Prognostic relevance of 18F-FDG PET/CT in newly diagnosed multiple myeloma patients receiving up-front autologous stem-cell transplantation: a prospective study

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BACKGROUND

- 18F-FDG PET/CT is a valuable method to carefully monitor response and predict clinical outcomes in various tumors, particularly lymphoma
- Incorporation of novel agents into ASCT affected unprecedented rates of CR in young MM patients
- More sensitive techniques for detecting MRD after ASCT are required

AIM OF THE STUDY

- To prospectively evaluate the prognostic significance of FDG-PET/CT at diagnosis, after induction therapy and after high dose therapy in patients with newly diagnosed MM who received thalidomide incorporated into up-front autologous stem cell transplantation (ASCT)

PATIENT POPULATION

- N° analyzed patients: 192

- Median follow-up: months 42
- Median follow-up of living patients: months 43

FDG-PET/CT STUDIES

- FDG-PET/CT performed:
  - at baseline
  - post induction therapy
  - 3 months after ASCT
  - every year during follow-up
  - at relapse
- Bone marrow involvement: negative, diffuse, number of focal lesions (> 0.5 cm)
- SUV value
- Presence of extramedullary disease

BASELINE PATIENT CHARACTERISTICS

N° patients	192
Median age (range)	56 (35-66)
% pts with creat >2	8
% pts with Ca > 10	9
ISS stage II-III (% pts)	45
% pts with del (13q)*	43
% pts with t(4;14)*	23
% pts with del(17p)*	15
ASCT -single (% pts) -double (%pts)	 40 60

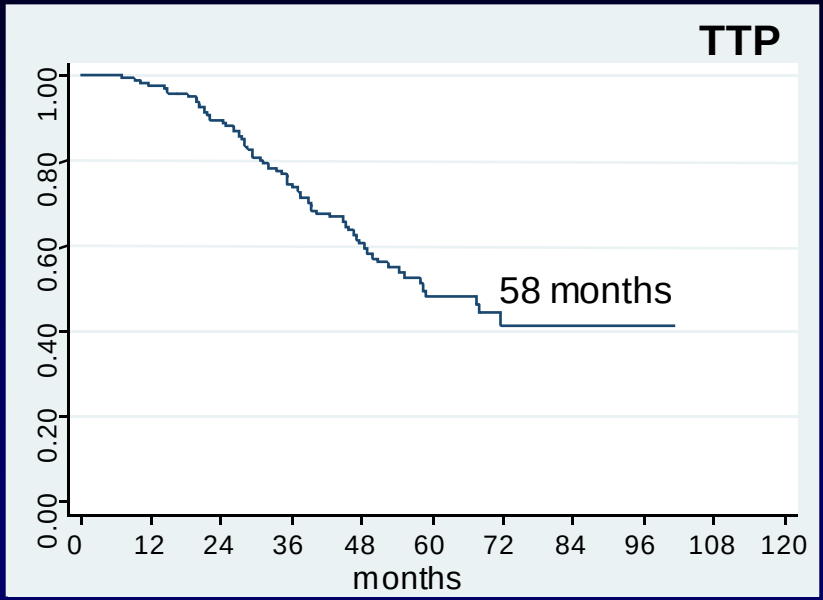
*80% pts screened for cytogenetic abnormalities (FISH) on CD 138+ bone marrow PC

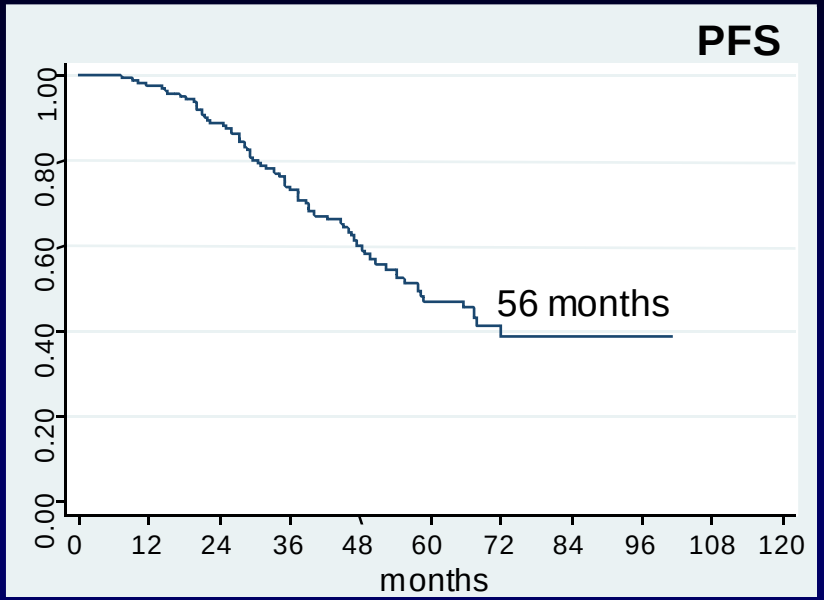
BASELINE FDG-PET/CT CHARACTERISTICS

N° patients	192
Negative (% pts) Positive (% pts)	24 76
1-3 focal lesions(% pts)	32
>3 FL or diffuse(% pts)	44
SUV(% pts) low (≤ 4.2) high (>4.2)	 54 46
Extramedullary disease (% pts)*	6

*defined as presence of FDG-avid soft tissue not contiguous to bone

CLINICAL OUTCOMES

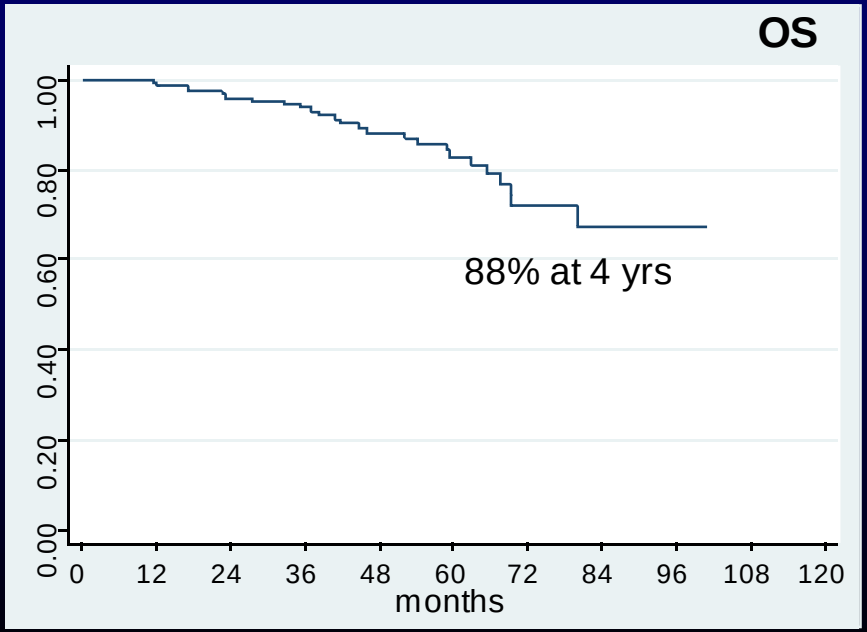




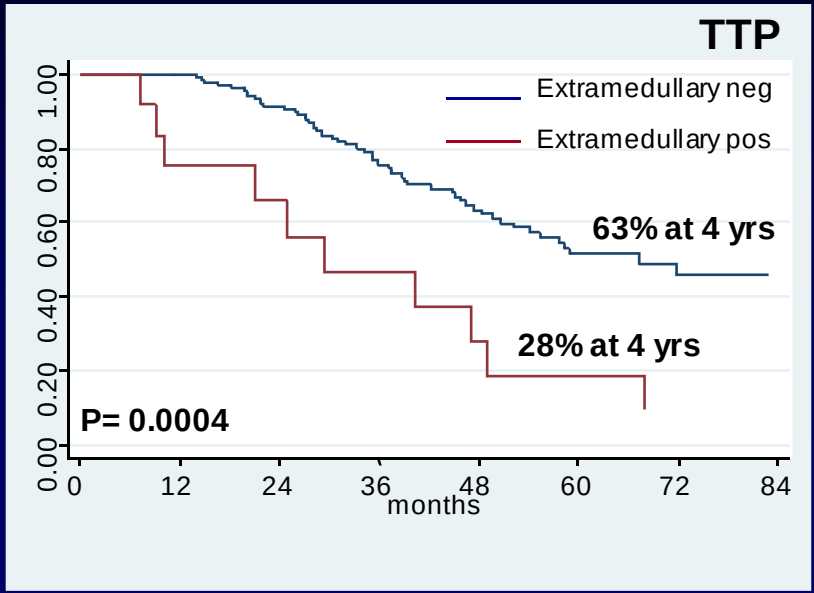
Best overall response:

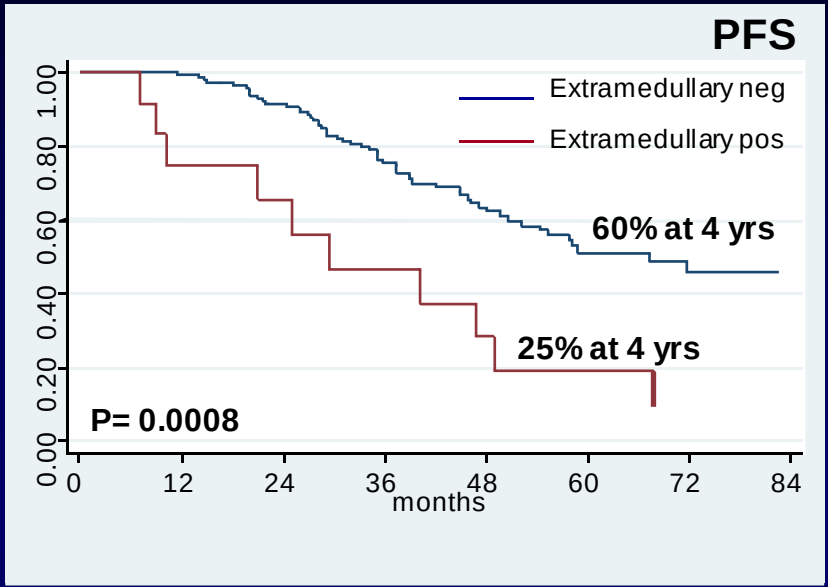
≥VGPR rate 80%

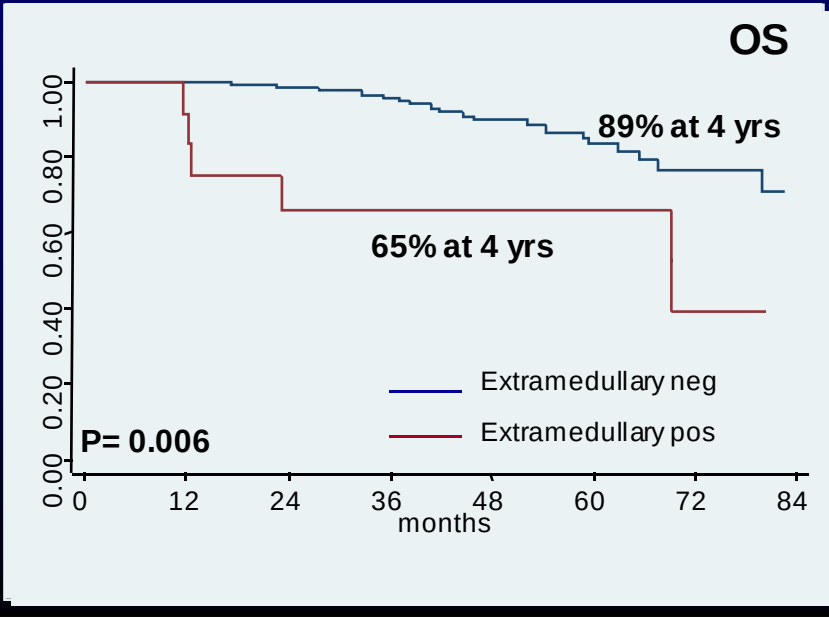
CR rate 52%



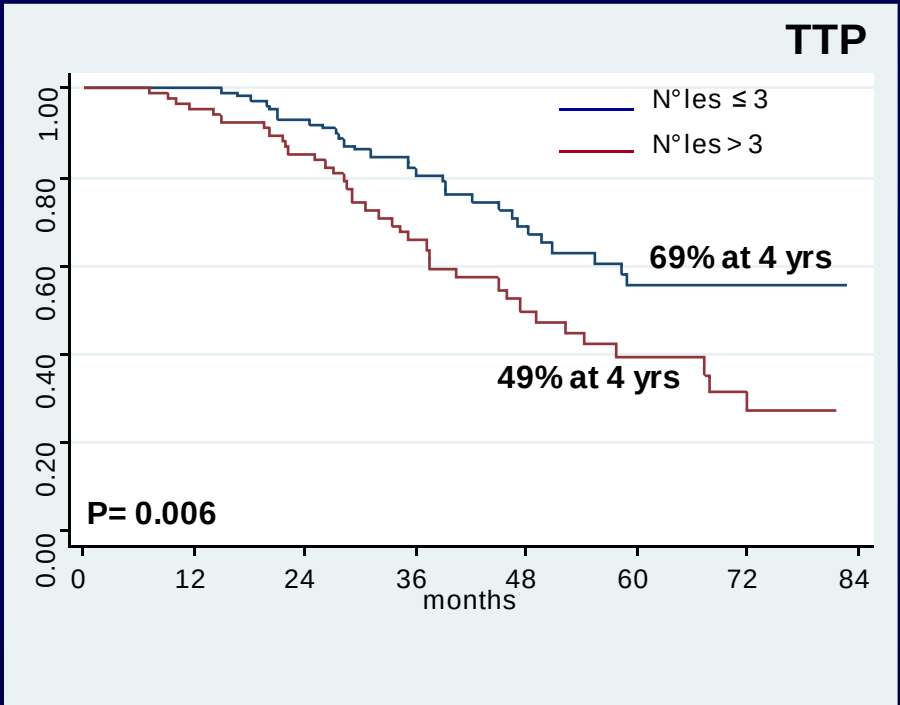
TTP, PFS AND OS IN PATIENTS WITH EXTRAMEDULLARY DISEASE

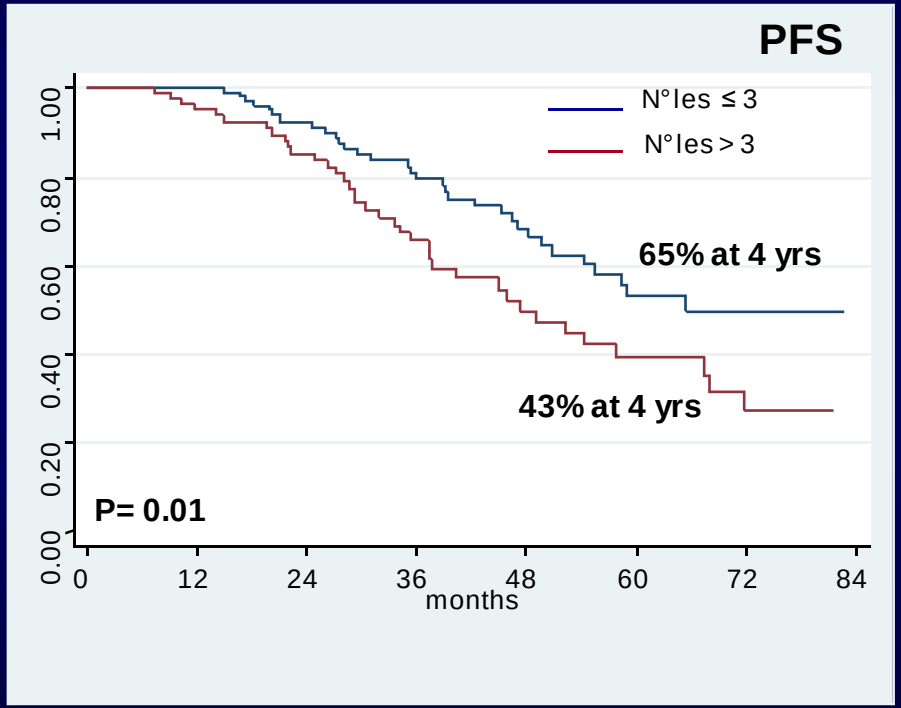




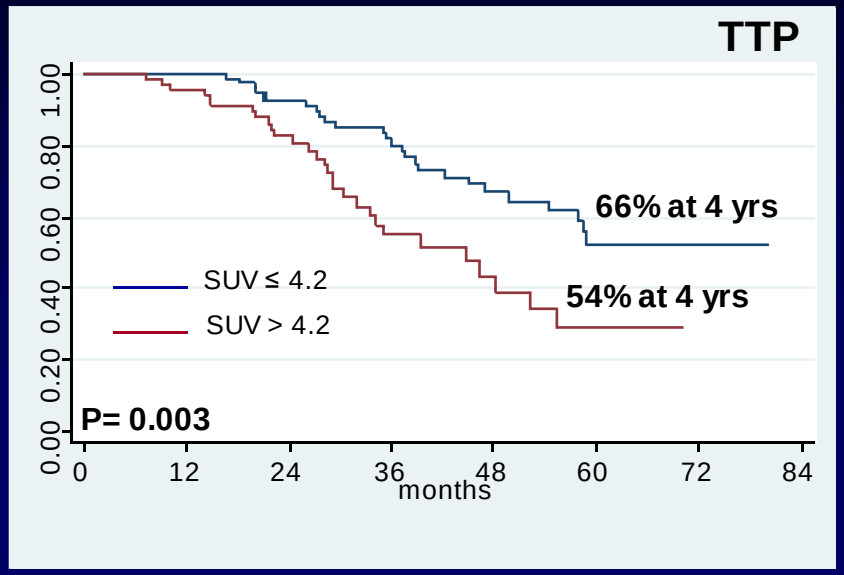


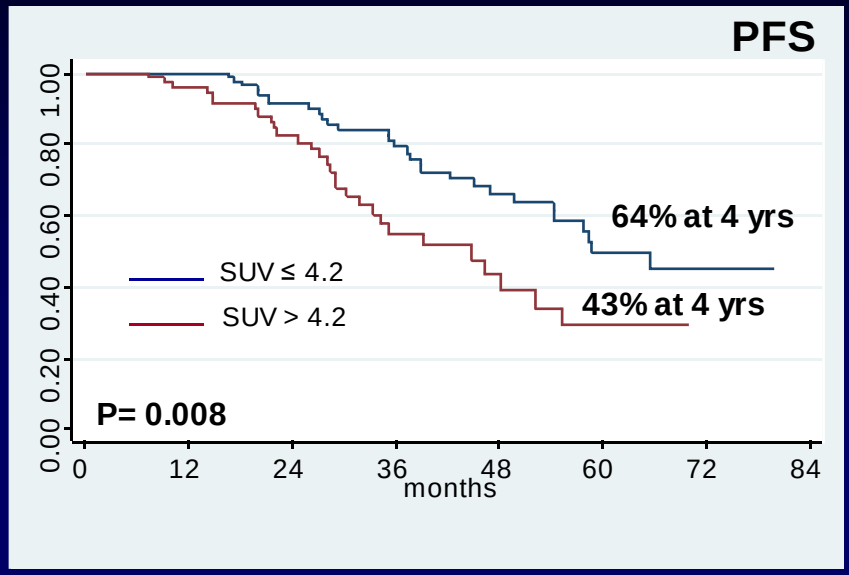
TTP AND PFS ACCORDING TO BASELINE FDG-PET/CT: NUMBER OF LESIONS

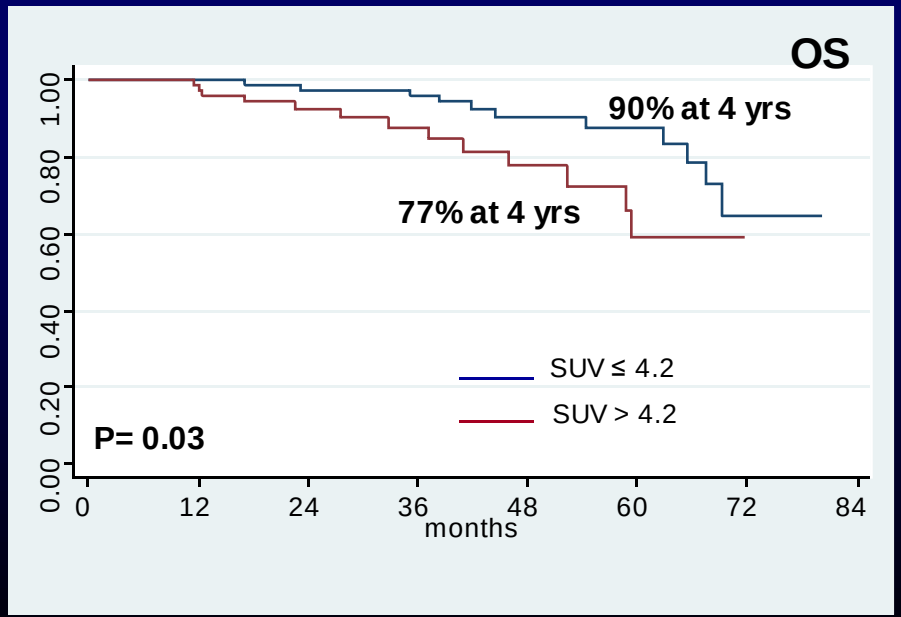




TTP, PFS AND OS ACCORDING TO BASELINE FDG-PET/CT: SUV VALUE







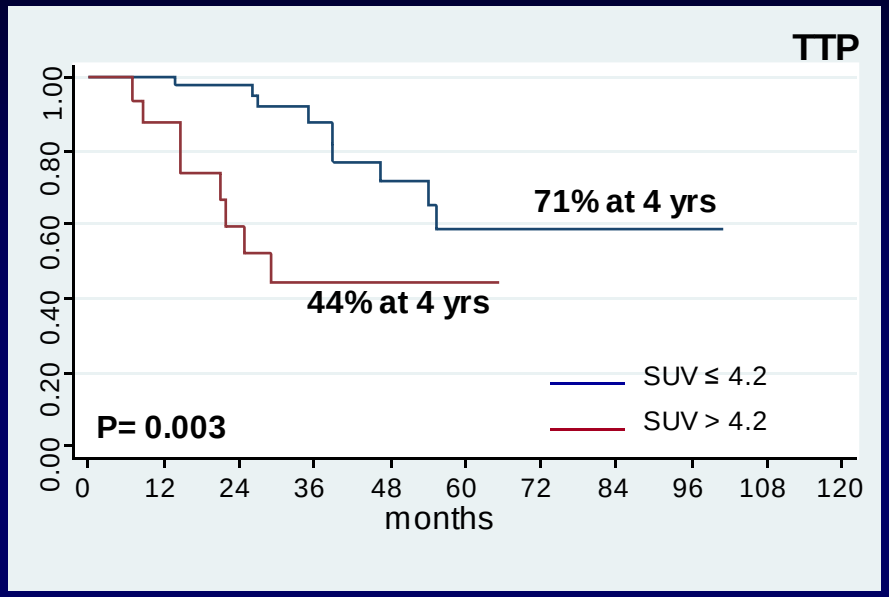
MULTIVARIATE ANALYSIS OF BASELINE UNFAVORABLE PROGNOSTIC FACTORS

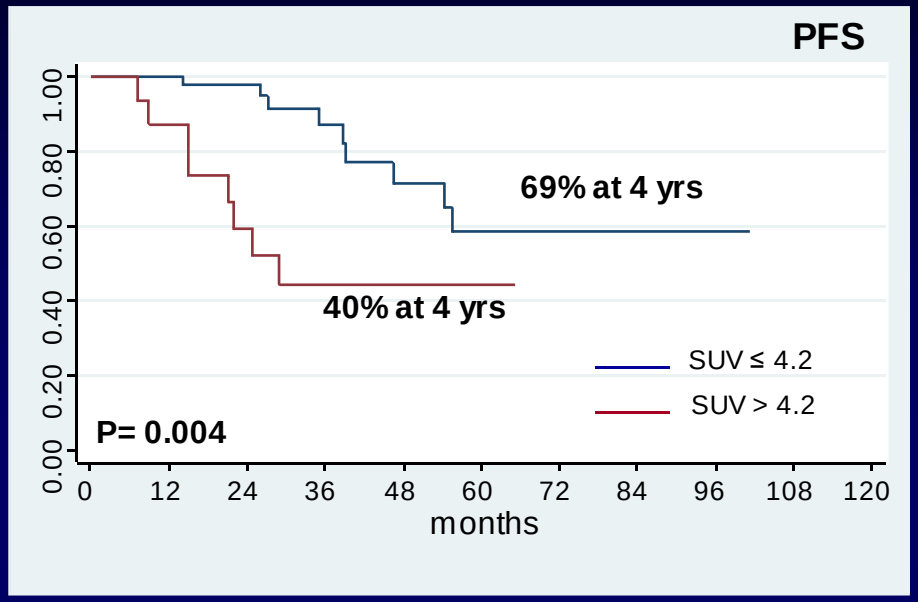
VARIABLES	HAZARD RATIO (95% CI)	P VALUE
TTP		
PET/CT > 4.2 SUV	2.37 (1.26-4.33)	0.007
Extramedullary disease	15. 43 (4.11-57.95)	0.000
del (17p) ± t(4;14)	1.86 (1.12-3.49)	0.05
PFS		
PET/CT > 4.2 SUV	2.05 (1.13-3.72)	0.018
Extramedullary disease	15. 00 (4.03-55.88)	0.000
del (17p) ± t(4;14)	2.03 (1.10-3.72)	0.02
OS		
Extramedullary disease	6. 99 (2.28-21.46)	0.001
del (17p) ± t(4;14)	2.36 (1.23-6.02)	0.05

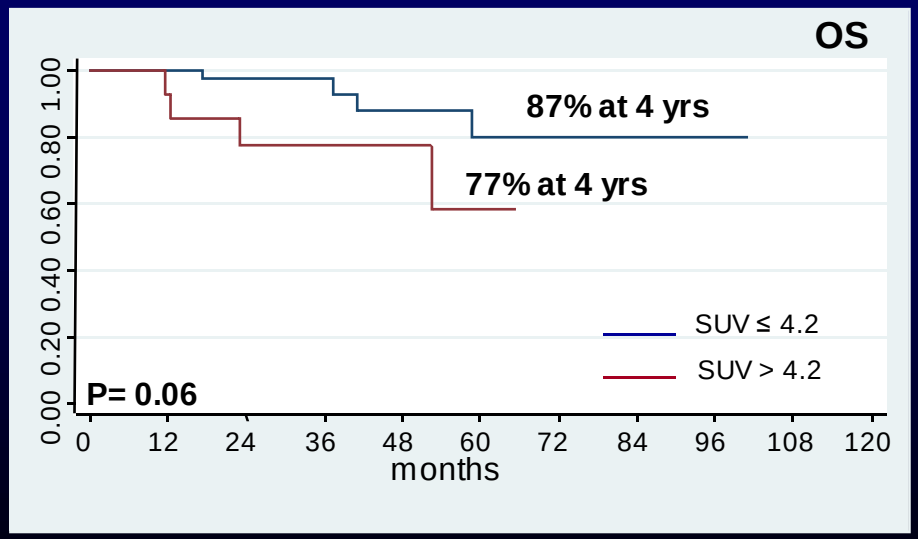
POST INDUCTION FDG-PET/CT CHARACTERISTICS

N° patients	85
Negative (%)	37
Positive (%)	63
-improved	14
-unchanged	43
-worstened	6

TTP, PFS AND OS ACCORDING TO POST-INDUCTION FDG-PET/CT





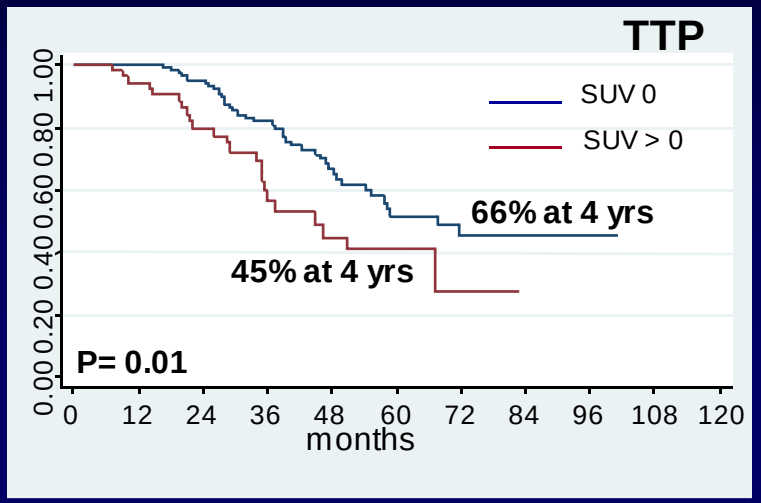


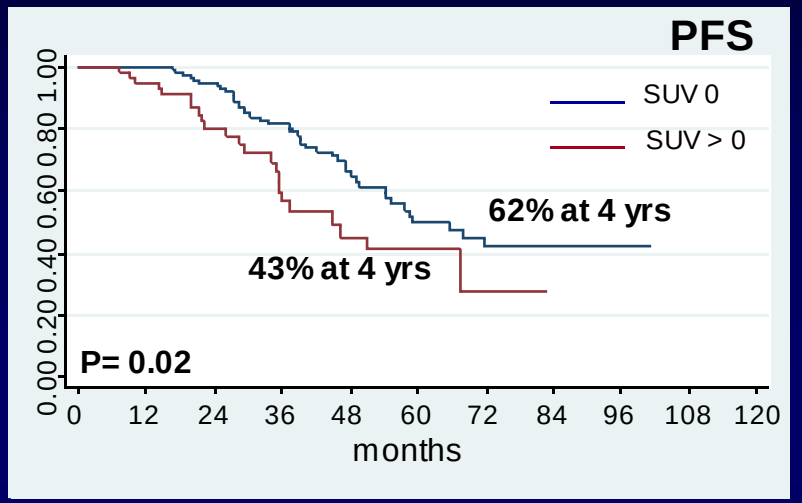
POST ASCT FDG-PET/CT CHARACTERISTICS

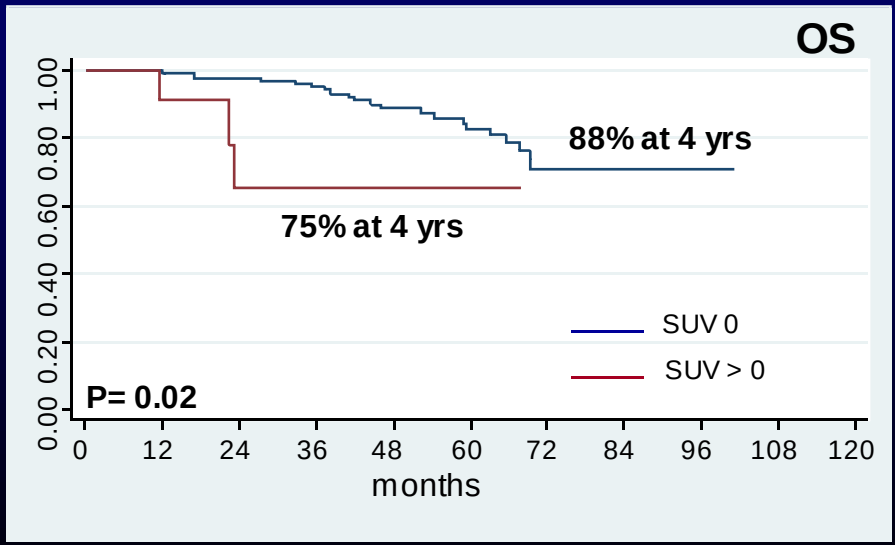
N° patients	192
Negative (%)	65
Positive (%)	35
-improved	17
-unchanged	14
-worstened	4
Negative + ≥ VGPR (%)	95
Positive + ≥ VGPR (%)	75

P = 0.001

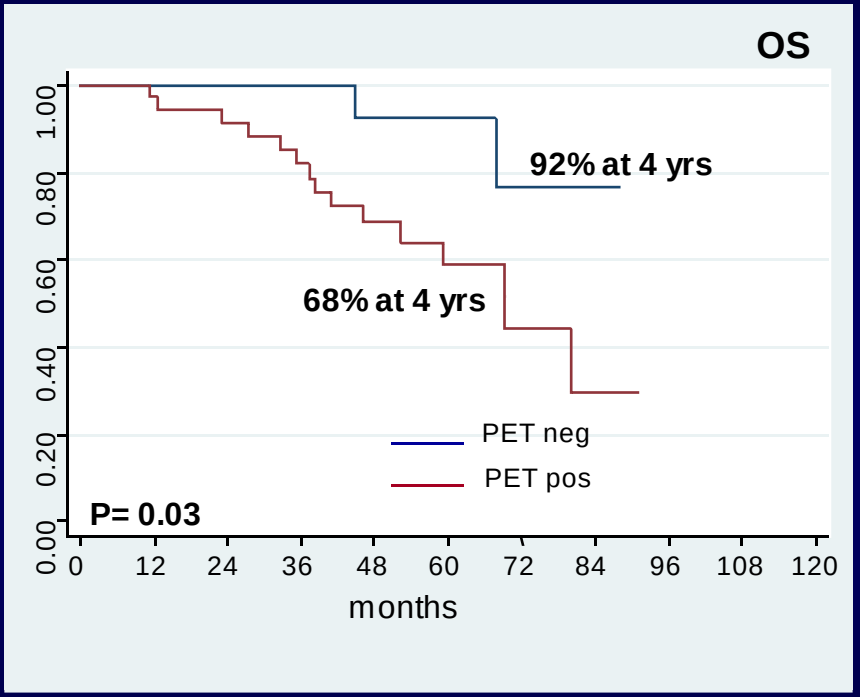
TTP, PFS AND OS ACCORDING TO POST ASCT FDG-PET/CT

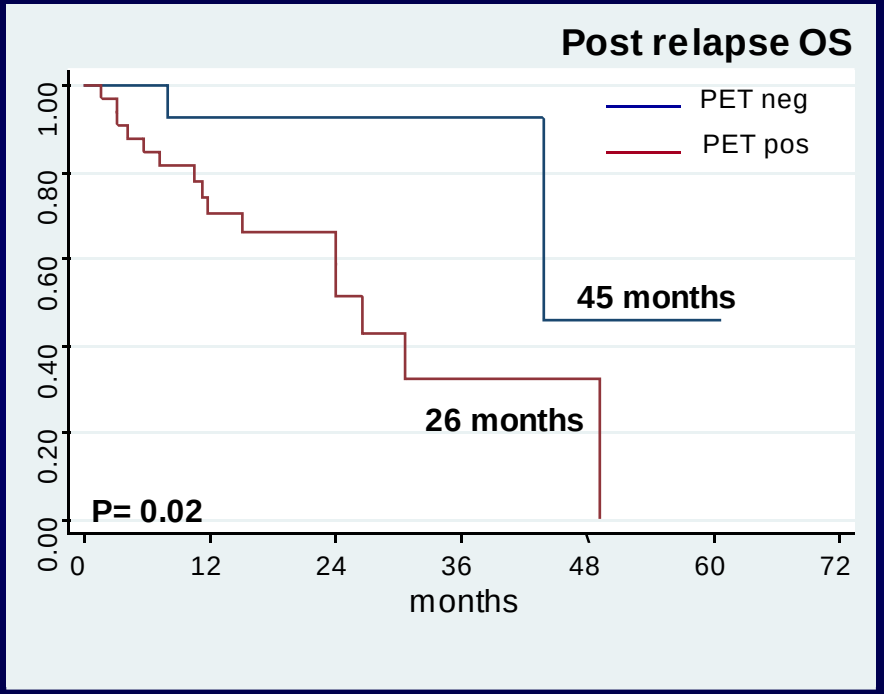






OS ACCORDING TO FDG-PET/CT IMAGING AT RELAPSE





MULTIVARIATE ANALYSIS OF BASELINE LABORATORY AND POST TREATMENT UNFAVORABLE PROGNOSTIC FACTORS

VARIABLES	HAZARD RATIO (95% CI)	P VALUE
TTP		
Not complete FDG PET suppression	2.12 (1.19-3.77)	0.01
Extramedullary disease	15. 43 (4.11-57.95)	0.000
del (17p) ± t(4;14)	1.86 (1.12-3.49)	0.05
< VGPR	2.10 (1.13-3.88)	0.017
PFS		
Not complete FDG PET suppression	2.12 (1.19-3.77)	0.023
Extramedullary disease	5. 47 (1.89-15.81)	0.002
del (17p) ± t(4;14)	1.92 (1.09-3.39)	0.025
< VGPR	2.11 (1.16-3.83)	0.013
OS		
Not complete FDG PET suppression	3.57 (1.03-12.39)	0.04
Relapse	9.56 (2.85-32.05)	0.000

CONCLUSION

- Independent impact of FDG-PET/CT at diagnosis on clinical outcomes (TTP, PFS and OS)
  - number of focal lesions
  - intensity of tumor metabolism (SUV)
  - EMD
- Persistence of high tumor metabolism (SUV) by FDG-PET/CT after induction therapy predicted worst outcome (TTP, PFS and OS)

CONCLUSION

- FDG-PET/CT after ASCT is a reliable tool to predict prognosis and identify patients at different risk of progression.
- Complete FDG suppression after ASCT was associated with extended PFS and OS both in univariate and multivariate analysis
- FDG-PET/CT involvement at the time of relapse was associated with shortened survival after relapse

CONCLUSION

•Based on these data and additional data from other groups, aims to evaluate MRD after ASCT should include also imaging techniques such as FDG-PET/CT and/or whole body MRI

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