

Supporting information 1. Summary of literature review of studies evaluating treatments and clinical outcomes of patients with mesenchymal chondrosarcoma.

Author, Year	Study design	Population (Male)	Median age (range), y	Metastatic at diagnosis (site)	Treatment	Chemotherapy agents	Median OS, m	Median PFS, m	Comment
Strach et al, (this study)	Retrospective review 2001-2022	22 MCS (45%)	28 (10-59)	3 (Lung, node)	17 S 2 preop CT 8 palliative CT 13 RT	D DI +Dz +Vinc +Da VDC/IE VIDE IrT M VDaC E GDo P Durvalumab + Tremilimumab Investigational	104	34	
Van Maldegem et al, 2019 ¹⁶	Retrospective review of 4 sarcoma centres 1980-2016	25 unresectable (36%)	27.5 (7-48)	NR	25 multidrug CT	D +Cis ++M +C I CisDzV Anastrozole Anti-TIM3 IDH inhibitor Durvalumab + Mogamulizumab		Mean 6.7	
Amer et al, 2019 ³	Retrospective review of SEER database 1973-2013	226 MCS (54%)	32 (NR)	24	86 RT	Not reported	34		CT and S not reported
Tsuda et al, 2017 ²²	Retrospective review, 1980-2013	57 MCS	33 (6-73)	17	Localised 34 S 13 CT+S 10 S+RT	D I Cis carboplatin	5y 66% 10y 56%	5y MFS 26%	

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					6 RT Advanced 16 CT	E C V M Da	CT 91% No chemo 57%		
Morioka et al, 2016 ²³	Randomised phase 2 prospective study of TRS 2012-2014	5 trabectedin (3 MCS) 3 BSC (3 MCS)	<40 (MCS)	all	MCS: 4/6 S 6 CT (3 preop) 1 RT (only reported in case study)	D DCis VDC VDC/IE	Trabectedin: 26 BSC: not reported	Trabectedin: 13 BSC: 1 (p)	1 PR, 2 SD Analysis of trabectedin grouped MCS with EMCS
Schniederman et al, 2016 ¹³	Retrospective review of SEER database, 1973-2011	205 (114)	37	Not reported	Not reported	Not reported	64m 5y 51% 10y 43%		Multivariate analysis on 104 due to missing data (tumour size)
Xu et al, 2015 ⁹	Systematic review 1994-2014 (included case reports)	107 MCS from 18 articles (56%)	88 <50yrs	24	93% S 63% CT 38% RT 40% S+CT 7% S+RT 15% S+CT+RT		80 5y OS 55% 10y OS 44% (no difference OS local v met p=0.095)	Median EFS 58	Excluded cases/series if patients died in 3m of FU
Frezza et al, 2015 ¹⁰	Retrospective review of EMSOS cases 1971-2012	113 (60)	30 (11-80)	17 (lung, bone)	Localised (96) 95 S 54 CT (21 preop, 30	Localised 96% anthracycline 70% alkylating	17 years Localised 20y Metastatic 3y	Localised 7yrs	Likely duplication of patients from previous analysis, 128

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					postop, 3 pre and postop) 40 RT (38 postop, 1 pre and postop) Metastatic (17) 2 S (primary, metastatectomy) postop RT 3 S (primary) 1 RT (primary)	Metastatic: Trabectedin Epl			cases, 15 excluded as no information
Kawaguchi et al, 2014 ²⁴	Retrospective review 1979-2010	37 (20)	33 (11 - 65)	7 (bone, breast, colon)	Primary: 8 S 13 S+CT (10 preop and 3 postop) 5 S+RT 8 S+CT+RT (1 preop CT+ RT, 2 preop CT and postop RT, 1 preop RT and postop CT, 4 postop CT+RT) 1 CT 1 RT 1 BSC	D (21) +C+Bleomycin +Cis +CDz DI +V +Dz Cis +Do +DzM	5y 51% 10y 37%	DFS 5y 23% 10y 5%	Localised: RT improved local RFS (p=0.037) No influence of CT on survival (p0.397)
Shakked et al, 2012 ²⁵	Retrospective review of records of senior bone pathologist 1964-2009	20 (9)	24 (7-37)		9 S 3 S+CT 1 S+RT 4 S+CT+RT	VDC/IE IE DI	Not reported for entire cohort		

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Italiano et al, 2013 ¹⁷	Retrospective review of 15 centres 1988-2011	112 CS – 17 MCS (CS: 62%)	CS: 52 (17-84)	All (135 lung, 40 bone, 8 liver, 39 other)	CT: Multidrug – 98 Single – 82 S: not stated	D +I +CisI +Cis +other PegD I +Cis GDo Imatinib Sirolimus+C Trabectedin Dz E IrT			Palliative surgery prognostic for OS (not hedgehog study)
Dantonello et al, 2008 ¹¹	Retrospective review of prospective CWS/COSS database 1977 - 2006	15 (33%)	16.6 (1-25)	1	S: All (8 complete) CT: 13 RT: 6	D +DaCV +DaIV +IMCis +IMCis, carboE→autosct Da + carboEIV→auto SCT +DEIMV	10y OS 67%	10y EFS 53%	7 induction CT (4 >50% tumour volume regression or histologic devitalisation)
Cesari et al, 2007 ¹⁵	Retrospective database review 1959-2003	28 (39%)	31 (20-71)	6 (Bone, lung, kidney, spleen, pancreas)	S: 24 RT: 5 CT: 12 (9 localised, 3 metastatic)	SE-91 protocol DI +CisM	10y OS Chemo 31% No chemo 19% (p=0.008)		

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Nakashima et al, 1986 ¹⁴	Case series retrospective review	111 (47%)	^a (5-74)	3 (2 lung, 1 LN)	^b 10 S+RT+CT 19 S+CT 8 S+RT		29% by 17y	DFS 20% (by 17y)	
Huvos et al, 1983 ⁵	Retrospective review 1931-1981	35 (57%)	mean 25 (6-70)	5 (2 bones, 1 lung, 1 chest wall, 1 breasts)	4 CT+S 8 RT+S 1 S+CT 10 S+RT	M	5yr OS 42% (n=32, 3 treatment to recent)		
Misc authors 1959-1983 ^{2, 26-30}		127	17-30						Not included here as historical
TOTAL		906	30 (1-84)				10y 19-67%		

Abbreviations: MCS, mesenchymal chondrosarcoma; S, surgery; RT, radiation therapy; CT, Chemotherapy; preop, preoperative; postop, postoperative; DFS, disease free survival; PFS, progression free survival; OS, overall survival; MFS, metastasis free survival; LN, lymph node; TRS, translocation-related sarcomas; BSC, best supportive care; ; D, doxorubicin; Ir, irinotecan; T, temozolamide; P= pazopanib; V, vincristine; Da, dactinomycin; I, ifosfamide; E, etoposide; Dz, dacarbazine; M, methotrexate; C, cyclophosphamide; G, gemcitabine; Do, docetaxel; Cis, Cisplatin; Ep, Epirubicin; PegD, pegylated doxorubicin; AutoSCT, autologous stem cell transplant; SE-91 protocol⁴²

^aaverage age not provided

^btreatment and follow up available for 78 patients