Interim PET evaluation in diffuse large B-cell lymphoma employing published recommendations:

Comparison of the Deauville 5-point scale and the ΔSUV_{max} method

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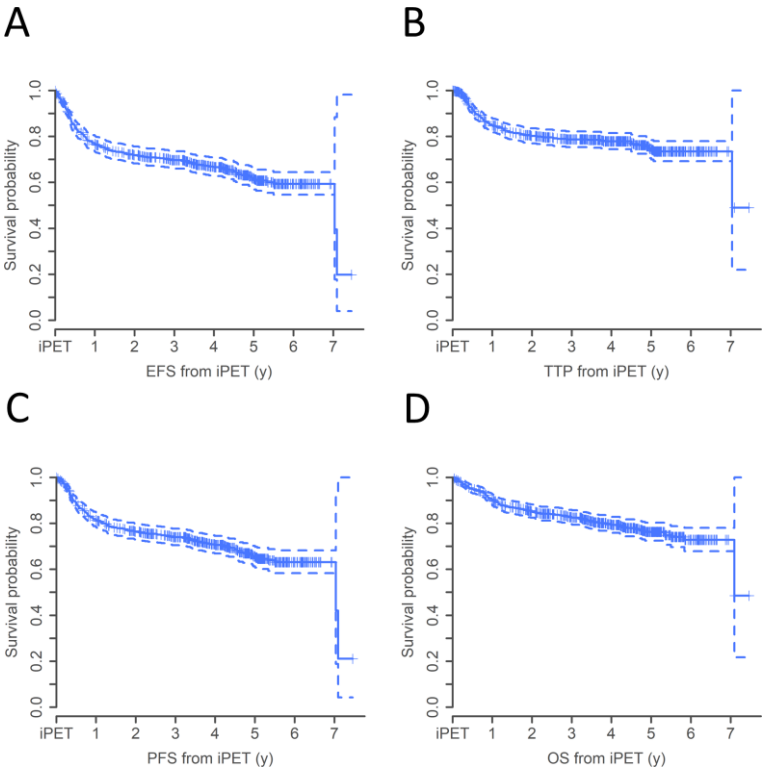
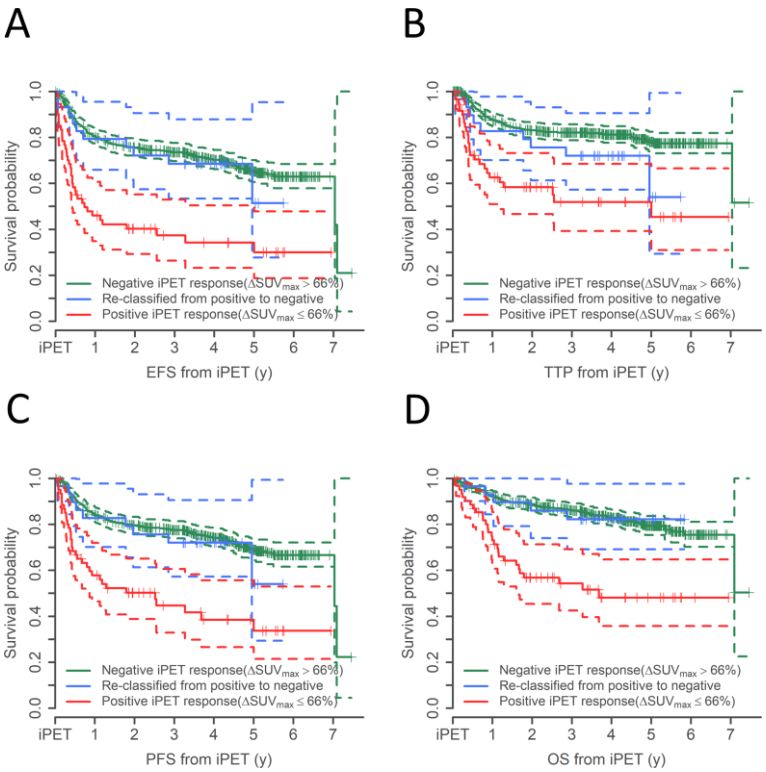
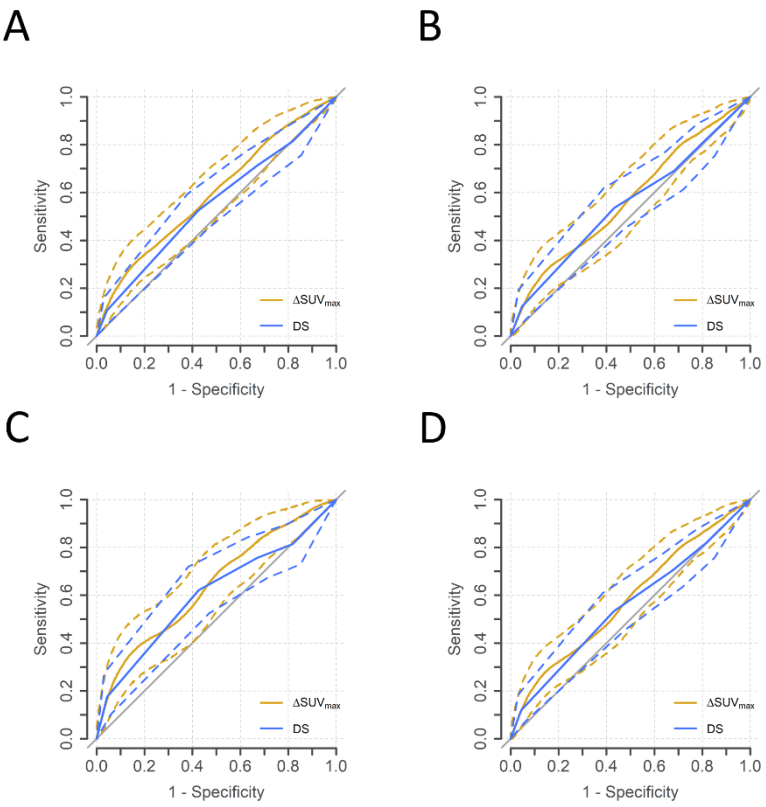
Supplemental Data



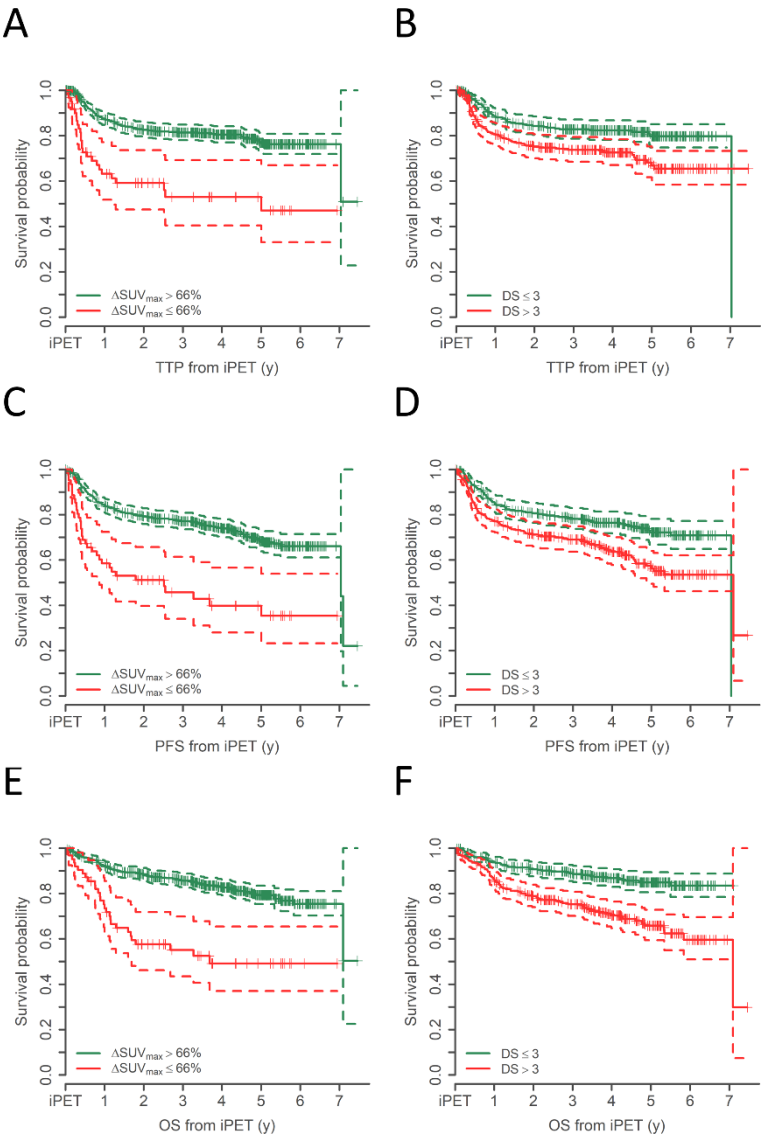
Supplemental Figure 1 Kaplan-Meier curves for the final analysis population (n = 596) for event-free survival (Panel A), time to progression (Panel B), progression-free survival (Panel C), and overall survival (Panel D). Dashed lines indicate 95% confidence intervals. EFS: event-free survival; iPET: interim positron emission tomography; OS: overall survival; PFS: progression-free survival; TTP: time to progression.



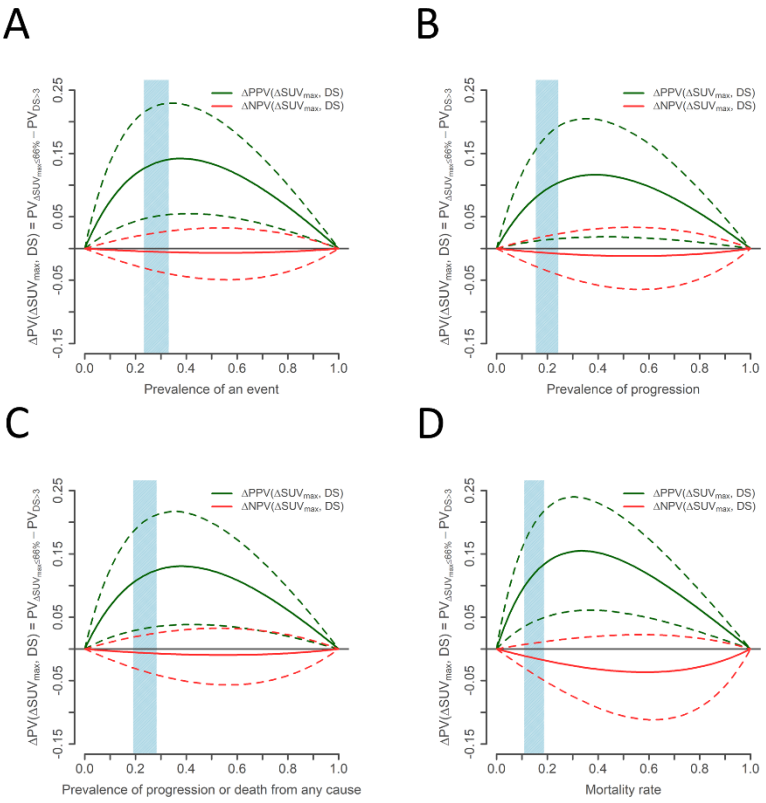
Supplemental Figure 2 Kaplan-Meier curves by ΔSUV_{max} interim positron emission tomography classification for event-free survival (Panel A), time to progression (Panel B), progression-free survival (Panel C), and overall survival (Panel D). The blue curves represent the group of patients lacking unphysiological ^{18}F-FDG uptake in interim positron emission tomography (n = 29) and being re-classified from positive response to negative response according to the modification of the ΔSUV_{max} method as described in the manuscript. Dashed lines indicate 95% confidence intervals. DS: Deauville score; ΔSUV_{max}: deltaSUVmax; EFS: event-free survival; iPET: interim positron emission tomography; OS: overall survival; PFS: progression-free survival; TTP: time to progression.



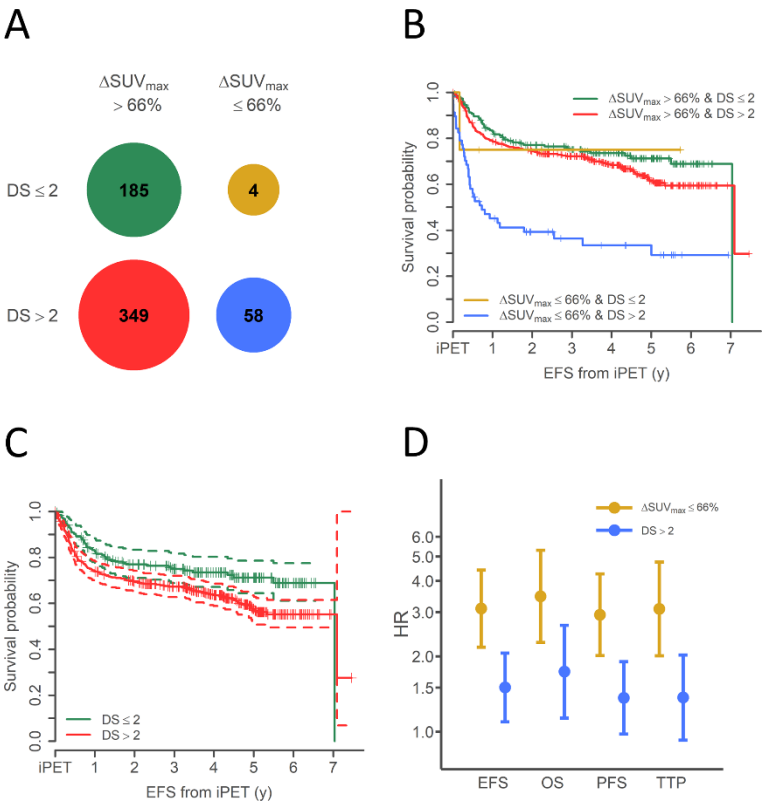
Supplemental Figure 3 Receiver operating characteristic curves for the ΔSUV_{max} approach and the Deauville score for event-free survival (Panel A), time to progression (Panel B), progression-free survival (Panel C), and overall survival (Panel D). Dashed lines indicate bootstrapped 95% confidence intervals. DS: Deauville score; ΔSUV_{max}: deltaSUVmax.



Supplemental Figure 4 Kaplan-Meier curves by early metabolic tumor response as assessed by the ΔSUV_{max} cut-off and the Deauville score cut-off for time to progression (Panels A & B), progression-free survival (Panels C & D), and overall survival (Panels E & F). Dashed lines indicate 95% confidence intervals. DS: Deauville score; ΔSUV_{max}: deltaSUVmax; EFS: event-free survival; iPET: interim positron emission tomography; OS: overall survival; PFS: progression-free survival; TTP: time to progression.



Supplemental Figure 5 Plot of predictive value differences for event-free survival (Panel A), time to progression (Panel B), progression-free survival (Panel C), and overall survival (Panel D). The x-axis spans the entire range of possible values for the unknown event prevalence of the respective endpoint (e.g., for the probability of an event in terms of overall survival, that is, mortality). The shaded blue rectangle represents a data-driven best guess for the true prevalence. Its interval on the x-axis refers to one minus the 99% confidence interval of the final analysis population's Kaplan-Meier estimator $\widehat{KM}$ at the time point of interest two years after interim positron emission tomography, e.g., for event-free survival it corresponds to the 99% confidence interval of $1-\widehat{KM}_{EFS}(t=2)$, where the left boundary x_1 of the blue rectangle refers to the lower confidence limit and its right boundary x_2 to the respective upper confidence limit. The y-axis indicates the difference between either the positive or negative predictive value of the ΔSUV_{max} ≤66% cut-off and the corresponding predictive value (positive or negative) of the Deauville score greater than three cut-off; in general notation for any of the two predictive values $\Delta PV(\Delta SUV_{max}, DS) = PV_{\Delta SUV_{max}\leq 66\%} - PV_{DS>3}$ as in the y-axis label. Plotted as a function of the unknown prevalence, the difference between the positive predictive value of the ΔSUV_{max} cut-off and the positive predictive value of the Deauville score cut-off ($\Delta PPV(\Delta SUV_{max}, DS)$ is shown in green. The difference between the negative predictive value of the ΔSUV_{max} cut-off and the negative predictive value of the Deauville score cut-off ($\Delta NPV(\Delta SUV_{max}, DS)$ is shown in red. Dashed lines indicate empirical 95% confidence intervals for the respective differences obtained by the bootstrap. DS: Deauville score; ΔSUV_{max}: deltaSUVmax; NPV: negative predictive value; PPV: positive predictive value; PV: predictive value.



Supplemental Figure 6 Results for the Deauville score cut-off defining an unfavorable early metabolic tumor response as an uptake above that of the mediastinum: Concordance between the ΔSUV_{max} and the Deauville score cut-off (Panel A). Kaplan-Meier event-free survival curves by concordance category (Panel B). Kaplan-Meier event-free survival curves by early metabolic tumor response (Panel C). Cox regression model hazard ratio with 95% confidence interval by method and time-to-event endpoint (Panel D). DS: Deauville score; ΔSUV_{max}: deltaSUVmax; EFS: event-free survival; HR: hazard ratio; iPET: interim positron emission tomography; OS: overall survival; PFS: progression-free survival; TTP: time to progression.

Supplemental Table 1 Numerical results of the time-dependent receiver operating characteristic curve analyses and the Cox regression model for event-free, progression-free, and overall survival as well as for time to progression. With regard to the area under the receiver operating characteristic curve, sensitivity, and specificity, confidence intervals relate to a simple bootstrap with 10,000 repetitions.

		EFS	TTP	PFS	OS
AUC (95% CI)	ΔSUV_{max}	0.597 (0.545–0.648)	0.581 (0.525–0.636)	0.641 (0.573–0.706)	0.572 (0.512–0.633)
	DS	0.552 (0.507–0.599)	0.554 (0.505–0.607)	0.605 (0.541–0.676)	0.552 (0.498–0.609)
HR (95% CI)	ΔSUV_{max}	3.10 (2.18–4.42)	3.09 (2.01–4.76)	2.93 (2.01–4.26)	3.47 (2.27–5.30)
	DS	1.70 (1.29–2.24)	1.72 (1.21–2.43)	1.68 (1.25–2.25)	2.54 (1.76–3.68)
Sensitivity (95% CI)	ΔSUV_{max}	0.246 (0.186–0.312)	0.247 (0.173–0.328)	0.249 (0.182–0.321)	0.325 (0.232–0.426)
	DS	0.525 (0.455–0.593)	0.537 (0.451–0.619)	0.533 (0.454–0.610)	0.621 (0.524–0.719)
Specificity (95% CI)	ΔSUV_{max}	0.888 (0.859–0.917)	0.874 (0.845–0.902)	0.881 (0.851–0.909)	0.880 (0.852–0.906)
	DS	0.575 (0.528–0.622)	0.567 (0.522–0.612)	0.570 (0.525–0.616)	0.574 (0.530–0.617)

AUC: area under the receiver operating characteristic curve; CI: confidence interval; DS: Deauville score; ΔSUV_{max}: deltaSUVmax; EFS: event-free survival; HR: hazard ratio; OS: overall survival; PFS: progression-free survival; TTP: time to progression.