SUPPLEMENTARY APPENDIX

Quantitative dynamic ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography before autologous stem cell transplantation predicts survival in multiple myeloma

Christos Sachpekidis, ^{1,2*} Maximilian Merz, ^{2,3*} Annette Kopp-Schneider, ⁴ Anna Jauch, ⁵ Marc-Steffen Raab, ² Sandra Sauer, ² Jens Hillengass, ⁶ Hartmut Goldschmidt^{2,3**} and Antonia Dimitrakopoulou-Strauss ^{1**}

*equal contribution as co-first authors; **share joint senior authorship

¹Clinical Cooperation Unit Nuclear Medicine, German Cancer Research Center (DKFZ), Heidelberg, Germany; ²Department of Internal Medicine V, University Hospital Heidelberg, Heidelberg, Germany; ³National Center for Tumor Diseases (NCT) Heidelberg, Heidelberg, Germany; ⁴Department of Biostatistics, German Cancer Research Center (DKFZ), Heidelberg, Germany; ⁵Institute for Human Genetics, University of Heidelberg, Heidelberg, Germany and ⁶Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

Correspondence: CHRISTOS SACHPEKIDIS - christos_saxpe@yahoo.gr doi:10.3324/haematol.2018.213041

Statistical analysis

Spearman correlation analysis was performed to investigate the correlation between quantitative PET parameters. PFS was measured from the date of start of treatment until disease progression or death from any cause. Kaplan-Meier estimates were generated and median PFS estimated. Median follow-up time was determined by inverse Kaplan-Meier estimation. For univariate comparison of PFS log-rank test was used. Multivariate Cox proportional hazards regression analysis was applied. Maximally selected rank statistics were used to identify the optimal cut point of quantitative covariables used for dichotomization of the cohort with respect to PFS. Statistical analysis was performed using R version 3.4.3 (The R Foundation for Statistical Computing 2017) and R packages survival and maxstat. The results were considered significant for p value less than 0.05 (p<0.05).

Supplementary Table 1 Descriptive statistics of SUV values and kinetic PET parameters for 18 F-FDG in reference BM and the hottest MM lesions. K_1 , k_3 and influx are expressed in 1/min. SUV and V_B have no unit.

Parameters	reference BM (os ilium)	MM lesions
SUV _{average}	median= 2.0, mean= 2.1, SD= 1.1	median= 5.2, mean= 6.1, SD= 3.6
SUV _{max}	median= 3.3, mean= 3.7, SD= 2.1	median= 8.5, mean= 9.3, SD= 5.3
V_{B}	median= 0.01, mean= 0.02, SD= 0.03	median= 0.04, mean= 0.07, SD= 0.11
K ₁	median= 0.18, mean= 0.21 , SD= 0.09	median= 0.30, mean= 0.30, SD= 0.14
k ₃	median= 0.05, mean= 0.05, SD= 0.03	median= 0.14, mean= 0.25, SD= 0.35
Influx (K _i)	median= 0.01, mean= 0.02, SD= 0.01	median= 0.04, mean= 0.05, SD= 0.02

SUV, standardised uptake value; PET, positron emission tomography; BM, bone marrow; MM, multiple myeloma

Supplementary Table 2 Effect of the previously established risk PET factors on PFS in MM.

Parameters	Median PFS at parameter positivity	Median PFS at parameter negativity	Statistical significance (p value)
>3 focal lesions	30.5 months (n= 19 patients)	59.4 months (n= 28 patients)	(p= 0.03)*
SUV _{max} >4.2 (reference BM)	21.3 months (n= 16 patients)	59.4 months (n= 31 patients)	(p<0.001)*
SUV _{max} >4.2 (MM lesions)	31.0 months (n= 24 patients)	39.7 months (n= 23 patients)	(p= 0.08)
EMD	17.2 months (n= 4 patients)	43.9 months (n= 43 patients)	(p= 0.02)*

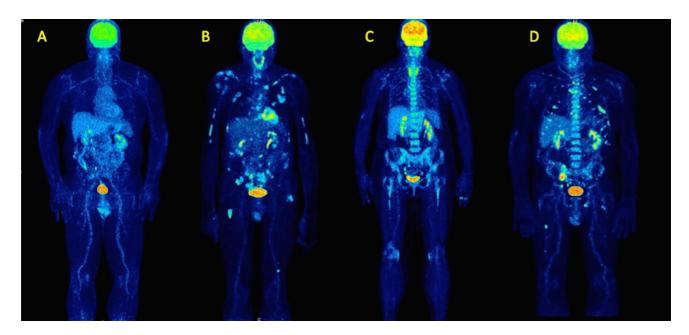
^{*} statistically significant differences

PET, positron emission tomography; PFS, progression-free survival; MM, multiple myeloma; SUV, standardised uptake value; BM, bone marrow

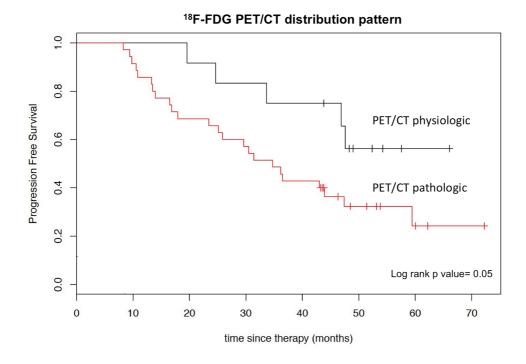
Supplementary Table 3 Multivariate Cox regression analysis of parameters unfavorably affecting PFS.

Parameters	HR	Lower 95% CI	Upper 95% CI	p-value
High cytogenetic risk	2.46	0.96	6.30	0.061
SUV _{max} reference	1.20	1.03	1.40	0.021
V _B reference (*1000)	1.01	1.00	1.02	0.009

HR, hazard ratio; 95% CI, 95% confidence intervals; SUV_{max}, maximum standardised uptake value



Supplementary Figure 1 The four different patterns of ¹⁸F-FDG uptake on PET/CT: negative (A), focal (B), diffuse (C) and mixed (D).



Supplementary Figure 2 PFS outcome according to physiologic and pathologic ¹⁸F-FDG PET/C distribution patterns.