Review

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Review

Management of PEComas: A Review of the Role of Radiotherapy

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Simple Summary

Malignant PEComa is an ultra-rare and aggressive subtype of sarcoma. Current treatment options mainly include surgery and systemic therapy for metastatic disease, while the role of radiotherapy (RT) remains unclear in all settings. This review summarizes published clinical reports on the use of radiotherapy for PEComa and describes treatment outcomes. Although the available evidence is limited to heterogeneous case reports and often includes additional therapies that make interpretation difficult, a considerable number of cases demonstrated local disease control and/or sustained disease stability after RT, suggesting that RT may be a possible therapeutic contributor and supporting the need for dedicated clinical studies evaluating RT in PEComa.

Abstract

Background/Objectives: Malignant PEComa is a rare sarcoma subtype and usually represents PEComa-NOS (not otherwise specified), one of the several entities of PEComa family. Surgery is the primary treatment; chemotherapy is used mainly for metastatic or unresectable cases. Radiotherapy (RT) may be considered in selected cases; however, its role remains unclear due to the rarity of the disease and limited radiotherapy-specific studies. **Methods**: This is a descriptive literature review of a limited number of reports on RT use in PEComa. Descriptive statistics were used to summarize reported case characteristics and outcomes. **Results**: We identified 28 publications reporting 33 cases. In neoadjuvant settings, there was a significant local response to RT in one case. In other neoadjuvant cases, although quantitative response assessments were not reported, most showed no recurrence during follow-up, with the longest follow-up at 34 months, suggesting that a possible benefit in local disease control may exist. In the adjuvant setting, some reports described prolonged disease-free survival following RT, though the lack of direct comparisons between surgery with versus without RT and heterogeneous follow-up limit definitive conclusions. In selected metastatic cases, palliative RT achieved notable local responses, potentially contributing to durable local control. **Conclusions**: In conclusion, although the only available data on RT in PEComas come from case studies with overall heterogeneous management approaches, RT has shown some potential as a therapeutic option across neoadjuvant, adjuvant, and palliative settings, warranting further dedicated clinical studies.

Keywords: PEComa; radiotherapy; local control; rare sarcoma; ultra-rare sarcoma

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1. Introduction

Perivascular epithelioid cell neoplasm (PEComa) is an ultrarare mesenchymal tumor that arises from the perivascular epithelioid cells (PEC) and may occur in any part of the body [1]. The entity was first formally described in 1992 where perivascular epithelioid cells were found in clear cell tumor of the lung (CCTL) as well as kidney angiomyolipoma (AML), and were characterized by strict association with the vessel smooth muscle walls and exhibited unusual histological features resembling both melanocytes and muscle cells. [2]. Later, Zamboni et al described a tumor found in the pancreas with similar pathohistological and immunochemical characteristics and the term PEComa was subsequently proposed to encompass this 'family' of tumours [3]. The World Health Organization included PEComa in its 2002 classification of diseases [4].

Historically, the PEComa family of tumors comprise of angiomyolipomas (AML), lymphangioleiomyomatosis (LAM), clear cell sugar tumor (CCST), and PEComa-not otherwise specified (PEComa-NOS). The first three subtypes are usually considered as noncancerous and are not included in this review. The term 'PEComa' is typically attributed to PEComa-NOS, which histopathology can be classified as benign, uncertain malignant potential (UMP) and malignant based on six high-risk criteria: tumor size ≥ 5 cm, infiltrative growth pattern, high nuclear grade cellularity, mitotic rate > 1/50 high-power fields (HPF), necrosis, and vascular invasion. PEComas with malignant histological features or uncertain malignant potential (UMP) often show aggressive behavior, extensive metastases and a poor prognosis [5].

Primary surgical excision with negative margins is crucial in treating PEComas [6]. With respect to pharmacotherapy, there is currently no clear consensus on the use of neoadjuvant or adjuvant drug-based regimens. Pharmacological treatment often reserved for progressive or inoperable disease, particularly with the use of mTOR inhibitors. [7-9]. Conventional systemic chemotherapy can be used although its objective response rate (ORR) is typically lower compared to that of mTOR inhibitors. [10, 11]. Other medical therapies, including Vascular Endothelial Growth Factor Receptor (VEGFR) and Programmed Cell Death Protein 1 (PD-1) inhibitors may be considered in cases of mTOR inhibitor resistance [12-14].

Another important clinical question that remains unanswered is the role of radiotherapy (RT) in the management of PEComa in the perioperative (neoadjuvant, adjuvant), palliative, and curative settings. Malignant PEComas exhibit features such as a high mitotic index and rich vascularization, which suggest they may have high cellular sensitivity to radiation [15]. This might support the use of radiotherapy as a therapeutic option for patients with PEComas. This study aimed to review available data on radiotherapy treatment of PEComa and their outcomes to enhance understanding of its application in these tumors.

2. Materials and Methods

The literature search started in April 2024 with final update of literature in May 2025 using different queries on the PubMed database. The following search terms, restricted to the title and/or abstract, were used: "PEComa" OR "Perivascular Epithelioid Cell Tumor" AND "treatment"; "PEComa" OR "Perivascular Epithelioid Cell Tumor" AND "radiotherapy"; "PEComa" OR "Perivascular Epithelioid Cell Tumor" AND "radiation therapy"; PEComa" OR "Perivascular Epithelioid Cell Tumor" AND "radiation" .

The selection criteria included case reports, case series, clinical trials involving patients with malignant and uncertain malignancy potential PEComa-NOS receiving radiotherapy in any settings (neoadjuvant, adjuvant, palliative, curative-intent) for PEComa-NOS with clinical and/or radiological follow-up reported for at least 3 months. The literature search included studies published since 1990 until May 2025. Given the rarity of the tumor and the limited number of studies focused specifically on radiotherapy for these tumors, detailed information on radiotherapy dosage was preferred but not mandatory for inclusion.

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We excluded non-English articles and those focusing on PEComa subtypes other than NOS including AML, LAM, CCST. We included only PEComa cases classified as malignant or having uncertain malignant potential, given the recognized overlap in pathological features between these categories and the fact that UMP tumors still retain malignant characteristics such as mitotic activity, nuclear atypia or pleomorphism, and larger tumor size, and can still demonstrate increased risk of recurrence and progression [16, 17].

Data collected from the included studies were: age, gender, size of the primary tumor, Folpe criteria (tumor size, mitotic activity, nuclear grade/cellular atypia, necrosis and infiltrative growth pattern if provided), Folpe risk category if provided, site of the primary tumor, site of metastatic lesions, treatment(s) received, follow-up periods, reported outcomes.

3. Statistical Analysis

As this is a descriptive literature review of limited number of available reports, no inferential statistical analysis was performed. Descriptive statistics, including means, medians, and proportions, were used to summarize reported case characteristics and outcomes.

Given the overall limited number of studies and heterogeneous outcome descriptors, most of which did not apply strict RECIST criteria, individual case outcomes were reported, and favorable disease courses were combined into a composite positive outcome for descriptive analysis grouped by RT setting. In neoadjuvant and adjuvant settings, this corresponded to no evidence of disease at last follow-up. In palliative settings, it included reported disease stability, local and/or systemic response, and/or symptom improvement after radiotherapy.

4. Results

A total of 1,805 abstracts and full-text articles were screened. A total of 28 publications reporting 33 cases were included in this review. Of these, 5 patients received neoadjuvant RT, 20 received adjuvant RT, and 8 received palliative RT (Figure 1). There were no cases of definitive or curative-intent radiotherapy identified.

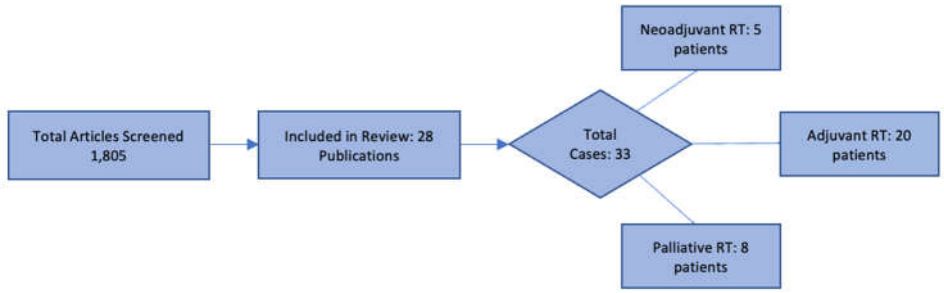

Figure 1.

4.1. Neoadjuvant Radiotherapy

The number of reports on neoadjuvant radiation for malignant PEComa treatment is limited. In total, we identified five cases that provided follow-up times and outcomes related to disease progression (Table 1). The median age was 49 years old, ranging from 28 to 68, with four of the five patients being females; the primary sites were musculoskeletal, oropharynx/neck, and liver. Follow-up times varied from 6 to 34 months with a median of 13 months. There was no evidence of disease recurrence (NED) reported in four out of five cases (80%).

Two cases included neoadjuvant chemotherapy in addition to radiotherapy [18], [19]. One of these cases demonstrated progression of a neck PEComa despite treatment with mTOR inhibitors and conventional chemotherapy with adriamycin and ifosfamide, which prompted the use of neoadjuvant radiotherapy, leading to a partial response and facilitating subsequent definitive

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surgical resection yet the exact post-RT volumetric change was not provided. The patient remained without evidence of disease (NED) at 6 months of follow-up [19]. In contrast, Osei et al. described a poor local response to neoadjuvant radiotherapy following neoadjuvant chemotherapy with doxorubicin and ifosfamide, initially resulting in tumor reduction but ultimately leading to a mild increase in tumor size before definitive surgical resection and the development of lung metastases by 13 months of follow-up [18].

Among all five cases, only one reported the exact dose of RT and associated volume reduction, where stereotactic RT of total 60 Gy in 8 fractions was applied to a liver PEComa lesion measuring 1280 cm^3 and resulting in a 50% reduction by week 17 and NED at 21 months post-resection [20].

Notably, all reported lesions were larger than 5 cm, marked by high mitotic counts and pleomorphism with locations seemingly challenging for upfront surgeries without attempting tumor downsizing first, which may have been a primary reason to proceed with neoadjuvant RT. Also, it is noted that two cases out of five did not demonstrate significant necrosis [21], [20]. These two cases had longer NED of 34 and 21 months-follow-up time.

Overall, neoadjuvant RT appeared to lead to some degree of response, although exact volumetric measurements were lacking except for the one case described above. In addition, two patients had follow-up periods over 20 months and remained with no evidence of disease (NED), suggesting that RT may have a potential role in durable disease control; however, very small sample size prevents making a firm conclusion. A detailed summary of the reported neoadjuvant cases is provided in Table 1, and a summary of RT treatments by treatment intent is presented in Appendix A.

Table 1.

Neoadjuvant Radiotherapy							
Author	**Patient information**	**Diagnosis**	**Location**	**Characteristics**	**Treatment**	**Follow-up (months)**	**Outcome**
Weinreb et al (2007)	68 y/o male	Malignant PEComa	Thigh	7.8 cm large areas of necrosis, high mitotic count (42 MFs per 10 HPFs), dedifferentiated patternless sarcoma areas	NR + resection	11	NED
Osei et al (2007)	49 y/o female	Malignant PEComa	Back/right shoulder	5.3 × 4.7 cm; undifferentiated and pleomorphic cells, focal islands of necrosis.	NC+NR+resection, 80% of tumor reduction after NC (doxorubicin and ifosfamide), size increase after NR.	13	Lung metastasis
Yamashita et al (2010)	39 y/o female	Malignant PEComa	Right proximal tibia	6.5 cm; prominent hypercellularit	NR+resection	34	NED

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				y with high mitotic activity			
Kirste et al (2018)	52 y/o female	Malignant PEComa	Liver	1280 cm^3 (around 10 cm in diameter) high proliferative activity, nuclear pleomorphism, multinuclear giant cells and lack of necrosis.	NR with 49% of tumor reduction + resection	21	NED
Saluja et al (2018) neoadjuvant	28 y.o female	Malignant Pecoma	Oropharynx	7.2 × 5.1 × 2.9 cm, high mitosis rate, nuclear atypia, area of necrosis	NC - 1 mo (mTORi, everolimus -1mo, then Adriamycin + Ifosfamide - 1 mo) + NR (palliative dose) + resection	6	NED

4.2. Adjuvant Radiotherapy

There were 20 cases (16 publications) with adjuvant RT identified. The median age was 51 years old, ranging from 9 to 92; and females accounted for 80% of the cases. The primary sites were musculoskeletal, gynecological, skin, neck, retroperitoneal, adrenal gland, falciform ligament and mesenteric, with the most prevalent being gynecological sites: 10/20 (50%). Of the cases, the median follow-up of the cases was 12 months (3-50 months). NED was reported in 15 of 20 cases (75%), and of these, combinations of high-risk features (high mitotic activity and/or necrosis and/or lymphovascular invasion) were described in 9 out of 15 cases (60%) [5, 22-29]. In addition, one patient with a large malignant PEComa remained NED at 50 months; however, no other pathomorphological features were described [29]. Of these 9 cases, 3 involved cutaneous PEComas, while the remaining were musculoskeletal, oropharynx/neck, adrenal gland and gynecological [22, 23, 25]. The follow-up periods for these nine cases varied between 6 to 24 months with a median of 12 months and a mean follow-up period of around 13.2 months. Among these nine cases with NED, both RT and chemotherapy were administered in three cases involving a high-risk cutaneous lesion larger than 5 cm and uterine/pelvis PEComas with local lymph node involvement and large size [23, 26, 29]. One of these cases reported by Jeon et al received adjuvant concurrent chemoradiation with NED at 18 months of follow-up [26].

Disease progression was observed in 5 out of 20 cases (25%) with four patients experiencing distant recurrence with metastasis to the lungs, liver, bones, small and large intestine, abdominal wall and one patient experiencing local recurrence [5, 30-33]. The median time to progression was 11 months (3-39 months). Primary tumor sites were falciform ligament (1/5), uterus (2/5), retroperitoneum (1/5), and mesentery (1/5). All five cases involved primary tumors of significant size ranging from 9 cm to 30 cm along with high-risk histopathological features. Vascular invasion was

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observed in two cases, necrosis in three, and all exhibited high mitotic activity. Two patients received both adjuvant radiotherapy and chemotherapy for uterine PEComa, one patient had concurrent adjuvant chemoradiation for mesenteric PEComa; progression time ranged between approximately 6 and 16 months [5, 31, 33].

Regarding RT doses, only 5 out of 20 cases reported total dosages, which varied between 45 and 60 Gy [22, 24, 26, 27, 33]. These cases involved PEComas of uterus, broad ligament, mesenteric region, adrenal gland, and skin**.** Among five cases, the mesentery PEComa, which received total 60 Gy of adjuvant concurrent RT with Ifosfamide and Adriamycin, recurred within 6 months [33].

Indications for adjuvant RT were not explicitly described in the presented case reports, except in two studies where it was administered for positive post-resection margins [27, 32]. It can be assumed that tumor size in combination with high-risk features and/or regional spread to lymph nodes would guide its use. At the same time, interestingly, there are a few cases where adjuvant RT was used in patients with PEComa of uncertain malignant potential, which are mainly characterized by size below 5 cm, low mitotic rate, and mild to moderate pleomorphism, suggesting unpredictable behaviour of this tumor despite fewer high-risk characteristics; all demonstrated NED at follow-up ranging between 6 and 30 months [5, 27, 34-36] .

Overall, some of the presented cases of malignant PEComa with high-risk features demonstrated prolonged periods of disease control [24-27, 37], with the longest NED observed at 50 months after complete resection of recurrent disease and adjuvant chemotherapy and radiotherapy [29]. However, given the heterogeneous follow-up periods, small sample size, lack of direct comparisons between adjuvant RT and no RT, and confounding from chemotherapy in some cases, conclusions regarding disease control remain difficult to draw. As for the reported progressed cases, a combination of large tumor size, intra-abdominal/pelvic primary location, high mitotic activity, and necrosis appeared to be associated with more unfavorable outcome. In addition, among the progressed cases, patients who received adjuvant radiotherapy and chemotherapy or concurrent radio-chemotherapy seemed to have a higher rate of progression (3 out of 8) compared to those receiving only adjuvant RT (2 out of 12). However, meaningful comparisons are limited by small number of cases, and the fact that multimodality approaches were typically used in the tumors exhibiting multiple unfavorable features, including vascular invasion, necrosis, a high mitotic index, and large size. Thus, these tumors were perhaps already predisposed to a more aggressive biological behavior, which may have warranted more intensive multimodality treatment. A detailed summary of adjuvant RT cases is provided in Table 2, and a summary of RT treatments by treatment intent is presented in Appendix A.

Table 2.

Adjuvant Radiotherapy							
Author	**Patient information**	**Diagnosis**	**Location**	**Characteristics**	**Treatment**	**Follow-up (months)**	**Outcome**
Folpe at al (2000)	21 y/o male	Malignant PEComa	Falciform ligament/ligamentum teres	20 cm; area of necrosis was not reported, low mitotic activity	Resection + AR	3	Lung metastasis
Folpe at al (2005)	71 y/o male	Malignant PEComa	Forearm	9 cm; high mitotic activity, high nuclear grade, mixed morphology with	Resection + AR	10	NED

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				multinucleated giant cells (MNGCs)			
Folpe at al (2005)	48 y/o female	PEComa with UMP	Cervix	2 cm; high nuclear grade, low mitosis, no necrosis, no vascular invasion, epithelioid and MNGC histology.	Resection + AR	21	NED
Folpe at al (2005)	77 y/o female	PEComa with UMP	Neck	2.6 cm; low mitotic rate, mixed histology and MNGC, no necrosis, no vascular invasion	Resection + AR	6	NED
Folpe at al (2005)	56 y/o female	Malignant PEComa	Uterus	9 cm; high cellularity, high nuclear grade, high mitotic activity, atypia, no necrosis, no vascular invasion	Resection + AR + AC	11	Lung and bone metastases
Hornick et al (2008)	50 y/o female	Malignant PEComa	Retroperitoneum	13 cm; pleomorphic morphology, with marked nuclear atypia, frequent mitoses (22/10 HPF), areas of necrosis	Resection + AR (for positive margins)	39	Lung, liver, abdominal wall metastasis
Fukunaga et al (2005)	40 y/o female	Malignant PEComa	Uterus	30 × 27 × 18 cm + local met; high mitotic activity, vascular invasion, moderate atypia, necrosis.	Resection + AC, AR	16	Died from multiple metastases
Silva et al (2004)	75 y/o female	PEComa with UMP	Uterus	Size – no reported; no necrosis, no high mitotic rate or invasion.	Resection + AR	8	NED
Vang et al (2004)	75 y/o female	PEComa with UMP	Uterus	5 cm; absence of necrosis, mitosis, pleomorphism, vascular invasion	Resection + AR	30	NED

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Jeon et al (2005)	9 y/o female	Malignant PEComa	Uterus	6.5 × 5 × 3.5 cm; no necrosis, mitosis but polymorphism and metastasis to one of the regional LN.	NC (VID) + resection +AC + adjuvant concurrent CRT (45 Gy + VID)	18	NED
Fink et al (2004)	51 y/o female	Malignant PEComa	Broad ligamentum	17 cm; pleomorphism, extensive areas of necrosis and hemorrhages	Resection + AR (50.4 Gy).	15	NED
Lai et al (2012)	59-y/o male	Malignant PEComa	Mesenteric	9 × 11 cm; high grade nuclear atypia, focal tumor necrosis, vascular invasion, and high mitotic rate	Resection + adjuvant concurrent CRT (IA + 60 Gy)	6	Recurrence
Cole et al (2021)	42 y/o female	Malignant PEComa	Skin (cutaneous form)	3.5 cm; increased mitotic activity, pleomorphism, nuclear atypia and hypercellularity	Resection +AR (60 Gy)	10	NED
Grevelin g et al (2013)	44 y/o male	Malignant PEComa	Cheek/cutaneous.	1cm; high mitotic activity, significant nuclear polymorphism, no necrosis.	Resection + AR	24	NED
Elousrou ti et al (2023)	92 y/o female	Malignant PEComa	Skin/cutaneous form.	7 × 5.5 × 5 cm; nuclear polymorphism, atypia, high mitotic activity, no necrosis, no vascular invasion	Resection + AR + AC (mTORi)	6	NED
Akay et al (2024)	24 y/o female	Malignant PEComa	Adrenal gland	10 cm, areas of necrosis, nuclear pleomorphism, high mitotic activity	Resection + AR (for positive margins)	17	NED

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					(46.8 Gy/26 fractions)		
Komune et al (2020)	24 y/o female	Malignant PEComa	Jugular foramen/neck	5 cm, infiltrative growth, vascular invasion, nuclear atypia, and high mitotic activity	Resection + AR	12	NED
Liu et al (2019)	80 y/o female	Malignant PEComa	Pelvis	10 cm, no microscopy reported	Resection + AR + AC (mTORi)	50	NED
Liu et al (2019)	51 y/o female	Malignant PEComa	Pelvis	8.3 cm, high mitotic rate, necrosis areas	Resection +AR+ AC (mTORi)	7	NED
Papoutsis et al (2019) adjuvant	67 y/o female	PEcoma UMP	Cervix	4.5cm × 2.5 cm, low mitotic index, modest nuclear polymorphism	Surgery, AR+AC	12	NED

4.3. Metastatic Disease, Advanced/Unresectable PEComa and Palliative Radiotherapy

In total, 8 case reports were identified that used palliative RT for PEComa metastases or inoperable disease [38-44]. The median age of patients was 46.5 years old (range 19-75) years old; and 5/8 (63%) were female. The primary PEComa sites were uterus, pelvis, retroperitoneum, lung, limbs, and one case with unknown primary tumor site. Follow-up periods after RT ranged between 4 to 48 months with median follow-up time of 15 months. All reported primary PEComa lesions were above 5 cm with high-grade histological malignancy features and abundant necrosis.

Out of eight cases, one case experienced both local and systemic progression 10 months after pelvic consolidative radiotherapy and chemotherapy for residual, non-operable disease following definitive resection [39]. De León et al. described two cases treated with palliative RT (13 Gy) for spinal metastases; however, no information on local control was provided. Both patients subsequently developed further disease progression involving additional spinal segments at 48th and 11th months [40].

Four cases described either disease stability or partial responses to palliative RT. [38, 41-44]. Separately, Lao et al. reported a case of metastatic malignant PEComa affecting the left femur for which the patient received palliative RT and was started on systemic chemotherapy, the patient was alive at 42 months, with no reported evidence of progression, although detailed response assessment and disease status were not provided [41].

Local RT responses were specifically highlighted in two cases. One reported a complete response by 4 months post-RT with 36 Gy (12 fractions) to a lung PEComa mass [38]. The other described a significant partial response to stereotactic body radiation therapy (SBRT) of 30 Gy (6 fractions) for a recurrent pelvic mass, along with an additional 24 Gy of SBRT delivered to a spine metastasis; the follow-up duration since treatment initiation was approximately 4 months [42]. However, the treatment also included PD-1 inhibitor, Tislelizumab, administered in the peri-radiotherapy period

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as well as granulocyte-macrophage colony-stimulating factor (GM-CSF), which was delivered concurrently with RT. Similarly, another patient with spinal metastasis treated with palliative radiotherapy alongside initiation of PD-L1 inhibitor therapy had stable disease for 12 months of follow-up [43]. Although positive RT response and/or RT-related local disease control is confounded by the use of immunotherapy in these cases, it does raise the question of a potential synergistic effect between radiotherapy and immunotherapy, which has been described in studies involving non-sarcoma tumors yet may be potentially applicable to sarcoma [45]. In addition, higher RT doses were reported in cases demonstrating positive local responses [38, 46]; however, the majority of case reports did not specify the exact palliative RT dose used, making interpretation of a dose-response relationship difficult.

Overall, both palliative radiotherapy and systemic therapy were reported in six out of eight cases, reflecting the standard approach for managing aggressive and metastatic PEComa. Although it is difficult to determine the individual contribution of RT versus systemic therapy to disease control, some cases demonstrated either prolonged stable disease during the follow-up period or local tumor regression after palliative RT. However, the small number of case reports, heterogeneous follow-up periods, and lack of RT-focused details limit the ability to draw clear conclusions. Reported cases are summarized in Table 3 and a summary of RT treatments by treatment intent is presented in Appendix A.

Table 3.

Metastatic Disease or PEComas not feasible for curative treatment							
Author	**Patient information**	**Diagnosis**	**Location**	**Characteristics**	**Treatment**	**Follow-up (months)**	**Outcome**
Bonetti et al (2001)	19 y/o female	Malignant PEComa	Uterine	5.5 cm, necrosis, atypia, nuclear polymorphism and lymphovascular invasion, rare mitotic figures	Resection, recurrence, another resection, inoperable residual disease, Postoperative chemotherapy (IA) + consolidative RT to the pelvic mass for residual disease	18	Multiple metastases + local progression by 10th month
De León et al (2010)	76 y/o female	Malignant PEComa	Retroperitoneum + vagina with mets to sacrum	15 × 15-cm and 4 × 4-cm; necrosis, mild atypia, atypical mitosis	Primary resection, then RT (13 Gy) for sacrum metastasis	48	Multiple mets to brain/spine
De León et al (2010)	38 y/o female	Malignant PEComa	Spine mets, NYD primary site	Extensive necrosis, mild atypia,	Palliative RT (13 Gy) for lumbar/sacral metastases.	18	Multiple mets to liver, lungs, spine by 11 months

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				atypical mitosis			post-RT for spinal metastases.
Lao W et al (2015)	47 y/o male	Malignant PEComa	Distal left femur + multiple lung metastases	5.2 × 3.2×2.6 cm; hypercellularity, nuclear atypia, atypical mitosis, necrosis	Palliative RT and systemic therapy, no details were reported. No RT site was reported (but likely distal femur given clinical description).	42	Alive at 42 months (no progression reported)
Bajaj, A et al (2021)	67 y/o male	Malignant PEComa	Primary site-lung + mets to ipsilateral lung, mediastinal, hilar nodes, ipsilateral malignant pleural effusion, chest wall, adrenal nodule etc	5.8x5 cm (primary mass) High-grade malignancy with abundant necrosis.	RT to the left lung mass (24 Gy + 12 Gy) + systemic therapy (mTORi)	4	Resolution of left lung mass, 2 new met in extrapulmonary sites.
Wang et al (2023)	63 y/o female	Malignant PEComa	Primary uterine, recurrent pelvic mass+mets to spine and lungs	10x10cm High-grade, necrosis, high proliferation index, primary site (uterine) –	Primary resection, resection of the recurred pelvic mass, second recurrence, SBRT 30 Gy/6 fractions delivered during cycles 1 and 4 of a 4-cycle (q3w) anti-PD-1 (Tislelizumab on Day8) + GM-CSF regimen (Day 1-7). GM-CSF concurrent; immunotherapy sequential. Subsequent SBRT 24 Gy/6 fractions delivered to spinal	4.3 (since progression in 2022 – second recurrence)	Significant shrinkage of the recurred pelvic mass, stable spine met post RT.

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					metastasis within the same anti-PD-1 + GM-CSF regimen.		
Alnajar et al (2018)	44 y/o male	Malignant PEComa	Popliteal Fossa + mets to spine	8.3 cm, nuclear atypia, areas of necrosis, rare mitotic figures	Resection + systemic therapy (Pazopanib+Nivolumab) + palliative RT to spine mets	12	Stable Disease
Ross et al (2011)	46 y/o Female	Malignant Pecoma	Pelvis (recurrent, non-operable)	10 × 10 cm, pleomorphism, scattered mitoses.	Palliative RT + sirolimus	12	Stable Disease

5. Conclusions

Although the role of RT remains unclear in the PEComa treatment due to limited data in this ultra-rare disease, this review highlights the emerging evidence that RT might contribute to disease control in both primary and metastatic settings in PEComa. Ongoing collaborative efforts such as the Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPSWG), CanSaRCC (Canadian Sarcoma Research and Clinical Collaboration) and similar initiatives, may help clarify further the role of RT in the management of PEComa.

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Abbreviations

The following abbreviations are used in this manuscript:

AC adjuvant chemotherapy
ACR adjuvant chemoradiotherapy
AR adjuvant radiotherapy
CRT chemoradiotherapy
CSF colony-stimulating factor
Gy Gray
HPF high-power field
IA Ifosfamide, Adriamycin

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LN lymph node
mTORi mammalian target of rapamycin inhibitor
NC neoadjuvant chemotherapy
NED no evidence of disease
NR neoadjuvant radiotherapy
PEComa perivascular epithelioid cell tumor
RT, radiotherapy
SBRT stereotactic body radiotherapy
UMP uncertain malignant potential
VID vincristine-ifosfamide-doxorubicin regimen

Appendix A

Summary of RT Treatments for PEComa by Treatment Intent

	Total Cases	Main Sites	Median Age	Females %	Males %	Mean Follow-Up (months)	Positive composite descriptive outcome (NED for neoadjuvant/adjuvant RT; for palliative RT: local response and/or local stability, and/or systemic disease stability and/or symptom relief)
Neoadjuvant RT	5	Musculoskeletal 60%	49	80%	20%	17 (6-34)	4 (80%)
Adjuvant RT	20	Gynaecological (including pelvis) - 50%	51	80%	20%	16.1 (3-50)	15(75%)
Palliative RT	8	Gynaecological (including pelvis) - 40%	46	62.5%	37.5%	20 (4-48)	4 (57%)*

*Lao et al. was excluded from outcome calculation because disease status was indeterminate (alive at 42 months without further clarification of response or progression).

References

1. Stacchiotti S, Frezza AM, Blay JY, Baldini EH, Bonvalot S, Bovée J, Callegaro D, Casali PG, Chiang RC, Demetri GD *et al*: **Ultra-rare sarcomas: A consensus paper from the Connective Tissue Oncology Society community of experts on the incidence threshold and the list of entities**. *Cancer* 2021, **127**(16):2934-2942. https://doi.org/10.1002/cncr.33618
2. Bonetti F, Pea M, Martignoni G, Zamboni G: **PEC and sugar**. *Am J Surg Pathol* 1992, **16**(3):307-308. https://doi.org/10.1097/00000478-199203000-00013
3. Zamboni G, Pea M, Martignoni G, Zancanaro C, Faccioli G, Gilioli E, Pederzoli P, Bonetti F: **Clear Cell "Sugar" Tumor of the Pancreas: A Novel Member of the Family of Lesions Characterized by the Presence of Perivascular Epithelioid Cells**. *The American Journal of Surgical Pathology* 1996, **20**(6):722-730.

 doi:10.20944/preprints202603.1475.v1

4. Fletcher CDM, Unni K, Mertens F: **World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of Soft Tissue and Bone.** . In., vol. 3rd ed Vol. 5. . IARC Press, Lyon; 2002: pp 221–222.
5. Folpe AL, Mentzel T, Lehr HA, Fisher C, Balzer BL, Weiss SW: **Perivascular epithelioid cell neoplasms of soft tissue and gynecologic origin: a clinicopathologic study of 26 cases and review of the literature**. *Am J Surg Pathol* 2005, **29**(12):1558-1575. https://doi.org/10.1097/01.pas.0000173232.22117.37
6. Zekry N, Rettenmaier MA, Abaid LN, John CR, Micha JP, Brown JV, 3rd, Goldstein BH: **Perivascular epithelioid cell neoplasms: a systematic review of prognostic factors**. *J Minim Invasive Gynecol* 2009, **16**(5):527-532. https://doi.org/10.1016/j.jmig.2009.04.017
7. Wagner A, Ravi V, Ganjoo K, Tine B, Riedel R, Chugh R, Cranmer L, Gordon E, Hornick J, Kwiatkowski D *et al*: **ABI-009 (nab -sirolimus) in advanced malignant perivascular epithelioid cell tumors (PEComa): Preliminary efficacy, safety, and mutational status from AMPECT, an open label phase II registration trial**. *Journal of Clinical Oncology* 2019, **37**:11005-11005. https://doi.org/10.1200/JCO.2019.37.15_suppl.11005
8. Wagner AJ, Ravi V, Riedel RF, Ganjoo K, Van Tine BA, Chugh R, Cranmer L, Gordon EM, Hornick JL, Du H *et al*: **nab-Sirolimus for Patients With Malignant Perivascular Epithelioid Cell Tumors**. *J Clin Oncol* 2021, **39**(33):3660-3670. https://doi.org/10.1200/jco.21.01728
9. Yates DH: **mTOR treatment in lymphangioleiomyomatosis: the role of everolimus**. *Expert Rev Respir Med* 2016, **10**(3):249-260. https://doi.org/10.1586/17476348.2016.1148603
10. Cao B, Huang Y: **Malignant perivascular epithelioid cell tumor (PEComa) of the uterus**. *BMC Womens Health* 2022, **22**(1):523. https://doi.org/10.1186/s12905-022-02119-9
11. Sanfilippo R, Jones RL, Blay JY, Le Cesne A, Provenzano S, Antoniou G, Mir O, Fucà G, Fumagalli E, Bertulli R *et al*: **Role of Chemotherapy, VEGFR Inhibitors, and mTOR Inhibitors in Advanced Perivascular Epithelioid Cell Tumors (PEComas)**. *Clin Cancer Res* 2019, **25**(17):5295-5300. https://doi.org/10.1158/1078-0432.Ccr-19-0288
12. Djerroudi L, Masliah-Planchon J, Brisse HJ, El Zein S, Helfre S, Tzanis D, Hamzaoui N, Bonnet C, Laurence V, Bonvalot S *et al*: **Metastatic Malignant Perivascular Epithelioid Cell Tumors With Microsatellite Instability Within Lynch Syndrome Successfully Treated With Anti-PD1 Pembrolizumab**. *JCO Precis Oncol* 2023, **7**:e2200627. https://doi.org/10.1200/po.22.00627
13. Liapi A, Mathevet P, Herrera FG, Hastir D, Sarivalasis A: **VEGFR Inhibitors for Uterine Metastatic Perivascular Epithelioid Tumors (PEComa) Resistant to mTOR Inhibitors. A Case Report and Review of Literature**. *Front Oncol* 2021, **11**:641376. https://doi.org/10.3389/fonc.2021.641376
14. Utpatel K, Calvisi DF, Köhler G, Kühnel T, Niesel A, Verloh N, Vogelhuber M, Neu R, Hosten N, Schildhaus HU *et al*: **Complexity of PEComas : Diagnostic approach, molecular background, clinical management**. *Pathologe* 2020, **41**(Suppl 1):9-19. https://doi.org/10.1007/s00292-019-0612-5
15. Zagardo V, Ferini G: **Is there any role for radiotherapy in the management of uterine perivascular epithelioid cell tumors (PEComas)?** *Arch Gynecol Obstet* 2024, **310**(3):1789-1791. https://doi.org/10.1007/s00404-024-07578-z
16. Garzon S, Caliò A, Ferrari FA, Iannicello CQ, Zorzato PC, Bosco M, Piazzola E, Martignoni G, Laganà AS, Mariani A *et al*: **Uterine perivascular epithelioid cell tumors (PEComa) and the accuracy of proposed classification systems in predicting the malignant versus non-malignant behavior**. *Gynecol Oncol* 2024, **188**:35-43. https://doi.org/10.1016/j.ygyno.2024.06.007
17. Gantzer J, Toulmonde M, Severac F, Chamseddine AN, Charon-Barra C, Vinson C, Hervieu A, Bourgmayer A, Bertucci F, Ryckewaert T *et al*: **PEC-PRO: A new prognostic score from a series of 87 patients with localized perivascular epithelioid cell neoplasms (PEComas) treated with curative intent**. *Cancer* 2024, **130**(13):2304-2314. https://doi.org/10.1002/cncr.35277
18. Osei DA, Alvandi F, Brooks JS, Ogilvie CM: **PEComa of the Upper Extremity: A Unique Case and Description of an Initial Response to Neoadjuvant Chemotherapy**. *Sarcoma* 2007, **2007**:53056. https://doi.org/10.1155/2007/53056
19. Saluja K, Thomas J, Zhang S, Sturgis EM, Jain KS, Prieto VG, El-Naggar AK, Bell D: **Malignant perivascular epithelioid cell tumor of the oropharynx with strong TFE3 expression mimicking alveolar soft part**

 doi:10.20944/preprints202603.1475.v1

sarcoma: a case report and review of the literature. *Hum Pathol* 2018, **76**:149-155. https://doi.org/10.1016/j.humpath.2017.11.016

20. Kirste S, Kayser G, Zipfel A, Grosu AL, Brunner T: **Unresectable hepatic PEComa: a rare malignancy treated with stereotactic body radiation therapy (SBRT) followed by complete resection**. *Radiat Oncol* 2018, **13**(1):28. https://doi.org/10.1186/s13014-018-0974-5
21. Yamashita K, Fletcher CD: **PEComa presenting in bone: clinicopathologic analysis of 6 cases and literature review**. *Am J Surg Pathol* 2010, **34**(11):1622-1629. https://doi.org/10.1097/PAS.0b013e3181f5974f
22. Cole DW, Menge TD, Renati S, Bresler SC, Patel RM, Fullen DR, Hamp LM: **Primary cutaneous malignant perivascular epithelioid cell tumor: Case of a rare tumor with review of the literature**. *J Cutan Pathol* 2021, **48**(8):1088-1093. https://doi.org/10.1111/cup.14034
23. Elousrouti LT, Mouaddine A, Fadlallah I, Elhitmy S, Elloudi S, Mernissi F, Elidrissi M, Hammas N, Elfatemi H, Chbani L: **Primary Cutaneous Malignant Perivascular Epithelioïd Cell Tumor (PEComa): Case Report With Review of the Literature**. *Clin Pathol* 2023, **16**:2632010x231178629. https://doi.org/10.1177/2632010x231178629
24. Fink D, Marsden DE, Edwards L, Camaris C, Hacker NF: **Malignant perivascular epithelioid cell tumor (PEComa) arising in the broad ligament**. *Int J Gynecol Cancer* 2004, **14**(5):1036-1039. https://doi.org/10.1111/j.1048-891X.2004.014549.x
25. Greveling K, Winnepenninckx VJL, Nagtzaam IF, Lacko M, Tuinder SMH, de Jong JMA, Kelleners-Smeets NWJ: **Malignant perivascular epithelioid cell tumor: a case report of a cutaneous tumor on the cheek of a male patient**. *J Am Acad Dermatol* 2013, **69**(5):e262-e264. https://doi.org/10.1016/j.jaad.2013.06.041
26. Jeon IS, Lee SM: **Multimodal treatment using surgery, radiotherapy, and chemotherapy in a patient with a perivascular epithelioid cell tumor of the uterus**. *J Pediatr Hematol Oncol* 2005, **27**(12):681-684. https://doi.org/10.1097/01.mph.0000193475.06870.d5
27. Akay SU, Kesen O, Küçük D, Yener E: **Adrenal PEComa Treated by Surgical Resection and Postoperative Radiotherapy: A Case Report**. *Am J Case Rep* 2024, **25**:e945177. https://doi.org/10.12659/ajcr.945177
28. Komune N, Masuda S, Yasumatsu R, Hongo T, Jiromaru R, Matsuo S, Akiyama O, Tsuchihashi N, Matsumoto N, Yamamoto H *et al*: **Malignant perivascular epithelioid cell tumor mimicking jugular foramen schwannoma: A case report and literature review**. *Heliyon* 2020, **6**(1):e03200. https://doi.org/10.1016/j.heliyon.2020.e03200
29. Liu CH, Chao WT, Lin SC, Lau HY, Wu HH, Wang PH: **Malignant perivascular epithelioid cell tumor in the female genital tract: Preferred reporting items for systematic reviews and meta-analyses**. *Medicine (Baltimore)* 2019, **98**(2):e14072. https://doi.org/10.1097/md.0000000000014072
30. Folpe AL, Goodman ZD, Ishak KG, Paulino AF, Taboada EM, Meehan SA, Weiss SW: **Clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres: a novel member of the perivascular epithelioid clear cell family of tumors with a predilection for children and young adults**. *Am J Surg Pathol* 2000, **24**(9):1239-1246. https://doi.org/10.1097/00000478-200009000-00007
31. Fukunaga M: **Perivascular epithelioid cell tumor of the uterus: report of four cases**. *Int J Gynecol Pathol* 2005, **24**(4):341-346. https://doi.org/10.1097/01.pgp.0000168515.83557.89
32. Hornick JL, Fletcher CD: **Sclerosing PEComa: clinicopathologic analysis of a distinctive variant with a predilection for the retroperitoneum**. *Am J Surg Pathol* 2008, **32**(4):493-501. https://doi.org/10.1097/PAS.0b013e318161dc34
33. Lai CL, Hsu KF, Yu JC, Chen CJ, Hsieh CB, Chan DC, Li HS, Hsu HM: **Malignant perivascular epithelioid cell tumor of the mesentery: a case report and literature review**. *Onkologie* 2012, **35**(3):114-117. https://doi.org/10.1159/000336826
34. Vang R, Kempson RL: **Perivascular epithelioid cell tumor ('PEComa') of the uterus: a subset of HMB-45-positive epithelioid mesenchymal neoplasms with an uncertain relationship to pure smooth muscle tumors**. *Am J Surg Pathol* 2002, **26**(1):1-13. https://doi.org/10.1097/00000478-200201000-00001
35. Silva EG, Deavers MT, Bodurka DC, Malpica A: **Uterine epithelioid leiomyosarcomas with clear cells: reactivity with HMB-45 and the concept of PEComa**. *Am J Surg Pathol* 2004, **28**(2):244-249. https://doi.org/10.1097/00000478-200402000-00013

 doi:10.20944/preprints202603.1475.v1

36. Papoutsis D, Sahu B, Kelly J, Antonakou A: **Perivascular epithelioid cell tumour and mesonephric adenocarcinoma of the uterine cervix: an unknown co-existence**. *Oxf Med Case Reports* 2019, **2019**(1):omy115. https://doi.org/10.1093/omcr/omy115
37. Tam CS, Brown JR, Kahl BS, Ghia P, Giannopoulos K, Jurczak W, Šimkovič M, Shadman M, Österborg A, Laurenti L *et al*: **Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial**. *Lancet Oncol* 2022, **23**(8):1031-1043. https://doi.org/10.1016/s1470-2045(22)00293-5
38. Bajaj A, Abazeed ME: **Molecularly Targeted Radiation Therapy Using mTOR Inhibition for the Management of Malignant Perivascular Epithelioid Cell Tumor (PEComa): A Case Report and Review**. *Adv Radiat Oncol* 2021, **6**(3):100657. https://doi.org/10.1016/j.adro.2021.100657
39. Bonetti F, Martignoni G, Colato C, Manfrin E, Gambacorta M, Faleri M, Bacchi C, Sin VC, Wong NL, Coady M *et al*: **Abdominopelvic sarcoma of perivascular epithelioid cells. Report of four cases in young women, one with tuberous sclerosis**. *Mod Pathol* 2001, **14**(6):563-568. https://doi.org/10.1038/modpathol.3880351
40. de León DC, Pérez-Montiel D, Bandera A, Villegas C, Gonzalez-Conde E, Vilchis JC: **Perivascular epithelioid cell tumor of abdominal origin**. *Ann Diagn Pathol* 2010, **14**(3):173-177. https://doi.org/10.1016/j.anndiagpath.2010.02.007
41. Lao IW, Yu L, Wang J: **Malignant perivascular epithelioid cell tumor (PEComa) of the femur: a case report and literature review**. *Diagn Pathol* 2015, **10**:54. https://doi.org/10.1186/s13000-015-0292-2
42. Wang Y, Li W, Zuo X, Min K, Tang Y, Chen H, Wang W, Zhou Y: **Anti-PD-1 immunotherapy combined with stereotactic body radiation therapy and GM-CSF for the treatment of advanced malignant PEComa: A case report**. *Front Oncol* 2023, **13**:1045119. https://doi.org/10.3389/fonc.2023.1045119
43. Alnajar H, Brickman A, Buckingham L, Arvanitis LD: **Metastatic malignant PEComa of the leg with identification of ATRX mutation by next-generation sequencing**. *Virchows Arch* 2018, **472**(3):499-503. https://doi.org/10.1007/s00428-017-2208-x
44. Ross C, Sharma S, Louca O, Scurr M, Hayes A, Judson I: **A patient presenting with a perivascular epithelioid cell tumor in the broad ligament: a case report**. *J Med Case Rep* 2011, **5**:383. https://doi.org/10.1186/1752-1947-5-383
45. Yin Z, Zhang H, Zhang K, Yue J, Tang R, Wang Y, Deng Q, Yu Q: **Impacts of combining PD-L1 inhibitor and radiotherapy on the tumour immune microenvironment in a mouse model of esophageal squamous cell carcinoma**. *BMC Cancer* 2025, **25**(1):474. https://doi.org/10.1186/s12885-025-13801-0
46. Wang Y, Li W, Zuo X, Min K, Tang Y, Chen H, Wang W, Zhou Y: **Anti-PD-1 immunotherapy combined with stereotactic body radiation therapy and GM-CSF for the treatment of advanced malignant PEComa: a case report**. *Front Oncol* 2023, **18**. https://doi.org/10.3389/fonc.2023.1045119.