Ifosfamide for Sarcoma

Vaccine-associated sarcomas (VASs) are locally invasive tumors that may develop in cats at a rate of 0.63 to 3/10,000 cats vaccinated annually. These tumors commonly recur after surgical excision, and up to one fourth may metastasize to the lungs and other sites. Surgical resection with or without radiation therapy remains the primary treatment for VAS in cats, and this combination has helped to improve control of these tumors. Still, treatment failure can result from local recurrence, metastasis, or both, and chemotherapy may be the 1 option that remains when surgery or radiation therapy is not possible or has failed. Few controlled studies have evaluated the response of VASs to various chemotherapeutic agents, and the clinical benefits have not been clearly defined. In this study, the clinical activity and toxic effects of ifosfamide were evaluated.

Ifosfamide is an isomer of cyclophosphamide; its antitumor and toxic effects differ from those of cyclophosphamide due to minor structural differences. It is currently used to treat several types of cancer in humans. In a previous study by the authors, the maximally tolerated dose, doselimiting toxicoses, and pharmacokinetic pattern of ifosfamide in cats with various sarcomas were determined. For this clinical trial, 27 cats with nonresectable, recurrent, or metastatic VASs were treated with IV ifosfamide (900 mg/m² body surface area) over a 30-minute period. Treatments were administered every 3 weeks, and tumor response was assessed after the second treatment. Ifosfamide was found to have antitumor activity against VAS, showing an overall response rate in 11 of 27 cats (47%). Responses lasted from 21 to 133 days (median 70 days). The major toxic effect was transient neutropenia. Adverse gastrointestinal effects (primarily salivation during infusion and inappetence after treatment) were reported in 9 cats (33%). Two cats developed renal toxicosis, and further studies to better define this risk are needed. The authors conclude that ifosfamide should be considered to treat cats with nonresectable, recurrent, or metastatic VASs and should be further evaluated as an adjunctive treatment in cats treated with surgery with or without radiotherapy.

COMMENTARY: The treatment of vaccine-associated sarcomas in cats remains challenging. The combination of radiation therapy and wide surgical excision has improved local control of the disease but recurrence and metastasis are still significant problems. The efficacy and optimal administration strategy of chemotherapeutics has not been clearly defined. The use of ifosfamide, as reported in this Phase II clinical trial, shows some promise but the results must be interpreted with particular caution because of the short duration of the study and the lack of long-term follow-up, particularly for tracking adverse side effects.—Eric R. Pope, DVM, MS, Diplomate ACVS