

Supplementary Material: A Retrospective Analysis of 10 Years of Liver Surveillance Undertaken in Uveal Melanoma Patients Treated at the Supraregional “Liverpool Ocular Oncology Centre”, UK

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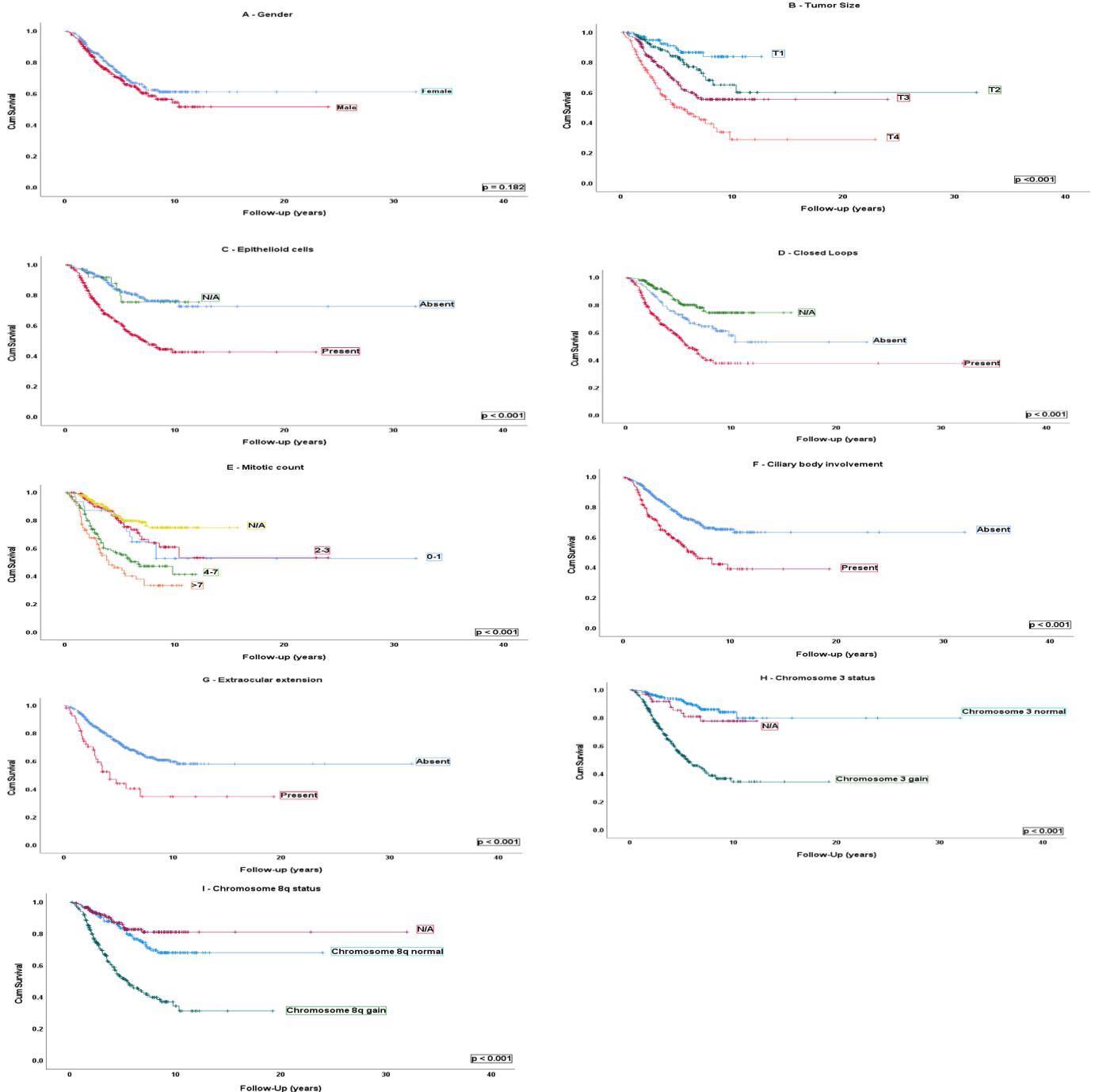
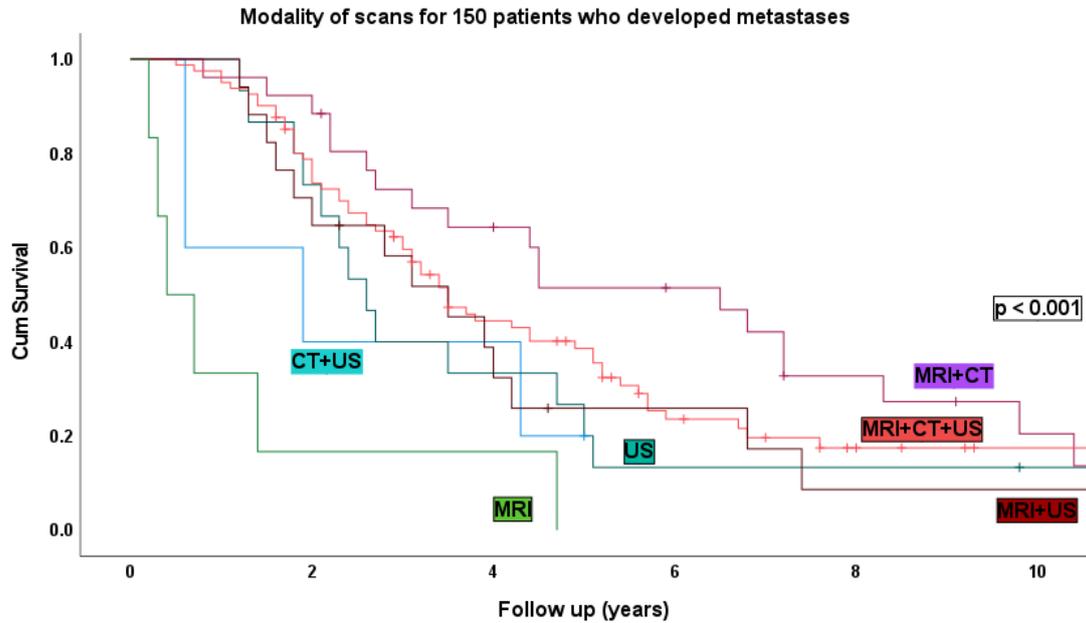


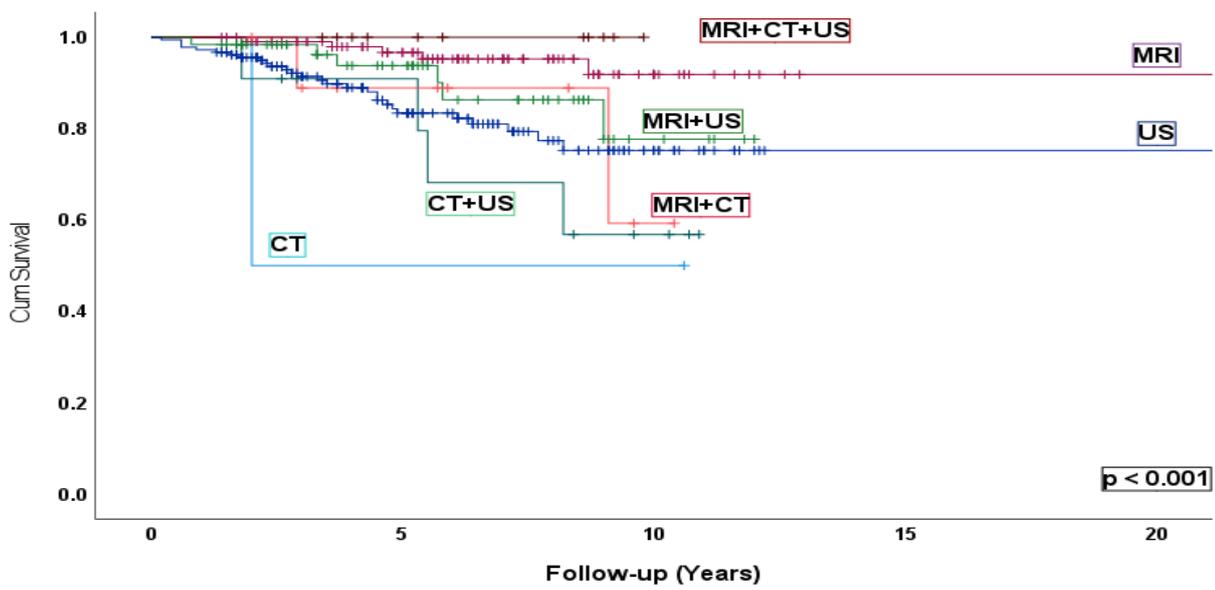
Figure S1: Kaplan-Meier plots (A-I). Overall survival for all patients stratified according to all predictor factors related to LUMPO3. All these predictor factors were associated to poor survival and metastatic mortality. A – Male gender, B – Increasing tumor size, C – presence of epithelioid cells, D – presence of closed loops, E – High mitotic count, F – Ciliary body involvement, G – Extraocular extension, H – Chromosome 3 alterations, I – Chromosome 8q alterations.



Modality of scans	Number of patients	(%)	Number of Scans	(%)	Number of Events	(%)	Censored	(%)	Median survival (years)	95% confidence interval	
										Lower	Upper
MRI	15	(10%)	74	(5%)	13	(87%)	2	(13.3%)	2.600	2.095	3.105
US	6	(4%)	6	(0.4%)	6	(100%)	0	(0%)	0.400	0.000	0.880
MRI + CT	26	(17%)	297	(19%)	19	(73%)	7	(26.9%)	6.500	3.817	9.183
MRI + US	17	(11%)	129	(8%)	14	(82%)	3	(17.6%)	3.500	2.123	4.877
CT + US	5	(3%)	27	(1.7%)	4	(80%)	1	(20.0%)	1.900	0.000	4.691
MRI + CT + US	81	(50%)	1067	(67%)	59	(73%)	22	(27.2%)	3.500	2.875	4.125
Overall	150		1600		115	(77%)	35	(23.3%)	3.500	2.875	4.125

Figure S2. Kaplan-Meier survival curve and table where 150 UM patients with metastases. detected through liver surveillance were stratified according to the modality of scan performed. MRI: 15 patients underwent 74 scans; US: 6 patients underwent 6 scans; MRI+CT: 26 patients underwent 297 scans; MRI+US: 17 patients underwent 129 scans; CT+US: 5 patients underwent 27 scans; MRI+CT+US: 81 patients underwent 1067 scans. Number of events indicates the number of deaths from metastatic disease.

Modality of scans for 386 patients who never demonstrate metastases



Modality of scans	Number of patients	(%)	Number of Scans	(%)	Number of Events	(%)	Censored	(%)	Median survival (years)	95% confidence interval	
										Lower	Upper
MRI	107	(28%)	871	(41%)	5	(87%)	102	(95.3%)	-	-	-
CT	2	(0.5%)	6	(0.3%)	1	(2.1%)	1	(50.0%)	-	-	-
US	183	(47%)	456	(22%)	28	(100%)	155	(84.7%)	-	-	-
MRI + CT	10	(3%)	103	(5%)	2	(73%)	8	(80.0%)	-	-	-
MRI + US	62	(16%)	488	(23%)	6	(82%)	56	(90.3%)	-	-	-
CT + US	11	(3%)	53	(3%)	4	(80%)	7	(63.6%)	-	-	-
MRI + CT + US	11	(3%)	137	(6%)	0	(73%)	11	(100%)	-	-	-
Overall	386		2114		46	(77%)	340	(80.1%)	-	-	-

Figure S3. “Kaplan-Meier survival curve and table where 386 UM patients who never demonstrated metastases were stratified according to the modality of scan performed”. MRI: 107 patients underwent 871 scans; CT: 2 patients underwent 6 scans; US: 183 patients underwent 456scans; MRI+CT: 10 patients underwent 103 scans; MRI+US: 62 patients underwent 488 scans; CT+US: 11 patients underwent 53 scans; MRI+CT+US: 11 patients underwent 137 scans. No survival statistics because all cases are censored. Number of events indicates the number of deaths.

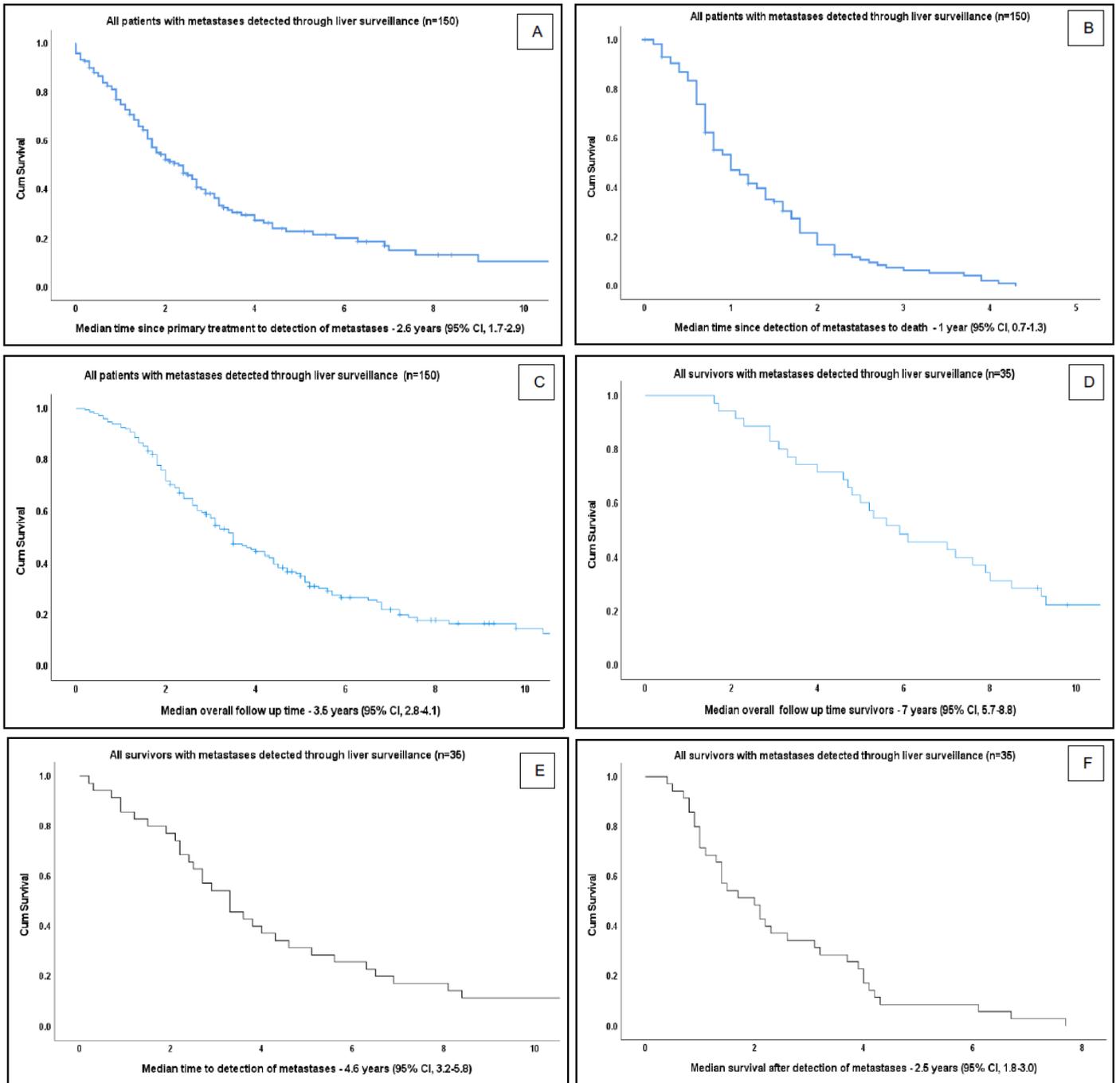


Figure S4. Kaplan Meier estimates for all 150 metastatic UM patients from primary treatment to detection of metastases, and from metastatic disease to death. A) Median time to detection of metastases. B) Median time from detection of metastases to death. C) Median follow-up time for all patients. D) Median overall follow-up time for survivors. E) Median time to detection of metastases for survivors. F) Median follow up time for survivors after detection of metastases.

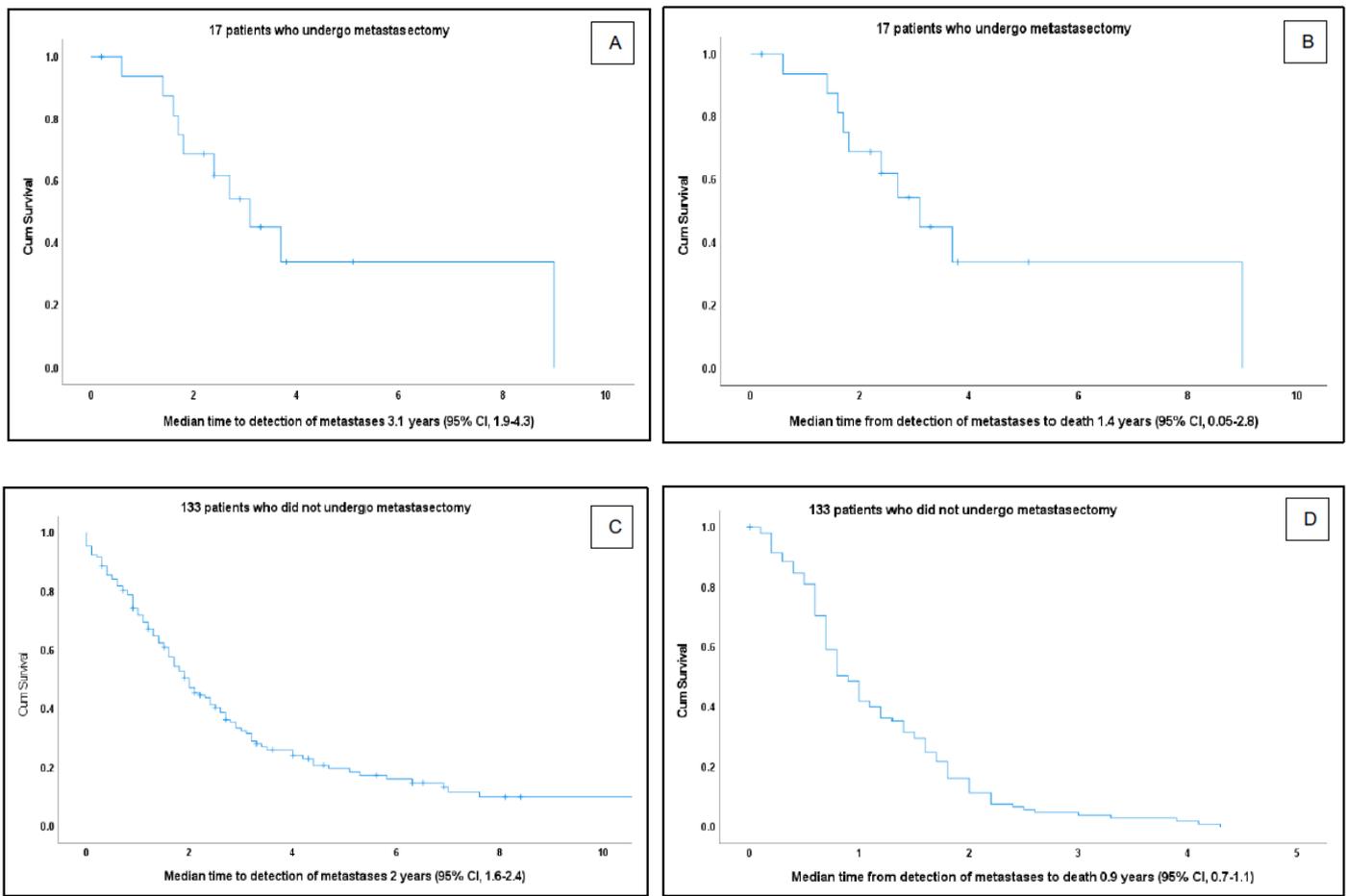
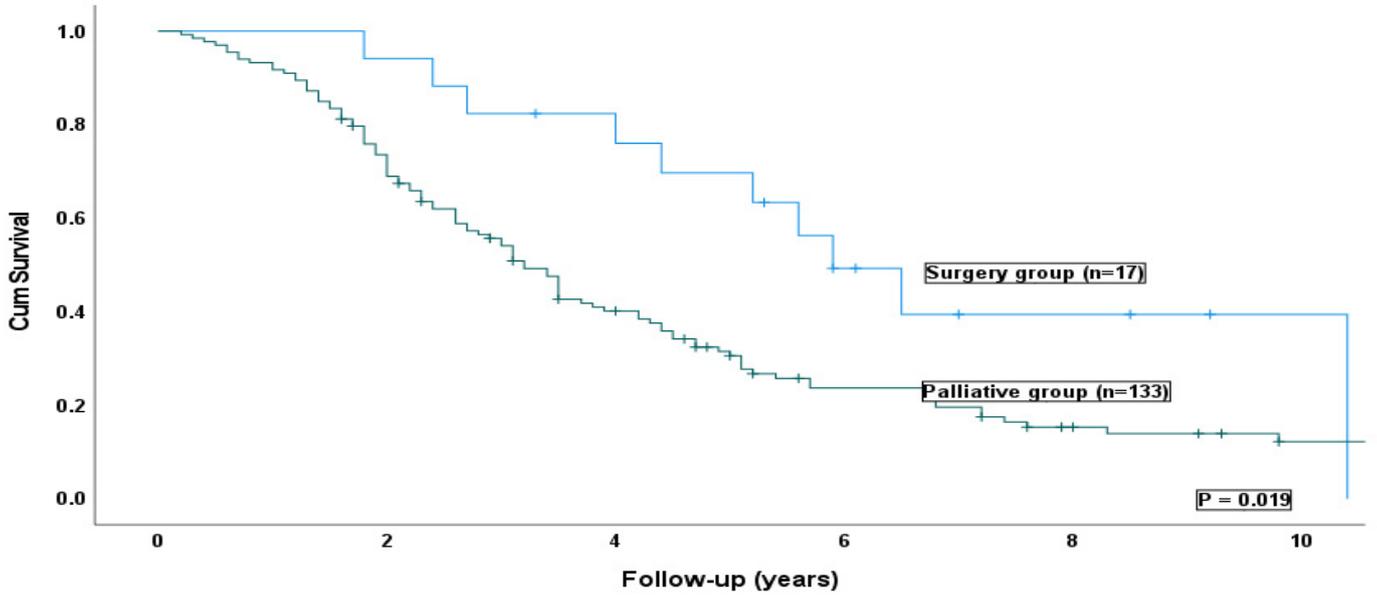


Figure S5. Kaplan-Meier estimates for all 150 metastatic UM patients stratified according to type of treatment post diagnosis of metastases. Metastasectomy was performed in 17 patients, while in the remaining 133 patients no metastasectomy event was recorded. Patients undergoing metastasectomy: A) Median time to detection of metastases, B) Median time from detection of metastases to death. Patients who did not undergo metastasectomy: C) Median time to detection of metastases, D) median time from detection of metastases to death.

Metastatic UM stratified according to the type of treatment post detection of metastases (n=150)



Groups	Number of patients (%)		Number of events %		Censored %		Sig.	Median survival (years)	95% confidence interval	
									Lower	Upper
Surgery	17	11%	10	59%	7	41.2%	P = 0.019	5.900	4.564	7.236
Palliative	133	89%	105	79%	28	21.1%	P = 0.019	3.200	2.803	3.597
Overall	150	100%	115	77%	35	23.3%		3.500	2.875	4.125

Figure S6. Kaplan-Meier survival curve and table for all metastatic UM stratified according to the type of treatment post detection of metastases. Patients were classified as: Surgery group ($n = 17$), and palliative group ($n = 133$), ($p = 0.019$).

Table S1. Summary of studies reporting outcome of UM metastatic disease.

Parameters	Studies				
	Cunha Rola et al.	Rietschel et al.	Rivoire et al.	Lane et al.	Lorigan et al.
Name of the Study	A retrospective analysis of 10 years of liver surveillance undertaken in UM patients treated at the supraregional LOOC	Variates of survival in metastatic UM	Treatment of liver metastases from UM	Survival rates in patients after treatment for metastases from UM	The prevalence and location of metastases from ocular melanoma: Imaging study 110 patients
Number of UM patients	615 UM patients	119 (stage IV UM)	602	3063	181
Time of the study	11 years	10 years	14 years	27 years	12 years
Metastatic disease	Total 229 (37%) UM metastases: 150 (66%) imaging 79 (34%) post-mortem	119 – UM metastases 77% - liver 43% - other sites	10.5% UM metastases	661 (21.6%) 12 (1.8%) excluded 87 (13%) no data 562 (85%) Metastases	110 (60.7%) MUM 101 (92%) liver + other sites 60 (55%) only liver
Metastases at time of diagnosis UM	7 (2.4%)	N/A	N/A	12 (1.8%) metastases within 6 months	3 (2.7%)
Parameters of the study	Diagnosed by imaging 65.5 % Diagnosed at autopsy 34.5 %	Diagnosed symptoms 40% Diagnosed imaging/others 60%	44% Liver surgery 56% Systemic chemotherapy	53% received treatment 47% untreated	Clinical and radiology reports

Time to metastases	2.6 years (0.1-17.8)	4.4 years (0-29.9)	2.4 years	3.45 years	4.3 years (0.2-36)
Time to death	12 months (1-52 months) < 2 years – 85% 2-3 years - 10% >3 years – 5%	9.5 months - Systemic treatment 32.4 months -Surgery/intrahepatic	13 months (2.5-110) 1 year – 59% 2 years – 29% 4 years – 13%	12 months– 21% 1.5 years – 11% 3 years – 4%	10 months (1-38) – 96%
Median survival after metastases	12 months (95% CI, 0.7-1.3)	12.5 months (95% CI, 9.5-15.7 months)	15 months (3-110 months)	3.9 months – received treatment 1.7 months – no treatment	N/A
Overall survival patients with metastases	3.5 years (95% CI, 2.8-4.1)	N/A	3.9 years (0.3-15.8)	8.9 years (0.1-29.6 years)	N/A
Survivors	(23.3%)	(22%)	(15.9%)	(30.2%) treated alive (5.6%) untreated alive <u>After 1 year of treatment</u>	(4.5%) (2.7%) – 22 months (1.8%) – 74 months
Median Follow-up survivors	30 months (4-92 months)	17 months (0-96 months)	29 months (16-110 months)	N/A	N/A