AAHA Oncology Guidelines for Dogs and Cats

Jaci Christensen, BAS, LVT, VTS (Oncology),† Kim Johnson, DVM, DACVIM (Oncology),†
Sue Ettinger, DVM, DACVIM (Oncology), Laura Garrett, DVM, DACVIM (Oncology), Ira Gordon, DVM, DACVR-RO, Shadi Ireifej, DVM, DACVS, Ashley Love, BVMS, DABVP (Feline Practice), Michelle Wisecup, DVM, MBA

ABSTRACT

Primary care veterinarians may diagnose, stage, and treat many canine and feline cancers while providing comprehensive patient health care in their practices. Collaboration between general practitioners and veterinary oncologists can optimize patient care and enhance client engagement, and referral is often necessary, especially in complex cases. These guidelines cover key fundamentals of, and new developments in, cancer diagnosis, staging, and treatment in dogs and cats, including patient supportive care and follow-up assessments. Therapy is based on identifying the tumor type, grade, and stage by using cytologic or histologic evaluation or both, combined with staging diagnostic testing such as imaging and lymph node sampling. Therapy is most often multimodal and may include chemotherapy, immunotherapy, radiation therapy, and surgery, along with nutritional support and pain management. Methods to protect patient, team, and client safety as related to handling cytotoxic chemotherapeutics are emphasized. In addition, strengthening the training, education, and responsibilities of veterinary technicians is encouraged to promote team engagement and practice efficiency, which is highly beneficial when managing complex cancer cases. These guidelines also highlight how to achieve successful collaboration between all members of primary care and referral practice teams, cover tools that can aid in referral to or consultation with veterinary oncologists, and describe communication skills that enhance client understanding and compliance. (*J Am Anim Hosp Assoc* 2026; 63:■■■–■■■. DOI 10.5326/JAAHA-MS-7549)

AFFILIATIONS

Texas A&M University, Veterinary Medical Teaching Hospital, College Station, Texas (J.C.); Mission Pet Health, Clinical Consultation Specialist, Memphis, Tennessee (K.J.); Dr Sue Cancer Vet PLLC and Guardian Veterinary Specialists, Brewster, New York (S.E.); University of Illinois College of Veterinary Medicine, Urbana, Illinois (L.G.); Veterinary Referral Associates, Gaithersburg, Maryland (I.G.); VetTriage, Las Vegas, Nevada (S.I.); Las Vegas Cat Hospital, Las Vegas, Nevada (A.L.); The Ohio State University, Columbus, Ohio (M.W.)

CONTRIBUTING REVIEWERS

Danielle DeCormier, LVT, VTS (Oncology) (MedVet, Whitmore Lake, Michigan); Michael Henson, DVM, PhD, DACVIM (Oncology) (University of Minnesota, St. Paul, Minnesota); Douglas Thamm, VMD, DACVIM (Oncology) (Colorado State University, Fort Collins, Colorado)

Correspondence: guidelines@aaha.org

†Jaci Christensen and Kim Johnson are the cochairs of the AAHA Oncology Guidelines task force.

These guidelines were prepared by a task force of experts convened by the American Animal Hospital Association. This document is intended as a guideline only, not an AAHA Standard of Care. These guidelines and recommendations should not be construed as dictating an exclusive protocol, course of treatment, or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to each individual practice setting. Evidence-guided support for specific recommendations has been cited whenever possible and appropriate. Other recommendations are based on practical clinical experience and a consensus of expert opinion. Further research is needed to document some of these recommendations. Drug approvals and labeling are current at the time of writing but may change over time. Because each case is different, veterinarians must base their decisions on the best available scientific evidence in conjunction with their own knowledge and experience.

Conflict of interest statement: Dr. Johnson is a key opinion leader for Hill's Pet Nutrition and was on a Zoetis Advisory Board. Dr. Ettinger has received speaking and consultation fees and honoraria from Antech, Dechra, Hills Jaguar Animal Health, Nutramax Laboratories, QBiotics Group, Virbac, Volition Veterinary, and Zoetis. Dr. Gordon is a scientific advisor for Jenga Biosciences.

AAHA gratefully acknowledges our task force facilitator, Mia Cary, DVM (she/her), of Cary Consulting, and Theresa Entriken, DVM, for developmental editing assistance.

The 2026 AAHA Oncology Guidelines for Dogs and Cats are generously supported by CareCredit, Hill's Pet Nutrition, Merck Animal Health, and Zoetis.

GUIDELINES TABLE OF CONTENTS

Sections

Tables

Abbreviations and acronyms

ATLS, acute tumor lysis syndrome; AUS, abdominal ultrasound; CA, conditionally approved; CBC, complete blood count; CID, chemotherapy-induced diarrhea; CINV, chemotherapy-induced nausea and vomiting; CNS, central nervous system; CT, computed tomography; FNA, fine-needle aspiration; GI, gastrointestinal; HD, hazardous drug; HSA, hemangiosarcoma; MCT, mast cell tumor; MST, median/mean survival time; MTD, maximally tolerated dose chemotherapy; NSAID, nonsteroidal anti-inflammatory drug; OVH, ovariohysterectomy; PD, progressive disease; PD-1, programmed cell death protein 1; PPE, personal protective equipment; PR, partial response; RT, radiation therapy; SHC, sterile hemorrhagic cystitis; SRT, stereotactic radiation therapy; TKI, tyrosine kinase inhibitor; USDA, United States Department of Agriculture; USP, United States Pharmacopeia; VCPR, veterinarian-client-patient relationship.

Introduction

Many clients anticipate that their primary care veterinarian is equipped to diagnose and treat their pet's cancer. These guidelines help veterinarians adopt an up-to-date and structured approach to managing each patient. The guidelines offer an overview of common canine and feline cancers, diagnostic testing and tumor staging recommendations, therapeutic options, and patient and caregiver safety in handling chemotherapeutic agents. Optimizing technicians' training and responsibilities, collaboration with and referral to oncologists, and communication strategies that are especially helpful when consulting with clients whose pets have cancer are also covered. All members of veterinary health care teams can work together to enhance clients' confidence in their practices to care for pets with cancer.

Section 1: Overview of Common Cancers

Overview of Common Cancers

Cancer is the leading cause of morbidity and mortality, affecting 50% of dogs and ~30% of cats over the age of 10 years.[1] It can arise in virtually any tissue and organ within the body. Understanding the common types of cancer in dogs and cats is essential for early detection, timely diagnosis, and appropriate treatment. Regular veterinary check-ups, awareness of clinical signs, and client education play critical roles in managing cancer in pets.

Commonly diagnosed canine and feline cancers are listed in **Table 1.1** and **Table 1.2**, respectively. These tables are intended for use as quick references and to facilitate initial conversations between practitioners and clients. They do not fully capture the variability in tumor behavior, cannot be used to predict the outcome in individual patients, and do not serve as primary resources for clinical decision making.

TABLE 1.1
Common Cancers of Dogs

Tumor Type *[Common Primary Anatomic Locations]*	**Behavior**	**Staging Tests**	**Treatment Options**	**Prognosis**	**Known Negative Prognostic Factors**
Anal sac carcinoma	• Locally aggressive; complete excision is difficult owing to proximity to anal sphincter. Metastatic rate is highly variable: <40% to >90%. LN metastasis is seen more commonly and earlier than systemic (liver, bone, pelvis, lung) metastasis. • Often slowly progressive unless diffuse metastasis is present at diagnosis or renal function is compromised from hypercalcemia.	• 3-view thoracic radiographs • AUS +/− abdominal/thoracic CT scan • Ionized calcium	Primary tumor • Surgery with preservation of fecal continence is the best first option. • Lymphadenectomy is an adjunct surgical approach for suspect/confirmed abdominal LN metastatic disease. • Primary RT (palliative or curative intent) can provide good local control for unresectable disease. Systemic treatment • Unproven survival benefit • Carboplatin-based chemotherapy • Mitoxantrone-based chemotherapy • Toceranib phosphate • NSAIDs • Metronomic chemotherapy • Bisphosphonates for hypercalcemia	Dogs with advanced systemic metastasis generally have survival times <1 yr. Dogs with surgical intervention can have survival times of 1.5 to >3 yr and cure. Local and nodal disease impacts quality of life early in the disease process.	• Hypercalcemia • Systemic (non-nodal) metastasis • Primary tumor size >10 cm^3
Lymphoma **[Multicentric (lymph node, liver, spleen), skin, mucocutaneous, central nervous system, bone, bone marrow, GI, mediastinal]**	• Considered a systemic disease, except for epitheliotropic lymphoma, which may be localized to primary sites (oral, skin) and some extranodal sites. • *All* forms of lymphoma have the potential to be disseminated. Some forms may be indolent and slow to progress (spleen or node). • ATLS is associated with extensive tumor burden.	• Immunophenotyping • Histopathology as indicated (inconclusive cytology, solitary node, slowly enlarging LNs, desire for more detailed histological information) • 3-view thoracic radiographs • Advanced imaging (CT/MRI if CNS involvement is suspected) • AUS	Systemic treatment • Prednisone alone • Single-agent chemotherapy • Multiagent chemotherapy • CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) protocol • +/− stem cell transplantation • +/− half-body RT • Rabacfosadine • Verdinexor	Prednisone alone • MST ~1–2 mo CHOP protocol • MST ~1 yr • Bone marrow transplantation and half-body RT may have an added survival benefit, but length of time is unknown Single agent • Highly variable response and durability, MST <1 yr Rabacfosadine • MST ~6 mo Verdinexor • MST ~2 mo	• T-cell phenotype • Stage V (extra nodal, bone marrow, GI) • Substage b (sick) • High grade, blastic

(Continued on next page)

TABLE 1.1, CONTINUED
Common Cancers of Dogs

Tumor Type *[Common Primary Anatomic Locations]*	Behavior	Staging Tests	Treatment Options	Prognosis	Known Negative Prognostic Factors
Mammary gland cancer	• OVH before first estrus dramatically reduces risk. Risk rises rapidly with additional cycles. • Individual tumors may progress from benign to malignant; the likelihood of malignancy increases with tumor size; dogs may present with multiple tumor types. • Metastatic rate of malignant tumors is likely <50%.	• Primary tumor FNA (may be helpful in ruling out non–mammary gland tumors) • 3-view thoracic radiographs • Regional LN FNA	Primary tumor Single malignant tumors: wide surgical excision with ~2-cm margins +/– deep fascia. Consider chain mastectomy (unilateral vs staged bilateral chain mastectomy) for dogs presenting with multiple tumors or developing multiple tumors over time. Systemic treatment • OVH concurrent with or within 2 yr before tumor removal may improve survival in a subset of dogs. Studies of various chemotherapy protocols have not definitively established a benefit.	• MSTs range widely for malignant tumors. • Consider the 50:50:50:50 rule: ~50% are benign, ~50% are malignant. Of the malignant tumors ~50% can be "cured" with appropriate surgery and ~50% will metastasize.	• Large tumor size • Skin ulceration • LN/distant metastases • High histologic grade • Histologic vascular or lymphatic invasion • Lack of hormone receptor expression • Sarcomas and inflammatory carcinomas are associated with poorer outcomes than carcinomas.
Mast cell tumor **[Skin and subcutaneous tissues]**	• Locally invasive; invasiveness increases with grade. • Metastatic potential (Patnaik system): • Grade 1: metastases are rare • Grade 2: ~20% • Grade 3: 50-100% Tumors may secrete histamine and heparin.	• Pretreatment staging is optional for small tumors exhibiting slow growth. Biopsy to determine histologic grade is advisable for any unresectable, large, or rapidly growing tumor. • FNA cytology of regional LN. • AUS and FNA of spleen or liver if enlarged; if LN metastases or systemic signs are present; or if known grade 3 tumor.	Primary tumor • Surgical excision with 2-cm or proportional margins wide (lateral margins equivalent to the widest measured diameter of the tumor) and 1 fascial plane deep. Wider margins may be necessary for high-grade tumors. • Scar excision may be considered if margins are histologically incomplete. • RT may be considered if adequate margins cannot be achieved or margins are histologically incomplete. • Tigilanol tiglate injection Systemic treatment • Vinblastine-based chemotherapy • CCNU • TKIs • Gilvetmab Ancillary therapy • Consider H1 and H2 blockers for patients with large tumors and/or GI signs.	Primary tumor • Grade 1 tumors and most grade 2 tumors are likely to be permanently controlled by appropriate surgery. • When margins are histologically incomplete, local recurrence rates are ~20–30%. • If wide margins cannot be achieved, RT provides 2 yr local control rates >85%. Metastases • Survival periods are highly variable. Prolonged MSTs and high 1 and 2 yr survival rates have been reported in "high risk" patients receiving prednisone and vinblastine. • TKIs produce a meaningful response rate in grossly measurable tumors; survival data in patients at high risk for metastases have not been reported.	• Large tumors • Higher histologic grades • Advanced LN or distant metastases • Mucous membrane locations • High mitotic index, proliferation indices, microvessel density • c-kit mutation • Histologically incomplete surgical margins • Local recurrence • Systemic illness

(Continued on next page)

TABLE 1.1, CONTINUED
Common Cancers of Dogs

Tumor Type *[Common Primary Anatomic Locations]*	Behavior	Staging Tests	Treatment Options	Prognosis	Known Negative Prognostic Factors
Oral malignant melanoma	• Metastatic rate ~80%, LN then lungs. • ~1/3 lack melanin and may be confused with sarcomas histologically.	• 3-view thoracic radiographs • FNA of regional LN (even if normal size) • Resection of medial retro-pharyngeal, parotid, and mandibular LN provides more complete staging. • CT/MRI facilitate surgical planning, particularly for large and caudal tumors.	Primary tumor • Surgery is generally the best first option. Mandibulectomy or maxillectomy is usually required, plus local LN excision. • Adjuvant RT with coarse fractionation if resection is known or suspected to be incomplete. Systemic treatment • Oncept vaccination • Carboplatin-based chemotherapy • Gilvetmab	• Reported local recurrence rates after surgery alone range from 0-48%. • Majority of measurable tumors treated with RT respond, and complete responses are common. • Local recurrence rate of ~26% when RT is used to treat microscopic residual disease. Reported MSTs when surgery is included in treatment range from 5 to 17 mo. Carboplatin produces responses in measurable disease in 30–50% of patients; studies regarding prolongation of survival are conflicting. Studies regarding the ability of DNA vaccination to prolong survival are conflicting.	• Large tumor size, caudal location, and previous local recurrence are risk factors for local recurrence and survival after surgery or RT. • Elevations in proliferation indices • LN or distant metastasis
Osteosarcoma **[Proximal humerus, distal radius, distal femur, proximal and distal tibia]**	• >90% of dogs have pulmonary micrometastases on presentation, rare skeletal metastases.	Essential • 3-view thoracic radiographs Optional • Bone scintigraphy or radiographic bone survey • Thoracic CT • AUS	Primary tumor • Amputation, limb-sparing surgery, or stereotactic RT • Palliative RT Systemic treatment • Carboplatin- or doxorubicin-based chemotherapy	• Amputation alone: MST ~4 mo • Amputation and chemotherapy: MST ~10–12 mo	• Elevated serum ALP • Proximal humeral location

(Continued on next page)

TABLE 1.1, CONTINUED
Common Cancers of Dogs

Tumor Type *[Common Primary Anatomic Locations]*	Behavior	Staging Tests	Treatment Options	Prognosis	Known Negative Prognostic Factors
Soft tissue sarcoma: mesenchymal tumors including fibrosarcoma, peripheral nerve sheath tumor, and others **[Skin and subcutaneous tissues]**	• Locally invasive; invasiveness increases with grade. • Overall metastatic rate is ~20% and increases with grade: Grade 1 and 2 ~15%, Grade 3 ~50%. Clinically apparent metastases develop relatively late (median ~1 yr).	• 3-view thoracic radiographs • CT/MRI may facilitate surgery for large or fixed tumors and tumors adjacent to key anatomic structures.	Primary tumor • Surgical excision with ≥3 cm margins including a fascial plane below if possible. Amputation may be considered if adequate margins cannot be provided. Scar excision may be considered if margins are histologically incomplete. • RT may be considered if adequate surgical margins could not be provided or margins are histologically incomplete. • Metronomic chemotherapy may improve duration of local control.	Primary tumor • When margins are histologically incomplete, local recurrence rate is ~20–35%. Recurrence rates are likely higher for high grade tumors. • RT for incompletely resected tumors provides local control rates: 75% at 1 yr; median time to local recurrence ~2 yr.[a] Systemic disease • Doxorubicin and other agents are known to produce responses in measurable disease. Data regarding treatment of micrometastases with conventional or metronomic chemotherapy are lacking.	• Local recurrence • Incomplete histologic margins • Large tumors • Metastases • High mitotic index/grade

Splenic hemangiosarcoma
Note: Some splenic masses are benign hematomas and cannot be definitively distinguished from HSA before splenectomy and biopsy.
	• Metastatic rate approaches 100%.
	• Liver is the most common metastatic site.
	• Survival times are highly correlated with clinical stage:
	  • Stage 1: No hemoabdomen; no clinically detectable metastases.
	  • Stage 2: Hemoabdomen, no clinically detectable metastases.
	  • Stage 3: Clinically detectable metastases.
		Essential
		• AUS for intra-abdominal metastases. Liver metastases cannot be definitively distinguished from hyperplastic nodules.
		• 3-view thoracic radiographs
		Optional
		• Echocardiography for concurrent right atrial mass; present in ~9% of dogs presenting for splenic HSA.
			Primary tumor
			• Splenectomy with biopsy of liver nodules
			Systemic treatment
			• Doxorubicin-based conventional chemotherapy and/or metronomic chemotherapy
				• Splenectomy alone: MST ~1.5–3 mo
				• Adjuvant chemotherapy: MST ~3–6 mo
					• Clinical stage

(Continued on next page)

TABLE 1.1, CONTINUED
Common Cancers of Dogs

Tumor Type *[Common Primary Anatomic Locations]*	**Behavior**	**Staging Tests**	**Treatment Options**	**Prognosis**	**Known Negative Prognostic Factors**
Transitional cell carcinoma/ urothelial carcinoma **[Urinary bladder, urethra, prostate]**	• Aggressive with tendency for local invasion and metastasis to regional LNs and lungs, high risk of urinary tract obstruction.	• Physical examination to include rectal exam • 3-view thoracic radiographs • AUS • Cystoscopy • Diagnostic catheterization • BRAF gene mutation test	• NSAIDs: piroxicam • Chemotherapy: mitoxantrone, carboplatin, vinblastine • Intensity-modulated RT	• NSAIDs alone: MST ~6 mo • NSAIDs with chemotherapy: MST ~12 mo • Intensity-modulated RT, NSAIDs, and chemotherapy: MST ~15-18 mo	• Clinical stage
Nasal tumors **[Carcinoma, adenocarcinoma, squamous cell carcinoma, osteosarcoma, fibrosarcoma, undifferentiated sarcoma, lymphoma]**	• Local invasion/ destruction with risk for regional and distant metastasis.	• 3-view thoracic radiographs • LN cytology • CT/MRI • Biopsy	• RT • Chemotherapy: carboplatin, doxorubicin, NSAID (palliative) • Toceranib	• RT: MST ~6-18 mo • Surgery or chemotherapy alone: MST ~3-6 mo	• Clinical stage • Squamous cell carcinoma

ALP, alkaline phosphatase; ATLS, acute tumor lysis syndrome; AUS, abdominal ultrasound; CNS, central nervous system; CT, computed tomography; FNA, fine needle aspirate; GI, gastrointestinal; HSA, hemangiosarcoma; LN, lymph node; MST, median survival time; NSAID, nonsteroidal anti-inflammatory drug; OVH, ovariohysterectomy; RT, radiation therapy; TKI, tyrosine kinase inhibitor.

a Hildebrandt IM, Skinner OT, Mickelson MA, et al. Surgery and postoperative definitive radiotherapy for management of canine soft tissue sarcoma: a multi-institutional retrospective study of 272 dogs (2010-2020). *J Am Vet Med Assoc.* 2024;263(3):1-12.

TABLE 1.2
Common Cancers of Cats

Tumor Type *[Common Primary Anatomic Locations]*	**Behavior**	**Staging Tests**	**Treatment Options**	**Prognosis**	**Known Negative Prognostic Factors**
Lymphoma **[Mediastinum, gastrointestinal, liver, spleen, kidney]**	• Considered a systemic disease except for rare solitary sites (e.g., nasal or skin lymphoma, which can be localized). Some forms may be indolent and slow to progress (e.g., spleen, lymph node, small cell lymphoma).	• FeLV/FIV testing • 3-view thoracic radiographs • AUS • Advanced imaging (CT/MRI if suspected CNS involvement) • Immunophenotype not critical in feline lymphoma	• Prednisolone alone • Prednisolone/ chlorambucil (low-grade GI) • Single-agent chemotherapy: CCNU (lomustine) • Multiagent chemotherapy: COP (cyclophosphamide, vincristine, prednisolone), CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) • RT	Prednisolone alone: • MST ~2–3 mo • Single agents: highly variable response and durability but MST ~4–6 mo CHOP protocols: • MST ~6–9 mo • Nasal lymphoma may have >2 yr controls with RT • Low-grade GI 8 mo to >2 yr	• FeLV+ • Grade/large cell • Stage • Substage b; most cats are b
Mammary gland cancer	• Incidence of feline mammary tumors is dependent on when OVH is performed. Cats who undergo OVH prior to 6 months of age have a 91% reduced risk of developing mammary cancer. • Locally aggressive. • Highly metastatic (80–90% to nodes, liver, lungs).	• 3-view thoracic radiographs • AUS • Regional LN FNA (even if normal size) • CT/MRI for surgical planning	Primary tumor • Surgery if possible. Unilateral radical mastectomy with regional node removal or staged bilateral radical mastectomy with 1 mo between sides (simultaneous bilateral not recommended) Systemic therapy • Chemotherapy value uncertain (doxorubicin, carboplatin, toceranib) • NSAIDs	• Guarded to poor prognosis. • Tumor size: <2 cm MST >3 years • Tumor size: >3 cm MST 4-12 mo • Surgery +/- chemotherapy: MST ~1 yr	• Tumor size >3cm • Lymphatic invasion • Higher clinical stage • High histologic grade • HER2 expression

(Continued on next page)

TABLE 1.2, CONTINUED
Common Cancers of Cats

Tumor Type *[Common Primary Anatomic Locations]*	Behavior	Staging Tests	Treatment Options	Prognosis	Known Negative Prognostic Factors
Squamous cell carcinoma **[Oral (mandible, maxilla, sublingual, gingival), retrobulbar, oropharynx, cutaneous, nasal planum, ear pinna, multifocal cutaneous in situ (Bowens)]**	• Locally aggressive. • Low metastatic rate. • Oral tends to be extremely aggressive. • Cutaneous is often slowly progressive.	• 3-view thoracic radiographs vs thoracic CT • Regional LN aspirate (even if normal size) • Biopsy • CT scan vs skull/oral radiographs • CT/MRI for surgical or RT planning	Oral primary tumor • Surgery if possible (small rostral lesions, but variable outcomes with eating). • Adjuvant RT if resection is known or suspected to be incomplete. • Primary RT (palliative or curative intent) provides poor local control for unresectable disease even if combined with chemotherapy. Systemic treatment (unproven survival benefit) • Carboplatin • Mitoxantrone • Toceranib phosphate • NSAIDs • Metronomic chemotherapy • Bisphosphonates (zoledronate, pamidronate and others) may help with bone integrity. Cutaneous primary tumor • Surgery, if possible, provides the best chance for cure. • Adjuvant RT if resection is known or suspected to be incomplete. • Strontium (for very superficial lesions). • Photodynamic therapy, electrochemotherapy are local options. • Topical imiquimod for early superficial lesions.	Oral • MST ~ 3–6 mo Cutaneous • Outcome associated with stage. • Early superficial lesions can be cured. • Bulky invasive lesions often cannot be surgically removed, rendering RT outcomes much more guarded.	• Oral location • Stage • Invasion beyond basement membrane (cutaneous)

(Continued on next page)

TABLE 1.2, CONTINUED
Common Cancers of Cats

Tumor Type *[Common Primary Anatomic Locations]*	Behavior	Staging Tests	Treatment Options	Prognosis	Known Negative Prognostic Factors
Soft tissue sarcomas (including injection site sarcoma) **[Cutaneous and subcutaneous tissue, interscapular, hind limb, flank]**	• Locally aggressive, especially injection site, with high (>50%) local recurrence. • Non-injection site sarcoma is less aggressive and location and grade dependent. Metastatic rate is <10% for low grade, non–injection site. • Metastatic rate >25% for high grade and/or injection-site sarcoma.	• CT/MRI for surgical and RT planning • Biopsy • +/- 3-view thoracic radiographs and AUS	Primary tumor • Surgery, if possible, is the initial treatment of choice. Preoperative radiation should be considered if gross disease is in a complex anatomic location. Adjuvant RT if resection is known or suspected to be incomplete. • Primary RT alone provides poor local control for unresectable disease but can provide palliation of signs. Systemic treatment • Doxorubicin • Carboplatin • NSAIDs • Metronomic chemotherapy	Injection site sarcoma • Median DFI <12 mo for wide surgery alone, even shorter for larger, more marginally excised tumors. Surgical cures possible with radical surgery (amputation or hemipelvectomy). • MST 1–2 yr with surgery and RT (pre- or postoperative) or surgery and doxorubicin.	• Injection-site location • Size ≥2 cm • Mitotic index >6 • Incomplete surgical excision • Malignant fibrous histiocytoma histology
Nasal tumors **[lymphoma, carcinoma, adenocarcinoma]**	• Local invasion/ destruction with risk for regional and distant metastasis.	• FeLV/FIV testing • 3-view thoracic radiographs • AUS • CT/MRI • Biopsy	• RT • CCNU (lomustine), COP or CHOP for lymphoma • NSAID/carboplatin for carcinoma	• MST 1–2 yr or normal lifespan for lymphoma • MST ~6–15 mo for carcinoma/ adenocarcinoma	• Clinical stage
Mast cell tumor **[Visceral, cutaneous (head, neck, trunk, limbs)]**	Intestine • Aggressive with metastasis to mesenteric LN and liver ± spleen, lung, and bone marrow. Visceral organ • Reported in ~20% of cats with cutaneous MCT.[a,b,c] Skin • Mastocytic: generally benign.	• AUS • FNA • Biopsy	• Surgery +/- chemotherapy with anecdotal efficacy • Medical therapy alone (lomustine, toceranib) associated with response rates >50%	Intestine • MST ~6 mo (one study has reported median survival times of 17+ months)[d] Spleen • MST ~ 1-2 yr Skin • Generally benign with excellent prognosis	• Clinical stage • Histologic grade • Anorexia • Weight loss

AUS, abdominal ultrasound; CNS, central nervous system; CT, computed tomography; DFI, disease-free interval; FeLV, feline leukemia virus; FIV, feline immunodeficiency virus; FNA, fine needle aspirate; MST, median survival time; NSAID, nonsteroidal anti-inflammatory drug; OVH, ovariohysterectomy; RT, radiation therapy.

a Arz R, Chiti LE, Krudewig C, et al. Lymph node metastasis in feline cutaneous low-grade mast cell tumours. *Journal of Feline Medicine and Surgery*. 2023;25(1):1098612X221138468.

b Henry C, Herrera C. Mast cell tumors in cats: Clinical update and possible new treatment avenues. *Journal of Feline Medicine and Surgery*. 2012;15(1):41–7.

c Dobromylskyj M. Feline cutaneous mast cell tumours; where are we now with prognostication? CVE Control & Therapy Series. 2016;284:45–9. Available at https://www.researchgate.net/profile/Melanie-Dobromylskyj/publication/312121164_Feline_cutaneous_mast_cell_tumours_-_where_are_we_now_with_prognostication/links/587006d008aebf17d3a9c2ed/Feline-cutaneous-mast-cell-tumours-where-are-we-now-with-prognostication.pdf. Accessed July 23, 2025.

d Barrett LE, Skorupski K, Brown DC, et al. Outcome following treatment of feline gastrointestinal mast cell tumours. *Vet Comp Oncol*. 2018;16(2):188–93.

Section 2: What's New in Veterinary Oncology

Top 3 Takeaways

1. Veterinary oncology is rapidly advancing, with novel therapeutics providing general practitioners and specialists with a growing arsenal of evidence-based tools to manage cancer, emphasizing individualized care and thoughtful selection of treatment strategies tailored to each patient.
2. Given the constantly evolving market and absence of oversight of cancer screening tests, it is crucial to assess the validity of such diagnostics before adopting their use.
3. Knowing the risks, benefits, costs, and FDA approval or US Department of Agriculture (USDA) licensing status of new oncology drugs is critical to using them appropriately and successfully.

Tremendous growth has occurred in diagnostic and therapeutic offerings in veterinary oncology. Additionally, direct-to-consumer advertising has increased client awareness of these options, which clients then want to discuss with primary care veterinarians. Veterinarians must recognize that regulatory oversight of marketing for veterinary diagnostic tests and many treatments is limited. A wide range of scientific levels of evidence for reliability and efficacy of products exists. Careful review of peer-reviewed publications regarding new tests or therapeutics and weighing the potential costs versus proven benefits of any new offering is crucial. In addition, with new veterinary drugs, it is important to understand the FDA's designation for drugs that have received conditional approval and how it affects the drug's use (see Box: Key Points About Conditionally Approved Drugs). Some products, such as vaccines, are regulated by the USDA (see Box: USDA Regulation of Biologics). Staying informed on licensing and approval regulations ensures that veterinarians provide safe, effective cancer care while avoiding legal risks.

Diagnostics

Many veterinary cancer screening tests are marketed with the stated goals of helping detect and treat cancer early. Assessing the efficacy of such tests requires understanding positive and negative predictive values and how disease prevalence affects those values. At this time, no blood or urine test can conclusively rule in or rule out cancer in a veterinary patient, so these tests must be used with caution to avoid providing a false sense of security or causing undue alarm. Studies are ongoing for some of these tests, with the hope of identifying more precise and accurate ways to leverage them for the benefit of patients.

Two new types of tests have emerged that are intended to aid in cancer diagnosis and treatment:

- *Liquid biopsy.* These blood or urine tests detect substances that may be used as biomarkers and are intended to diagnose, screen for, or monitor cancer.
- *Personalized/precision medicine profiles.* These blood and tumor sample tests use various forms of biologic tumor profiling, which are intended to identify treatments that the tumor may be most susceptible to based on its genome rather than its histology (tumor type).

Key Points About Conditionally Approved Drugs

Conditional approval is a regulatory pathway granted by the FDA for veterinary drugs that have demonstrated complete and acceptable safety and have a "reasonable expectation of effectiveness" when they are used according to the label.[a]

Under this designation, it is a violation of federal law to use these products in a manner other than what is specified on their label. Therefore, during the time a drug is sold under conditional approval, extralabel use is illegal. Extralabel use is allowed only for drugs that are fully approved. Because more than 90% of drugs used in veterinary oncology are not approved in veterinary species and thus are used extralabel, the legal limitations in using conditionally approved drugs are often, and understandably, missed.

An FDA conditionally approved (CA) drug is noted by the drug's trade name followed by CA and a number (DRUG NAME-CA1). For example, CA1 indicates that it is the first CA application for that drug, and CA2 indicates a second CA application for that drug. If a CA drug receives full FDA approval, the CA notation and number are no longer listed. During the conditional approval period, these drugs can be legally marketed and prescribed. This allows veterinarians earlier access to promising medications for conditions where fully approved alternatives do not exist. If the effectiveness standard for full approval is not shown within 5 years, the drug can no longer be sold.

a U.S. Food and Drug Administration. Conditional approval explained: a resource for veterinarians. FDA.gov. 9/17/2020. Available at https://www.fda.gov/animal-veterinary/resources-you/conditional-approval-explained-resource-veterinarians. Accessed May 8, 2025.

USDA Regulation of Biologics

The USDA regulates biologics (e.g., vaccines, monoclonal antibodies) used in veterinary oncology, whereas the FDA oversees chemical-based drugs. USDA-licensed products, such as the Oncept canine melanoma vaccine and gilvetmab (anti–programmed cell death protein 1 [PD-1] monoclonal antibody), are often restricted to specific indications and may be available only through specialists.

USDA-regulated biologics offer valuable options for hard-to-treat cancers, but their efficacy data may be less extensive. Veterinarians must critically assess available evidence and consult specialists as needed. Compliance involves adhering to label instructions and maintaining treatment records. These products enhance therapeutic choices but require careful consideration of their regulatory restrictions and clinical applications.

These are exciting developments; however, at this time, insufficient data exists to conclude whether these tests meaningfully improve outcomes in animals. General practitioners and specialists should be aware of the data and limitations of these tests before recommending or interpreting them.[2]

Choose cancer diagnostic tests and methods wisely. In contrast to drugs, minimal to no regulatory approval process exists for veterinary cancer diagnostics and medical devices. Accordingly, a product's presence in the marketplace does not establish that it has demonstrated accuracy or patient benefit.

Newer Therapeutics

Systemic therapies

Rabacfosadine[3–11] is fully approved by the FDA to treat canine lymphoma. It is a double prodrug of a nucleotide analog that inhibits DNA synthesis by inhibiting DNA polymerases. The drug is administered as a 30-minute IV infusion, given once every 3 weeks for up to five doses. It is generally well tolerated, with gastrointestinal (GI) upset and neutropenia being the main side effects; cutaneous reactions and pulmonary fibrosis are less common but also of note. Publications describe its use in rescue therapy and naive lymphomas. It may also be combined in multidrug protocols. As it is a fully approved drug, extralabel use is permitted. In early studies, dogs with multiple myeloma showed strong therapeutic responses.[12]

Verdinexor[3,5,8,10] is FDA conditionally approved to treat canine lymphoma. It is a selective inhibitor of nuclear export. It is given orally twice a week. Adverse reactions include anorexia, vomiting, diarrhea, and lethargy. In the initial approval study, all 58 dogs had at least one adverse reaction, and 36% of dogs had a severe or life-threatening reaction.[8] Response rates are limited, and studies are ongoing for full FDA approval.

Crofelemer-CA1 is conditionally approved for managing chemotherapy-induced diarrhea in dogs.[13] Crofelemer-CA1 is an oral antisecretory medication used to manage chemotherapy-induced diarrhea in dogs by regulating chloride and water secretion in the GI tract. It works locally in the gut and is minimally absorbed systemically.

Gilvetmab is a caninized monoclonal antibody against canine PD-1, which leads to a decrease in tumor-induced immune suppression and thus improves the immune system's ability to destroy cancer cells.[14] It is conditionally licensed by the USDA for use in dogs with mast cell tumors (MCTs) or melanomas and is available only through veterinary specialists practicing oncology. Studies are ongoing for full licensure.

Cell therapies (e.g., adoptive cell therapy, ELIAS cancer immunotherapy, and chimeric antigen receptor T-cell therapy) are another growing area for cancer treatment, and further research needs to be done.[15–17]

Autologous cancer vaccines (e.g., Torigen) represent a personalized immunotherapeutic approach by using a patient's own tumor tissue to stimulate an immune response. Although they are appealing because of their individualized nature and ease of administration, there remains limited peer-reviewed evidence supporting their efficacy in veterinary oncology. Further research is needed to better understand their clinical benefit, mechanisms of action, and potential role within a multimodal treatment plan.

Local therapies

Tigilanol tiglate[18–20] is an FDA-approved local therapy for nonmetastatic canine MCTs. Cutaneous tumors anywhere on the body can be treated. To treat subcutaneous tumors, they must be located at or distal to the elbow or hock. Restrictions for use also exist for tumor size and total dose. Injection is restricted to intratumoral (avoiding the margins, periphery, and deep to the tumor) and leads to hemorrhagic necrosis of the tumor. Wound healing is usually complete within 4–8 weeks.

Electrochemotherapy[21–26] is another area of research and growth in local tumor treatment. A special unit generates an electrical field to increase cancer cell permeability, which can enhance chemotherapeutic efficacy.

Section 3: Tumor Diagnostics & Staging

Top 3 Takeaways

1. Cancer is frequently treatable or manageable in veterinary patients. A suspicion or diagnosis of cancer should be the beginning and not the end of the diagnostic process.
2. To assess a cancer patient's prognosis and develop an optimal treatment plan, a cytologic or histopathologic diagnosis is needed, and in many cases, it is necessary to determine the tumor stage or tumor grade or both.
3. Appropriate tumor staging tests vary and should be selectively performed based on their diagnostic relevance, prognostic value, and compatibility with the pet's needs and the client's priorities and limitations.

Making the Diagnosis

Suspicion of neoplastic disease in a patient often stems from identifying a mass on physical examination or imaging tests. The type and potential behavior of a mass cannot be determined based solely on palpation or imaging. To assess patient prognosis and develop an optimal treatment plan, a specific diagnosis and in many cases identification of the tumor stage or tumor grade or both is needed (Table 3.1).

Most tumors present as a mass or lump, although many non-neoplastic conditions can present identically. Accordingly, when physical examination or imaging reveals a mass, sampling the mass for microscopic evaluation is indicated.

Cytologic examination of a fine-needle sample (obtained with or without aspiration) of a mass often provides a definitive diagnosis of benign lesions (e.g., dermal cyst, lipoma, inflammation) and round cell tumors (e.g., lymphoma, MCT, plasma cell tumor) and can be helpful in categorizing other masses as mesenchymal or epithelial and at times benign versus malignant. In most cases, submission of cytology samples to a clinical pathologist for interpretation is recommended and may preclude the need for histopathology (Table 3.2).

Obtaining a tissue sample for biopsy and histopathology can provide a definitive diagnosis in nearly all accessible masses (Table 5.7). It also frequently provides additional information that cytology cannot (Table 3.3), such as tumor grade, mitotic index, and invasiveness that may impact prognosis and treatment recommendations.

Ancillary Diagnostic Tests

In some cases, a mass may not be amenable to sampling, initial test results may be inconclusive, or no mass lesion exists, but cancer is suspected. In these cases, tests such as organ sampling (e.g., bone marrow or splenic aspirates), immunohistochemistry, proliferation markers, special tissue stains, polymerase chain reaction for antigen receptor rearrangement, and flow cytometry can provide additional diagnostic and prognostic information.[27]

Consult with a veterinary pathologist or oncologist to identify which ancillary tests may be indicated, how to perform them, and how they might be beneficial.

Staging

The staging process identifies the extent and distribution of cancer in a patient. For solid tumors, such as sarcomas and carcinomas, this usually involves the size of a patient's local disease and whether regional or distant metastasis is present (Table 3.1).

Evaluating locoregional disease starts with a physical examination to determine the primary tumor's size and appearance and its mobility or fixation to adjacent tissues. If the neoplasm is internal or a concern exists about bone or other tissue involvement, ultrasonography, radiography, computed tomography (CT), or MRI may be needed to assess the extent of local disease. It is best practice for a board-certified veterinary radiologist to review the images.

TABLE 3.1
Tumor Grade and Stage Features

	Tumor Grade	Tumor Stage
Definition	Describes the microscopic appearance of cancer cells and tissue	Describes the size and extent of local disease and presence of regional and distant metastasis
Features of low grade/stage	Well-differentiated cells that closely resemble normal tissue with minimal invasion or disruption of surrounding normal tissue	Small tumors without evidence of regional and/or distant metastasis
Features of high grade/stage	Poorly differentiated cells without normal tissue architecture or pattern	Large/infiltrative tumors or tumors with regional and/or distant metastasis

TABLE 3.2
Indications for In-Clinic Versus Diagnostic Laboratory Cytologic Examination (Selected Examples)

Cytologic Examination In-Clinic by a General Practitioner or Specialist	Cytologic Examination by a Clinical Pathologist (Typically After Initial Review by a General Practitioner or Specialist)
Clinician is confident in cytologic diagnosis (e.g., mast cell tumor)	Clinician is uncertain of malignancy or cell type
Client financial constraints	No client financial constraints
Sufficient information has been obtained to recommend and plan biopsy	No additional diagnostics are planned before instituting therapy
Aspirating a fatty mass, which may be poorly cellular	Additional tumor characterization affects treatment recommendations (e.g., benign vs malignant, cytologic grading)

TABLE 3.3
Overview of Cytologic Versus Histopathologic Examination

	Cytologic Examination	Histopathologic Examination
Sampling	Minimally invasive, often requires no sedation or anesthesia	Curative-intent surgery vs several incisional biopsy options (e.g., needle core, punch, wedge)
Results turnaround time	0–2 days	3–7 days
Information provided	• Epithelial, mesenchymal, or round cell appearance • Benign vs malignant	• Specific tumor histology in most cases • Benign vs malignant with higher confidence than cytology • Width of surgical margins • Tumor grade +/− other prognostic factors (if relevant for that specific tumor type)
Allows grading	No (rare exceptions for cytologic grading schemes)	Yes
Allows determination of tumor type	Commonly allows determination of tumor category (e.g., round cell, epithelial, and mesenchymal) and sometimes allows a specific diagnosis	Nearly all tumors (special stains or immunohistochemistry may be required)

Carefully assess regional lymph nodes by palpation and, when indicated, further evaluate lymph nodes with imaging tests and cytologic or histopathologic examination. Evaluating lymph nodes by palpation and size are not always reliable indicators of metastasis. Lymph nodes may be enlarged because of metastatic disease or non-neoplastic causes such as infection or other inflammatory processes. Similarly, normal-sized lymph nodes may harbor metastatic disease. To more accurately determine whether lymph node metastasis has occurred, perform fine-needle aspiration (FNA) or biopsy. Cytologic or histopathologic examination of these samples provides a more definitive diagnosis and allows identification of metastatic cells. This approach is critical for accurate staging and treatment planning in patients with cancer.

Assess a patient's systemic health status by obtaining a minimum database, which includes a complete blood count (CBC), chemistry panel, urinalysis, and viral testing in cats (feline leukemia virus/feline immunodeficiency virus). For potentially malignant tumors, screen for cancer spread to distant organs. Confirmed distant metastasis generally implies a worse prognosis and may dramatically affect therapeutic decisions. Staging tests to screen for distant metastasis vary, but the most common staging tests (beyond the physical examination) include thoracic radiography, abdominal ultrasonography, lymph

The 3 P's of Staging Test Decision Making

Prognostic—Perform tests that impact prognosis or treatment recommendations. For example, for canine osteosarcoma, thoracic radiography is important because patients who have pulmonary metastasis have a worse prognosis and limb amputation is recommended with caution. For canine lymphoma, staging with examination of splenic or liver aspirates is unlikely to change the prognosis or treatment, but immunophenotyping tests may.

Practical—If a client has a limited budget for their pet's care, avoid spending the majority on diagnostic testing and leaving little for treatment. Prioritize diagnostic tests that confirm a diagnosis and evaluate the patient's health.

Pertinent—For a specific tumor, screen the sites of most frequent early metastasis. For example, for dogs with an MCT, use FNA and cytology of locoregional lymph nodes, +/− liver and spleen to screen for metastasis versus thoracic radiography, because pulmonary metastasis is less common in these patients. For dogs with osteosarcoma involving a limb, first screen for metastasis with thoracic radiography, but if the dog has an elevated serum alanine aminotransferase, abdominal ultrasound (AUS) may be recommended as part of the workup.

node sampling, and/or CT. The tests selected depend on the tumor type and the impact of potential findings from each test on prognosis or treatment or both. Client education is critical at this step, and clinicians should aim to avoid unnecessary or redundant tests.

Section 4: Client Communication

Top 3 Takeaways

1. To best serve each client and patient, understand that a multitude of life factors affect a client's decision regarding their pet's medical care and remain conscientious of the verbal and nonverbal exchanges between the veterinary team and the client.
2. By providing a safe space for discussion and education, veterinary teams can support each client's decision-making process for their pet's medical care.
3. Veterinarians are no strangers to having difficult and emotional conversations with their clients, and oncologic case management relies on detailed and empathetic discussions—from diagnosis and treatment options to end-of-life expectations and care.

Veterinarians face tremendous pressure while delivering bad news—a frequent occurrence in oncology cases—and it is a common occupational stress factor in the veterinary profession.[28] Relationships created and grown through trust propel patient care.[29] Health care teams establish trust by acknowledging client perspectives and providing nonjudgmental support. Clients who feel understood and validated by their pet's health care providers may be more inclined to accept medical recommendations and adhere to treatment plans.[29] When the deep feelings that people have about their pets are trivialized or ignored or when their concerns are not acknowledged with sincerity and respect, clients can become dissatisfied, disillusioned, and hostile.[30] The best outcomes for the family unit occur when veterinarians can offer an array of options to find the best diagnostic and treatment combination for the patient and client within the context of their needs and abilities.[29] Clients are more engaged in decision making when health care options are presented within a context of pros and cons, expected and unexpected outcomes, anticipated impact on patient diagnosis and prognosis, cost-benefit ratios, and possible additional patient support needs.[31]

Communication skills especially relevant to contextualized care conversations include open-ended inquiry, reflective listening (paraphrasing what a client has expressed back to the client), transparency, and unconditional positive regard (the veterinarian accepts the client for who they are and "meets them" where they are).[31] Perspective taking and perspective seeking are also skills that require drawing upon cultural humility and recognizing that clients view their pets' care journeys through a unique lens that will be influenced by personal, familial, cultural, and societal perspectives on their relationships with animals and the uniqueness of their bond with their pet.[31]

Oncologic case management relies on detailed and empathetic discussion that surrounds the entire patient care conversation—from diagnosis and treatment options to end-of-life expectations and care. General practitioners are encouraged to become acquainted with and consult veterinary oncologists to help guide them in educating clients about the complexities related to their pet's cancer and determining treatment expectations. Oncologists' experience and access to oncological medical literature and educational resources are valuable tools that can be shared with primary care practitioners and clients.

Section 5: Therapeutic Interventions

Top 3 Takeaways

1. Most veterinary cancer patients have treatment options that can improve or extend their quality of life and survival.
2. Once a cancer diagnosis is made, treatment may involve surgery, chemotherapy, immunotherapy, radiation therapy, or a combination of these interventions, and identifying the most appropriate therapeutic approach can be challenging. It includes considering reasonable clinical goals based on the diagnosis and an understanding of the client's priorities and constraints.
3. Although more study and innovation are needed, the emergence of new therapies, including advances in immunotherapy, radiation therapy, and personalized medicine, provides hope that future cancer care becomes more targeted, nuanced, and effective.

Therapeutic Modalities: Chemotherapy

Chemotherapy is commonly used in veterinary cancer medicine and offers a variety of approaches tailored to small animal patients. Conventional chemotherapy, metronomic chemotherapy, and targeted therapies, including tyrosine kinase inhibitors (TKIs), are all available to small animal practitioners and differ in their indications and goals (Table 5.1). To use these modalities effectively, clinicians must understand the basic principles of each approach. This includes knowing the regulatory agency approval or licensing status of the drugs (Section 2) and appropriate extralabel administration techniques, adhering to proper safety protocols for handling chemotherapy agents (see Safety Considerations in this section), and understanding the potential side effects of the drugs (see Chemotherapy Side Effects in this section). Table 5.1 provides an overview of chemotherapeutics and immunotherapeutics with antineoplastic activity that are commonly used in veterinary medicine.

Educating clients about chemotherapy is equally important. It involves setting realistic expectations, discussing potential side effects, and giving guidance on monitoring and home care. Effective communication with clients not only helps manage their concerns but also contributes greatly to the overall success of the treatment plan (see Section 4, Client Communication).

General Principles of Conventional Chemotherapy

Conventional chemotherapy, also known as maximally tolerated dose (MTD) chemotherapy, involves administering chemotherapeutic agents at the highest tolerated dose, with the primary goal of targeting and killing rapidly dividing cancer cells. However, because some normal cells also have a high turnover rate, they can be temporarily damaged by MTD chemotherapy (see Chemotherapy Side Effects).

TABLE 5.1
Overview of Antineoplastic Chemotherapy and Immunotherapy Agents Commonly Used in Veterinary Medicine

Chemotherapy Agent/Anticancer Agent	Principal Indications	Type of Drug	Route of Administration	Toxicities/Side Effects	Special Considerations for Monitoring or Treatment
Asparaginase	• Lymphoma • Leukemia	• Bacterial enzyme	• IM • SC	• Hypersensitivity reaction after administration	Bone marrow suppression is rare; prior administration can increase risk of hypersensitivity; use with caution in patients with prior hypersensitivity, history of pancreatitis.
Carboplatin	• Osteosarcoma • Melanoma • Carcinoma • Sarcoma	• Platinum drug	• IV • Intracavitary	• Myelosuppression • GI upset • Nephrotoxicity	Less nephrotoxic and fewer GI adverse effects compared with cisplatin. Myelosuppression is typically the DLT with a "later nadir." Neutrophil nadir typically occurs around day 10 to 14 (or 21) in dogs and day 7 to 28 in cats.

(Continued on next page)

TABLE 5.1, CONTINUED
Overview of Antineoplastic Chemotherapy and Immunotherapy Agents Commonly Used in Veterinary Medicine

Chemotherapy Agent/Anticancer Agent	Principal Indications	Type of Drug	Route of Administration	Toxicities/Side Effects	Special Considerations for Monitoring or Treatment
Chlorambucil	• Lymphoma • Chronic lymphocytic leukemia • MCT • Transitional cell carcinoma	• Alkylating agent (nitrogen mustard derivative)	• Oral	• Myelosuppression • GI toxicity	Monitoring is essential. Myelosuppression is typically more gradual and may occur 7–14 days after start, and recovery is similar. Severe myelosuppression may occur with chronic use and can take months to years to recover. Frequent blood work monitoring is recommended even with chronic use (every 6–12 weeks). Use disposable chemotherapy-resistant gloves when handling pills and the pet's bodily fluids and waste.
Cyclophosphamide	• Lymphoma • Carcinoma • Sarcoma	• Alkylating agent	• IV • Oral • SC • IP	• Myelosuppression • GI upset • SHC in dogs (rare in cats)	Administer with furosemide in dogs to decrease SHC; educate owners about this side effect and ways to decrease it (frequent walks after treatment, encourage additional access to water for 3 days after treatment). Use disposable chemotherapy-resistant gloves when handling pills and the pet's bodily fluids and waste.
Doxorubicin	• Lymphoma • Osteosarcoma • Hemangiosarcoma • Carcinoma • Sarcoma	• Anthracycline antibiotic	• IV	• Myelosuppression • GI upset • Perivascular damage with extravasation • Myocardial toxicity • Hypersensitivity during administration • Nephrotoxicity (cats)	Vesicant injuries can be severe; contraindicated in dogs with impaired cardiac function or that have reached a total cumulative dose of doxorubicin (180–240 mg/m^2). Use with caution in dogs with MDR1 genetic mutation and breeds predisposed to cardiomyopathy.

(Continued on next page)

TABLE 5.1, CONTINUED
Overview of Antineoplastic Chemotherapy and Immunotherapy Agents Commonly Used in Veterinary Medicine

Chemotherapy Agent/Anticancer Agent	Principal Indications	Type of Drug	Route of Administration	Toxicities/Side Effects	Special Considerations for Monitoring or Treatment
Gilvetmab	• Canine MCT (stages I, II, and III) • Melanoma (stages II and III) (USDA conditionally licensed)	• Monoclonal antibody immune checkpoint inhibitor	• IV	• Lethargy/fatigue • Decreased appetite • Vomiting • Increased liver enzymes	Currently available only to oncologists. Premedicate with diphenhydramine to reduce risk of infusion reaction.
Lomustine (also known as CCNU)	• Lymphoma • MCT • Brain tumors • Histiocytic sarcoma • Hemangiosarcoma	• Alkylating agent	• Oral	• Myelosuppression • Idiosyncratic hepatotoxicity	CBC nadirs in dogs generally occur at day 7 but can vary to 1 to 3 weeks after treatment. In cats, nadir is variable, usually 1–6 weeks. Thrombocytopenia may also occur and is typically cumulative. Use disposable chemotherapy-resistant gloves when handling pills and the pet's bodily fluids and waste.
Mitoxantrone	• Transitional cell carcinoma • Anal sac carcinomas • Carcinomas • Lymphoma	• Antitumor antibiotic	• IV	• Myelosuppression • GI upset • Perivascular damage with extravasation • Nephrotoxicity	Less cardiotoxic than doxorubicin, so commonly used as an alternative to doxorubicin in patients with cardiac dysfunction. In cats, it is less nephrotoxic than doxorubicin and may be a safer option for those with renal insufficiency.
Oncept canine melanoma vaccine	• Malignant melanoma (USDA licensed)	• Xenogeneic DNA vaccine	• Transdermal	• No known contraindications • Transient low-grade fever may be noted • Possible bruising and soreness at vaccination site	Most effective when local disease control has been achieved. Only available from a specialist. Requires special injection device.

(Continued on next page)

TABLE 5.1, CONTINUED
Overview of Antineoplastic Chemotherapy and Immunotherapy Agents Commonly Used in Veterinary Medicine

Chemotherapy Agent/Anticancer Agent	Principal Indications	Type of Drug	Route of Administration	Toxicities/Side Effects	Special Considerations for Monitoring or Treatment
Prednisone/ Prednisolone	• Lymphoma • MCT • Myeloma • Chronic lymphocytic leukemia Noncytotoxic indications are: • Central nervous system tumors • Insulinoma • Management of hypercalcemia	• Glucocorticoid	• Oral	• Polyuria • Polyphagia • Polydipsia • Muscle wasting • Behavioral changes	Steroid hepatopathy with chronic use. Do not use in conjunction with NSAIDs. A washout period between using NSAIDs and steroids may be indicated.
Rabacfosadine	• Lymphoma (FDA approved for canine lymphoma)	• Guanine nucleotide analogue prodrug	• IV	• Decrease or loss of appetite • Vomiting • Diarrhea • Cumulative dermatopathy • Neutropenia • Perivascular irritation upon extravasation • Rare idiopathic pulmonary fibrosis	Recommend being proactive with nausea and appetite stimulant medications. Rare life-threatening pulmonary fibrosis reported. Contraindicated in West Highland white terriers.
Tigilanol tiglate	• MCT (FDA approved for nonmetastatic dermal MCT and SC MCT at or distal to elbow or hock)	• Protein kinase C activator	• IT	Most commonly related to MOA: • Wound formation and swelling • Injection site reactions (pain, swelling, erythema, bruising, lameness in treated limb) • Wound formation may be extensive GI effects: • Hyporexia • Vomiting • Diarrhea	Must be used with concomitant medications (corticosteroid, H1 and H2 blockers) to minimize effects of degranulation; MCT volume ≤10 cm^3 and total dose must not exceed 5 mL/dog and 0.25 mL/kg.

(Continued on next page)

TABLE 5.1, CONTINUED
Overview of Antineoplastic Chemotherapy and Immunotherapy Agents Commonly Used in Veterinary Medicine

Chemotherapy Agent/Anticancer Agent	Principal Indications	Type of Drug	Route of Administration	Toxicities/Side Effects	Special Considerations for Monitoring or Treatment
Toceranib	• MCT (FDA approved for grade 2 and 3 MCT in dogs) • Used extralabel in a variety of canine sarcomas, carcinomas, melanoma, heart-based tumors • In cats MCT, oral SCC	• TKI: Primary targets include KIT, VEGFR2 and PDGFR	• Oral	• Anorexia/hyporexia • Weight loss • Vomiting • Diarrhea • Hypertension • Proteinuria • Cytopenias Less common: • Lameness	Monitoring blood work, body weight, blood pressure, and urinalysis for potential proteinuria is essential. Label dosage for dogs is considered by most clinicians to be higher than is necessary and associated with more side effects. Use disposable chemotherapy-resistant gloves when handling pills and the pet's bodily fluids and waste.
Verdinexor	• FDA conditionally approved for canine lymphoma	• Selective inhibitor of nuclear export	• Oral	Predominantly GI: • Anorexia • Vomiting • Diarrhea • Weight loss • Lethargy Less common: • Polydipsia • Polyuria • Elevated liver enzymes • Thrombocytopenia	Give with food. Use disposable chemotherapy-resistant gloves when handling pills and the pet's bodily fluids and waste.
Vinblastine	• MCT • Lymphoma • Transitional cell carcinoma	• Vinca alkaloid antitubulin agent	• IV	• Myelosuppression (more than vincristine) • Perivascular vesicant • Tends to cause less nausea and vomiting than vincristine	Use with caution in dogs with MDR1 genetic mutation.
Vincristine	• Lymphoma • MCT • Transmissible venereal tumor • Leukemia	• Vinca alkaloid antitubulin agent	• IV	• Myelosuppression (less myelosuppressive than vinblastine) • Perivascular vesicant • Peripheral neuropathy • Ileus (cats)	Use with caution in dogs with MDR1 genetic mutation. For cats that develop neurotoxicity, can substitute vinblastine.

DLT, dose-limiting toxicity; GI, gastrointestinal; IM, intramuscular; IP, intraperitoneal; IT, intratumoral; MCT, mast cell tumor; MDR1, multidrug resistance 1; MOA, method of administration; NSAID, nonsteroidal anti-inflammatory drug; SC, subcutaneous; SCC, squamous cell carcinoma; SHC; sterile hemorrhagic cystitis; TKI, tyrosine kinase inhibitor.

Appropriate Extralabel Drug Use in Veterinary Cancer Patients

Extralabel use of medications is common in veterinary oncology owing to the limited number of drugs specifically approved for animals. For example, toceranib phosphate is FDA approved for MCTs in dogs, but it is often used extralabel for other cancers like anal sac adenocarcinoma and thyroid carcinoma. Veterinarians frequently rely on clinical experience and/or published evidence to apply these treatments to different cancers. Additionally, most chemotherapy drugs used in veterinary medicine, such as doxorubicin and carboplatin, are approved for human use and are administered extralabel in animals. Understanding and appropriately prescribing extralabel treatments is essential to providing optimal care for veterinary cancer patients, and this includes knowing the legal limitations of using FDA CA drugs (see Section 2, What's New in Veterinary Oncology).

This necessitates a recovery period between treatments to allow these normal cell populations, such as those in the bone marrow and GI tract, to recover. MTD chemotherapy is typically administered weekly to every 3 weeks (e.g., CHOP protocols to treat lymphoma or giving carboplatin every 3 weeks to treat osteosarcoma).

Although this approach maximizes tumor cell death and is generally associated with a low chance of serious side effects, the intervals between treatments may also allow for tumor regrowth. Depending on the tumor type being treated and the stage of the disease, MTD chemotherapy may be administered alone or as an adjuvant to surgery or radiation therapy. It is indicated for the treatment of tumors known to be sensitive to drug therapy, such as hematologic malignancies (e.g., lymphoma, leukemia, multiple myeloma), and highly metastatic malignancies, such as osteosarcoma, hemangiosarcoma, and high-grade MCTs.

When conventional chemotherapy is used against solid tumors such as osteosarcoma, it is often applied in an adjuvant setting after primary tumor treatment to slow the progression of occult micrometastatic disease. Occasionally, drugs are also administered in the neoadjuvant setting to downstage a chemosensitive primary tumor (e.g., MCT) before definitive surgery or radiation therapy. Table 5.1 provides an overview of chemotherapeutics and immunotherapeutics with antineoplastic activity that are commonly used in veterinary medicine.

The main objectives of conventional chemotherapy are tumor control, maintaining or improving the patient's quality of life, and improved disease-free interval.

Metronomic Chemotherapy

Metronomic chemotherapy involves the continuous administration of low-dose cytotoxic drugs, typically given orally by the pet caregiver on a daily or every-other-day schedule, usually in combination with nonsteroidal anti-inflammatory drugs (NSAIDs). This approach reduces the tumor's ability to repair damage or adapt to its microenvironment by targeting angiogenesis. Unlike conventional chemotherapy, which aims to reduce tumor burden, metronomic chemotherapy focuses on disease stabilization. Early studies show it may be effective against several tumor types, with benefits such as reduced toxicity, ease of administration, and lower costs.[32] It is often considered when conventional protocols fail or are declined by the client. Side effects are generally mild and transient.

Despite the promise of metronomic chemotherapy, this approach is currently limited by significant gaps in knowledge regarding best indications as well as optimal dosing schedules and drug combinations. The types of cancer best suited to metronomic therapy and the best methods to gauge tumor treatment response are also not fully understood. However, several published studies in veterinary medicine, mostly prospective phase 1 and phase 2 trials, have investigated the use of metronomic chemotherapy and reported generally positive responses. The most commonly evaluated neoplasms in these studies were hemangiosarcoma, soft tissue sarcoma, and transitional cell carcinoma. An assortment of other neoplasms, such as osteosarcoma, melanoma, and various carcinomas, were also evaluated, although in a smaller number of patients.[33–37]

In the majority of these studies, the oral chemotherapy drug cyclophosphamide was used.[34–36] Other chemotherapeutic agents that have been assessed include lomustine (also known as CCNU) and chlorambucil.[33,37] These oral chemotherapeutics were often combined with an NSAID because of the antiangiogenic properties of the NSAID drug class.[38] Toceranib is also used with metronomic cyclophosphamide.[39]

Because sterile hemorrhagic cystitis is a risk associated with cyclophosphamide chemotherapy, whether administered as metronomic or MTD, this sequela should be monitored with periodic urinalysis of a voided sample.[36] Furthermore, because other unanticipated toxicities may occur when multiple agents are combined in a protocol, close monitoring of patients is imperative.[33]

Targeted Chemotherapy Using TKIs

Tyrosine kinases are enzymes that activate proteins involved in the signaling pathways to regulate normal cell proliferation and survival. Because many of these pathways are dysregulated in cancer cells,

TKIs are anticancer drugs that block signal transduction, thereby preventing tumor growth. TKIs target specific signal transduction pathways, and they can induce toxicities to rapidly dividing normal cells that also rely on these pathways (see Chemotherapy Side Effects).

Currently, only one oral TKI, toceranib phosphate, is FDA approved for use in dogs with cancer in the United States. Toceranib is approved to treat grade 2 or 3 recurrent cutaneous MCTs with or without regional lymph node involvement.

Toceranib may prove useful for treating a variety of tumors in dogs extralabel, including heart-base tumors,[40] sarcomas, carcinomas, and melanomas. Toceranib has been investigated in combination with radiation therapy[41] and in combination with other therapies such as prednisone, low-dose continuous (metronomic) cyclophosphamide alone[39] or with piroxicam,[42] piroxicam[43] and MTD chemotherapy including doxorubicin,[44] lomustine,[45–47] carboplatin,[48] and vinblastine.[49–51] More widespread use of TKIs awaits further investigation of several important questions, such as the tumor types in which TKIs are most likely to be effective and their optimal combination with conventional chemotherapy agents.

Safety Considerations

Personnel Safety

Research has shown that human health care personnel working with hazardous drugs have higher instances of reproductive difficulties, fetal loss, DNA alterations, and cancer.[52–57] Similar studies have been performed rarely in veterinary medicine, but exposure of veterinary personnel handling hazardous drugs could be comparable to human medical personnel owing to lack of regulations, challenges with patient compliance, frequent exposure to contaminated patient excrement, inconsistent personnel training, and variable access to safety equipment.[58] Veterinarians have legal and ethical responsibilities to educate their staff on the safe handling of chemotherapeutic agents.

In these guidelines, the terms hazardous drugs (HDs) and chemotherapeutic agents will be used interchangeably. The Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health have compiled a comprehensive list of HDs.[59] Additionally, the United States Pharmacopeia (USP) provided updated guidelines in 2017 titled "USP General Chapter 800," which outline standards regarding personnel protection for preparation and handling of HDs. Because an in-depth discussion of HD controls is beyond the scope of these guidelines, readers can refer to the USP for detailed information on this topic at usp.org.

Exposure to HDs can occur at any point from the receipt of the drug to when it is excreted from the animal and into the environment. The routes of exposure for health care workers include skin or eye contact, inhalation, ingestion, or sharps injury.[58] Table 5.2 outlines various safety equipment that should be used when working with HDs. Clearly label all HDs with chemotherapy warning labels. Individuals who are pregnant, trying to conceive, breastfeeding, or immunocompromised should not handle HDs.

If chemotherapy is uncommon in your practice, consider ordering premeasured single-dose chemotherapeutics to reduce hazardous drug manipulation in the clinic. This option negates the need for a biological safety cabinet and may decrease costs for clients.

After administering chemotherapeutic agents, discard the administration materials and personal protective equipment (PPE) into chemotherapy waste receptacles. Use PPE while thoroughly cleaning all areas and equipment that came into contact with HDs (Table 5.3). To prevent aerosolization, avoid spraying cleaning products directly on spills or contaminated surfaces.

TABLE 5.2
Safety Equipment Necessary for Handling Hazardous Drugs

Personal Protective Equipment (PPE)	• Double glove with ASTM D6319 standard* gloves • Disposable, impermeable single-use gowns • Eye protection • Mouth protection
Supplementary Controls	• Closed system transfer devices • Needleless systems • Hazardous drug labels • Readily available spill kits • Chemotherapy disposal bin
Engineering Controls	• Class II Biological Safety Cabinet

*ASTM D6319, American Society for Testing and Materials standard D6978

TABLE 5.3
Summary and Sequence of Spill Management Cleaning Steps*

Sequence of Cleaning Steps	Purpose	Agents
Deactivation	Render compound inert or inactive	As listed in the hazardous drug labeling. If no specific information is available, sodium hypochlorite or other EPA-registered oxidizer is used.
Decontamination	Remove inactivated residue	Sterile alcohol, sterile water, peroxide, or sodium hypochlorite
Cleaning	Remove organic and inorganic material	Germicidal detergent and sterile water
Disinfection	Destroy microorganisms	Sterile alcohol or other EPA-registered disinfectant appropriate for use

Adapted from International Society of Oncology Pharmacy Practitioners Standards of Practice.
*Reprinted with permission from Biller B, Berg J, Garrett L, et al. 2016 AAHA Oncology Guidelines for Dogs and Cats. *J Am Anim Hosp Assoc.* 2016;52(4):181-204.
EPA, Environmental Protection Agency.

Properly trained technicians play a key role in ensuring that crucial HD cleaning procedures are followed.

Client Safety

HD exposure risk does not end at the hospital. Clients with pets undergoing chemotherapy may be exposed to HDs through their pet's urine and feces and by administering oral cytotoxic drugs. Clients or other individuals caring for the pet should:

- Avoid exposure to the pet's waste for 72 hours after chemotherapy administration. If exposure must occur (cleaning litter boxes, waste cleanup), wear gloves and a mask.
- Do not split or crush oral HDs. Compounded liquid of HDs is available but not recommended because of exposure risk.
- Wear gloves when handling oral HDs, and do not handle oral HDs in food storage or preparation areas.

Patient Safety

In veterinary medicine, chemotherapeutic agents are often dosed in milligrams per meter squared (mg/m^2), which offers ample opportunity for drug calculation errors. Given the narrow therapeutic index of these drugs and the potential for serious side effects, adhering to precise drug dosing is essential. It is recommended that two individuals calculate chemotherapeutic doses to double-check accuracy before administration.

Technicians proficient in medical math can assist in double-checking chemotherapy drugs and dosing.

Some of the most common chemotherapeutics are irritants and vesicants. Drug extravasation can result in discomfort, swelling, redness, blistering, and necrosis. Make every effort to avoid extravasation by performing clean-stick IV catheter placement, using proper patient restraint, flushing the catheter adequately, and delivering the drug manually (syringe pumps are discouraged). If an extravasation occurs, withdraw as much drug as possible (do not flush) and implement a mitigation protocol (see Chemotherapy Extravasation Management at http://aaha.org/chemo-extravasation).[60]

Chemotherapy Side Effects

The primary goal of chemotherapy in veterinary oncology is to maintain the best possible quality of life for pets while effectively managing their cancer. Most veterinary chemotherapy protocols are well tolerated, with side effects that are typically mild and manageable. Studies show that approximately 15–30% of dogs undergoing chemotherapy experience side effects, most of which are mild (e.g., vomiting, diarrhea, or lethargy) and manageable with medical intervention. Severe, life-threatening side effects, such as febrile neutropenia, which may require hospitalization, occur in ~5–7% of cases.[61] In most cases, patients will complete treatment without the need for dose adjustments or early discontinuation because of toxicity.

Febrile neutropenia, although uncommon, is a recognized potential complication. In a retrospective study of 673 chemotherapy treatments in dogs with lymphoma, febrile neutropenia was documented in 12 cases (1.8%), most often after the first CHOP cycle.[61] A broader multiprotocol retrospective study reported neutropenia in 23 of 155 dogs (14.8%), with 17 of those dogs (11.0%) also

developing fever consistent with febrile neutropenia.[62] Although many neutropenic dogs remain clinically stable, a prospective study found bacteremia in 4 of 34 neutropenic patients (12.3%), emphasizing the importance of individualized monitoring and supportive care.[63]

Cats tend to tolerate chemotherapy even better than dogs, with a lower overall toxicity rate. Only ~10–15% of cats experience side effects, and severe reactions are even less common, likely affecting fewer than 5% of cases.[64] A proactive approach to treatment, including preventive medications, can help minimize the occurrence and duration of side effects.

MTD chemotherapy primarily damages rapidly dividing cells, which include cancer cells and certain normal cells. The tissues most sensitive to MTD chemotherapy are the bone marrow, hair follicles, and gastrointestinal lining, often referred to collectively as the "BAG" (bone marrow, alopecia, gastrointestinal) effects.

The most common side effects from toceranib are GI, including diarrhea, decrease or loss of appetite, weight loss, and hematochezia. Other less common side effects are hepatotoxicity, neutropenia, lameness or muscle pain, coagulopathies, proteinuria, hypertension, and, rarely, pancreatitis.

Bone Marrow Suppression and Neutropenia

Bone marrow suppression most commonly results in neutropenia, which is the dose-limiting toxicity in veterinary oncology. Neutrophils and platelets are particularly at risk owing to their shorter circulating lifespan. Cats tend to be more tolerant of these adverse effects compared with dogs.

The degree of myelosuppression varies depending on the chemotherapy drug:

- Mild to none: corticosteroids, L-asparaginase
- Moderate: vincristine, vinblastine, cyclophosphamide, melphalan, rabacfosadine
- High: doxorubicin, lomustine, mitoxantrone, carboplatin, combination protocols

Neutropenia in cancer patients can also result from bone marrow infiltration by neoplastic cells (e.g., leukemia, advanced lymphoma, multiple myeloma) or from increased neutrophil consumption because of infection.

Neutropenia is the primary dose-limiting toxicity in veterinary oncology.

Prophylactic antibiotics are sometimes prescribed to be given at the expected neutropenic nadir (lowest neutrophil count), although this practice is controversial. Commonly used antibiotics include trimethoprim sulfamethoxazole and amoxicillin-clavulanic acid. Some oncologists may consider prophylactic antibiotic use when administering highly myelosuppressive agents like doxorubicin, carboplatin, or lomustine, particularly in high-risk patients, but not all task force members agreed with this practice. In a double-blind, placebo-controlled study, prophylactic trimethoprim-sulfadiazine was associated with fewer hospitalizations and reduced nonhematologic toxicities during chemotherapy for lymphoma and osteosarcoma.[65] However, a more recent multi-institutional retrospective study in dogs treated with lomustine found no significant reduction in febrile neutropenia with antimicrobial prophylaxis, reinforcing the importance of individualized decision making and antibiotic stewardship.[66]

For chemotherapy drugs with high potential for bone marrow suppression (e.g., doxorubicin, carboplatin, lomustine), a CBC is typically checked after treatment to monitor the nadir, which is the lowest neutrophil count. This check helps determine if antibiotics or a dose reduction is necessary. The nadir usually occurs 7 days after treatment, although it can vary, especially for drugs like carboplatin and lomustine. Chlorambucil and melphalan can cause irreversible, delayed thrombocytopenia after long-term use, necessitating discontinuation of the drug.

At the nadir appointment, it is important to run a CBC, gather a thorough history, take vital signs (especially temperature, as identifying fever is crucial in neutropenic patients), and conduct a complete physical examination. The neutrophil count, not the total white blood cell count, is the primary indicator of concern (Table 5.4). Antibiotics are recommended if the neutrophil count drops

TABLE 5.4
Nadir Appointment Action Plan

Neutrophil Count/μL	Fever and Systemic Signs	Plan
1000 to 2000	No	• Monitor, antibiotics not necessary • Delay chemotherapy if due for treatment
<1000	No	• Prescribe oral antibiotics • Delay chemotherapy if due for treatment • Consider dose reduction if next chemotherapy is delayed
<1500	Yes	• Hospitalize, give IV fluid therapy and IV antibiotics • Delay chemotherapy if due for treatment • Chemotherapy dose reduction

IV, intravenous

below 1000/μL, although a recent publication suggested that a cutoff of 750/μL is safe and may reduce unnecessary antimicrobial use.[67] If the patient is afebrile and feeling well, they can often be managed as an outpatient. However, if the neutrophil count is <1500/μL and the patient is febrile or showing signs of illness, hospitalization with supportive care is required.

Febrile neutropenia is an oncologic emergency and requires hospitalization.

Alopecia

Alopecia occurs as a result of damage to the rapidly dividing hair follicles. Dog breeds with continuously growing coats, such as poodles, Scottish terriers, and West Highland white terriers, are more likely to experience this effect. Alopecia is rare in cats, but shaved areas (e.g., from limb catheters or AUS) may take longer to regrow, and cats may lose their whiskers. Hair and whiskers typically regrow once treatments are completed, but hair may sometimes grow back with a different texture or color. Although pets are unaffected by this cosmetic side effect, it is important to inform clients about potential changes in whiskers and hair coat to avoid surprises.

GI Toxicity

Drugs used in veterinary oncology have varying risks of chemotherapy-induced nausea and vomiting (CINV):

- Low risk: L-asparaginase, chlorambucil
- Moderate risk: vincristine, vinblastine, lomustine, cyclophosphamide, mitoxantrone, carboplatin, toceranib
- High risk: doxorubicin, rabacfosadine, cisplatin

CINV is classified as either acute (within 24 hours) or delayed (1–5 days after chemotherapy). Acute CINV is primarily mediated by serotonin (5-HT3) pathways, whereas delayed CINV is associated with substance P neurokinin-1 (NK1) receptor pathways.

GI toxicity, including vomiting, diarrhea, decreased appetite, and nausea, is usually self-limiting and lasts an average of 3 days. These side effects are less common in cats than in dogs. Taking a proactive approach to prevent these side effects is helpful, and appropriate medications can be used as needed to minimize and manage them.

Importance of Managing and Preventing GI Side Effects

One of the most common reasons clients stop chemotherapy prematurely is because their pet has hyporexia or anorexia. This side effect can be distressing for pet caregivers and can lead to unnecessary discontinuation of treatment. It is crucial to emphasize to clients that appetite loss is often manageable with proper intervention and addressing it early can help keep pets on their treatment plan.

Educate clients about the likelihood of appetite changes and reassure them that this is a manageable side effect.

Encourage clients to report even mild changes in their pet's eating habits so that supportive measures can be implemented quickly. By addressing appetite loss early, pets can remain on their cancer treatment plan and their overall well-being during therapy can be substantially improved.

Prevention Strategies

Nausea is often a primary cause of appetite loss. Proactively using maropitant or other antiemetic drugs after chemotherapy can help reduce nausea and improve appetite. For acute CINV, pretreatment with maropitant IV or subcutaneously or ondansetron may be useful for high-risk drugs (e.g., doxorubicin, rabacfosadine). To prevent delayed CINV, especially in dogs, administer oral maropitant for 4–5 days after chemotherapy. Cats typically require less preventive treatment unless they have experienced prior GI issues. If breakthrough CINV occurs, additional antiemetic therapy may be needed.

In addition, proactive use of appetite stimulants can be very helpful. Appetite stimulants such as capromorelin or mirtazapine, particularly transdermal mirtazapine in cats, can be useful for stimulating appetite and preventing anorexia. Administering these at the first sign of decreased appetite can prevent prolonged periods of inappetence. Both antinausea and appetite stimulant medications may be needed concurrently in some patients. For pets with pre-existing inappetence, additional medications may be prescribed at treatment to prevent worsening of appetite loss during chemotherapy.

It is highly beneficial for chemotherapy patients to go home with "just in case" medications if side effects occur after hours, clients can start treatment promptly, preventing unnecessary discomfort or emergency visits. Provide a client information sheet that explains how to manage side effects at home and details the proper usage of these medications.

Management for diarrhea may include dietary modifications and probiotics. Crofelemer-CA1 may be of benefit, and antibiotics such as tylosin or metronidazole have anecdotally been useful. For more information on antimicrobial stewardship and treatment of diarrhea, see the *2022 AAFP/AAHA Antimicrobial Stewardship Guidelines* at aaha.org.

Encourage clients to provide small, frequent meals of palatable foods to entice pets to eat. Offering a variety of textures (e.g., wet food, homemade diets) can help stimulate interest in food. In addition, close monitoring of a pet's appetite and body weight and adjusting the treatment plan as needed can make a substantial difference. If appetite continues to be an issue, adjusting chemotherapy doses, adding supportive care, or delaying chemotherapy can often resolve the problem without completely stopping treatment.

In-Hospital Versus Outpatient Treatment of GI Side Effects

With a proactive approach and early recognition, most cases of inappetence, CINV, and diarrhea can be managed at home. However, in more severe cases where there is a concern for dehydration or oral medications are ineffective, IV treatment may be necessary.

When a patient is brought to the hospital, the goal is to determine whether outpatient or inpatient care is required, based on the physical examination findings, clinical signs, and diagnostic workup. Consider running a CBC, chemistry panel, and urinalysis or urine specific gravity and possibly fecal floatation and/or bacterial cultures (blood and/or urine). If abdominal pain is present, radiography or ultrasonography may be necessary to rule out foreign bodies, obstruction, or intussusception. For pets with GI neoplasia, distinguishing between chemotherapy side effects and the disease can be challenging, and obtaining a thorough history, including the timing of symptoms, is essential.

Outpatient treatment typically includes a period of nothing by mouth, followed by a bland diet, IV or subcutaneous fluids, injectable antiemetics, appetite stimulants, and antidiarrheals as needed. It is also important to temporarily discontinue any oral chemotherapy or medications contributing to inappetence, with appropriate adjustments made for future treatments.

Some patients may require hospitalization because of side effects. In such cases, patients are typically hospitalized for 24–48 hours for supportive care, including IV fluids, injectable antiemetics, and possibly antibiotics. It is important to reassure clients not to consider euthanasia at this stage, as many patients show rapid improvement with supportive care. Most can resume treatment with dose reductions and additional prophylactic measures.

Other Toxicities

In addition to general side effects, certain chemotherapy drugs are known to cause specific and unique toxicities. For example:

- Doxorubicin is contraindicated in dogs with impaired cardiac function or those that have reached a total cumulative dose of 180–240 mg/m^2. It can also exacerbate renal disease in cats.
- Cyclophosphamide has the potential to cause sterile hemorrhagic cystitis in dogs, and rarely in cats, leading to bladder irritation and discomfort.
- Rabacfosadine can cause cumulative dermatopathy and, in rare cases, life-threatening pulmonary fibrosis.

For more detailed information on chemotherapy drug–specific toxicities, refer to Table 5.1, consult resources such as veterinary drug formularies, or seek advice from a veterinary oncologist (see Section 6).

Therapeutic Modalities: Immunotherapy

Harnessing the immune system's ability to fight cancer holds significant promise for treating aggressive malignancies, particularly in preventing or controlling metastatic disease. Since the introduction of the Oncept canine melanoma vaccine in 2007, which was the first USDA-licensed immunotherapeutic agent for dogs with stage II or III oral melanoma, the field of veterinary immunotherapy has seen notable advancements as well as challenges. Oncept marked a significant step forward, but both progress and setbacks have occurred in developing further immunotherapeutics. To date, options remain limited, and some immunotherapies have been discontinued because of safety concerns or lack of efficacy identified in larger studies.

One of the notable recent developments is gilvetmab, which targets the PD-1 pathway in dogs. It is the first conditionally licensed caninized anti-PD-1 monoclonal antibody in veterinary medicine. It is labeled for use in dogs with stage I, II, or III MCTs and stage II or III melanoma. Gilvetmab results in immune checkpoint inhibition by preventing the suppression of T cells and enabling them to recognize and kill tumor cells. This therapeutic approach is designed to boost the immune system's response against cancer cells, essentially "unmasking" the cancer cells to allow the dog's immune system to target and attack them. Currently, this immunotherapeutic agent is only available through veterinary oncologists.

In addition to monoclonal antibodies like gilvetmab, ongoing research is exploring other immunotherapeutic approaches, including cancer vaccines, checkpoint inhibitors, and adoptive T-cell therapies. These therapies aim to bolster the body's immune response against cancer cells and provide new treatment options, particularly for cancers that are resistant to conventional therapies.

Combination therapy will be crucial in the success of immunotherapy. Just as in human oncology, the effectiveness of immunotherapy in veterinary medicine often hinges on its integration with other treatment modalities, such as surgery, radiation therapy, and chemotherapy. These combinations can significantly enhance outcomes, offering new hope for patients with difficult-to-treat cancers. As the field of veterinary immunotherapy continues to advance, ongoing clinical trials and research are critical for determining the most effective therapies and combinations.

Therapeutic Modalities: Radiation Therapy

Radiation therapy (RT) involves the targeted delivery of ionizing radiation to damage and kill cancer cells. RT is a localized therapy (like surgery) and is therefore intended to reduce the size or stop the growth of a solitary or regionally isolated area of disease (i.e., primary tumor and regional lymph nodes). It is generally not used to address the risk or presence of systemic metastatic disease (except for palliation of specific metastatic lesions and half-body RT for lymphoma).

Owing to the equipment, shielding, and expertise requirements of radiation therapy, its use is typically limited to veterinary specialty facilities.

Goals of Radiation Therapy

The classic paradigm of RT categorized radiation as either definitive intent (aka curative intent) or palliative intent.

Definitive-intent RT involves dose-intense treatment courses with the goal and expectation of providing prolonged tumor control and survival. With these goals in mind, moderate, acute, and temporary toxicity is expected and considered tolerable. In contrast, palliative-intent RT involves less dose-intense treatments intended to minimize toxicity, as the primary goal is improvement or extension of quality of life, usually over the short to medium term (e.g., 3–9 months) (Table 5.5).

Historically, definitive-intent RT has involved "finely fractionated" courses of treatment where the total radiation dose is divided into many (e.g., 10–20) total treatments at relatively low doses per treatment and high cumulative radiation doses. In contrast, palliative-intent RT was often delivered in more "coarsely fractionated" courses of 1–5 treatments with a higher dose per treatment.

Despite this useful framework, current radiation practices have blurred the distinctions between definitive intent and palliative intent for several reasons:

- Although curative outcomes are common for localized tumors that are treated with a combination of surgery (to remove all gross disease) and RT (to sterilize residual microscopic disease), many other tumors treated primarily with definitive-intent radiation have high rates of eventual recurrence. In addition, palliative-intent RT can be intensified with the goal of providing more durable palliation or local tumor control.
- Innovation in clinical practice and publication of various studies have introduced treatment courses that fall between finely and coarsely fractionated protocols that improve convenience, response rates, or toxicity rates compared with previous protocols.
- Newer technologies (see Box) have collectively allowed for significant reduction in volume and severity of radiation toxicity and the introduction of definitive RT protocols delivered in short (coarsely fractionated) treatment courses (Table 5.5). In certain clinical situations (e.g., brain tumors, nasal tumors), this has made it possible to give much higher doses per treatment without an unacceptable increase in toxicity to surrounding tissues (i.e., stereotactic RT [SRT]). For example, 15 years ago, nearly all brain tumors were treated with 16–21 courses of radiation, but today, most brain tumors treated at facilities with capable equipment receive 1–5 radiation treatments with similar outcomes for response, survival, and toxicity. In these cases, this has allowed prescription of high radiation doses in short courses that are definitive intent rather than palliative intent.[68]

TABLE 5.5
Common Fractionated Radiation Therapy Protocols

	Finely Fractionated Radiation	Coarsely Fractionated Radiation
Number of fractions*	10-20	1 to 8
Schedule*	Daily, EOD	Daily, EOD, or weekly
Treatment intent	Usually definitive	Usually palliative (except for SRT)
Common protocols	18 daily treatments Mon–Fri over 3.5–4 weeks 10 daily treatments Mon–Fri over 2 weeks 12 treatments (e.g., Monday/Wednesday/Friday) over 4 weeks	2 treatments on back-to-back days 3–5 daily treatments in 1 week 6–7 weekly treatments 5 treatments, twice weekly over 2–2.5 weeks

*In most veterinary settings.
EOD, every other day; SRT, stereotactic radiation therapy.

Advances in Radiation Technology and Therapy

3D treatment planning—Volumetric imaging (e.g., CT, MRI) and radiation treatment planning software simulates a variety of treatment plans and calculates the radiation dose delivered anywhere within the scanned volume.

Intensity-modulated radiation therapy—Radiation beams are shaped and controlled by a computer to precisely conform the radiation dose to the shape of a target. This allows a decreased radiation dose and reduces radiation side effects to surrounding normal tissues.

Stereotactic (body) radiation therapy (SRT/SBRT)—Often used to deliver high radiation doses targeted only to the visible tumor in shortened treatment protocols. Minimal radiation is delivered to the margins outside of the target.

On-board imaging (OBI)—Diagnostic quality digital imaging incorporated onto a linear accelerator (most commonly cone-beam CT) allows precise verification and adjustment of radiation delivery settings and patient positioning immediately before treatment.

Normal Tissue Response and Radiation Side Effects

Normal tissue responses to radiation are generally limited to the tissues near the target/tumor and are divided between acute effects and late effects.

Acute effects are seen in tissues with rapidly dividing cells (skin, mucosa, bone marrow) between 2 weeks and 2–3 months from the start of a treatment course. Examples of acute effects include radiation dermatitis (dry or moist desquamation), or mucositis. These effects are expected (although severity varies) with definitive doses of radiation and typically resolve over a few weeks with supportive care. Accordingly, acute effects are not usually dose limiting but can impact quality of life during and for a few weeks after the treatment period.

Late effects typically develop many months to years after radiation. Mild late effects may be cosmetic such as leukotrichia (whitening of fur) or permanent alopecia. Other late effects can significantly impact function (e.g., cataract). Severe late effects such as necrosis (e.g., bone, brain), ulceration, and new cancers caused by radiation are potentially irreversible and life threatening. Radiation is often dose limited because of the desire to keep the incidence of severe late effects below 5% of treated patients. Definitive radiation courses have been traditionally delivered over many treatment fractions because giving the same total dose over more treatments is preferentially sparing of late-responding tissues like brain and bone compared with cancer cells and acute-responding tissues.

Tumor-Specific Radiation Therapy Considerations

A complete listing of the tumors that are treatable with radiation and their associated goals and outcomes is beyond the scope of these guidelines. Table 5.6 summarizes typical clinical scenarios when radiation is considered, with their associated treatment goals and examples. Generally, most localized tumors can be targeted with radiation. Response rates and durations vary by tumor type and disease stage and grade. Tumors that can be cytoreduced to microscopic disease before radiation have the highest rates of long-term control.

Therapeutic Modalities: Surgery

Generally, if a primary tumor can be completely excised "en bloc" with acceptable morbidity, surgery is the best treatment. The first attempt at surgical excision always offers the best opportunity to completely remove the tumor. For this reason, appropriately assessing the patient before surgical excision of a mass is indicated (see Tumor Diagnostics and Staging). Locally recurrent tumors are often more difficult to remove than the initial tumor because more extensive involvement of normal tissues in the region occurs and normal tissue planes are distorted by scar tissue.

An en bloc excision is derived from French, meaning "as a whole." In surgical oncology it refers to the removal of a margin of healthy tissue (e.g., normal skin, muscle) around the tumor in one piece, having never cut into the tumor itself.

For tumors that are large, fixed, or located adjacent to critical normal structures, preoperative CT or MRI may be helpful in planning the surgical excision.

TABLE 5.6
Considerations for Radiation Therapy and Treatment Goals

Clinical Scenario	Treatment Goals	Examples
Large and unresectable or invasive tumors	Palliation or temporary reduction in size or cessation of growth	Soft tissue sarcoma, thyroid carcinoma, subcutaneous hemangiosarcoma
Tumors located where surgery is excessively invasive or challenging	Durable reduction in tumor size and alleviation or prevention of tumor-associated signs Downstage tumor to allow resection	Brain, pituitary gland, nasal, bladder, prostate, oral, or anal sac tumors
Invasive tumors that can only be resected narrowly with a high risk of recurrence Incompletely resected tumors	Long-term tumor control	Soft tissue sarcoma, mast cell tumor, oral, limb, or spinal tumors
Tumors causing or at risk of causing pain or dysfunction (particularly in patients that are not candidates for definitive therapy)	Reduction in tumor-associated signs or tumor size (palliation)	Osteosarcoma; oral, nasal, joint, vertebral, or spinal tumors

TABLE 5.7
Special Considerations in Oncologic Surgery

Principles of Oncologic Surgery	Rationale	Examples
Complete tumor excision with adequate margins when possible	Adequate excision decreases the risk of tumor recurrence.	Adequate margins vary by tumor type; examples include: • Low-grade mast cell tumors: 2 cm or proportional margins wide (lateral margins equivalent to the widest measured diameter of the tumor) and 1 fascial plane deep • Canine soft tissue sarcoma: >3 cm laterally and 1 fascial plane deep • Feline injection site sarcoma: 5 cm laterally and 2 fascial planes deep • Osteosarcoma: the entire affected bone or organ, or 2–3 cm of healthy bone (amputation is most frequent)
Ink specimen margins	Allows pathologists to distinguish actual margins from margins introduced during tissue processing. Also allows identification of which margins were closest, narrow, or incomplete.	Identify deep margin, lateral margins, proximal/distal, cranial/caudal, and dorsal/ventral as appropriate to the site.
Add markers/ hemoclips around the surgical field	If postoperative imaging and radiation are pursued, such markers can aid in defining the target and act as fiducial markers for treatment setup.	Mark the circumference and deep margins of the surgical field.
Assess lymph nodes	Lymph node biopsy or excision is frequently a helpful and prognostic staging test that can be performed at the time of surgery.	Examples include: • Cervical lymph node excision when removing an oral tumor • Thoracic lymph node biopsy when removing a lung tumor • Popliteal lymph node excision when removing a mast cell tumor of the distal hindlimb
Minimize tumor seeding and contaminating other tissues	Tumor cells are easily seeded on instrument tracks and throughout the surgical site during mass removal. Seeding can result in regional recurrence.	• Avoid tumor manipulation and rupture during surgery. • Perform thorough lavage after mass removal (e.g., splenectomy). • Minimize bleeding in the surgical field. • Change instruments and gloves immediately after removal of the tumor (before reconstruction and closure).
Reconstruction and function preservation	Reconstruction should preserve function and minimize tension to the greatest extent possible. It should consider the impact of reconstruction on additional therapy (i.e., second surgery or radiation therapy).	In general, orient incisions along naturally existing tension lines, dependent on location. For example, orient incisions on the limb from proximal to distal rather than circumferentially.

The usual objective of surgery is to obtain wide surgical margins in all directions surrounding the tumor; that is, to remove the tumor with a grossly visible intact cuff of surrounding normal tissue. The necessary margin often depends on the tumor type and, in some cases, the tumor grade, as well as the type of tissues that are adjacent to the tumor. For example, fascial planes generally provide a good physical barrier to tumor growth, so excision of an intact fascial plane below a tumor is an excellent way to optimize the chance of a complete excision. Subcutaneous fat is poorly resistant to tumor growth and should always be aggressively excised with the tumor mass.

A marginal excision refers to "shelling out" a tumor or excising it just outside its pseudocapsule. Because the pseudocapsule often consists of compressed cancer cells, marginal excisions risk leaving microscopic quantities of tumor cells in the patient and are associated with higher rates of local recurrence than wide excisions. As a rule, marginal excisions should be avoided when possible unless postoperative RT is planned, or if the client's only goal is temporary palliative care for a local tumor causing concerning symptoms, with no foreseeable plans of pursuing additional definitive therapies.

Although most general surgery principles apply to oncologic surgery, a few additional practices to implement in cancer surgeries are listed in Table 5.7.

All excised tumors should be submitted for histopathologic examination and margin analysis. Because pathology laboratories typically prepare representative samples from a given specimen, a report of complete margins does not necessarily guarantee that an excision was complete. A report of incomplete margins means the resection was histologically incomplete in at least one location. Although overall recurrence rates are consistently greater for tumors with incomplete margins than for tumors with complete margins, clients should be aware that tumors with complete margins can recur locally and, conversely, many tumors with incomplete margins do not recur. Following a report of incomplete margins, options include close monitoring (if an appropriate re-excision will be feasible should local recurrence develop), immediate wide excision of the surgical scar, or postoperative RT.

Section 6: Consultations and Referrals

Top 3 Takeaways

1. Referring veterinarians who proactively reach out to the specialty team before their first referral will be in the best position to establish an evolving relationship between the referring veterinarian, specialist, and client, sharing the goal of providing the best possible care and service along an efficient timeline for patients and clients.
2. Collaboration between specialists and referring veterinarians to develop postreferral plans will optimally aid each client and patient.
3. Veterinary telehealth is a versatile and powerful adjunctive tool that improves access to specialty care through teleconsultations.

General practitioners often refer patients who have a diagnosis of neoplasia to their local board-certified veterinary oncologist. Direct and open communication, advice seeking, and eventual referral ought to be a stress-free, collaborative, and fluid process between the referring veterinarian and the oncologist, as well as a seamless, tension-free process in the eyes of the client.[69]

Referrals occur when a referring veterinarian, who is the patient care provider before and during the referral process, transfers a patient's care to a receiving veterinarian, who is then the one providing care from the moment the referral is complete until an appropriate endpoint.[69] Collaboration, communication, and shared goals are essential for a working relationship among all individuals involved in the referral process, which includes not only clinicians but also veterinary technicians, referral coordinators, and client service representatives. A working relationship between teams committed to the

TABLE 6.1
Referral Considerations for Oncology Cases

Referral Considerations	Example
Determine whether the desired oncological services are provided by the oncologist.	A patient who needs radiation therapy is referred to a facility that provides it.
Outline the costs of the referral consultation and the anticipated recommendations for the patient, which helps inform client expectations and clarify the purpose of the referral.	A client desires a referral oncologist consultation to discuss their pet's palliative treatment options because financial limitations preclude them from pursuing an ideal intervention of re-excision surgery followed by chemotherapy.
Balance the urgency of the referral with the oncologist's availability to accept that referral within the appropriate timeline.	A lymphoma patient who requires immediate chemotherapeutic induction because of upper airway obstruction from submandibular lymphadenopathy is referred to an oncologist who can accept the patient that same day.
Transfer the medical documents for the referral before the referral appointment.	Blood work, radiographs, and cytology results are provided (e.g., via email, online portal, other online platform) to the oncologist before the referral appointment, including specialist interpretations (e.g., radiologist, pathologist) where applicable.
Collaborate to ensure proper and timely postreferral care.	Per the oncologist's recommendation, the client approves adding immunohistochemistry to the biopsy sample that the referring veterinarian submitted. The laboratory requires the practice that submitted the sample to approve the test and receive the results. The oncologist must inform the referring veterinarian of the added test, and the referring veterinarian must approve the test in a timely manner and share the results with the oncologist upon receipt.
Provide complete oncologist medical records and availability for follow-up questions to the referring veterinarian in a timely manner.	Timely receipt of referral letters can avoid issues if chemotherapy-induced complications arise.

highest quality of care, education, and service enhances the client's experience and the patient's outcome during a referral. Factors to consider when referring are listed in Table 6.1.

The recommendations in Table 6.1 include direct and open communication with the oncologist, which is vital to a successful referral. Such communication must be welcomed at both ends of the referral process. Telecommunication via the telephone or an online referral portal are immediate, direct, and convenient methods to initiate a referral and clarify what all parties need and expect. For additional guidance on well-ordered referral processes, see the *2025 AAHA Referral Guidelines* at aaha.org/referral.

Telehealth Consultations in Oncology Cases

Veterinary telehealth is the overarching term that defines remote care using telecommunication technologies between two individuals who are in two different geographical locales.[70] Veterinary telehealth is now a commonplace, versatile, and powerful adjunctive tool to in-person brick and mortar practice that promotes contextualized care while improving access to specialty care through teleconsultations.[71–73]

For more information on telehealth for small animal practices, see the *AAHA/AVMA Telehealth Guidelines* at aaha.org/telehealth.

Section 7: Supportive and Symptomatic Care

Top 3 Takeaways

1. Thoroughly evaluate the patient—including evaluation for potential comorbidities—when instituting symptomatic care to improve overall quality of life.
2. Pain and discomfort may arise from the cancer itself (e.g., pain from osteosarcoma), from side effects of cancer treatment (e.g., RT or chemotherapy), or secondary to another disease process.
3. Routinely assess oncology patients' nutritional status, beginning with diagnosis and continuing throughout treatment.

The primary objective of symptomatic therapy for oncology patients is to maintain or improve quality of life by mitigating discomfort and resolving or alleviating clinical signs. Supportive and symptomatic care are essential components of patient management and are aimed at enhancing quality of life throughout treatment. Given that clients often prioritize their pet's quality of life, it is crucial to consider the client's goals, preferences, and limitations when developing a care plan. Effective case management requires coordinated communication between general practitioners and oncologists, as the former frequently play a vital role in administering care. Comprehensive patient evaluation, including the identification of comorbidities that may affect the treatment protocol, is imperative. Supportive therapies are summarized below and in Table 7.1.

Common Side Effects of Chemotherapy

Dogs and cats generally tolerate chemotherapy well, but side effects such as vomiting, nausea, anorexia, diarrhea, and bone marrow suppression may occur. These side effects can lead to muscle wasting and weight loss, which clients may perceive as a decline in quality of life.

Supportive Medications

1. Nausea/Vomiting

See Table 7.1 for options to treat nausea and vomiting in patients.

2. Hyporexia Management

Hyporexia may occur secondary to the primary disease process, such as GI lymphoma, or may be secondary to treatment such as chemotherapy. Along with options listed in Table 7.1, the appetite stimulants capromorelin and mirtazapine can be given orally to manage

TABLE 7.1
Supportive and Symptomatic Care Options

Vomiting	Hyporexia	Diarrhea	Pain	Other GI Support	Bone Marrow Suppression
• Maropitant • Ondansetron • Metoclopramide	• Capromorelin oral solution • Mirtazapine • Prednisone/ prednisolone	• Crofelemer-CA1 • Probiotics • Smectite +/- metronidazole, fiber	• NSAIDs • Bedinvetmab • Frunevetmab • Buprenorphine • Opioids • Gabapentin/ pregabalin • Bisphosphonates	• Dietary support • Therapeutic diet • Antacids • Motility drugs • Vitamin B12 • Probiotics • Feeding tube	• See "Section 5, Bone Marrow Suppression and Neutropenia" for management of neutropenia

GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs.

hyporexia in feline and canine patients,[74–77] and mirtazapine is available as a transdermal ointment for use in cats. If nausea is suspected underlying the hyporexia, treat for nausea first.

3. Diarrhea Management

Therapeutic recommendations for managing diarrhea after chemotherapy have been updated. Because other acceptable treatment options are effective, the current trend is a shift away from empirical antibiotic use to treat acute diarrhea to support antibacterial stewardship and avoid the negative impacts of disrupting the normal GI biome.[78–80]

Crofelemer-CA1 delayed-release tablets, which the FDA conditionally approved for treatment of chemotherapy-induced diarrhea (CID) in dogs, is one therapy to consider. And in one small study, a highly potent probiotic reduced the incidence of CID in canine patients receiving multiagent chemotherapy and may be considered as an additional supportive care option.[81] Another option is smectite (medical aluminosilicate clay), which in one study led to a faster resolution of clinical signs when compared with metronidazole in dogs with CID.[82]

4. Pain Management

Recognizing and alleviating pain in oncology patients is essential for maintaining quality of life. Pain may be caused by the cancer itself (e.g., osteosarcoma pain), a treatment modality (e.g., RT or chemotherapy), or a concurrent disease (e.g., osteoarthritis). To adequately control pain, use a multimodal approach. Refer to the *2022 AAHA Pain Management Guidelines for Dogs and Cats* for current recommendations on a multimodal approach to pre-empting and controlling pain.

The most effective pain management is usually achieved by treatment of the underlying disease, so consider the cancer-specific therapies discussed above. When these are not feasible or desired, the second most effective option for the most consistent and durable pain control for most malignant tumors is palliative-intent radiation therapy. Based on studies in humans and animals, between 70 and 90% of patients with cancer-related pain will have significantly reduced pain in response to palliative-intent radiation therapy. Response durations vary widely, from a few months to more than a year depending on the tumor type.

New pain management products are available and may complement standard pain therapy. Two monoclonal antibody therapies that target nerve growth factor to manage chronic pain are available for dogs (bedinvetmab)[83] and cats (frunevetmab).[84] Two drugs often used postoperatively in feline patients are injectable buprenorphine, which can control pain for 24 hours, or buprenorphine transdermal solution, which can control pain for 4 days.[85–87] Gabapentin or pregabalin have mixed effectiveness in adjunctive pain management in dogs and cats and can also be considered in chemotherapy patients.[88] IV bisphosphonates can help reduce bone pain.

5. Nutritional Support

Routinely assess the nutritional status of oncology patients at the time the diagnosis is made and throughout treatment. Customize diets based on the patient's cancer diagnosis, any additional health issues (e.g., pancreatitis, renal disease), and nutritional needs. Also consider environmental factors, such as other household pets and the client's ability to adhere to feeding recommendations.

The primary dietary goal is to ensure that the food is highly palatable and consumed. A complete and balanced diet, whether commercial or homemade, is essential. A newly released therapeutic diet (ONC Care) has high palatability and positively affects body weight in tumor-bearing dogs.[89] Consulting a veterinary nutritionist is advisable, especially if a homemade diet is chosen, as creating a balanced diet is challenging.[90] Feeding raw diets to oncology patients is not recommended because these patients are immunocompromised, and feeding raw meat–based diets poses increased risks of *Salmonella* and *Escherichia coli* infections for patients and for caregivers who may touch saliva or fur or clean up after meals.[91–93]

If anorexia persists despite medical management, discuss feeding tube (e.g., esophagostomy, nasoesophageal, and percutaneous endoscopic gastrostomy) placement with the client. This can be particularly crucial early in the disease or postoperatively to aid recovery while awaiting therapeutic responses. Consideration of the overall goals, quality of life, and prognosis is essential for feeding tube placement in hospice cases.

Section 8: Technician and Team Optimization

Top 3 Takeaways

1. Technician training and education are essential to providing optimal patient care while utilizing technicians to their full extent.
2. Effective client communication, education, and support can often be provided by technicians and benefits the health care team and client.
3. Delegating more clinical responsibilities to veterinary technicians enables veterinarians to focus on diagnosing, prognosing, prescribing, and surgery and increases practice efficiency. Providing and encouraging specific training in cancer patient care optimizes team utilization.

Technician and Team Optimization

Credentialed veterinary technicians are often underutilized in practice, leading to inefficiencies and poor job satisfaction. Recognizing what veterinary technicians can legally do, while also mentoring them to augment their training and education, will lead to better team utilization. Refer to the *2023 AAHA Technician Utilization Guidelines* at aaha.org/technician-utilization for more information and resources.

A good patient history for an oncology patient includes gathering information regarding all current medications and supplements, the patient's diet, and the patient's status since the last treatment.

Credentialed Technicians' Key Duties During Oncology Appointments

- Obtain a detailed patient history relevant to the reason for the visit and the patient's vital signs.
- Collect most diagnostic samples required for an oncologic visit including blood, urine, and fine-needle aspirates of masses or lymph nodes.
- Assist with cytologic evaluation, manual differentials for hematology, initial screening of laboratory work, and sample preparation (e.g., cytology, histopathology, flow cytometry).
- Perform patient body mapping and obtain mass measurements.
- Double-check chemotherapy calculations, prepare and administer chemotherapeutics, and monitor patients throughout the infusion.

Consider scheduling technician appointments for laboratory visits. These visits often entail phlebotomy and vital signs check but commonly do not require direct veterinarian oversight unless concerns are noted by the veterinary technician or client.

Credentialed Technicians' Key Duties During and After Patient Discharge

- Discharge patients and discuss routine test results, potential side effects of treatment, supportive care and medications, chemotherapy exposure risks, and follow-up plan.
- Provide a phone call follow-up after treatments or procedures at an appropriate time interval (e.g., after chemotherapy: 3–5 days, after procedure: 1–2 days).
- Play a key role in quality-of-life conversations and end-of-life discussions.
- Assist in internal recordkeeping, making external referrals, and obtaining and evaluating records in practices that accept referrals.
- Alert the attending veterinarian to evaluate the CBC immediately if cytopenias are present or the patient has a fever.

Whenever feasible, consider having technician consistency with cancer patients. This helps build a trusting relationship between the technician and client.

Technician Training

Although a credentialed veterinary technician is highly skilled and educated, specific training related to oncologic patients and care will be essential. Technicians should have access to training or pursue continuing education on chemotherapy administration, HD safety, oncology diagnostics, supportive care for the chemotherapy patient, palliative care, and disease-specific courses.

For clinics with a high oncology caseload, credentialed technicians may also pursue a specialty certification in oncology, surgery, anesthesia, and/or emergency and critical care to further enhance their knowledge base and capabilities. See navta.net/veterinary-technician-specialties/ for more information.

Awareness of state regulations is the responsibility of the credentialed technician and the management team, and all actions taken must fall within the scope of the technician's license. The entire veterinary team should become familiar with the scope of practice for credentialed technicians in their state.

Section 9: Post-Treatment Monitoring and Follow-Up Care

Top 3 Takeaways

1. Regular monitoring of oncology patients is important and rechecks should be scheduled based on tumor behavior/grade, stage, and treatment protocol.
2. Monitoring for and addressing recurrent disease, late side effects from treatment, or concurrent conditions is imperative to assess and maintain patients' quality of life.
3. Sustain client communication throughout the treatment time frame and long term to enhance patients' and clients' quality of life.

Assessing Response

What constitutes a patient's response to therapy can be difficult to generalize because each cancer process is unique. Response to therapy must be viewed in the context of the original therapy, whether it be cure or palliation. Assessing response in oncology patients is categorized as:[94]

- Complete response (CR): regression of all evidence of disease with normal-sized lymph nodes.
- Partial response (PR): greater than a 30% reduction in the sum of longest diameters of target lesions (up to five specific lesions measured at the start of treatment and tracked throughout therapy), with no new lesions appearing.
- Progressive disease (PD): increase of at least 20% in the sum of the longest diameters of target lesions or the appearance of new lesions.
- Stable disease (SD): neither sufficient shrinkage to qualify as PR nor sufficient increase to qualify as PD.

New Clinical Signs in Cancer Patients

Because many patients receiving treatment are geriatric, it is common for them to develop new conditions or symptoms. Whenever a patient presents after cancer treatment with a new clinical sign, consider the possibility that the new sign can be caused by one of the following three things:

- Tumor progression
- Treatment toxicity
- An unrelated new problem

If the new clinical sign is not one that would be expected as a result of tumor progression or treatment toxicity, it is more likely that the pet has a new and potentially undiagnosed problem not related to the tumor or treatment.

For patients with PD, restaging is appropriate to look for systemic changes/metastasis before initiating another treatment modality (see Section 5, Therapeutic Interventions).

Post-RT Monitoring

Many patients, especially those treated with definitive intent, have a fair-to-excellent prognosis following initial RT. Acute effects of RT often resolve with minimal intervention. Late side effects can develop more than a year after therapy and are more common in patients receiving higher doses but typically occur in less than 5% of patients. Although rare, they can be permanent. Supportive care is often sufficient and includes pain management (opioids or NSAIDs), pentoxifylline, and vitamin E. Side effects are rarely life threatening, so euthanasia is seldom the best option (see Section 5, Therapeutic Modalities: Radiation Therapy for a description of acute and late side effects).

Patients must have periodic post-therapy examinations to assess for recurrence, metastasis, new tumor development, or complications of initial therapy.

Upon completion of initial therapy, patients are often restaged to determine the extent of disease. Patients should be monitored for resolution, improvement, progression, or recurrence of their initial presenting signs and for new signs potentially associated with recurrence, metastasis, new tumor development, or complications of initial therapy (see Box). The frequency of such evaluations should be based on the patient's condition, diagnosis, time since therapy, and client preferences and limitations. It is common for pets to be evaluated every 2–4 weeks for 2–3 months after they complete radiation therapy (usually by the treating oncologist), then every 2–3 months for the first year after treatment, followed by every 3–6 months during the second year. In many cases, this long-term follow-up may include evaluations by the primary care veterinarian.

Continuous Therapy

Continuous therapy is used either after an intense induction period or as the primary intervention. Additional chemotherapy, metronomic chemotherapy, or TKIs and cyclooxygenase-2 inhibitors have been used as ongoing therapy in such cases. During this time, continued diagnostic monitoring is tailored to the patient's therapeutic plan.

Monitoring for Recurrent or Metastatic Disease

PD can occur at any time during the therapeutic or remission stages. All patients must have a follow-up after receiving any cancer diagnosis regardless of their status. This allows the practitioner to monitor for recurrent or progressive disease. Follow-up is tailored to the patient and their tumor type. Keep in mind that abnormalities found during this period are not always related to the primary condition. Side effects secondary to treatment may arise or new problems often occur. It is important to be vigilant and distinguish the cause of clinical signs because it is common for clients to attribute changes in their pet to their cancer diagnosis, even when other etiologies are more likely.

As a general guideline, reassessments are recommended every 4–6 months for patients with low-grade tumors and every 1–3 months for those with high-grade tumors. Although not required at all visits, reassessment may include a physical examination, minimum database (CBC, serum chemistry, urinalysis, blood pressure), and radiographs. If disease recurs, it may indicate a guarded prognosis and return to normalcy may not be possible, so assessing these patients' quality of life is critical. Goals of therapy in such cases are often dynamic and affected by the extent of disease, expectations for the patient's quality of life, and client wishes.

Continuing Care

Veterinarians and clients often question whether cancer patients should continue to receive vaccines. The published veterinary literature does not support a consensus on this topic and opinions vary with the cancer type, so consult with an oncologist for their recommendations regarding specific patients.

Supportive care for cancer patients does not stop after the intense induction period of therapy. The postdiagnosis and post-therapy time frames are crucial for communication between the client

and the veterinary team. It is important to reinforce the client-clinic relationship, so patients receive ideal care. Follow-up care includes open communication, long-term pain management, recognizing and treating secondary conditions, and improving quality of life for as long as possible (See also Section 7, Supportive and Symptomatic Care).

Summary

Cancer is all too common in adult animals and is especially prevalent in senior pets. Diagnosing, staging, and treating cancer in dogs and cats and establishing a collaborative local or virtual relationship with veterinary oncologists for patient referrals and consultations are essential offerings in most full-service veterinary practices. Identifying the tumor type and stage are vital when selecting treatment and supporting clients as they weigh their options. Chemotherapy, surgery, immunotherapy, adjunctive treatments, and RT may be used alone or in combination depending on patient needs and client preferences. Therapeutic response must be assessed in the context of whether the original therapy was intended as cure or palliation. Managing quality of life in veterinary patients is especially meaningful for everyone involved and includes anticipating and preventing or minimizing discomfort and cancer treatment side effects, providing regular patient follow-up assessments, and maintaining transparent, relationship-focused communication with clients.

REFERENCES

1. Withrow SJ, Vail DM, Page RL. *Withrow and MacEwen's Small Animal Clinical Oncology*. 5th ed. Saunders; 2013.
2. Chon E, Hendricks W, White M, Rodrigues L, Haworth D, Post G. Precision medicine in veterinary science. *Vet Clin North Am Small Anim Pract* 2024;54(3):501–21.
3. Breit MN, Kisseberth WC, Bear MD, et al. Biologic activity of the novel orally bioavailable selective inhibitor of nuclear export (SINE) KPT-335 against canine melanoma cell lines. *BMC Vet Res* 2014;10:160.
4. Cawley JR, Wright ZM, Meleo K, et al. Concurrent use of rabacfosadine and L-asparaginase for relapsed or refractory multicentric lymphoma in dogs. *J Vet Intern Med* 2020;*34*(2):882–9.
5. London CA, Bernabe LF, Barnard S, et al. Preclinical evaluation of the novel, orally bioavailable Selective Inhibitor of Nuclear Export (SINE) KPT-335 in spontaneous canine cancer: results of a phase I study. *PLoS One* 2014;*9*(2):e87585.
6. Saba CF, Clifford C, Burgess K, et al. Rabacfosadine for naive canine intermediate to large cell lymphoma: Efficacy and adverse event profile across three prospective clinical trials. *Vet Comp Oncol* 2020;18(4):763–9.
7. Saba CF, Vickery KR, Clifford CA, et al. Rabacfosadine for relapsed canine B-cell lymphoma: Efficacy and adverse event profiles of 2 different doses. *Vet Comp Oncol* 2018;16(1):E76–E82.
8. Sadowski AR, Gardner HL, Borgatti A, et al. Phase II study of the oral selective inhibitor of nuclear export (SINE) KPT-335 (verdinexor) in dogs with lymphoma. *BMC Vet Res* 2018;14(1):250.
9. Thamm DH, Vail DM, Post GS, et al. Alternating rabacfosadine/doxorubicin: efficacy and tolerability in naive canine multicentric lymphoma. *J Vet Intern Med* 2017;31(3):872–8.
10. Vlodaver EM, Keating MK, Bidot WA, et al. Efficacy of verdinexor for the treatment of naive canine epitheliotropic cutaneous T-cell lymphoma: An open-label pilot study. *Vet Dermatol* 2024;35(5):536–46.
11. Weishaar KM, Wright ZM, Rosenberg MP, et al. Multicenter, randomized, double-blinded, placebo-controlled study of rabacfosadine in dogs with lymphoma. *J Vet Intern Med* 2022;36(1):215–26.
12. Thamm DH, Vail DM, Kurzman ID, et al. GS-9219/VDC-1101–a prodrug of the acyclic nucleotide PMEG has antitumor activity in spontaneous canine multiple myeloma. *BMC Vet Res* 2014;10:30.
13. U.S. Food and Drug Administration. FDA conditionally approves first oral tablet to treat chemotherapy-induced diarrhea in dogs. December 21, 2021. Fda.gov. Available at https://www.fda.gov/news-events/press-announcements/fda-conditionally-approves-first-oral-tablet-treat-chemotherapy-induced-diarrhea-dogs. Accessed July 23, 2025.
14. Gilvetmab [package insert]. Rahway, New Jersey: Merck Animal Health. Available at https://merckusa.cvpservice.com/product/basic/view/1047586. Accessed July 23, 2025.
15. Cockery JR, Leifer CA. Racing CARs to veterinary immuno-oncology. *Front Vet Sci* 2023:10(2):1130182.
16. Xia YY, Chi KH, Liao AT, et al. Limited clinical efficacy with potential adverse events in a pilot study of autologous adoptive cell therapy for canine oral malignant melanoma. *Vet Sci* 2024;11(4):150.
17. McCafferty C. USDA approves new canine cancer therapy. DVM360. March 19, 2025. Available at https://www.dvm360.com/view/usda-approves-new-canine-cancer-therapy. Accessed July 23, 2025.
18. De Ridder TR, Campbell JE, Burke-Schwarz C, et al. Randomized controlled clinical study evaluating the efficacy and safety of intratumoral treatment of canine mast cell tumors with tigilanol tiglate (EBC-46). *J Vet Intern Med* 2021;35(1):415–29.
19. Jones PD, Campbell JE, Brown G, et al. Recurrence-free interval 12 months after local treatment of mast cell tumors in dogs using intratumoral injection of tigilanol tiglate. *J Vet Intern Med* 2021;35(1):451–5.
20. Reddell P, De Ridder TR, Morton JM, et al. Wound formation, wound size, and progression of wound healing after intratumoral treatment of mast cell tumors in dogs with tigilanol tiglate. *J Vet Intern Med* 2021;35(1):430–41.
21. de Castro Cunha RM, Lavalle GE, Nunes FC, et al. Canine squamous cell carcinoma: Electrochemotherapy association with surgery and correlation with overall survival. *Vet Comp Oncol* 2023;21(2):240–54.
22. Dos Anjos DS, Bueno C, Magalhães LF, et al. Electrochemotherapy induces tumor regression and decreases the proliferative index in canine cutaneous squamous cell carcinoma. *Sci Rep* 2019;9(1):15819.
23. Moretti G, Dentini A, Beccati F, et al. Palliative repeated electroporations of oral tumors in dogs: A case series. *Front Vet Sci* 2022;9:1004811.
24. Ramos SC, Dias-Pereira P, Luís AL, et al. Electrochemotherapy in dogs and cats-A review. *Vet Comp Oncol* 2024;22(3):311–21.
25. Santos Dos Anjos D, Rossi YA, Sierra OR, et al. Outcome following curative-intent electrochemotherapy for extramedullary plasmacytoma in dogs - case reports. *Top Companion Anim Med* 2020;40:100441.
26. Tellado M, Mir LM, Maglietti F. Veterinary guidelines for electrochemotherapy of superficial tumors. *Front Vet Sci* 2022;9:868989.
27. Thalheim L, Williams LE, Borst LB, et al. Lymphoma immunophenotype of dogs determined by immunohistochemistry, flow cytometry, and polymerase chain reaction for antigen receptor rearrangements. *J Vet Intern Med* 2013;27:1509–16.

28. Pun JKH. An integrated review of the role of communication in veterinary clinical practice. *BMC Vet Res* 2020;16(1):394.
29. Englar R. Recasting the gold standard – part I of II: delineating healthcare options across a continuum of care. *J Feline Med Surg* 2023;25(12): 1098612X231209855.
30. Carson CA. Nonverbal communication in veterinary practice. *Vet Clin North Am Small Anim Pract* 2007;37(1):49–63.
31. Englar R. Recasting the gold standard – part II of II: communicating healthcare options along a continuum of care. *J Feline Med Surg* 2023; 25(12):1098612X231215639.
32. Gaspar TB, Henriques J, Marconato L, et al. The use of low-dose metronomic chemotherapy in dogs—Insight into a modern cancer field. *Vet Comp Oncol* 2018;16:2–11.
33. Biller B. Metronomic chemotherapy in veterinary patients with cancer: Rethinking the targets and strategies of chemotherapy. *Vet Clin North Am Small Anim Pract* 2014;44(5):817–29.
34. Burton JH, Mitchell L, Thamm DH, et al. Low-dose cyclophosphamide selectively decreases regulatory T cells and inhibits angiogenesis in dogs with soft tissue sarcoma. *J Vet Intern Med* 2011;25(4):920–6.
35. Lana S, U'ren L, Plaza S, et al. Continuous low-dose oral chemotherapy for adjuvant therapy of splenic hemangiosarcoma in dogs. *J Vet Intern Med* 2007;21(4):764–9.
36. Elmslie RE, Glawe P, Dow SW. Metronomic therapy with cyclophosphamide and piroxicam effectively delays tumor recurrence in dogs with incompletely resected soft tissue sarcomas. *J Vet Intern Med* 2008;22(6): 1373–9.
37. Tripp CD, Fidel J, Anderson CL, et al. Tolerability of metronomic administration of lomustine in dogs with cancer. *J Vet Intern Med* 2011; 25(2):278–84.
38. Kerbel RS, Kamen BA. The anti-angiogenic basis of metronomic chemotherapy. *Nat Rev Cancer* 2004;4(6):423–36.
39. Mitchell L, Thamm DH, Biller BJ. Clinical and immunomodulatory effects of toceranib combined with low-dose cyclophosphamide in dogs with cancer. *J Vet Intern Med* 2012;26(2):355–62.
40. Lew FH, McQuown B, Borrego J, Cunningham S, Burgess KE. Retrospective evaluation of canine heart base tumours treated with toceranib phosphate (Palladia): 2011-2018. *Vet Comp Oncol* 2019;17(4):465–71.
41. Carlsten KS, London CA, Haney S, Burnett R, Avery AC, Thamm DH. Multicenter prospective trial of hypofractionated radiation treatment, toceranib, and prednisone for measurable canine mast cell tumors. *J Vet Intern Med* 2012;26(1):135–41.
42. London CA, Gardner HL, Mathie T, et al. Impact of toceranib/piroxicam/cyclophosphamide maintenance therapy on outcome of dogs with appendicular osteosarcoma following amputation and carboplatin chemotherapy: A multi-institutional study. *PLoS One* 2015;29:10(4): e0124889.
43. Chon E, McCartan L, Kubicek LN, et al. Safety evaluation of combination toceranib phosphate (Palladia®) and piroxicam in tumour-bearing dogs (excluding mast cell tumours): a phase I dose-finding study. *Vet Comp Oncol* 2012;10(3):184–93.
44. Pellin MA, Wouda RM, Robinson K, et al. Safety evaluation of combination doxorubicin and toceranib phosphate (Palladia®) in tumour bearing dogs: a phase I dose-finding study. *Vet Comp Oncol* 2017;15(3): 919–31.
45. Burton JH, Venable RO, Vail DM, et al. Pulse-administered toceranib phosphate plus lomustine for treatment of unresectable mast cell tumors in dogs. *J Vet Intern Med* 2015;29(4):1098–104.
46. Pan X, Tsimbas K, Kurzman ID, et al. Safety evaluation of combination CCNU and continuous toceranib phosphate (Palladia(®)) in tumour-bearing dogs: a phase I dose-finding study. *Vet Comp Oncol* 2016;14(2):202–9.
47. Bavcar S, de Vos J, Kessler M, et al. Combination toceranib and lomustine shows frequent high grade toxicities when used for treatment of non-resectable or recurrent mast cell tumours in dogs: A European multicentre study. *Vet J* 2017;224:1–6.
48. Wouda RM, Hocker SE, Higginbotham ML. Safety evaluation of combination carboplatin and toceranib phosphate (Palladia) in tumour-bearing dogs: A phase I dose finding study. *Vet Comp Oncol* 2018;16(1):E52–E60.
49. Robat C, London C, Bunting L, et al. Safety evaluation of combination vinblastine and toceranib phosphate (Palladia®) in dogs: a phase I dose-finding study. *Vet Comp Oncol* 2012;10(3):174–83.
50. Olsen JA, Thomson M, O'Connell K, et al. Combination vinblastine, prednisolone and toceranib phosphate for treatment of grade II and III mast cell tumours in dogs. *Vet Med Sci* 2018;4(3):237–51.
51. Rippy SB, Gardner HL, Nguyen SM, et al. A pilot study of toceranib/vinblastine therapy for canine transitional cell carcinoma. *BMC Vet Res* 2016;12(1):257.
52. Falck K, Gröhn P, Sorsa M, et al. Mutagenicity in urine of nurses handling cytostatic drugs. *Lancet* 1979;1(8128):1250–1.
53. Hon CY, Teschke K, Shen H, et al. Antineoplastic drug contamination in the urine of Canadian healthcare workers. *Int Arch Occup Environ Health* 2015;88(7):933–41.
54. Roussel C, Witt KL, Shaw PB, et al. Meta-analysis of chromosomal aberrations as a biomarker of exposure in healthcare workers occupationally exposed to antineoplastic drugs. *Mutat Res Rev Mutat Res* 2019;781: 207–17.
55. Smerhovsky Z, Landa K, Rössner M, et al. Risk of cancer in an occupationally exposed cohort with increased level of chromosomal aberrations. *Environ Health Perspect* 2001;109(1):41–5.
56. Anderson RW, Puckett WH, Dana WJ, et al. Risk of handling injectable antineoplastic agents. *Am J Hosp Pharm* 1982;39:1881–7.
57. Arnon J, Meirow D, Lewis-Roness H, et al. Genetic and teratogenic effects of cancer treatments on gametes and embryos. *Hum Reprod Update* 2001;7:394–403.
58. Christensen J. Hazardous drugs: The hidden threat to veterinary nurses. *Today's Veterinary Nurse*. Winter 2023; 46–55.
59. National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2024. December 2024. Available at https://www.cdc.gov/niosh/docs/2025-103/default.html. Accessed November 18, 2025.
60. Pérez Fidalgo JA, García Fabregat L, Cervantes A, et al. Management of chemotherapy extravasation: ESMO-EONS Clinical Practice Guidelines. *Ann Oncol* 2012;23(suppl 7):vii167–vii173.
61. Fournier Q, Serra JC, Handel I, et al. Impact of pretreatment neutrophil count on chemotherapy administration and toxicity in dogs with lymphoma treated with CHOP chemotherapy. *J Vet Intern Med* 2018;32(1): 384–93.
62. Chavalle T, Chamel G, Denoeux P, et al. Are severe adverse events commonly observed in dogs during cancer chemotherapy? A retrospective study on 155 dogs. *Vet Comp Oncol* 2022;20(2):393–403.
63. Shaffer K, Bach J, Chun R. Prospective study evaluating the incidence of bacteraemia and bacteruria in afebrile and febrile neutropaenic dogs undergoing chemotherapy. *Vet Med Sci* 2016;2(4):281–94.
64. Cunha SC dos S, Silva FB, Corgozinho KB, et al. Retrospective study of adverse events of chemotherapy in cats. *Acta Sci Vet* 2018;46(1).
65. Chretin JD, Rassnick KM, Shaw NA, et al. Prophylactic trimethoprim-sulfadiazine during chemotherapy in dogs with lymphoma and

osteosarcoma: A double-blind, placebo-controlled study. *J Vet Intern Med.* 2007;21(1):141–148.
66. Gumash M, Martin OA, Lindley SES, Zhu X. Prophylactic antimicrobials for prevention of febrile neutropenia in tumour-bearing dogs treated with lomustine. *Vet Comp Oncol* 2025;23(1):30–6.
67. Bisson JL, Fournier Q, Johnston E, et al. Evaluation of a 0.75×10^9/L absolute neutrophil count cut-off for antimicrobial prophylaxis in canine cancer chemotherapy patients. *Vet Comp Oncol* 2020;18(3):258–68.
68. Dunfield EM, Turek MM, Buhr KA, et al. A survey of stereotactic radiation therapy in veterinary medicine. *Vet Radiol Ultrasound* 2018;59: 786–95.
69. Burney D, Jones G, Byers C, et al. 2025 AAHA Referral Guidelines. *J Am Anim Hosp Assoc* 2025;61(2):28–45.
70. AVMA. Veterinary telehealth: The basics. 2024. Available at https://www.avma.org/resources-tools/animal-health-and-welfare/telehealth-telemedicine-veterinary-practice/veterinary-telehealth-basics. Accessed May 21, 2025.
71. Simonsen A. States must lift restrictions on telemedicine: Veterinary telemedicine saves lives, alleviates suffering and preserves the human-animal bond. June 12, 2023. Humanepro.org. Available at https://humanepro.org/blog/blog-states-must-lift-restrictions-telemedicine. Accessed May 21, 2025.
72. ASPCA. Position Statement on Veterinary Telemedicine. 2024. Available at https://www.aspca.org/about-us/aspca-policy-and-position-statements/position-statement-veterinary-telemedicine. Accessed May 21, 2025.
73. VVCA. 2024 Industry Report: Embracing the Future of Veterinary Care: Virtual Care. February 21, 2024. Available at https://vvca.org/embracing-the-future-of-veterinary-care-virtual-care/. Accessed May 21, 2025.
74. Johannes CM, Musser ML. Anorexia and the cancer patient. *Vet Clin North Am Small Anim Pract* 2019;49(5):837–54.
75. Rathore M, Das N, Ghosh N, et al. Insights on discovery, efficacy, safety and clinical applications of ghrelin receptor agonist capromorelin in veterinary medicine. *Vet Res Commun* 2024;48(1):1–10.
76. Rhodes L, Zollers B, Wofford JA, et al. Capromorelin: a ghrelin receptor agonist and novel therapy for stimulation of appetite in dogs. *Vet Med Sci* 2018;4(1):3–16.
77. Zollers B, Wofford JA, Heinen E, et al. A prospective, randomized, masked, placebo-controlled clinical study of capromorelin in dogs with reduced appetite. *J Vet Intern Med* 2016;30(6):1851–7.
78. Ellis C, Odunayo A, Tolbert MK. The use of metronidazole in acute diarrhea in dogs: a narrative review. *Top Companion Anim Med* 2023; 56-57:100824.
79. Holden R, Brennan M. Does metronidazole increase the speed of recovery in dogs with acute diarrhoea? *Vet Rec* 2021;188(1):33–4.
80. Stübing H, Suchodolski JS, Reisinger A, et al. The effect of metronidazole versus a synbiotic on clinical course and core intestinal microbiota in dogs with acute diarrhea. *Vet Sci* 2024;11(5).
81. Jugan MC, Wouda RM, Higginbotham ML. Preliminary evaluation of probiotic effects on gastrointestinal signs in dogs with multicentric lymphoma undergoing multi-agent chemotherapy: A randomised, placebo-controlled study. *Vet Rec Open* 2021;8(1):e2.
82. Fournier Q, Serra JC, Williams C, et al. Chemotherapy-induced diarrhoea in dogs and its management with smectite: Results of a monocentric open-label randomized clinical trial. *Vet Comp Oncol* 2021;19(1):25–33.
83. Gildea E, North C, Walker K, et al. Use of bedinvetmab (Librela®) for canine osteoarthritis in France, Germany, Italy, Spain, and the UK: Quantitative analysis of veterinarian satisfaction and real-world treatment patterns. *Animals (Basel)* 2024;14(15):2231.
84. Walters RR, Boucher JF, De Toni F. Pharmacokinetics and immunogenicity of frunevetmab in osteoarthritic cats following intravenous and subcutaneous administration. *Front Vet Sci* 2021;8:687448.
85. Clark TP, Linton DD, Freise KJ, et al. Multicentered masked placebo-controlled phase 2 clinical study of an extended duration transdermal buprenorphine solution for postoperative pain in cats. *J Vet Pharmacol Ther* 2022;45(S1)(suppl 1):S40–S51.
86. Clark TP, Linton DD, Freise KJ, et al. Multicentered masked placebo-controlled phase 3 clinical study of an extended duration transdermal buprenorphine solution for post-operative pain in cats. *J Vet Pharmacol Ther* 2022;45(S1)(suppl 1):S52–S66.
87. Clark TP, Linton DD, Freise KJ, et al. Margin of safety of extended-duration transdermal buprenorphine solution following multiple-dose administrations to cats. *J Vet Pharmacol Ther* 2022;45(S1)(suppl 1):S67–S84.
88. Di Cesare F, Negro V, Ravasio G, et al. Gabapentin: clinical use and pharmacokinetics in dogs, cats, and horses. *Animals (Basel).* 2023;13(12):2045.
89. Anthony RM, Amundson MD, Brejda J, et al. Acceptance of a novel, highly palatable, calorically dense, and nutritionally complete diet in dogs with benign and malignant tumors. *Vet Sci* 2023;10(2):148.
90. Stockman J, Fascetti AJ, Kass PH, et al. Evaluation of recipes of home-prepared maintenance diets for dogs. *J Am Vet Med Assoc* 2013;242(11): 1500–5.
91. Candellone A, Badino P, Girolami F, et al. Concomitant campylobacteriosis in a puppy and in its caregiver: A One Health perspective paradigm in human-pet relationship. *Vet Sci* 2023;10(4):244.
92. Davies RH, Lawes JR, Wales AD. Raw diets for dogs and cats: a review, with particular reference to microbiological hazards. *J Small Anim Pract* 2019;60(6):329–39.
93. Ribeiro-Almeida M, Mourão J, Magalhães M, et al. Raw meat-based diet for pets: a neglected source of human exposure to *Salmonella* and pathogenic *Escherichia coli* clones carrying *mcr*, Portugal, September 2019 to January 2020. *Euro Surveill* 2024;29(18):2300561.
94. Nguyen SM, Thamm DH, Vail DM, et al. Response evaluation criteria for solid tumours in dogs (v1.0): a Veterinary Cooperative Oncology Group (VCOG) consensus document. *Vet Comp Oncol* 2015;13(3):176–83.