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

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Supplementary Data

Statistics:

At initial staging, FDG-PET results were compared to the status of the disease determined by histology findings (if available), clinical and imaging follow-up. For each of FDG-PET potential metrics, a threshold value was determined using X-tile software (Yale University, New Haven, CT). For visual analysis, three positivity cut-off were studied DS =5, DS ≥4 and DS≥3. End points studied were PFS and OS, determined by clinical and imaging follow-up. Survival functions were calculated using Kaplan-Meier estimates and comparison between categories was made with the log-rank test. Univariate and multivariable analyses were performed using Cox proportional hazards models. Because survival was significantly prolonged in the RM group in the LyMa population, treatment arm was also considered in this analysis along with other baseline factors (aggressive morphological variants, Ki67>30%, MIPI score). The association between SUVmax at diagnosis and these baseline factors was evaluated using the Fisher's exact test. Only p-values< 0.05 were considered as statistically significant.

Multivariate analysis was conducted by first determining the best baseline model for survival using baseline clinical information (including treatment arm and MIPI score) and FDG-PET measures. Because SUVmax and SUVpeak showed similar prognostic values, we chose to assess FDG-uptake only as measured with SUVmax, this metric being the most widely used. For both PFS and OS, the base model was study arm (Non-randomized vs Obs vs RM), MIPI (Low vs Intermediate vs High) and SUV max (<=10.3 vs >10.3). There was no evidence of interaction effects across the three factors. Each metric was added to this model to determine if it provided any additional prognostic value.

Tables:

Table S1-Demographical and baseline characteristics

	LYMA-PET population N=104	LYMA population N=299	Test
Age at inclusion (years)			Wilcoxon
n	104	299	P = 0.523
Missing	0	0	
Median	57.0	57.0	
Min ; Max	41.0 ; 65.0	27.0 ; 65.0	
Sexe			Fisher Exact
Male / Female	78 /26 (75.% / 25%)	236/63 (79%/21%)	P = 0.236
Arm (randomized patients)			Fisher Exact
OBSERVATION	44 (47.8%)	120 (50.0%)	P = 0.691
RITUXIMAB	48 (52.2%)	120 (50.0%)	
LDH			Fisher Exact
N	61 (58.7%)	184 (61.5%)	P = 0.943
> N	40 (38.4%)	108 (36.2%)	
Not done	3 (2.9%)	7 (2.3%)	
Ann Arbor Staging			Fisher Exact
Missing	0	1	P = 0.089
2	4 (3.8%)	18 (6.0%)	
3	16 (15.4%)	31 (10.4%)	
4	84 (80.8%)	249 (83.6%)	
MIPI			Fisher Exact
Low	55 (52.9%)	159 (53.2%)	P = 0.507
Int	32 (30.8%)	82 (27.4%)	
High	17 (16.3%)	58 (19.4%)	

Statistical tests performed between LYMA-PET and Non LYMA-PET populations

Table S2- Description of FDG-PET metrics studied at baseline

	N=103
SUVmax	
Mean (SD)	8.7 (5.0)
Median	7.39
Q1 ; Q3	5.27 ; 11.64
Min ; Max	1.82 ; 33.85
SUVpeak	
Mean (SD)	4.81 (2.59)
Median	4.18
Q1 ; Q3	2.84 ; 6.74
Min ; Max	0 ; 13.96
Metabolic Tumor Volume (cm3)	
Mean (SD)	192.8655 (435.536)
Median	24.39
Q1 ; Q3	9.712 ; 124.890
Min ; Max	0.870 ; 2482.570
Total Lesion Glycolysis (cm3)	
Mean (SD)	820.5 (1667.83)
Median	105.18
Q1 ; Q3	32.93 ; 535.40
Min ; Max	0 ; 9384.41

Table S3- Multivariate survival analyses

Based on the LYMA-PET patient set the best Cox model for PFS includes study arm (Non-randomized vs Observation vs Rituximab), MIPI (Low vs Intermediate vs High) and SUV max (<=10.3 vs > 10.3). There was no evidence of interaction effects across the three factors.

Table S3.1 - Cox Model (Arm, SUVmax and MIPI) for PFS

Parameter	Modality tested	Hazard Ratio	95% Hazard Ratio Confidence Limits		Pr>ChiSq
			Lower	Upper	
SUVmax	>10.3	5.415	2.489	11.779	<.0001
MIPI SCORE	High	2.137	0.808	5.652	0.1257
	Int	2.562	1.133	5.796	0.0239
D arm	Non-randomized	17.454	6.539	46.588	<.0001
	RITUXIMAB	0.358	0.134	0.952	0.0395

Model is based on 103 patients (33 with events and 70 censoring).

Table S3.2 - Cox Model (Arm SUVmax and MIPI) for OS

Parameter	Modality tested	Hazard Ratio	95% Hazard Ratio Confidence Limits		Pr>ChiSq
			Lower	Upper	
SUVmax	>10.3	6.318	2.584	15.445	<.0001
MIPI SCORE	High	4.966	1.548	15.934	0.0071
	Int	3.134	1.172	8.375	0.0228
D arm	Non-randomized	10.507	3.784	29.178	<.0001
	RITUXIMAB	0.900	0.304	2.669	0.8499

Model is based on 103 patients (24 with events and 79 censoring).

Table S4- Description of FDG-PET metrics studied after induction therapy and at end of treatment

	Before transplantation N=64	End of Treatment N=44
SUVmax		
Median	1.9	1.9
Range	[0.5-16]	[0.5-24.1]
ΔSUVmax		
Median	- 68%	- 76 %
Range	[-100% - +271%]	[-100% - +17%]
SUVpeak		
Median	1.4	1.4
Range	[0.3-20.3]	[0.4-17.2]
ΔSUVpeak		
Median	69%	-78%
Range	[-95% - +278%]	[-96% - + 13%]
Deauville Score		
1	19 (29.6%)	23 (52.3%)
2	23 (35.9%)	12 (27.3%)
3	8 (12.5%)	6 (16.6%)
4	6 (9.3%)	1 (2.3%)
5	8 (12.5%)	2 (4.5%)

Table S5-Prognostic values (p-value and Hazard Ratios when p-value < 0.05) of metrics derived FDG-PET before transplantation and end of treatment.

		Metrics	Modality	P-value	Hazard Ratio	95% Hazard Ratio Confidence	
						Lower	Upper
Before Transplantation (n=64)	*PFS*	$SUVmax_{iPET}$	>6,3	0.0977	3.627	0.789	16.667
	OS	$SUVmax_{iPET}$	>6,3	0.0199	6.927	1.357	35.351
	PFS	$\Delta SUVmax_{iPET}$	>-29.65%	0.2976	-	-	-
	OS	$\Delta SUVmax_{iPET}$	>-29.65%	0.1089	-	-	-
End of Treatment (n=41)	*PFS*	$SUVmax_{eotPET}$	>1,18	0.3879	-	-	-
	OS	$SUVmax_{eotPET}$	>1,18	0.0708	0.228	0.046	1.134
	PFS	$\Delta SUVmax_{eotPET}$	>-90.88%	0.0209	0.196	0.049	0.781
	OS	$\Delta SUVmax_{eotPET}$	>-90.88%	0.1836	-	-	-