1457P - A UK multicentre retrospective review of metastatic renal cell carcinoma (mRCC) patients (pts) outcomes with brain metastases (BM) in the modern era

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INTRODUCTION

- The evolving landscape of systemic therapies (ST) in metastatic renal cell carcinoma (mRCC) in recent years has led to greater options and better outcomes, including Tyrosine Kinase Inhibitors (TKI) and Immunotherapy (IO).
- Brain metastases (BM) form an important group of mRCC pts, with historically poorer outcomes expected.
- We conducted a UK multicentre retrospective individual case review of outcomes in mRCC pts with BM in the era of IO.

METHODS

- 1173 individual pt data collated from 15 UK centres from pts commencing first line (1L) ST between 01/01/2018 and 30/06/2021 (censored at 30/06/2021).
- Data on BM, IMDC scores, ST and local therapies (LT) were collected and median Overall Survival (mOS) were analysed using Kaplan Meier Analyses (log rank test).

RESULTS

- At data cutoff, 105 pts had <6months (m) follow up from metastatic diagnosis (FUm), 405 pts <12mFUm, and 676 pts <24m FUm.
- The breakdown of the baseline characteristics of the mRCC pts by group (All, No BM, BM) are seen in **Table 1**.
- 154 mRCC pts with BM were identified from a total of 1173 mRCC eligible pts (13.1%), of which 80% were symptomatic at BM diagnosis (**Figure 1**).
- Only 225 pts (19.2%) underwent brain imaging (BI) within 3 months of starting 1L ST, of which 26 pts had BM diagnosed.
- 28 of 245 pts (11.4%) who had BI within 3 months of metastatic diagnosis, had BM.
- Most BM pts commenced 1L with a TKI (108), 35 pts with Double IO as 1L ST, 8 with IO+TKI and 3 with Single IO.

		All		No BM		BM	
		Number	%	Number	%	Number	%
Number		1173	-	1019	-	154	-
Median Age		65	-	66	-	62	-
Sex	M	845	72.04	735	72.13	110	71.43
	F	328	27.96	284	27.87	44	28.57
Prior Nephrectomy	Y	598	-	511	-	87	-
	N	523	-	457	-	66	-
	Missing	52	-	51	-	1	-
Lines of Treatment	1	605	51.58	530	52.01	78	50.65
	2	395	33.67	339	33.27	53	34.42
	3	132	11.25	115	11.29	17	11.04
	4	36	3.07	30	2.94	6	3.90
	5	5	0.43	5	0.49	0	0.00
	6	0	0.00	0	0.00	0	0.00
IMDC Group	Favourable	241	20.55	221	21.69	20	12.99
	Intermediate	567	48.34	476	46.71	91	59.09
	Poor	282	24.04	244	23.95	38	24.68
	Missing	83	7.08	78	7.65	5	3.25
Histology	Clear Cell	915	78.01	781	76.64	134	87.01
	Papillary	79	6.73	76	7.46	3	1.95
	Chromophobe	10	0.85	9	0.88	1	0.65
	Collecting duct	2	0.17	2	0.20	0	0.00
	Undifferentiated	7	0.60	7	0.69	0	0.00
	Unclassified	20	1.71	19	1.86	1	0.65
	Other	16	1.36	16	1.57	0	0.00
	missing	132	11.25	117	11.48	15	9.74
	mixed	8	0.68	8	0.79	0	0.00
Sarcomatoid	Yes	95	8.10	79	7.75	16	10.39
	No	855	72.89	743	72.91	112	72.73
	Missing	223	19.01	197	19.33	26	16.88
Site of metastases	Adrenal	172	14.66	149	14.62	23	14.94
	Lung	769	65.56	647	63.49	122	79.22
	Liver	174	14.83	158	15.51	16	10.39
	Bone	339	28.90	295	28.95	44	28.57
	Pancreatic	59	5.03	52	5.10	7	4.55
	Nodal	511	43.56	452	44.36	59	38.31
	Other	166	14.15	148	14.52	18	11.69
	Brain only					9	5.84
Number of additional Metastatic sites (in addition to BM)	0					9	5.84
	1					52	33.77
	2					54	35.06
	3					27	17.53
	4					12	7.79
	4+					0	0.00

TABLE 1: Baseline pt characteristics by group (all, no-BM and BM pts).

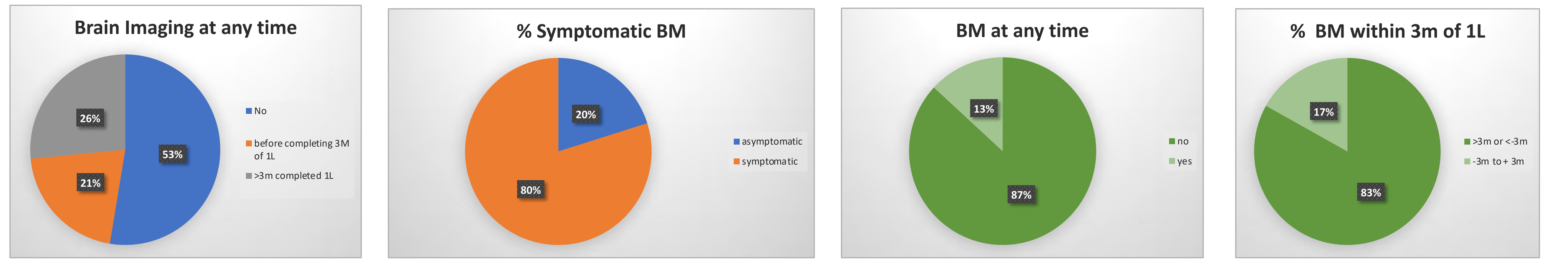
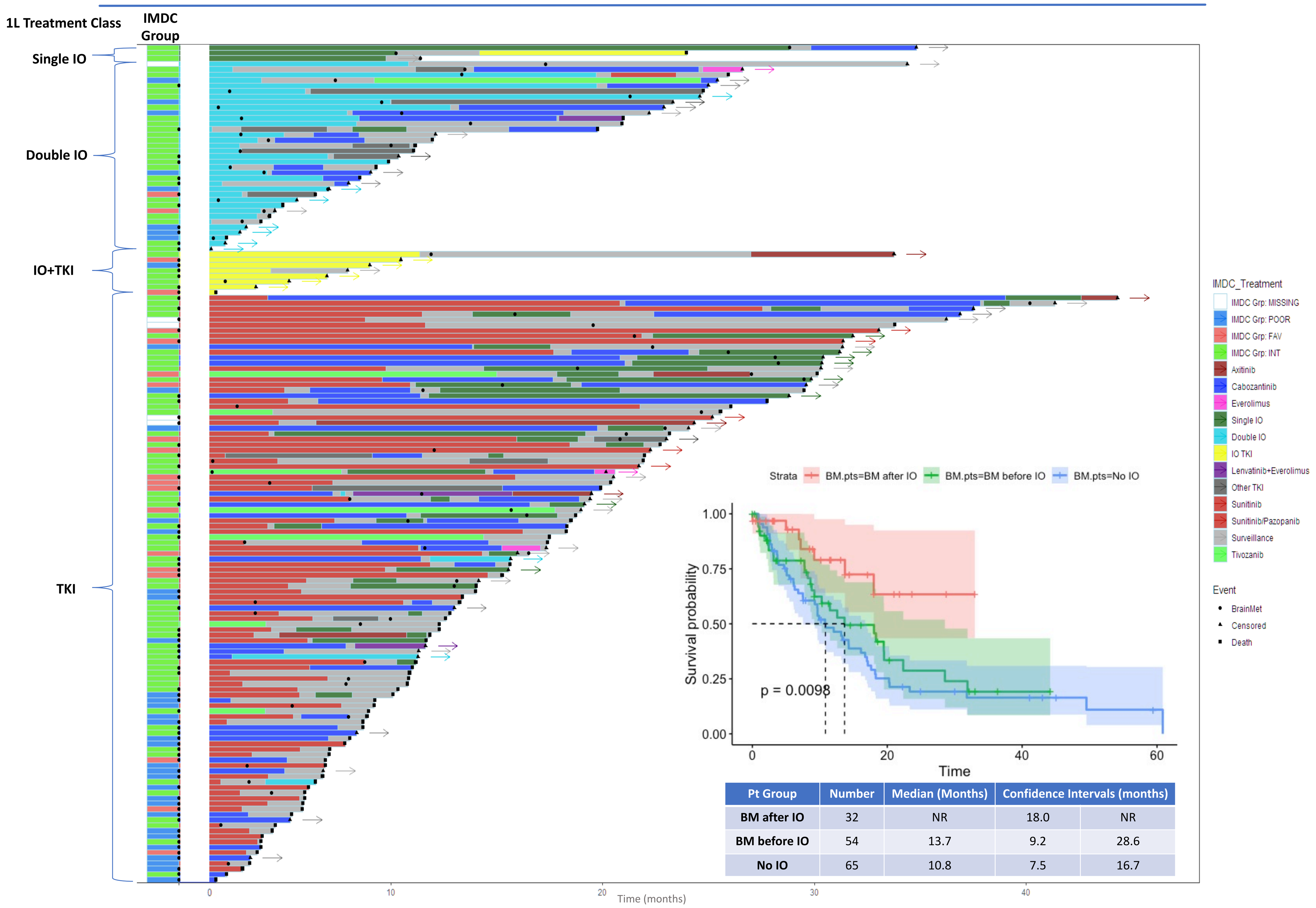


FIGURE 1: Proportion of mRCC pts undergoing BI, clinically presenting with and detecting BM at any time, and within 3 months of starting 1L

RESULTS (continued)

- Patients receiving IO before BM diagnosis had a statistically greater mOS than IO before BM or no IO (NR vs 13.7m vs 10.8m, p=0.0098) (**Figure 2**)
- The majority of BM pts only received 1 or no further ST lines after BM diagnosis (**Figure 3**).
- The mOS for BM mRCC pts is 21.03 months from start of 1L and 14.30 months from BM diagnosis (**Figure 4**).



Pt Group	Number	Median (Months)	Confidence Intervals (months)	
BM after IO	32	NR	18.0	NR
BM before IO	54	13.7	9.2	28.6
No IO	65	10.8	7.5	16.7

FIGURE 2: Stacked Swimmer's Plot of all BM pts , including time of BM diagnosis on ST, grouped by class of 1L ST (Single agent IO, Double IO, IO+TKI, and TKI), and identified by IMDC score. KM analysis of pts who received No IO vs IO before and after BM.

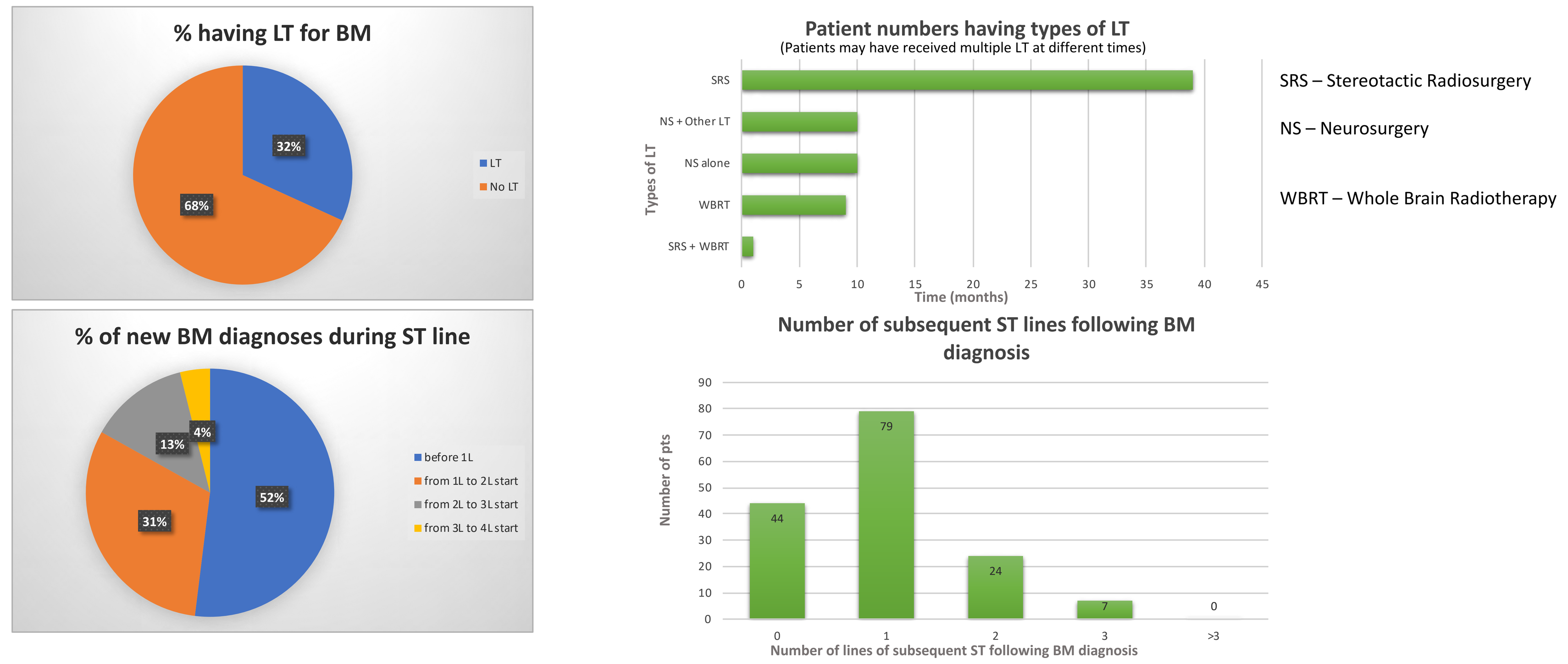
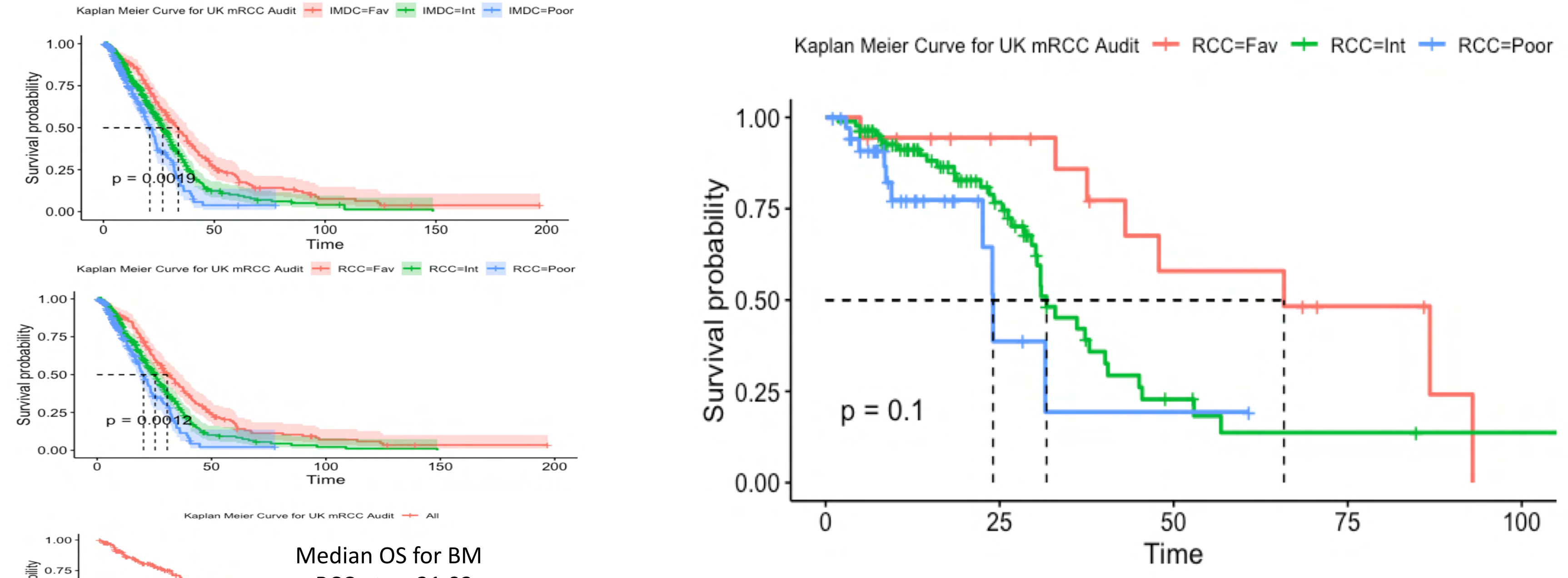


FIGURE 3: BM pts undergoing LT, type of LT, and breakdown of developing BM by ST line, with number of subsequent ST lines following BM diagnosis.



IMDC	All		no BM		BM	
	%	OS(m)	%	OS(m)	%	OS(m)
Favourable	20.5	33.8	22.5	30.7	13.0	65.8
Intermediate	48.3	26.7	49.0	25.3	59.1	31.7
Poor	24.0	20.9	25.1	20.3	24.7	24.1
Missing	7.1	n/a	3.4	n/a	3.2	n/a

FIGURE 4: KM curves for estimation of mOS in All, No-BM and BM pt groups, stratified by IMDC score. The mOS for BM pts was 21.03m, and 14.30m from BM diagnosis.

CONCLUSIONS

- In our series, there is a greater incidence of BM in mRCC pts than with historical data.
- mOS for BM pts receiving IO before BM diagnosis is significantly better than those receiving IO after BM diagnosis or no IO.
- There is a strong argument for the use of IO as 1L ST to improve mOS in patients who develop BM.
- Identifying BM is important with modern LT and better ST to help improve long term outcomes in this cohort, suggesting more routine BI is important. More mature data will be collected in this cohort.

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