PEComa Care Delivery Across the Academic–Community Oncology Continuum: A Case Study in Diagnosis, Treatment, and Clinical Coordination

Prepared by NCODA with support from Aadi Bioscience I December 2025

Introduction

Perivascular epithelioid cell tumors (PEComas) are a rare and heterogeneous group of mesenchymal neoplasms characterized by the co-expression of melanocytic and smooth muscle markers. These tumors may arise in various anatomic locations including the uterus, retroperitoneum, lung, and gastrointestinal tract. PEComas may present with nonspecific symptoms such as abdominal pain, bleeding, or incidental mass findings.[1,2] PEComas are frequently misdiagnosed or detected late in the disease course due to their rarity and clinical overlap with other soft tissue malignancies like leiomyosarcoma, gastrointestinal stromal tumor (GIST), or renal cell carcinoma.[2]

Historically, treatment options for unresectable or metastatic PEComa were limited to off-label use of oral mTOR inhibitors, which often resulted in variable efficacy and inconsistent tolerability.[2] However, the FDA approval of *nab*-sirolimus (Fyarro®), the first and only approved therapy for malignant PEComa, has reshaped the treatment paradigm.[3] *Nab*-sirolimus offers a targeted approach that improves tumor control and progression-free survival while providing a manageable safety profile.[4]

Because of its rarity, optimal PEComa care requires collaboration across healthcare settings. Academic medical centers play a critical role in establishing the diagnosis through expert pathology and molecular diagnostics, initiating evidence-based therapy, and offering access to clinical trials. Yet, the majority of ongoing cancer care in the U.S. takes place in community settings, where patients receive most of their treatment and follow-up.[5,6] As a result, a shared care model, anchored in communication, continuity, and aligned protocols is essential to ensure that patients with PEComa benefit from cutting-edge science without losing access to local support.

This case study explores the real-world experiences of both an academic sarcoma center and a high-volume community oncology network. It highlights the institutional pathways, treatment decision-making, and coordination mechanisms that have been implemented to optimize PEComa diagnosis, treatment with *nab*-sirolimus, patient support, and long-term outcomes. By examining care delivery from both ends of the referral spectrum, this report provides a comprehensive model for how to operationalize rare tumor care through collaboration, education, and clinical leadership.

Challenges in Diagnosing PEComa Across Sites of Care

Diagnosing PEComa is inherently complex due to its rarity, histologic variability, and overlapping clinical features with other more common tumors.[2] These challenges manifest differently in academic and community oncology settings, though both environments face critical diagnostic inflection points that influence patient outcomes.

1. Diagnostic Complexity at Academic Medical Centers

At academic institutions, providers are more likely to encounter referrals for second opinions on difficult-to-classify soft tissue tumors. Despite this, PEComa can still elude immediate recognition, particularly in its uterine or retroperitoneal forms, where symptoms are often vague or mimic other gynecologic or abdominal conditions.[7] Patients may present with abnormal bleeding, nonspecific pelvic pain, or incidental mass findings during unrelated imaging studies.

Even in highly specialized settings, diagnosis hinges on expert pathology review. Immunohistochemistry for melanocytic markers (HMB-45, Melan-A) and muscle markers (SMA, desmin) are essential for accurate identification.[1] The academic site highlighted in this case study noted that most of their PEComa cases were originally misdiagnosed as leiomyosarcoma, GIST, or renal cell carcinoma. Only through multidisciplinary tumor board review and high-level pathology collaboration was the correct diagnosis made.

The academic team emphasized the importance of internal communication between departments, particularly gynecologic oncology and sarcoma services, to ensure uterine PEComa cases are appropriately classified and co-managed. Furthermore, they often serve as the "diagnostic endpoint" for patients who had previously seen multiple providers without definitive answers.

> ***"We frequently see second opinions initiated by referring providers, often after pathology was inconclusive or misclassified. Pathology is central to the diagnostic process in PEComa."***
>
> – Academic Medical Center Provider

2. Diagnostic Gaps in the Community Setting

In the community oncology environment, providers face the additional challenge of identifying PEComa among a broad and diverse case mix. While large practices may see thousands of cancer cases annually, the appearance of a PEComa diagnosis is rare and often unexpected. As such, it is common for patients to first be treated under the assumption of a more typical soft tissue malignancy.

Community oncologists typically rely on external referrals from academic centers for the diagnosis of PEComa. These patients arrive with diagnostic workups and treatment plans already in place. However, when the diagnosis originates locally, delays may occur due to limited access to comprehensive molecular testing or a lack of familiarity with the disease.

Community practices may also face practical constraints when pursuing confirmatory diagnostics, such as limited in-house pathology resources or delays in outsourcing biopsies for advanced staining or NGS. These barriers can lead to reliance on empirical treatment approaches that are not tailored to PEComa biology, further underscoring the value of collaboration with academic sarcoma programs.

> ***"We most often see patients with PEComa after they've been diagnosed at a tertiary center. In some cases, we've treated them based on a preliminary diagnosis that later changed after academic pathology review."***
>
> - Community Oncology Provider

3. Shared Challenges and Points of Convergence

Both academic and community sites encounter overlapping diagnostic challenges, particularly around:

- Limited clinical suspicion for PEComa due to its rarity
- Overlap in presentation with more common malignancies
- Lack of standardized diagnostic algorithms or screening criteria
- Difficulty in accessing timely and definitive molecular results

As a result, establishing the correct diagnosis of PEComa remains a pivotal moment in the patient journey as it determines treatment eligibility, prognosis, and long-term care strategy. The data gathered from both sites reinforce the critical role of pathology, the value of multidisciplinary review, and the necessity of maintaining strong academic-community referral pathways to expedite diagnosis and avoid inappropriate treatment.

Treatment Decision-Making and Adoption of *Nab*-sirolimus: Divergent Paths, Aligned Purpose

Once PEComa is accurately diagnosed, treatment decisions must be made rapidly and thoughtfully, balancing disease aggressiveness with therapeutic efficacy, toxicity profiles, and patient preferences. The approval of *nab*-sirolimus in 2021 marked a significant milestone in PEComa care, offering the first FDA-approved therapy specifically indicated for this rare malignancy.[3] Both academic and community sites now use *nab*-sirolimus, but their paths to adoption and the decision-making frameworks differ in meaningful ways.

1. Academic Centers: Data-Driven Adoption

Academic institutions, often at the forefront of clinical trial participation and guideline development, were among the first to adopt *nab*-sirolimus into routine practice. In the highlighted academic sarcoma center, the medical team had been closely following the AMPECT trial results and was prepared to integrate *nab*-sirolimus into clinical pathways as soon as it received FDA approval.

Adoption was facilitated by multidisciplinary tumor boards, institutional protocols, and a culture of rapid knowledge translation. For unresectable or metastatic PEComa, *nab*-sirolimus quickly replaced off-label mTOR inhibitors like sirolimus and everolimus, which had shown inconsistent efficacy and higher toxicity in the real-world setting.[2]

> ***"We transitioned to Fyarro based on both trial data and our early patient experiences. It's more effective, better tolerated, and easier to manage than the oral agents we previously used."***
>
> - Academic Medical Center Provider

Academic teams emphasized the value of *nab*-sirolimus' albumin-bound formulation, which enhances drug delivery and reduces systemic side effects. Side effect profiles are closely tracked using standardized grading systems, and internal supportive care protocols (including dexamethasone mouthwash and proactive fatigue management) were rapidly implemented across departments.

2. Community Practices: Guided by Expertise, Grounded in Access

In the community setting, *nab*-sirolimus adoption has been equally important but followed a more consultative path. Community oncologists often initiate treatment based on detailed recommendations from academic partners who made the initial diagnosis. These handoffs include dosing guidelines, toxicity monitoring parameters, and clear escalation pathways should complications arise.

"We usually follow the academic center's plan. They help us interpret the data and guide when to initiate Fyarro. Our focus is delivering that care safely and consistently, close to the patient's home."

- Community Oncology Provider

While community practices don't typically drive the initial treatment decision for PEComa, they play a crucial role in continuity by administering infusions, managing side effects, and supporting adherence. Community clinicians report high patient satisfaction with receiving treatment locally, particularly when supported by regular check-ins with academic colleagues and shared EMR access.

Importantly, community teams had to navigate unique challenges with access and logistics such as securing prior authorizations, coordinating co-pay assistance, and managing drug supply. In some cases, institutional policies required the drug to be "formulary, non-stocked" to reduce the risk of wastage due to low patient volume.

3. Shared Principles, Local Adaptations

Despite the differences in adoption timeline and workflow, both academic and community settings are aligned in several key areas:

- **Commitment to evidence-based treatment:** Both sites trust the AMPECT data and NCCN Guidelines®, using them as a foundation for therapeutic decisions.
- **Patient-centered adaptation:** Academic centers initiate treatment, but community settings adjust supportive care and monitoring based on patient needs and treatment tolerance.
- **Collaborative communication:** Regular touchpoints through shared records, direct calls, or pharmacist consults, ensure that treatment stays on course regardless of location.

Managing Side Effects and Supporting the PEComa Patient Experience: A Shared Commitment

As with many cancer treatments, the success of *nab*-sirolimus in clinical practice is defined not only by tumor control, but also by its manageability and impact on the patient's day-to-day life. While academic and community sites may differ in how they monitor, document, and adjust care, both prioritize minimizing toxicity and supporting patients through treatment. Their approaches, while shaped by setting, converge on a shared philosophy: proactive side effect management equals better adherence, and ultimately, better outcomes.

1. Academic Centers: Multidisciplinary Support

Academic centers have the advantage of larger care teams, established clinical pathways, and access to institutional resources for managing rare cancer therapies. From the outset, patients receiving *nab*-sirolimus are counseled on expected toxicities, symptom tracking, and supportive interventions. Side effects are graded using CTCAE criteria and discussed at regular clinic visits or tumor board reviews.

The most commonly observed side effects include:

- Stomatitis (mouth sores)
- Fatigue
- Rash
- Nausea
- Edema
- Diarrhea

To preempt complications, patients are prescribed dexamethasone mouthwash at treatment initiation and receive education on oral hygiene, including the use of non-alcoholic rinses and soft toothbrushes. If stomatitis progresses to Grade 2 or higher, magic mouthwash is promptly prescribed. Dose modifications are guided by established protocols, with reductions or holds implemented for Grade 3+ toxicities.

"Tolerance has been generally favorable. When side effects do emerge, we intervene early. Stomatitis and fatigue are the most common, but they're manageable with the right tools."

- Academic Medical Center Provider

In addition to symptom control, academic teams emphasize patient education—using visual aids, printed materials, and reputable online resources such as the Sarcoma Foundation of America. Still, providers note that more tailored resources for PEComa patients, especially multimedia and multilingual tools, are sorely needed.

2. Community Oncology Practices: Real-World Flexibility and Personal Connection

In the community setting, care teams focus on delivering guideline-concordant treatment while navigating real-world barriers: transportation, time off work, and local pharmacy limitations among them. Providers rely heavily on the treatment plans and education materials shared by academic centers at the time of handoff.

> ***"We follow their protocols closely. We'll adjust the dose if needed and manage side effects per guidance. But we also spend a lot of time listening, patients want to know they're not alone in this."***
>
> - Community Oncology Provider

Community clinicians report similar side effect patterns, with stomatitis and fatigue being the most troublesome. However, access to compounding pharmacies or specific formulations (magic mouthwash) may be more limited, prompting creative substitutions. In these cases, care teams often consult with academic partners or pharmacists for alternatives.

Importantly, the community environment allows for more frequent touchpoints, shorter wait times for appointments, quicker phone follow-ups, and ongoing relationships with nurses and support staff. Patients often express gratitude for being able to receive rare cancer treatment close to home, provided the care is clearly coordinated with their academic specialists.

3. Common Themes: Anticipation, Adaptation, and Empathy

Despite differences in infrastructure, both care settings demonstrate:

- Anticipatory management of known side effects like stomatitis and fatigue.
- Early dose modifications to preserve quality of life without compromising efficacy.
- Proactive communication to align academic guidance with real-world delivery.
- Commitment to reassurance, education, and minimizing fear in patients facing a rare diagnosis.

Yet, both settings also acknowledge opportunities for improvement:

- More targeted patient education materials, especially ones specific to PEComa.
- Expanded access to supportive medications in rural or under-resourced areas.
- Symptom tracking tools (digital apps) to help patients report and manage toxicity in real time.

Access, Affordability, and Financial Navigation: Overcoming Barriers to *Nab*-Sirolimus

1. Academic Medical Centers: Navigating Complexity with Infrastructure

Academic institutions typically have well-established pathways for managing high-cost therapies. Pharmacy and financial navigation teams review each new therapy order for coverage requirements, prior authorizations, and patient assistance eligibility.

Still, even within these systems, challenges persist. Many academic centers classify *nab*-sirolimus as "formulary, non-stocked" due to concerns about vial wastage and shelf life, requiring just-in-time ordering and close coordination between clinics and pharmacies.

> ***"Our team works with AadiAssist and other programs to reduce barriers. When we anticipate a delay, we reach out early so the patient isn't left waiting."***
>
> - Academic Medical Center Provider

Patient assistance programs like AadiAssist have significantly reduced financial barriers. These programs have been particularly effective in smoothing the initiation of therapy for uninsured or underinsured patients. Nonetheless, providers emphasized the need for expanded eligibility, transportation assistance, and multilingual financial education materials to better serve diverse populations.

2. Community Oncology Practices: Sustaining Treatment and Access

Community practices are on the front lines of patient affordability. Financial counselors and nurses play an active role in helping patients navigate insurance approvals, co-pay accumulators, and manufacturer support resources. However, practices without institutional pharmacy teams may face more time-consuming hurdles in medication procurement and delivery.

> ***"The co-pay support programs have made a huge difference, but the logistics are on us to coordinate, especially in practices that serve a wide geographic area."***
>
> - Community Oncology Provider

Community teams report high variability in payer requirements and turnaround times. Delays in approval can threaten continuity of care unless proactively managed. When patients are handed off from academic centers with a prescription in hand, the burden of follow-through falls on the local team.

Despite these challenges, many community providers go beyond clinical responsibilities to help secure therapy by making calls to foundations, following up with insurers, and advocating directly with manufacturers.

3. Shared Solutions and Systemic Gaps

Across both settings, the consensus is clear: manufacturer-supported assistance programs have been a lifeline, but broader systemic reforms are needed. Recommendations include:

- Real-time benefits verification tools at the point of care.
- Simplified prior authorization workflows, particularly for FDA-approved rare cancer therapies.
- Collaborative education between manufacturers and practices to ensure that staff understand the nuances of drug access and reimbursement.

Together, these strategies can ensure that treatment decisions are made based on clinical need, not cost, coverage, or paperwork delays.

Continuity Across Settings: The Architecture of Shared Care

For a disease as rare and complex as PEComa, no single site of care can meet every need. What makes successful treatment possible is the structure of collaboration between academic and community providers. From diagnosis to survivorship, these partnerships ensure that patients receive expertise where needed and support where they live.

1. Academic Centers: Establishing the Care Framework

Academic centers often initiate care and define the treatment roadmap. After confirming diagnosis and initiating *nab*-sirolimus, they develop comprehensive shared care plans, including dosing schedules, side effect protocols, imaging timelines, and escalation criteria.

> ***"We provide the structure: treatment summaries, monitoring protocols, pharmacy guidance. But we also remain available to consult, to support, and to step back in if needed."***
>
> - Academic Medical Center Provider

Academic pharmacists and physicians remain on call for toxicity management and treatment questions. EMR integration and secure communication channels enable real-time updates, especially when community teams need to adapt the plan to patient realities.

2. Community Practices: Sustaining the Journey

Community oncologists take ownership of longitudinal care, administering *nab*-sirolimus, monitoring labs and imaging, managing symptoms, and maintaining patient confidence. Their proximity to patients allows for regular check-ins and supportive relationships that academic centers cannot always provide.

Patients benefit most when the transition feels seamless. This requires:

- Timely sharing of diagnostic materials.
- Clarity on roles and responsibilities between sites.
- Ongoing communication about treatment response and side effects.

> ***"Our job is to carry out the plan, monitor closely, and loop back in with the academic team when needed. We want the patient to feel supported every step of the way."***
>
> - Community Oncology Provider

3. A Model of Coordinated Rare Cancer Care

The PEComa care journey exemplifies how rare disease treatment must bridge institutional lines. Best practices identified in this case study include:

- Early and frequent provider-to-provider communication.
- Standardized handoff protocols and documentation.
- Clear escalation pathways for re-referral.
- Mutual respect for the different strengths of each setting.

As the cancer care landscape continues to evolve, this model of academic–community integration may serve as a blueprint not just for PEComa, but for other rare diseases, where diagnosis may be delayed, and care is complex.

Conclusion: A Collaborative Framework for Advancing PEComa Care

The management of PEComa demands precision, speed, and an integrated approach across all levels of the cancer care system. As this case study demonstrates, academic medical centers and community oncology practices each play a vital, complementary role in delivering high-quality care to patients with this ultra-rare sarcoma.

Academic institutions excel at early diagnosis, leveraging advanced pathology and molecular tools to identify PEComa accurately and initiate evidence-based therapies such as *nab*-sirolimus. Their leadership in clinical trial engagement and treatment standardization sets the foundation for therapeutic success.

Community oncology practices ensure that this success extends beyond the academic walls, translating protocols into personalized, accessible care close to home. Their strengths lie in the longitudinal relationships they build with patients, their agility in managing real-world challenges, and their commitment to continuity of care.

What binds these settings together is a shared commitment to:

- Accurate, timely diagnosis through expert collaboration.
- Use of *nab*-sirolimus as the evidence-based standard of care for advanced PEComa.
- Proactive management of toxicity to preserve quality of life.
- Coordinated care transitions that prioritize the patient experience.
- Financial navigation that makes treatment access possible for all.

Together, academic and community sites form a coordinated care continuum that supports patients with PEComa through consistent communication, shared expertise, and collaborative treatment planning across care settings.

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