Patient Population

Inclusion criteria:
• ≥ 18 years old, WHO performance status ≤ 2, adequate lab values, ASA score < 3
• Histologically proven primary high risk leiomyosarcoma (LMS) or liposarcoma (LPS) of retroperitoneal space or infra-peritoneal spaces of pelvis
  ◦ LMS: Grades 2 and 3, of minimum size 5 cm
  ◦ LPS (diagnosed on IHC, MDM2 and CDK4 expression): Grade 3 DDLPS, or confirmed grade 2 DDLPS on biopsy only if 1) FNCLCC score = 5 and clear necrosis on imaging (whether or not present on biopsy), or 2) high risk gene profile as determined by the Complexity Index in Sarcomas
• Unifocal tumor; resectable tumor (details per protocol)
• Radiologically measurable disease (RECIST 1.1), as confirmed by imaging within 28 days of randomization

Exclusion criteria:
• Sarcoma originating from bone structure, abdominal or gynecological viscera; metastatic disease
• Extension through the sciatic notch/across the diaphragm
• Tumor grading not assessable from biopsy
• Any previous surgery (excluding diagnostic biopsy), radiotherapy or systemic therapy for the present tumor
• Hypersensitivity to doxorubicin, ifosfamide, dacarbazine, or any of their metabolites/exipients
• Congestive heart failure, angina pectoris, acute inflammatory heart disease, myocardial infarction within 1 year of randomization, uncontrolled arterial hypertension, or uncontrolled cardiac arrhythmia
• Active and uncontrolled infections (especially urinary)
• Inflammation of the urinary bladder (interstitial cystitis) and/or obstructions of the urine flow

Treatment Plan

See Protocol Section 6 for Complete Treatment Details

- Standard arm: large en-bloc curative intent surgery within 4 weeks following randomization (see protocol for details)
- Experimental arm: 3 cycles of neoadjuvant chemotherapy starting within 2 weeks from randomization according to histology (high grade LPS/LMS) followed by reassessment of operability and curative intent surgery within 3-6 weeks after day 1 of last cycle of chemotherapy
  ◦ High grade LPS: Doxorubicin 75 mg/m² (or the equivalent epirubicin 120 mg/m²) + ifosfamide 9 g/m² Q3 weeks
  ◦ LMS: Doxorubicin 75 mg/m² (or the equivalent epirubicin 120 mg/m²) + dacarbazine 1 g/m² Q3 weeks

- Tumor assessments will be performed every 12 weeks until week 48. Then tumor assessments will be performed every 6 months until progression or death
  - CT thorax abdomen pelvis with IV contrast is preferred; use the same modality throughout the study

Note: Some procedures noted in the protocol should only be done as clinically indicated in the US (i.e., LDH [mandatory prior to randomization], CRP, proteinuria, 12-lead ECG, IV pyelogram [done during the baseline CT]/differential renal isotope scan); see US Appendix Section 5

For more guidance on treatment, please see the EA7211 EMR template posted under Protocol Related Documents on the CTSU

Patient Enrollment
All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org/open

Protocol Information

Please Enroll Your Eligible Patients!
Accrual: 250 patients

- Resection specimen + blood samples
  - Large en-bloc
  - Surgery

- Neoadjuvant Chemotherapy
  - 3-6 weeks

- Resection + Debulking
  - LMS: 3 cycles

- Pathologic Response
  - 3 weeks

- PET scan
  - 4 weeks

- Eligibility check
  - Randomization
  - Treatment

- Follow-up

- High Risk Resectable LPS or LMS

Diagnosis biopsy
- Quality of life questionnaire
- Pregnancy test
- ASA score > 3
- Adverse hematologic and organ function
- Predictive chemotherapy
- Physical examination
- Medical history
- Informed consent

IF: 1.1
- Bone function
  - Imaging
  - MRI