ECONOMIC AND UTILITY EVIDENCE FOR METASTATIC SYNOVIAL SARCOMA AND MYXOID ROUND CELL LIPOSARCOMA: A SYSTEMATIC LITERATURE REVIEW

EPH134

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Background

- Soft tissue sarcomas (STS) are a rare and heterogenous group of mesenchymal cancers that originate from soft tissues and account for <1% of all adult tumours
- Synovial sarcoma (SS) and myxoid/round cell liposarcoma (MRCLS) are rare subtypes of STS
- Outcomes for patients with advanced/metastatic SS/MRCLS (mSS/mMRCLS) are poor and systemic treatment options are limited
- New cell therapies are being investigated for mSS/mMRCLS, and economic and utility evidence will be required by health technology assessment (HTA) bodies to evaluate these new treatments

Study Objective

- To systematically review the economic and utility evidence for previously treated mSS/mMRCLS and the broader STS population

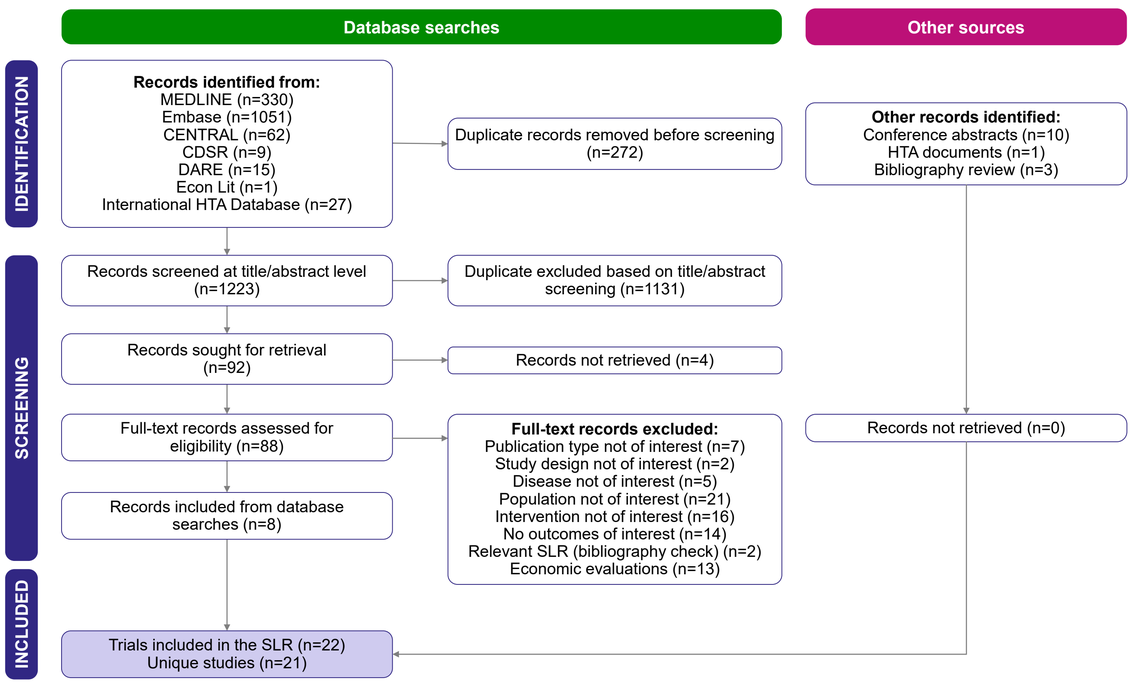
Study Design

- Searches were conducted in Embase, MEDLINE, EconLit, Cochrane and DARE (2000–2022), complemented with selected conferences (2020–2022) and HTA websites, published in English
- Observational studies, clinical trials and economic studies reporting on patients with mSS/mMRCLS, STS results stratified by SS/MRCLS or >80% study population with SS/MRCLS, were eligible for inclusion
- Advanced/metastatic STS population studies were flagged for additional consideration
- No restriction was placed on interventions or comparators. Outcomes included economic evaluations, cost, HCRU or utility values

Results

- Titles and abstracts of 1223 studies were screened; of these, 88 full-text studies were reviewed. None of these studies met the inclusion criteria for the mSS/mMRCLS population; hence, no evidence was identified on the economic burden or utilities
- However, for the broader STS population, 21 relevant studies were identified **(Figure 1): three utility studies (Table 1), 10 HTAs were identified (Table 2) and eight costs/HCRU studies (Table 3)**
- Utility values for the progressive disease health state were lower compared with stable disease and response to treatment/pre-progression health states, highlighting the substantial impact on quality of life associated with mSTS
- HTA reviews for treatments for STS (i.e., eribulin, pazopanib, olaratumab and trabectedin) noted evidence gaps for drug administration, wastage, adverse events, and identification and costing of subsequent treatments. Efficacy results primarily driven by PFS increased the scrutiny of disease management costs pre- and post-progression
- Cost/HCRU studies on STS revealed that cost drivers included drug, inpatient hospitalization and outpatient cost

Figure 1. PRISMA Diagram



CDSR, Cochrane Database of Systematic Reviews; DARE, Database of Abstracts of Reviews of Effects; HTA, health technology assessment; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses; SLR, systematic literature review; SS, synovial sarcoma.

Table 1. Utility evidence in STS

Author, Year	Study design	Country	Samples size	Tool	Progressive disease	Stable disease	Response
Guest, 2013[1]	Cross-sectional survey	UK	207	Time trade-off	**Mean:** 0.3	**Mean:** 0.43	Complete: **Mean:** 0.60 Partial: **Mean:** 0.51
				Standard gamble	**Mean:** 0.17	**Mean:** 0.31	Complete: **Mean:** 0.51 Partial: **Mean:** 0.43
Shinger, 2013[2]	Cross-sectional survey	UK	100	Time trade-off	**Mean (SD):** 0.263 (0.231)	**Mean (SD):** 0.736 (0.231)	**Mean (SD):** 0.792 (0.169)
Reichardt, 2012[3]	Cross-sectional survey	Canada, USA, Germany, France, Italy, the Netherlands, Spain, UK, Sweden	116	EQ-5D	**Mean (SD):** 0.56 (0.27) **Median, (95% CI):** 0.66, 0.46–0.67	NR	**Mean (SD), Median, (95% CI)** 1L chemotherapy, pre-progression: 0.72 (0.31), 0.76, (0.56, 0.88) 2L chemotherapy, pre-progression: 0.64 (0.33), 0.73, (0.49, 0.78) 3L+ chemotherapy, pre-progression: 0.77 (0.14), 0.75, (0.68, 0.86)

CI, confidence interval; EQ-5D, EuroQol five-dimensional; 1L, first line, 2L, second line; 3L, third line; NR, not reported; SD, standard deviation.

Table 2. Health Technology Assessment studies in STS[4–13]

Country/HTA Body	Appraisal ID	Year	Therapy	Recommended for reimbursement
Australia/PBAC	NA	2012	Pazopanib	No (high ICER)
	NA	2013 (resubmission)	Pazopanib	Yes (based on high unmet need)
	NA	2016	Eribulin	Yes (risk sharing agreement)
	NA	2021	Trabectedin	Yes (pricing arrangement)
Canada/CADTH	PC0111-000	2016	Trabectedin	No (no clinical benefit, high ICER)
	PC0111-000	2018	Olaratumab	Yes (time-limited pending phase 3 study)†
UK/NICE	TA185	2010	Trabectedin	Yes (patient access scheme)
Scotland/SMC	SMC820/12	2012	Pazopanib	No (uncertainty, high ICER)
	SMC2210	2019	Trabectedin	No (uncertain clinical and economic benefit)
	SMC2283	2020 (resubmission)	Trabectedin	Yes (high ICER, orphan medicine)

†Reimbursement was contingent on more robust clinical data, Jan 30, 2019, phase 3 study did not confirm the clinical benefit and recall alert was issued by Health Canada.
CADTH, Canadian Agency for Drugs and Technologies in Health; ICER, incremental cost-effectiveness ratio; NA, not available; NICE, National Institute for Health and Care Excellence; PBAC, Pharmaceutical Benefits Advisory Committee; SMC, Scottish Medicines Consortium; STS, soft tissue sarcoma.

Results (continued)

Table 3. Cost and resource use evidence in STS

Author, Year	Study design	Country/region	Patient accrual dates	Cost/resource use outcomes reported
Nadler, 2020[14]	Retrospective observational cohort study	USA	July 2015 to August 2018 n=376	• HCRU during the study period[a] • 1L and 2L treatment regimens distribution for overall population, for those who started 1L pre-October 2016 and 1L post-October 2016 • 1L and 2L treatment regimens in the pre- and post-October 2016 periods received by at least five patients
Duh, 2013[15]	Retrospective, longitudinal study	USA	January 2005 to April 2012 n=1228	• Costs of IV therapy for metastatic soft tissue sarcoma • Subcategories of cost include IV administration • Other visit-related services
Jönsson, 2016[16]	Multi-country, multi-centre retrospective chart review and cross-sectional patient survey	Canada, France, Germany, Italy, the Netherlands, Spain, Sweden, UK and USA	January 2004 to December 2009 n=213	• Expected mean per-patient lifetime resource use (only sarcoma related resource use) • Expected lifetime cost per mSTS patients, by each health state and all health states, for total population • Expected lifetime cost per mSTS patients, by type of resource for each health state • Expected lifetime chemotherapy cost per patient, total population for each IV chemotherapy and oral chemotherapy • Expected lifetime cost of care for mSTS patients by resource type across countries
Mytelka, 2018[17]	Retrospective review of medical records	UK, Germany, Spain and France	UK: August 2015 to October 2015 Germany: August 2015 to November 2015 Spain: August 2015 to January 2016 France: February 2016 to May 2016 n=807	• Outpatient consult/office visits (UK, Spain, Germany and France) • Outpatient hospital visits (Spain, Germany and France) • Palliative care & outpatient nurse visits (UK) • Accident and emergency or ED visits inpatient hospitalisations, and transfers to long-term or hospice care • Patients' use of specific categories of supportive/palliative medications was collected • Estimated health care costs related to treatment of advanced STS per country and per treatment line • Other direct health care costs[b]
Guest, 2013[1]	Survey of clinicians[c]	Italy, Spain and Sweden	NR Six clinicians	• HCRU associated with diagnosis • Treatment assumptions including, probability of receiving 2L therapy • HCRU associated with the evaluation of response to chemotherapy • Use of pre-and post-chemotherapy tests to assess haematological and renal function • Clinician visits & follow-up test and procedures • Pre- and post-chemotherapy medication use • Costs associated with managing haematological toxicities • Palliative care costs
Judson, 2007[18]	Retrospective chart review	UK	NR n=47	• Mean cost per patient for disease management and costs associated with key drivers of overall cost • Estimates the annual cost of mSTS from the perspective of the UK NHS
Sharma, 2021[19]	Retrospective cohort study	India	January 2013 to December 2019	• Average cost of pazopanib and oral metronomic regimen acquisition per patient per month assuming equivalent outcomes for both treatments (PFS and OS). No further outcomes reported
Rajan, 2019[20]	Retrospective database analysis	Taiwan	2007 to 2014 n=3529	• Hospitalisation length of stay • Emergency room visits • Outpatient visits

[a]Hospitalisation, ED visits, surgeries, outpatient visits, laboratory procedures, receiving growth factors (G-CSF and ESA) and receiving dexrazoxane.
[b]Costs calculated as the sum of all costs associated with outpatient and ED visits, inpatient stays not adverse event-related, selected supportive care services, and inpatient long-term care and hospice care.
[c]This article is an economic evaluation; no HCRU data in Italy, Spain and Sweden was identified so primary data collection was performed to derive model inputs.
ED, emergency department; ESA, erythropoiesis-stimulating agent; G-CSF, granulocyte colony stimulating factor; HCRU, health care resource utilisation; IV, intravenous; mSTS, metastatic soft tissue sarcoma; PFS, progression-free survival; NHS, national health service; NR, not reported; OS, overall survival.

Conclusions

- Published literature has established that STS has a detrimental impact of patients' quality of life, particularly in patients with progressive disease. The economic burden of STS has also been characterized in the literature.[1–3] However, there is a dearth of evidence on HCRU, cost and utility evidence for histology subtypes, specifically patients with SS/MRCLS
- HTA reviews have also noted these evidence gaps in their reviews for treatments in STS populations (that include mSS/mMRCLS), which has led to pricing arrangements when recommended for reimbursement[4–13]
- Further research is required to elucidate the effect of mSS/mMRCLS on patient utilities and economic burden

Disclosures

MP is an employee of GSK. **YS** is an employee and shareholder of GSK. **SD**, **EZ** and **DT** are employed by Evidera, which provides consulting and other research services to pharmaceutical, medical device and other related organizations. In their salaried positions, they work with a variety of companies and organizations, and are precluded from receiving payment or honoraria directly from these organizations for services rendered. Evidera received funding from GSK to participate in the study.

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