# cancer

## Veterinary technical bulletin

STANGEST

## Cancer

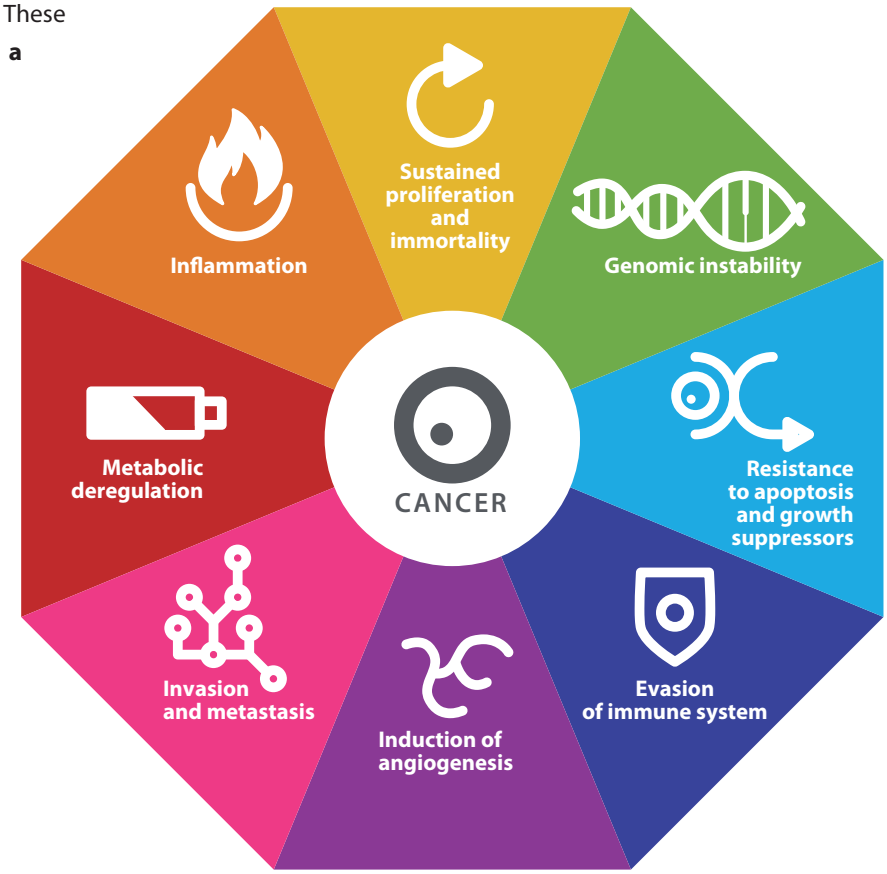
Cells can divide to replace the ones that are dead or damaged, maintaining tissue homeostasis (normal function and morphology of the tissue). This balance relies on a precise regulation of cell proliferation and cell death. **Cancer** is a disease characterized by an unbalance between these two processes, causing an uncontrolled cell proliferation. The accumulation of cells can result in a tissue mass **(tumor)**, although some type of cancers like leukemia or lymphoma do not present solid tumors. There are benign tumors, formed by cells that are not capable of invading other organs. The term cancer refers to malign tumors, those that possess the capability of invading nearby tissues and disseminate to distant parts of the organism. The evolution of each type of cancer depends on different factors both from the tumor and the patient that influence each other.

## Hallmarks of cancer

During cancer development, tumor cells acquire functional characteristics that clearly differentiate them from healthy cells. This evolution towards malignancy is enabled by the **genomic instability** of tumor cells: DNA repair systems are frequently altered, which impedes error repair during cellular division and increases sensitivity to exogenous or endogenous mutagenic agents, such as oxidative stress. Hence, tumor cells acquire a succession of alterations in the genome that will give rise to their typical biological capabilities. These include the ability of **proliferating in a constant and unlimited manner** by means of several mechanisms, such as the activation of growth signaling pathways, the inhibition of cell cycle arrest signals, etc. The process of tumor growth involves stressing states like hypoxia, the alteration of signaling pathways or DNA damage. In a healthy cell, the detection of these unfavorable conditions activates **apoptosis or programmed cell death**. On the contrary, tumor cells have acquired the capacity of inhibiting this process and keep growing. Moreover, tumor cells can **migrate** to other parts of the organism via the circulatory or the lymphatic system, where a secondary tumor can develop.

## Relationship with the microenvironment

For cancer progression, it is of utmost importance the interaction of tumor cells with their microenvironment, which includes the extracellular matrix and the immune and circulatory systems. Hence, tumor cells utilize surrounding healthy cells to their advantage. An example of this is the induction of **angiogenesis**, the formation of new blood vessels that provide oxygen and nutrients to cancer cells. In addition, this neovascularization also facilitates intravasation and the posterior migration of tumor cells to other tissues. In a healthy organism, the **immune system** would detect tumor cells as abnormal and induce their death. Cancer cells are frequently capable of evading the immune response by directly inhibiting the activity of cytolytic cells or even by utilizing immune cells that inhibit the response of T lymphocytes or natural killer cells. Likewise, stromal **fibroblast** activity is regulated by tumor cells: they can induce the production of growth factors by fibroblasts, promoting the proliferation of the tumor; or they can remodel the **extracellular matrix**, which facilitates the dissemination to other organs. For all these reasons, cancer is not simply studied as a homogeneous mass of transformed cells, but as a complex network of different cell types having multiple interactions with each other.



## Causes

Cancer is the result of an alteration in gene expression, caused by DNA mutations or by the alteration in gene regulation mechanisms: epigenome, miRNAs, etc. These mutations provide tumor cells with their previously mentioned functional characteristics.

A low percentage of cancers are due to inherited mutations, the vast majority of genomic alterations are acquired during life. Among them, there are spontaneous genetic alterations that are produced during cellular replication; and the mutations caused by environmental factors, namely carcinogens able to modify the genome or the epigenome to finally induce a cancer (see graphic in the next page).

Moreover, there are **risk factors** which are related to a higher cancer incidence: age, diet, obesity, the lack of physical activity, chronic inflammation, exposition to certain hormones, immunosuppression processes, etc.

The development of cancer will depend on the genetic factors of the patient, the amount and time of exposure to carcinogens and the behavior towards risk factors. Therefore, it is possible to reduce the risk of developing certain types of cancer by avoiding exposure to carcinogenic substances or by modifying our lifestyle and diet habits.

Cancer already represents the first death cause in pets. In studies including more than 2000 autopsies, it was shown than 45% of dogs from age 10 and above died due to cancer. Developing a cancer depends on genetic factors, the amount and exposure time to carcinogens and the behavior in relation to risk factors. Consequently, the risk of developing a cancer can be reduced by avoiding the exposure to certain carcinogenic substances or modifying our habits and diet.

## Cancer and oxidative stress

**Reactive oxygen species** (ROS) are generated as a consequence of different cellular biochemical processes, such as mitochondrial respiration or the oxidation of proteins and lipids. ROS are highly reactive and cells have different **antioxidant** systems to neutralize them and maintain redox homeostasis, a balance between ROS production and elimination.

Cancer cells present high levels of ROS as a consequence of alterations in different signaling pathways and metabolism. It is considered that ROS can contribute to tumor formation by activating proliferation pathways or by generating mutations in the DNA, affecting lipids and proteins.

Certain antioxidants, such as Vitamin C and alpha-lipoid acid, present pro-oxidant activity specifically in tumor cells, which contributes to the fight against the tumor. Moreover, radiotherapy and systemic chemotherapy have a relative selectivity for cancer cells, so healthy tissues are also affected by the treatment. Likewise, organs such as the liver and kidneys work more intensively in order to metabolize the components of chemotherapy. This increased performance can lead to inflammation and oxidative stress. Hence, themodulation of ROS by antioxidants will have a considerable impact in tumor initiation and progression, as well as in the mutagenesis in healthy cells caused by the treatment.

## Cancer treatments

### Conventional treatments

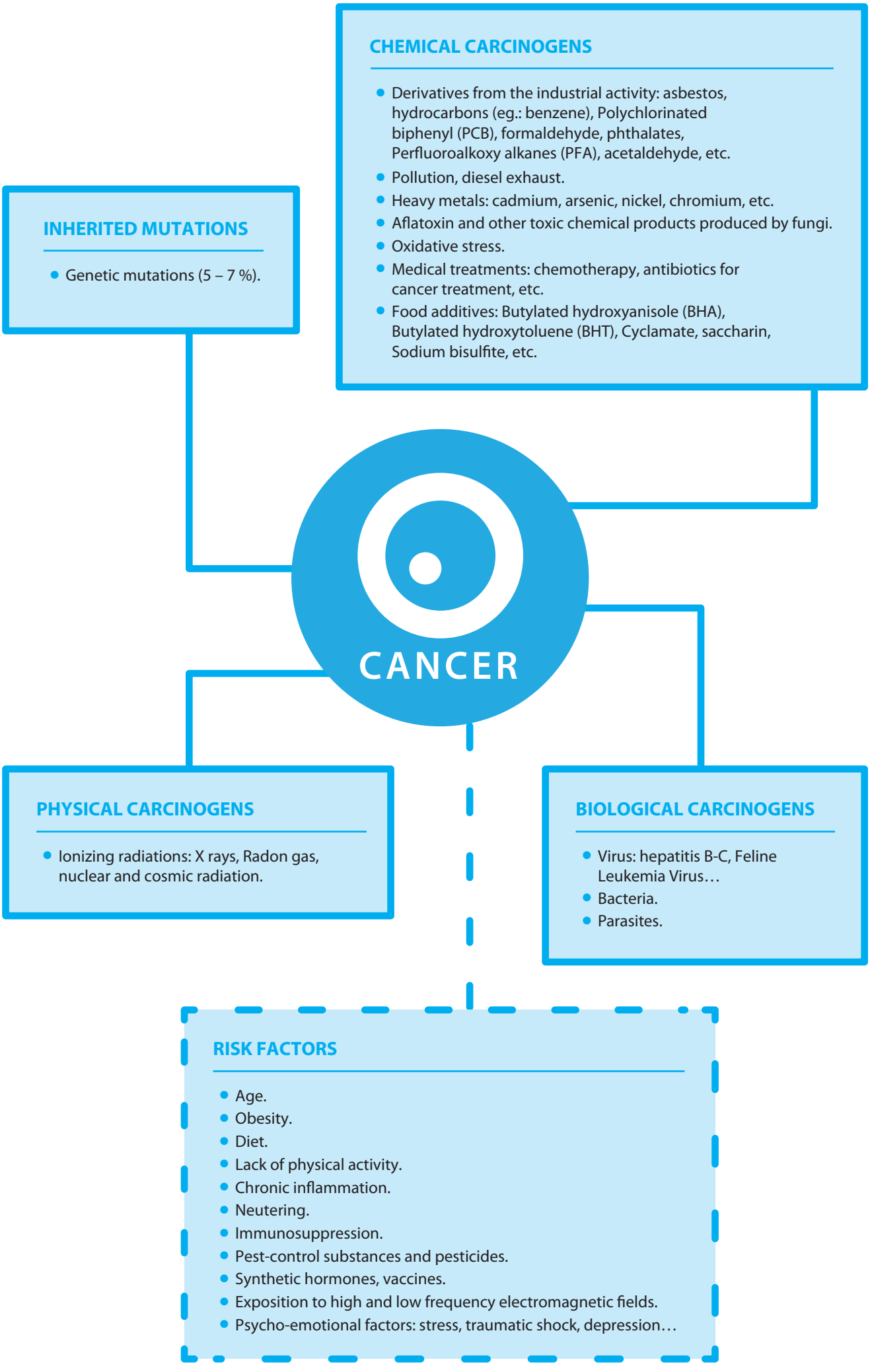
The main cancer treatments are surgery, radiotherapy and chemotherapy. For certain tumors there are other therapeutic options, such as immunotherapy or hormone therapy. The therapeutic options will depend on factors related to the tumor, such as the type of tumor, the progression state and the dissemination to other tissues; as well as the age and health status of the patient.

Cancer treatments have a strong toxic effect over healthy cells, which derives to side effects that vary depending on the patient, the diet, the treatment received, etc. The most frequent ones in animals are: pain, colitis, cystitis, constipation, lack of appetite, nausea and vomit, diarrhea, dehydration, leukopenia (with the subsequent risk of infection) and inflammation of the mouth, skin, eyes, intestine and others.

**Integrative oncology**

Integrative oncology is a combination of conventional treatments with complementary therapies of maximum efficacy and scientific rigor. The essential part of oncologic therapy is still the conventional treatment, although additional measures are implemented by taking into account the maximum number of factors related to cancer development. The objective of complementary therapies is to promote the patients' quality of life by:

- Preventing malnutrition
- Reducing the side effects of chemo- and radiotherapy
- Modulating the immune system
- Supporting hepatic detoxification


CHEMICAL CARCINOGENS
Derivatives from the industrial activity: asbestos, hydrocarbons (eg.: benzene), Polychlorinated biphenyl (PCB), formaldehyde, phthalates, Perfluoroalkoxy alkanes (PFA), acetaldehyde, etc.
Pollution, diesel exhaust.
Heavy metals: cadmium, arsenic, nickel, chromium, etc.
Aflatoxin and other toxic chemical products produced by fungi.
Oxidative stress.
Medical treatments: chemotherapy, antibiotics for cancer treatment, etc.
Food additives: Butylated hydroxyanisole (BHA), Butylated hydroxytoluene (BHT), Cyclamate, saccharin, Sodium bisulfite, etc.
INHERITED MUTATIONS
Genetic mutations (5 – 7 %).
CANCER
PHYSICAL CARCINOGENS
Ionizing radiations: X rays, Radon gas, nuclear and cosmic radiation.
BIOLOGICAL CARCINOGENS
Virus: hepatitis B-C, Feline Leukemia Virus…
Bacteria.
Parasites.
RISK FACTORS
Age.
Obesity.
Diet.
Lack of physical activity.
Chronic inflammation.
Neutering.
Immunosuppression.
Pest-control substances and pesticides.
Synthetic hormones, vaccines.
Exposition to high and low frequency electromagnetic fields.
Psycho-emotional factors: stress, traumatic shock, depression…

# Integral Protocol for cancer in pets

Here we propose an Integral Protocol to deal with cancer in pets. Implementing this Protocol in a gradual and organized manner, within existing possibilities, implies developing a personalized procedure, according to the cancer type and the patient's condition at the time of diagnosis. It consists of the following 4 phases:

## 1. Identify and neutralize the causes that might be at the origin of cancer

There is a wide range of factors that can lead to cancer development, and it is difficult to identify which ones are involved. Nevertheless, there are common points among cancer patients: a high toxic load as well as nutritional deficiencies, which compromise the normal function of the organism. These issues can be improved by taking different measures:

**1.1 Change some aspects of the way of life.** This step involves being aware of the unlimited substances linked to our lifestyle that contribute to cancer development. Consequently, the exposition of our pets and ourselves to this kind of substances should be reduced.

**1.2 Establish protocols for hepatic detoxification.** It is advisable to help the organism in the removal of xenobiotic compounds by assisting the involved organs with a nutritional support.

## 2. Target the main hallmarks of cancer cells

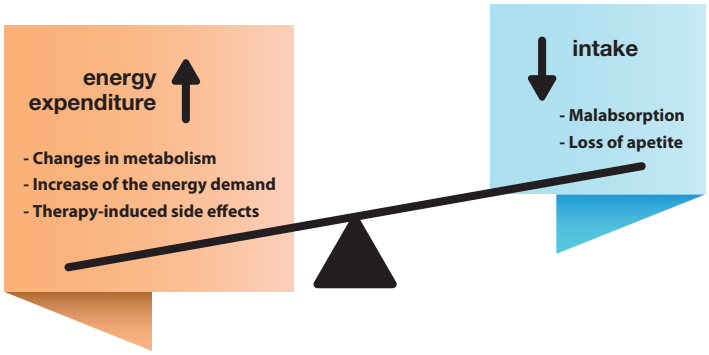
Chemotherapy and radiotherapy have an impact on this step. However, they also have their limitations: toxicity for healthy cells, high cost and relapses along time. Considering the hallmarks of cancer cells, the actions to be taken are the following:

**1.** Reduce the genomic instability
**2.** Promote a controlled proliferation
**3.** Reestablish programmed apoptosis and senescence
**4.** Harmonize the immune response
**5.** Inhibit aberrant angiogenesis
**6.** Block invasion and metastasis
**7.** Neutralize a pro-inflammatory environment

These actions can also be taken through the administration of nutrients, natural substances of plant origin, vitamins and amino acids that have specific anticancer properties with proven efficacy *in vitro* and *in vivo*. Furthermore, many of them exert an antioxidant function that can protect healthy cells from chemo- and radiotherapy side effects.

## 3. Improve the nutritional status of the patient

Many cancer patients present cachexia, a syndrome characterized by a lack of appetite, fatigue, systemic inflammation and anemia, which involves a severe loss of weight. Cachexia is caused by multiple factors and affects various organs. Its main characteristic is energetic unbalance, caused by a diminishment of intake and/or an increase of energy expenditure. The reduced intake may be caused by the loss of appetite, due to either the pathology itself (a physical interference in the intake process, changes in the senses of taste and smell, alteration of the intake regulation pathways) or the side effects of the treatment (vomit, nausea, mouth inflammation, etc.). Likewise, dysfunctions in the digestive system have been described to difficult the absorption of nutrients and therefore contribute to the malnutrition status.




Cancer development and treatment involve changes in carbohydrate, lipid and amino acid metabolism. The processes of energy production are altered, being much more inefficient than the ones that occur in a healthy organism. This implies an increase of energy expenditure to maintain energetic homeostasis and to compensate the resources used by the tumor. When the ingested nutrients are not enough to cover the demand, the body begins to degrade muscle and fat, from which useful substrates are extracted for energy production. For this reason, cachexia is characterized by the loss of muscular mass and adipose tissue. Therefore, cachexia is not only caused by a lack of intake, but also by a severe alteration of metabolic pathways. Even though the animal eats in a normal manner, loss of weight and cachectic symptoms can appear.

The emergence of cachexia in a cancer patient reduces his welfare, worsens the side effects of the treatment and reduces the survival rate. Complications can appear, such as secondary immunosuppression, delay of wound healing and tissue repair, alteration in the protein and lipid profiles, dysfunctions in the respiratory and cardiovascular systems, etc.

For this reason, it is essential to compensate malnutrition with an appropriate nutritional therapy. We propose two steps in this regard:

**3.1. Introduce an individualized, free from additives, natural diet.** Carbohydrates should be avoided, as they are the main source of energy of cancer cells. Under veterinarian supervision, diets such as Bones and Raw Food (BARF), ketogenic or paleolithic can be followed.

Commercial foods are not recommended due to their high content in hydrocarbons, the protein origin (frequently it is sub-products), additives, and mutagens produced during the production, among other reasons.

**3.2. Compensate nutritional deficiencies.** Many cancer patients present specific nutritional deficiencies, compromising the right function of the organism. In fact, nutritional deficiencies themselves represent a risk factor for cancer development. For this reason, it is essential to compensate malnutrition with an appropriate nutritional therapy. Compensating the specific nutritional lack derived from cancer would allow to improve the response to treatment, reduce post-operational complications, extend the survival rate, and ameliorate the quality of life of the patients.

## 4. Manage side effects derived from chemo- and radiotherapy

Side effects are generally treated with symptomatic medication, although it would be better to prevent them. To this end, intake of certain nutrients before, during and after conventional treatment reduces the side effects of cancer therapy.

As part of this protocol, Stangest offers two dietary supplements: OncoVet I and II. They are formulated with plant extracts, vitamins, amino acids and trace elements that participate in all the stages of the protocol: support hepatic detoxification, target the different hallmarks of cancer cells to restore the normal equilibrium of the organism, compensate nutritional deficiencies and reduce side effects derived from treatment. The main goal is to optimize the patient's health situation to improve its quality of life.

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**INTEGRATIVE ONCOLOGY**

**Conventional Protocol**
- Surgery
- Radiotherapy
- Chemotherapy
- Others: immunotherapy, hormone therapy, etc.
- Symptomatic medication for the side effects

**Integral Protocol**
- Identify and neutralize the causes
  - Change some aspects of the way of life
  - Establish protocols for hepatic detoxification
- Target the main hallmarks of cancer cells
- Improve the nutritional status of the patient
  - Diet
  - Compensate nutritional deficiencies
- Prevent side effects with natural supplements
- Other possible complementary therapies: phytotherapy, ozone therapy, acupuncture, etc.

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- National Cancer Institute at the National Institutes of Health
- National Toxicology Program, U.S. Department of Health and Human Services
- National Center for Complementary and Integrative Health
- Organización Mundial de la Salud
- International Agency for Research on Cancer

# OncoVet I

**Nutritional support for cancer patients. Their natural ingredients facilitate detoxification and elimination of carcinogenic agents that harm the organism.**


The utilization of specific nutrients and antioxidants reduces the toxicity produced by radiotherapy and chemotherapy. It reduces the side effects such as constipation or nausea. It ameliorates the degree of immunization, inhibits metastasis and reduces the risk of relapse. It increases the quality of life of the patients.

**Composition per tablet:**
L-glutamic acid: 150 mg, *Silybum marianum* (Milk thistle extract, silymarin): 100 mg, *Punica granatum* (Pomegranate): 125 mg, *Camellia sinensis* (Green tea): 100 mg, *Curcuma longa* (Curcumin): 50 mg, *Vitis vinifera* (Grape seed): 20 mg, L-selenomethionine: 1 mg (Selenium: 0,02 mg), Excipients q.s.

**L-Glutamic Acid**
Amino acid that takes part in numerous biochemical reactions, including the formation of nucleotides, amino acids and glycogen. L-Glutamic Acid is a substrate for the *de novo* synthesis of glutamine. Glutamine acts directly on the lymphoid tissue associated with the intestine, stimulating the immune system and protecting the intestinal mucosa.

**Milk thistle extract *(Silybum marianum)***
Its main component is silymarin (>80%), which acts as an antioxidant. It also increases the endogenous antioxidant capacity by means of an increase of glutathione concentration and superoxide dismutase activity. Silymarin has antimetastasic, antiangiogenic and anti-inflammatory activities. It inhibits cellular proliferation and induces apoptosis.

**Pomegranate extract *(Punica granatum)***
It is rich in ellagic acid (>40%), which adheres to several carcinogenic substances and deactivates them. Therefore, it has anti-mutagenic properties. It inhibits angiogenesis and the cell cycle. It has anti-inflammatory and antioxidant effects.

**Green tea extract *(Camellia sinensis)***
It is a powerful antioxidant due to its high polyphenol content (>50%). With immunomodulatory and anticarcinogenic properties: it is capable of inhibiting proliferation, metastasis and angiogenesis, as well as inducing apoptosis.

**Curcumin *(Curcuma longa)***
It has antioxidant and antiviral properties. It exerts an anti-inflammatory function by the regulation of important signaling pathways and it is capable of inducing the programmed cell death of cancer cells. *In vivo* studies have demonstrated that it sensitizes the effects of chemo- and radiotherapy.

**Grape seed extract *(Vitis vinifera)***
Thanks to its high content in proanthocyanidins (>90%), it presents a great antioxidant effect against free radicals, preventing lipidic peroxidation. It protects against the side effects of chemotherapy, probably by means of its antioxidant properties. It also presents antimutagenic and immunomodulator activities.

**L-Selenomethionine**
It acts as a free radical scavenger and promotes the synthesis and activity of endogenous antioxidants, protecting against cell damage. It stimulates the immune system, regulates cell proliferation and apoptosis. It has been reported its influence in suppressing the growth of blood vessels that bring nutrients to the tumor.

**Administration:**
1 tablet per 10 kg of weight, twice a day.

**Presentations:**
- 60-tablet container
- 300-tablet clinical container
- 300-tablet clinical blister pack


# OncoVet II

**Formulated with amino acids, vitamins, antioxidants and minerals to compensate nutritional deficiencies derived from oncological processes and treatments, to reinforce the immune system and to improve the quality of life of the patient.**

Dietary supplement based on essential nutrients that exert their function in a synergic manner, acting directly on cancer cells and reinforcing the extracellular matrix. It complements the antioxidant and anticancer properties of OncoVet I. Cancer cells produce enzymes that digest collagen, which affects the interstitial tissue and facilitates growth and invasion. The amino acids lysine and proline, together with the action of vitamin C, reinforce the structure of collagen and hinder the action of these enzymes. This way, the conjunctive tissue becomes more stable, preventing cancer cell penetration.

**Composition (in 3 grams):**
Whey protein: 2000 mg, L-Proline: 75 mg, L-Lysine: 50 mg, L-Arginine: 150 mg, Niacinamide (Vitamin B3): 200 mg, Sodium ascorbate (Vitamin C): 300 mg, Vitamin D3: 300 UI, Vitamin K3: 3 mcg, Lipoid acid: 10 mg, Magnesium gluconate: 100 mg (Magnesium: 5.4 mg), Zinc chelate: 30 mg (Zinc: 6 mg), Excipients q.s.

**Total amino acid content (whey protein AA + added AA) in 3 g:**
Arg: 196.2 mg, Pro: 189.8 mg, Lys: 229.4 mg, Ala: 95.8 mg, Asn: 214.4 mg, Cys: 43.6 mg, Phe: 61.6 mg, Gly: 34.8 mg, Gln: 379 mg, His: 52.6 mg, Ile: 115.4 mg, Leu: 207.4 mg, Met: 42.6 mg, Ser: 99.6 mg, Tyr: 43.8 mg, Thr: 135.4 mg, Trp: 32 mg, Val: 102 mg.

**Whey Protein**
Among the most important biologic components of whey protein we find lactoferrin, α-lactoglobulin, β-globulin and other immunoglobulins, all of them with immunomodulatory properties. Lactoferrin also acts by inducing apoptosis, inhibiting angiogenesis and modulating the activity of carcinogen metabolizing enzymes. Whey protein has an antioxidant effect on healthy cells, inducing an increase of glutathione synthesis. On the contrary, glutathione concentration is reduced in cancer cells, sensitizing them to chemotherapy.

**L-Proline**
It is a conditionally essential amino acid: the organism is capable of producing it, but in certain situations (illnesses, stress...) its demand increases and it needs to be assimilated from diet. Proline favors collagen formation thus reinforcing the extracellular matrix and difficulting tumor cell migration to the surrounding tissues. Moreover, collagen degradation releases proline, which is captured by tumor cells. When it is metabolized, it generates reactive oxygen species which initiate a wide variety of effects, including blockage of the cell cycle, autophagy and apoptosis.

**L-Lysine**
It is an essential amino acid, so it is not synthetized by the organism and therefore it is necessary to ingest it from diet. It is another fundamental component for collagen fibers and therefore its administration favors their formation and reinforces the extracellular matrix. Moreover, lysine inhibits the action of plasmin, protein responsible for triggering the activation of collagenases and other enzymes that dissolve the extracellular matrix. Consequently, it hinders the dissemination of tumor cells to other tissues.

**L-Arginine**
This amino acid is also conditionally essential. Besides its most known function in the urea cycle, arginine is able to boost the immune system. It is an essential nutrient of cells with cytolytic activity and defends the organism from implantation of tumor cells. It has been demonstrated that supplementing with arginine reduces tumor growth *in vivo*, metastasis incidence and the tumorigenesis potential of the present carcinogens.

**Niacinamide (Vitamin B3)**
Niacinamide or nicotinamide is the amide of niacin (nicotinic acid or Vitamin B3). It is the primary precursor of NAD+, the essential coenzyme in ATP production. Niacin deficiency is a common characteristic in cancer. A high content of NAD+ is necessary to maintain genome stability since it facilitates DNA repair. Consequently, niacinamide supplement reduces the short- and long-term side effects of chemotherapy.

**Sodium ascorbate (Vitamin C)**
Vitamin C can be useful in preventing and treating of cancer. It acts as an antioxidant, neutralizing free radicals. It is also an immunomodulator, improving leukocyte activity while protecting them from oxidative damage derived from their cytolytic activity. Vitamin C is also essential in collagen formation: together with proline and lysine, it reinforces the extracellular matrix, thus hindering the invasion of surrounding tissues by tumor cells.

**Vitamin D3**
Vitamin D3 directly and indirectly regulates more than 2000 genes, including a multitude of processes: it is capable of enhancing apoptosis and diminishing cellular proliferation, the formation of new blood vessels and metastasis. It has anti-inflammatory effects. Chronic inflammation is implicated in a large number of disorders including cancer. In dogs and humans, it has been demonstrated that low levels of vitamin D correlate with a higher cancer incidence. Moreover, vitamin D boosts the anti-cancer effects of several chemotherapeutical agents, improving the response to anticancer therapy and the heath of the animal.

**Vitamin K3**
Recent discoveries show that the use of vitamin K3 as a specific nutrient can participate in almost all development phases of different types of cancer. Vitamin K3 induces oncosis, a sort of cellular death by ischemia, against which cellular cells are particularly susceptible. Recently, other three vitamin K3-mediated anticancer mechanisms, which act in a synergic manner, have been identified. Moreover, this vitamin blocks angiogenesis, thus complicating tumor tissue progression.

**Alpha-lipoid acid**
It is known as "the universal antioxidant". It acts as an antioxidant, it increases glutathione synthesis and it recycles endogenous antioxidants, specially vitamins C and E. Being lipophilic and hydrophilic, it can exert its function both in the membranes and inside the cell. Moreover, it is a metal ion chelator.

Alpha-lipoid acid regulates key enzymes of metabolism. Thanks to this, it is capable of slowing tumor progression by means of the metabolic reprogramming of tumor cells. Alpha-lipoid acid regulates different cell signaling pathways. It has anti-metastasic and anti-inflammatory capacities and the administration of alpha-lipoid acid allows the reduction of the side effects of conventional chemotherapeutic agents.

**Magnesium**
There is a clear epidemiologic relationship between magnesium deficiency and cancer. The majority of chemotherapy treatments induce a magnesium deficiency, which conditions the transformation of the precancerous cell.
Magnesium acts as a cofactor in more than 300 enzymes that have a notable influence in carbohydrate, amino acid, nucleic acid and protein metabolism. Its role in fatty acid and phospholipid metabolism is key for the correct permeability of the cellular membrane.

**Zinc**
Zinc deficiencies are very common in cancer patients and it is in fact a good indicator of the nutritional status of the patient. Zinc ameliorates cellular immunity functions such as the activity of natural killer cells. It acts as an antioxidant, induces inflammatory cytokines and favors the apoptosis of malignant cells.

**Administration:**
- Small animals:
  0.6 g / 2 kg body weight, twice a day.
- Medium and large animals:
  3 g / 10 kg body weight, twice a day.

**Presentations:**
- Small animals:
120 g container, with 0.6 g measuring spoon.
- Medium and large animals:
240 g container, with 3 g measuring spoon.

## OBJECTIVES OF ORTHOMOLECULAR NUTRITION IN CANCER

- Compensate nutritional deficiencies
- Support the phases of hepatic detoxification
- Target the cancer cell hallmarks: apoptosis, proliferation, inflammation, genomic stability, angiogenesis and metastasis
- Modulate the activity of the immune system
- Diminish the side effects derived from cancer treatment
- Improve the quality of life of the patient

**Watch our video explaining the role of dietary supplements for cancer patients:**
http://bit.ly/2fA3iHv

# How do Oncovet I & II act?

Cancer is a consequence of an uncontrolled proliferation of cells capable of invading the surrounding tissue and disseminating to other parts of the organism. Their hallmarks include genomic instability (which allows them to acquire mutations), sustained proliferation, evasion of apoptosis, the ability of metastasizing, etc.

**OncoVet I & II are formulated based on components with anticancer properties like the inhibition of proliferation or the induction of apoptosis**

Nowadays, the relationship of tumor cells with their microenvironment and how they relate with healthy cells is considered of high importance. The aim is to try to understand and treat cancer from a wider perspective, taking into account various aspects of the organism, both cancerous and healthy, which include:

- The relation with the **immune system**: organism defenses are able to detect when a cell is abnormal and induce its death. Cancer cells will avoid this response of the immune system against them.
- **Inflammation**: a chronic inflammation can induce cancer. An inflamed tissue contains molecules that facilitate tumor growth.

**The immunomodulator and anti-inflammatory properties of OncoVet I & II will contribute to the fight against the tumor**

- **Angiogenesis**: it is the generation of new blood vessels that provide oxygen and nutrients to tumor cells and allow them to disseminate to other parts of the body. Reducing angiogenesis will block this supply, which can hinder tumor growth, and reduce its metastatic ability.

**Several components of OncoVet I & II are capable of inhibiting angiogenesis, thus hampering tumor nutrient supply and metastasis**

Cancer induces changes in metabolism, both at a cellular and an organism level. There is an increase of energy expenditure since a lot of material is needed to keep growing. Moreover, there is frequently a reduction of food intake owing to the pathology itself (tumors in the mouth, for example) or to the side effects of the treatment (nausea, etc.). This causes nutritional deficiencies in many cancer patients (magnesium, zinc, vitamin D, among others). Another aim of OncoVet I & II is to compensate these nutritional deficiencies and try to optimize the general condition of the patient so that they can face the tumor.

**Formulated to compensate nutritional deficiencies associated with the progression and the treatment of cancer**

One might think that, by means of this nutritional complementation, the growth of the tumor is promoted since these nutrients also reach the tumor. However, we must take into account that cancer continuously mutates and acquires new characteristics that allow it to grow in very adverse conditions. For example, tumor cells frequently overexpress glucose receptors. In the case of low levels of this molecule, tumor cells are much more efficient in its uptake. Another example is that, in a nutritional deficiency, cancer cells degrade muscle and fat in order to obtain energy. Therefore, in reality, the tumor creates mechanisms to obtain nutrients in a very efficient way: it will gather energy, even if this implies leaving healthy cells without it. With the supply of nutrients, we intend to reinforce healthy cells and the health status of the patient in general.

Another property of OncoVets, especially OncoVet I, is the **antioxidant** capacity. Antioxidants neutralize reactive oxygen species (ROS). ROS are generated, for example, in the liver, which works a lot to detoxify the body from xenobiotics (during chemotherapy it degrades the drug…).

**OncoVet's formulation is designed to protect healthy cells from the oxidative damage that might be caused by the growth of the tumor or its treatment**

The use of antioxidants in cancer treatment remains controversial. Can it minimize the effectiveness of chemotherapy? Radiation and some chemotherapeutic agents induce cellular death through the generation of ROS, so antioxidants can interfere with these treatments. However, we must consider that tumor cells have very high levels of ROS as well as high levels of antioxidants to neutralize them as a defensive mechanism. Moreover, many chemotherapeutic agents induce death without the need of increasing ROS levels. ROS can be detected as a consequence of cellular death, but it is not their mechanism of action. Therefore, adding antioxidants can protect from the side effects of the treatment without interfering with its mechanism of action. There are many clinical studies that demonstrate the benefits of the co-treatment of chemotherapeutic and antioxidant agents, such as doxorubicin and the Q10 co-enzyme, or cisplatin and glutathione. It has been proved that vitamin C reduces the side effects and ameliorates the quality of life of the cancer patient and also acts as a pro-oxidant on cancer cells.

In brief, supplementing with OncoVet I & II will facilitate the detoxification of the organism, reduce side effects and enhance the immune system to fight the tumor.

**The ultimate objective is to optimize the health status of the patient in order to improve his quality of life**

# Mechanism of action of OncoVet I & II components

| | | PHASE 1 | PHASE 2 | | | | | | | | PHASE 3 | PHASE 4 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Detoxification | Oxidative stress | Inflammation | Proliferation | Genomic instability | Apoptosis | Immune system | Angiogenesis | Invasion and metastasis | Nutrition and metabolism | Side effects |
| OncoVet I | L-GLUTAMIC ACID | | | | | | | ● | | | ● | ● |
| | MILK THISTLE EXTRACT | ● | ● | ● | ● | | ● | | ● | ● | | |
| | POMEGRANATE EXTRACT | | ● | ● | ● | ● | ● | | ● | | | |
| | GREEN TEA EXTRACT | ● | ● | | ● | | ● | ● | ● | ● | | |
| | CURCUMIN | ● | ● | ● | | | ● | ● | | | | |
| | GRAPE SEED EXTRACT | ● | ● | | | ● | | ● | | | | ● |
| | SELENIUM | ● | ● | | ● | | ● | ● | ● | | ● | |
| OncoVet II | WHEY PROTEIN | ● | ● | | | ● | ● | ● | ● | ● | ● | |
| | PROLINE | ● | | | | | | | ● | ● | ● | |
| | LYSINE | ● | | | | | | | | ● | ● | |
| | ARGININE | | | | ● | ● | | ● | | ● | ● | |
| | VITAMIN B3 | | | | | ● | | | | | ● | ● |
| | VITAMIN C | ● | ● | ● | | | ● | ● | | ● | ● | ● |
| | VITAMIN D3 | | | ● | ● | | ● | | ● | ● | ● | |
| | VITAMIN K3 | | | | ● | | ● | | ● | | | |
| | ALPHA-LIPOIC ACID | ● | ● | ● | | ● | | | | ● | ● | ● |
| | MAGNESIUM | ● | | | | | | | | | ● | |
| | ZINC | ● | ● | ● | | | ● | ● | | | ● | |

# OncoVet

## Nutritional support for cancer patients


## Antioxidant, anticancer and anti-inflammatory substances

## Reinforce of the immune system and the extracellular matrix

**For further information:**

**Technical bulletin**

http://bit.ly/2eVBWL1

**Video**

http://bit.ly/2fA3iHv

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