What the Milken Institute Guide Changes

Source: ***Uterine Leiomyosarcoma: A Giving Smarter Guide***, Milken Institute Science Philanthropy Accelerator, June 2025. Authors Mawla, Barrett, Altimus. Produced with the Briger Foundation for Oncology Research, drawing on 40 key opinion leaders — scientists, clinicians, biotech.

This is a **philanthropy roadmap**, not a treatment guide. It was written to tell wealthy donors where money moves the needle in uLMS. That makes it unusually useful here for two reasons: it is disease-specific rather than sarcoma-general, and it is candid about what the field cannot yet do.

Two findings are **time-critical and actionable this week**. The rest is context.

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1. THE ONE THAT CANNOT WAIT — tissue preservation

> "Practices like **storing viably frozen tissue, flash-frozen tumor samples, or presurgical blood are not standardized, and clinicians often do not routinely do them, even at top-tier cancer centers.** These early procedural choices, if not proactively considered, can **severely limit future options** for therapeutic decision-making." — p. 27

And, listing what patients typically never learn in time:

> "…practical steps, like **requesting that clinicians preserve live tissue samples** so the patient can choose further biological profiling." — p. 27

Why this is different from the slide request already in motion

They are not the same thing, and this is the part that is easy to miss.

	WHAT IT IS	WHAT IT ENABLES
Paraffin blocks / slides	Tissue fixed in formalin and wax. What every pathology lab keeps by default	Diagnosis, IHC, most sequencing. **Already being requested**
Viably frozen / flash-frozen tissue	Living or snap-frozen tumour cells. Kept only if someone asks, in advance	**Organoids, cell lines, patient-derived xenografts** — growing her actual tumour to test drugs against it

Formalin kills the cells. Once a specimen goes into a standard pathology workflow, the organoid option is gone for that specimen — permanently.

What this means for her, concretely

She has **no viably frozen tissue** from the September 2024 hysterectomy. That was routine benign-fibroid processing; nobody had any reason to preserve live cells.

The next procedure is the opportunity. If there is a metastasectomy, a repeat biopsy, or any further tissue sampling, the request has to be made **before it happens** — and per this guide, it will not happen automatically even at an excellent centre.

Add this to the video follow-up

> **"If there is any further tissue procedure — a repeat biopsy or a lung resection — can we arrange in advance to have a portion sent as viably frozen or flash-frozen tissue rather than all of it going to formalin? And is pre-treatment blood worth banking at the same time?"**

Also worth asking whether the **23 July lung biopsy** left any frozen or unstained material, or whether all of it was fixed.

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2. FREE PROGRAMMES THAT TAKE HER TISSUE AND RUN THE SCIENCE

These are patient-initiated. She does not need a research centre to sponsor her, and there is no cost. Any of them can be started now.

PROGRAMME	WHAT IT DOES
LMSproject — Count Me In, with the Broad Institute	A patient-partnered study **open to LMS specifically**. Patients share samples, clinical information, and their experience. Backed by a $13M Broad-led project building an LMS database
Rare Cancer Research Foundation (RCRF)	Patients donate tissue **directly** to researchers. Has already produced 65+ rare cancer research models
Cancer Cell Line Factory — Broad Institute	Converts a tumour sample into **organoids and cell lines** researchers can use

The through-line: **the family can put her tumour into the research pipeline themselves.** They do not have to wait to be invited, and it does not depend on which hospital treats her.

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3. DR. RIRIE'S PLAN LOOKS BETTER, NOT WORSE

Worth saying plainly, because it is reassuring and it is evidence-based.

The guide tabulates every major chemotherapy trial in LMS. Of the **eight** listed, five first-line trials were **negative**. Exactly one first-line combination came back **positive**:

> **Trabectedin + doxorubicin** (NCT02997358), Phase 3, first line — progression-free survival — **Positive**

That is precisely the combination named in his 29 July plan. The other two positives (trabectedin alone, eribulin) are third-line-plus.

Do not read this as "the plan is settled." Read it as: the plan is the current best-evidence option, so the questions worth asking are about *sequencing and trials*, not about substituting the drug.

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4. IMMUNOTHERAPY — the evidence says do not chase it

> "In two clinical trials, patients with advanced uLMS **didn't benefit much from immune checkpoint inhibitor drugs like nivolumab or pembrolizumab**, even when combined with chemotherapy." — p. 24

Checkpoint inhibitors are the immunotherapy most people have heard of, and a well-meaning relative will suggest them. The guide explains the mechanism: the uLMS tumour microenvironment physically blocks immune cells from reaching the tumour, so a drug that releases the brakes on T cells has nothing to work with.

CAR-T, NK cell therapy, TILs and cancer vaccines have **not been tested in uLMS at all**.

This is worth knowing so the family can decline that conversation with a reason rather than a shrug.

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5. NAMED THINGS TO ASK ABOUT

A short list of specifics the guide surfaces that a general oncology practice may not raise.

NCT04076579	Phase 2, **trabectedin + olaparib** (a PARP inhibitor) in advanced sarcomas including uLMS. Rationale: uLMS tumours often have DNA repair defects, so pairing DNA-damaging chemo with a repair blocker is a real mechanistic bet
NCT06088290	PharmaMar, **Zepzelca (lurbinectedin)**, Phase 2b/3, specifically **metastatic LMS**
NCT06263231	Intensity Therapeutics INT230-6, Phase 3, metastatic soft tissue sarcoma

NCT05712694	Polaris, pegargiminase, Phase 3, soft tissue sarcoma and LMS
LMS SPORE	NIH Specialized Program of Research Excellence in LMS, **led by the University of Michigan** since 2022, multi-institutional and international. If a trial-capable centre matters, Michigan is where the federal money went
MRD / liquid biopsy	Signatera, FoundationOne Tracker, and others. **Not standard in uLMS**, no approved test, and thresholds vary by company. Some firms will run assays on an individual basis for patients who know to ask

On morcellation — the guide confirms the mechanism directly: power morcellation "dispersed tumor tissue, promoting metastases, which significantly increased mortality in uLMS patients." Her 2024 specimen was recorded as **disrupted**. That makes the existing question about specimen disruption more pointed, not less.

6. THE ANSWER TO "COULD THE FAMILY FUND A STUDY?"

This document *is* that answer. It is the roadmap, already built, by the people who do this professionally.

The gap, in one line

Endometrial cancer — a cancer arising inches away in the same organ — received **over $885 million** in NIH funding from 2014 to 2024. **uLMS received $9.5 million.** Normalised per case, uLMS gets $1.2M per million women affected against $30.6M for ovarian.

Even inside sarcoma it is a rounding error: 4% of sarcoma research funding goes to soft tissue sarcoma; 8% of that to LMS; a third of that to uLMS.

The starkest number: NIH-funded projects 2014–2024 mentioning **leiomyoma** (benign fibroids) — **621**. Mentioning **leiomyosarcoma** — **28**.

What this means for a family with money

Philanthropic dollars go further here than almost anywhere in oncology. The entire decade of federal uLMS funding is $9.5M. A single well-placed gift is material at that scale, which is simply not true in breast or lung cancer.

The guide ranks six opportunities by fit for philanthropy. The top two:

1. **A comprehensive natural history study of uLMS** — ranked most suited to philanthropy. There is no good longitudinal dataset. The FDA now accepts external control data for rare diseases, so this dataset could serve as the comparator arm for future single-arm trials, de-risking every drug development programme that follows.
2. **Map the biological fingerprint** — multiomic profiling, biobanking, tumour models.

The honest timing answer

Funding a study will not change her treatment. A natural history study takes years to design, enrol, and read out. Nothing here arrives in time to alter what happens in the next twelve months.

What *can* happen on her timeline is section 1 and section 2 of this document — preserving her tissue properly and putting it into research programmes. That is free, takes a phone call, and is the version of "contributing to the science" that is actually available right now.

If the family wants to give, the people to talk to are named in the guide: the **Milken Institute Science Philanthropy Accelerator**, which built this roadmap, and the **Briger Foundation for Oncology Research**, which funded it. Both have already done the diligence.

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7. TWO CONTEXT FACTS WORTH CARRYING

There are roughly 50 sarcoma specialists in the entire United States. That single number explains why travel is normal for this disease, why a general oncology practice seeing a uLMS case is not unusual, and why the second-opinion push is not a criticism of anyone.

She is unusually young for this. uLMS typically presents between 45 and 60, peaking at 50–54. She is 39. Young age in a rare cancer is one of the standard prompts for a germline conversation — which, combined with the 2021 thyroid cancer, strengthens the existing question about genetic testing.

WHAT TO ACTUALLY DO WITH THIS

1. **Add the tissue-preservation question to the video follow-up.** Time-critical and free.
2. **Ask whether the 23 July lung biopsy left any frozen or unstained material.**
3. **Look at LMSproject / Count Me In and RCRF.** Patient-initiated, no cost, no gatekeeper.
4. **Stop worrying about checkpoint immunotherapy.** The evidence is in and it is negative.
5. **Park the study-funding question** until after treatment starts. It is real, it is worth doing, and it is not urgent in the way tissue is.

Nothing here is medical advice. It is a summary of a published research roadmap, translated into questions to ask.