6. SUPPLEMENTARY FILES

SUPPLEMENTARY TABLE 1: Risk factors and risk categories based on pre-treatment characteristics for the MSKCC (2) and IMDC (3) model.

Risk factors	**MSKCC**	**IMDC**
Karnoskfy Performance Score < 80%*	X	X
Time from diagnosis to treatment < 1 year**	X	X
Haemoglobin < LLN	X	X
Corrected serum calcium > ULN	X	X
Lactate dehydrogenase > 1.5 ULN	X	
Neutrophil count > ULN		X
Platelet count > ULN		X

Risk group	**MSKCC**	**IMDC**
Favourable risk group	0 risk factors	0 risk factors
Intermediate risk group	1 or 2 risk factors	1 or 2 risk factors
Poor risk group	≥3 risk factors	≥3 risk factors

Abbreviations: MSKCC, Memorial Sloan Kettering Cancer Center; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; ULN, upper limit of normal; LLN, lower limit of normal.
* In this study we used WHO≥1 as a risk factor which equals KPS≤ 80.
** Diagnosis including original localized disease.

SUPPLEMENTARY TABLE 2: Examples of logical imputation for the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) model in 4 hypothetical patients

	Observed information							**Logical imputation patterns**						
Patient	KPS < 80% **Factor 1**	Time diagnosis -treatment < 1 y **Factor 2**	Hb < LLN **Factor 3**	Corrected serum calcium > ULN **Factor 4**	Neutrophil Count > ULN **Factor 5**	Platelet count > ULN **Factor 6**	**IF**	KPS < 80% **Factor 1**	Time diagnosis -treatment < 1 y **Factor 2**	Hb < LLN **Factor 3**	Corrected serum calcium > ULN **Factor 4**	Neutrophil Count > ULN **Factor 5**	Platelet count > ULN **Factor 6**	**Group**
#1	Y	N	N	N	?	N	Factor 5 → Y	Y	N	N	N	Y	N	Intermediate
							Factor 5 → N	Y	N	N	N	N	N	Intermediate
Conclusion: Unambiguous classification → intermediate risk group														
#2	N	N	?	N	N	N	Factor 3 → Y	N	N	Y	N	N	N	Intermediate
							Factor 3 → N	N	N	N	N	N	N	Favourable
Conclusion: Ambiguous classification → unclassifiable patient														
#3	?	Y	Y	?	Y	N	Factor 1 → Y Factor 4 → Y	Y	Y	Y	Y	Y	N	Poor
							Factor 1 → Y Factor 4 → N (or vice versa)	Y	Y	Y	N	Y	N	Poor
							Factor 1 → N Factor 4 → N	N	Y	Y	N	Y	N	Poor
Conclusion: Unambiguous classification → poor risk group														
#4	N	?	?	?	N	N	Factor 2 → Y Factor 3 → Y Factor 4 → Y	N	Y	Y	Y	N	N	Poor
							Factor 2 → Y Factor 3 → N Factor 4 → Y (or 2 or 4 N)	N	Y	N	Y	N	N	Intermediate
							Factor 2 → Y Factor 3 → N Factor 4 → N (or 3 or 4 Y)	N	Y	N	N	N	N	Intermediate
							Factor 2 → N Factor 3 → N Factor 4 → N	N	N	N	N	N	N	Favourable
Conclusion: Ambiguous classification → unclassifiable patient														

Abbreviations: Y, Yes; N, No; KPS, Karnofsky Performance Score; Hb, haemoglobin; LLN, lower limit of normal; ULN, upper limit of normal.

SUPPLEMENTARY TABLE 3: Examples of logical imputation for the Memorial Sloan Kettering Cancer Center (MSKCC) model in 4 hypothetical patients

	Observed information						**Logical imputation patterns**					
Patient	KPS < 80% **Factor 1**	Time diagnosis - treatment < 1 y **Factor 2**	Hb < LLN **Factor 3**	Corrected serum calcium > ULN **Factor 4**	Lactate dehydrogenase > 1.5x ULN **Factor 5**	**If**	KPS < 80% **Factor 1**	Time diagnosis - treatment < 1 y **Factor 2**	Hb < LLN **Factor 3**	Corrected serum calcium > ULN **Factor 4**	lactate dehydrogenase > 1.5x ULN **Factor 5**	**Group**
#1	Y	N	N	N	?	Factor 5 → Y	Y	N	N	N	Y	Intermediate
						Factor 5 → N	Y	N	N	N	N	Intermediate
Conclusion: Unambiguous classification → intermediate risk group												
#2	N	N	?	N	N	Factor 3 → Y	N	N	Y	N	N	Intermediate
						Factor 3 → N	N	N	N	N	N	Favourable
Conclusion: Ambiguous classification → unclassifiable patient												
#3	?	Y	Y	?	Y	Factor 1 → Y Factor 4 → Y	Y	Y	Y	Y	Y	Poor
						Factor 1 → Y Factor 4 → N (or vice versa)	Y	Y	Y	N	Y	Poor
						Factor 1 → N Factor 4 → N	N	Y	Y	N	Y	Poor
Conclusion: Unambiguous classification → poor risk group												
#4	N	?	?	?	N	Factor 2 → Y Factor 3 → Y Factor 4 → Y	N	Y	Y	Y	N	Poor
						Factor 2 → Y Factor 3 → N Factor 4 → Y (or 2 or 4 N)	N	Y	N	Y	N	Intermediate
						Factor 2 → Y Factor 3 → N Factor 4 → N (or 3 or 4 Y)	N	Y	N	N	N	Intermediate
						Factor 2 → N Factor 3 → N Factor 4 → N	N	N	N	N	N	Favourable
Conclusion: Ambiguous classification → unclassifiable patient												

Abbreviations: Y, Yes; N, No; KPS, Karnofsky Performance Score; Hb, haemoglobin; LLN, lower limit of normal; ULN, upper limit of normal.

SUPPLEMENTARY TABLE 4: EuroTARGET consensus and hospital-specific cut-off values for laboratory-based pre-treatment characteristics.

Laboratory-based characteristic	EuroTARGET consensus values	Hospital-specific values[#]		
		Minimum	**Mode**	**Maximum**
Haemoglobin				
for males	13 g/dL	12 g/dL	13.7 g/dL	14 g/dL
(LLN)	(=8.1 mmol/L)	(=7.5 mmol/L)	(=8.5 mmol/L)	(=8.7 mmol/L)
for females	11.5 g/dL	11.3 g/dL	12.0 g/dL	13.7 g/dL
(LLN)	(=7.1 mmol/L)	(=7.0 mmol/L)	(=7.5 mmol/L)	(=8.5 mmol/L)
Corrected calcium	10 g/dL	5.24 g/dL	10.2 g/dL	11.0 g/dL
(ULN)	(=2.5 mmol/L)	(=1.31 mmol/L)	(=2.55 mmol/L)	(=2.75 mmol/L)
Neutrophil count (ULN)	7.5 x 10^9/L	4.8 x 10^9/L	7.5 x 10^9/L	9.0 x 10^9/L
Platelet count (ULN)	400 x 10^9/L	350 x 10^9/L	400 x 10^9/L	450 x 10^9/L
LDH (ULN)*	250 IU/L	190 IU/L	250 IU/L	495 IU/L

Abbreviations: LLN, lower limit of normal; ULN, upper limit of normal; LDH, lactate dehydrogenase; IU, International Units; dL, deciliter; mmol, millimoles per liter; L, liter

[#] *based on 49 hospitals.*

**presented is the ULN, not 1.5xULN as used for the MSKCC risk group classification.*

SUPPLEMENTARY TABLE 5: MSKCC and IMDC risk group classification for patients without missing pre-treatment characteristics using consensus cut-off values. Overlap in patient classification for the two models is printed in bold.

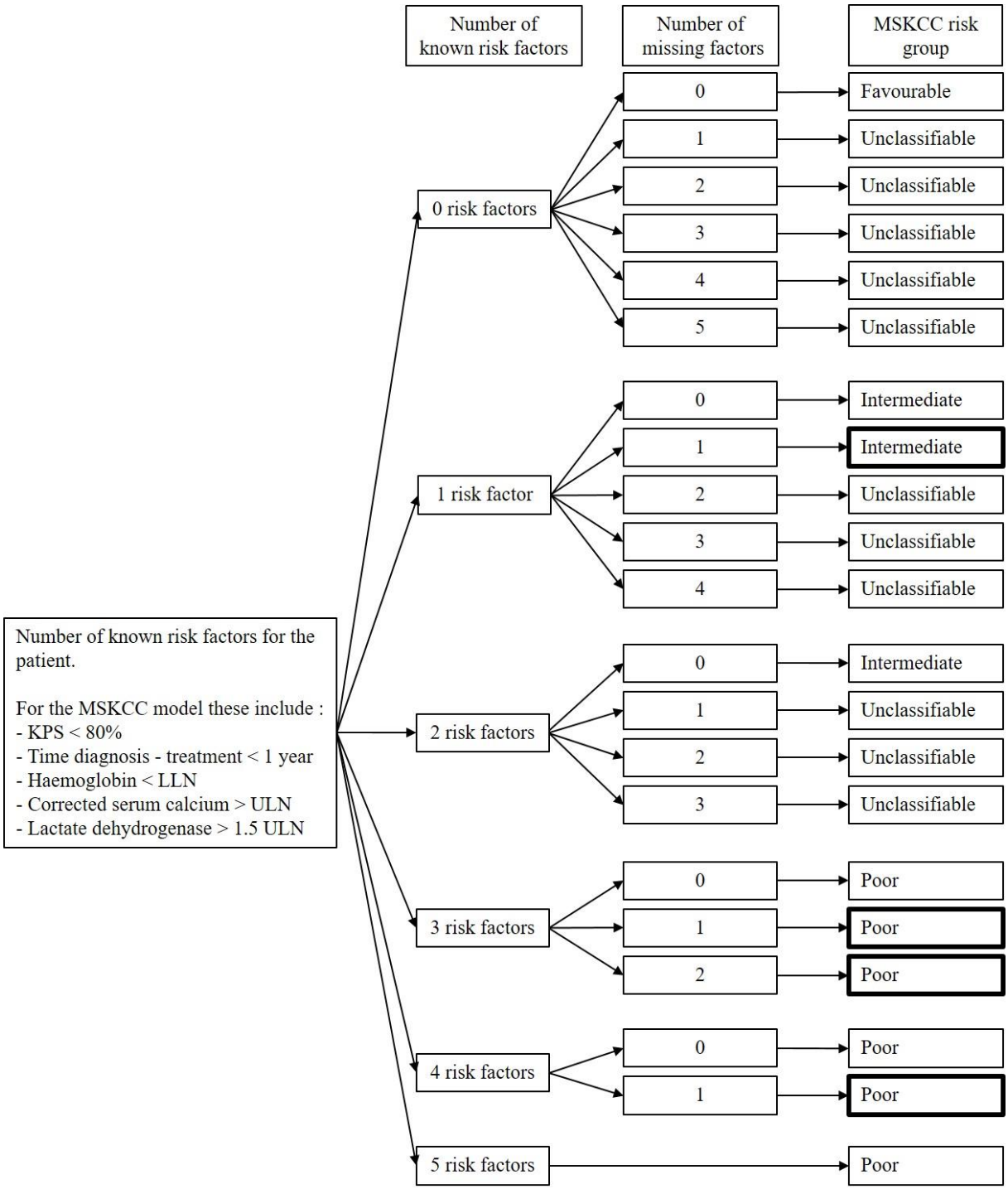
MSKCC risk group	**IMDC risk group**				**Total**	**Total MSKCC**
	Favourable	Intermediate	Poor	Unclassified		
Favourable	**55**	1	0	2	58	
Intermediate	9	**165**	20	12	206	**N = 396**
Poor	0	15	**110**	7	132	
Unclassified	1	7	4	305	317	
Total	65	188	134	326	713	
Total IMDC	**N = 387**					

SUPPLEMENTARY TABLE 6: MSKCC and IMDC risk group classification for patients using consensus versus hospital-specific cut-off values for the risk factors. Overlap for the two classifications is printed in bold.

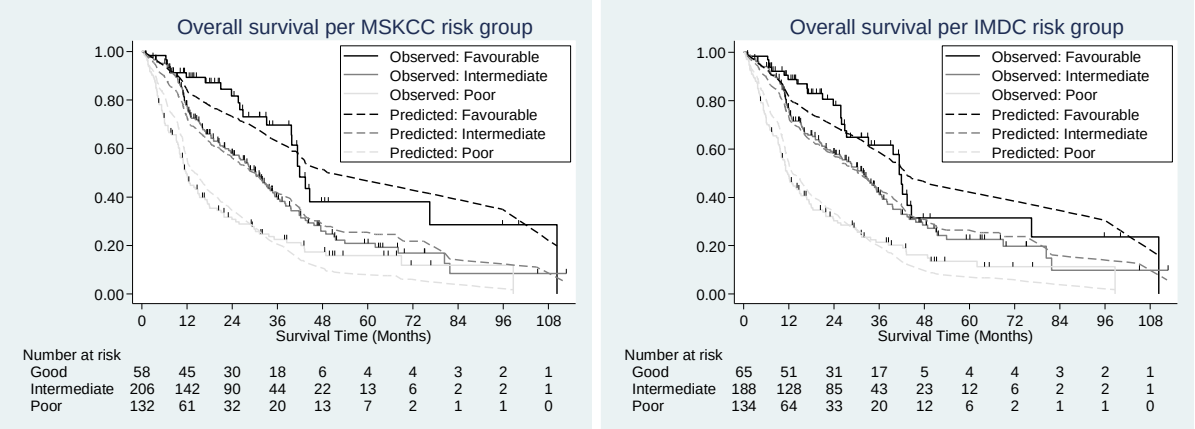
MSKCC risk group consensus values	**MSKCC risk group using hospital-specific cut-off values**				
	Favourable	Intermediate	Poor	Unclassified	**Total**
Favourable	**29**	6	0	23	58
Intermediate	3	**117**	9	77	206
Poor	0	11	**70**	51	132
Unclassified	0	0	0	**317**	317
Total	32	134	79	468	713

IMDC risk group consensus values	**IMDC risk group using hospital-specific cut-off values**				
	Favourable	Intermediate	Poor	Unclassified	**Total**
Favourable	**35**	4	0	26	65
Intermediate	3	**113**	5	67	188
Poor	0	5	**77**	52	134
Unclassified	0	0	0	**326**	326
Total	38	122	82	471	713

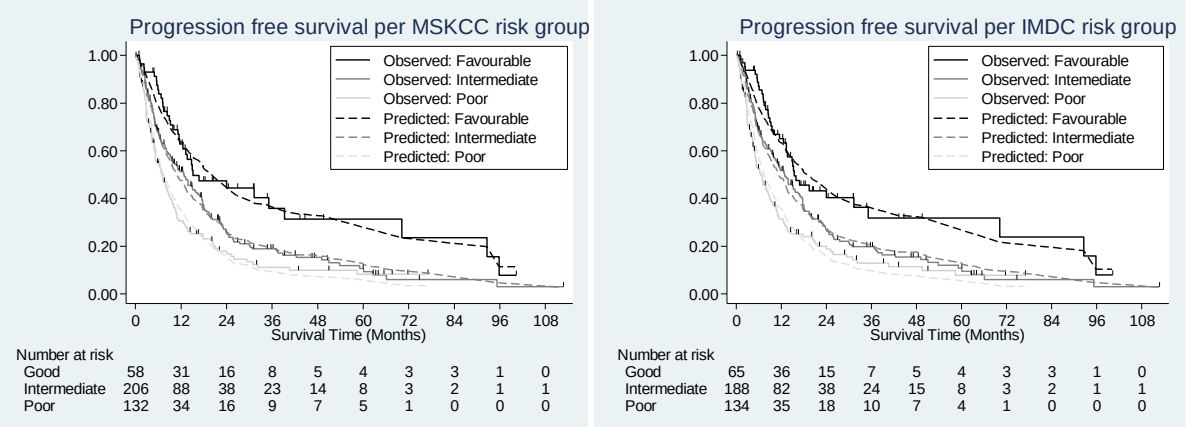
Abbreviations: MSKCC, Memorial Sloan Kettering Cancer Center; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium.



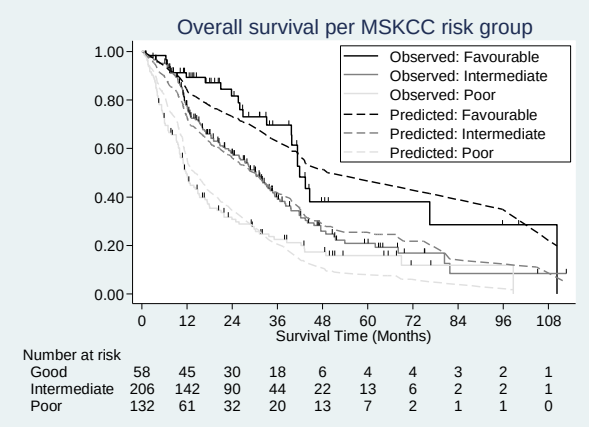
SUPPLEMENTARY FIGURE 1: Rules for logical imputation of the Memorial Sloan Kettering Cancer Center (MSKCC) risk groups. The bold outlined boxes are the additional classifications obtained by using this imputation procedure. Abbreviations: LLN, lower limit of normal; ULN, upper limit of normal.

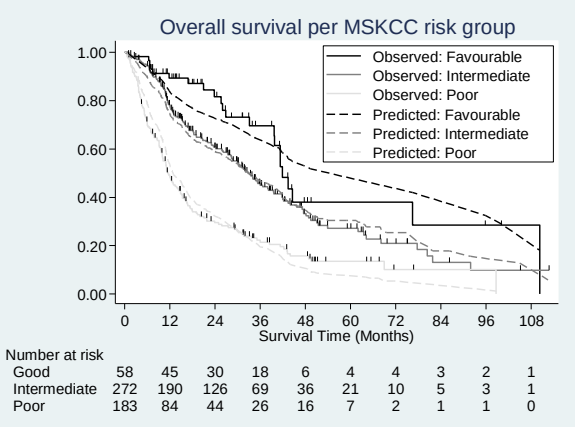


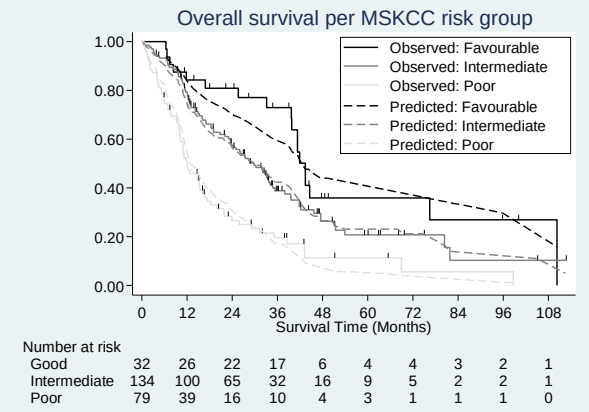
SUPPLEMENTARY FIGURE 2: Observed Kaplan-Meier curves (solid lines) with corresponding risk table and predicted curves using Cox regression (dashed lines) of overall survival for MSKCC (**left side**) and IMDC (**right side**) risk groups, using patients with complete information on pre-treatment characteristics and consensus cut-off values.



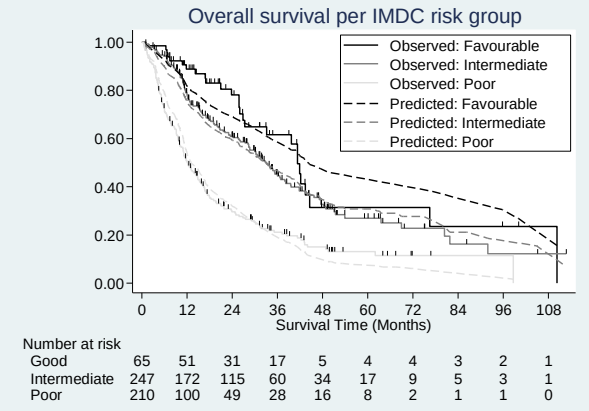
SUPPLEMENTARY FIGURE 3: Observed Kaplan-Meier curves (solid lines) with corresponding risk table and predicted curves using Cox regression (dashed lines) of progression-free survival for MSKCC (**left side**) and IMDC (**right side**) risk groups, using patients with complete information on pre-treatment characteristics and consensus cut-off values .

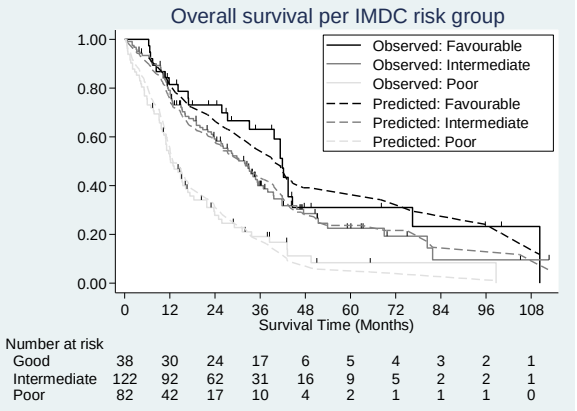


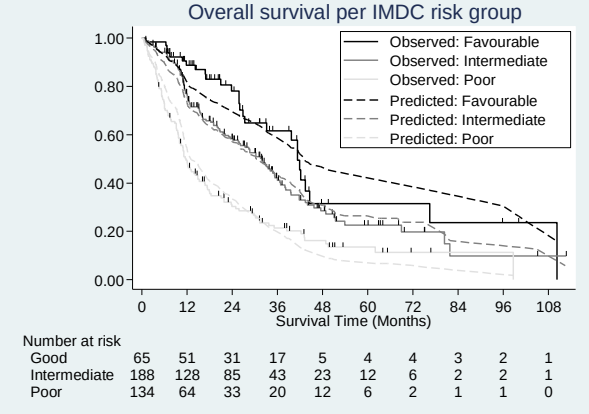




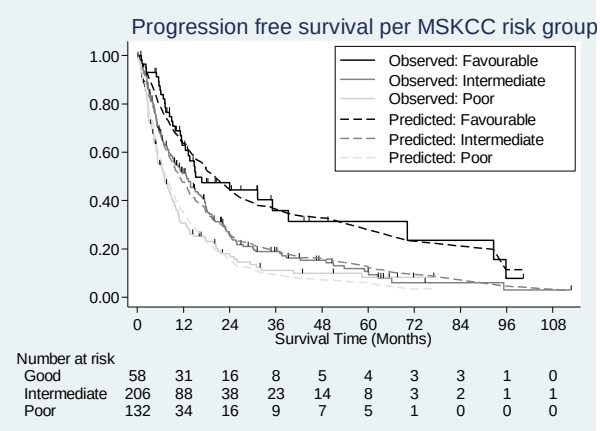
SUPPLEMENTARY FIGURE 4: Observed Kaplan-Meier curves (solid lines) with the corresponding risk table, and the predicted survival curves (dashed lines) per MSKCC risk group for overall survival, using patients with complete information on pre-treatment characteristics only (**top left**), including patients with missing pre-treatment characteristics (**top right**), and using hospital-specific cut-off values (**bottom left**).

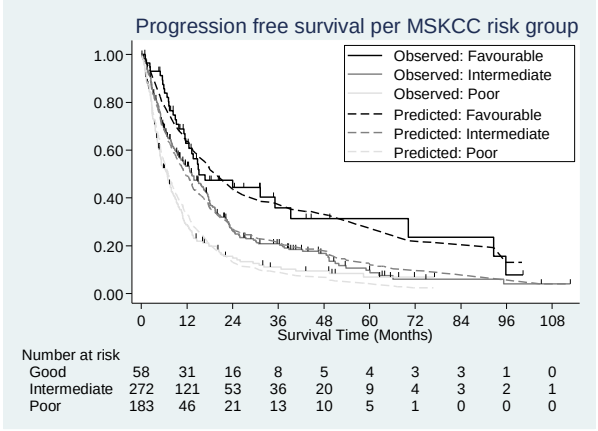


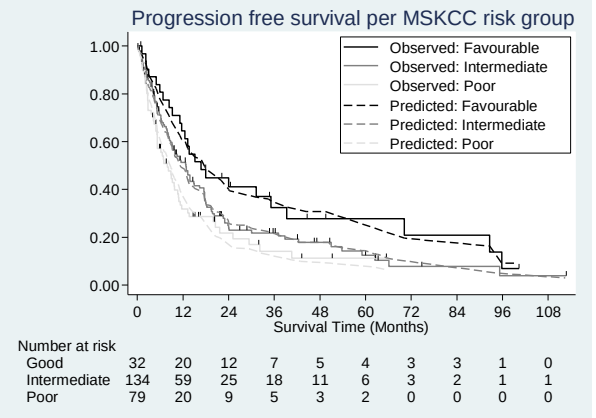




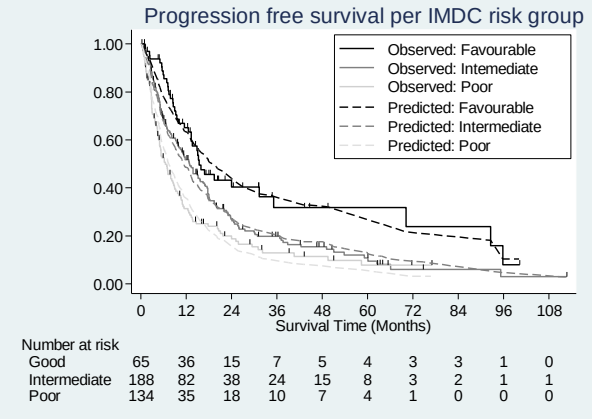
SUPPLEMENTARY FIGURE 5: Observed Kaplan-Meier curves (solid lines) with the corresponding risk table, and the predicted survival curves (dashed lines) per IMDC risk group for overall survival, using patients with complete information on pre-treatment characteristics only (**top left**), including patients with missing pre-treatment characteristics (**top right**), and using hospital-specific cut-off values (**bottom left**).

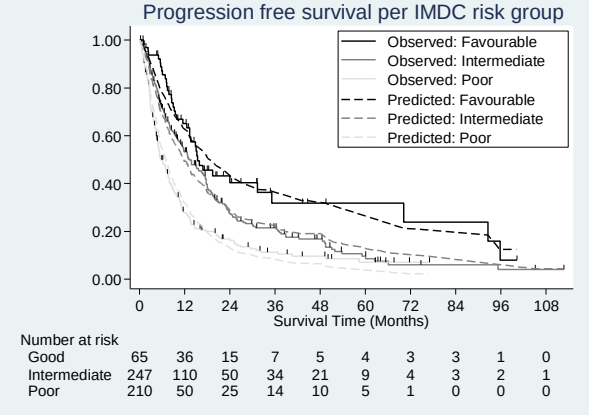


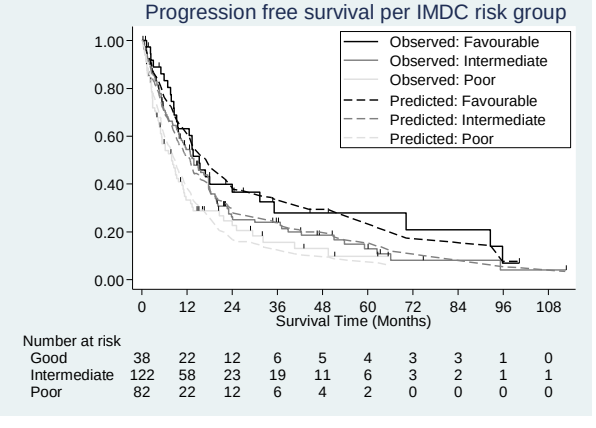




SUPPLEMENTARY FIGURE 6: Observed Kaplan-Meier curves (solid lines) with the corresponding risk table, and the predicted survival curves (dashed lines) per MSKCC risk group for progression-free survival, using patients with complete information on pre-treatment characteristics only (**top left**), including patients with missing pre-treatment characteristics (**top right**), and using hospital-specific cut-off values (**bottom left**).







SUPPLEMENTARY FIGURE 7: Observed Kaplan-Meier curves (solid lines) with the corresponding risk table, and the predicted survival curves (dashed lines) per IMDC risk group for progression-free survival, using patients with complete information on pre-treatment characteristics only (**top left**), including patients with missing pre-treatment characteristics (**top right**), and using hospital-specific cut-off values (**bottom left**).