

## Supplementary Material

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### **Supplementary Figures:**

Supplementary Figure S1: PFS by treatment type

Supplementary Figure S2: OS by treatment type

### **Supplementary Tables:**

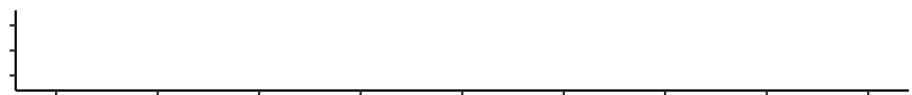
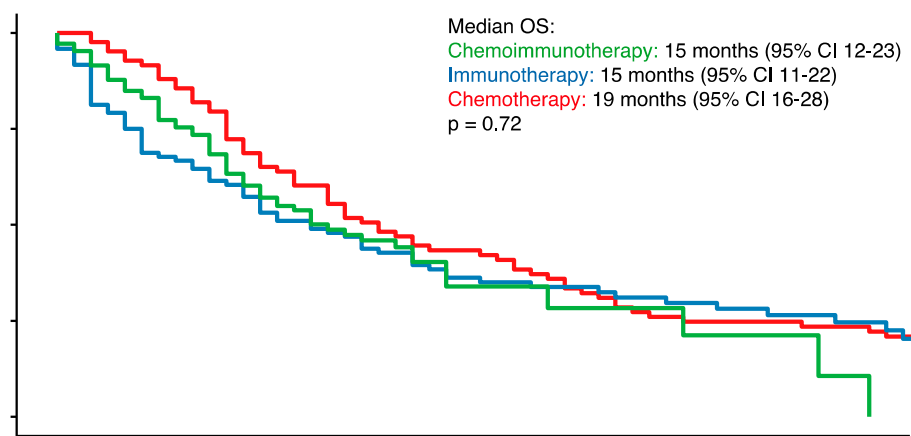
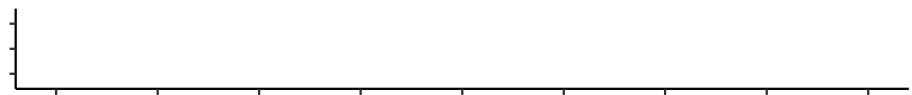
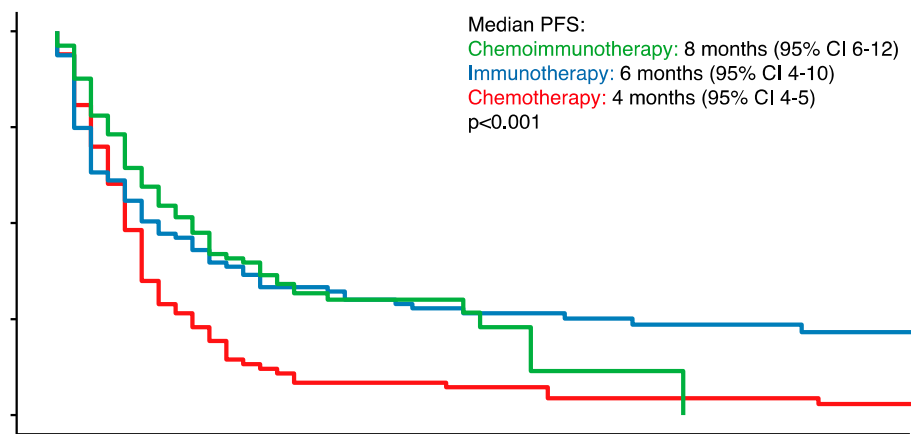
Supplementary Table S1: Univariate and Multivariate analysis for ORR

Supplementary Table S2: Univariate and Multivariate analysis for PFS

Supplementary Table S3: Univariate and Multivariate analysis for OS

Supplementary Table S4: OS and PFS for bone metastases by treatment type

Supplementary Table S5: OS and PFS for liver metastases by treatment type



**Legend:** : PFS: Progression Free Survival; OS: Overall Survival; CI: Confidence Interval

**Supplementary Table S1: Univariate and Multivariate analysis for ORR**

	Univariate			Multivariate		
Characteristic	OR <sup>†</sup>	95% CI <sup>†</sup>	p-value	OR <sup>†</sup>	95% CI <sup>†</sup>	p-value
<b>Lung Metastases</b>			0.20			0.40
Not present	1.00	—		1.00	—	
Present	1.38	0.85, 2.27		1.28	0.68, 2.44	
<b>Lymph Node Metastases</b>			0.53			0.20
Not present	1.00	—		1.00	—	
Present	0.82	0.43, 1.55		0.57	0.26, 1.25	
<b>Liver Metastases</b>			0.32			0.30
Not present	1.00	—		1.00	—	
Present	1.40	0.72, 2.73		0.66	0.28, 1.52	
<b>Brain Metastases</b>			0.25			0.14
Not present	1.00	—		1.00	—	
Present	0.70	0.37, 1.28		1.95	0.81, 4.79	
<b>Adrenal Metastases</b>			0.97			0.60
Not present	1.00	—		1.00	—	
Present	0.99	0.53, 1.82		0.83	0.39, 1.73	
<b>Pleural Metastases</b>			0.06			<b>0.05</b>
Not present	1.00	—		1.00	—	
Present	1.66	0.99, 2.79		1.93	1.01, 3.74	
<b>Bone Metastases</b>			<b>&lt;0.001</b>			<b>&lt;0.01</b>
Not present	<b>1.00</b>	—		<b>1.00</b>	—	
Present	<b>0.37</b>	<b>0.20, 0.66</b>		<b>0.35</b>	<b>0.16, 0.73</b>	
<b>Volume of metastases</b>			0.68			0.70
<20 metastases	1.00	—		1.00	—	
≥20 metastases	0.87	0.44, 1.68		1.16	0.48, 2.74	
<b>Metastatic lesion ≥5cm</b>			0.08			0.20
Not present	1.00	—		1.00	—	
Present	1.63	0.94, 2.82		1.55	0.79, 3.03	
<b>Age</b>			0.38			0.4
<65 years	1.00	—		1.00	—	
≥65 years	1.01	0.99, 1.04		1.01	0.98, 1.05	
<b>Sex</b>			0.75			>0.9
Female	1.00	—		1.00	—	
Male	1.08	0.66, 1.80		1.01	0.54, 1.90	
<b>Smoking Status</b>			0.13			<b>&lt;0.01</b>
Never-Smoker	1.00	—		1.00	—	
Ex-Smoker	1.63	0.77, 3.64		<b>3.06</b>	<b>1.11, 9.19</b>	
Current Smoker	2.32	1.02, 5.55		<b>6.67</b>	<b>2.09, 23.3</b>	
<b>PD-L1 Status</b>			0.54			0.90
<1%	1.00	—		1.00	—	
≥1%	0.96	0.43, 2.15		1.06	0.39, 2.84	
≥50%	1.51	0.76, 3.01		1.14	0.49, 2.67	
Not Tested	1.17	0.56, 2.43		0.82	0.31, 2.16	
<b>Tumour Type</b>			0.80			0.80
Adenocarcinoma	1.00	—		1.00	—	
SCC	1.04	0.57, 1.88		0.74	0.34, 1.58	

ULCC	0.74	0.31, 1.65		0.64	0.23, 1.71	
NOS	0.35	0.02, 2.43		0.49	0.02, 6.58	
<b>Treatment Type</b>			0.38			0.20
Chemotherapy	1.00	—		1.00	—	
Immunotherapy	0.87	0.46, 1.65		0.48	0.17, 1.36	
Chemoimmunotherapy	1.30	0.71, 2.40		1.61	0.58, 4.59	
<b>Radiotherapy</b>			0.13			0.60
No Upfront RT	1.00	—		1.00	—	
Upfront RT	0.66	0.38, 1.12		0.84	0.42, 1.66	

Legend: n: number; SCC: Squamous Cell Carcinoma; ULCC: Undifferentiated Large Cell Carcinoma; NOS: Not otherwise specified; PD-L1: Programmed Cell death ligand 1 receptor; RT: Radiotherapy

**Supplementary Table S2: Univariate and Multivariate analysis for PFS**

	Univariate			Multivariate		
Characteristic	HR <sup>†</sup>	95% CI <sup>†</sup>	p-value	HR <sup>†</sup>	95% CI <sup>†</sup>	p-value
<b>Lung Metastases</b>			0.88			0.70
Not present	1.00	—		1.00	—	
Present	1.02	0.79, 1.33		0.94	0.67, 1.33	
<b>Lymph Node Metastases</b>			0.19			0.60
Not present	1.00	—		1.00	—	
Present	1.27	0.88, 1.82		0.88	0.58, 1.34	
<b>Liver Metastases</b>			0.74			0.50
Not present	1.00	—		1.00	—	
Present	0.95	0.68, 1.31		1.16	0.75, 1.80	
<b>Brain Metastases</b>			0.02			0.60
Not present	1.00	—		1.00	—	
Present	1.56	1.10, 2.21		1.13	0.72, 1.77	
<b>Adrenal Metastases</b>			0.20			0.60
Not present	1.00	—		1.00	—	
Present	0.80	0.56, 1.14		0.88	0.58, 1.34	
<b>Pleural Metastases</b>			0.60			0.30
Not present	1.00	—		1.00	—	
Present	1.08	0.82, 1.41		1.21	0.86, 1.69	
<b>Bone Metastases</b>			0.001			<0.01
Not present	1.00	—		1.00	—	
Present	1.63	1.23, 2.17		1.70	1.17, 2.47	
<b>Volume of metastases</b>			0.03			0.20
<20 metastases	1.00	—		1.00	—	
≥20 metastases	1.50	1.07, 2.12		1.31	0.85, 2.00	
<b>Metastatic lesion ≥5cm</b>			0.01			<0.01
Not present	1.00	—		1.00	—	
Present	1.45	1.09, 1.93		1.74	1.21, 2.50	
<b>Age</b>			0.17			0.06
<65 years	1.00	—		1.00	—	
≥65 years	1.01	1.00, 1.02		1.02	1.00, 1.03	
<b>Sex</b>			0.91			>0.9
Female	1.00	—		1.00	—	
Male	1.02	0.78, 1.32		0.99	0.71, 1.38	
<b>Smoking Status</b>			0.02			0.02
Never-Smoker	1.00	—		1.00	—	
Ex-Smoker	0.58	0.40, 0.83		0.51	0.32, 0.82	
Current Smoker	0.62	0.41, 0.94		0.61	0.35, 1.06	
<b>PD-L1 Status</b>			<0.001			0.01
<1%	1.00	—		1.00	—	
≥1%	0.57	0.37, 0.88		0.74	0.44, 1.24	
≥50%	0.52	0.36, 0.74		0.63	0.41, 0.97	
Not Tested	0.95	0.66, 1.37		1.26	0.77, 2.07	
<b>Tumour Type</b>			0.10			0.20
Adenocarcinoma	1.00	—		1.00	—	
SCC	1.56	1.14, 2.12		1.58	1.06, 2.34	

ULCC	1.23	0.80, 1.90		1.05	0.62, 1.78	
NOS	1.23	0.46, 3.34		0.63	0.15, 2.71	
<b>Treatment Type</b>			<b>&lt;0.001</b>			<b>&lt;0.001</b>
Chemotherapy	<b>1.00</b>	—		<b>1.00</b>	—	
Immunotherapy	<b>0.56</b>	<b>0.41, 0.78</b>		<b>0.52</b>	<b>0.31, 0.86</b>	
Chemoimmunotherapy	<b>0.54</b>	<b>0.40, 0.75</b>		<b>0.34</b>	<b>0.21, 0.56</b>	
<b>Radiotherapy</b>			0.64			0.80
No Upfront RT	1.00	—		1.00	—	
Upfront RT	1.07	0.80, 1.43		1.04	0.72, 1.50	

Legend: n: number; SCC: Squamous Cell Carcinoma; ULCC: Undifferentiated Large Cell Carcinoma; NOS: Not otherwise specified; PD-L1: Programmed Cell death ligand 1 receptor; RT: Radiotherapy

**Supplementary Table S3: Univariate and Multivariate analysis for OS**

	Univariate			Multivariate		
Characteristic	HR	95% CI	p-value	HR	95% CI	p-value
<b>Lung Metastases</b>			0.88			0.40
Not present	1.00	—		1.00	—	
Present	1.02	0.78, 1.34		1.15	0.81, 1.64	
<b>Lymph Node Metastases</b>			0.16			0.70
Not present	1.00	—		1.00	—	
Present	1.32	0.89, 1.95		1.09	0.69, 1.72	
<b>Liver Metastases</b>			0.90			0.09
Not present	1.00	—		1.00	—	
Present	1.02	0.73, 1.44		1.52	0.95, 2.43	
<b>Brain Metastases</b>			<0.01			>0.9
Not present	1.00	—		1.00	—	
Present	1.64	1.15, 2.34		1.00	0.62, 1.63	
<b>Adrenal Metastases</b>			0.61			0.30
Not present	1.00	—		1.00	—	
Present	0.91	0.63, 1.31		0.80	0.51, 1.24	
<b>Pleural Metastases</b>			0.94			0.40
Not present	1.00	—		1.00	—	
Present	1.01	0.76, 1.35		1.17	0.82, 1.68	
<b>Bone Metastases</b>			<0.001			<0.001
Not present	1.00	—		1.00	—	
Present	1.95	1.45, 2.62		2.01	1.37, 2.97	
<b>Volume of metastases</b>			<0.01			0.03
<20 metastases	1.00	—		1.00	—	
≥20 metastases	1.77	1.24, 2.53		1.66	1.05, 2.62	
<b>Metastatic lesion ≥5cm</b>			0.06			0.07
Not present	1.00	—		1.00	—	
Present	1.35	0.99, 1.83		1.44	0.98, 2.14	
<b>Age</b>			0.02			<0.001
<65 years	1.00	—		1.00	—	
≥65 years	1.02	1.00, 1.03		1.03	1.01, 1.05	
<b>Sex</b>			0.97			0.6
Female	1.00	—		1.00	—	
Male	1.00	0.76, 1.33		0.91	0.64, 1.28	
<b>Smoking Status</b>			0.13			0.20
Never-Smoker	1.00	—		1.00	—	
Ex-Smoker	0.68	0.46, 1.01		0.78	0.47, 1.28	
Current Smoker	0.84	0.54, 1.30		1.05	0.59, 1.87	
<b>PD-L1 Status</b>			0.06			0.40
<1%	1.00	—		1.00	—	
≥1%	0.74	0.48, 1.16		0.92	0.53, 1.60	
≥50%	0.58	0.40, 0.86		0.69	0.43, 1.10	
Not Tested	0.69	0.47, 1.01		0.71	0.41, 1.23	
<b>Tumour Type</b>			0.02			<0.01
Adenocarcinoma	1.00	—		1.00	—	
SCC	1.76	1.29, 2.40		2.05	1.39, 3.04	

ULCC	0.96	0.58, 1.60		0.88	0.47, 1.63	
NOS	1.06	0.34, 3.33		0.36	0.05, 2.74	
<b>Treatment Type</b>						
Chemotherapy	1.00		0.72	1.00		0.20
Immunotherapy	1.07	0.77, 1.48		1.65	0.98, 2.77	
Chemoimmunotherapy	1.16	0.82, 1.64		1.27	0.74, 2.17	
<b>Radiotherapy</b>						
No Upfront RT	1.00	—	0.43	1.00	—	0.70
Upfront RT	1.13	0.83, 1.54		1.07	0.73, 1.56	

Legend: n: number; SCC: Squamous Cell Carcinoma; ULCC: Undifferentiated Large Cell Carcinoma; NOS: Not otherwise specified; PD-L1: Programmed Cell death ligand 1 receptor; RT: Radiotherapy



**Supplementary Table S4: OS and PFS for bone metastases by treatment type**

Outcome	Immunotherapy				Chemoimmunotherapy				Chemotherapy			
	Bone	No Bone	HR	p-value	Bone	No Bone	HR	p-value	Bone	No bone	HR	p-value
<b>Median OS months (95% CI)</b>	5 (4-15)	21 (13-33)	<b>2.10</b>	<b>&lt;0.01</b>	10 (8-21)	21 (16-NA)	<b>1.99</b>	<b>&lt;0.01</b>	15 (9-35)	21 (16-30)	1.49	0.17
<b>1-year OS (%)</b>	32.0	60.6			40.7	68.5			56.2	67.2		
<b>2-year OS (%)</b>	16.0	43.3			21.5	43.8			25.0	47.7		
<b>Median PFS months (95% CI)</b>	2 (1-6)	9 (5-17)	<b>3.19</b>	<b>&lt;0.001</b>	4 (4-9)	9 (7-NA)	<b>1.98</b>	<b>&lt;0.01</b>	3 (1-10)	5 (4-5)	1.44	0.20
<b>6-month PFS (%)</b>	20.9	56.2			41.8	63.6			31.3	28		

Legend: HR: Hazard Ratio; CI: Confidence Interval; OS: Overall Survival; PFS: Progression Free Survival

**Supplementary Table S5: OS and PFS for liver metastases by treatment type**

Outcome	Immunotherapy				Chemoimmunotherapy				Chemotherapy			
	Liver	No Liver	HR	p-value	Liver	No Liver	HR	p-value	Liver	No Liver	HR	p-value
<b>Median OS months (95% CI)</b>	6 (2-NA)	16.5 (12-25)	<b>2.04</b>	<b>0.05</b>	9 (7-NA)	18 (14-29)	<b>1.80</b>	<b>0.05</b>	19.0 (12-35)	18.5 (14-30)	1.46	0.19
<b>1-year OS (%)</b>	30.0	55.8			33.4	63.2			66.7	64.7		
<b>2-year OS (%)</b>	10.0	39.3			0	35.1			40	44.1		
<b>Median PFS months (95% CI)</b>	1 (1-NA)	7 (5-12)	<b>3.19</b>	<b>&lt;0.001</b>	4 (2-NA)	9 (6-13)	1.33	0.40	4 (3-5)	4 (3-9)	1.12	0.68
<b>6-month PFS (%)</b>	20.0	50.4			43.1	57.5			33.3	27.9		

Legend: HR: Hazard Ratio; CI: Confidence Interval; OS: Overall Survival; PFS: Progression Free Survival