Title: Undifferentiated Sarcomas Treated with Immune Checkpoint Blockade: The MD Anderson Cancer Center Experience

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Supplemental Table S1. Overall Survival according to clinical characteristics.

Variable	Number of Patients	Median OS (months, IQR)	Univariate HR (95%CI)	p-Value
Sex	-	-	1.04 (0.43-2.55)	0.93
Male	24	14.6 (1.1-67.8)	-	-
Female	12	12.9 (5-35.2)	-	-
Race	-	-	0.25 (0.05-1.2)	0.08
Caucasian	31	14.6 (1.3-67.8)	-	-
African American	5	5.3 (1.1-13.1)	-	-
Age	-	-	1.4 (0.6-3.4)	0.92
0-65	25	12.9 (5.5-17.6)	-	-
>65 years	11	18.6 (3.5-20.3)	-	-
Histology	-	-	0.95 (0.4-2.25)	0.90
UPS	26	8.9 (5.3-18.4)	-	
Other unclassified pleomorphic	10	10.2 (5-19.8)	-	
Previous Radiotherapy	-	-	**0.44 (0.2-0.99)**	**0.047**
Yes	22	7.9 (2.1-14.5)	-	-
No	14	17.5 (8.1-34.4)	-	-
ICB Combination Type	-	-	0.5 (0.23-1.12)	0.094
Standalone	15	13.1 (3.6-32.3)	-	-
Combination	21	8 (5.2-17.6)	-	-
Number of previous Systemic Therapies	-	-	0.78 (0.35-1.7)	0.53
≤2	19	12.9 (5-18.1)	-	-
>2	17	7.5 (5.2-20.9)	-	-
Lung Metastasis	-	-	1.02 (0.4-2.59)	0.96
Yes	26	12 (5.7-20.4)	-	-

No	10	5.8 (4.2-12.9)	-	-
Liver Metastasis	-	-	0.88 (0.24-3.1)	0.84
Yes	4	6.5 (4.8-22.9)	-	-
No	32	10.3 (5.2-19.2)		-

OS = overall survival; ICB= Immune Checkpoint Blockade; HR = hazard ratio; RT = Radiotherapy; UPS = undifferentiated pleomorphic sarcoma; Values in bold have p-value < 0.05

Supplemental Table S2. Patient and disease characteristics stratified by exposure to RT prior to ICB

Characteristic	Category	N (%) / median [range]		
		Previous RT N= 22	No prior RT N=14	p-value
Age at first ICB (years)	All	53 [22-79]	52 [33-78]	0.8
	>65 years	6 (27)	5 (36)	
Sex	Male	17 (77)	7 (50)	0.2
	Female	5 (23)	7 (50)	
Race	Caucasian	19 (86)	12 (86)	0.9
	African American	3 (14)	2 (14)	
ECOG performance status	0	5 (23)	6 (43)	0.3
	1	15 (68)	8 (57)	
	2	2 (9)	0 (0)	
BMI		32 [20-50]	28 [24-52]	0.3
Histology	UPS	17 (77)	9 (64)	0.6
	Other unclassified pleomorphic	5 (23)	5 (36)	
Biggest tumor diameter at start of ICB (cm)		7.7 [1.3,25]	4 [1.5,14.2]	**0.027**
Lung metastasis		16 (73)	10 (71)	1
Liver metastasis		3 (14)	1 (7)	1
Site of primary tumor	Extremities	9 (41)	6 (43)	
	Chest	10 (45)	5 (36)	
	Other*	3 (14)	3 (21)	
Number of surgical resections prior to ICB		2 [0-8]	2 [0-4]	0.3
Number of lines of systemic therapy prior to ICB		2 [0-10]	3 [0-5]	0.3
Type of ICB** treatment	Standalone ICB	11 (50)	4 (29)	
	Combination of ICB + ICB	10 (45)	6 (43)	
	Combination of ICB + RT	0 (0)	3 (21)	0.11
	Combination of ICB + chemo or antiangiogenic	1 (5)	1 (7)	
Received ICB as part of a clinical trial		14 (64)	11 (79)	0.6
Best response to ICB	Partial/complete Response	2 (9)	1 (7)	0.074
	Stable Disease	2 (9) 16 (73)	7 (50)	

Progressive		5 (36)
Disease	2 (9)	
Unknown		1 (7)

*Other sites of disease include abdomen, heart, and lumbar spine
** ICB drugs used: atezolizumab, durvalumab, ipilimumab, nivolumab, pembrolizumab, tremelimumab

Abbreviations: ICB, immune checkpoint blockade; ECOG, Eastern Cooperative Oncology Group; BMI, Body Mass Index; UPS, undifferentiated pleomorphic sarcoma; RT, radiotherapy

Supplemental Table S3. Patient and disease characteristics by type ICB treatment

| Characteristic	Category	N (%) / median [range]		p-value
		Standalone ICB N= 15	Combination N=21	
Age at first ICB (years)	All	57 [36, 79]	51 [22, 78]	0.064
Sex	Female	3 (20)	9 (43)	0.3
	Male	12 (80)	12 (57)	
Race	African American	4 (27)	1 (5)	0.2
	Caucasian	11 (73)	20 (95)	
ECOG performance status	0	4 (27)	7 (33)	0.2
	1	9 (60)	14 (67)	
	2	2 (13)	0 (0)	
BMI		30 [24, 52]	31 [20, 44]	0.2
Histology	UPS	11 (73)	15 (71)	1
	Other unclassified pleomorphic	4 (27)	6 (29)	
Biggest tumor diameter at start of ICB (cm)		9.5 [1.5, 22.0]	5.0 [1.3, 25.0]	0.2
Lung metastasis		10 (67)	16 (76)	0.8
Liver metastasis		1 (7)	3 (14)	0.9
Site of primary tumor	Chest	5 (33)	10 (48)	0.7
	Extremities	7 (47)	8 (38)	
	Other*	3 (20)	3 (14)	
Number of surgical resections prior to ICB		1 [0, 3]	2 [0, 8]	**0.013**
Number of lines of systemic therapy prior to ICB		2 [0, 5]	3 [0, 10]	0.062
Previous RT prior to ICB		11 (73)	11 (52)	0.4
Received ICB as part of a clinical trial		6 (40)	19 (90)	**0.004**
Best response to ICB	Partial/complete Response	2 (14)	1 (5)	0.6
	Stable Disease	3 (20)	13 (61)	
	Progressive Disease	8 (53)	6 (29)	
	Unknown	2 (13)	1 (5)	

Abbreviations: ICB, immune checkpoint blockade; ECOG, Eastern Cooperative Oncology Group; BMI, Body Mass Index; UPS, undifferentiated pleomorphic sarcoma; RT, radiotherapy
* Other sites of disease include abdomen, heart, and lumbar spine

Supplemental Figure S1. Progression-free survival in patients with previous RT comparing peri-op vs metastatic RT

	N	Events	Median PFS
Peri-op RT	14	13	2.5 months
Other RT	8	7	1.2 months

p= 0.52
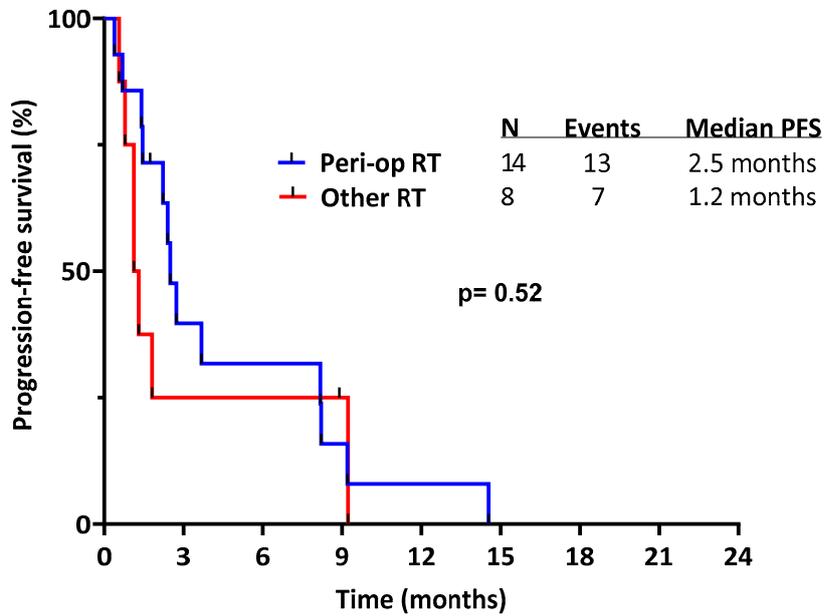
Number at risk (number censored)									
Peri-op RT	14 (0)	5 (1)	4 (1)	2 (1)	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)
Other RT	8 (0)	2 (0)	2 (0)	1 (1)	0 (1)	0 (1)	0 (1)	0 (1)	0 (1)

Supplemental Figure S2. Overall Survival stratified by exposure to RT prior to ICB
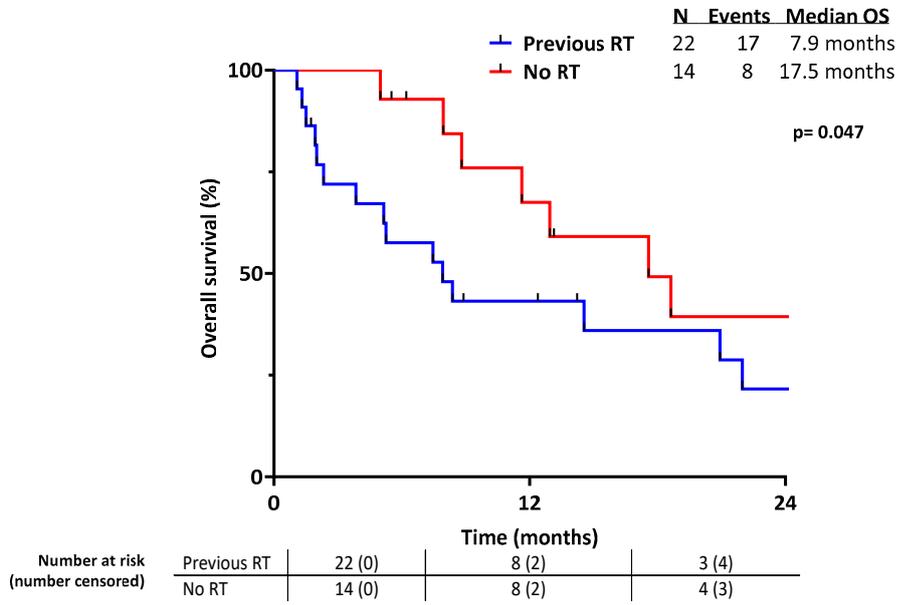
Supplemental Figure S3. Overall Survival stratified by number of lines of systemic therapy prior to ICB

	N	Events	Median OS
≤ 2	19	12	14.6 months
> 2	17	13	11.6 months

p= 0.5315
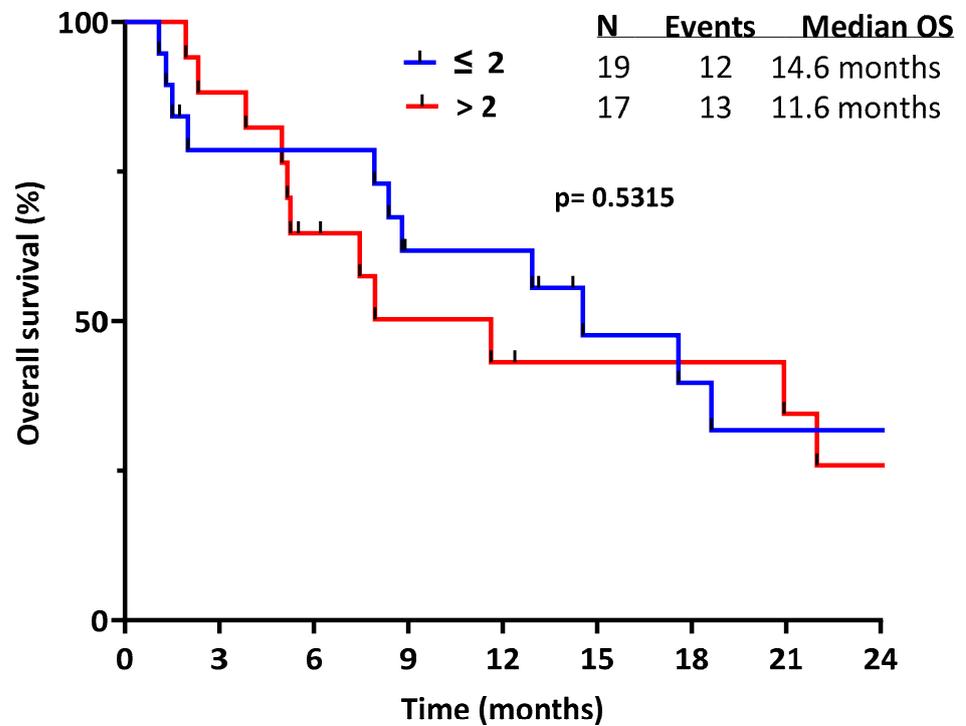
Number at risk (number censored)										
≤2	19 (0)	14 (1)	14 (1)	10 (2)	10 (2)	6 (4)	5 (4)	4 (4)	4 (4)
>2	17 (0)	15 (0)	10 (1)	7 (2)	6 (2)	5 (3)	5 (3)	4 (3)	3 (3)

Supplemental Figure S4. Overall Survival stratified by type of ICB treatment

		N	Events	Median OS
Standalone		15	8	29.5 months
Combination		21	17	8.8 months

p= 0.0936
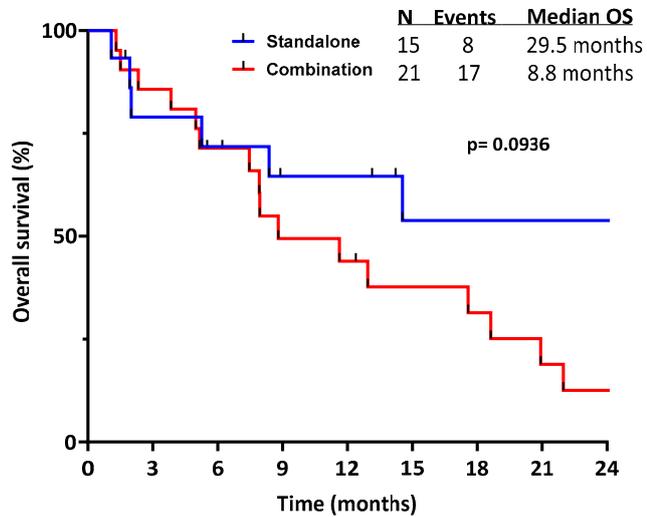
Number at risk (Number censored)										
Standalone	15 (0)	11 (1)	10 (1)	8 (2)	8 (2)	5 (3)	5 (3)	5 (3)	5 (3)
Combination	21 (0)	18 (0)	14 (1)	9 (2)	8 (2)	6 (3)	5 (3)	3 (3)	2 (3)