Systemic Anti-Cancer Therapy in Synovial Sarcoma: A Systematic Review

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Table S1. Search Strategies implemented in each database. Note that the search was originally designed to also include myxoid and round cell liposarcoma.

| #   | Search terms                                                                 | Results returned |
|-----|-----------------------------------------------------------------------------|------------------|
| 1   | Sarcoma, Synovial/                                                          | 2958             |
| 2   | ((synovi* or tendosynovial) adj2 (sarcoma or malignant)).tw.                | 3175             |
| 3   | (synoviasarcoma or synoviosarcoma or synovioma).tw.                        | 211              |
| 4   | Liposarcoma/                                                               | 3965             |
| 5   | (myxosarcoma or myxoid liposarcoma or round cell liposarcoma or MRCLS).tw. | 966              |
| 6   | mixed type liposarcoma.tw.                                                 | 28               |
| 7   | or/1-6                                                                     | 8587             |
| 8   | Case study/ or case reports/                                               | 1,878,316        |
| 9   | (case adj2 (stud * or report *)).tw.                                       | 588,258          |
| 10  | 8 or 9                                                                     | 2,141,590        |
| 11  | 7 not 10                                                                   | 4602             |
| 12  | limit 11 to yr="2000-current" [April 19 2017] *                            | 2353             |

Database searched: Embase 1974 to 2017 [Searched 19th April 2017; updated 30th January 2018]

| #   | Search terms                                                                 | Results returned |
|-----|-----------------------------------------------------------------------------|------------------|
| 1   | exp * synovial sarcoma/                                                     | 2325             |
| 2   | ((synovi* or tendosynovial) adj2 (sarcoma or malignant)).tw.                | 3953             |
| 3   | (synoviasarcoma or synoviosarcoma or synovioma).tw.                        | 193              |
| 4   | exp * Liposarcoma/                                                         | 3934             |
| 5   | (myxosarcoma or myxoid liposarcoma or round cell liposarcoma or MRCLS).tw. | 1177             |
| 6   | mixed type liposarcoma.tw.                                                 | 36               |
| 7   | or/1-6                                                                     | 8957             |
| 8   | Case study/ or case reports/                                               | 2,307,885        |
| 9   | (case adj2 (stud * or report *)).tw.                                       | 750,563          |
| 10  | 8 or 9                                                                     | 2,526,844        |
| 11  | 7 not 10                                                                   | 4737             |
| 12  | limit 11 to yr="2000 -Current" [April 19 2017] *                          | 3116             |
| 13  | conference.so.                                                            | 2,542,009        |
| 14  | 12 not 13                                                                  | 2225             |

Database searched: EBM Reviews - Cochrane Central Register of Controlled Trials [Searched 19th April 2017; updated 30th January 2018]

| #   | Search terms                                                                 | Results returned |
|-----|-----------------------------------------------------------------------------|------------------|
| 1   | sarcoma, synovial/                                                         | 0                |
| 2   | ((synovi* or tendosynovial) adj2 (sarcoma or malignant)).tw.                | 22               |
| 3   | (synoviasarcoma or synoviosarcoma or synovioma).tw.                        | 0                |
Liposarcoma/ (myxosarcoma or myxoid liposarcoma or round cell liposarcoma or MRCLS).tw.
mixed type liposarcoma.tw.

or/1-6 [April 19 2017] *

* Searches were updated on 30th January 2018; the following numbers of additional references were identified from all databases combined (From 1st January 2017-30th January 2018): 408 abstracts.

Table S2. Reported objectives of studies included in review.

| Author, Publication Year | Objectives |
|--------------------------|------------|
| **Localized**            |            |
| De Silva, 2004 [1]       | To study the association of clinicopathologic variables with recurrence, metastases, and tumor-related death in patients with synovial sarcoma who did not have metastases at presentation. |
| Scheer, 2016 [2]         | Assess the outcomes, identify prognostic factors, and to analyse treatment strategies in synovial sarcoma patients with metastases at diagnosis. |
| Krieg, 2011 [3]          | To investigate the extent to which individual clinical tumor-specific factors as well as surgical approach affect the outcome of patients with synovial sarcoma with at least 10-year follow-up. |
| Beaino, 2016 [4]         | To determine the local recurrence-free survival and distant recurrence-free survival in patients with T1 (<5 cm) localized synovial sarcoma; To identify what determines local recurrence and metastasis; To assess if radiation and chemotherapy affect local recurrence and metastasis in early stage disease. |
| Orbach, 2011 [5]         | To determine if the modified indications for radiotherapy or radical surgery, according to the quality of initial resection and response to initial chemotherapy, had an impact on survival. |
| Shi, 2013 [6]            | To review the outcomes of a cohort of synovial sarcoma patients at single institution, identify prognostic factors impacting both local and distant disease control, and document acute and late toxicity related to treatment. |
| Eilber, 2007 [7]         | To determine if ifosfamide-based chemotherapy offers a survival benefit to adult patients with primary extremity synovial sarcoma. |
| Al-Hussaini, 2011 [8]    | To investigate the impact of chemotherapy on survival in both paediatric and adult patients with localized synovial sarcoma treated at two specialized sarcoma centres. |
| Trassard, 2001 [9]       | To identify most significant and therapeutically relevant prognostic factors in adults with localized primary synovial sarcomas and to confirm the usefulness of the French Federation of Cancer Centers (FNCLCC) grading system. |
| Ferrari, 2015 [10]      | To assess survival rates and treatment failure patterns; the role of ifosfamide–doxorubicin chemotherapy in improving response rates in patients with unresectable synovial sarcoma; and to determine the impact of omitting adjuvant chemotherapy in patients with low-risk synovial sarcoma. |
| Brecht, 2006 [11]       | To identify risk and treatment factors which influence survival rates in patients with synovial sarcoma. |
| Italiano, 2009 [12]     | To clarify the prognosis factors and the impact of neo-adjuvant/adjuvant chemotherapy for adult patients with localized synovial sarcoma. |
| Canter, 2008 [13]       | To analyse the clinicopathologic predictors of distant recurrence and sarcoma-specific death. |
| Vlenterie, 2015 [14]    | To explore age as a prognostic factor in synovial sarcoma patients. |
| Vining, 2017 [15]       | To study the effect of adjuvant chemotherapy on OS among a large cohort of patients undergoing curative-intent resection of synovial sarcoma. |
| Gronchi, 2017 [16]      | Show the superiority of the neoadjuvant administration of histotype-tailored regimen to standard chemotherapy. |

**Locally advanced or metastatic**
| Author(s) | Year | Reference Details | Summary |
|----------|------|-------------------|---------|
| Takenaka, 2008 | [17] | To clarify the prognostic impact of SYT-SSX fusion type, in association with other clinical factors, in patients with synovial sarcoma in Japan. | |
| Setsu, 2013 | [18] | To investigate the phosphorylation status of Akt (protein kinase B), mTOR, 4E-BP1, and S6 in a large series of synovial sarcoma and evaluated the relation between Akt/mTOR pathway activation and clinical and histopathologic features. | |
| Deshmukh, 2004 | [19] | To determine whether distal or truncal location of synovial sarcoma is of prognostic significance for survival when corrected for tumor size. | |
| Guillou, 2004 | [20] | To assess the prognostic value of SYT-SSX fusion type, in comparison with other factors, in patients with synovial sarcoma. | |
| Palerini, 2009 | [21] | To retrospectively examine all synovial sarcoma patients treated at our institution to identify tumor-related and treatment-related factors influencing survival. | |
| Ferrari, 2004 | [22] | To retrospectively analyse a large series of synovial sarcoma patients of all ages who were treated at a single centre. | |
| Vlenterie, 2016 | [23] | Compared the demographics and outcome of a large subset of advanced synovial sarcoma patients treated in first-line palliative chemotherapy studies between 1976 and 2012 and compared these results with other advanced STS patients treated in these studies. | |
| Brennan, 2016 | [24] | To assess the role of age, socioeconomic status and other prognostic factors on outcome for synovial sarcoma. | |
| Corey, 2014 | [25] | To determine demographic and survivorship of 34 soft tissue sarcomas. | |
| Spurrell, 2005 | [26] | To look specifically at a cohort of patients with advanced synovial sarcoma and to identify potential prognostic factors. | |

### Metastatic disease

| Author(s) | Year | Reference Details | Summary |
|----------|------|-------------------|---------|
| Sanfilippo, 2015 | [27] | To review all patients with advanced synovial sarcoma treated with trabectedin at four European sarcoma reference centers and within the Italian Rare Cancer Network. | |
| Savina, 2017 | [28] | To utilized a unique set of data to assess the modalities of treatment of patients with metastatic STS in a real-life setting, to evaluate their impact on the outcome according to the histological subtype. | |

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