1   Supplementary material


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┌──────────────────────────────┐
│  213 adult sarcoma patients   │
│       treated with ICE        │
└──────────────────────────────┘
                 │          ┌──────────────────────────────────┐
                 │          │ 103 excluded                     │
                 │          │  •  16 osseous sarcoma           │
                 │          │  •  15 non-eligible STS          │
                 │          │  •  10 G1 grading                │
                 │          │  •  29 non-progressive           │
                 │          │     disease                      │
                 │          │  •  29 no RHT treatment          │
                 │          │  •  4 ICE as firstline-          │
                 │          │     treatment                    │
                 │          └──────────────────────────────────┘
     ┌──────────────────────────────┐
     │  110 patients included in     │
     │          analysis             │
     └──────────────────────────────┘
        ┌───────────────┴───────────────┐
┌──────────────────────┐      ┌──────────────────────┐
│  54 patients with     │      │  56 patients with     │
│  locally advanced     │      │  metastatic disease   │
│  disease              │      │                       │
│  (LA-STS)             │      │  (M-STS)              │
└──────────────────────┘      └──────────────────────┘
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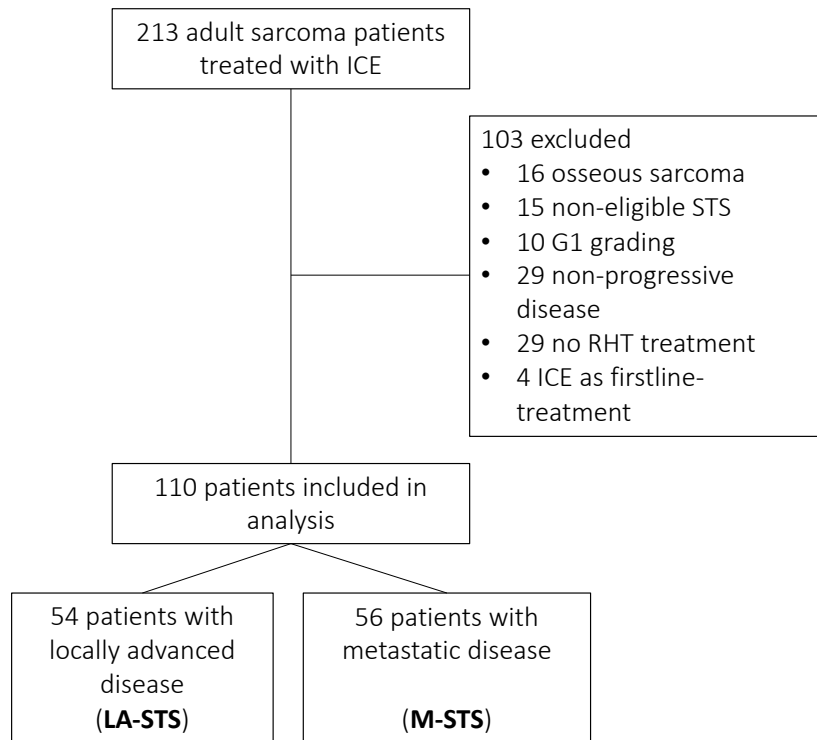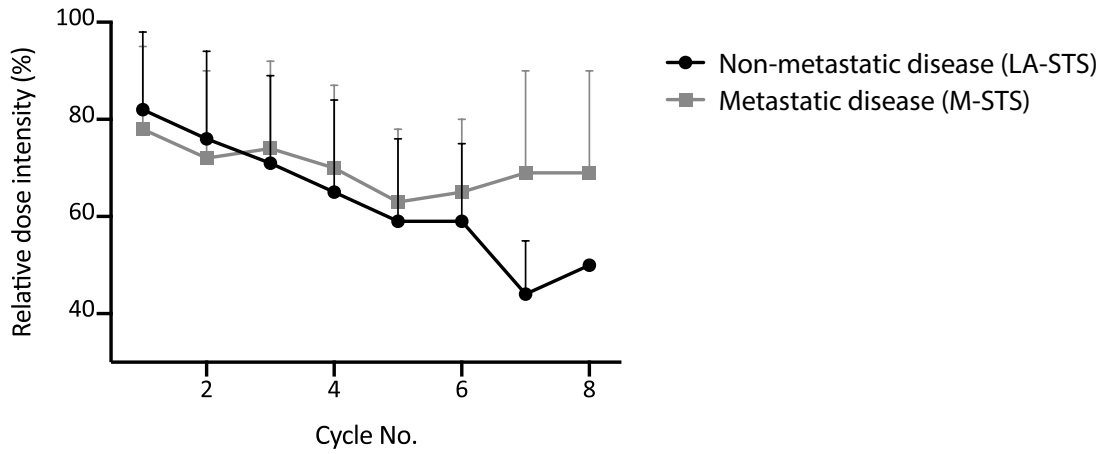
2   Supplementary Figure 1: Selected patient populations. **Abbreviations:** STS: soft-tissue sarcoma

3   Supplementary Figure 2: Relative dose intensity of applied ICE cycles. Full-dosed ICE (as described in the
4   patients and methods paragraph) over four days was considered 100%.

5 Supplementary Table 1: Prognostic factors for progression-free survival for LA-STS patients. P values were
6 calculated using the log-rank test for univariate analysis. For multivariate analysis using a Cox model, only
7 parameters with a p <0.10 in univariate analyses were considered. **Abbreviations:** HR: Hazard ratio, mo:
8 months, NA: not assessable, OS: overall survival.

Parameter	N	Univariate analysis		Cox model	
		Median PFS, mo (95% CI)	p	HR (95% CI)	p
Age			0.29		
>50 years	38	10 (8-15)			
≤50 years	16	9 (6-29)			
Sex			0.49		
Male	31	10 (8-12)			
Female	23	9 (6-22)			
Treatment line			0.15		
2nd line	46	10 (9-15)			
> 2nd line	8	9 (6-NA)			
Grading			**0.003**	3.10 (1.028-9.34)	**0.045**
3	32	9 (5-10)			
2	22	20 (11-36)			
Histologic sub-entity			**0.043**	0.88 (0.395-1.98)	0.762
Lipo-/Leiomyosarcoma	28	11 (6-29)			
Non-Lipo-/Leiomyosarcoma	26	9 (7-11)			
Surgery			**0.008**	0.45 (0.196-1.02)	0.054
Yes	31	11 (9-21)			
No	23	8 (5-11)			
Response/Disease stabilization as best radiographic response with ICE+RHT			**<0.0001**	0.15 (0.054-0.39)	**<0.001**
Yes	26	10 (9-27)			
No	9	3 (2-NA)			
Type of progression			**0.0002**	0.42 (0.175-0.99)	**0.048**
Progression after response to prior chemotherapy	32	11 (9-27)			
Primary refractory disease	22	5 (4-10)			

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10 Supplementary Table 2: Prognostic factors for overall survival for M-STS patients. P values were calculated
11 using the log-rank test for univariate analysis. For multivariate analysis using a Cox model, only parameters with
12 a p <0.10 in univariate analyses were considered. **Abbreviations:** HR: Hazard ratio, mo: months, NA: not
13 assessable, OS: overall survival.

Parameter	N	Univariate analysis		Cox model	
		Median OS, mo (95% CI)	p	HR (95% CI)	p
Age			0.24		
>50 years	27	15 (11-27)			
≤50 years	29	11 (8-19)			
Sex			0.56		
Male	26	11 (7-19)			
Female	30	13 (10-31)			
Treatment line			0.12		
2nd line	40	11 (8-17)			
> 2nd line	16	15 (11-42)			
Grading			0.07	1.33 (0.68-2.60)	0.406
3	39	10 (7-19)			
2	17	15 (13-NA)			
Histologic sub-entity			0.19		
Lipo-/Leiomyosarcoma	22	11 (7-17)			
Non-Lipo-/Leiomyosarcoma	34	17 (11-34)			
Surgery			0.52		
Yes	15	15 (11-35)			
No	41	11 (7-19)			
Response/Disease stabilization as best radiographic response with ICE+RHT			**<0.0001**	0.36 (0.19-0.70)	**0.002**
Yes	26	18 (15-35)			
No	24	7 (5-19)			
Type of progression			0.33		
Progression after response to prior chemotherapy	19	15 (11-34)			
Primary refractory disease	37	10 (7-17)			

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