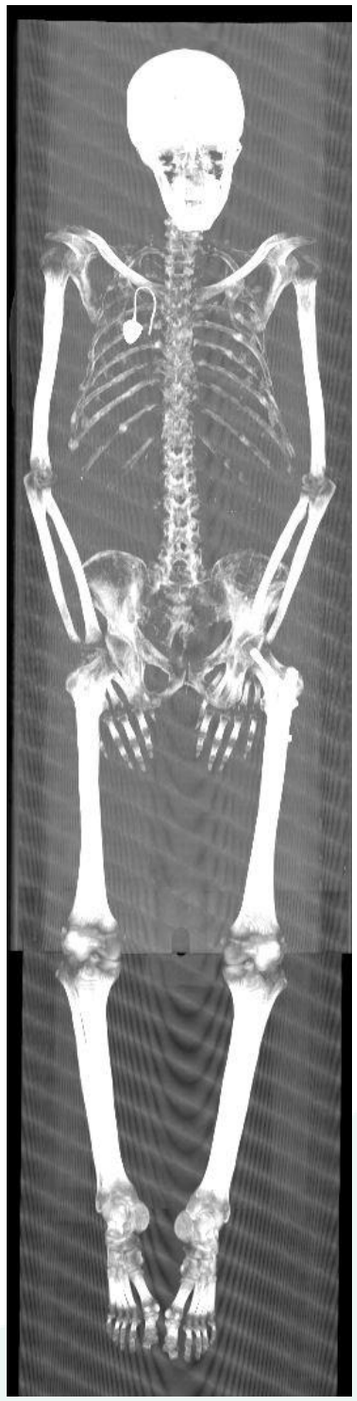
- **Diagnosis**
- Prognostic biomarker
- Treatment assessment

[^{18}F]FDG PET/CT procedure for MM

Low dose CT part quality is important

Different parameters are acceptable as long as they produce images of diagnostic quality with low effective dose to patient



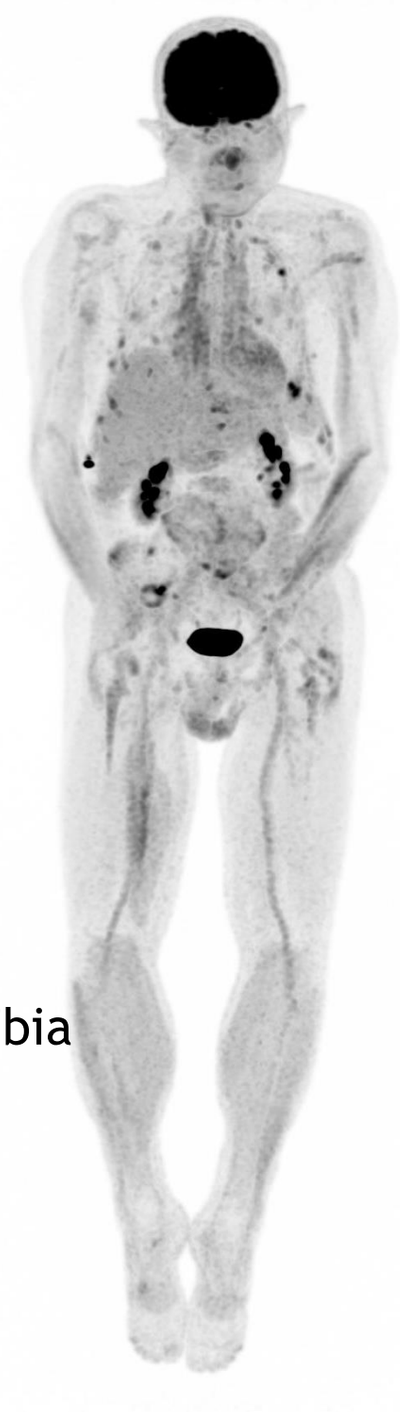


Cranial vault

Proximal tibia

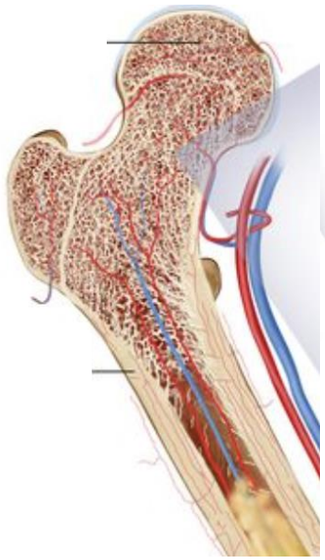
Toes

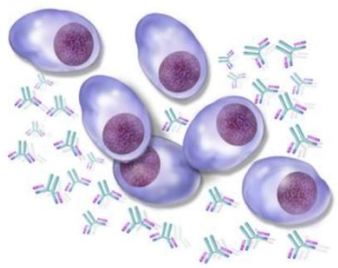
Extent



Blood Cancer J. 2018 Oct 4;8(10):95; Eur Radiol. 2018 Feb;28(2):683-691.

Development of plasma cell disorders





Bone marrow clonal plasma cells

Progression

Bone marrow

MGUS → Smouldering multiple myeloma → Multiple myeloma

MGUS
< 3 mg/dl serum M protein
and <10% BMPC
and no MDE

Smouldering MM
≥ 3 mg/dl serum M protein or
≥ 500 mg/24 h urine M protein
and/or 10-59% BMPC
and no MDE or amyloidosis

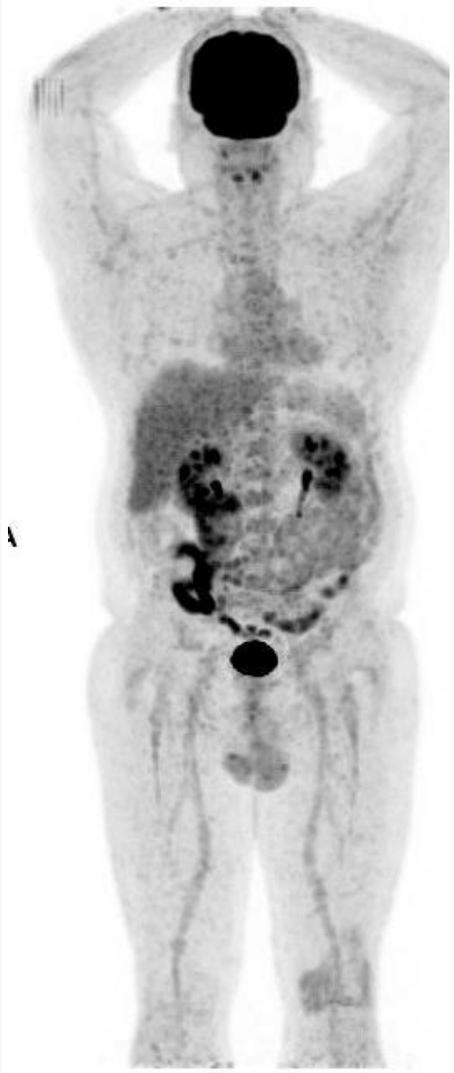
Active MM
≥ 10% BMPC or
biopsy-proven plasmacytoma
and MDE

MDE = Myeloma defininghevent
MGUS = Monoclonal gammopathy of undetermined significance

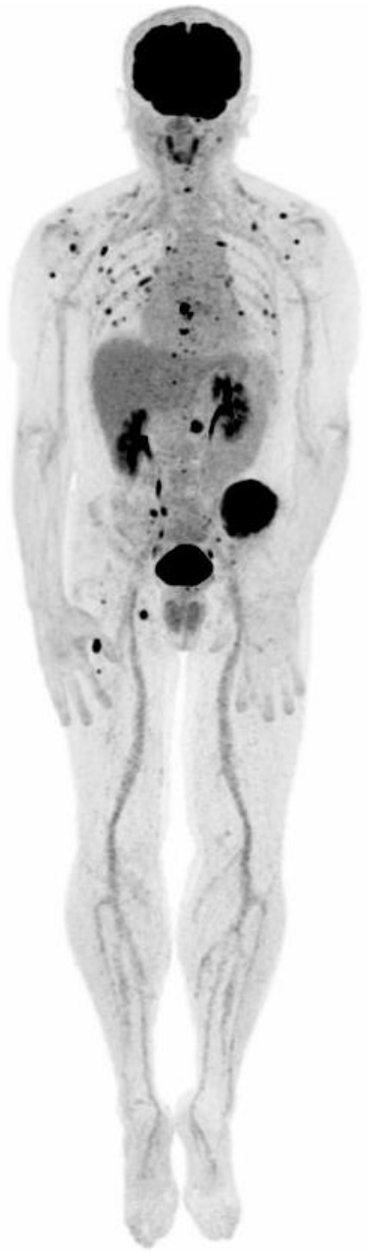
Nature Reviews Disease Primers volume 3, Article number: 17046 (2017)

Various patterns of bone infiltration

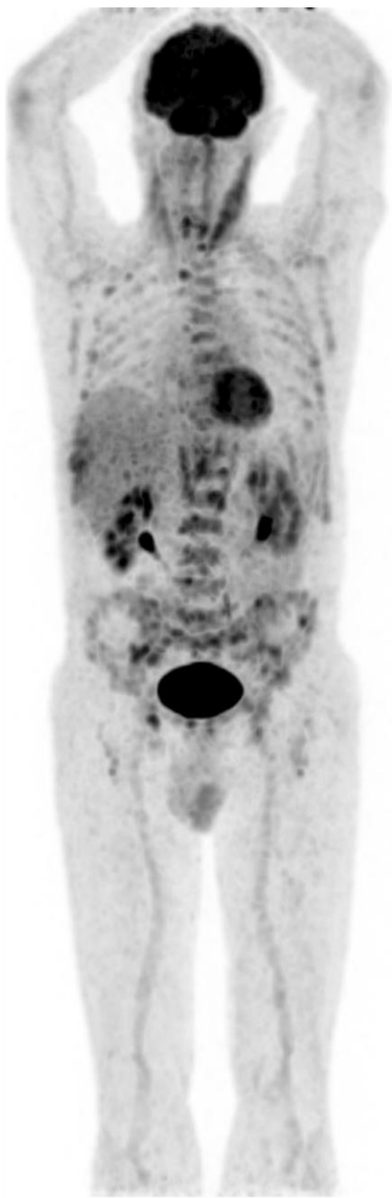
Negative PET



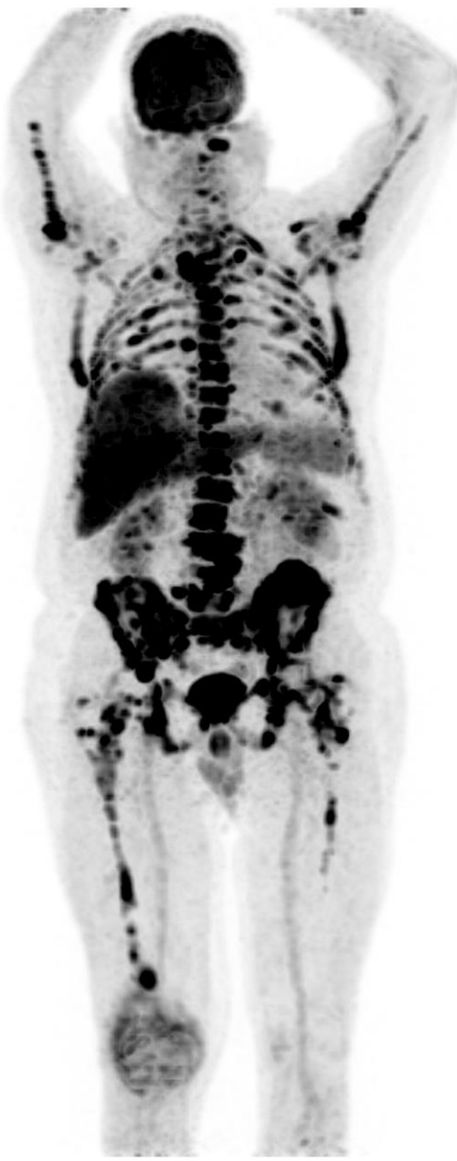
Focal lesions (FL)



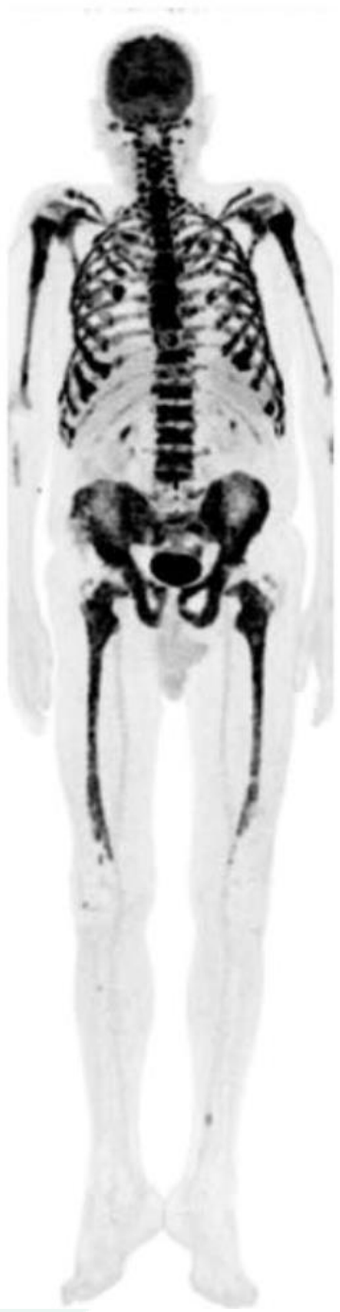
Diffuse pattern



BMPC 20%

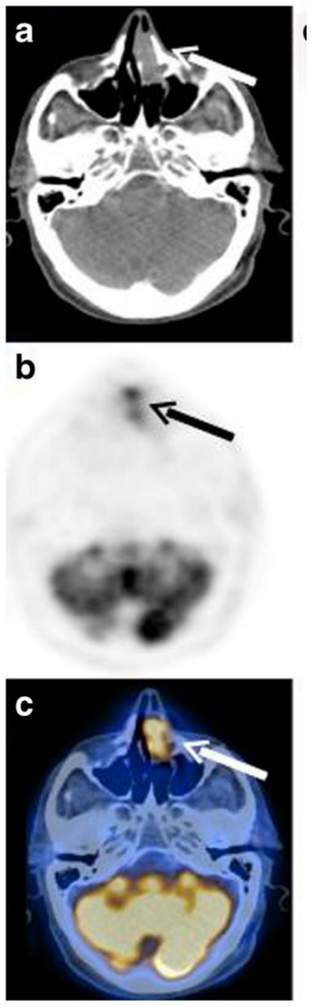


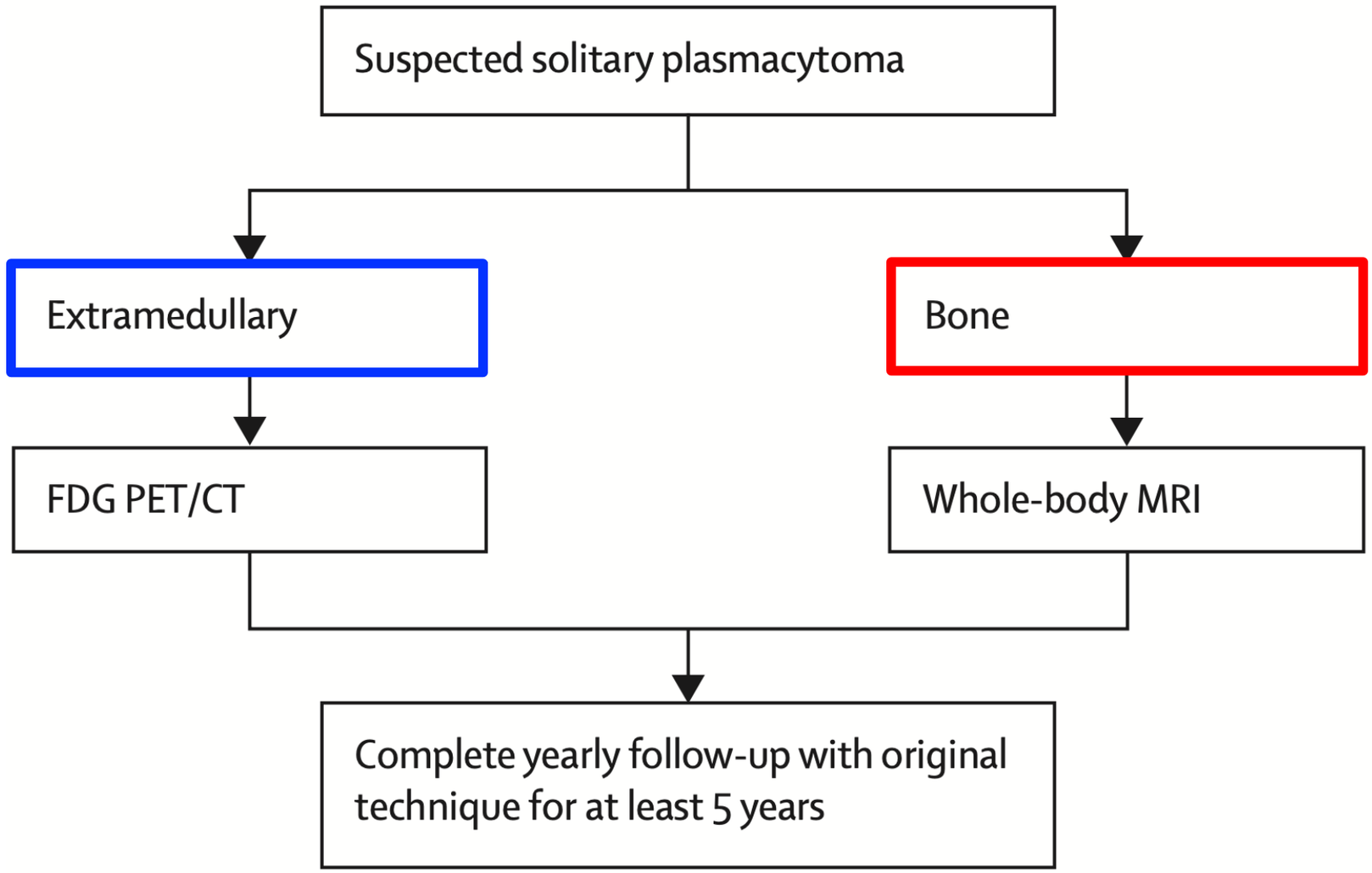
BMPC 22%

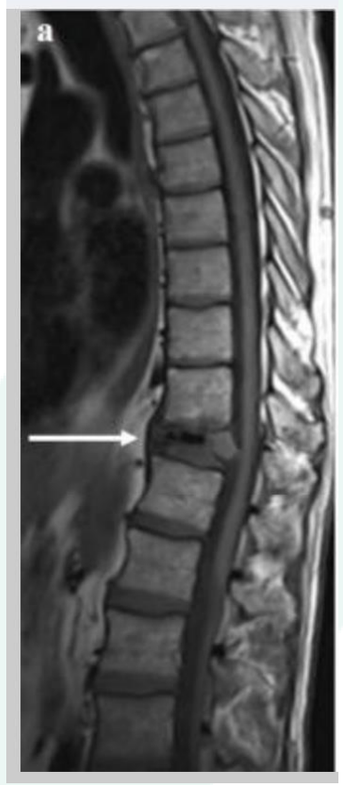


Imaging solitary plasmacytoma

Additional lesion in ∽1/3 of cases



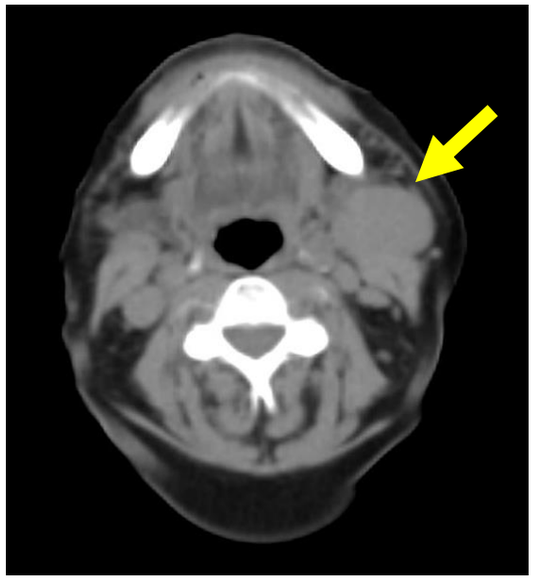




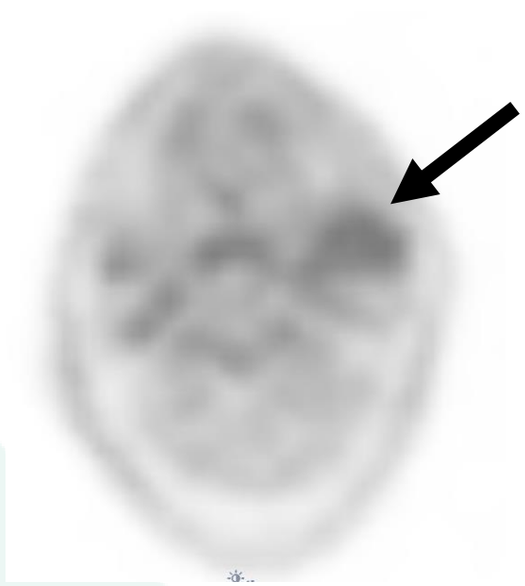
IMWG 2019 consensus. Hillengass J et al. Lancet Oncol. 2019 Jun;20(6):e302-e312

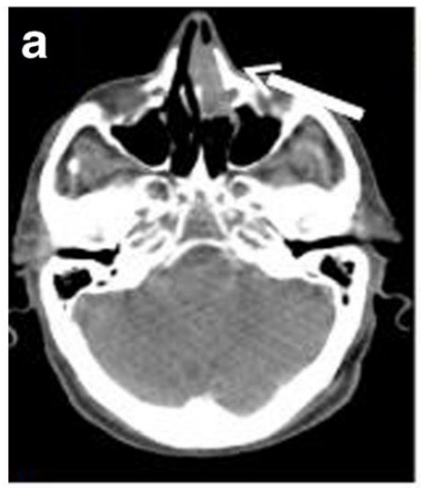
Frequent location of extramedullary SP

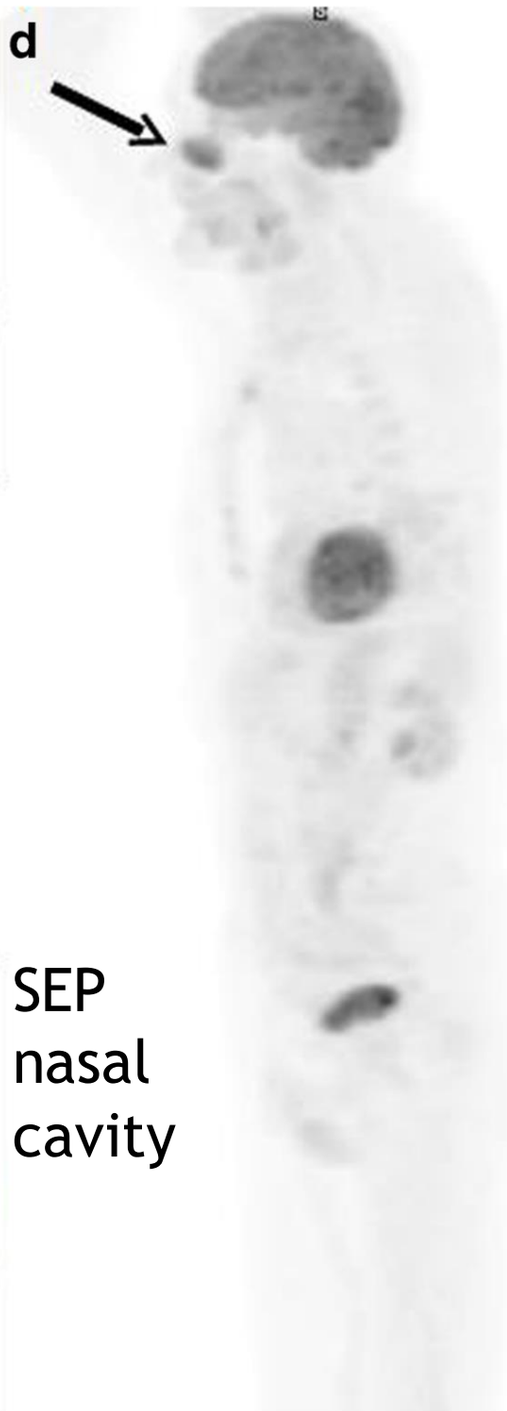
Head & neck area

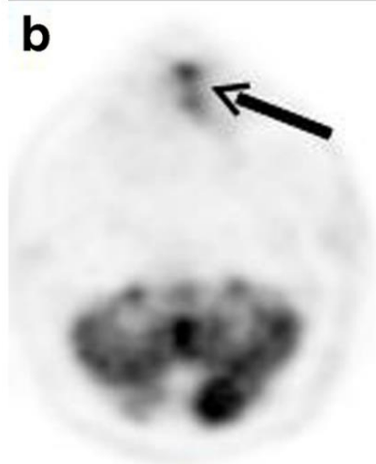


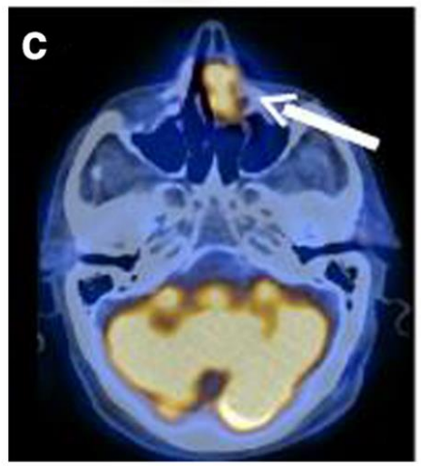
SEP
Cervical LN









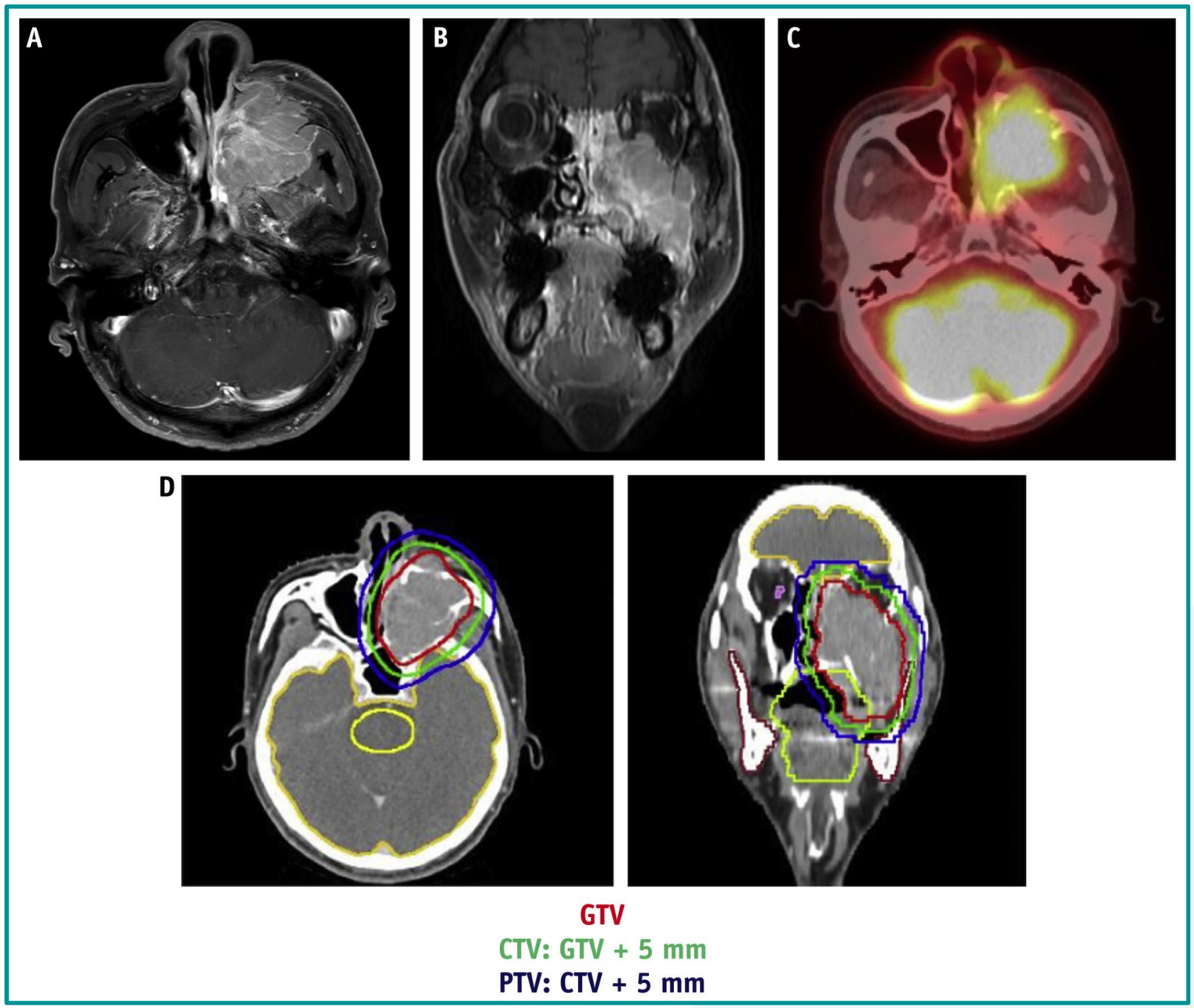


SEP
nasal
cavity

Albano et al. Eur J Nucl Med Mol Imaging. 2018 Jan;45(1):77-84.

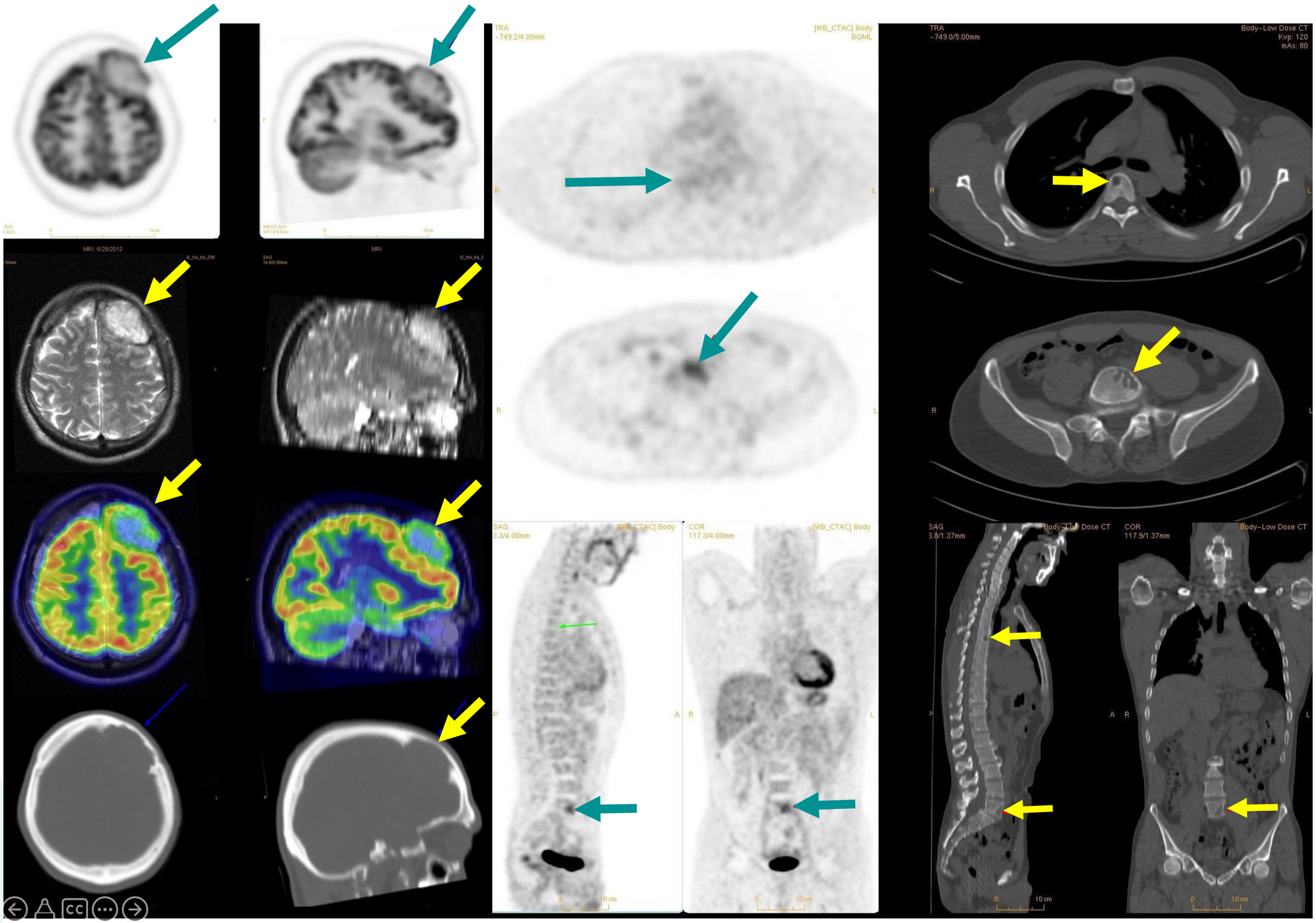
Radiation therapy for extramedullary SP

→ Long-term remission & even cure



Guidelines From the International Lymphoma Radiation Oncology Group. Int J Radiat Oncol Biol Phys. 2018 Jul 15;101(4):794-808.

[^{18}F]FDG PET/CT
Diagnosis from bone SP to active MM



Diagnosis of active MM

≥ 10% BMPC or biopsy-proven plasmacytoma
and **≥ 1 MDE:**

CRAB

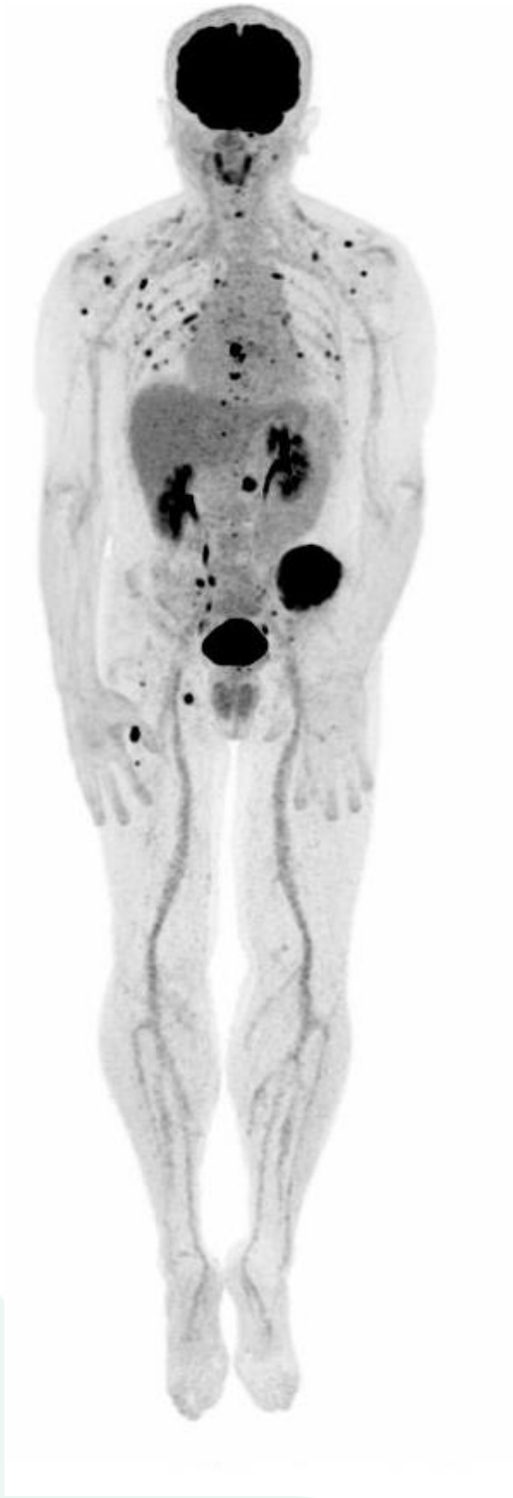
- **C** • Hypercalcaemia: serum calcium >0·25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2·75 mmol/L (>11 mg/dL)
- **R** • Renal insufficiency: creatinine clearance <40 mL per min† or serum creatinine >177 µmol/L (>2 mg/dL)
- **A** • Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value <100 g/L
- **B** • Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT‡

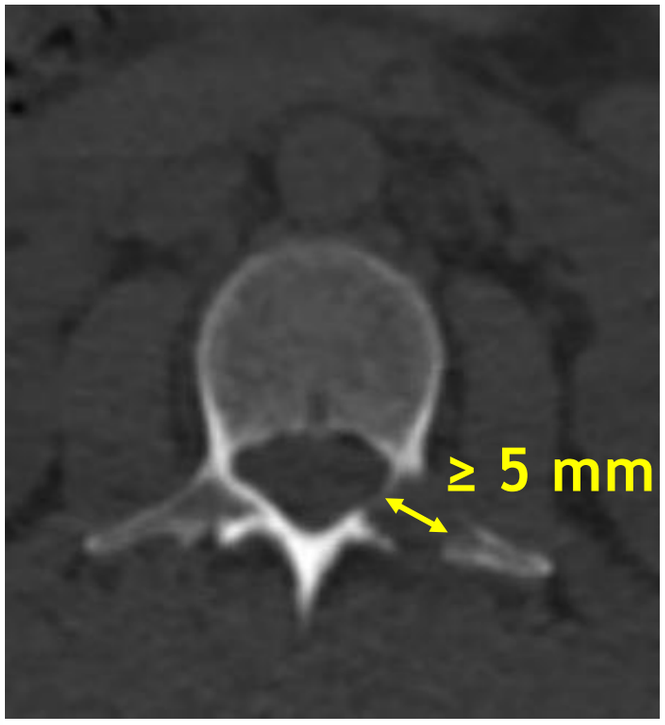
SLiM

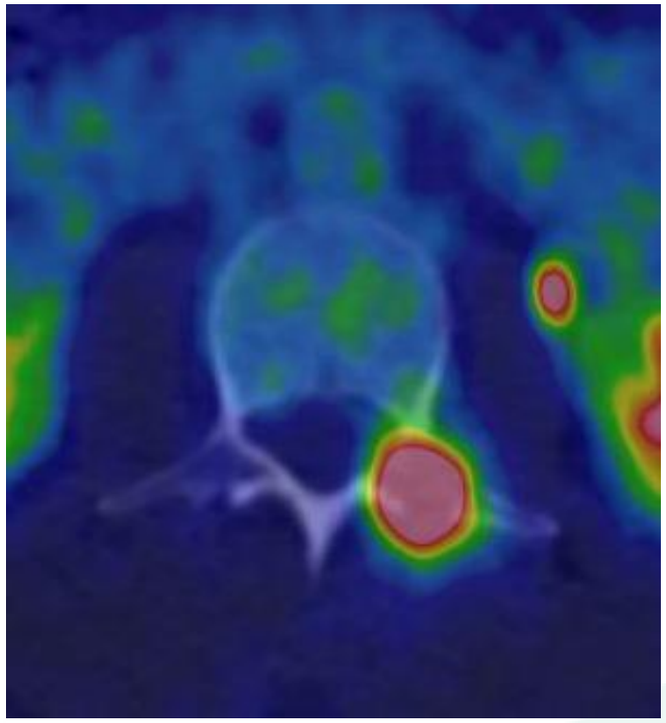
- Any one or more of the following biomarkers of malignancy:
- **S** • Clonal bone marrow plasma cell percentage* ≥60%
- **Li** • Involved:uninvolved serum free light chain ratio§ ≥100
- **M** • >1 focal lesions on MRI studies¶

Rajkumar S.V. et al. Lancet Oncol. 2014 Nov;15(12):e538-48

[^{18}F]FDG PET/CT in active MM
Bone focal lesion (FL)







≥1 osteolytic FL ≥5 mm

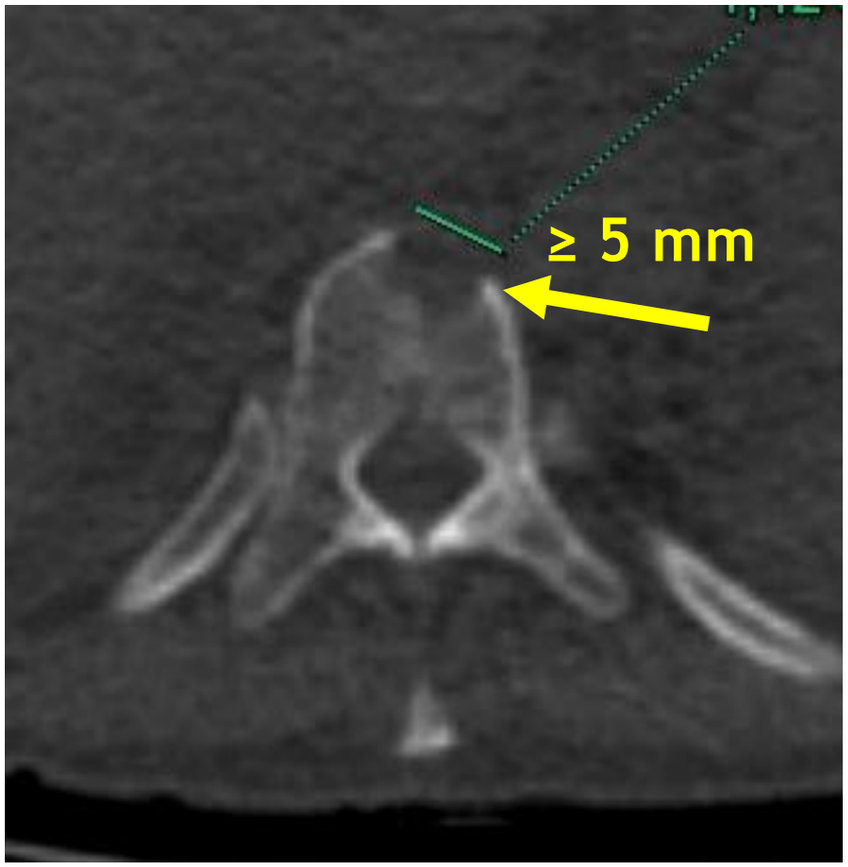
= CRA**B** = MDE

= Active MM requiring treatment

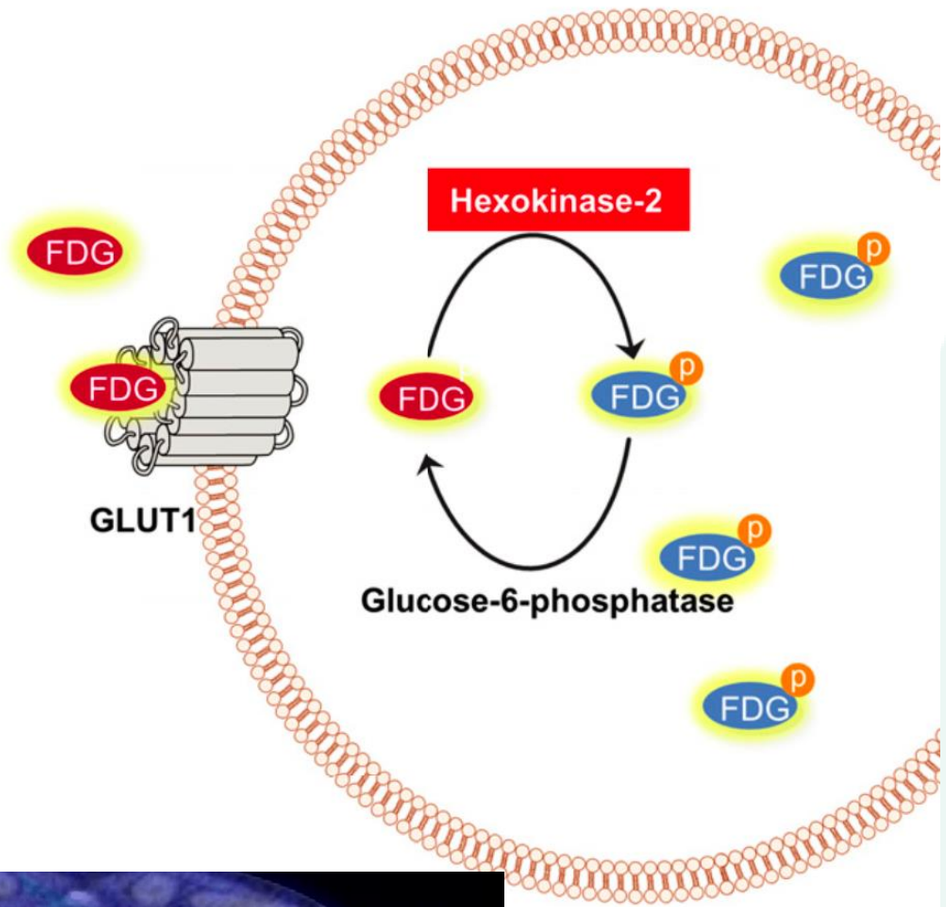
Rajkumar S.V. et al. Lancet Oncol. 2014 Nov;15(12):e538-48

The low dose CT part is as important as PET to detect FL

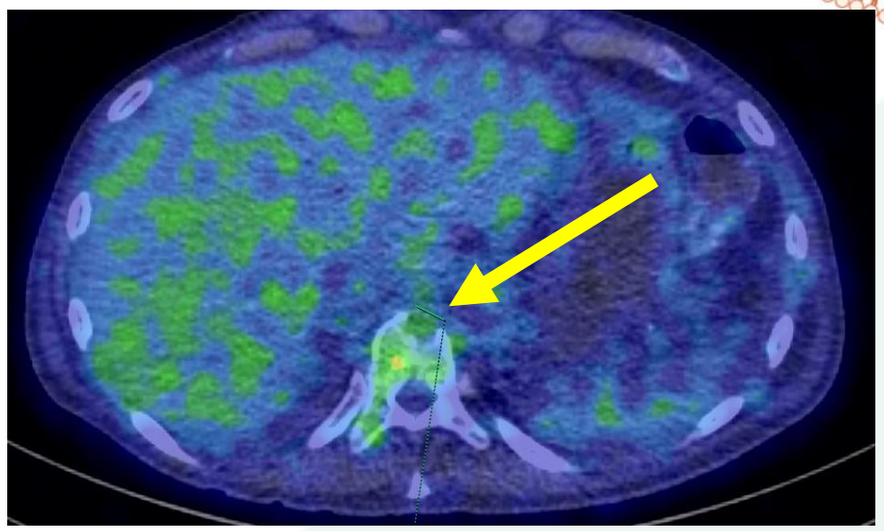
10-20% no [^{18}F]FDG uptake due to low hexokinase-2 &/or GLUT-1 transporter



CRA**B**

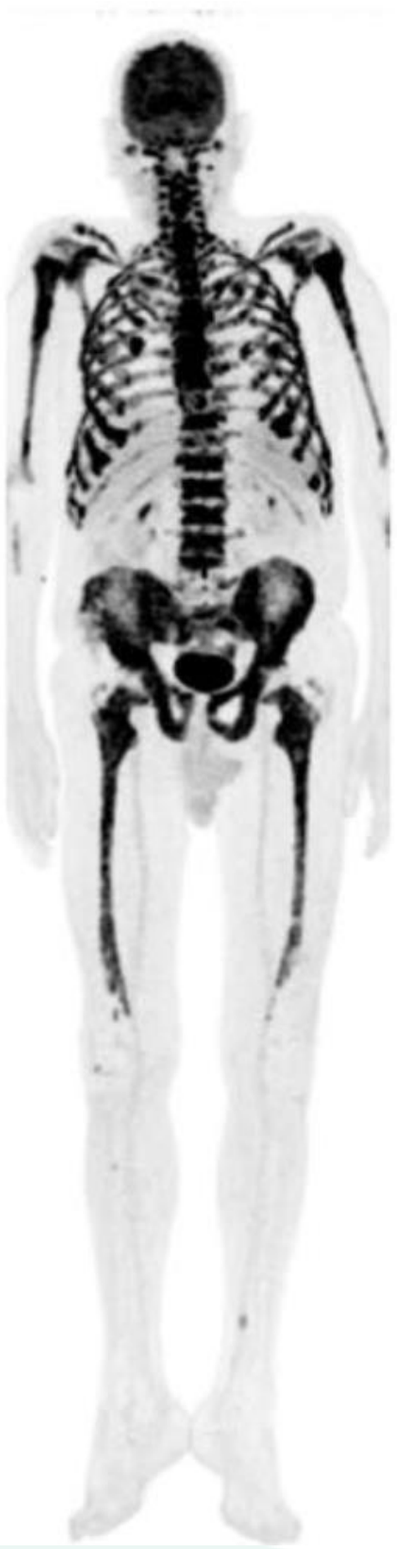


No [^{18}F]FDG uptake



Rasche et al. Blood. 2017 Jul 6;130(1):30-34.

[^{18}F]FDG PET/CT in the diagnostic work up
Diffuse bone marrow uptake



Definition:
Heterogeneous or homogenous **diffuse** uptake of the axial skeleton (that may extend to the periphery) **> liver** uptake

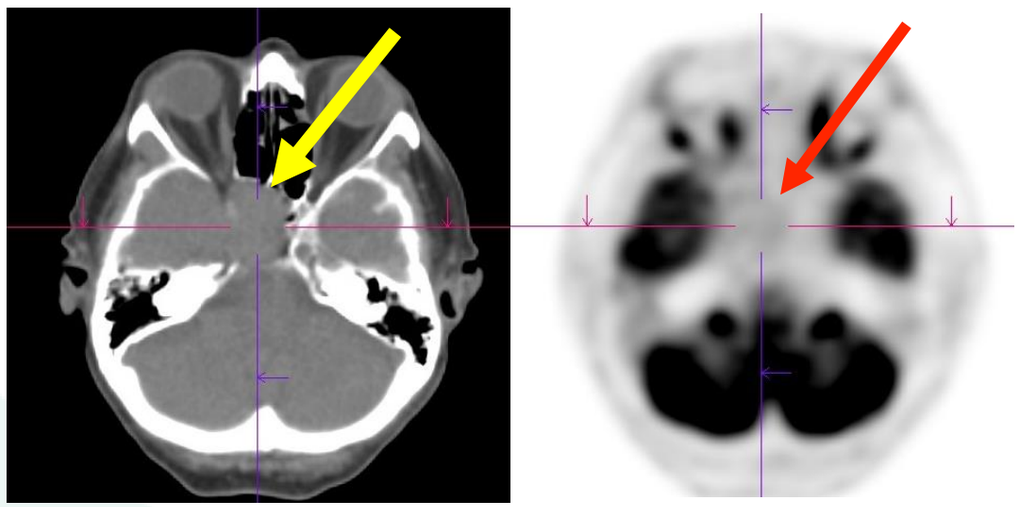
This **NOT a MDE** according to 2014 IMWG MM diagnosis criteria due to the limited specificity (reactive BM hyperplasia related to anaemia)

Nanni C et al. Eur J Nucl Med Mol Imaging. 2016 Mar;43(3):414-21;
Eur J Nucl Med Mol Imaging. 2018 May;45(5):712-719.
Takahashi et al. Sci Rep. 2019 Nov 11;9(1):16429.

[^{18}F]FDG PET pitfalls

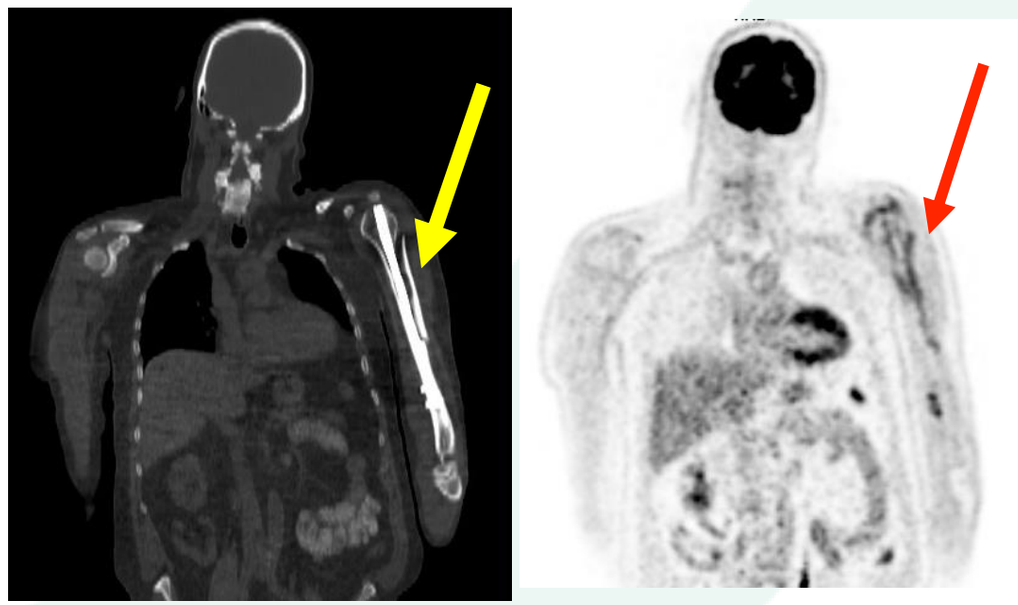
FALSE NEGATIVE

- Hyperglycaemia
- Recent administration of high-dose steroids
- No [^{18}F]FDG uptake (10-20% cases)



FALSE POSITIVE

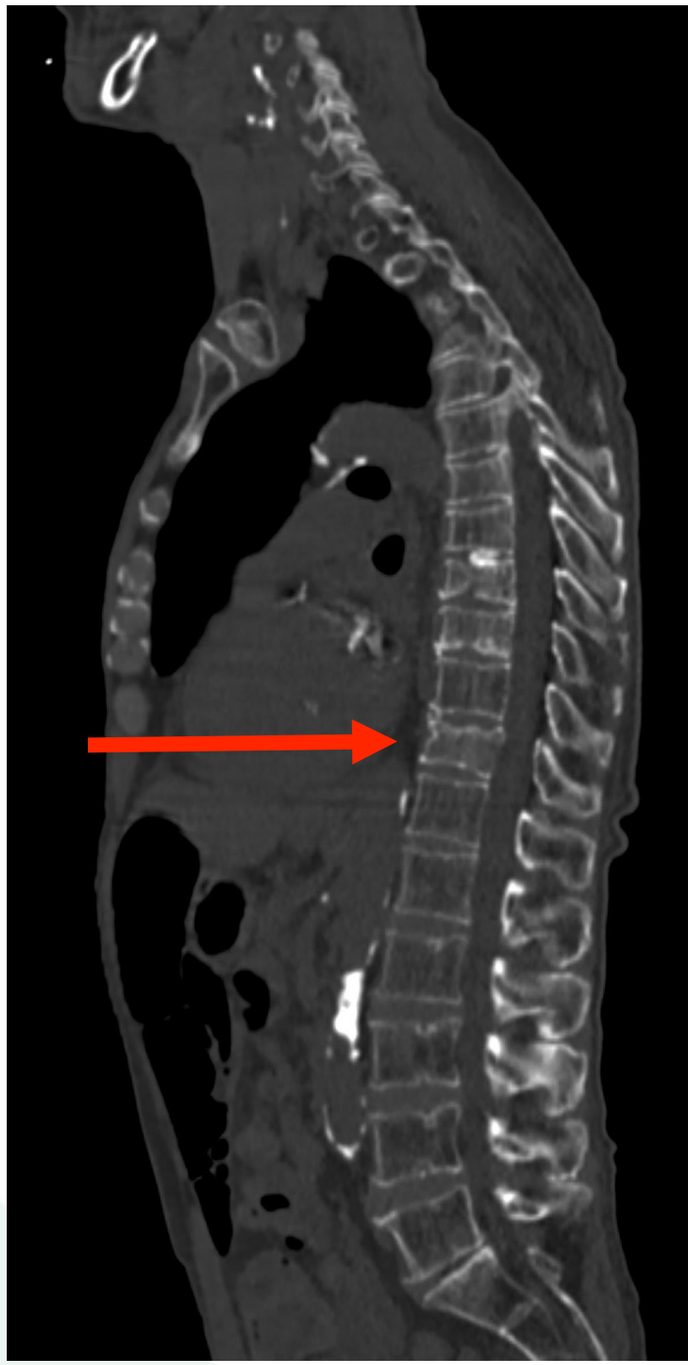
- Vertebral collapse (osteoporosis)
- Inflammation
- Reactive diffuse BM uptake
- Recent bone fracture and surgery

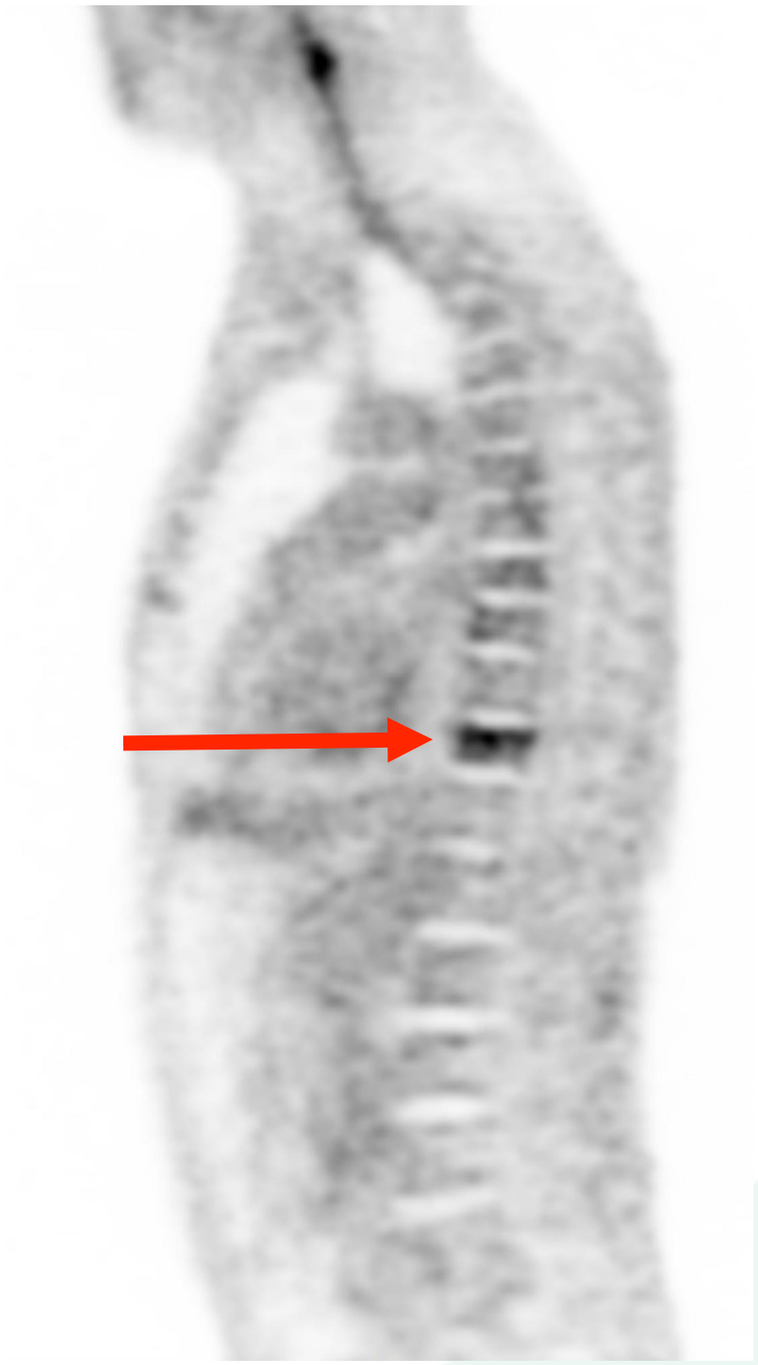


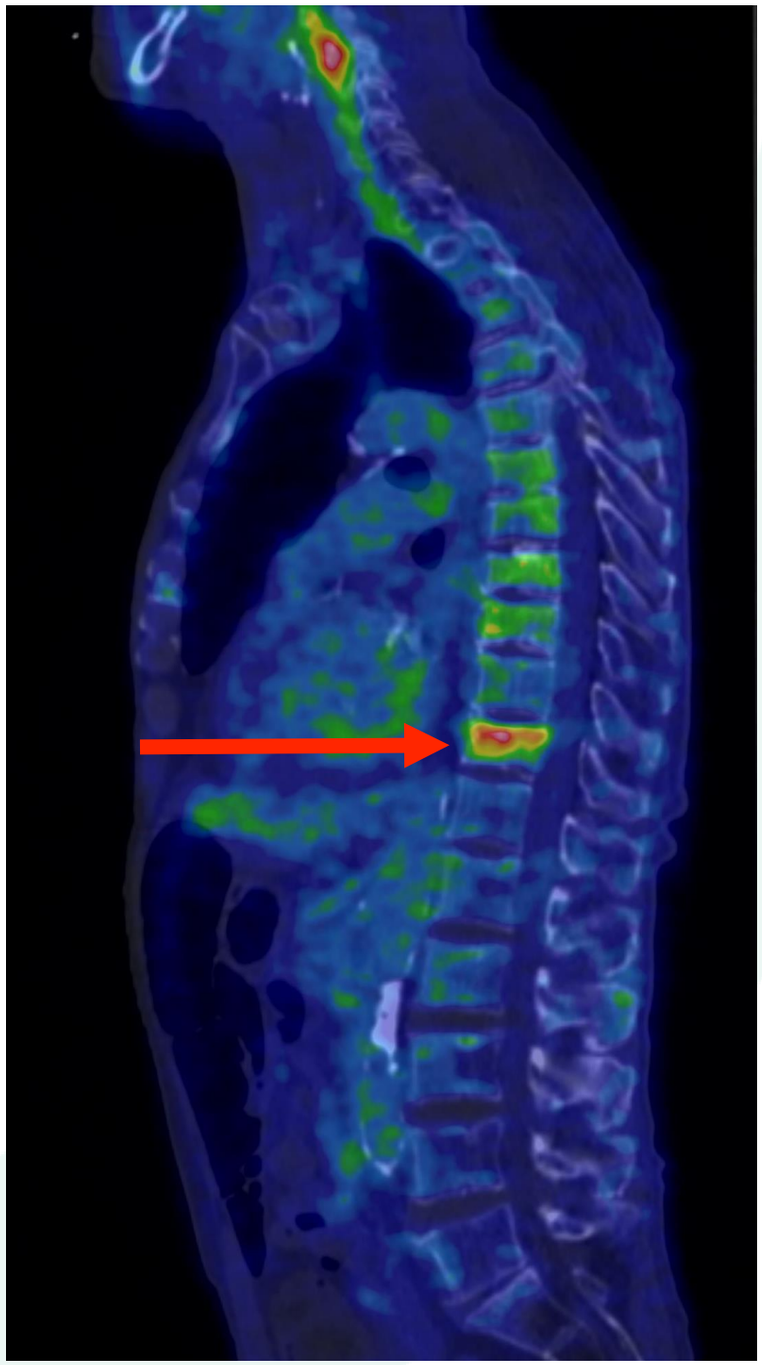
Blood. 2017 Jul 6;130(1):30-34; J Nucl Med. 2018 Nov 2; Rasche et al. Blood. 2017 Jul 6;130(1):30-34.

Vertebral collapse

Patients at increased risk of osteoporosis and vertebral collapse





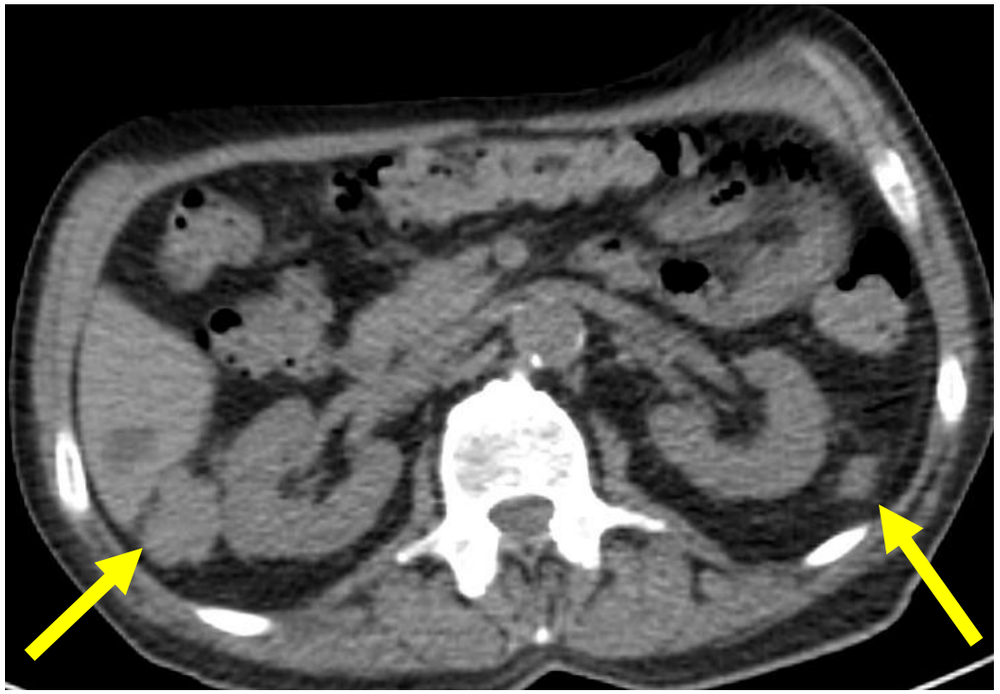


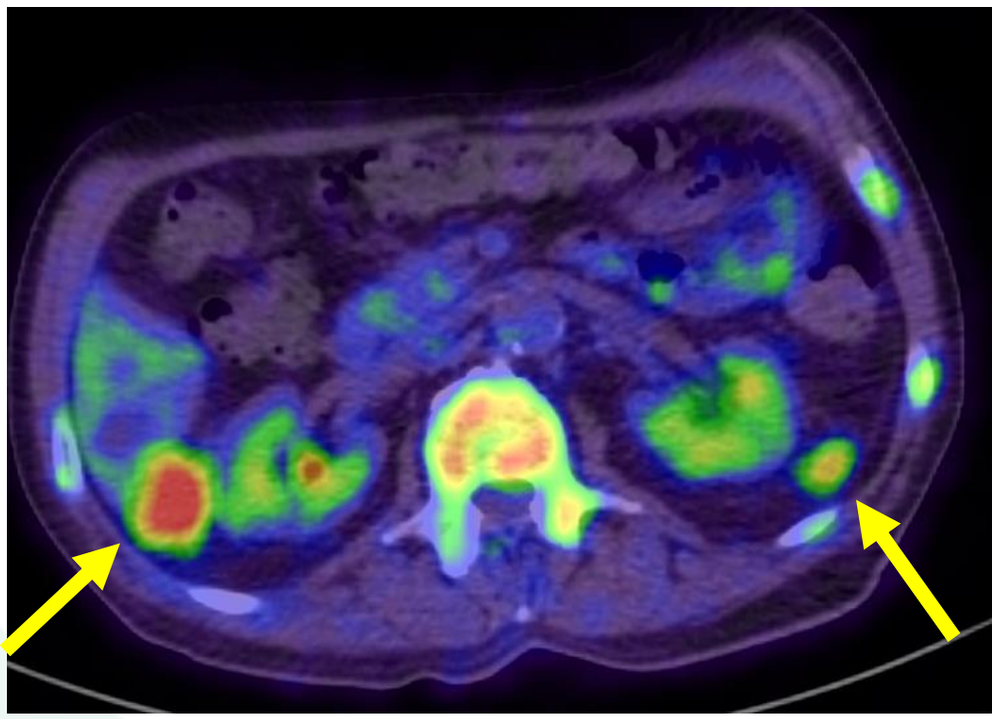
Outline

[^{18}F]FDG PET/CT in multiple myeloma

- Diagnosis
- **Prognostic biomarker**
- Treatment assessment

Extramedullary disease (EMD)





[^{18}F]FDG PET/CT detects EMD with high sensitivity

Nanni C et al. Eur J Nucl Med Mol Imaging. 2016 Mar;43(3):414-21; Eur J Nucl Med Mol Imaging. 2018 May;45(5):712-719.

EMD is an independent prognostic factor

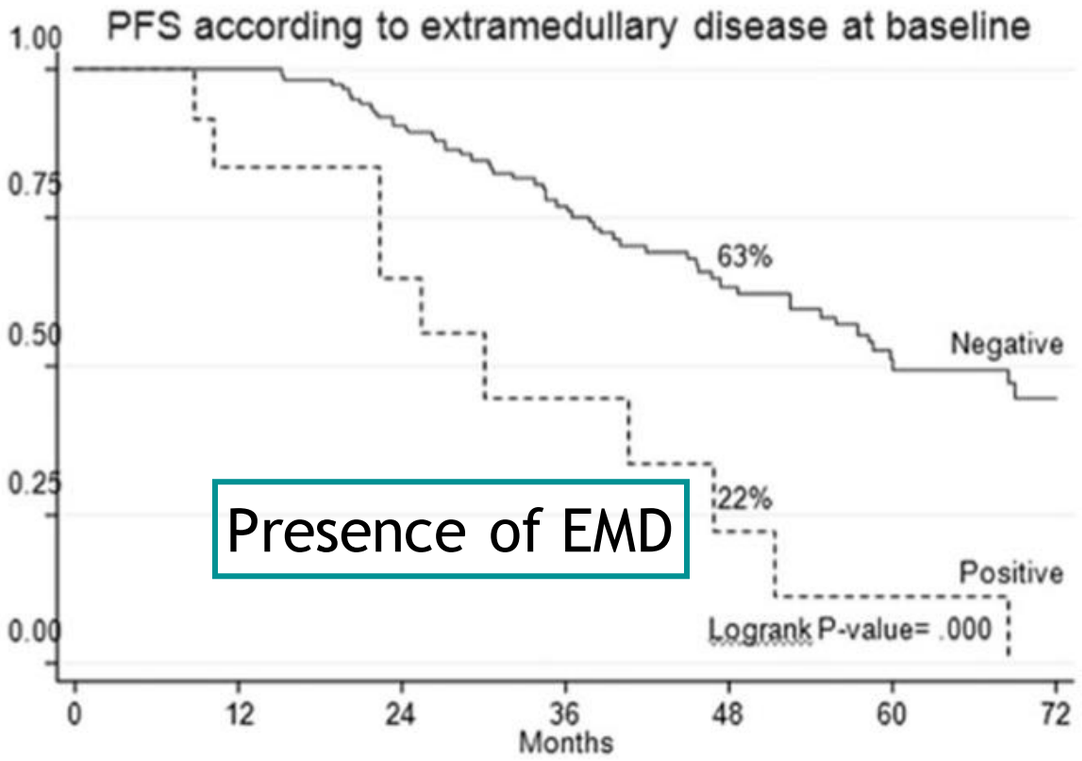


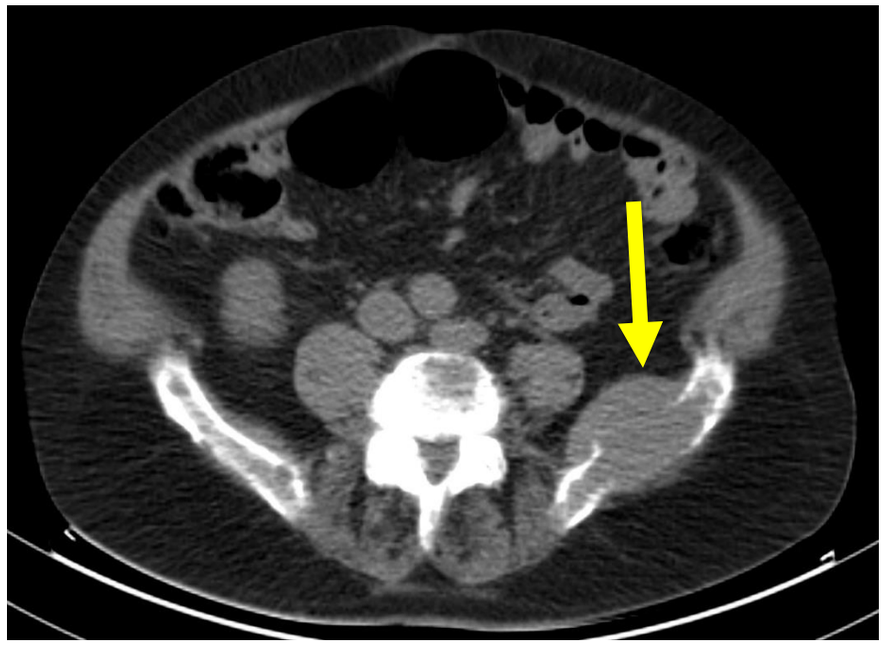
Table 4. Multivariate Cox regression analysis of baseline variables adversely affecting PFS and OS

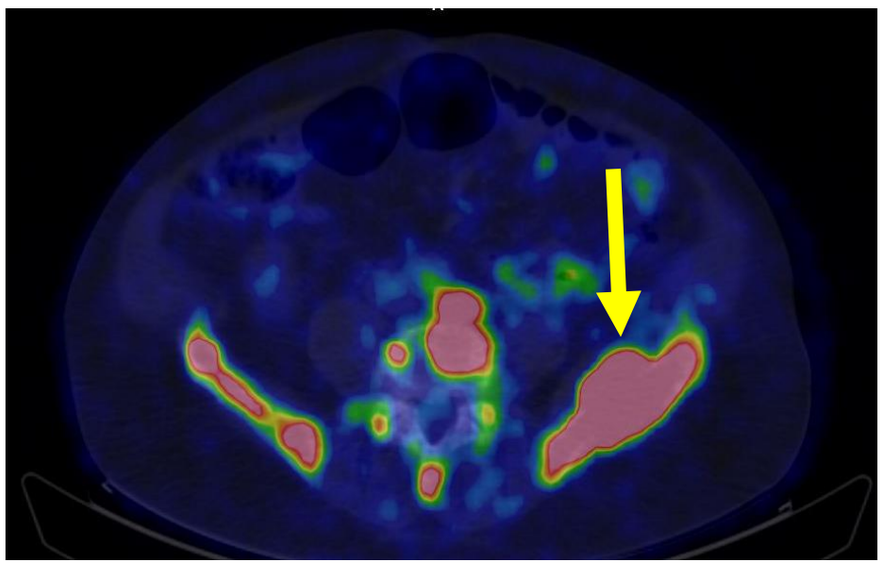
Variables	HR (95% CI)	*P*
PFS		
EMD	5.28 (1.43-19.53)	.013
SUV > 4.2	2.13 (1.10-4.12)	.024
ISS stage II-III	2.12 (1.13-3.98)	.020
del(17p) ± t(4;14)	2.00 (1.03-3.88)	.040
OS		
EMD	9.75 (3.44-27.65)	.000
SUV > 4.2	3.23 (1.35-7.72)	.008

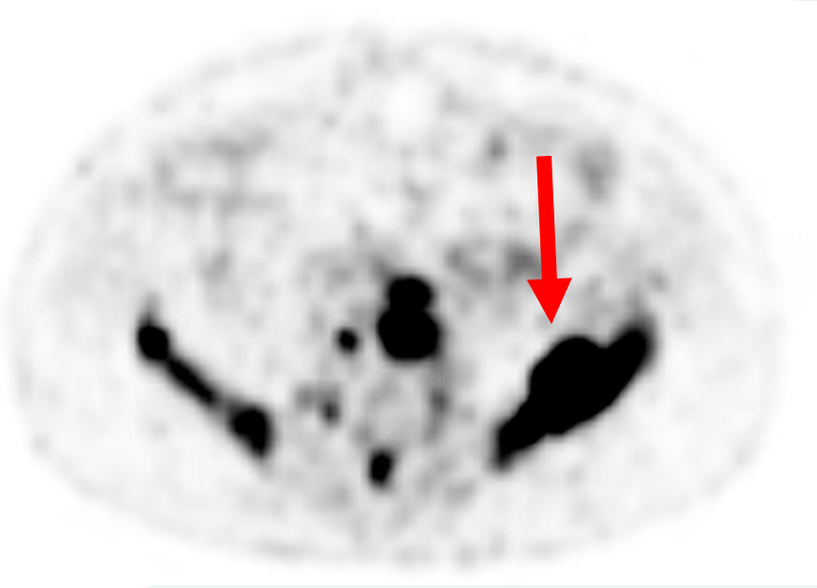
Zamagni E. et al. Blood. 2011 Dec 1;118(23):5989-95

Paramedullary disease (PMD)

Definition: Bone lesion involving surrounding soft tissues with bone cortical interruption

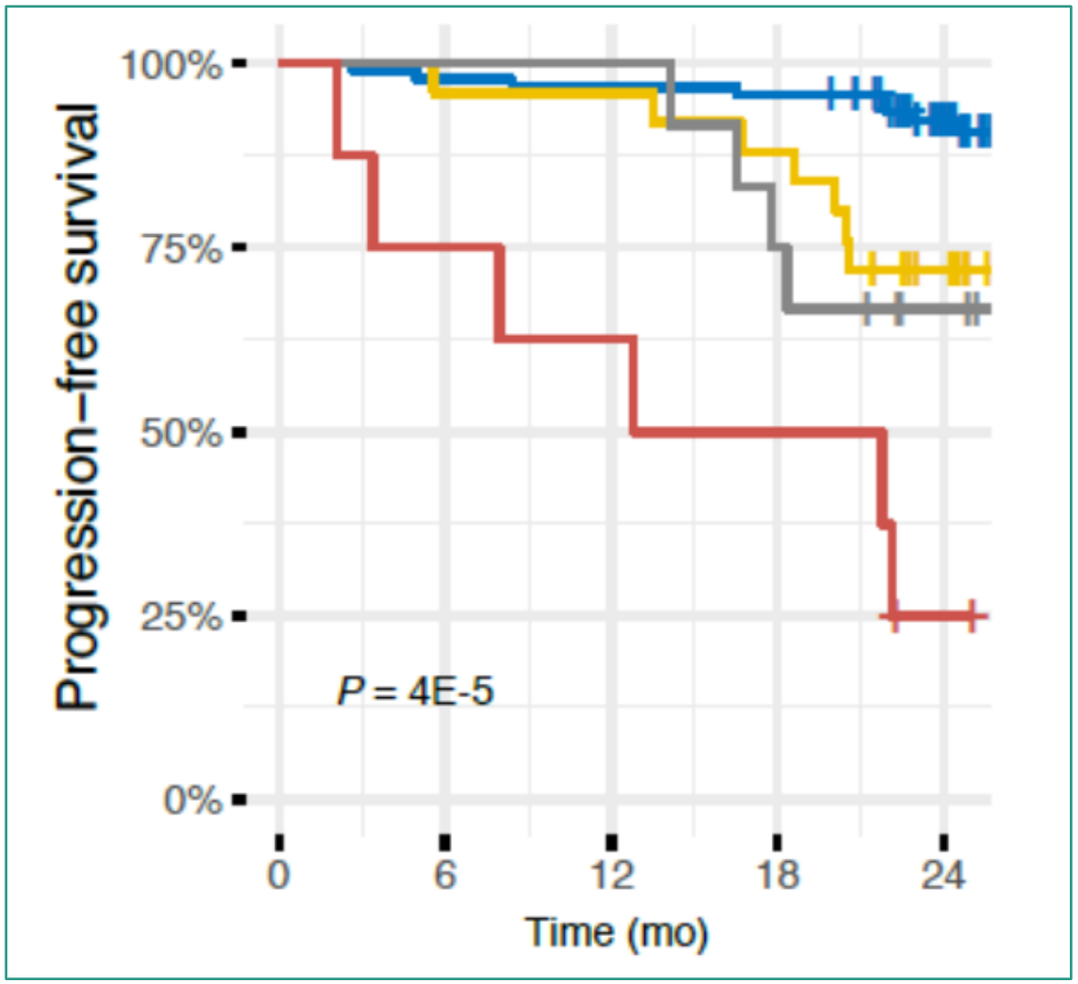




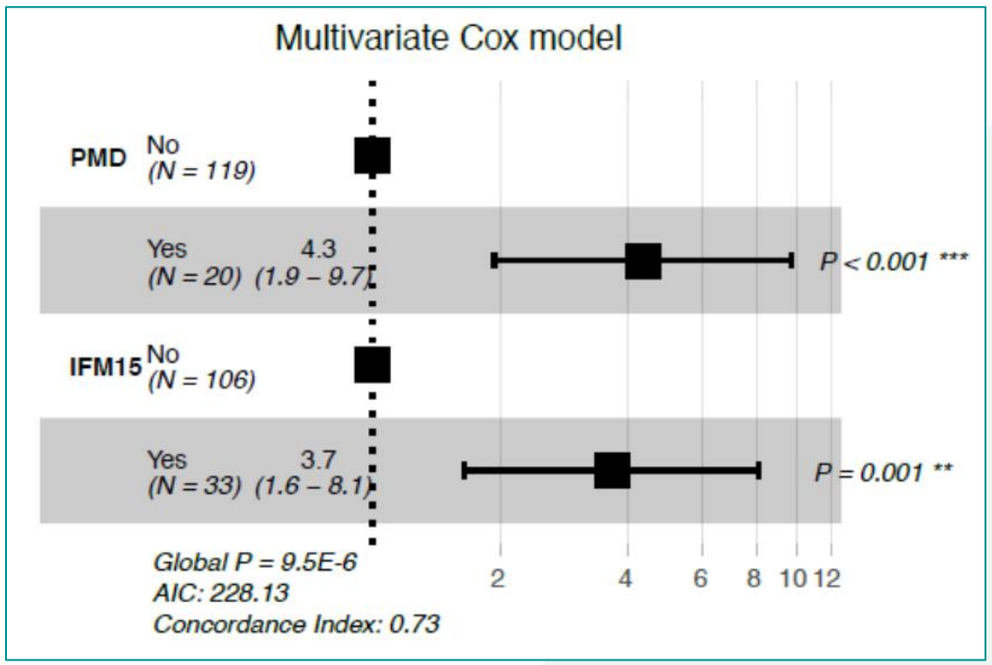


Nanni C et al. Eur J Nucl Med Mol Imaging. 2016 Mar;43(3):414-21; Eur J Nucl Med Mol Imaging. 2018 May;45(5):712-719.

PMD is a prognostic factor



High risk of progression:
[^{18}F]FDG PET paramedullary disease
+ high-risk gene expression signature IFM15

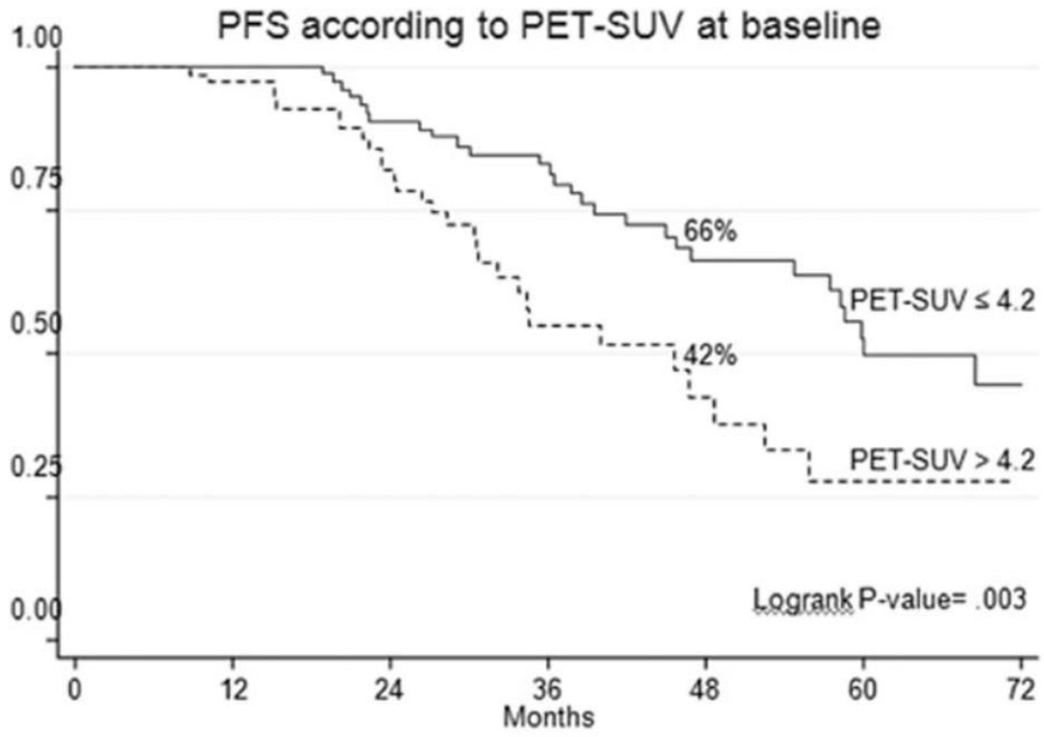


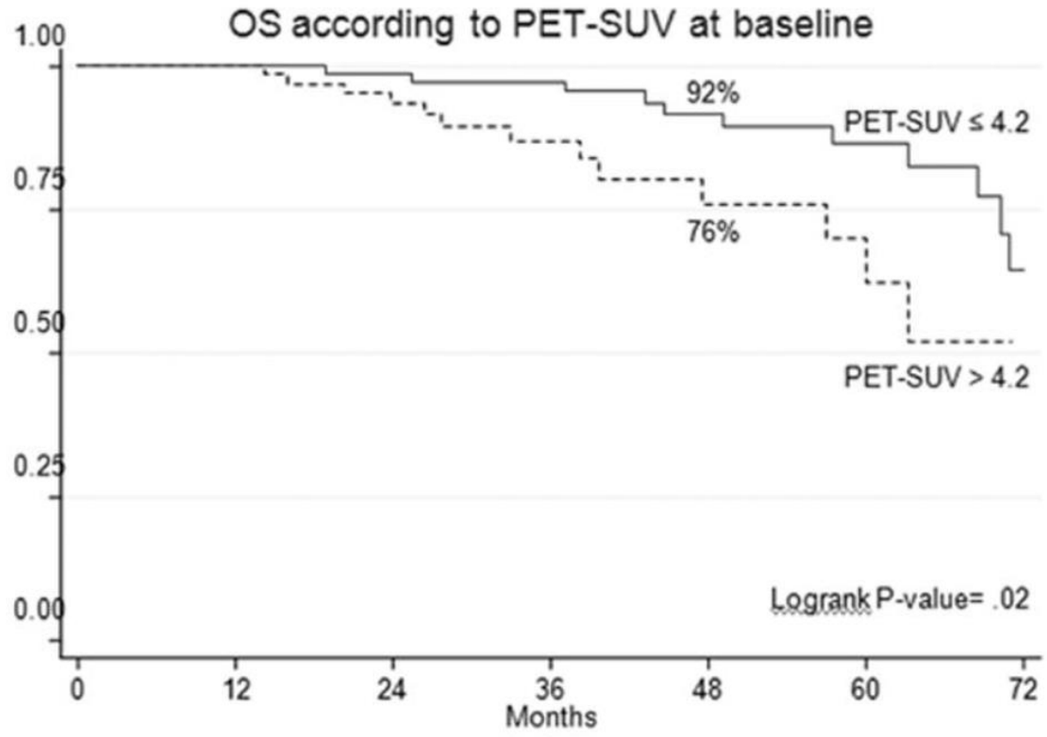
CASSIOPET trial

Alberge JB; Kraeber-Bodere, F. et al. J Nucl Med. 2022 Jan 27.

Baseline [^{18}F]FDG uptake associated with shorter PFS & OS

OS (multivariate analysis)	NDMM	Variable	HR (95%CI), p value
Zamagni, 2011	n = 192	SUVmax > 4.2	3.23 (1.35-7.72), p = 0.008
Michaud-Robert, 2020	n = 227	Bone SUVmax > 7.1	2.020 (1.140-3.592), p = 0.016
Li, 2023	n = 133	SUVmax ≥ 5.3	2.488 (1.387-4.462), p = 0.000*

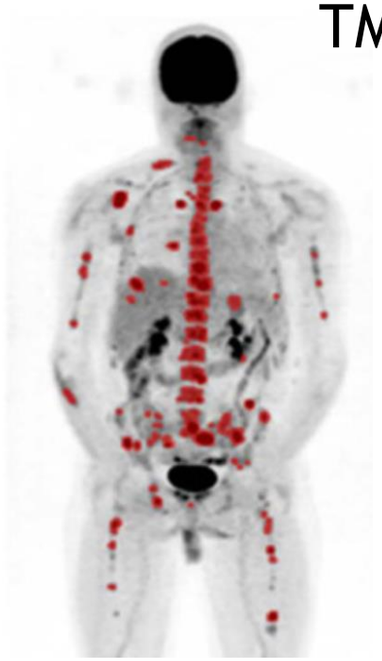




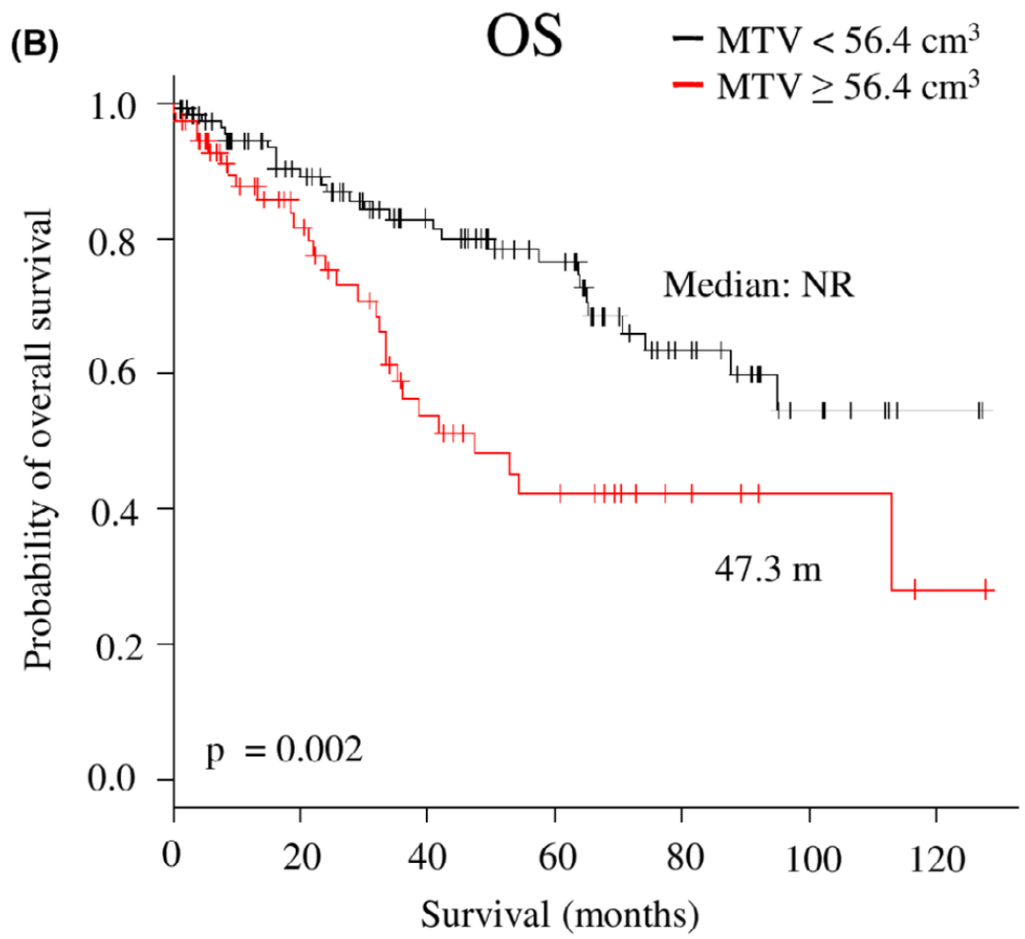
Blood. 2011 Dec 1;118(23):5989-95; Cancers (Basel). 2020 Sep 6;12(9):2532; Eur J Nucl Med Mol Imaging. 2023 May;50(6):1665-1670.

Ongoing trials: Total metabolic tumour volume

TMTV is complementary to R-ISS stage



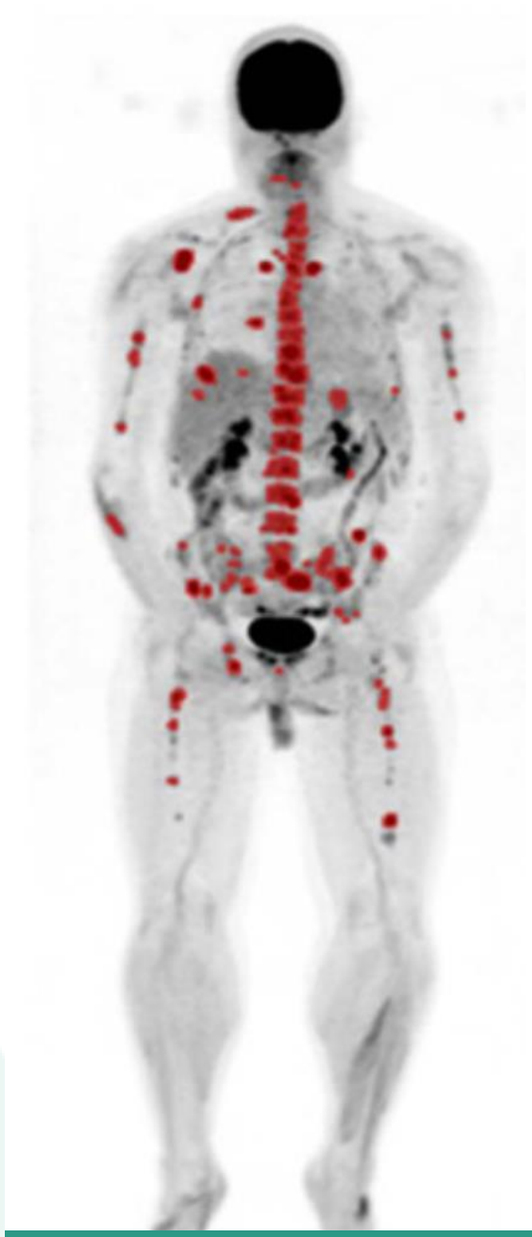
	Variable	Including MTV	
		HR (95% CI)	*P*
PFS	MTV ≥56·4 cm^3	1·53 (1·04, 2·25)	0·03
	TLG ≥166·4 g	–	–
	R-ISS Stage III†	1·45 (0·98, 2·15)	0·06
	High-risk PET/CT findings	1·29 (0·85, 1·95)	0·23
OS	Age ≥75 years	3·24 (1·83, 5·75)	<0·001
	MTV ≥56·4 cm^3	2·10 (1·32, 3·62)	0·007
	TLG ≥166·4 g	–	–
	R-ISS Stage III†	2·65 (1·41, 4·97)	0·002
	High-risk PET/CT findings	1·66 (0·87, 3·16)	0·12



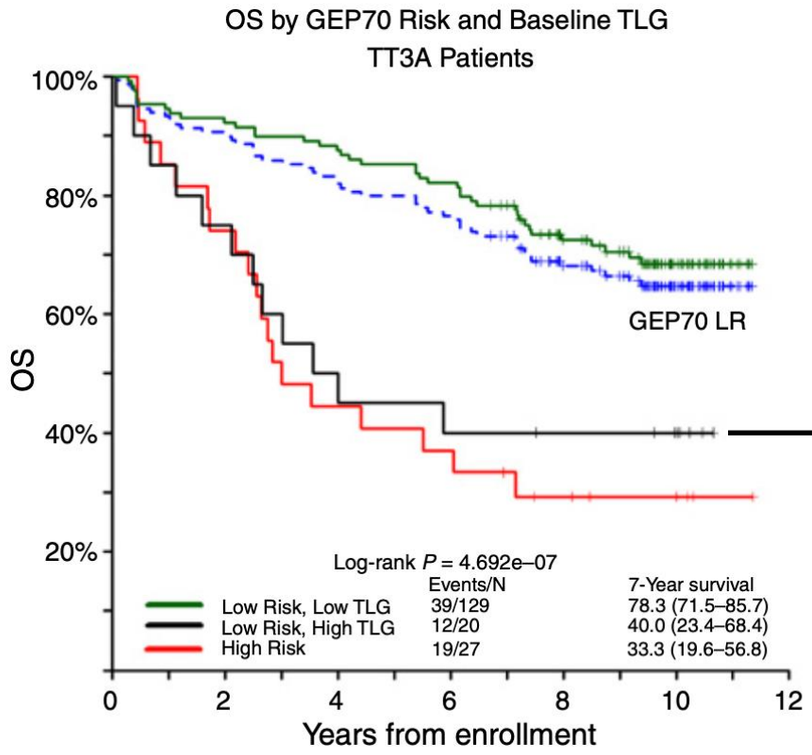
Terao et al. Br J Haematol. 2020 Oct;191(2):223-230.

Ongoing trials: [^{18}F]FDG PET total lesion glycolysis

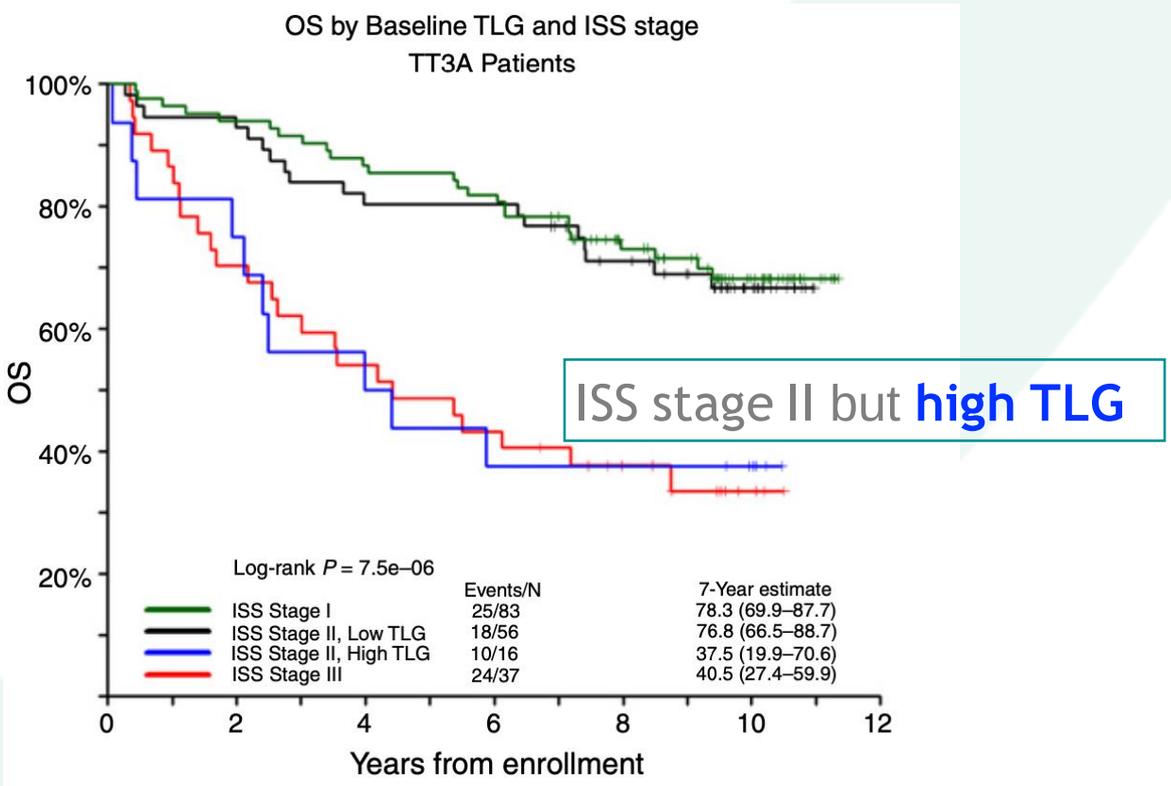
TLG is complementary to gene expression profile GEP70 & ISS stage



n = 192 patients
from the TT3A trial



GEP70 low-risk but **high TLG**

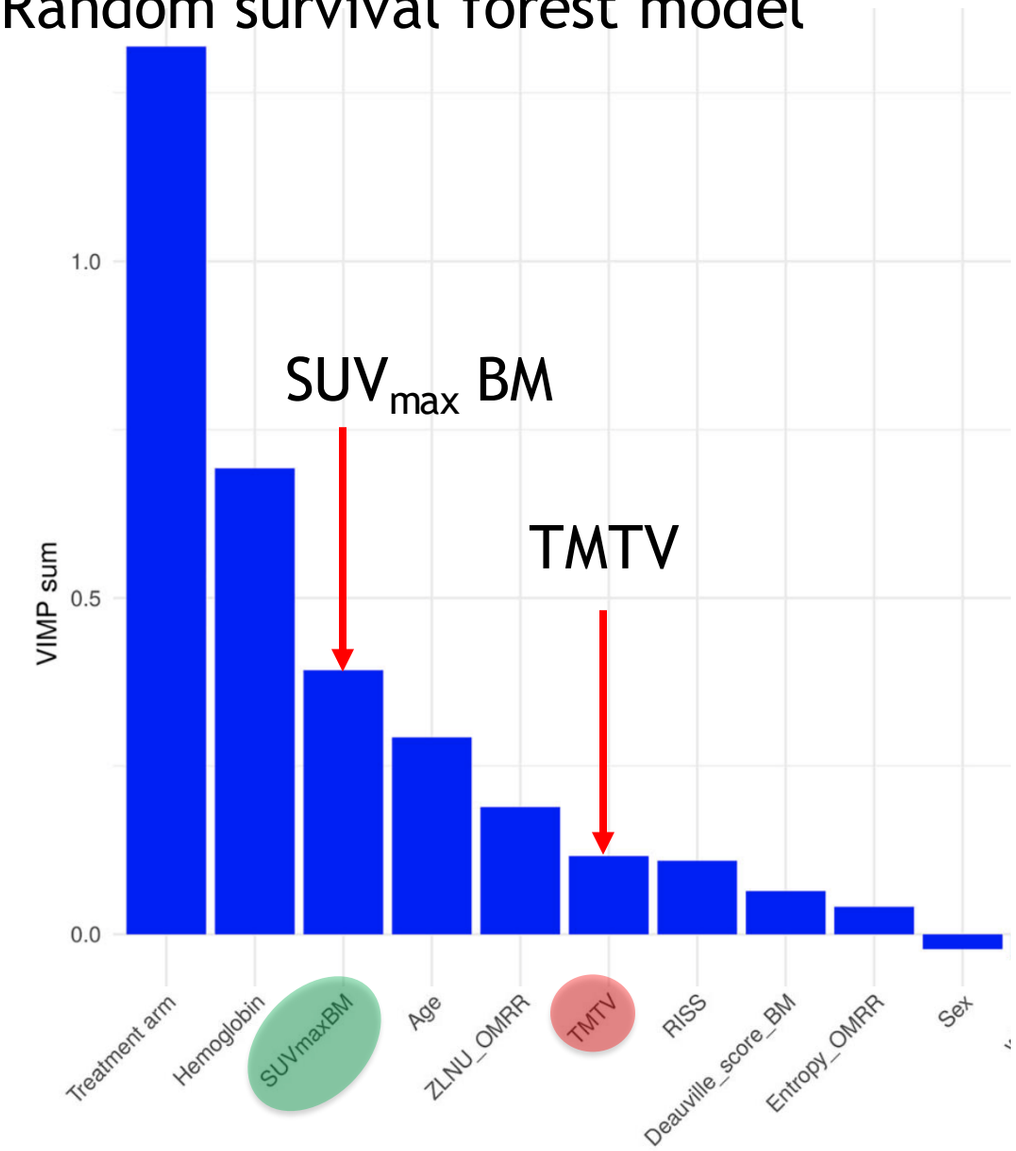


ISS stage II but **high TLG**

McDonald et al. Clin Cancer Res. 2017 Apr 15;23(8):1981-1987.

Ongoing trials
[^{18}F]FDG PET volumetric parameters

Random survival forest model



No volume-derived metabolic parameter (TMTV or TLG) in the final model, suggesting less prognostic importance in this population

n = 139 patients from
IFM/DFCI2009 &
EMN02/HO95 phase III trials

Eur J Nucl Med Mol Imaging. 2021 Apr;48(4):1005-1015.

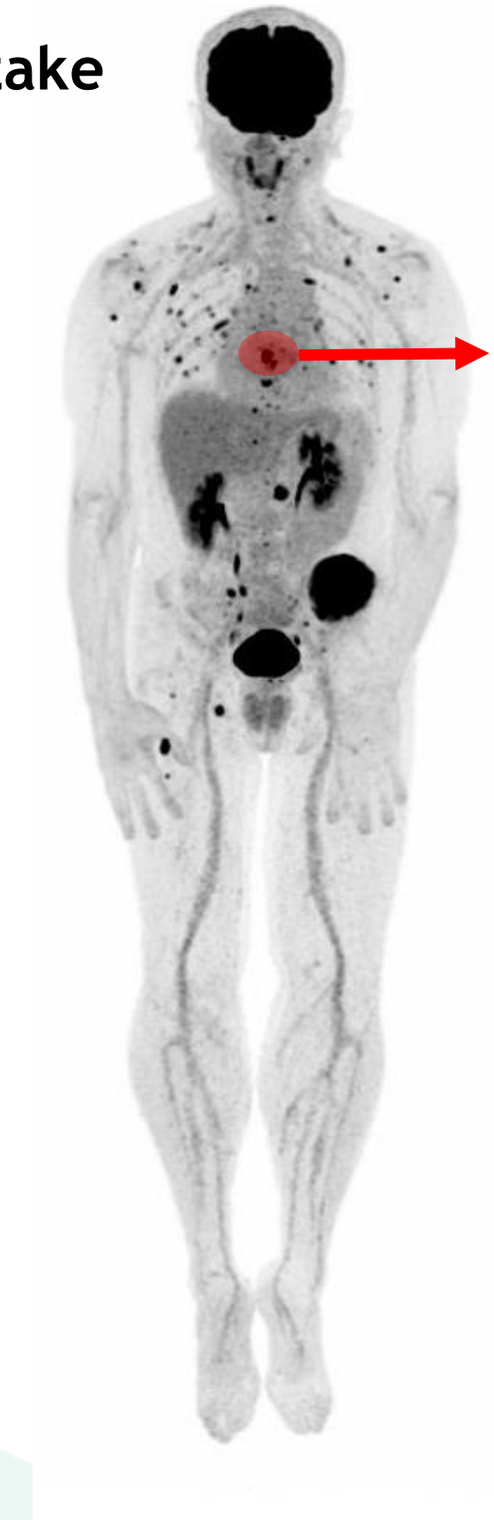
IMPeTUs (Italian Myeloma criteria for PET Use)

Lesion type	Site	Number of lesions (x)	Grading
PET Diffuse	Bone marrow[a]		Deauville five-point scale
Focal (F)	Skull (S)	x = 1 (no lesions)	Deauville five-point scale
	Spine (SP)	x = 2 (1 to 3 lesions)	SUV_{max} (hottest)
	Extraspinal (ExP)	x = 3 (4 to 10 lesions)	
		x = 4 (>10 lesions)	
CT Lytic (L)		x = 1 (no lesions) x = 2 (1 to 3 lesions) x = 3 (4 to 10 lesions) x = 4 (>10 lesions)	+ Size
Fracture (Fr)	At least one		
Paramedullary (PM)	At least one		
Extramedullary (EM)	At least one	N/EN (nodal/extranodal)[b]	Deauville five-point scale

Nanni C et al. Eur J Nucl Med Mol Imaging. 2016 Mar;43(3):414-21; Eur J Nucl Med Mol Imaging. 2018 May;45(5):712-719.

IMPeTUs: Example

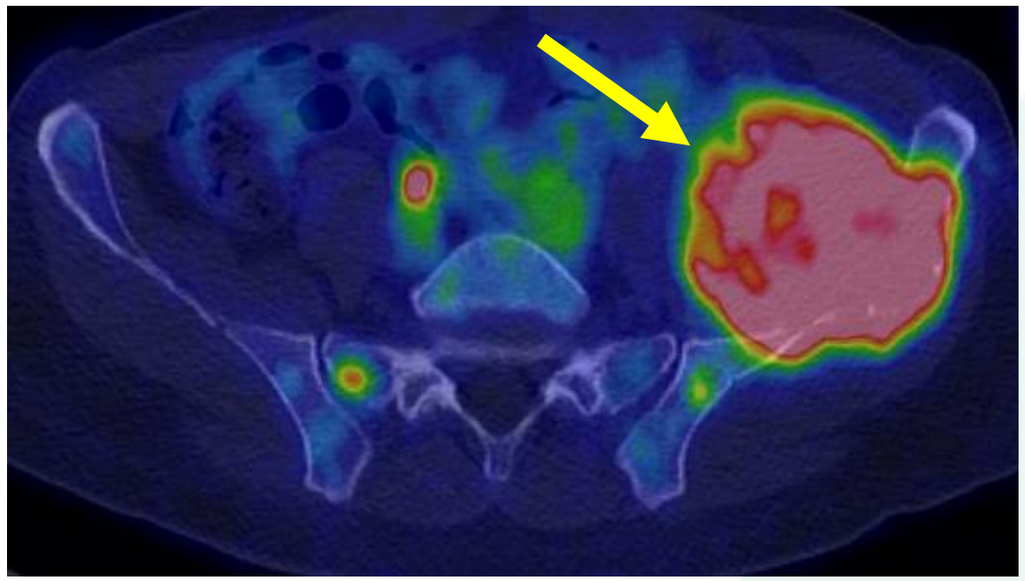
BM uptake
DS 2

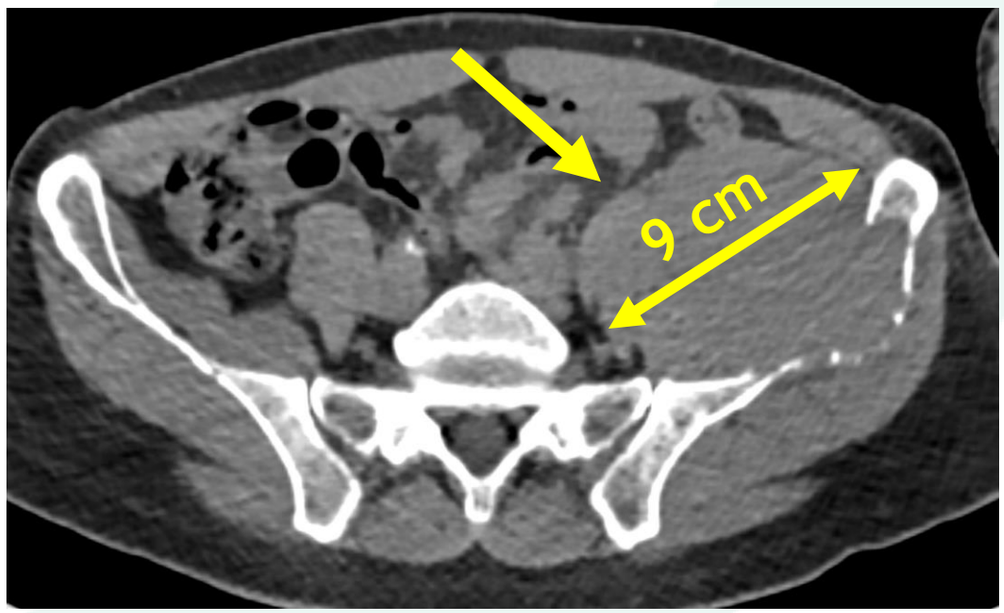


FL
Number > 10

Hottest FL
DS 5
SUV_{max} 13.6

Paramedullary disease





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	Extraspinal (ExP)	x = 3 (4 to 10 lesions)	
		x = 4 (>10 lesions)	
Lytic (L)		x = 1 (no lesions)	
		x = 2 (1 to 3 lesions)	
		x = 3 (4 to 10 lesions)	
		x = 4 (>10 lesions)	
Fracture (Fr)	At least one		
Paramedullary (PM)	At least one		
Extramedullary (EM)	At least one	N/EN (nodal/extranodal)[b]	Deauville five-point scale

BM DS 2

FL DS 5
SUV_{max} 13.6

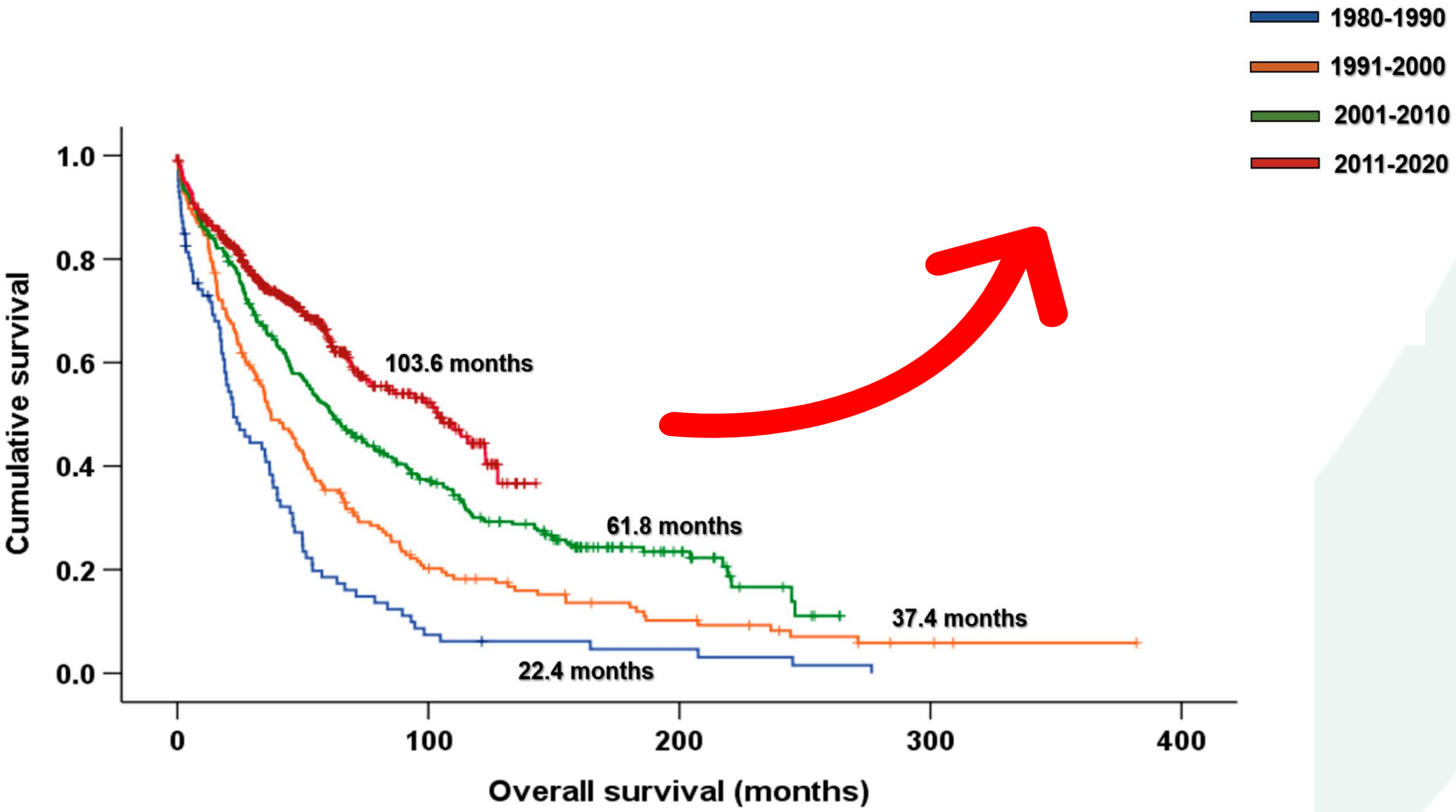
Nanni C et al. Eur J Nucl Med Mol Imaging. 2016 Mar;43(3):414-21; Eur J Nucl Med Mol Imaging. 2018 May;45(5):712-719.

Outline

[^{18}F]FDG PET/CT in multiple myeloma

- Diagnosis
- Prognostic biomarker
- **Treatment assessment**

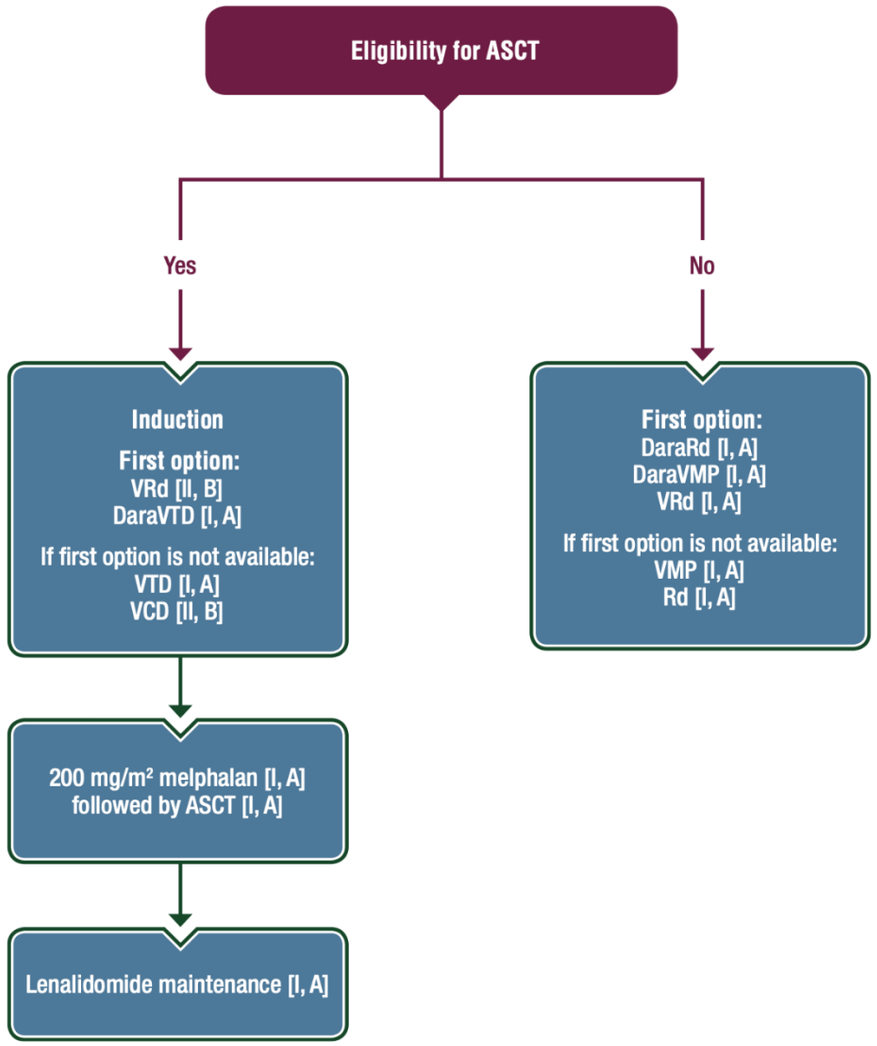
Therapeutic strategies improved survival in MM



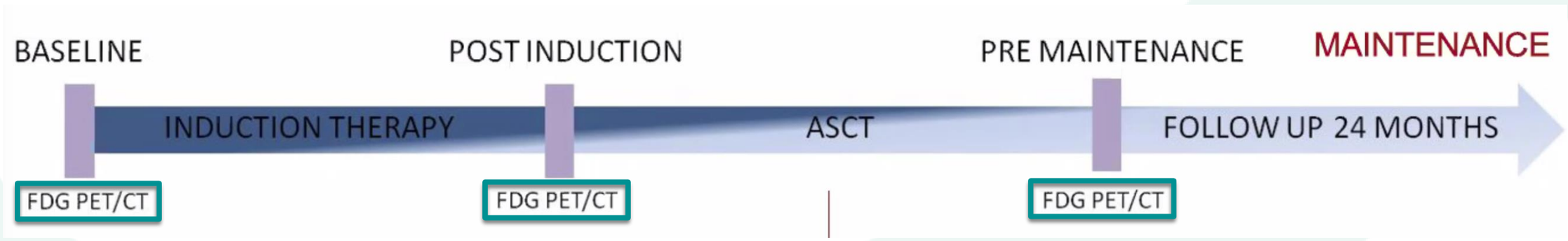
2011-2020 *vs*. 1980-1990: HR 3.5 [95% CI, 2.5-4.4]; *P*=0.000
2011-2020 *vs*. 1991-2000: HR 2.1 (95% CI, 1.7-2.7]; *P*=0.000
2011-2020 *vs*. 2001-2010: HR 1.4 [95% CI, 1.2-1.8]; *P*=0.001

Cancers (Basel). 2023 Mar 2;15(5):1558.

General therapeutic flow chart in MM patients



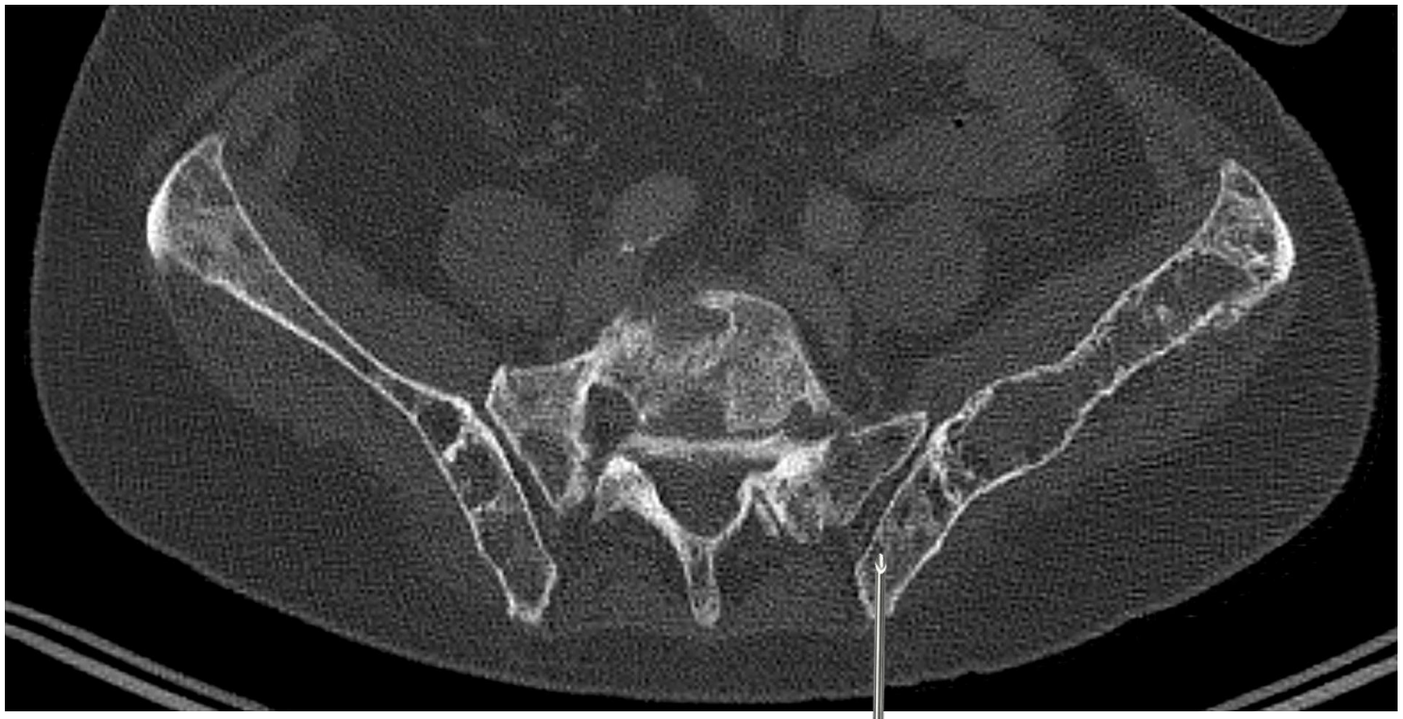
ASCT = Autologous stem cell transplantation

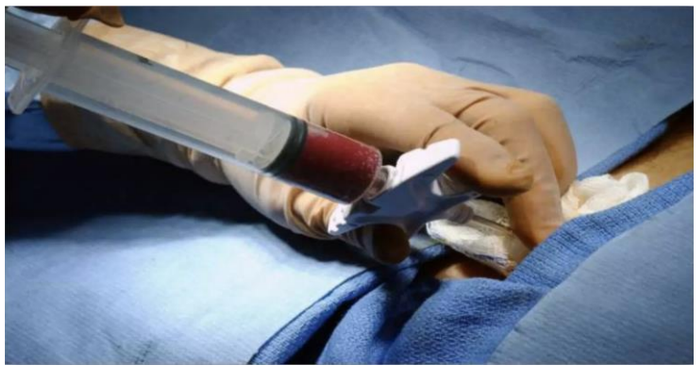


C. Nanni, ESMIT webinar on Spotlight on FOCUS Meeting 2022; EHA-ESMO Clinical Practice Guidelines. Ann Oncol. 2021 Mar;32(3):309-322.

Minimal Residual Disease Status

Post-treatment single BM biopsy





MRD status
Flow cytometry or
next generation sequencing (NGS)
High sensitivity up to 10^{-5} and 10^{-6}

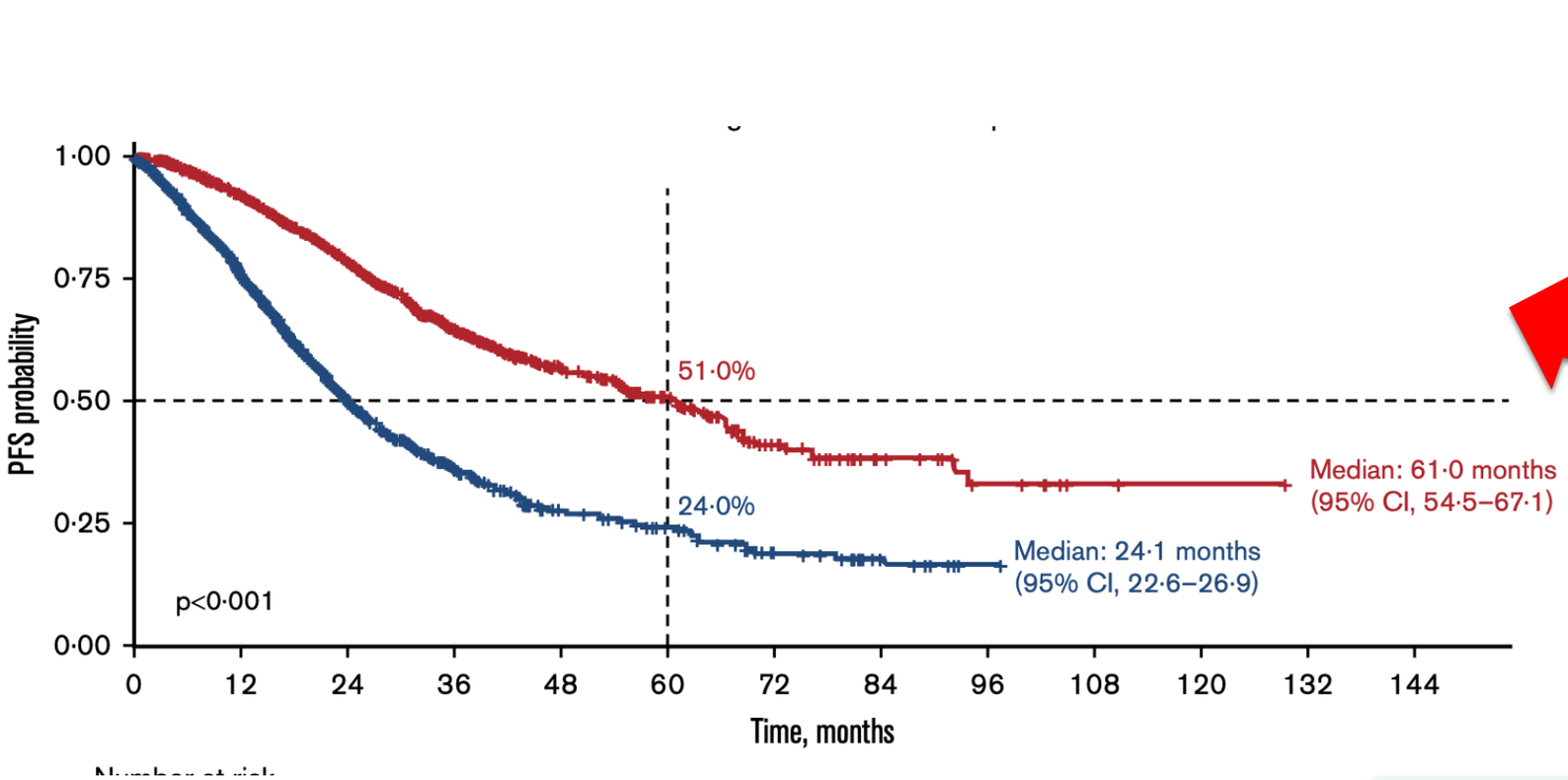
Cavo et al. Lancet Oncol 2017; 18: e206–17; Kumar et al. Lancet Oncol 2016; 17: e328-46

Depth of response to therapy

IMWG response criteria

PR → VGPR → CR → sCR → MRD-

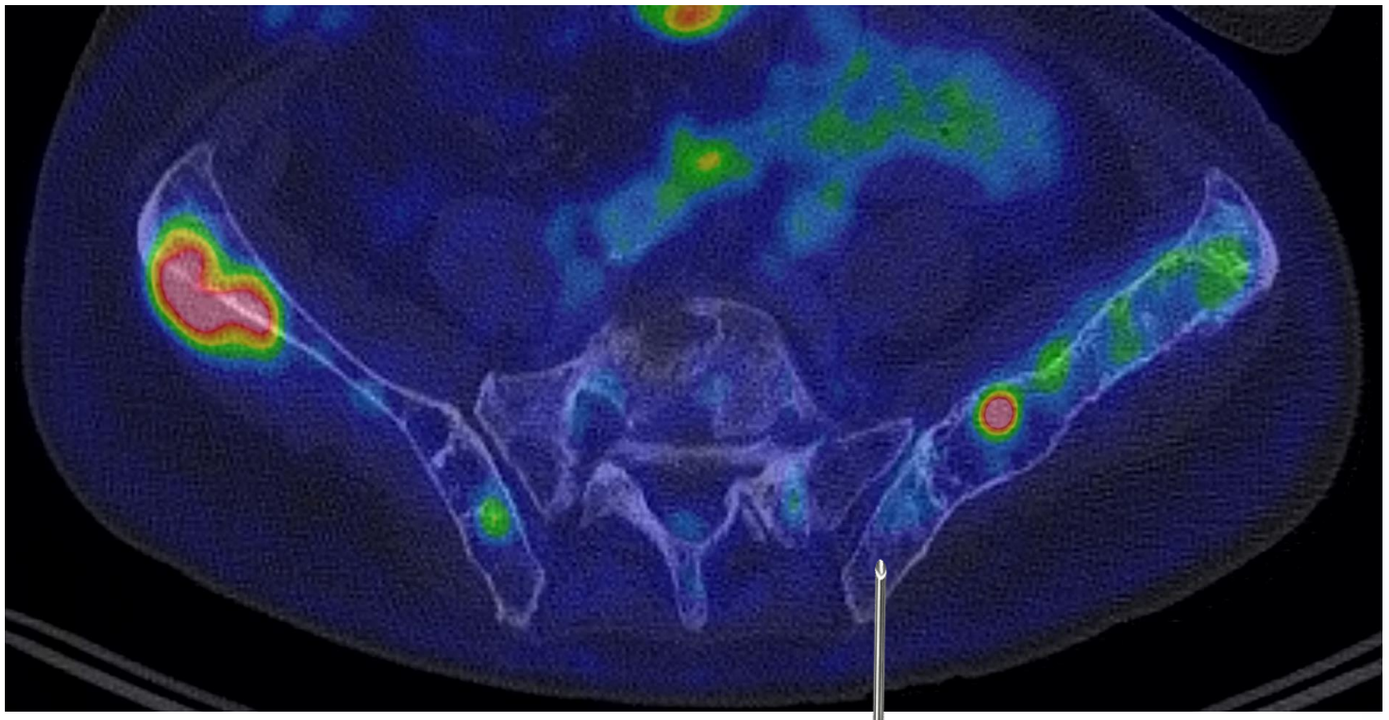
Negative
Minimal Residual Disease

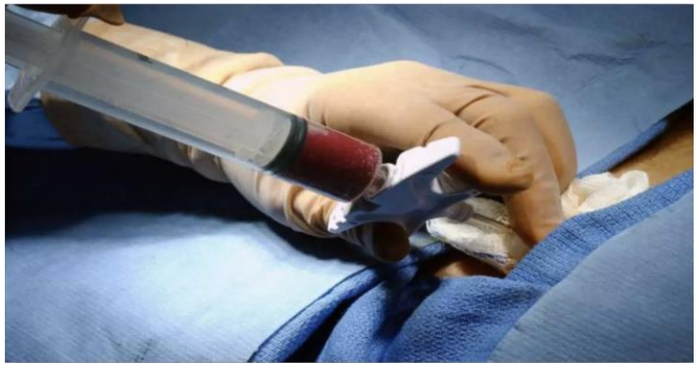


Transplant eligible newly diagnosed MM

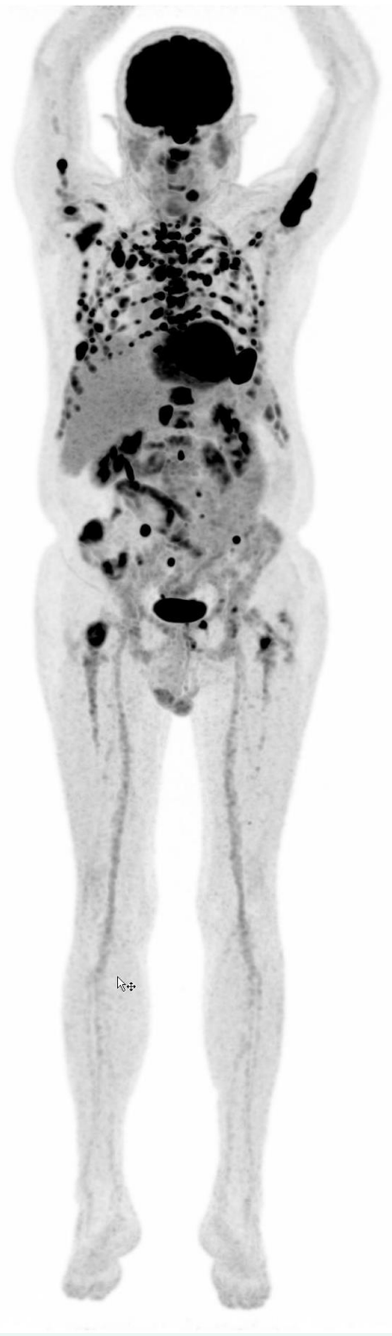
The Lancet Oncology. 2016;17(8):e328-e346; Blood Adv. 2020 Dec 8;4(23):5988-5999.

Whole body [^{18}F]FDG PET/CT to confirm MRD negativity outside the BM

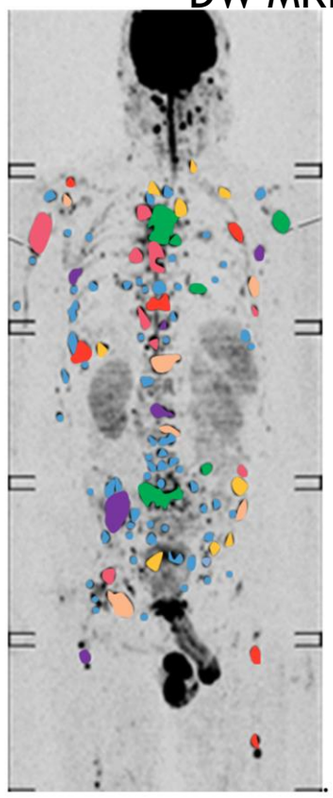




Patchy BM infiltration
& pesrsitance of EMD



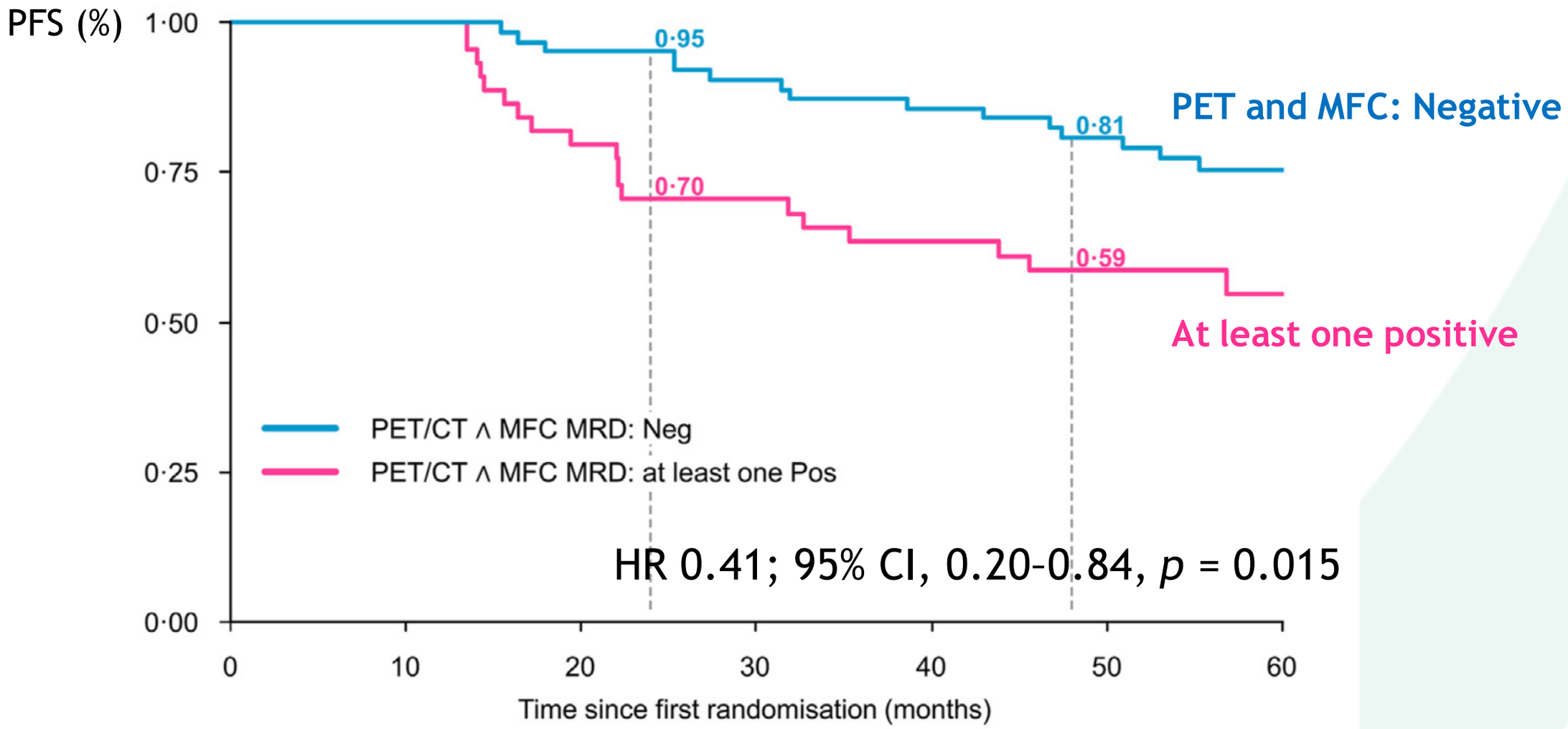
DW MRI



Genomic spatial heterogeneity

Int J Mol Sci. 2019 Mar 12;20(5):1248

[^{18}F]FDG PET/CT CMR + negative BM MFC



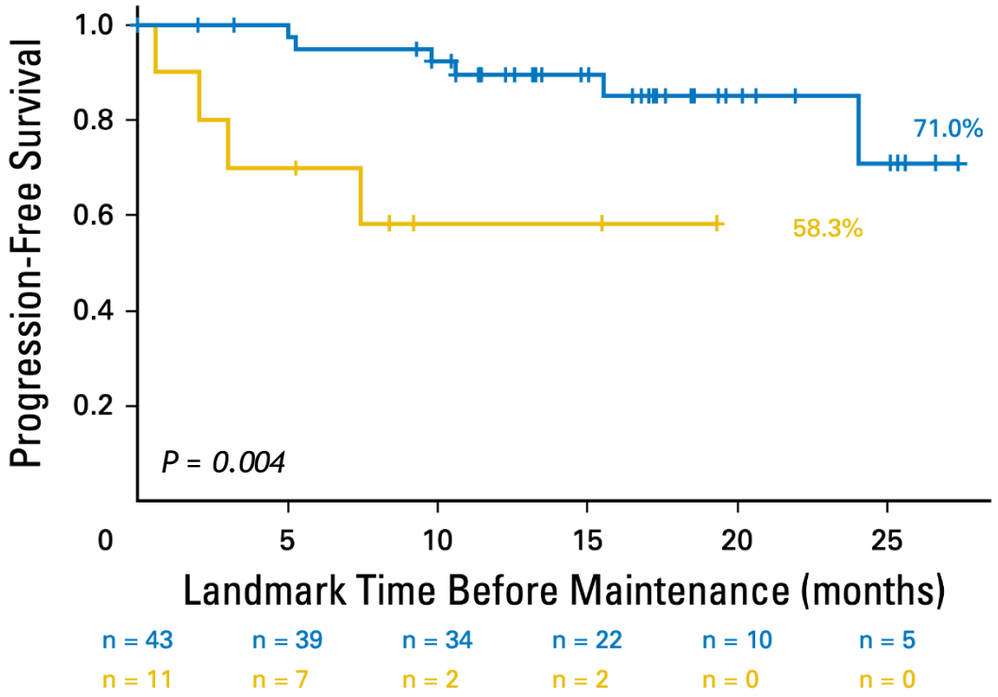
Imaging substudy of FORTE trial
n = 109/474 transplant-eligible NDMM

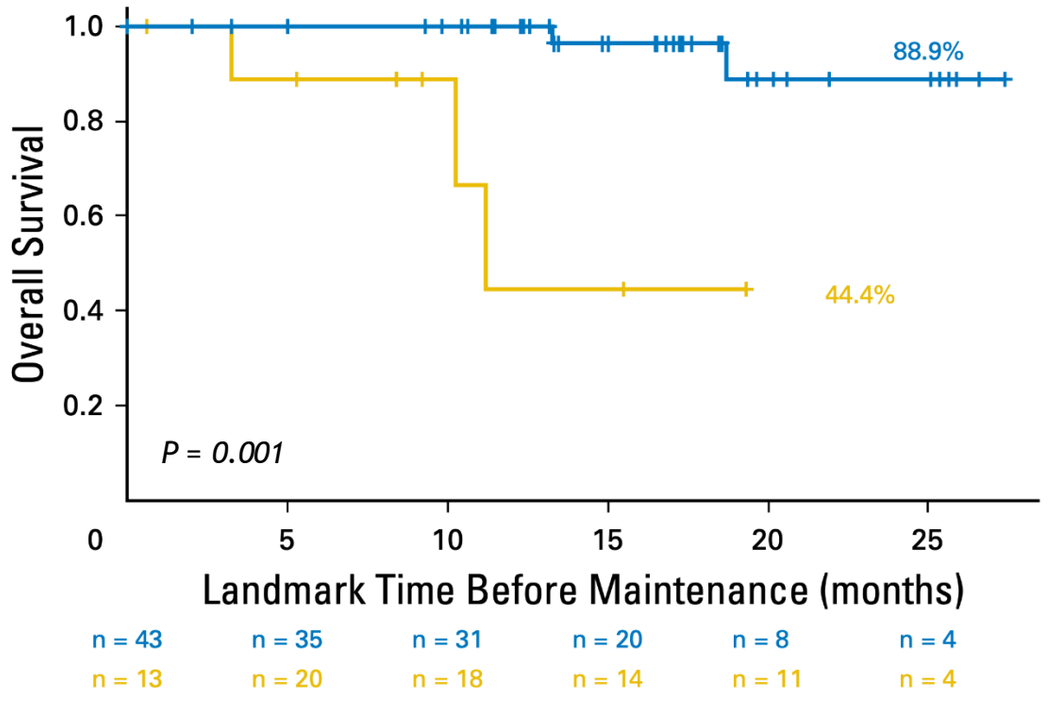
MFC = multiparameter flow cytometry (MFC) at 10^{-5}

EClinicalMedicine. 2023 Jun 9;60:102017.

Whole-body [^{18}F]FDG PET/CT to monitor therapy response

[^{18}F]FDG PET normalization after ASCT is a prognostic factor for PFS and OS



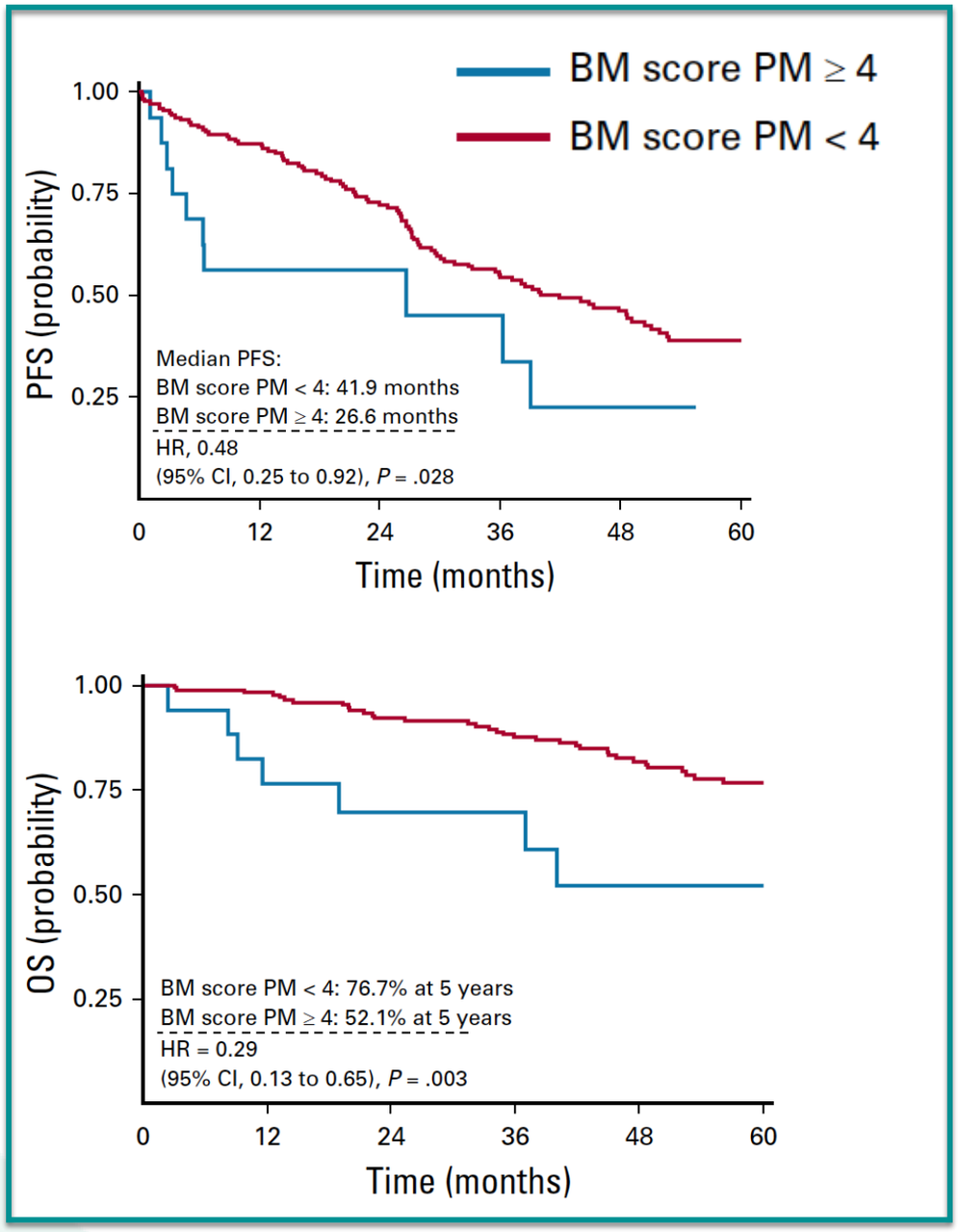


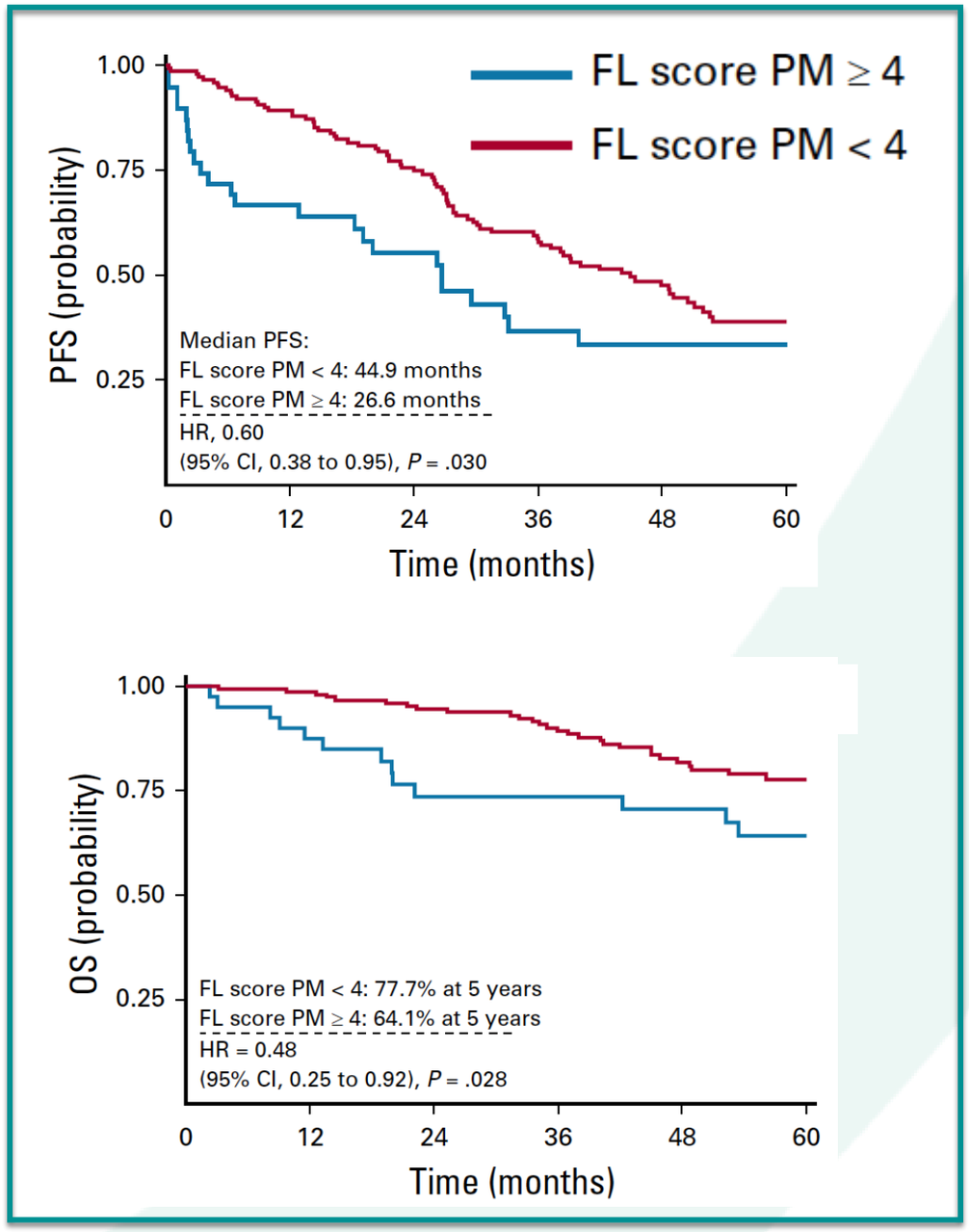
Note MRI: Low rate of “early” normalisation and no association with survival

IMAJEM (IFM/DFCI 2009 Trial) Moreau et al. J Clin Oncol. 2017 Sep 1;35(25):2911-2918;
Cavo et al. Lancet Oncol 2017; 18: e206-17; Kumar et al. Lancet Oncol 2016; 17: e328-46

5-point Deauville scale score for metabolic response

Complete Metabolic Response = DS score 1-3





n = 228 pts
French IFM/DFCI2009 + Italian EMN02/HO95 trials

PM = Pre-maintenance

Zamagni et al. J Clin Oncol. 2021 Jan 10;39(2):116-125.

IMPeTUs classification
[^{18}F]FDG PET/CT for therapy response assessment

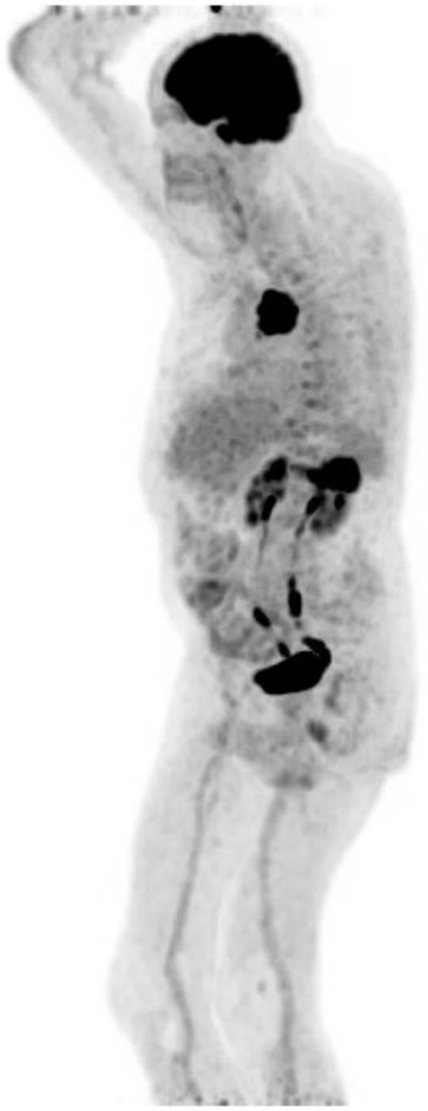
Complete MR	No lesion uptake higher than the liver activity (DS score 1-3)*
Partial MR	Persistent lesion(s) with uptake > liver activity (DS score 4-5) with decrease in number and/or activity compared to baseline*
Stable MD	No significant change in BM/FLs compared with baseline
Progressive MD	New FL(s) compared with baseline consistent with MM

* lesions present at baseline: BM; FLs; EMD and PMD

Note: If baseline [^{18}F]FDG PET is negative, criteria do not apply

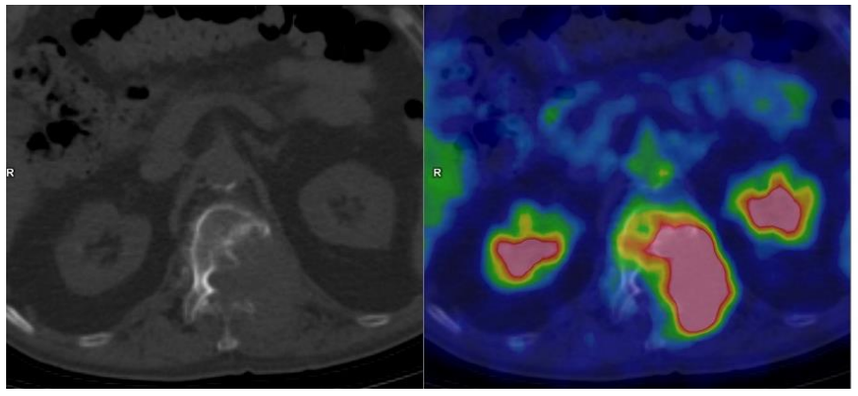
J Clin Oncol. 2021 Jan 10;39(2):116-125.

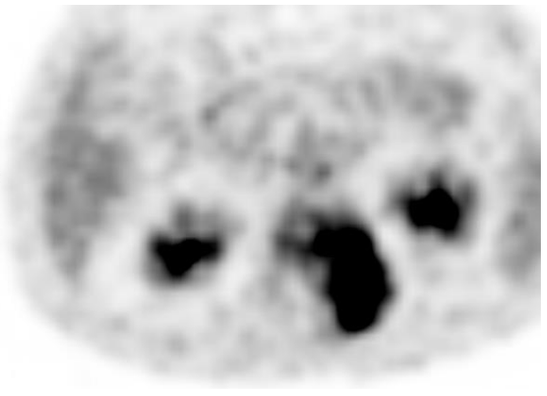
Case of [^{18}F]FDG PET normalisation

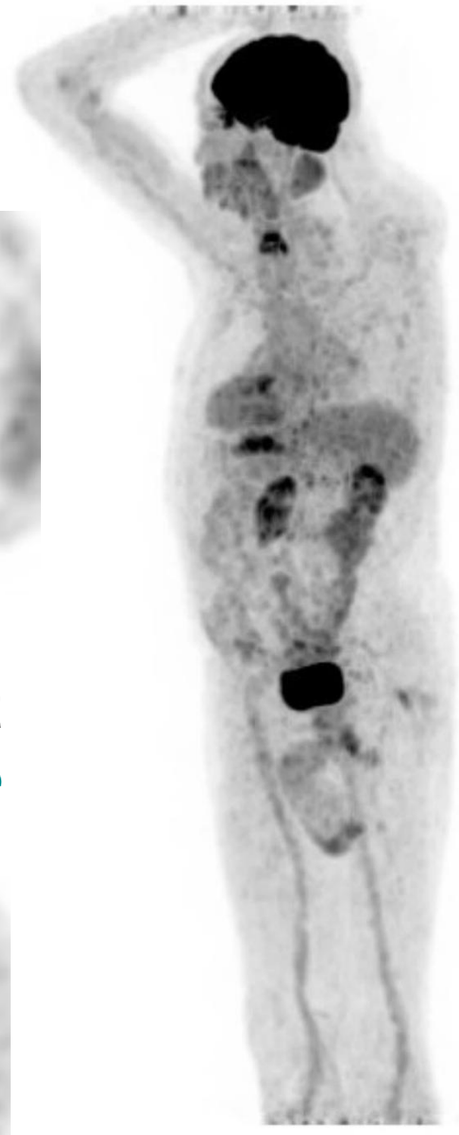


Baseline

n = 4 FL; **DS score 5 + PMD**

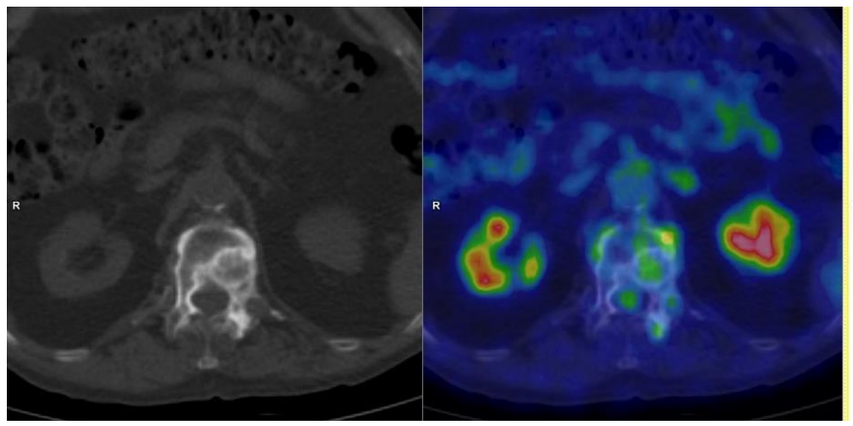






Post-treatment

DS score 2 : Complete metabolic response

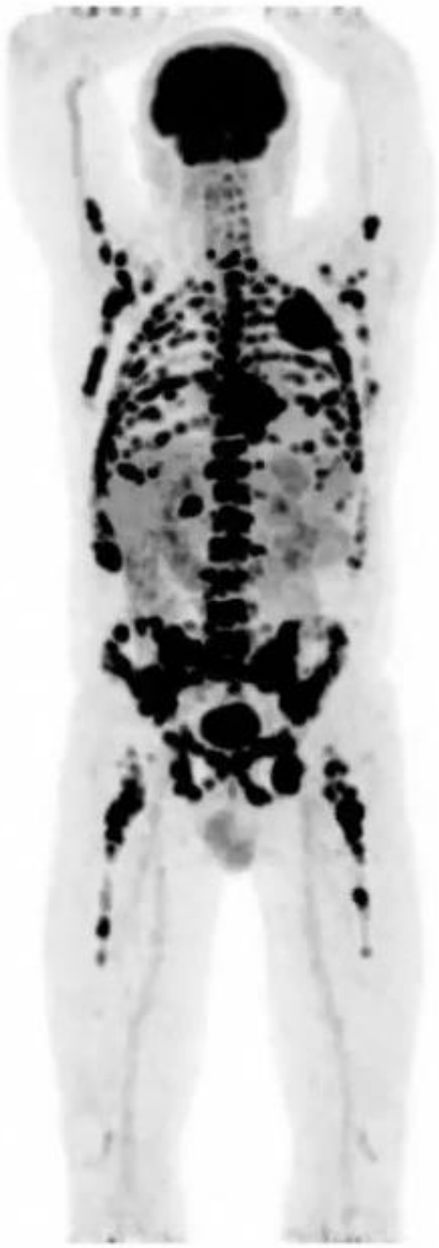


88 y-o man
MM IgG lambda

Rev-Dex
Zoledronic Acid

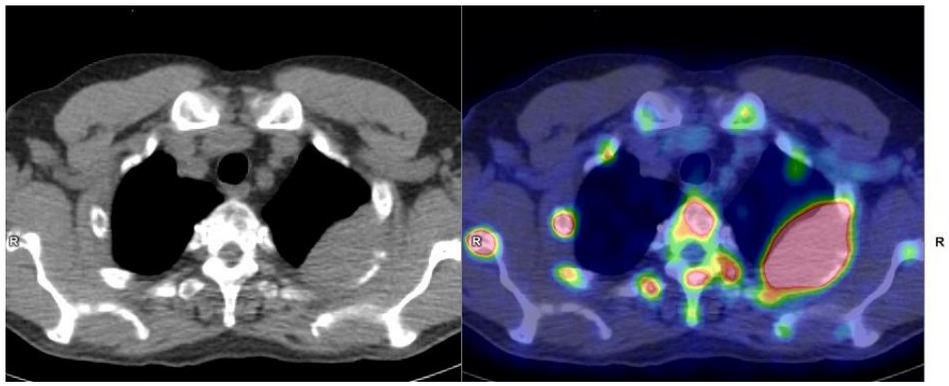
Biological CR
+ FDG PET CR

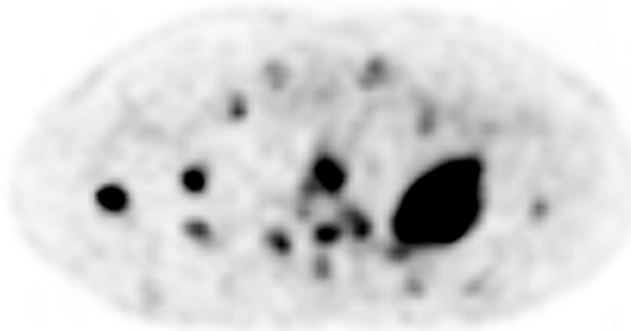
Case of persistent positive [^{18}F]FDG PET/CT

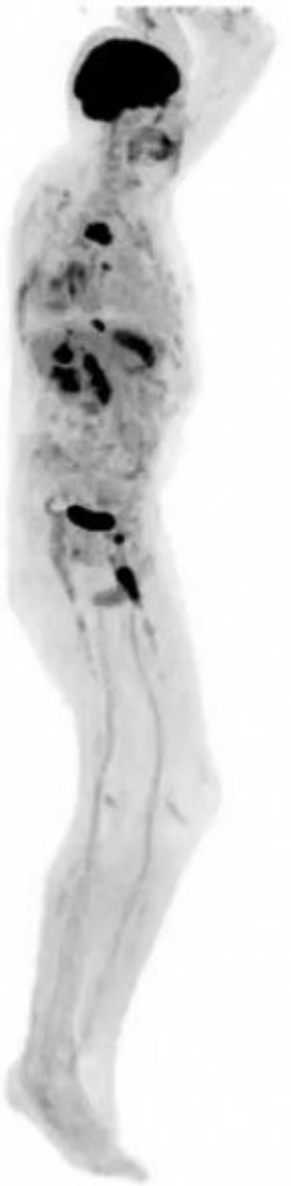


Baseline

Extensive BM involvement FL>10; **DS score 5 + PMD**

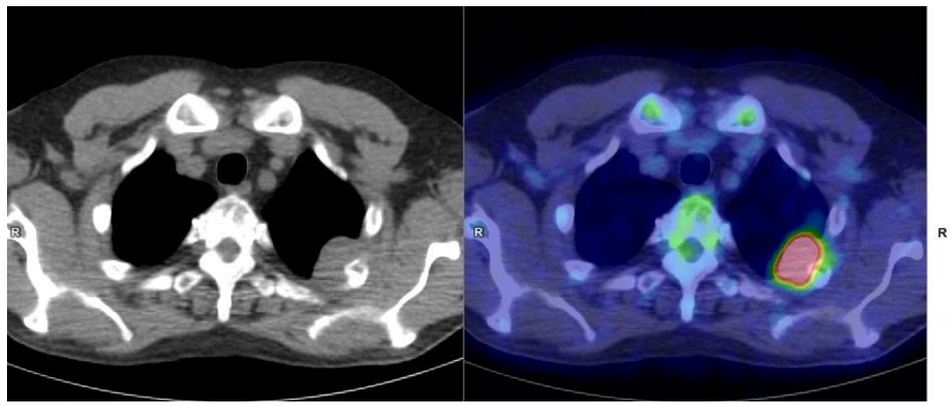


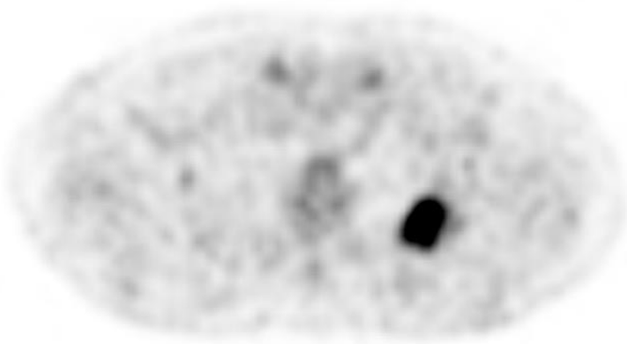




Post-induction

DS score 5: Partial metabolic response





49 y-o man
MM IgA kappa;
ISS 3; t(4;14)

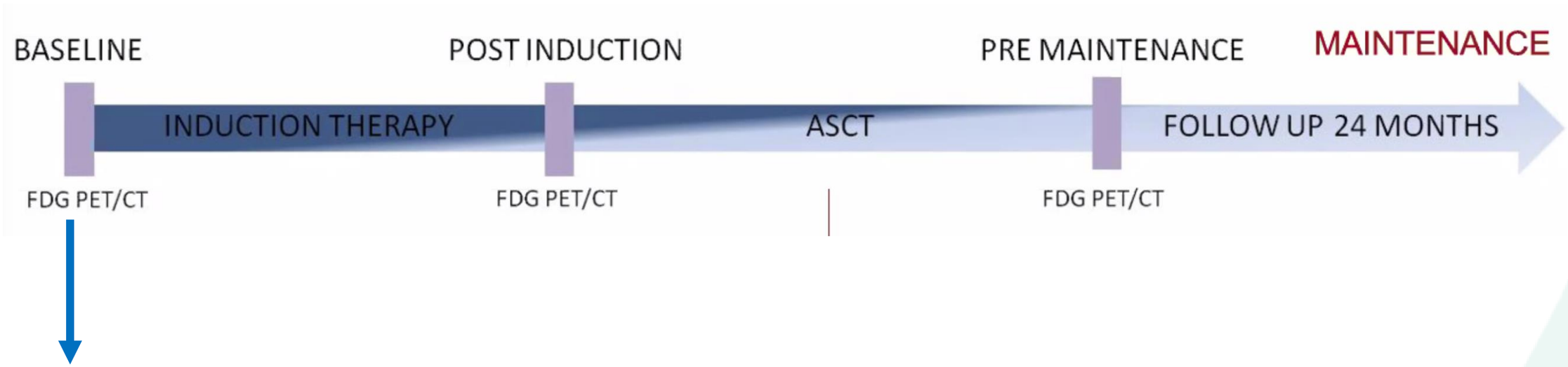
→

VTD x 3
Zoledronic Acid
T9 lesion treated by RT

→

VGPR
& positive FDG PET

Take aways
[^{18}F]FDG PET/CT in MM



CT → MDE: ≥ 1 bone osteolytic lesion 5 mm

[^{18}F]FDG PET → Prognostic biomarker

EMD (head and neck)

PMD (size)

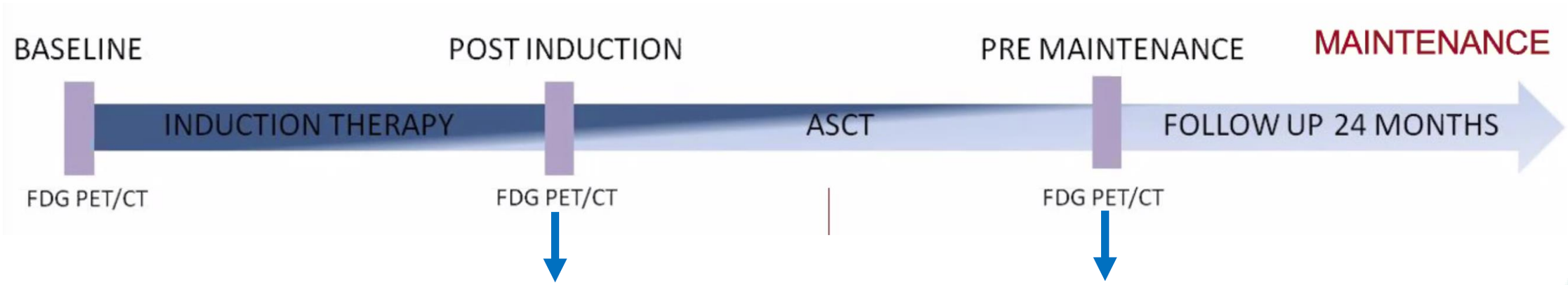
Number of FL + intensity (SUV_{max} & DS score of the hottest)

Diffuse BM DS score 4-5

Fracture

Nanni C et al. Eur J Nucl Med Mol Imaging. 2016 Mar;43(3):414-21; Eur J Nucl Med Mol Imaging. 2018 May;45(5):712-719.

Take aways
[^{18}F]FDG PET/CT in MM



Treatment response IMPeTUs classification:

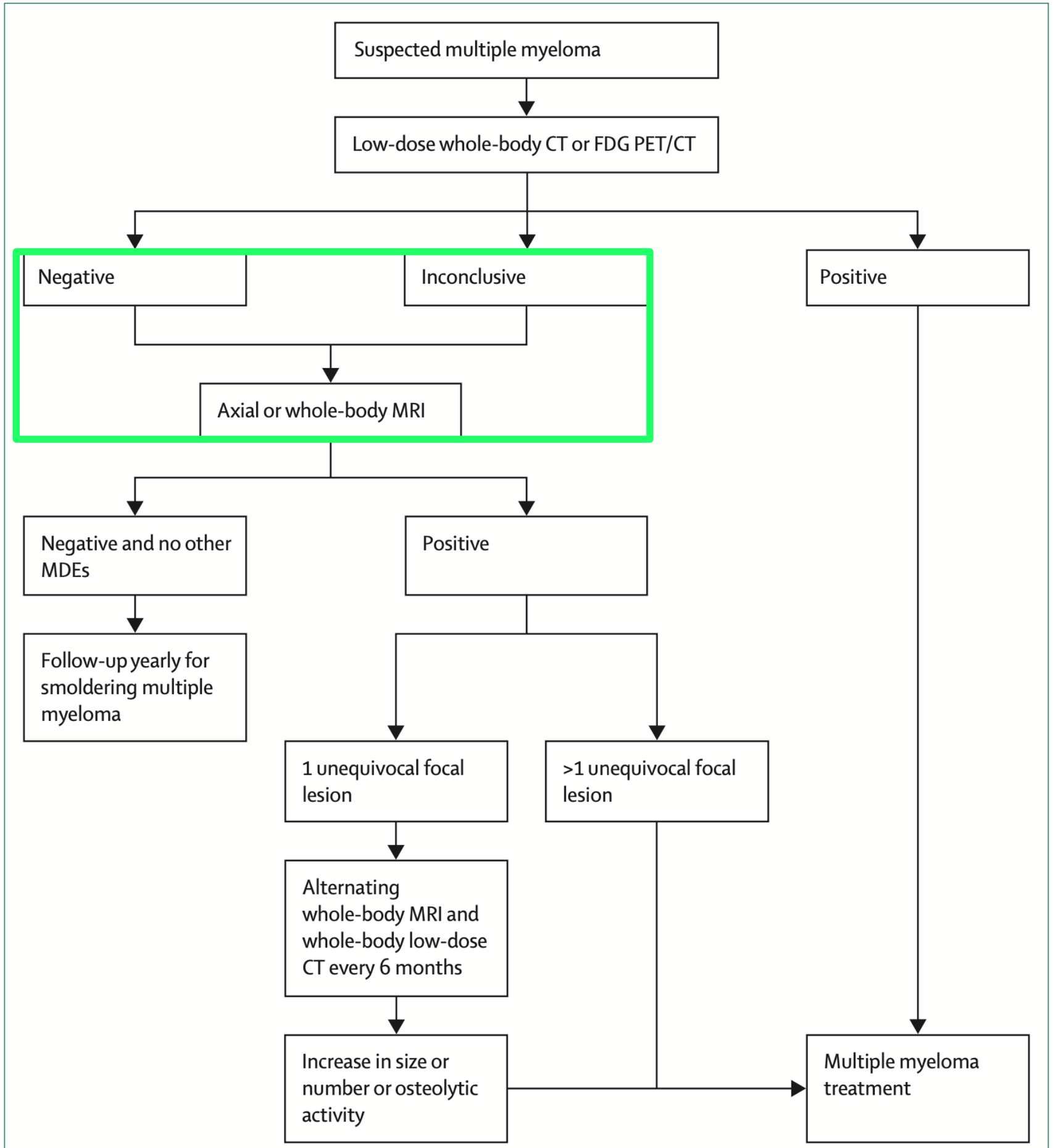
Complete MR	No lesion uptake higher than the liver activity (DS score 1-3)*
Partial MR	Persistent lesion(s) with uptake > liver activity (DS score 4-5) with decrease in number and/or activity compared to baseline*
Stable MD	No significant change in BM/FLs compared with baseline
Progressive MD	New FL(s) compared with baseline consistent with MM

* lesions present at baseline: BM; FLs; EMD and PMD

Zamagni et. al. J Clin Oncol. 2021 Jan 10;39(2):116-125.

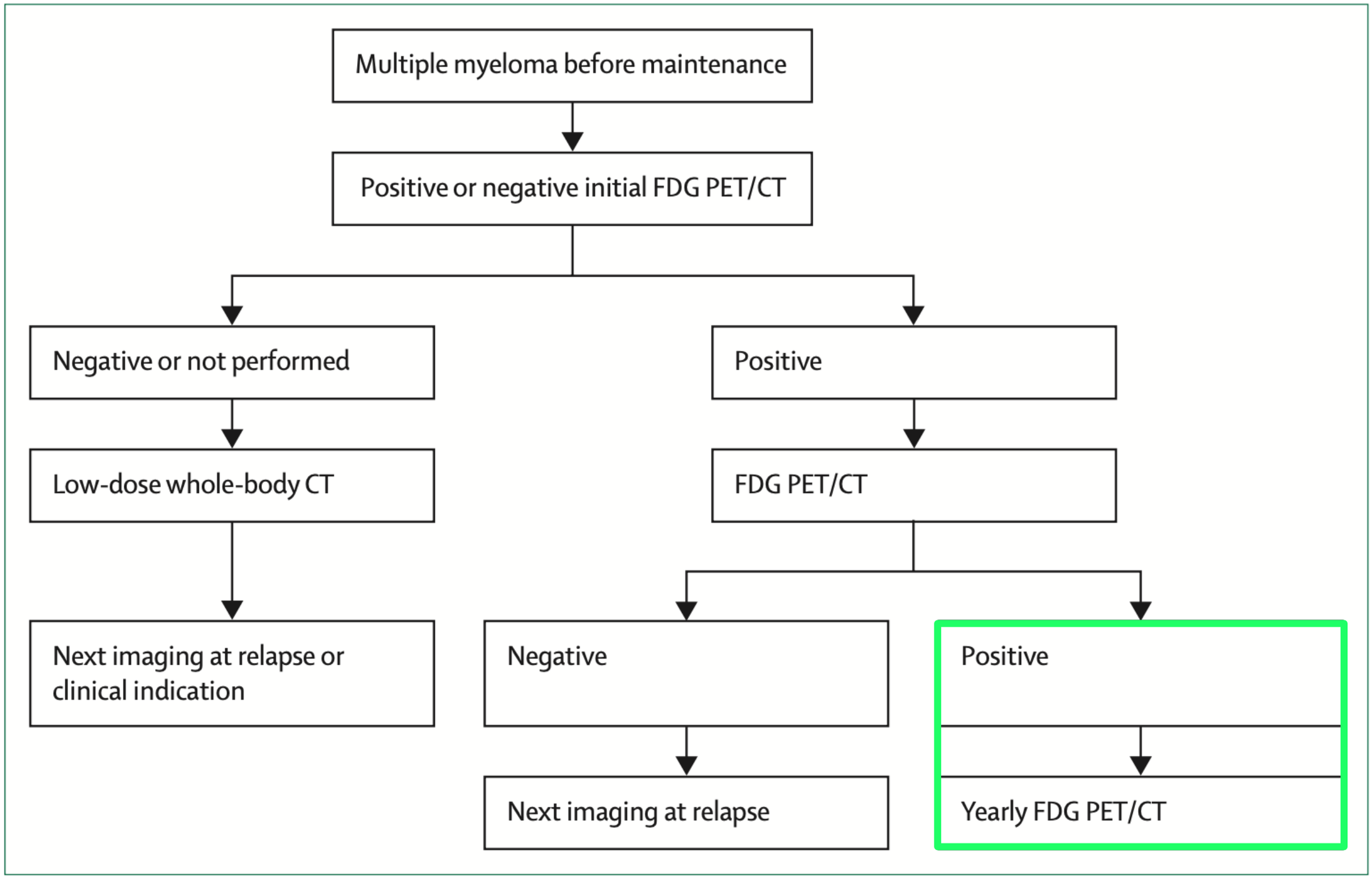

EASY!

MRI if negative or inconclusive PET



Lancet Oncol. 2019 Jun;20(6):e302-e312

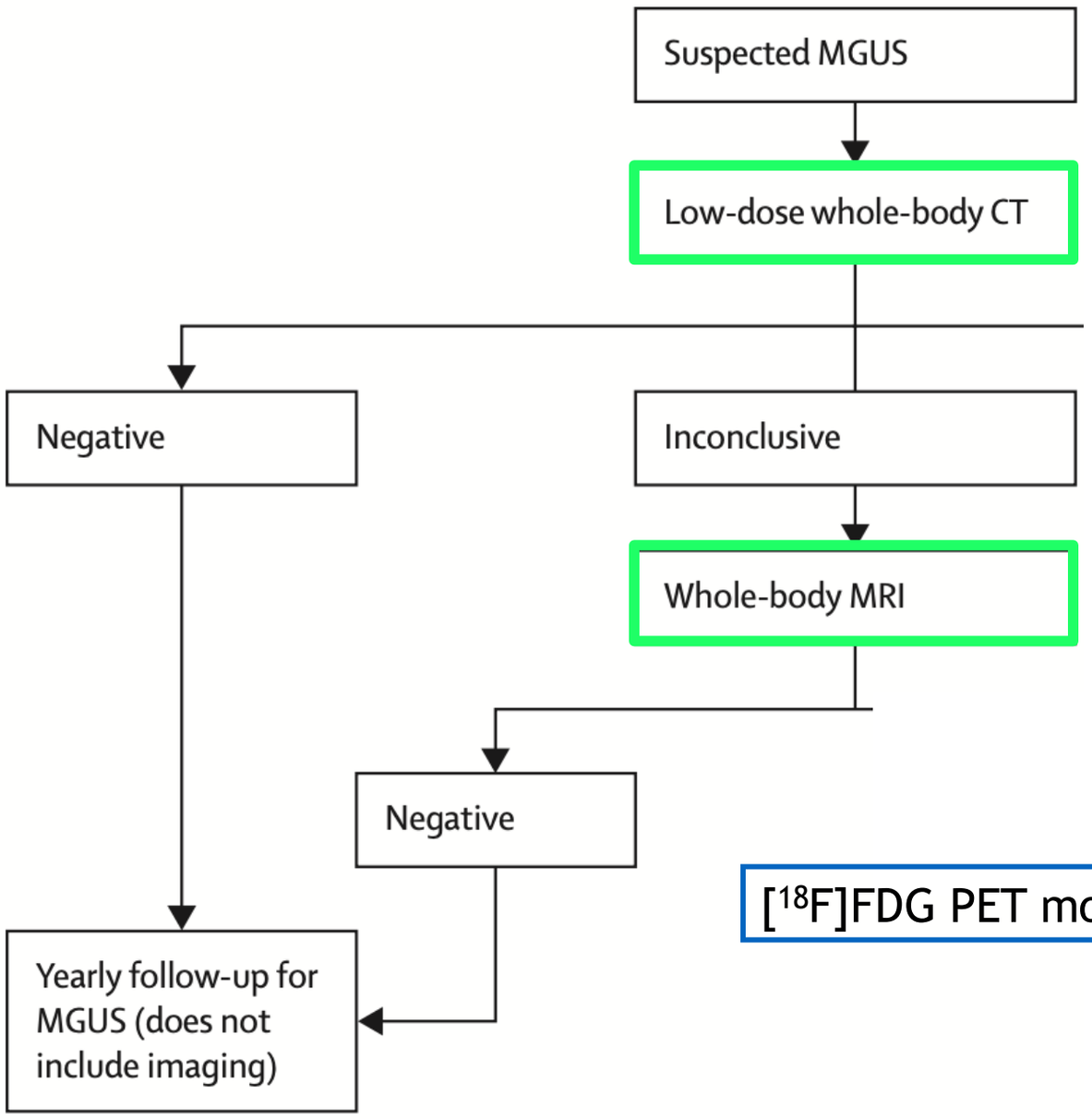
Positive post-treatment PET at higher risk of relapse



Lancet Oncol. 2019 Jun;20(6):e302-e312

Suspected MGUS
WBLDCT is the first-line imaging

MGUS: Low risk of progression to active MM (~1% per year)



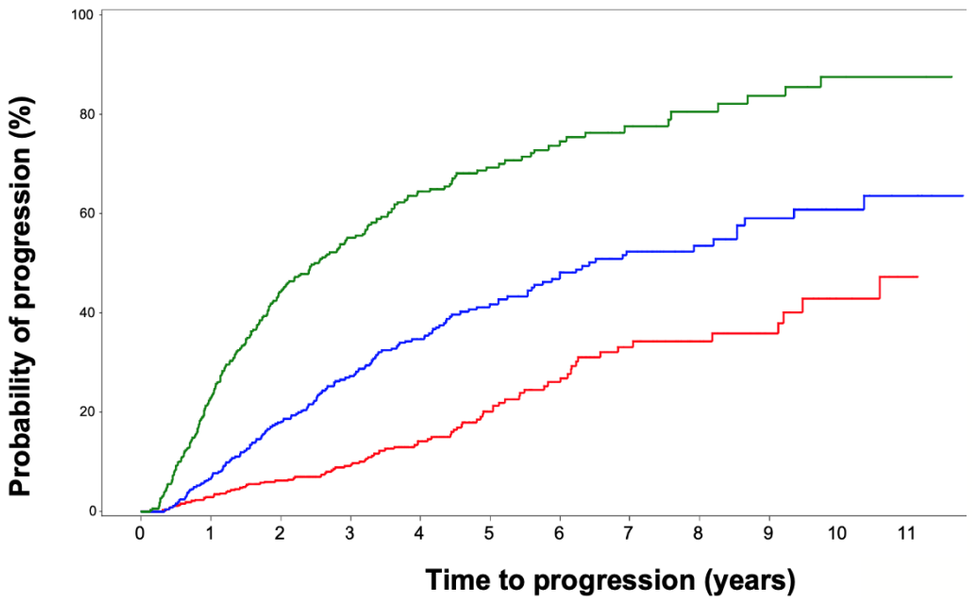
[^{18}F]FDG PET most of the time negative → Not recommended

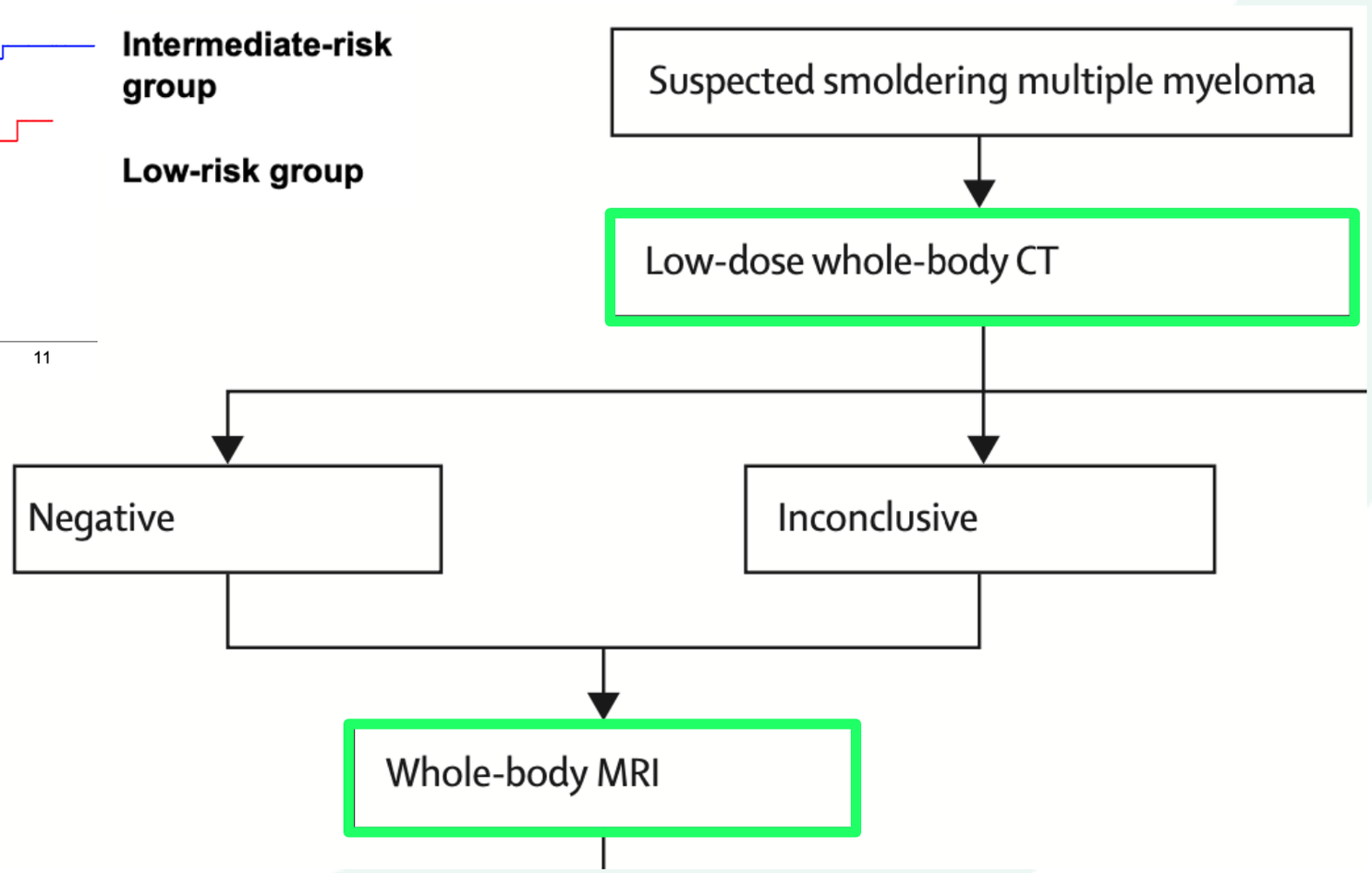
Lancet Oncol. 2019 Jun;20(6):e302-e312

Suspected smouldering MM
WBLDCT is the first-line imaging

Smouldering MM

Higher (variable) risk of progression to active MM





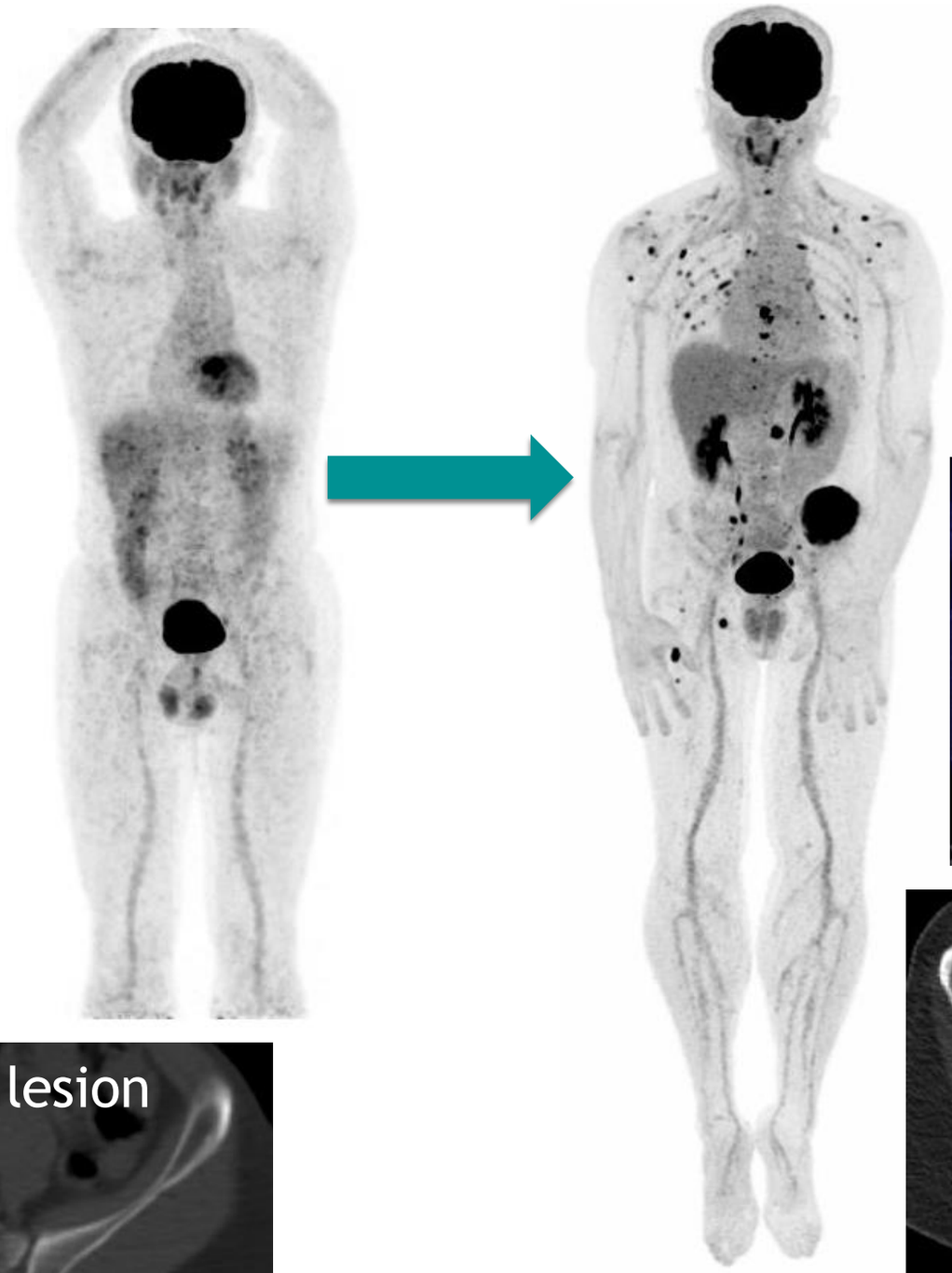
Lancet Oncol. 2019 Jun;20(6):e302-e312; Mateos, M. V. et al. Blood Cancer J. 2020 Oct 16;10(10):102

Evolution of smouldering to active MM

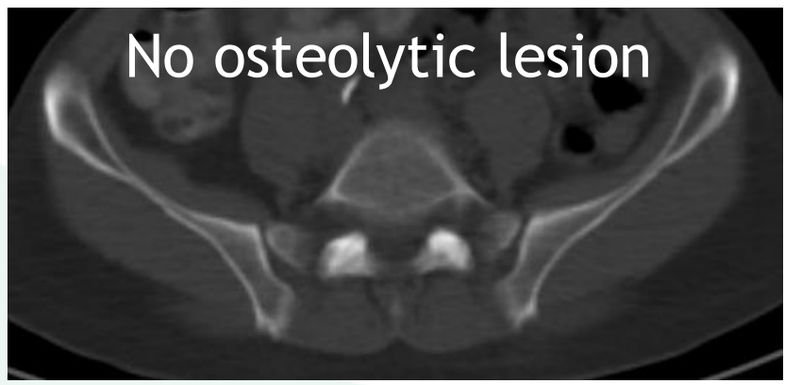
Negative [^{18}F]FDG PET/CT

November 2021

Smouldering MM



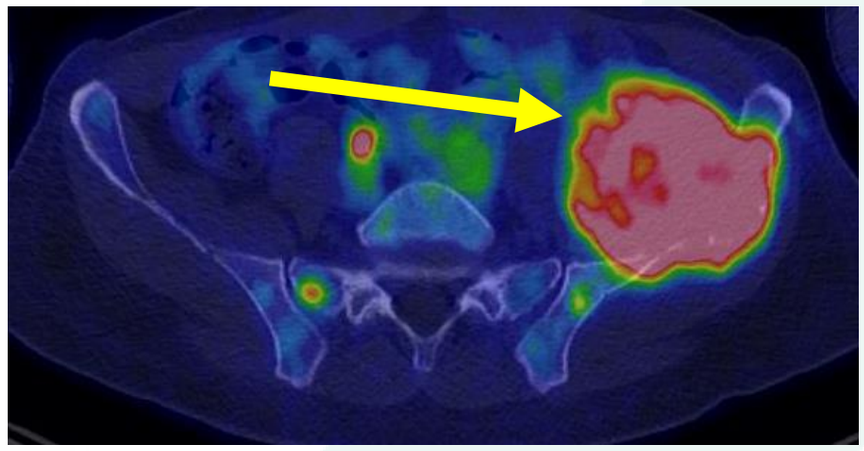
No osteolytic lesion

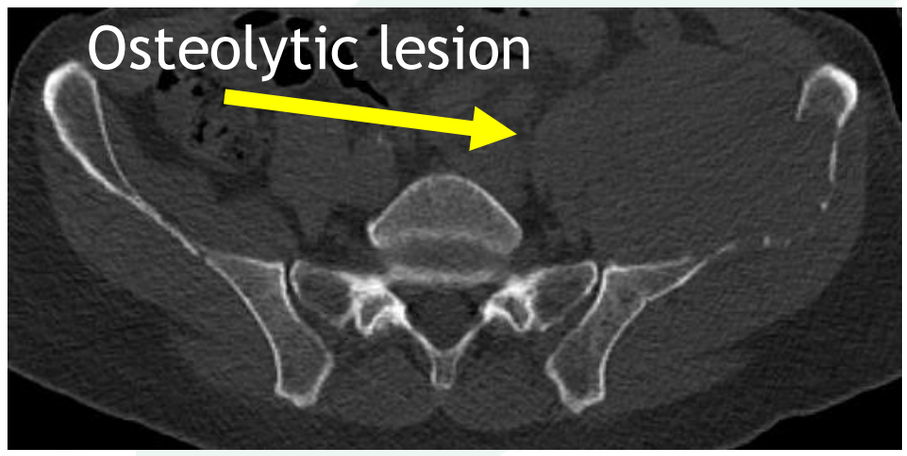


Positive [^{18}F]FDG PET/CT

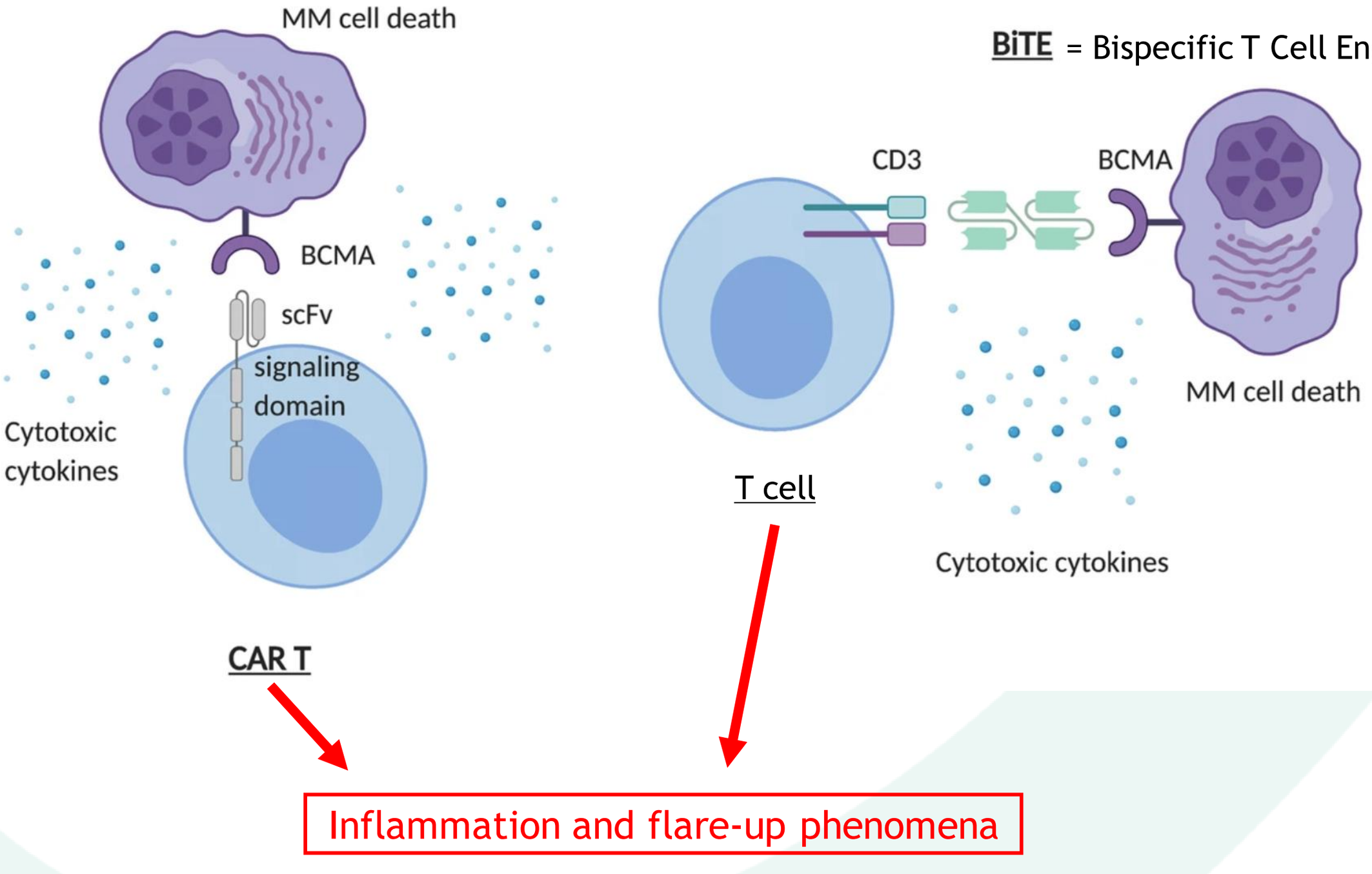
November 2022

Active MM





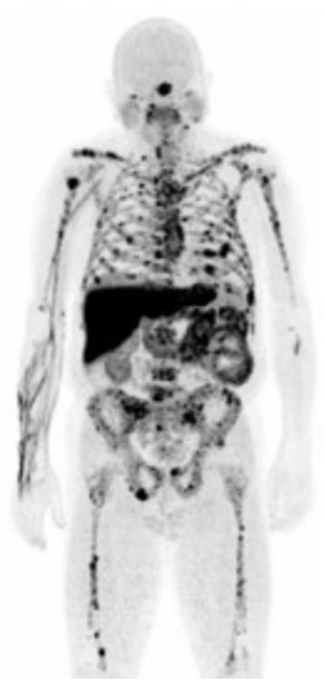
Targeted immunotherapy in relapsed or refractory MM
Pitfalls !



J Hematol Oncol. 2020 Sep 17;13(1):125; Clin Nucl Med. 2023 May 1;48(5):e230-e231.

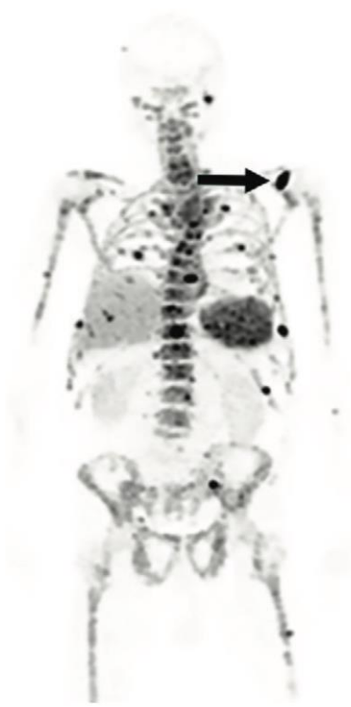
And non [^{18}F]FDG PET/CT in MM …

[^{11}C]methionine

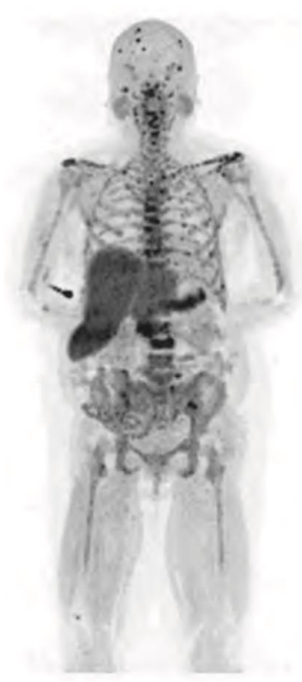


[^{68}Ga]Ga-CXCR4-ligand

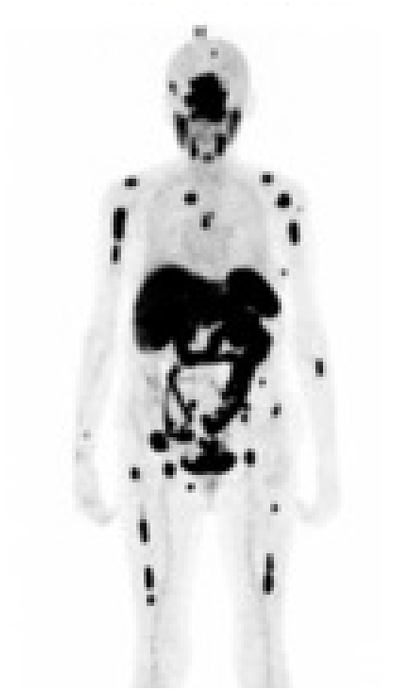
[^{89}Zr]DFO-daratumumab anti-CD38



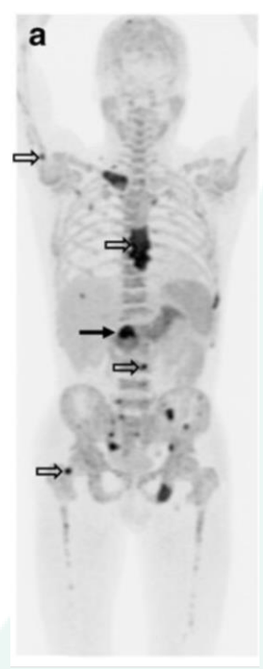
[^{18}F]fluciclovine



[^{68}Ga]Ga-PSMA-ligand



[^{11}C]acetate



Limited number of patients and/or various MM settings (diagnosis/relapse)

Lapa et al. Theranostics. 2017 Jan 1;7(1):205-212; Ulaner et al. Radiology. 2020 Jun;295(3):606-615; Morales-Lozano et al. Cancers (Basel). 2020 Apr 23;12(4); Stokke et al. EP1022. EHA25-Abstracts-2020; Ramos et al. eposter-078 EANM 2019 ; Lin et al. Eur J Nucl Med Mol Imaging. 2014 Jan;41(1):41-9.

DS criteria for CMR [^{18}F]FDG PET/CT

Imaging substudy of FORTE trial (n = 109/474)

All PET pts (*n* = 109)	B-PET_FLs	B-PET_BMs	PM-PET_FLs	PM-PET_BMs
Positive[a], n (%)	98 (93)	106 (99)	43 (40)	97 (89)
Negative, n (%)	7 (7)	1 (1)	65 (60)	12 (11)
Missing, n	4	2		
EMD, n (%)		8 (7)		
Deauville scores				
DS 1, n (%)	7 (7)	1 (1)	65 (60)	12 (11)
DS 2, n (%)	1 (1)	34 (32)	2 (2)	52 (48)
DS 3, n (%)	4 (4)	7 (7)	14 (13)	28 (26)
DS 4, n (%)	93 (89)	65 (61)	27 (25)	16 (15)
Missing, n	4	2	1	1
SUV max, median (IQR)	6.04 (4.31–8.29)	3.5 (2.8–4.37)	3.04 (2.2–5.39)	2.8 (2.3–3.44)
CMR[b], n (%)			69 (63)	

Abbreviations. B, Baseline; BM, Bone marrow; CMR, Complete metabolic response; DS, Deauville scores; EMD, Extramedullary disease; FLs, Focal lesions; IQR, Interquartile range; n, Number; PET, Positron emission tomography; PM, Pre-maintenance; pts, Patients; SUV, Standardised uptake value. [a]Defined as DS >1. [b]Defined as DS <4 both in the FLs and BM.

Table 2: **Baseline (B) and pre-maintenance (PM) PET characteristics.**

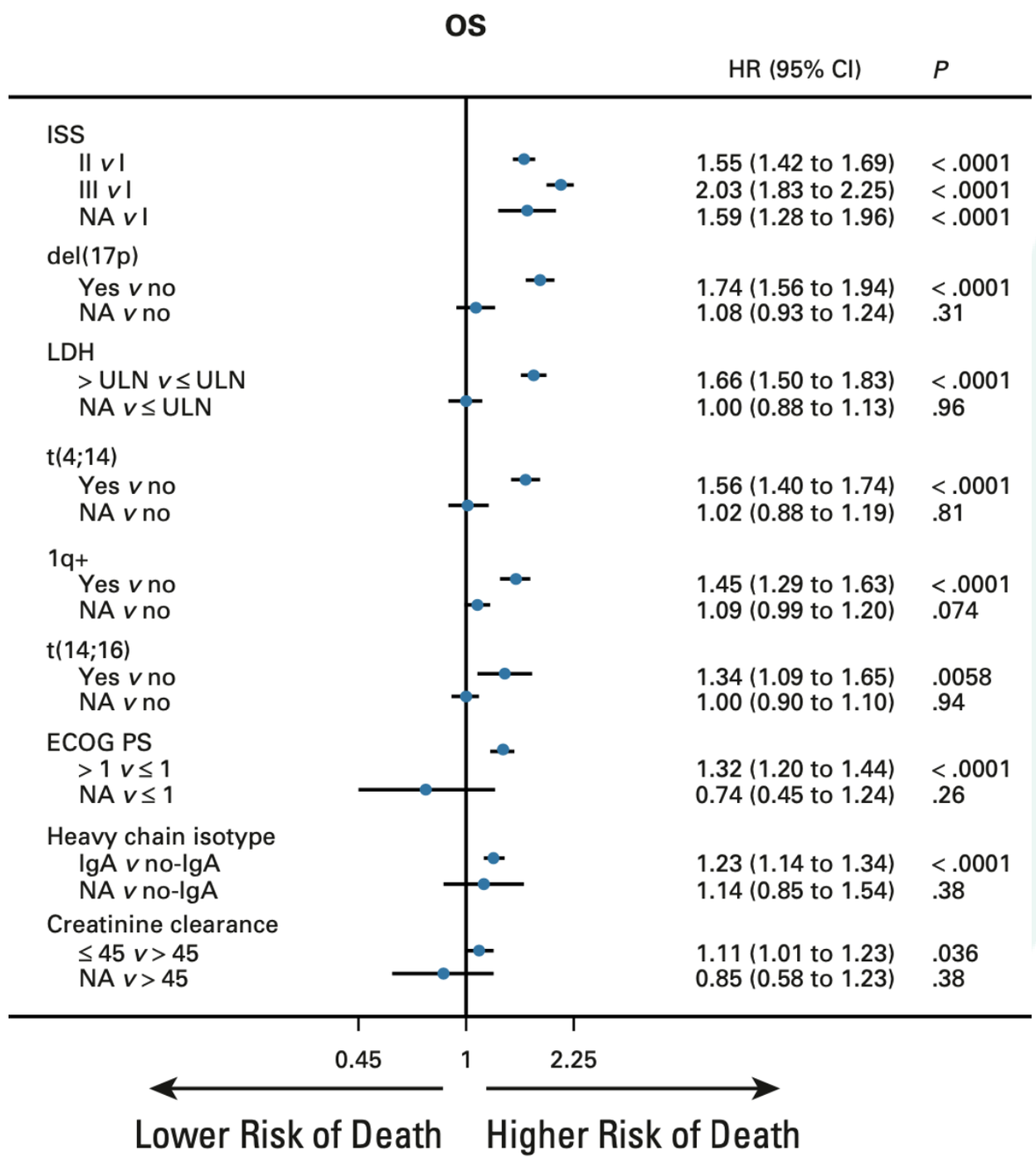
EClinicalMedicine. 2023 Jun 9;60:102017.

International staging system (ISS)

Table 1. Standard Risk Factors for MM and the R-ISS

Prognostic Factor	Criteria
ISS stage	
I	Serum β_2-microglobulin < 3.5 mg/L, serum albumin ≥ 3.5 g/dL
II	Not ISS stage I or III
III	Serum β_2-microglobulin ≥ 5.5 mg/L
CA by iFISH	
High risk	Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)
Standard risk	No high-risk CA
LDH	
Normal	Serum LDH < the upper limit of normal
High	Serum LDH > the upper limit of normal
A new model for risk stratification for MM	
R-ISS stage	
I	ISS stage I and standard-risk CA by iFISH and normal LDH
II	Not R-ISS stage I or III
III	ISS stage III and either high-risk CA by iFISH or high LDH

Abbreviations: CA, chromosomal abnormalities; iFISH, interphase fluorescent in situ hybridization; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma; R-ISS, revised International Staging System.



J Clin Oncol. 2005 May 20;23(15):3412-20; J Clin Oncol. 2015 Sep 10;33(26):2863-9; J Clin Oncol. 2022 Oct 10;40(29):3406-3418.