

## Immunotherapy of dogs in case of oncological diseases

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Last 5-10 years there was observed growth of oncological diseases among fine animals. Swedish veterinaries led by Dr. Bonett have carried out a research among 222000 dogs. According to results of this research, the amount of animals with oncological pathologies varies (depending on a breed) between 12 and 45%. At the moment there is observed growing of the pathology [11].

According to the latest 3-year statistics of veterinary clinic "KAVET" (Latvia, Riga) there was observed growth of breast, liver, pancreatic, bones and joint malignant and benign tumours in dogs. The most frequent oncopathologies are benign and malignant tumour-formations of skin. Because of the low pain threshold in animals their owners do not notice the beginning of the disease. They turn to a veterinary clinic with already very neglected processes of malignant new growth. In this case the animal begins to feel discomfort or pain, its behaviour and appearance change, the appetite comes down. At that, as there are no methods of treating the pathology in veterinary practice, the animal is usually narcotized.

Such a high amount of growing of oncological pathology is connected with development of secondary immunodeficiency in animals, which can be effect of either social or medically biological factors [7, 12, 13, 18].

It is known that in case of oncologic diseases there changes the control mechanisms from the side of immune system above the processes of cell proliferation and defference of cells because of the active suppression of its functions. The malignated cell is not recognized by immunocompetent cells of the diseased organism. Their common property is the ability of uncontrolled reproduction, invasion and metastasing. As the processes of metabolism pass rapidly in animals, ether quantitative or qualitative neoplastic processes often develop very fast.

The therapy that is practiced in the present-day complex treating usually induces immunosuppression of cell type. It is a dangerous way of treating because tumour-cells suppress the response of organism on their presence. At that, functions of the specific and non-specific factors of immune protection of organism significantly descend. In the result of this develops state of secondary immunodefficiency, increases risk of secondary bacterial-viral infections and reactivation of present inflammation hearths. Therefore, it is important to include immune products which are able to change relationship between a tumour and organism in treating program.

At that, creation of new products which have anti-tumour effect is one of the most important medically biological problems. Despite the urgency of the problem in veterenary, people have started to solve it not so long ago [9, 10, 17].

In common with staff of P. Stradina Medical Academy of Latvia we have developed, obtained and licenced a new product Rimolan for veterinary practice.

Rimolan is a natural biologically active product. It contains cytokine complexes, reproductive hormones, which are also immunomodulators, AFP and other proteinic components. A study about composition of Rimolan has shown that it contains cytokines: TNF- $\alpha$ , IL-2, IL-8, IFN- $\alpha$ , IL-1 and other. Rimolan in high concentration contains ferritin. Owing to presence of cytokines immunotherapy has become adequate and clinically effective [8,16]. The role of IL-2 is especially important, because it has the main role in development of immune response. It is established that it purposefully affects growth and activation of T- and B-lymphocytes and other immunocompetent cell populations (such as monocytes, macrophages and other) [6,14, 15]. It is known that all these factors of immune system have anti-tumour, and anti-bacterial-viral protection of organism.

Rimolan contains IFN- $\alpha$ , which promotes activation of macrophages and NK-cells and in this way promotes synthesis of IL-1, IL-2, IL-4, IL-6 and TNF- $\alpha$ . As a result macrophages and NK-cells become able to destroy neoplastic and virus-infected cells, which is proved by results of our pre-clinical investigations [1,2,3,4,19].

According to a high concentration of ferritin in the product, it is assumed that Rimolan has also an anti-oxidant effect.

Practically this difficult multifunctional immunoregulation can be reached only with multicomponent substance, which is near to natural. Rimolan is a substance of this kind.

It is proved by experimental investigations that Rimolan:

- ✓ shows a wide spectrum of immunotrope activity;
- ✓ stimulates cell-mediated and humoral immune response reactions in case of either primary normal or secondary immunodeficiency situation;
- ✓ increases activity of T-lymphocytes in reactions of cell immunity of hypersensitivity and host transplantant;
- ✓ stimulates and regulates phagocytic activity of neutrophils in case of primary normal showings and in case of secondary immunodeficiency;
- ✓ does not affect hematological activity of complement and migration of haematogenous rotting cells;
- ✓ has got a reliable effect of inhibition of tumour growing either in case of treating or prophylaxis (the experiment was done on lungs adenocarcinoma of Luis (LLC) and solid variant of lympholeucosis – P-388);
- ✓ has got a reliable effect of life extension (the experiment was done using the same tumours);
- ✓ has not got high cytotoxicity (object of the investigations in vitro were interweaved human cell lines: breast adenocarcinoma – MCF-7, carcinoma of ovaries – SKOV-3, throat epidermal carcinoma – Hep-2);
- ✓ has not got mutagen activity;
- ✓ does not induce gene mutation by maximal mechanism of action;
- ✓ is not embryotoxic.

In pre-clinical experimental studies there was proved that Rimolan is non-toxic, non-teratogenic, demonstrates a wide spectrum of immunotrope activity and has reliable effect of inhibition of tumour growth either in case of treating or prophylactic variant.

Average lethal dose (LD50), when injecting it subcutaneously to white mice, is more than 2000 mg/kg. Practically lethal dose (LD50) of the product in the experiment was not found.

In experiments with white mice and dogs, in case of therapeutically recommended dose, the product does not cause any essential changes in organism of the animals.

### Results of clinical practice of Rimolan:

Treating with Rimolan was done on 28 dogs with oncological diseases of different localization. The control group consisted of 12 animals, which obtained therapy, accepted in veterinary practice in case of this pathology (Table 1).

The malignant course of disease was confirmed histologically in the both groups of animals. Metastases in the basic group were recognized in case of rectum, prostate cancer. The operation was done for 20 dogs.

All the animals of the control group were operated (three of them – twice).

Table 1

### Diagnosis of the Animals

Diagnose	Basic group, n=28		Control group, n=12	
	Абсолютное число	%	Абсолютное число	%
Ca gl. Mammae	13	46,4	6	50
Osteosarcoma	3	10,7	1	8,3
Hondroma			1	8,3
Ca Pulmonum	1	3,6	-	
Ca Prostatae	1	3,6	1	8,3
Ca Rectum	1	3,6	-	
Lymphoma	2	7,1	-	
Ca Prepuca	3	10,7	-	
Melanoma	-		1	8,3
Hemangioma	-		2	16,6
Ca ovarii	2	7,1	-	
Adenocarcinoma	2	7,1	-	

How the animals were divided in age groups is shown in Table 2.

Table 2

### Age Groups of the Animals

Groups	6 years	7 years	8 years	10 years	11 years	12 years	13 years	14 years
Basic group, n=28	3	1	2	5	6	1	4	6
Control group, n=12	4	2	2	2	2	-	-	-
%	17,5	7,5	10,0	17,5	20,0	2,5	10,0	15,0

The dose of Rimolan and the scheme of its injecting was worked out considering the main diagnosis, weight of an animal and showings of its immunogram (Picture 1). There were no toxic or allergic reactions observed in the animals when injecting the product.

When animals of the both groups before treatment were examined, there was discovered statistically reliable decreasing of showings of phagocytosis, there were recognized high levels of circulating immune complexes, anemia, lymphopenia (absolute quantity), increased showings of alkaline phosphatase, ALAT, decreased concentration of albumen and glucose. After treatment the given parameters of blood were statistically authentically normalized in researched groups at 78 % and 47 % of animals accordingly. At all animals of the basic group growth inhibition of a tumour, after surgical intervention - fast healing of seams, normalization of behaviour and a feed is marked.

The outcome of treating in the both groups at the moment is shown in Table 3.

Table 3

**The Result of Outcome of the Therapy in the Animals of the Basic and of the Control Groups**

<b>Groups (alive at the moment)</b>	<b>Ca gl. Mammae</b>	<b>Osteo-sarcoma</b>	<b>Hondroma</b>	<b>Ca Pulmonum</b>	<b>Ca Prostatae</b>	<b>Ca Rectum</b>	<b>Lymphoma</b>	<b>Ca Prepuccia</b>	<b>Melanoma</b>	<b>Hemangioma</b>
<b>Basic group, n=27</b>	12	2	1	1	1	1	2	2	-	-
<b>Control group, n=12</b>	-	-	-	-	-	-	-	-	-	-

However, owners of 5 animals of the basic group (in spite of significant improvement of their general state and paraclinical showings) decided to narcotize their dogs.

The average extension of their life after the treatment was from 6 month to 2 years – 19 animals, 4 – Continue treatment

On the Photo there is shown a dog Serra before and after the treating course in connection with generalized papillomatosis (the diagnosis was confirmed by biopsy).

The outcome in the control group:

All the animals died during 6 months after operation.

**Conclusions:**

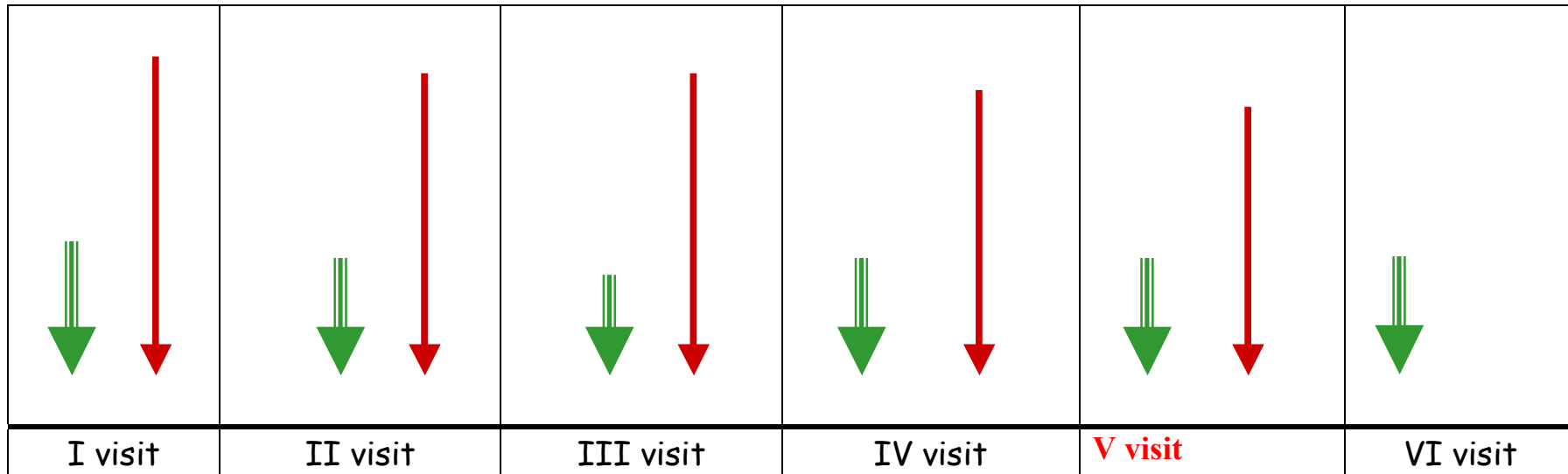
1. The greatest densities in structure of oncological diseases borrows a cancer of a mammary gland, on the average 48,2 %.
2. Disease among dogs in the age of till 10 years has made 35 % from 10 till 14 years of 65 %.
3. Rimolan is a clinically effective product for animals with oncopathology of different localization.
4. Rimolan has immunomodulatory effect. After the course of injecting the product there is observed positive dynamics of showings of immunogram (growth till physiological levels of absolute amount of lymphocytes, showings of phagocytal activity of neutrophils, circulating immune complexes and immunoglobulins) among animals with malignant tumours.


5. Rimolan rises life quality of diseased animals and extends life of animals with oncopathology.
6. The product should be recommended in complex treating of animals with malignant tumours on purpose of correction of disorders of immune system's functions and for prophylaxis in case of the given pathology of bacteriological-viral infections.


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### Scheme of Injecting the Product Rimolan and Control of Blood Tests



Doing tests (surveying): 

Injecting of "Rimolan": 

## Clinical Example (a bandog Serra)



**a photo before treating**



**a photo 6 months after treating**

Diagnosis – Generalized malignant papylamathosis (the diagnosis confirmed by biopsy). The treating course was started 3 months after the beginning of the disease. The disease began at age of 8 years.

The animal stayed alive for 2 years after the treating.