Concurrent Chemoradiotherapy: What Is the Risk?

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In the Literature

Stibirova K, Treggiari E, Amores-Fuster I, et al. Haematologic toxicity in dogs with mast cell tumours treated with vinblastine/prednisolone chemotherapy with/without radiotherapy. *J Small Anim Pract*. 2019;60(9):534-542.

FROM THE PAGE ...

Chemoradiotherapy is considered the standard of care for certain cancers in humans and, although less common, has been used in veterinary patients. Chemoradiotherapy involves administration of chemotherapeutic agents prior to and during the course of radiation therapy as a radiation sensitizer to improve the response to local radiation, for the treatment of advanced locoregional disease, or for both local and systemic effects on tumors with a high metastatic potential.

Patients with incompletely excised high-grade or metastatic tumors require adjunctive therapy (ie, radiation and chemotherapy) to provide both adequate local and systemic control of their tumors. Although using these treatment modalities simultaneously can shorten overall treatment time, the risk for hematologic toxicity can be increased. This study aimed to determine whether dogs with microscopic mast cell tumors treated with radiation therapy and vinblastine/prednisolone demonstrated increased myelosuppression as compared with dogs treated with only vinblastine/prednisolone.

Forty-three dogs were treated with a combination of radiation therapy and vinblastine/prednisolone (RT/VBL/Pred); another 43 dogs were treated with vinblastine/prednisolone alone (VBL/Pred). Eight dogs (19%) in the RT/VBL/Pred group experienced neutropenia (6 VCOG [Veterinary Cooperative Oncology Group] grade I, 1 VCOG grade II, and 1 VCOG grade IV neutropenia) that resulted in a delay of chemotherapy, and 1 dog had a 10% dose reduction. Ten dogs (23%) in the VBL/Pred group experienced neutropenia (4 VCOG grade I, 2 VCOG grade II, and 4 VCOG grade III neutropenia), necessitating a dose delay in 10 dogs and a 10% dose reduction in 1. There was no significant difference in the frequency of neutropenia between the RT/VBL/Pred and VBL/Pred groups. The authors state that the study may have been underpowered to detect a difference.

Although no increased risk for myelosuppression was shown when radiation therapy was administered simultaneously with vinblastine and prednisolone, this may not be the case when other chemotherapy agents are used. Other factors that can influence the risk for myelosuppression when combining radiation with chemotherapy include the radiation protocol (ie, number of fractions and total radiation dose) and the amount of bone marrow in the radiation field. In humans, a major factor associated with neutropenia or thrombocytopenia during radiation therapy is the percent of marrow being irradiated.

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… TO YOUR PATIENTS

Key pearls to put into practice:

1. Treating dogs concurrently with radiation and vinblastine can decrease overall treatment time without increasing the risk for myelosuppression, but different radiation protocols may not have the same result.
2. There may be an increased risk for myelosuppression associated with concurrent radiation therapy and chemotherapy when other chemotherapy agents are used and a greater amount of bone marrow is being irradiated.
3. Multimodal cancer therapy must be carefully planned and pet owners educated about the risk versus benefit for the patient.

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Suggested Reading

Hume KR, Johnson JL, Williams LE. Adverse effects of concurrent carboplatin chemotherapy and radiation therapy in dogs. *J Vet Intern Med*. 2009;23(1):24-30.

Seiwert TY, Salama JK, Vokes EE. The concurrent chemoradiation paradigm—general principles. *Nat Clin Pract Oncol*. 2007;4(2):86-100.

Veterinary Cooperative Oncology Group—common terminology criteria for adverse events (VCOG-CTCAE) following chemotherapy or biological antineoplastic therapy in dogs and cats v1.1. *Vet Comp Oncol*. 2016;14(4):417-446.

Selarid™
(selamectin)

Topical Parasiticide For Dogs and Cats

BRIEF SUMMARY:
See Package Insert for full Prescribing Information

CAUTION:
US Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATIONS:
Selarid is recommended for use in dogs six weeks of age or older and cats eight weeks of age and older for the following parasites and indications:
Dogs:
Selarid kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mite (*Otodectes cynotis*) infestations. Selarid also is indicated for the treatment and control of sarcoptic mange (*Sarcoptes scabiei*) and for the control of tick infestations due to *Dermacentor variabilis*.
Cats:
Selarid kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mite (*Otodectes cynotis*) infestations. Selarid is also indicated for the treatment and control of roundworm (*Toxocara cati*) and intestinal hookworm (*Ancylostoma tubaeforme*) infections in cats.

WARNINGS:
Not for human use. Keep out of the reach of children.
In humans, Selarid may be irritating to skin and eyes. Reactions such as hives, itching and skin redness have been reported in humans in rare instances. Individuals with known hypersensitivity to Selarid should use the product with caution or consult a health care professional. Selarid contains isopropyl alcohol and the preservative butylated hydroxytoluene (BHT). Wash hands after use and wash off any product in contact with the skin immediately with soap and water. If contact with eyes occurs, then flush eyes copiously with water. In case of ingestion by a human, contact a physician immediately. The safety data sheet (SDS) provides more detailed occupational safety information. For a copy of the SDS or to report adverse reactions attributable to exposure to this product, call 1-866-591-5777.
Flammable – Keep away from heat, sparks, open flames or other sources of ignition.
Do not use in sick, debilitated or underweight animals (see SAFETY).

PRECAUTIONS:
Prior to administration of Selarid, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. Selarid is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, Selarid is not effective for microfilariae clearance.
Hypersensitivity reactions have not been observed in dogs with patent heartworm infections administered three times the recommended dose of selamectin solution. Higher doses were not tested.

ADVERSE REACTIONS:
Pre-approval clinical trials:
Following treatment with selamection solution, transient localized alopecia with or without inflammation at or near the site of application
was observed in approximately 1% of 691 treated cats. Other signs observed rarely (≤0.5% of 1743 treated cats and dogs) included vomiting, loose stool or diarrhea with or without blood, anorexia, lethargy, salivation, tachypnea, and muscle tremors.
Post-approval experience:
In addition to the aforementioned clinical signs that were reported in pre-approval clinical trials, there have been reports of pruritus, urticaria, erythema, ataxia, fever, and rare reports of death. There have also been rare reports of seizures in dogs (see **WARNINGS**).

SAFETY:
Selamectin solution has been tested safe in over 100 different pure and mixed breeds of healthy dogs and over 15 different pure and mixed breeds of healthy cats, including pregnant and lactating females, breeding males and females, puppies six weeks of age and older, kittens eight weeks of age and older, and avermectin-sensitive collies. A kitten, estimated to be 5–6 weeks old (0.3 kg), died 8 ½ hours after receiving a single treatment of selamectin solution at the recommended dosage. The kitten displayed clinical signs which included muscle spasms, salivation and neurological signs. The kitten was a stray with an unknown history and was malnourished and underweight (see **WARNINGS**).
DOGS: In safety studies, selamectin solution was administered at 1, 3, 5, and 10 times the recommended dose to six-week-old puppies, and no adverse reactions were observed. The safety of selamectin solution administered orally also was tested in case of accidental oral ingestion.
Oral administration of selamectin solution at the recommended topical dose in 5- to 8-month-old beagles did not cause any adverse reactions.
In a pre-clinical study selamectin was dosed orally to ivermectin-sensitive collies. Oral administration of 2.5, 10, and 15 mg/kg in this dose escalating study did not cause any adverse reactions; however, eight hours after receiving 5 mg/kg orally, one avermectin-sensitive collie became ataxic for several hours, but did not show any other adverse reactions after receiving subsequent doses of 10 and 15 mg/kg orally. In a topical safety study conducted with avermectin-sensitive collies at 1, 3 and 5 times the recommended dose of selamectin solution, salivation was observed in all treatment groups, including the vehicle control. Selamectin solution also was administered at 3 times the recommended dose to heartworm infected dogs, and no adverse effects were observed.
CATS: In safety studies, selamectin solution was applied at 1, 3, 5, and 10 times the recommended dose to six-week-old kittens. No adverse reactions were observed. The safety of selamectin solution administered orally also was tested in case of accidental oral ingestion. Oral administration of the recommended topical dose of selamectin solution to cats caused salivation and intermittent vomiting. Selamectin solution also was applied at 4 times the recommended dose to patent heartworm infected cats, and no adverse reactions were observed.
In well-controlled clinical studies, selamectin solution was used safely in animals receiving other frequently used veterinary products such as vaccines, anthelmintics, antiparasitics, antibiotics, steroids, collars, shampoos and dips.

STORAGE CONDITIONS: Store below 86°F (30°C).

HOW SUPPLIED: Available in seven separate dose strengths for dogs and cats of different weights (see **DOSAGE**). Selarid for puppies and kittens is available in cartons containing 3 single dose applicators.
Selarid for cats and dogs is available in cartons containing 6 single dose applicators.
Approved by FDA under ANADA # 200-663

Manufactured by:
Norbrook Laboratories Limited
Newry, BT35 6PU, Co. Down,
Northern Ireland

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