

# Traditional Treatment Modalities for Canine Transmissible Venereal Tumor (TVT): An Overview

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## ABSTRACT

Canine Transmissible Venereal Tumor (TVT) is a contagious cancer with a worldwide presence, making it a problem in veterinary oncology. The rise of TVT cases resistant to treatment has driven the development of new alternatives. Diagnosis can be made through clinical exam, molecular testing, or serological testing. Conventional treatments like chemotherapy, radiation, and surgery have evolved. This article examines and explores current approaches to treat TVT, highlighting innovative medications that are being researched or are already in use.

### Introduction

Canine transmissible venereal tumor (CTVT), often referred to as venereal sarcoma, infectious sarcoma, venereal granuloma, or Sticker's tumor, is a type of tumor that affects the reticuloendothelial system in dogs [1]. Canine transmissible venereal tumor (CTVT) is a malignant neoplasm that arises in the connective tissue and is characterized by its capacity for horizontal transmission, mostly targeting the external reproductive organs of canines [2]. The growth of this tumor is not caused by chance but rather is transmitted by coitus, licking, and/or sniffing, which sets it apart from other neoplasms in terms of pathophysiology [3]. Tumor cells did not contain any infectious particles, such as bacteria or viruses, despite the transmission having occurred [4]. This disease is prevalent in around 90 countries globally [5]. CTVT is categorized into two distinct types: genital CTVT and extragenital CTVT. Genital CTVT predominantly impacts the reproductive region of canines. It mainly affects the lower part of the male genitalia, particularly the foreskin, causing disorders such as phimosis or paraphimosis. Lesions frequently manifest in the posterior vaginal region of female dogs, specifically in close proximity to the vestibulovaginal junction [6]. Because of its deep location, it may sometimes go unnoticed until it becomes significantly large [7]. Extragenital tumor cases are linked to the characteristics of tumor transmission, which can be transmitted through licking and sniffing [8]. Nevertheless, there is a substantial amount of recorded evidence regarding extragenital CTVT, which includes tumors discovered in the eyes, mouth area, and skin. These cases have been managed with diverse therapeutic strategies [9].

Currently, there are several therapeutic options accessible for cases of CTVT, such as surgery, chemotherapy, and radiotherapy [10]. Vincristine sulfate chemotherapy is frequently used as a treatment due to its proven clinical effectiveness and lower occurrence of significant risks and adverse effects [11]. Despite the use of conventional therapy for TVT, resistance has become more common, leading to the need for alternative treatments. Various options are currently available, ranging from well-established methods to those still in experimental stages. This study aims to review the recent conventional treatment approaches for Canine Transmissible Venereal Tumor (TVT).

### Diagnosis of TVT

Various methods are used to diagnose Canine Transmissible Venereal Tumor (TVT), including: Physical examination, Molecular tests and Blood tests.

### Traditional Treatment Modalities:

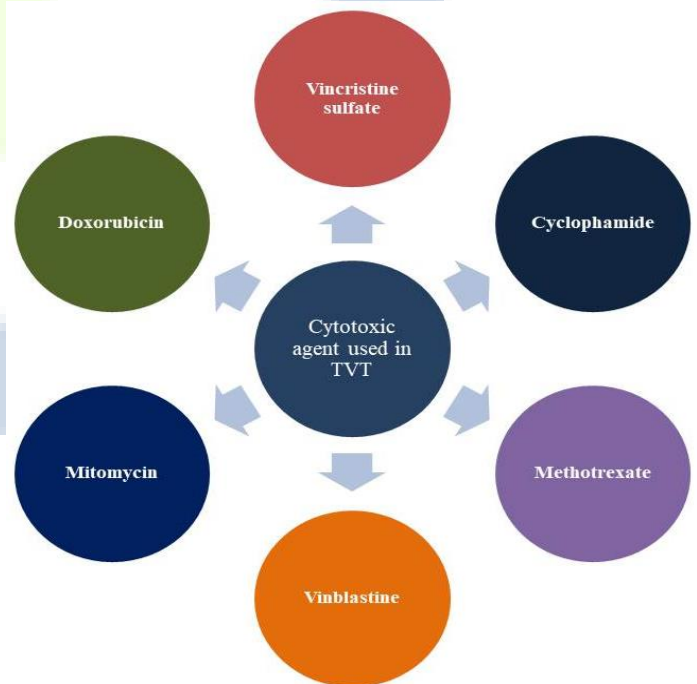
Currently, there are multiple therapy alternatives accessible for instances of transmissible venereal tumor (TVT) in canines. Certain treatments have undergone clinical trials, while others are still being examined in clinical research to determine their effectiveness.

### Chemotherapy for TVT

Cytotoxic medications are categorized into alkaline agents, antimetabolites, antitumor (cytotoxic) antibiotics, vinca alkaloids, hormones, enzymes, and other agents based on their mechanism of action, specific tissues they target, and their antitumor actions [17].

**Table 1** provides details on the specific diagnostic methods used for TVT.

3-	Histopathology	A biopsy is performed on the tumor, and then the tissue samples are examined with a microscope to verify the presence of TVT cells and assess their microscopic appearance.	[14]
4-	Immunohistochemistry (IHC)	Detection of specific markers (e.g., vimentin, leukocyte common antigen) in tissue samples to further confirm the diagnosis of TVT.	[15]
5-	Polymerase chain reaction (PCR)	Molecular analysis to detect TVT-specific DNA sequences in biopsy samples, providing highly sensitive and specific confirmation of the disease.	[16]
6-	Imaging techniques	Radiography or ultrasonography of the affected area to evaluate tumor size, location, and involvement of nearby structures, aiding in treatment planning.	[12]
7-	Serology	Detection of antibodies against TVT antigens in serum samples, although less commonly used for diagnosis due to variations in sensitivity and specificity.	[15]



**Fig. 1** this figure show some cytotoxic agents used in the treatment of Canine transmissible venereal tumor (CTVT).

	Diagnostic methods	Descriptions	Reference
1-	Clinical examination	Assessment of physical signs such as genital masses, bleeding, or lymphadenopathy.	[12]
2-	Cytology	Fine-needle aspirate of the tumor mass to identify characteristic TVT cells, which are large round cells with prominent nuclei and scant cytoplasm	[13]

Vincristine sulfate is administered to treat lymphoproliferative malignancies, transmissible venereal tumors, thrombocytopenia, and other related conditions [18]. The process of involution is initially quick during the early stages of treatment, but gradually slows down with time. The lesions also undergo a progressive involution. Complete healing is often attained after undergoing 2-8 therapy sessions, with a success rate of 90%. Certain side effects are anticipated. Vincristine, a cytotoxic drug, can lead to side effects such as myelosuppression and gastrointestinal issues, which may result in leucopenia and vomiting in approximately 5-7% of patients [19].

Cyclophosphamide is administered in conjunction with other chemotherapeutic agents to treat lymphoma, some carcinomas, and sarcomas [20]. Methotrexate is administered in conjunction with other chemotherapeutics to treat lymphomas in cats and dogs [21]. In addition, it can be utilized in the management of myoproliferative diseases and transmissible venereal tumors [22]. The medicine doxorubicin is utilized to treat lymphoma, osteosarcoma, hemangiosarcoma, thyroid carcinoma, and many other carcinomas [23]. Mitomycin is used in the treatment of adenocarcinoma as well as carcinomas affecting the breast gland, cervix, colon, rectum, bladder, neck, and pancreas [24]. Vinblastine is used therapeutically to treat mast cell malignancies and lymphomas in canines. Furthermore, it is extremely effective in the treatment of malignant testicular cancers [25].

#### Radiation Therapy

Radiotherapy has proven time and time again to be an effective local tumor control method, especially when surgical excision is not an option or when the tumor has spread locally extensively [26]. Radiation treatment, which uses focused radiation administration, is a non-invasive way to kill tumor cells without damaging healthy tissue around them [27]. Radiotherapy procedures such as brachytherapy and fractionated external beam radiation have been investigated, enabling the development of individualized treatment plans according to tumor size, site, and stage [28]. In addition, tumor regression and long-term disease-free survival have been achieved with radiotherapy, which supports its use as either the main or supplementary treatment for TVT [29]. To further advance the therapeutic landscape for this common canine tumor, additional research is needed to optimize treatment procedures, minimize side effects, and evaluate long-term outcomes.

#### Surgical Treatment

Surgical techniques are essential for diagnosing and treating cancers, especially solid tumors, and they have a high success rate in treatment. Surgery is contraindicated for diffuse cases of TVT [3]. In this case, the surgery effectively treated the diagnostic, spinal cord decompression, collection of biopsy material, and provided treatment. The current analysis suggests that for dogs with small, easily accessible, non-invasive tumor nodules, surgical excision is the suggested approach. This method ensures the total removal of the mass with adequate surgical margins [30]. Surgical intervention can yield positive results for tiny and circumscribed tumors. Nevertheless, when the disease has metastasized, the probability of recurrence after surgery might vary between 30% and 75% [31]. Surgical operations carry the risk of TVT cells spreading to the surgical area, which may increase the likelihood of the condition recurring [32].

#### Immunotherapy

Immunotherapy is now recognized as an effective treatment for this type of cancer. In the past, treatments involved using blood or serum from recovered animals to provide temporary immunity, or creating vaccines from tumor cells or bacterial toxins to trigger the body's immune system. Today, treatments use substances like interleukins and viruses to stimulate the immune system actively. In particular, BCG therapy has proven successful in treating canine venereal cancers. [33]. Instead of using TVT, a different treatment involves injecting genes that produce immune-boosting proteins called IL-6, IL-12, and IL-15 into the body using an electrical procedure called electroporation. [34].

#### Challenges and Future Directions

Traditional treatments for Canine Transmissible Venereal Tumor (TVT), including chemotherapy, radiation, and surgery, have limitations. Resistance to medications, side effects, and the need for more precise treatments pose challenges. Emerging therapies for TVT offer potential solutions, especially for tumors resistant to traditional methods. One example is using lomustine for tumors that have become resistant to vincristine sulfate. These new approaches provide hope for improved treatment outcomes in dogs with TVT. Agents that have not yet undergone clinical testing will likely require additional research to clarify and study. A number of innovative therapeutic approaches are garnering significant interest due to their potential to increase treatment efficacy while decreasing side effects. Two such examples are immunotherapy and targeted molecular medicines. Consistent professional practice and improved treatment outcomes are both facilitated by standardized protocols and guidelines. Researchers should focus their efforts in the future on two main areas: (1) better understanding the fundamental mechanisms of tumor growth and treatment resistance, and (2) identifying biomarkers that consistently predict treatment response and direct personalized therapy

tactics. Collaborative efforts involving oncologists, immunologists, molecular biologists, and veterinarians are crucial to overcome these obstacles and discover the future of TVT treatment.

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