

**SUPPLEMENTAL TABLE 1 Uni- and multivariable Cox Proportional Hazard analyses including baseline MTV for 2-year PFS (n=296)**

	2-year PFS			
	Univariate HR (95%CI)	p-value	Multivariable HR (95%CI)	p-value
<b>Age (≤60 vs &gt;60)</b>	1.44 (0.80-2.59)	0.222	1.83 (1.01-3.32)	0.046
<b>aaPI (low/low-intermediate vs high-intermediate/high)</b>	2.83 (1.50-5.34)	0.001*		
<b>B symptoms (no vs yes)</b>	1.97 (1.18-3.30)	0.010*	1.75 (1.04-2.98)	0.036
<b>Baseline MTV log-transformed</b>	1.43 (1.16-1.76)	0.001*	1.32 (1.07-1.62)	0.010
<b>ΔSUVmax (&gt;70% vs ≤70%)</b>	7.44 (4.29-12.92)	<0.0001*	7.87 (4.48-13.83)	<0.0001*
<b>Gender (male vs female)</b>	0.73 (0.44-1.23)	0.240		
<b>Treatment arm (R-CHOP14 vs RR-CHOP14)</b>	0.85 (0.51-1.42)	0.539		

\* Statistically significant difference

Abbreviations: 95%CI= 95% confidence interval; aaPI= age-adjusted international prognostic index; HR= Hazard Ratio; LDH= lactate dehydrogenase; MTV=metabolic tumor volume; PFS= progression-free survival; WHO= world health organization

**SUPPLEMENTAL TABLE 2 I-PET4 and EoT-PET 2x2 contingency table**

	<b>EoT-PET positive (DS 4-5)</b>	<b>EoT-PET negative (DS 1-3)</b>	<b>Total</b>
<b>I-PET4 positive (DS 4-5)</b>	54	42~	96
<b>I-PET4 negative (DS 1-3)</b>	20^	358	378
<b>Total</b>	74 *	400 †	474

*Abbreviations: DS= Deauville 5-point scale; EoT-PET= end-of-treatment <sup>18</sup>F-FDG PET(/CT); I-PET4= interim <sup>18</sup>F-FDG PET(/CT) after four treatment cycles.*

*\*No I-PET4 was performed in 5 patients with positive EoT-PET (reasons unknown)*

*†No I-PET4 was performed in 14 patients with negative EoT-PET(reasons unknown), in 3 patients I-PET4 was not available for qualitative analysis (high glucose, poor visual quality and not interpretable due to missing baseline scan, respectively)*

*^ Twenty patients (4.2%) switched from a negative I-PET4 to a positive EoT-PET, sixteen of these patients had a high-intermediate or high aalPI and had a 2-year PFS of 40% (95%CI 18-62%).*

*~ Forty-two patients (8.9%) had a positive I-PET4 and turned negative at EoT-PET, of these only 4 patients had progressive disease within 2 years after randomization of whom 2 died within this period. These converting patients had a 2-year PFS of 90% (95%CI 81-99%).*

**SUPPLEMENTAL TABLE 3** Diagnostic and prognostic measures for aaIPI, baseline MTV, for different cut-off values of the Deauville 5-point scale at I-PET4, and  $\Delta$ SUVmax for 2-year PFS for subset of patients with baseline MTV analysis ( $n=296$ )

		Diagnostic information				Prognostic information		Discrimination	
		Number of patients (n)	Negative Predictive Value %(95%CI)	Positive Predictive Value %(95%CI)	Sensitivity %(95%CI)	Specificity %(95%CI)	Univariate Hazard Ratio (95%CI)	p-value	AUC (95%CI)
<b>AaIPI</b>	<b>L/LI vs HI/H</b>	118 vs 178	89.8 (83.1-94.1)	26.4 (20.5-33.3)	79.7 (67.7-88.0)	44.7 (38.5-51.2)	2.83 (1.50-5.34)	0.0013	0.61 (0.55-0.67)
<b>Baseline MTV</b>	<b>≤345ml vs &gt;345ml</b>	137 vs 159	86.1 (79.4-90.9)	25.2 (19.2-32.4)	67.8 (55.1-78.3)	49.8 (43.5-56.1)	1.96 (1.13-3.38)	0.0161	0.58 (0.52-0.65)
<b>I-PET4</b>	<b>DS1 vs DS2-5</b>	88 vs 208	84.1 (75.1-90.7)	21.6 (16.6-27.7)	76.3 (64.0-85.3)	31.2 (25.7-37.4)	1.42 (0.78-2.59)	0.252	0.54 (0.48-0.59)
	<b>DS1-2 vs DS3-5</b>	159 vs 137	86.8 (80.7-91.2)	27.7 (20.9-35.8)	64.4 (51.7-75.4)	58.2 (51.9-64.3)	2.39 (1.40-4.07)	0.0014	0.61 (0.55-0.67)
	<b>DS1-3 vs DS4-5</b>	226 vs 70	86.7 (81.7-90.5)	41.4 (30.6-53.1)	49.2 (36.8-61.6)	82.7 (77.4-87.0)	3.99 (2.39-6.66)	<0.0001	0.65 (0.60-0.70)
	<b>DS1-4 vs DS5</b>	280 vs 16	83.2 (78.4-87.1)	75.0 (50.5-89.8)	20.3 (12.0-32.3)	98.3 (95.7-99.3)	9.49 (5.00-18.01)	<0.0001	0.59 (0.57-0.62)
<b><math>\Delta</math>SUVmax</b>	<b>&gt;70% vs ≤70%</b>	266 vs 30	85.0 (80.2-88.8)	63.3 (45.5-78.1)	32.2 (21.7-44.9)	95.4 (91.9-97.4)	7.46 (4.30-12.95)	<0.0001	0.64 (0.61-0.67)

*Abbreviations: 95%CI= 95% confidence interval; AaIPI= age-adjusted international prognostic index; AUC= area under the receiver*

*operating curve; DS= Deauville 5-point scale;  $\Delta$ SUVmax= reduction of maximum standardized uptake value between baseline and interim*

*18F-FDG PET(/CT); H=high risk group; HI= high-intermediate risk group; I-PET= interim 18F-FDG PET(/CT) after four cycles; MTV= metabolic*

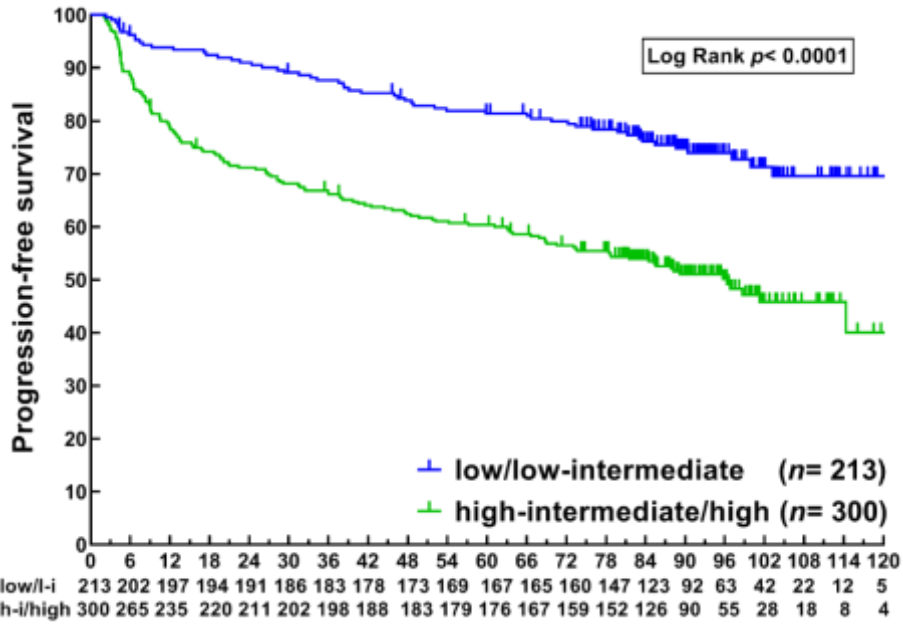
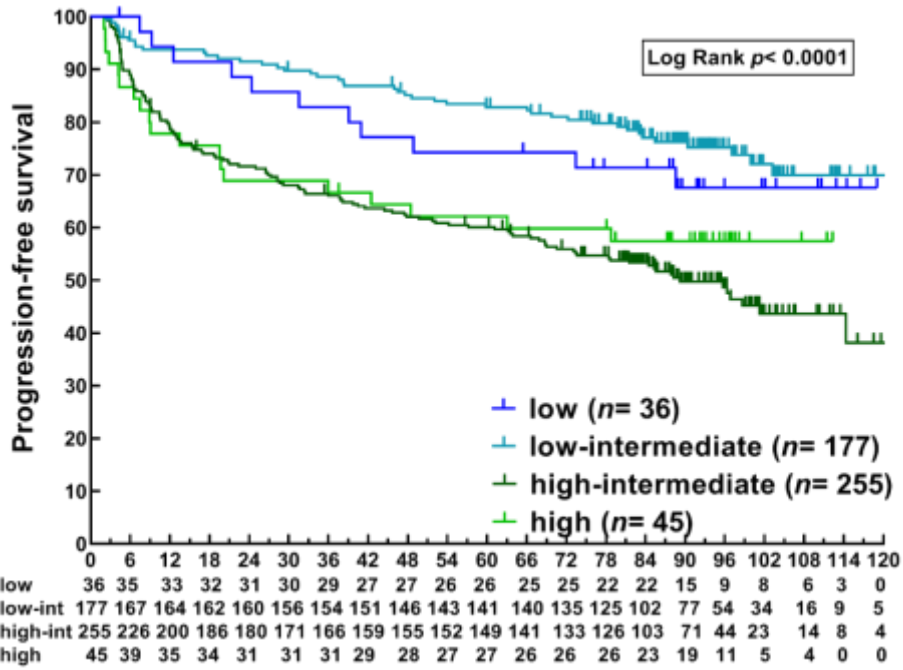
*tumor volume; PFS= progression-free survival*

**SUPPLEMENTAL TABLE 4 Uni- and multivariable Cox Proportional Hazard analyses of  $\Delta$ SUVmax analysis-group for 2-year PFS (n=367)**

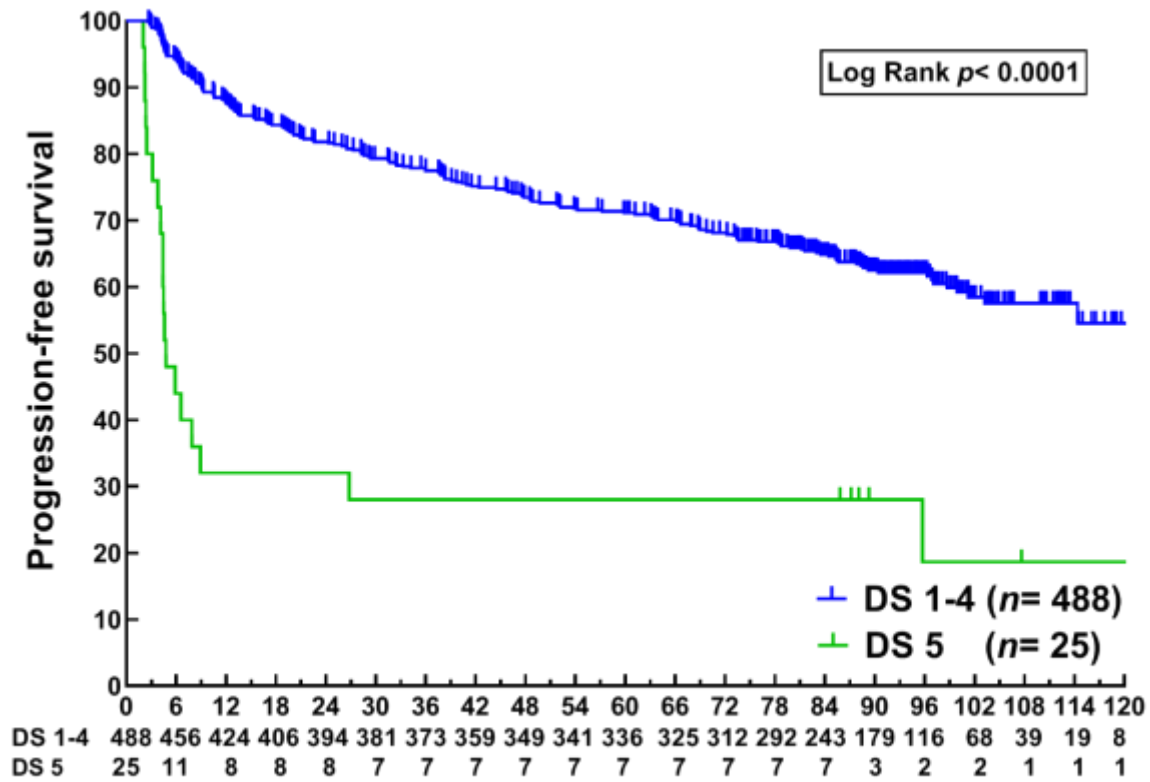
	2-year PFS			
	Univariate HR (95%CI)	p-value	Multivariable HR (95%CI)	p-value
<b>Age (<math>\leq 60</math> vs <math>&gt;60</math>)</b>	1.60 (0.95-2.69)	0.075		
<b>aaPI (low/low-intermediate vs high-intermediate/high)</b>	3.16 (1.80-5.55)	<0.0001*	3.27 (1.86-5.75)	<0.0001*
<b>B symptoms (no vs yes)</b>	1.67 (1.07-2.61)	0.025*		
<b><math>\Delta</math>SUVmax (<math>&gt;70\%</math> vs <math>\leq 70\%</math>)</b>	4.80 (2.88-8.00)	<0.0001*	5.01 (3.00-8.36)	<0.0001*
<b>Gender (male vs female)</b>	1.25 (0.80-1.96)	0.335		
<b>Treatment arm (R-CHOP14 vs RR-CHOP14)</b>	0.99 (0.63-1.54)	0.957		

\* Statistically significant difference

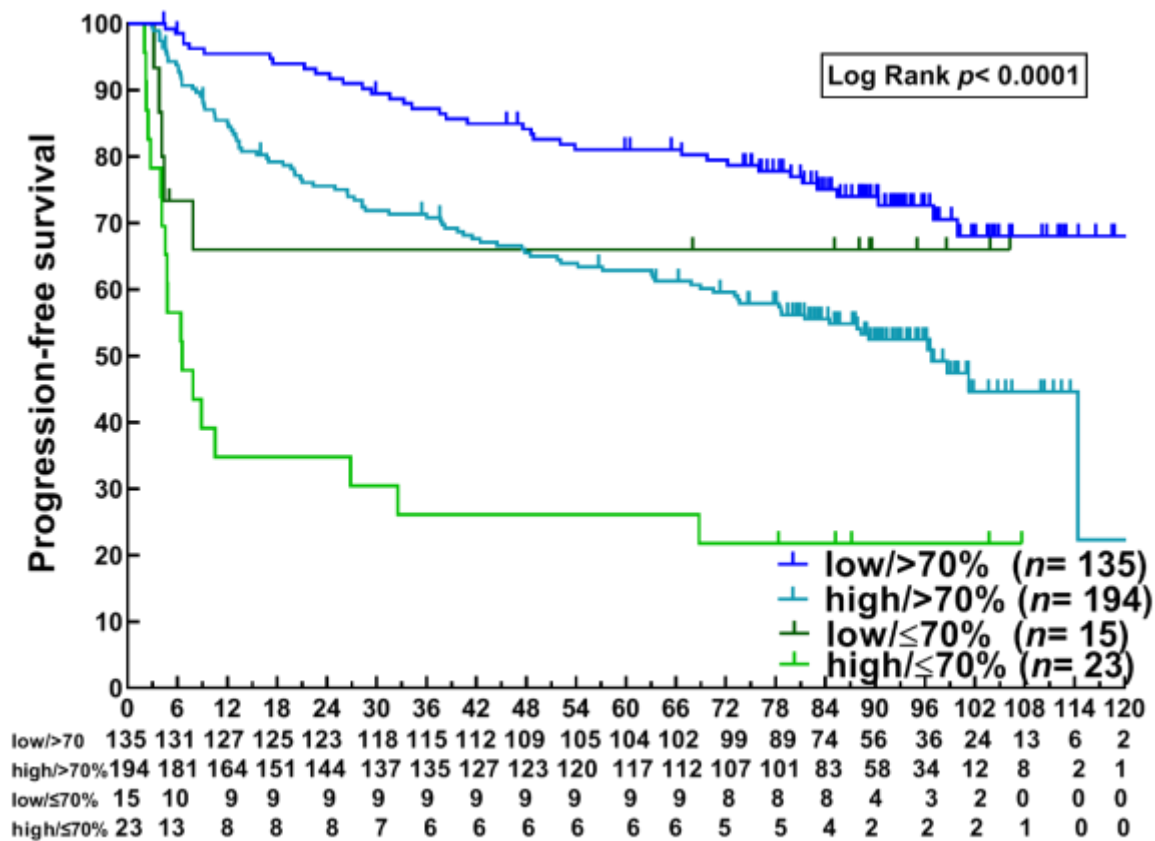
Abbreviations: 95%CI= 95% confidence interval; aaPI= age-adjusted international prognostic index;  $\Delta$ SUVmax= reduction of maximum standardized uptake value between baseline and interim 18F-FDG PET(/CT); HR= Hazard Ratio; LDH= lactate dehydrogenase; PFS= progression-free survival; WHO= world health organization



**SUPPLEMENTAL FIGURE 1** Kaplan-Meier curves for progression-free survival in months stratified by ordinal aaPI (1a) and dichotomized aaPI (1b)



SUPPLEMENTAL FIGURE 2 Kaplan-Meier curves for I-PET4 with numbers at risk for progression-free survival in months stratified by DS1-4 vs DS5 result.



SUPPLEMENTAL FIGURE 3 Kaplan-Meier curves for progression-free survival in months stratified by combined aaPI and  $\Delta$ SUVmax subgroups.

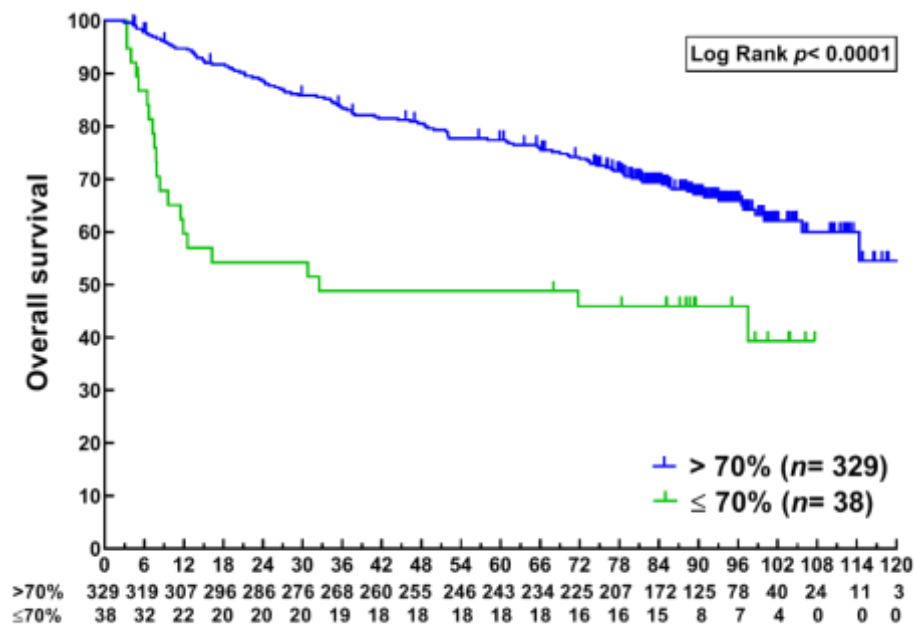
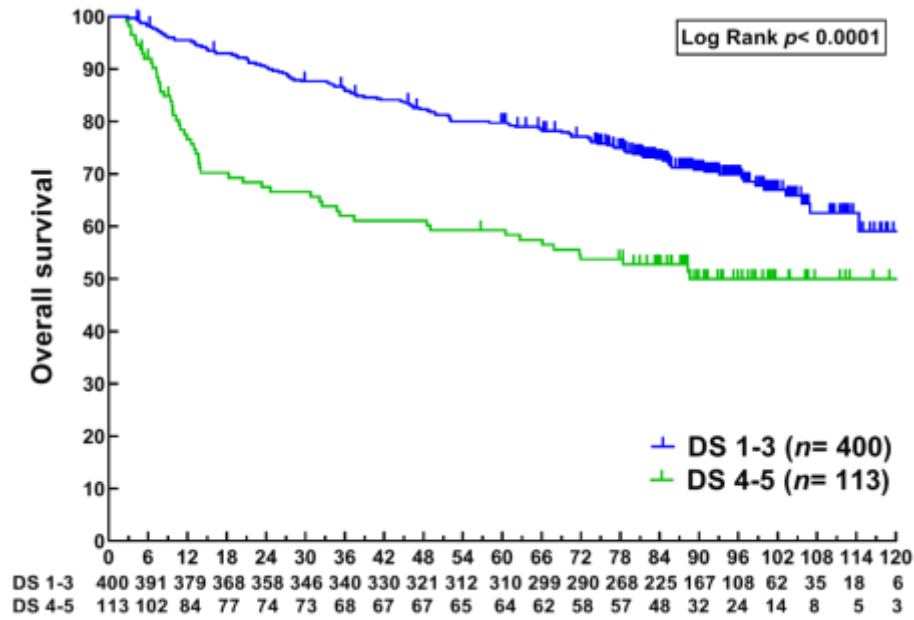
### **3. SECONDARY OUTCOME MEASURES**

#### **Definitions:**

Overall survival (OS) was defined as time from randomisation to death, patients still alive were censored at date of last contact.

#### **Kaplan-Meier curves for OS**





**SUPPLEMENTAL FIGURE 4** Kaplan-Meier curves with numbers at risk for overall survival in months stratified by I-PET4 result according to DS (4a) and according to  $\Delta$ SUVmax result (4b).

**SUPPLEMENTAL TABLE 5 Diagnostic and prognostic measures for baseline MTV, for different cut-off values for the Deauville 5-point scale at I-PET4, and  $\Delta$ SUVmax for 2-year OS**

		Diagnostic information				Prognostic information	Discrimination
		Negative Predictive Value % (95%CI)	Positive Predictive Value % (95%CI)	Sensitivity % (95%CI)	Specificity % (95%CI)	Univariate Hazard Ratio (95%CI)	AUC (95%CI)
<b>Baseline MTV</b>	<b>≤345ml vs &gt;345ml</b>	90.5 (84.4-94.4)	20.1 (14.6-27.0)	71.1 (56.6-82.3)	49.9 (43.3-55.6)	2.23 (1.17-4.24)	0.59 (0.52-0.66)
<b>I-PET4</b>	<b>DS1 vs DS2-5</b>	87.6 (82.0-91.7)	15.5 (12.0-19.8)	70.3 (59.1-79.5)	35.5 (31.2-40.1)	1.29 (0.79-2.13)	0.53 (0.47-0.64)
	<b>DS1-2 vs DS3-5</b>	90.3 (86.4-93.2)	20.6 (15.8-26.4)	62.2 (50.8-72.4)	59.7 (55.0-64.2)	2.35 (1.47-3.75)	0.61 (0.55-0.66)
	<b>DS1-3 vs DS4-5</b>	90.5 (87.2-93.0)	31.6 (24.0-40.9)	48.7 (37.6-59.8)	82.5 (78.6-85.7)	4.02 (2.55-6.35)	0.65 (0.61-0.70)
	<b>DS1-4 vs DS5</b>	88.3 (85.2-90.9)	68.0 (48.4-82.8)	23.0 (14.9-33.7)	98.2 (96.5-99.1)	9.85 (5.69-17.03)	0.60 (0.58-0.62)
<b><math>\Delta</math>SUVmax</b>	<b>&gt;70% vs ≤70%</b>	88.8 (84.9-91.7)	44.7 (30.2-60.3)	31.5 (20.7-44.7)	93.3 (90.0-95.6)	5.52 (3.10-9.83)	0.62 (0.59-0.66)

*Abbreviations: 95%CI= 95% confidence interval; AUC= area under the receiver operating curve; DS= Deauville 5-point scale;  $\Delta$ SUVmax= reduction of maximum standardized uptake value between baseline and interim 18F-FDG PET(/CT); I-PET= interim 18F-FDG PET(/CT) after four cycles; MTV= metabolic tumor volume; OS= overall survival*

**SUPPLEMENTAL TABLE 6 Uni- and multivariable Cox Proportional Hazard analyses of  $\Delta$ SUVmax analysis-group for 2-year OS ( $n=367$ )**

	2-year OS			
	Univariate HR (95%CI)	<i>p</i> -value	Multivariable HR (95%CI)	<i>p</i> -value
<b>Age (<math>\leq 60</math> vs <math>&gt;60</math>)</b>	1.65 (0.88-3.08)	0.116	1.92 (1.01-3.62)	0.046*
<b>aaIPI (low/low-intermediate vs high-intermediate/high)</b>	2.85 (1.47-5.52)	0.0002*	2.42 (1.24-4.76)	0.010*
<b>B symptoms (no vs yes)</b>	2.12 (1.23-3.65)	0.0007*	1.82 (1.01-3.16)	0.036*
<b><math>\Delta</math>SUVmax (<math>&gt;70\%</math> vs <math>\leq 70\%</math>)</b>	5.52 (3.10-9.83)	$<0.0001^*$	6.03 (3.36-10.81)	$<0.0001^*$
<b>Gender (male vs female)</b>	0.68 (0.40-1.18)	0.172	0.55 (0.31-0.95)	0.034*
<b>Treatment arm (R-CHOP14 vs RR-CHOP14)</b>	1.01 (0.59-1.72)	0.969		

\* Statistically significant difference

Abbreviations: 95%CI= 95% confidence interval; aaIPI= age-adjusted international prognostic index;  $\Delta$ SUVmax= reduction of maximum standardized uptake value between baseline and interim  $^{18}$ F-FDG PET(/CT); HR= Hazard Ratio; OS= overall survival

**SUPPLEMENTAL TABLE 7 Uni- and multivariable Cox Proportional Hazard analyses including baseline MTV for 2-year OS (n=296)**

	2-year OS			
	Univariate HR (95%CI)	p-value	Multivariable HR (95%CI)	p-value
<b>Age (≤60 vs &gt;60)</b>	1.36 (0.70-2.62)	0.367		
<b>aalPI (low/low-intermediate vs high-intermediate/high)</b>	2.43 (1.20-4.91)	0.013*		
<b>B symptoms (no vs yes)</b>	2.15 (1.19-3.91)	0.012*		
<b>Baseline MTV log-transformed</b>	1.62 (1.25-2.08)	0.0002*	1.55 (1.20-2.00)	0.001*
<b>ΔSUVmax (&gt;70% vs ≤70%)</b>	7.33 (3.97-13.55)	<0.0001*	6.75 (3.63-12.55)	<0.0001*
<b>Gender (male vs female)</b>	0.67 (0.37-1.21)	0.182		
<b>Treatment arm (R-CHOP14 vs RR-CHOP14)</b>	0.97 (0.54-1.74)	0.923		

\* Statistically significant difference

Abbreviations: 95%CI= 95% confidence interval; aalPI= age-adjusted international prognostic index; HR= Hazard Ratio; MTV=metabolic tumor volume; OS= overall survival