

Supplementary figures and tables

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Table S1: Neuroblastoma classification according to the International Neuroblastoma Risk Group staging system

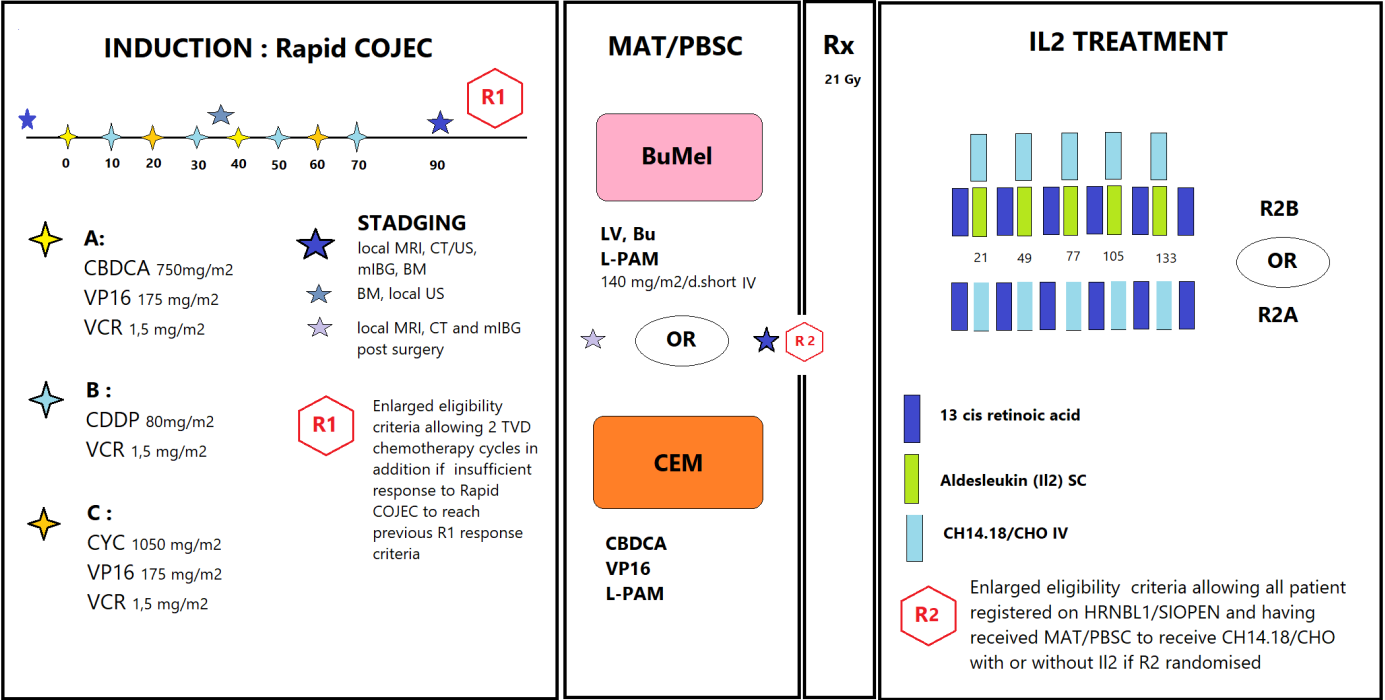
INRG Stage	Age	Histologic Category	Grade of Tumor Differentiation	MYCN	11q Aberration	Ploidy	Pretreatment Risk Group
L1/2		GN maturing GNB intermixed					Very Low
L1		Any except GN maturing or GNB intermixed		NA			Very Low
				Amplified			High
L2	< 18 months	Any except GN maturing or GNB intermixed		NA	No		Low
					Yes		Intermediate
	> 18 months	GNB nodular, Neuroblastoma	Differentiating	NA	No		Low
					Yes		Intermediate
			Poorly or un - differentiated	NA			High
					Amplified		High
M	< 18			NA		Hyperdiploid	Low
	> 12			NA		Diploid	Intermediate
	12 to <18			NA		Diploid	Intermediate
	< 18			Amplified			High
	> 18						High
MS				NA	No		Very Low
					Yes		High
				Amplified			High

Adapted from ref [6]. GN: Ganglioneuroma. GNB: Ganglioneuroblastoma. NA: Non Amplified.

Table S2: Cox analysis of progression-free survival

	Hazard ratio	p	coef lower 95%	coef upper 95%
age	0.998	0.784	0.983	1.01
sex	1.2	0.652	0.545	2.64
log(LDH)	1.69	0.0922	0.918	3.1
SIOPEN	1.01	0.241	0.99	1.04
MYCN	1.1	0.85	0.416	2.9
$\log(\mu)$	0.932	0.248	0.827	1.05
visible threshold	0.998	0.482	0.991	1

Figure S1: HRNBL1 protocol

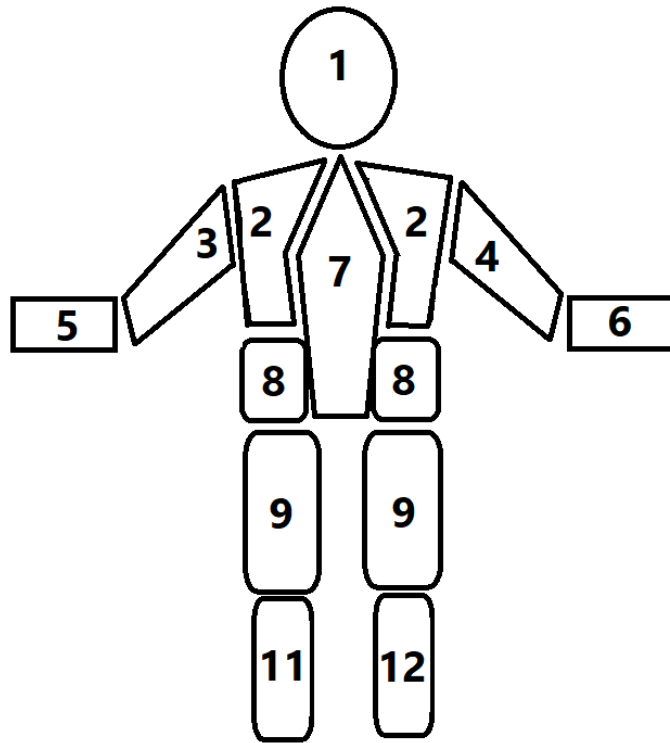


Time is in days.

Staging: MRI: Magnetic Resonance Imaging. CT: Computerized tomography. US: Ultrasound. mIBG: meta-iodo-benzyl-guanidine scintigraphy. BM: Medullar Bone exploration.

Treatments: CBDCA: Carboplatine, VP16: Etoposide, VCR: Vincristine, CDDP: Cisplatin. MAT: Myeloablative therapy. PBSC: Peripheral Blood Stem Cell. Bu Mel: Busulphan Mephalan. Rx: Radiotherapy.

Figure S2: SIOPEN scoring



To score patients, the skeleton is divided into 12 segments, and for each of them extension of the lesions is scored as:

- 0: no lesion
- 1 for 1 lesion
- 2 for 2 lesions
- 3 for 3 lesions
- 4 for > 3 lesions but $< 50\%$ of the concerned segment
- 5 for diffuse disease but $< 95\%$ of the whole segment
- 6 for difsuse disease $> 95\%$ of whole segment

The SIOPEN score is then defined as the sum of each segment's score.

Figure S3: Primary tumor and metastases location

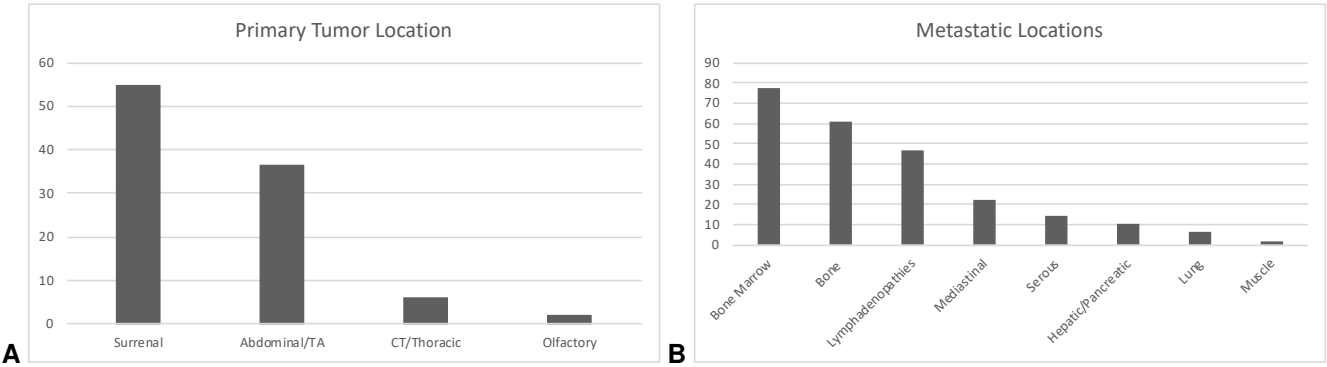
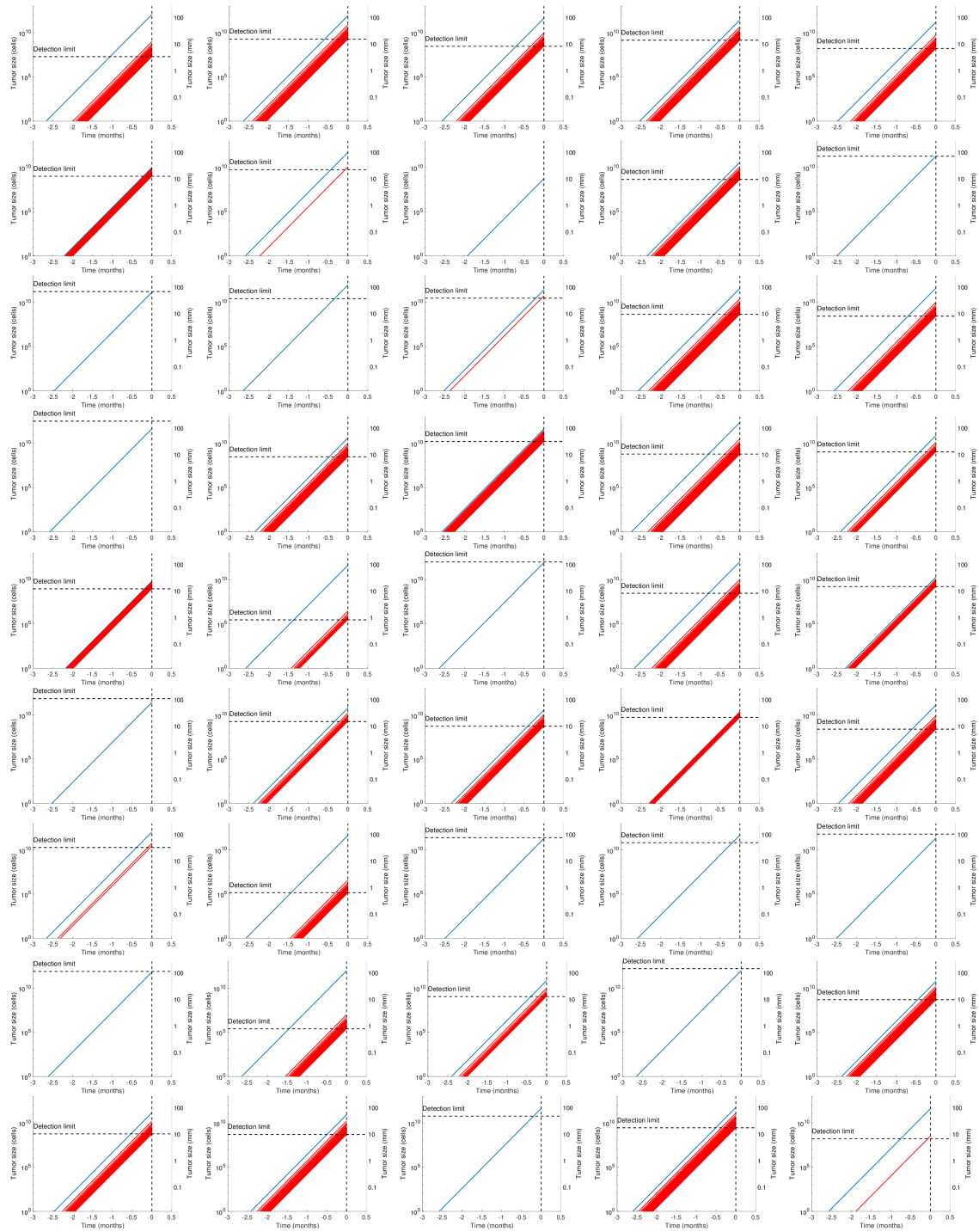
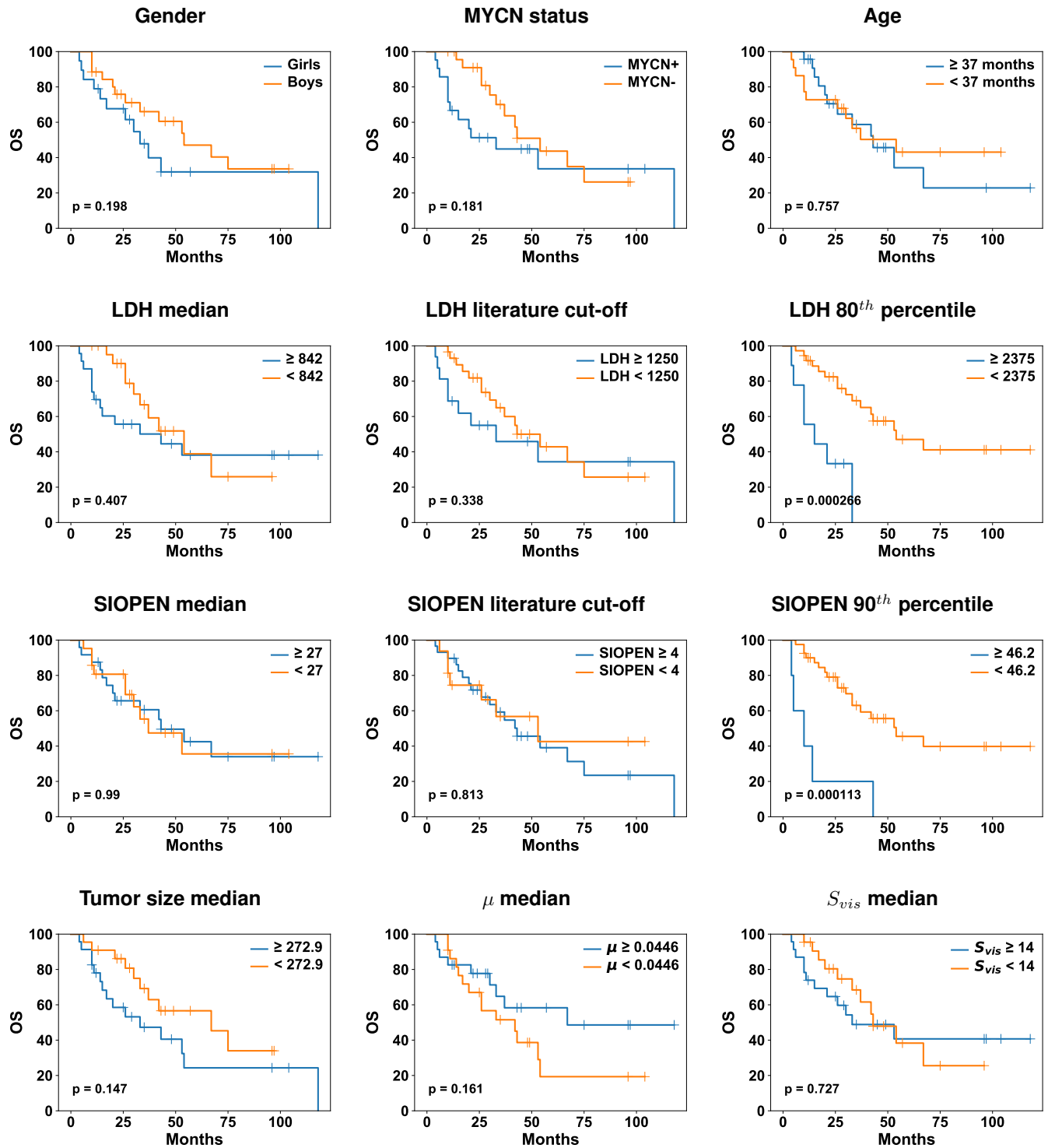


Figure S4: Simulations of all patients



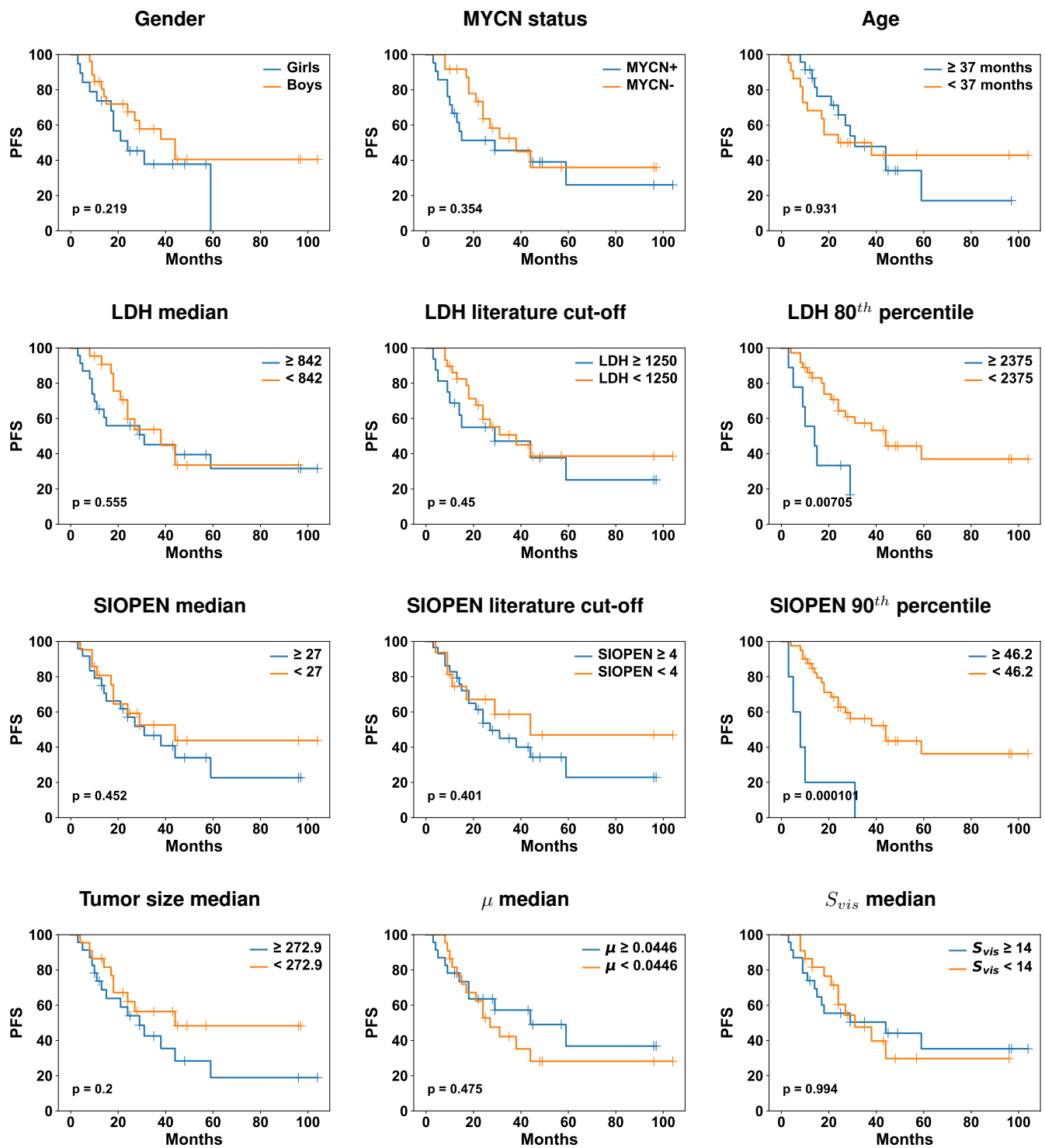
Simulations of the mechanistic model for all patients in the cohort. Blue line is the size of the primary tumor. Red lines are the predicted sizes of the metastases.

Figure S5: Overall survival analysis in dichotomized groups



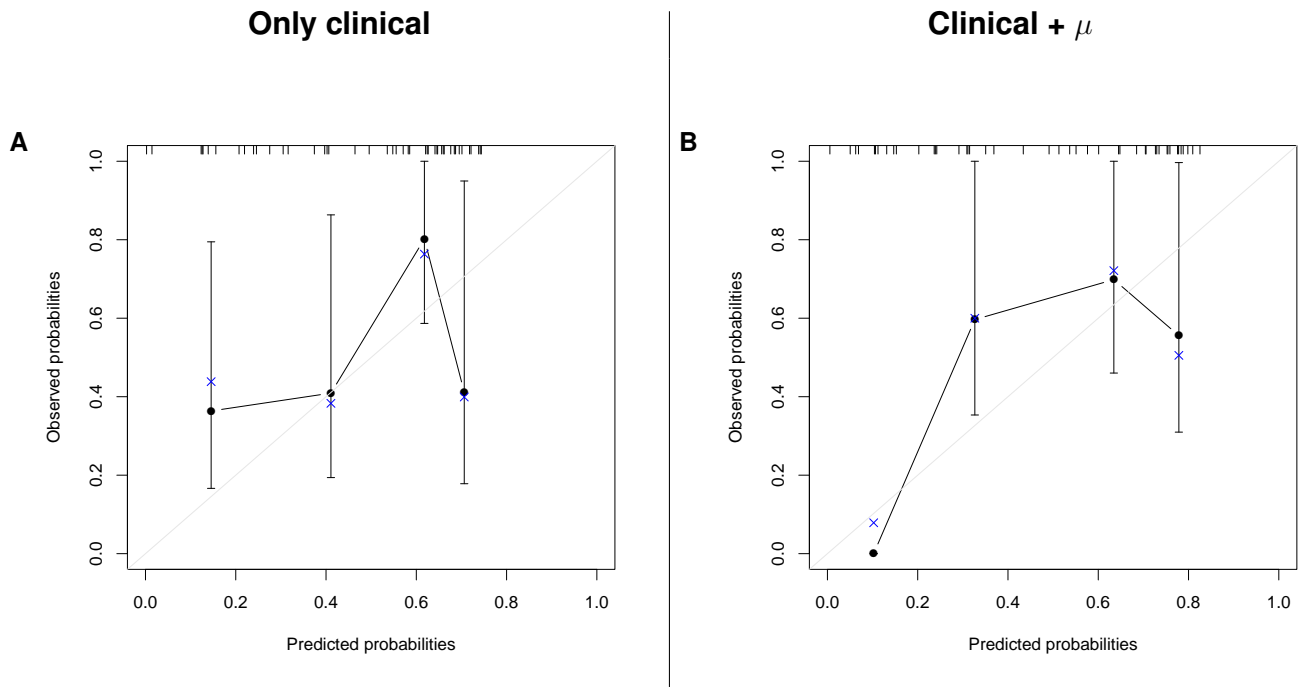
Dichotomized analysis of overall survival (OS) according to the different variables, at median or literature cut-offs.

Figure S6: Progression-free survival analysis in dichotomized groups



Dichotomized analysis of progression-free survival (PFS) according to the different variables, at median or literature cut-offs.

Figure S7: Calibration plots



A. Calibration plots of the prediction model with only clinical variables (i.e. tumor size and log(LDH) after variable selection). Crosses mark the bootstrap corrected estimates. B. Same as A. for the prediction model using the mathematical biomarkers as additional variables in the model (i.e. $\log(\mu)$ and log(LDH)) after variable selection).