

Challenges in the treatment of soft-tissue plasmacytoma: a retrospective analysis of 120 patients with extramedullary multiple myeloma

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Figures:

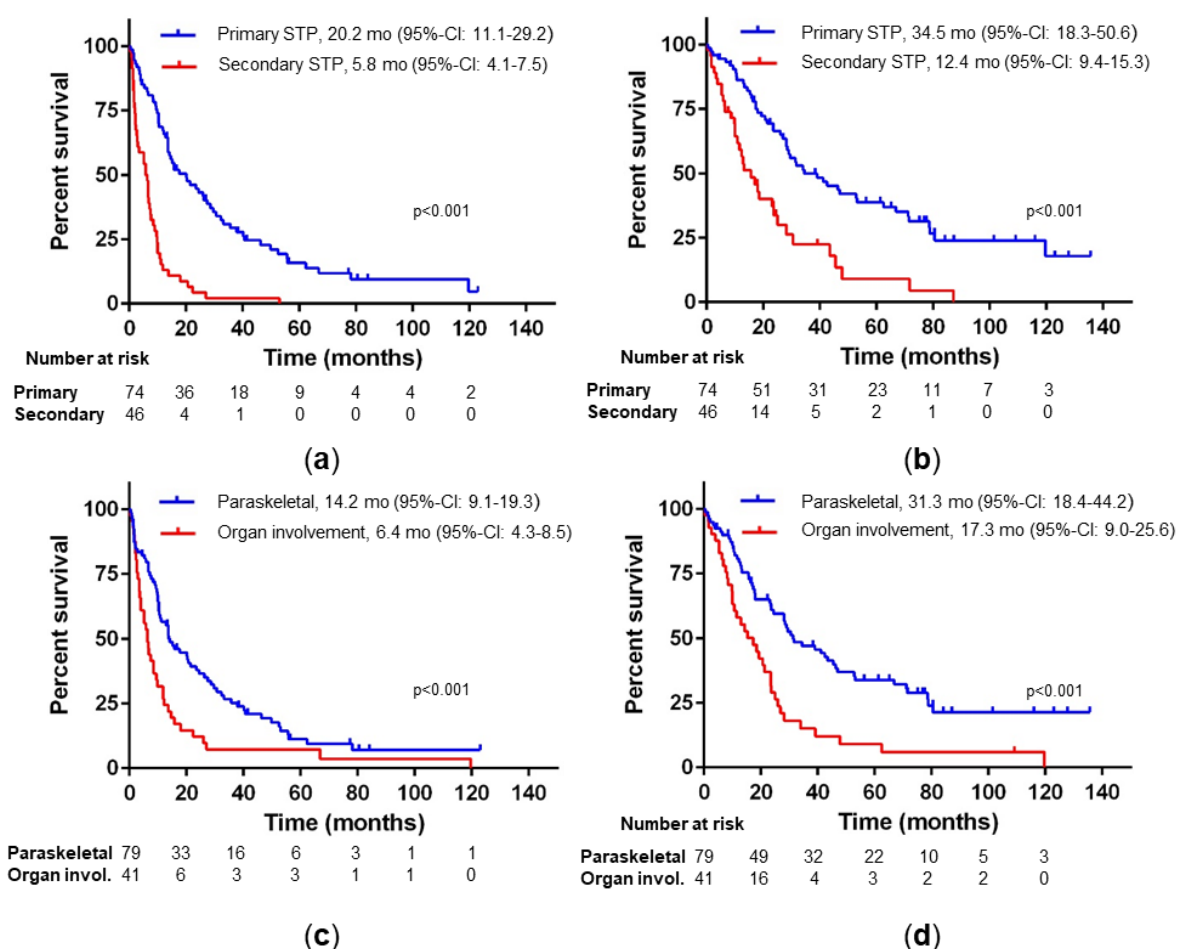


Fig. S1 Progression-free survival (a, c) and overall survival (b, d) in STP patients stratified by primary and secondary STP (a and b) or stratified by parasketal plasmacytomas and STP with organ involvement (c and d)

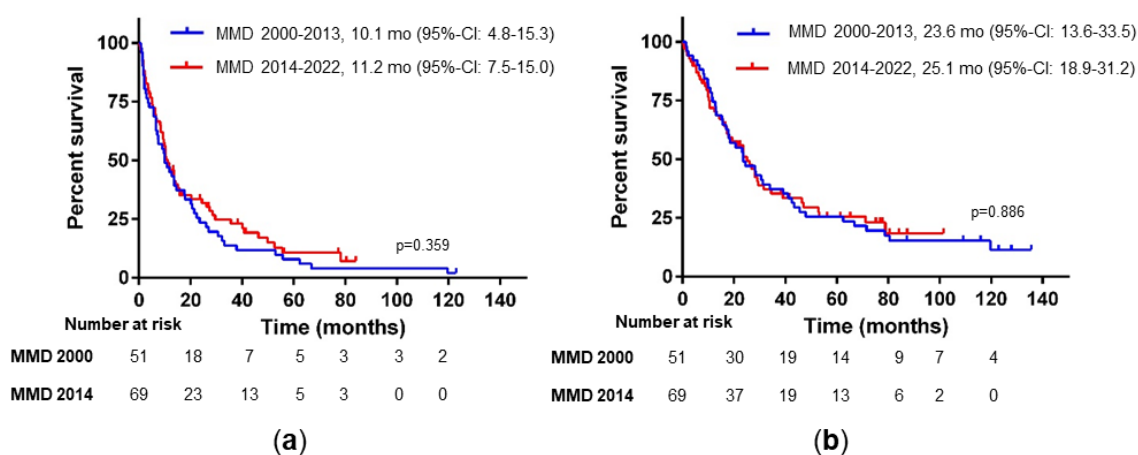


Fig. S2 Kaplan-Meier curves including median duration for (a) progression-free survival and (b) overall survival in STP patients stratified by year of multiple myeloma diagnosis (MMD)

Tables:

Table S1 Pretreatment of secondary STP pts (n=46)

		Number	%
Median no. of regimens, range		2 (1-9)	
Drugs	PI	14	30
	IMiD	1	2
	anti-CD38-mAB	0	0
	PI + IMiD	19	41
	anti-CD38-mAB + PI	0	0
	anti-CD38-mAB + IMiD	0	0
	anti-CD38-mAB + PI + IMiD	11	24
	Others ¹	1	2
Novel Drug classes²	0	1	2
	1	15	33
	2	19	41
	3	11	24
Prior HCT	Yes	36	78
	1 autologous	19	53
	≥2 autologous	12	33
	Allogeneic	2	6
	Auto-Allo	3	8

¹ including classical chemotherapy; ² PI, IMiD and anti-CD38-mAB.

Table S2 Patient characteristics stratified by year of diagnosis of multiple myeloma [n (%)]

Characteristics		MM Diagnosis 2000-2013 n=51 (43%)	MM Diagnosis 2014-2022 n=69 (57%)	p-value ⁵
Median Age (years, range)		68 (37-84)	68 (40-87)	0.256
Sex	Male	38 (75%)	41 (59%)	0.119
	Female	13 (25%)	28 (41%)	
MM type	IgG	28 (55%)	45 (65%)	0.357
	IgA	9 (18%)	13 (19%)	
	IgD	2 (4%)	0 (0%)	
	Kappa-LC	6 (12%)	6 (9%)	
	Lambda-LC	6 (12%)	4 (6%)	
	Asecretoy	0 (0%)	1 (1%)	
LC involvement¹	Kappa	32 (63%)	47 (68%)	0.557
	Lambda	19 (37%)	21 (30%)	
STP type	Primary STP	23 (45%)	51 (74%)	0.002
	Secondary STP	28 (55%)	18 (26%)	
STP Localization	Paraskeletal	33 (65%)	46 (67%)	0.966
	Organ involvement	9 (18%)	12 (17%)	
	Both	9 (18%)	11 (16%)	
Disease status	Newly diagnosis	23 (45%)	51 (74%)	0.007
	First relapse	12 (24%)	8 (12%)	
	Multiple relapse	11 (22%)	5 (7%)	
	Primary refractory	0 (0%)	3 (4%)	
	Refractory relapse	5 (10%)	2 (3%)	
LDH	Normal	29 (57%)	37 (54%)	0.853
	Elevated	22 (43%)	32 (46%)	
Serum Albumin	< 3.5 mg/L	13 (25%)	22 (32%)	0.448
	≥ 3.5 mg/L	38 (75%)	47 (68%)	
Serum β2-Microglobulin	< 3.5 mg/L	7 (58%)	14 (31%)	0.201
	3.5-5.5 mg/L	2 (17%)	13 (28%)	
	> 5.5 mg/L	3 (25%)	19 (41%)	
R-ISS²	R-ISS I	3 (27%)	5 (11%)	0.243
	R-ISS II	7 (64%)	29 (63%)	
	R-ISS III	1 (9%)	12 (26%)	
HRCA³	t(4;14)	5 (10%)	10 (14%)	0.585
	t(14;16)	1 (2%)	1 (1%)	1
	del17p13	3 (6%)	7 (10%)	0.523
	ampl1q21	3 (6%)	11 (16%)	0.151
	Yes ⁴	9 (19%)	17 (25%)	0.504
	no	39 (81%)	52 (75%)	

¹data available in 119 patients (1 asecretoy); ²data available in 57 patients (11 patients / 46 patients); ³data available for 117 patients (48 patients / 69 patients); ⁴patients with at least 1 HRCA ⁵determined by two-sided t-test (continuous variables) or Chi² or Fisher's exact test (categorical variables). HCT: Hematopoietic cell transplantation; HRCA: High-risk cytogenetic aberrations; IMiD: Immunomodulatory drugs; LC: Light chain; mAB: monoclonal antibody; MM: Multiple myeloma; PI: Proteasome inhibitors; PS: Paraskeletal; STP: Soft-tissue plasmacytoma.

Table S3 STP first-line treatment including systemic therapy with novel drugs categorized by primary and secondary STP [n (%)]

		Primary STP (n=74)	Secondary STP (n=46)
Drugs	PI	41 (55)	11 (24)
	IMiD	2 (3)	11 (24)
	anti-CD38-mAB	0 (0)	1 (2)
	PI + IMiD	20 (27)	10 (22)
	anti-CD38-mAB + PI	3 (4)	5 (11)
	anti-CD38-mAB + IMiD	2 (3)	2 (4)
	anti-CD38-mAB + PI + IMiD	4 (5)	0 (0)
	Others ¹	2 (3)	6 (13)
Novel drug classes²	0	2 (3)	6 (13)
	1	43 (58)	23 (50)
	2	25 (34)	17 (37)
	3	4 (5)	0 (0)
HCT	Yes	38 (51)	4 (9)
	1 autologous	35 (92)	3 (75)
	≥2 autologous	3 (8)	0 (0)
	allogeneic	0 (0)	1 (25)

¹ including classical chemotherapy; ² Proteasome inhibitors (PI), immunomodulatory drugs (IMiD) and anti-CD38-monoclonal antibodies (mAB). HCT: Hematopoietic cell transplantation; STP: Soft-tissue plasmacytoma

Table S4 Median a) progression-free survival and b) overall survival and Hazard Ratios (HR) of univariate proportional hazards analysis for potential prognostic factors

(a) - Progression-free survival					
Prognostic Factor	N	Parameter	Median PFS (months; 95%-CI)	HR_{PFS} (95%-CI)	P-value
Age	45	<65	13.7 (9.3-18.0)	1.258	0.255
	75	≥65	10.3 (9.4-11.3)	(0.847-1.868)	
Sex	79	Male	13.8 (10.0-17.6)	1.688	0.010
	41	Female	6.6 (1.4-11.9)	(1.131-2.520)	
STP type	74	Primary	20.2 (11.1-29.2)	3.801	<0.001
	46	Secondary	5.8 (4.1-7.5)	(2.503-5.773)	
Organ involvement	79	No	14.2 (9.1-19.3)	2.106	0.001
	41	Yes	6.4 (4.3-8.5)	(1.350-3.009)	
Non-paravertebral plasmacytoma	37	No	13.6 (8.9-18.3)	0.901	0.633
	62	Yes	11.8 (8.4-15.2)	(0.587-1.383)	
CNS involvement	114	No	10.4 (7.7-13.0)	1.348	0.481
	6	Yes	12.1 (3.8-20.4)	(0.587-3.095)	
R-ISS¹	44	I+II	20.4 (7.6-33.1)	3.904	<0.001
	13	III	5.4 (0.0-11.1)	(1.916-7.953)	
Beta-2-Microglobulin²	36	≤5.5 mg/L	23.6 (11.5-35.7)	2.285	0.006
	22	>5.5 mg/L	8.5 (2.9-14.2)	(1.264-4.130)	
Albumin	85	≥3.5 g/dL	10.5 (4.5-16.6)	1.341	0.179
	35	<3.5 g/dL	10.8 (8.1-13.6)	(0.874-2.057)	
LDH	66	Normal	18.0 (9.4-26.6)	1.934	0.001
	54	Elevated	8.3 (5.2-11.3)	(1.306-2.865)	
High-risk aberration³	91	No	10.5 (7.6-13.5)	1.149	0.551
	26	Yes	11.2 (6.8-15.7)	(0.727-1.817)	
del17p13	107	No	11.8 (8.9-14.7)	1.815	0.076
	10	Yes	6.7 (0.0-16.7)	(0.940-3.502)	
t(4;14)	102	No	10.4 (8.0-12.7)	0.870	0.638
	15	Yes	13.6 (10.6-16.6)	(0.468-1.556)	
t(14;16)	115	No	10.8 (8.3-13.4)	1.769	0.427
	2	Yes	3.7 (3.7-3.7)	(0.433-7.227)	
ampl1q21	103	No	12.8 (9.40-16.2)	1.833	0.038
	14	Yes	6.9 (0.0-15.1)	(1.034-3.249)	
dupl1q21	83	No	11.8 (7.8-15.8)	1.039	0.857
	34	Yes	10.5 (9.2-11.8)	(0.682-1.584)	
tripl1q21	99	No	13.6 (10.3-17.0)	1.476	0.145
	18	Yes	10.8 (8.3-15.9)	(0.874-2.493)	
Year of MM diagnosis	51	2000-2013	10.1 (4.8-15.3)	0.837	0.361
	69	2014-2022	11.2 (7.5-15.0)	(0.572-1.225)	
LC involvement⁴	79	Kappa-LC	11.2 (7.1-15.4)	1.320	0.176
	40	Lambda-LC	10.5 (8.0-13.0)	(0.883-1.973)	
Prior AHCT⁵	10	No	6.3 (0.0-12.7)	1.184	0.648
	31	Yes	5.8 (1.6-9.9)	(0.573-2.447)	
STP first-line treatment with-AHCT⁶	78	No	6.7 (4.9-8.4)	0.388	<0.001
	41	Yes	26.3 (17.8-34.9)	(0.256-0.589)	
STP first-line therapy with PI+IMiD	90	No	9.6 (7.7-11.6)	0.552	0.009
	30	Yes	20.7 (8.1-33.4)	(0.353-0.862)	
STP first-line therapy with PI+IMiD and/or CD38-mAb	73	No	9.6 (7.7-11.6)	0.614	0.016
	47	Yes	17.7 (7.3-28.1)	(0.413-0.912)	

(b) - Overall survival

Prognostic Factor	N	Parameter	Median OS (months; 95%-CI)	HR _{OS} (95%-CI)	p-value
Age	45	<65	39.1 (23.6-54.5)	1.871	0.005
	75	≥65	18.0 (12.4-23.5)	(1.206-2.902)	
Sex	79	Male	28.2 (21.2-35.2)	1.886	0.004
	41	Female	17.3 (10.1-24.5)	(1.228-2.897)	
STP type	74	Primary	34.5 (18.3-50.6)	3.062	<0.001
	46	Secondary	12.4 (9.4-15.3)	(1.996-4.697)	
Organ involvement	79	No	31.3 (18.4-44.2)	2.334	<0.001
	41	Yes	17.3 (9.0-25.6)	(1.522-3.579)	
Non-paravertebral plasmacytoma	37	No	30.5 (11.9-49.2)	1.146	0.574
	62	Yes	23.7 (13.8-33.7)	(0.713-1.840)	
CNS involvement	114	No	25.1 (20.7-29.4)	2.116	0.079
	6	Yes	14.3 (0.8-27.9)	(0.916-4.891)	
R-ISS¹	44	I+II	47.0 (16.2-77.8)	4.309	<0.001
	13	III	14.3 (2.4-26.2)	(2.008-9.243)	
Beta-2- Microglobulin²	36	≤5.5 mg/L	52.8 (14.9-90.7)	2.840	0.003
	22	>5.5 mg/L	23.6 (11.1-36.1)	(1.441-5.597)	
Albumin	85	≥3.5 g/dL	26.1 (0.0-57.4)	1.174	0.491
	35	<3.5 g/dL	23.6 (17.3-29.9)	(0.744-1.851)	
LDH	66	Normal	29.5 (21.8-37.1)	1.736	0.009
	54	Elevated	19.4 (10.2-28.6)	(1.148-2.628)	
High-risk aberration³	91	No	24.5 (17.8-31.1)	1.006	0.982
	26	Yes	23.7 (8.9-38.6)	(0.611-1.655)	
del17p13	107	No	26.1 (21.8-30.3)	1.543	0.218
	10	Yes	10.3 (0.4-20.2)	(0.774-3.077)	
t(4;14)	102	No	23.6 (16.6-30.6)	0.713	0.314
	15	Yes	33.9 (16.1-51.8)	(0.369-1.378)	
t(14;16)	115	No	25.1 (20.8-29.2)	3.878	0.063
	2	Yes	6.8 (6.8-6.8)	(0.932-16.141)	
ampl1q21	103	No	28.1 (22.7-33.7)	2.111	0.023
	14	Yes	12.4 (3.9-20.8)	(1.107-4.024)	
dupl1q21	83	No	23.7 (16.5-31.0)	0.809	0.382
	34	Yes	26.9 (13.6-40.2)	(0.503-1.302)	
tripl1q21	99	No	26.1 (21.2-31.0)	1.499	0.156
	18	Yes	17.8 (3.2-32.4)	(0.875-2.622)	
Year of MM diagnosis	51	2000-2013	23.6 (13.6-33.5)	0.970	0.886
	69	2014-2022	25.1 (18.9-31.2)	(0.642-1.467)	
LC involvement⁴	79	Kappa-LC	28.5 (21.7-35.2)	1.256	0.297
	40	Lambda-LC	19.4 (12.4-26.4)	(0.819-1.925)	
Prior AHCT⁵	10	No	9.9 (4.2-15.7)	0.523	0.093
	31	Yes	12.4 (9.7-15.0)	(0.245-1.114)	
STP first-line treatment with-AHCT⁶	78	No	16.7 (10.0-24.0)	0.283	<0.001
	41	Yes	66.9 (25.8-108.0)	(0.173-0.463)	
STP first-line therapy with PI+IMiD	90	No	20.7 (15.0-26.4)	0.405	0.001
	30	Yes	71.2 (21.6-120.8)	(0.238-0.690)	
STP first-line therapy with PI+IMiD and/or CD38-mAb	73	No	20.7 (14.4-27.1)	0.555	0.009
	47	Yes	34.5 (21.7-47.2)	(0.375-0.863)	

¹data available for 57 patients; ²data available for 58 patients; ³data available for 117 patients; ⁴data available for 119 patients (1 asecreatory patient); ⁵only for patients with secondary STP (n=46, 5 patients with allogeneic or autologous-allogeneic HCT censored); ⁶data available for 119 patients (1 patient with allogeneic HCT censored). AHCT: Autologous hematopoietic cell transplantation; IMiD: Immunomodulatory drugs; mAb: monoclonal antibody; PI: Proteasome inhibitors; STP: Soft-tissue plasmacytoma.

Table S5 Hazard Ratios (HR) of multivariate Cox proportional hazards analysis for potential prognostic factors for progression-free survival (HR_{PFS}) and overall survival (HR_{OS}) – complete model

Factor	HR_{PFS} (95%-CI) p-value	HR_{OS} (95%-CI) p-value
Sex (male vs. female)	1.258 (0.591-2.679) (p=0.551)	1.524 (0.670-3.468) (p=0.315)
Age (<65 years vs. ≥65 years)	-	1.252 (0.531-2.951) (p=0.608)
STP type (primary vs. secondary)	2.748 (1.002-7.533) (p=0.049)	3.753 (1.005-14.023) (p=0.049)
Organ involvement (no vs. yes)	2.654 (1.164-6.051) (p=0.020)	2.884 (1.221-6.812) (p=0.016)
R-ISS (I+II vs. III)	1.829 (0.746-4.482) (p=0.187)	2.203 (0.758-6.407) (p=0.147)
ampl1q21 (no vs. yes)	1.216 (0.460-3.215) (p=0.693)	1.615 (0.474-5.498) (p=0.443)
STP first-line treatment with AHCT (no vs. yes)	0.426 (0.202-0.894) (p=0.024)	0.580 (0.227-1.477) (p=0.253)
STP first-line therapy with PI+IMiD (no vs. yes)	0.671 (0.339-1.327) (p=0.252)	0.431 (0.178-1.044) (p=0.062)

AHCT: Autologous hematopoietic cell transplantation; IMiD: Immunomodulatory drugs; PI: Proteasome inhibitors; STP: Soft-tissue plasmacytoma