Metastatic Pattern of Truncal and Extremity Leiomyosarcoma: Retrospective Analysis of Predictors, Outcomes, and Detection

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Research

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Abstract

Background

Leiomyosarcomas (LMS) are a heterogenous group of malignant mesenchymal neoplasms with smooth muscle origin and are classified as either non-uterine (NULMS) or uterine (ULMS). Metastatic pattern, prognostic factors, and ideal staging/surveillance studies for truncal and extremity LMS have not been defined.

Methods

A retrospective analysis of patients diagnosed with histopathology-confirmed truncal or extremity LMS between 2009-2019 was conducted. Data collected included demographics, tumor characteristics, staging, surveillance, and survival endpoints. Primary site was defined as either 1. Extremity, 2. Flank/Pelvis, or 3. Chest wall/Spine.

Results

We identified 73 patients, 23.3% of which had metastatic LMS at primary diagnosis, while 68.5% developed metastatic disease at any point. The mean metastatic-free survival from primary diagnosis of localized LMS was 3.0±2.8 years. Analysis of prognostic factors revealed that greater age (≥50 years) at initial diagnosis (OR=3.74, p=0.0003) and higher tumor grades II (OR=16, p=0.019) and III (OR=13, p=0.025) were significantly associated with metastases.

Conclusions

Truncal and peripheral extremity LMS is an aggressive tumor with high metastatic potential. While there is a significant risk of metastases to lungs, extra-pulmonary tumors are relatively frequent. Older patients and patients with higher-grade (II/III) tumors carry an increased risk of developing metastatic disease.

Introduction

Leiomyosarcomas (LMS) are a heterogenous group of malignant mesenchymal neoplasms with smooth muscle origin typically divided into non-uterine (NULMS) and uterine (ULMS) classifications. LMS is one of the most common subtypes of soft-tissue sarcomas (STS) with an incidence of 1.2 cases per 100,000 person-years and represents between 10–20% of all newly diagnosed STS [1]. In general, the overall prognosis for leiomyosarcomas is poor with a reported 5-year survival rate of 35% across all grades [2]. Incidence of LMS increases with age and shows worse prognosis in patients over 50 years old [3, 4]. Specifically, LMS can arise in any smooth muscle location, with common sites including the retroperitoneum (20–67% of cases), and peripheral soft tissues (12–41%) including the extremities, skin, and head/neck [2]. To date, there are a small number of studies describing the metastatic rate and pattern for ULMS [4–7], however the metastatic characteristics for truncal and extremity LMS are not well defined.
Management of LMS includes staging studies to assess metastasis and prognosis at the time of initial diagnosis. Treatment is centered around surgical resection with or without radiation therapy for localized disease and chemotherapy is utilized in select circumstances or in established metastatic disease. Patients with no evidence of disease after initial treatment are followed with surveillance imaging given the high risk of developing metastatic disease (40–80%) [2, 4, 8, 9]. Early detection of metastatic disease has several potential advantages including initiation of palliative therapy, avoiding progression of occult metastasis to the point of severe pain or other morbidity, patient counseling, and comfort planning. Patients with known metastatic disease are followed with periodic scans to assess response to treatment and tumor stability. While the role of imaging of LMS is pivotal, there is a paucity of evidence-based recommendations on best practices for staging and surveillance imaging of truncal and extremity LMS.

We therefore sought to answer three questions: (1) What is the anatomical distribution and frequency of metastatic disease in truncal/extremity LMS? (2) Are factors such as age at primary diagnosis, tumor grade, tumor size, and primary tumor location associated with metastatic risk or overall survival after primary diagnosis of truncal/extremity LMS? (3) Is imaging modality associated with a greater frequency of metastatic disease detection?

**Patients And Methods**

In this institutional review board-approved retrospective study, the electronic medical records of patients diagnosed with histopathology-confirmed truncal or extremity LMS at our cancer center between 2009–2019 were reviewed. Exclusion criteria included uterine, retroperitoneal, head and neck, cutaneous tumor origin, and patients with incomplete records or surveillance/follow-up.

**Patient demographics, presentation, and treatment**

A total of 73 patients met inclusion criteria for truncal or extremity LMS, 30 (41.0%) of which were female (Table 1). Four patients were lost to follow-up and at a mean follow-up period of 40.4 months (range, 4.1–126.4 months), 53 patients were alive. The mean age at initial diagnosis was 58.2 ± 14.3 years (range, 17–87 years), with 55 (75.3%) patients ≥ 50 years of age. The mean primary tumor size was 8.4 cm (range, 1.0–23.0 cm) measured as the longest dimension, with 19 (26.0%) tumors ≥ 10 cm in size. The most common primary tumor site was peripheral extremity (50 patients, 68.0%), followed by flank/pelvis (13 patients, 18.0%), and chest wall/spine (10 patients, 14%). There were 7 (10.0%) patients with FNCLCC tumor grade I, 24 (34.0%) patients with tumor grade II, and 39 (56.0%) patients with tumor grade III.
### Table 1
Patient Demographics and Tumor Characteristics

| Variable                        | n, mean | %, range |
|---------------------------------|---------|----------|
| **Gender**                      |         |          |
| Female                          | 30      | 41.0%    |
| Male                            | 43      | 59.0%    |
| **Mean Age (Years)**            | 58.2    | 17.0–87.0|
| ≥ 50 years                      | 55      | 75.3%    |
| < 50 years                      | 18      | 24.7%    |
| **Tumor Size (cm)**             | 8.4     | 1.0–23.0 |
| ≥ 10 cm                         | 19      | 26.0%    |
| < 10 cm                         | 54      | 74.0%    |
| **Primary Tumor Site**          |         |          |
| Extremity                       | 50      | 68.0%    |
| Flank/Pelvis                    | 13      | 18.0%    |
| Chest Wall/Spine                | 10      | 14.0%    |
| **Histological Grade**          |         |          |
| I                               | 7       | 10.0%    |
| II                              | 24      | 34.0%    |
| III                             | 39      | 56.0%    |
| **Presentation Status**         |         |          |
| Primary Disease                 | 56      | 76.7%    |
| Metastatic Disease              | 17      | 23.3%    |
| **Development of Metastatic Disease by Histological Grade** | | |
| I                               | 1       | 14.3%    |
| II                              | 17      | 70.8%    |
| III                             | 32      | 82.1%    |
| **Time to Metastatic Disease from Diagnosis (Years)** | 3.0 | 0.5–11.0 |
| **Metastasis Locations**        |         |          |
| Any Location                    | 50      | 68.5%    |
| Variable                              | n  | mean  | %, range |
|---------------------------------------|----|-------|----------|
| Lung                                  | 42 |       | 84.0%    |
| Abdomen/Thorax/Visceral Organ         | 26 |       | 52.0%    |
| Bone                                  | 17 |       | 34.0%    |
| Skin/Soft Tissue                      | 14 |       | 28.0%    |
| Lymph Node                            |  3 |       |  6.0%    |
| Brain                                 |  2 |       |  4.0%    |
| Vessel                                |  1 |       |  2.0%    |
| Local Recurrence                      |    |       |          |
| Yes                                   | 24 |       | 36.4%    |
| No                                    | 42 |       | 63.6%    |
| Mean Survival After Primary Diagnosis, All Grades (Years) | 4.7 |       | 1–14     |

**Variables, outcome measures, data sources, and bias**

Clinicopathologic data included age at first diagnosis, sex, primary tumor site, tumor size, tumor grade (Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) system), presence of metastatic disease at diagnosis, number of metastatic sites at first presentation, initial staging imaging modality, treatment type, presence of local recurrence, time to metastasis, survival after primary diagnosis, and surveillance/treatment response imaging modalities. Primary site was defined as either 1. Peripheral extremity, 2. Flank/pelvis, or 3. Chest wall/spine. Recurrent or metastatic disease was confirmed either by biopsy or by the presence of progression on serial surveillance imaging.

**Statistical Analysis**

Patient demographics are presented as means and range for continuous variables and by frequency and percentage for categorical variables. Metastatic-free survival and overall survival were calculated as the interval from the date of primary diagnosis to detection of metastatic disease, or date of death, respectively. The prognostication of age, tumor grade, tumor size, and surveillance frequency on survival was evaluated. The Kaplan-Meier method, log-rank test, multivariable Cox proportional hazards regression models, and Chi-Square tests were used for estimation, testing, and multivariable modeling of overall survival. Analyses were considered significant with a $p$ value < 0.05. All analyses were done using RStudio version 1.1.456 (Boston. MA).

**Results**
Anatomical distribution and frequency of metastatic disease in truncal/extremity LMS

At the time of primary diagnosis, 17 (23.3%) patients had metastatic disease. Of the 56 patients that did not have metastatic disease at the time of primary diagnosis, 33 (58.9%) subsequently developed metastases. A total of 50 (68.5%) patients had metastatic disease develop at any point in the mean follow-up period of 40.4 months (range, 4.1-126.4 months) (Table 1). In patients with primary tumors classified as grade I, II, or III, there was metastatic progression in 1 (14.3%), 17 (70.8%), and 32 (82.1%) patients, respectively. The mean tumor size was 8.35 cm (Range, 1–23). The mean metastatic-free survival from primary diagnosis of localized LMS of any grade was 3.0 ± 2.8 years (range, 0.5–11). The mean metastatic-free survival from primary diagnosis for patients with grade III LMS was 1.6 ± 1.7 years (range, 0.5–8). The rate of metastatic disease after primary diagnosis in patients without initial metastases, and not including local recurrence, was 42% at 1 year, 64% at 5 years, 84% at 10 years, and 92% at 11 years. (Fig. 1).

Amongst the 50 patients with metastatic disease, the most common site of metastasis was lung (42 patients, 84.0%), followed by abdomen/thorax/visceral organs (26 patients, 52.0%), bone (17 patients, 34.0%), skin/soft tissue (14 patients, 28.0%), lymph nodes (3 patients, 6.0%), brain (2 patients, 4.0%), and vessels (1 patient, 2.0%) with 30 (41.1%) patients having metastatic disease in 3 or more of these sites (Table 1). Of patients with metastatic disease, the first detected metastatic site was located outside of the lungs in 22 (44.0%) patients. Following surgical resection of primary tumors, local recurrence occurred in 24/66 (36.4%) patients, 12 (50.0%) of which microscopic positive margins.

Prognostic factors associated with metastatic risk or overall survival after primary diagnosis of truncal/extremity LMS

Univariate analysis of metastatic prognosticators revealed that age at initial diagnosis (≥ 50 years), and tumor grade (II/III), were significantly associated with the development of metastatic disease (Table 2). Patients aged 50 and above had a significantly higher rate of metastatic disease compared to patients under the age of 50 (Odds Ratio (OR) = 3.74, p = 0.0003) after adjusting for tumor size and grade, with 42/55 patients ≥ 50 years old developing metastatic disease, compared to 8/18 patients < 50 years old. Tumor grade was significantly associated with the development of metastatic disease: compared with low grade (I) tumors, the OR for the development of metastatic disease amongst grade II and III tumors was 16 (p = 0.019) and 13 (p = 0.025), respectively, after controlling for tumor size. Additionally, grade III, but not grade II tumors showed a significant predilection for metastasis to the lungs, with an odds ratio of 9.74 (p = 0.046). Tumor size (p = 0.515), or primary tumor location (p = 0.355) was not associated with metastatic disease.
The mean overall survival after primary diagnosis was 4.7 ± 3.3 years (range, 1–14 years) (Table 1), with a survival rate after primary diagnosis of 59% at 5 years, 34% at 10 years, and 19% at 13 years (Fig. 2). After detection of metastatic disease, the survival rate was 60% at 1 year, 45% at 2 years, 36% at 3 years, 5% at 4 years (Fig. 3). High-grade tumors (II/III) showed significantly worse survival with hazard ratios (HR) of 7.66 (p = 0.048) and 8.57 (p = 0.036), respectively (Table 3). Additionally, older patients (≥ 50 years) showed worse survival, with a HR = 4.76 (p = 0.017) and patients with larger tumors (≥ 10 cm) showed worse survival, with a HR = 1.92 (p = 0.029). Primary tumor site was not associated with overall survival. Primary tumor location, either flank/pelvis or chest wall/spine, does not influence overall survival (HR = 1.37, p = 0.412, HR = 1.73, p = 0.174, respectively).

### Table 2
**Multivariate Analysis of Prognostic Factors for Metastatic Disease**

| Location         | Factor  | OR   | Lower 95% | Upper 95% | p-value |
|------------------|---------|------|-----------|-----------|---------|
| Any Metastasis   | Age ≥ 50 years | 4.0  | 1.32      | 12.36     | 0.015*  |
| Grade II         | 16.0    | 2.13 | 337.57    |           | 0.019*  |
| Grade III        | 13.0    | 1.89 | 262.64    |           | 0.025*  |
| Tumor Size       | 1.04    | 0.93 | 1.17      |           | 0.515   |
| Lung Metastasis  | Grade II | 7.1  | 0.97      | 145.60    | 0.093   |
| Grade III        | 9.7     | 1.43 | 195.57    |           | 0.046*  |

### Table 3
**Multivariate Analysis of Prognostic Factors for Overall Survival**

| Variable         | Level            | Hazard Ratio | Lower 95% | Upper 95% | p-value |
|------------------|------------------|--------------|-----------|-----------|---------|
| Primary Site     | Flank/Pelvis     | 1.37         | 0.65      | 2.90      | 0.412   |
|                  | Chest Wall/Spine | 1.73         | 0.78      | 3.82      | 0.174   |
| Grade            | II               | 7.66         | 1.02      | 57.75     | 0.048*  |
|                  | III              | 8.57         | 1.15      | 63.75     | 0.036*  |
| Age              | ≥50              | 4.76         | 0.06      | 0.75      | 0.017*  |
| Surveillance     | (≤ 4 mo)         | 2.7          | 0.17      | 0.79      | 0.010*  |

**Impact of imaging modality on frequency of metastatic disease detection?**

A total of 84 imaging studies were performed across 73 patients for initial staging. These included CT scans (n = 47, 56.0%), PET/CT (n = 25, 30.0%), Nuclear bone scan (n = 7, 8.3%) and chest x-ray alone (n = 5, 6.0%) (Table 4). Comparing the rate of primary tumor detection and metastatic disease at baseline based on the imaging modality used at initial staging, PET/CT imaging was found to be associated with
a significantly greater rate of tumor detection, identifying 20 instances of metastatic disease when compared to CT CAP imaging, which identified 14 instances (Chi-square = 16.5, p < 0.0001) (Table 5).

| Variable                        | n  | %   |
|---------------------------------|----|-----|
| **Initial Staging Studies**     |    |     |
| CT Chest/Abdomen/Pelvis        | 47 | 56.0% |
| PET/CT                          | 25 | 30.0% |
| Nuclear Bone Scan               | 7  | 8.3% |
| Chest X-Ray                     | 5  | 6.0% |
| **Radiological Surveillance Studies** |    |     |
| CT chest/abdomen/pelvis        | 343| 51.6% |
| PET/CT                          | 166| 25.0% |
| Chest X-Ray                     | 134| 20.2% |
| Nuclear Bone Scan               | 22 | 3.2% |

| Variable                        | n  |     |
|---------------------------------|----|-----|
| **Mean Annual Surveillance Frequency (Months)** | 5.0 | 1.0–13.0 |
| **Mean Number of Lifetime Surveillance Scans** | 11.0 | 1.0–51.0 |

During the follow-up period, there were a total of 665 follow-up visits for surveillance/treatment response imaging (Table 4). Imaging studies included CT CAP (n = 343, 68%), PET/CT (n = 166, 19%), and chest x-rays (n = 134, 15.4%), and nuclear bone scan (n = 22, 3.2%). On average, patients underwent surveillance
imaging every 2.4 months, for an average of 5 visits per year (range, 1–13 visits/year), with an average lifetime total of 11 studies performed (range, 1–51 studies).

We compared the rate of detection of tumor metastases during this period, based on surveillance imaging modality utilized (CT CAP vs PET/CT). PET/CT imaging detected new tumor metastases significantly more often, when compared to CT CAP (Chi-square = 11.32, p < 0.001) (Table 5). An analysis of site-specific detection reveals that PET/CT was associated with significantly more frequent metastatic tumor detection in the abdomen/visceral organs (Chi-square = 8.18, p = 0.004), and skin/soft tissue (Chi-square = 9.97, p = 0.0016) than CT CAP.

Comparing the effects of surveillance frequency on survival, patients that underwent surveillance more frequently than every 4 months showed a worse mean overall survival of 4.1 years compared to patients that underwent surveillance less frequently (> 4 months apart on average) (5.89 years, p = 0.0245). Patients that underwent more frequent surveillance (≤ 4 months apart) had worse survival, with a HR = 2.7, relative to patients that underwent less frequent surveillance (p = 0.010) after adjusting for grade (Fig. 4).

Discussion

Despite the relatively poor prognosis of LMS, one of the more common soft-tissue sarcoma subtypes, there is a paucity of data describing the metastatic pattern, prognostic factors, and efficacy of specific staging or surveillance imaging modalities [10–13]. We therefore sought to answer three questions: (1) What is the anatomical distribution and frequency of metastatic disease in truncal/extremity LMS? (2) Are factors such as age at primary diagnosis, tumor grade, tumor size, and primary tumor location associated with metastatic risk or overall survival after primary diagnosis of truncal/extremity LMS? (3) Is imaging modality associated with a greater frequency of metastatic disease detection? Here, we show that truncal/extremity LMS has a high rate of metastasis, with significantly higher rates in older patients and those with higher grade tumors at initial diagnosis. We show that truncal/extremity LMS has a high rate of metastases to extra-pulmonary sites, and the use of PET/CT imaging, both at initial staging and throughout surveillance, was associated with a greater rate of metastatic tumor detection.

This study has several limitations, including its retrospective nature and non-randomized design. As a retrospective study, we were reliant on the accuracy of patient records. Further, as we collected data from our single cancer institution, bias in patient referral should be considered. As a retrospective, non-randomized investigation, this study was not designed to parse out the utility of each imaging modality for surveillance or progression of disease/response to treatment. The use of imaging modalities is often influenced factors such as patient insurance. Also, this study was not designed to evaluate how the type and frequency of imaging studies impact clinical outcomes such as survival and quality of life.

In this retrospective analysis, we identified 73 patients with truncal or extremity LMS. Consistent with the findings of others, the lung was the most common metastatic site [6, 7], with a relatively high rate of metastatic disease arising in the abdomen, thorax, visceral organs, bone, and skin or soft tissues. We
show that grade III tumors are significantly more likely to metastasize to the lungs compared to low-grade tumors, with an odds ratio of 9.74 ($p = 0.046$). The 5-year overall survival rate in this cohort was 59%, while Shoushtari et al. reported a 5-year survival rate of under 25% in an analysis of only metastatic LMS', and Lamm et al. reported a 5-year survival rate of 44.4% [6, 7]. The lower 5-year survival rates previously reported likely represent the difference in proportions of high vs low-grade LMS. The largest study focusing on LMS to date, conducted by Shoushtari and colleagues in 2016, provides a description of the overall survival and response to systemic therapy in extrauterine metastatic LMS [6] but lacks a precise description of metastatic pattern. Further, in 2014, Lamm et al. compared uterine to non-uterine LMS, showing that lungs are the most common metastatic site in both uterine and non-uterine LMS, with initial metastatic disease serving as a prognostic factor for overall survival [7]. More recently, Lee et al. compared the response to radiation treatment of truncal/extremity LMS versus non-LMS soft-tissue sarcomas. Lee and colleagues describe and similar average age and tumor size of 63 years and 6.0 cm, respectively [11]. Similarly, Gladdy et al. describe a median age of 57 years, and average tumor size of 6.0 cm and identified high grade tumors as predictive of disease-specific survival [10].

In this study, 10.0% of patients were classified as grade I, compared to 3% and 2% in the studies by Shoushtari et al. and Lamm et al [6, 7]. In our analysis of metastatic prognosticators, we identified high-grade tumors (II/III) and patients over the age of 50 showed significantly greater rates of metastasis, consistent with current reports of ULMS and NULMS [4–7]. We also show that tumor size is not associated with metastatic risk ($OR = 1.04$, $p = 0.515$), and primary tumor location, either flank/pelvis or chest wall/spine, does not influence overall survival ($HR = 1.37$, $p = 0.412$, $HR = 1.73$, $p = 0.174$, respectively).

Effective detection, diagnosis, and surveillance are vital in the treatment and management of LMS. Analyses of efficacy of radiological staging and surveillance modalities for LMS are also sorely needed. Here, we found a significantly worse overall survival in patients that underwent more frequent radiological surveillance. We believe this represents positive clinical decision-making, in that patients that were deemed to have more aggressive tumors at diagnosis subsequently underwent more frequent surveillance. While Chest CT with or without contrast remains the benchmark for assessing lung metastases, there is conflicting evidence for obtaining an abdomen/pelvis CT for staging [9]. Reports of incidence rates of metastatic disease in the abdomen or pelvis vary – one report from a single institution suggests a 16.0% incidence rate [14], supporting routine abdomen/pelvis CT, while another retrospective review reported only a 2.9% incidence rate; this would argue against routine use of abdomen/pelvis CT for staging and monitoring in the setting of soft-tissue sarcoma of the extremity [15]. There is also a growing role for PET/CT for staging, surveillance, and gauging treatment response of soft-tissue sarcomas [16–18]. In two studies of LMS, tumor $^{18}$F-FDG uptake, as measured by the maximum standardized uptake value ($SUV_{max}$) was a powerful prognostic factor for overall survival correlating with tumor grade and size [17, 19]. In this study, we show that the risk of metastatic disease to any extra-pulmonary area after primary LMS diagnosis occurred in 36/73 patients (49.3%). Of those 50 patients that developed metastatic disease, 35 (72.0%) developed metastatic sites outside of the lungs,
supporting the use of imaging that extends beyond routine chest CT. Despite the potential strength of PET/CT imaging, there have been relatively few reported series, with low case numbers to justify the routine application of PET/CT imaging of LMS. In this study, we provide the largest comparison known to date of metastatic tumor detection between PET/CT imaging and CT CAP in a cohort of patients with truncal/extremity LMS.

In comparing the rate of tumor detection between the two most common and comparable imaging modalities, CT CAP and PET/CT, we found that PET/CT imaging detected significantly more tumors both at initial staging (Chi-square = 4.7, p = 0.03), and throughout surveillance/treatment response (Chi-square = 11.32, p < 0.001). In this study, we show that metastases to extra-pulmonary sites are relatively frequent, suggesting a particular important utility for PET/CT imaging in detecting metastatic disease at sites that are not readily detected on conventional CT imaging. In particular, PET/CT imaging had a greater rate of detecting tumors in the abdomen/visceral organs, and skin/soft tissue – areas that might be missed using CT Chest/Abdomen/Pelvis imaging. However, caution is warranted as Hensley et al. have suggested that PET has not been shown to be superior for staging of uterine and ovarian LMS, and may miss small volume lung metastatic tumors, often necessitating chest CT imaging in conjunction with whole body PET/CT imaging [20]. Moreover, our study was not designed to parse out the utility of each imaging modality for surveillance or progression of disease/response to treatment. The use of PET/CT versus CT CAP was not always dictated by care algorithms. Further investigations are needed to elucidate the clinical benefit of specific staging and surveillance techniques and timing.

Conclusions

Truncal and peripheral extremity LMS is an aggressive tumor with high metastatic potential. Notably, over 30% of all primary metastatic sites were not in the lungs, suggesting thorough staging and surveillance imaging beyond the lungs is warranted. Grade II and III tumors carry a high-risk of developing metastatic disease. Five and 10-year overall survival rates across all grades are low, with older patients and higher grades having worse survival. Historically, CT scans have been primarily used for initial staging and disease surveillance/treatment response, however in our study PET/CT scans were found to detect overall metastatic sites more frequently and were not inferior to CT CAP in detecting lung metastases in our series. This suggests that PET/CT may be preferred over conventional CT for staging and surveillance of LMS. Further investigation into the optimal imaging techniques for LMS staging and surveillance are needed.

Declarations

Ethics approval and consent to participate

The present study was approved by the Stanford Institutional Review Board. All patients involved in the present study provided written informed consent.
Consent for publication
Not applicable

Availability of data and materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests
Not applicable

Funding
Not applicable

Authors’ contributions
RSA, RJS, DGM, CF, SST initiated and designed the study, wrote the manuscript, and contributed to scientific discussions. SST, CF, and NS collected and analyzed the data, created figures, and synthesized results.

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Not applicable

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**Figures**

![Time to Metastasis](image)

**Figure 1**

Kaplan-Meier analysis of metastatic-free survival after initial diagnosis of localized LMS.
Figure 2

Kaplan-Meier analysis of overall survival, stratified by tumor grade I, II, or III, after initial diagnosis of localized LMS.
Figure 3

Kaplan-Meier analysis of overall survival after detection of metastatic disease.
Figure 4

Kaplan-Meier analysis of overall survival after primary tumor detection in patients with frequent (≤4 months), or infrequent (>4 months) surveillance.