# Angiosarcomas and Other Sarcomas of Endothelial Origin

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**KEYWORDS**

• Angiosarcoma • Epithelioid hemangioendothelioma • Vascular sarcoma
• Kaposi sarcoma • VEGF • KDR • FLT4 • Translocation • Organ transplant

**KEY POINTS**

- Vascular sarcomas are rare and collectively affect fewer than 600 people a year in the United States (incidence approximately 2/million).
- Because angiosarcomas, hemangioendotheliomas, and other vascular tumors have unique embryonal derivation, it is not surprising that they have a unique sensitivity pattern to chemotherapy agents.
- Surgery, when possible, remains the primary treatment for angiosarcomas.
- Adjuvant radiation for primary disease seems prudent for at least some angiosarcoma, given the high local-regional recurrence rate of these tumors. Angiosarcomas also have a high rate of metastasis, but it is not clear that adjuvant chemotherapy improves survival.
- Epithelioid hemangioendothelioma is a unique form of sarcoma often presenting as multifocal disease. Most patients can do well with observation alone, although a fraction of patients have more aggressive disease and have difficulties in both local control and metastatic disease.

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- Anthracyclines, alkylating agents such as ifosfamide, are active against at least some vascular sarcomas. Angiosarcomas demonstrate a unique sensitivity to taxanes, and gemcitabine, vinorelbine, and vascular endothelial growth factor (VEGF) or vascular endothelial growth factor receptors (VEGFR) antagonists all have at least some activity against these tumors.
- New targets to consider for therapy include angiopoietin antagonists as well as inhibitors notch or ephrin signaling pathways.

## INTRODUCTION

Of the 14,000 cases of sarcoma diagnosed in the United States annually, sarcomas arising from endothelium and other elements of blood vessels constitute ~2% to 3%, and thus it is likely that fewer than 600 people in the United States are affected each year.[1] This fact is surprising, given the common nature of the benign counterpart of these tumors, hemangiomas, arteriovenous malformations, and other lesions in the population.

In this review, examined are some of the unique characteristics and therapeutic options for patients with tumors that arise from endothelium or its precursors, highlighting the potential of new agents for these tumors. Given the activity of antiangiogenic therapy in both vascular sarcomas and other cancers, new agents will have an impact on both vascular sarcomas and more common cancers.

## SCOPE OF THE DIAGNOSES DISCUSSED

The World Health Organization (WHO) fascicle for soft tissue sarcomas was updated in 2013. The terminology for soft tissue vascular sarcomas is largely unchanged from the prior 2002 version. For bone vascular tumors, changes are anticipated to make terminology for both groups of vascular tumors more consistent. Technically, leiomyosarcoma could be considered vascular sarcomas, because they frequently arise from branches of veins, presumably from smooth muscle cells of blood vessels or their precursors, but they are not discussed here. For space considerations, also not addressed are other tumors that arise from other cellular structures associated with blood vessels (eg, solitary fibrous tumor or intimal sarcoma, each of which has unique biology and sensitivity to systemic therapeutics as well). Finally, there are also vascular components of other tumors such as angiomyolipoma, but these are also not discussed in this review.

## DEMOGRAPHICS

Kaposi sarcoma (KS) is an AIDS (acquired immune deficiency syndrome)-defining diagnosis and happily has been observed less frequently, with the advent of newer generations of anti-retroviral therapy for people with human immunodeficiency virus (HIV) infections. KS also arises in approximately 1 in 200 patients with organ transplants due to immunosuppressive drugs. KS is also seen in an endemic form in patients from the Mediterranean basin and endemically in Africa and the Mideast as well. In the United States, what was a rare cancer became common with the advent of AIDS, with a peak incidence of 10 to 20/1000 HIV-positive patients per year in the United States, but an ~80% decrease with the broad use of multitargeted anti-retroviral therapy.[2] Nonetheless, KS remains more common than other vascular sarcomas.