

# EVALUATION OF THE EFFICIENCY OF TREATMENTS AGAINST THE CANINE LYMPHOMA

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## 1. INTRODUCTION

The canine lymphoma is a malignant proliferation of lymphocytes that mainly affects the lymph nodes, spleen and liver. It represents between roughly a 7-24% of all the canine's neoplasias, with an annual incidence of 114/100.000 individuals. The etiology in this species is consider multifactorial, since it has not been identified an etiologic agent isolated.

The diagnostic of lymphoma is based on making cytology and hystopathology and the precision and the sensitivity increase if you make flow cytometry, immunohistochemistry or molecular proofs, like PCR or PARR (polymerase chain reaction for antigen receptorrearrangement), helping to differentiate the type of tumoral proliferation.

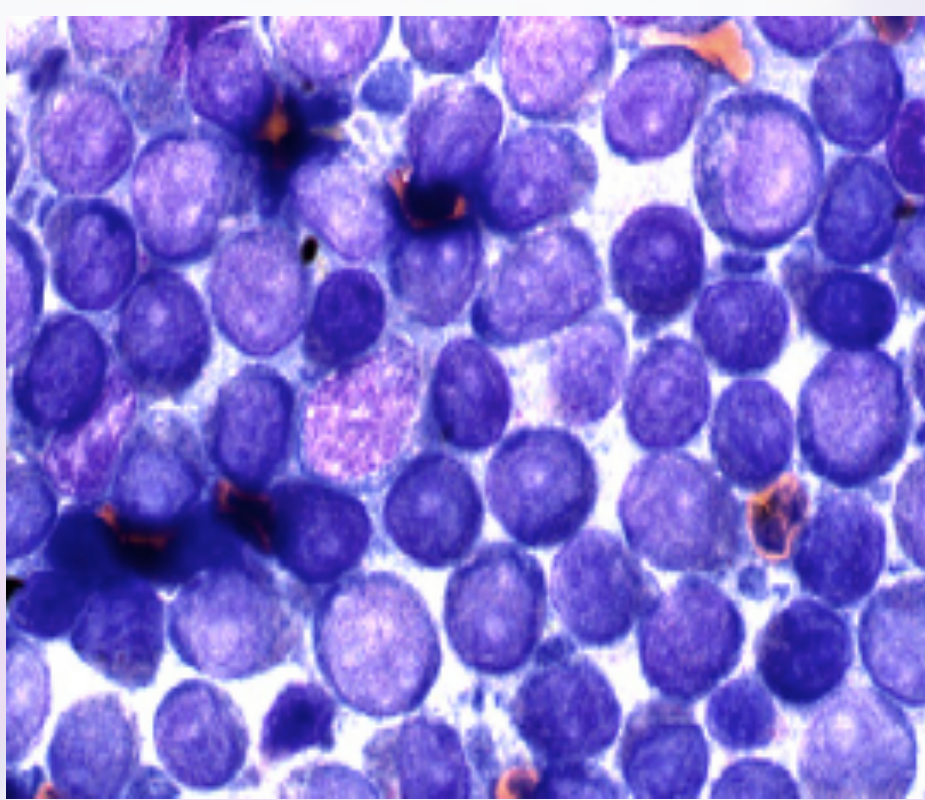


Fig. 1. Cytology of a lymph node. Diffuse large B-cell lymphoma (DLBCL) (Bienzle and Vernau, 2011)

According to its clinical presentation, the canine lymphoma is classified in **multicentric**, **gastrointestinal**, **mediastinum** and **extranode**; besides subclasiffy according to the grade of progression of the disease or the presence of clinical symptomatology.

## 2. AIMS

The main aims are described next:

1. Enumerate the different chemotherapeutic agents used in the treatment against the canine lymphoma and understand his action's mechanism.
2. Know the different vaccines against the canine lymphoma that are still being developed and his therapeutic target.
3. Compare the efficiency of the different therapeutic options indicated in the canine lymphoma based on studies made *in vivo*.

## 3. TREATMENTS AGAINST THE CANINE LYMPHOMA

### CHEMOTHERAPY

In veterinary medicine exists several protocols and combinations of chemoterapic drugs. One of the most popular protocol is CHOP which combines cyclophosphamide (C), doxorubicin (H for hydroxydaunorubicin), vincristine (O for Oncovin) and prednisone (P).

### RADIOTHERAPY

The radiation of half or whole body has been evaluated as a way to keep the remision after doing chemotherapy in canine lymphoma patients. However, the dose of radiation that can be administered safely to the whole body of dogs at one time is too low to effectively reduce tumor cell burden.

### IMMUNOTHERAPY

The immunotherapy is designed to activate cellular components of the immune anti-tumoral response or to go directly headed to determinate characteristic criticisms of the own tumor.

Noeadays, there are 2 vaccines that are used like adjuvants of the chemotherapy treatment. One of them goes directly against the heat shock proteins, specifically Hsp70 and the other one, against the telomerase reverse transcriptase (cTERT).

## 6. CONCLUSIONS

1. Nowadays, the aim of the treatments against canine lymphoma is to increase the time of remision. At the moment, all the treatments are palliative and is rarely that they cure the disease. For that reason, we need to focus on other systemic treatment modalities like immunotherapy.
2. The autologous HSPPC-vaccine and the vaccine against the cTERT show that, in combination with the chemotherapy, increase the presentation of antigens and activate the proliferation of lymphocytes T CD8<sup>+</sup> and Natural Killers cells. In this way, they decrease the load tumoral and, thus, delay the relapse and prolong the time of survival.
3. Actually, the results of the different studies using different and varied protocols of chemotherapy agents, show that it is unlikely the cure of the dogs with lymphoma. The immunotherapy can be considered a big strategy to provide an effective therapy without causing toxicity. This represents a significant step toward the development of a new class of therapeutics with a more precise and targeted approach to the treatment of canine lymphoma.

## 4. THERAPY EFFICIENCY

### CHEMOTHERAPY

Agents	Risk of side efects	Average survival time	Cost
<b>Prednisone</b>	Low	2 months	Very low
<b>H</b>	Moderate	7 months	Moderate
<b>H + C</b>	Moderate to High	12-14 months	Moderate
<b>COP</b>	Low to Moderate	6 months	Moderate
<b>CHOP</b>	Moderate to High	12-14 months	Higher

Table 1. A brief synopsis of the most common treatment protocols for canine lymphoma

### RADIOTHERAPY

The radiotherapy is considered a part from chemotherapy. The lymphocytes are especially sensitive to this treatment and, besides, does not affect to the resistance of the drugs used in the chemotherapy protocol. The TTP (time to progresion) and the AST (average survival time) is used to be some 15 and others 18 months, respectively.

### IMMUNOTHERAPY

#### Autologous HSPPC-vaccine

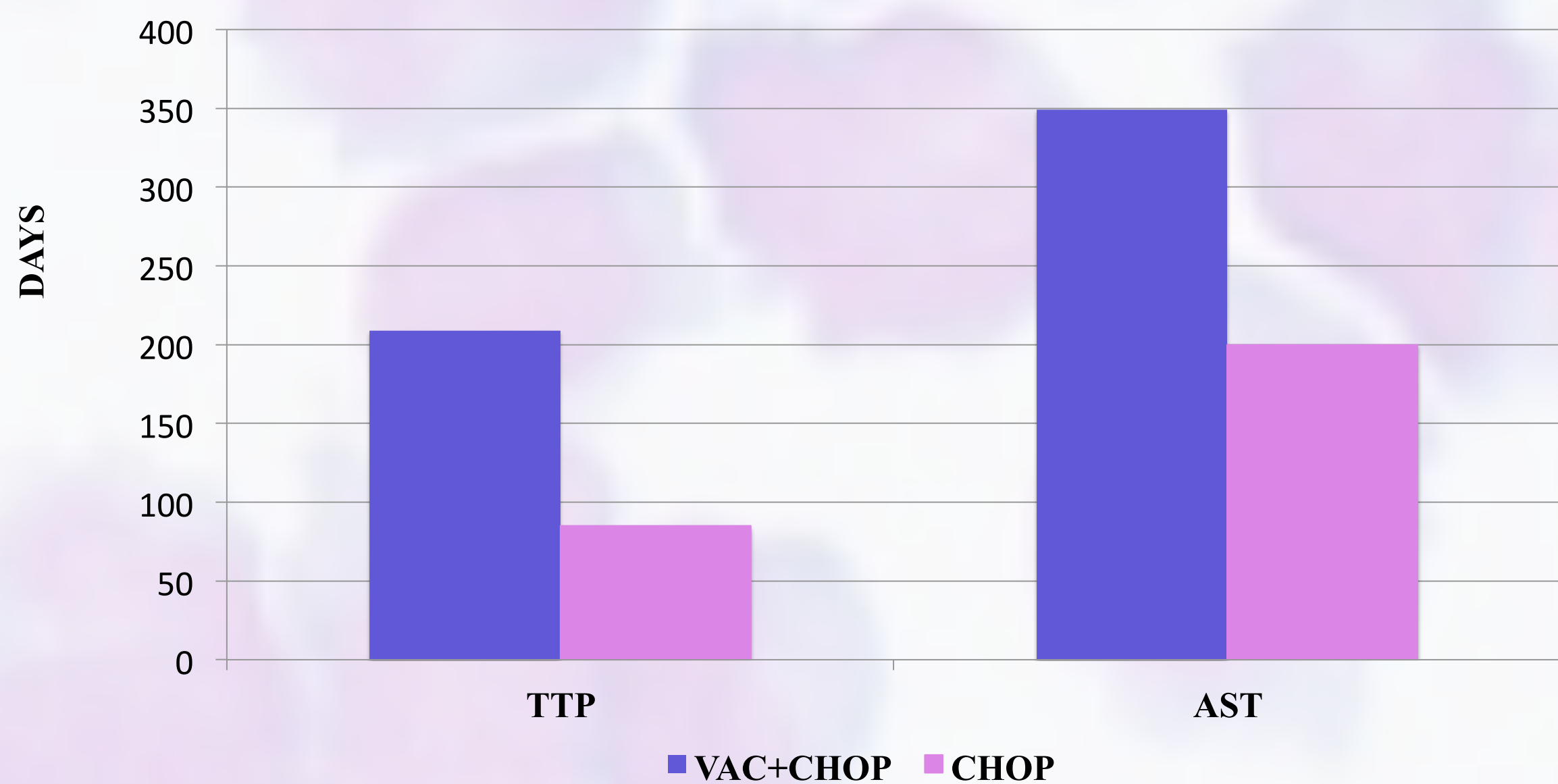


Fig. 2. TTP and AST of VAC+CHOP and CHOP. The average for all the dogs was 192 days. In VAC+CHOP this was significantly longer (209 days) compared with CHOP (85 days). The TTP in both groups was an average of 274 days. The average was significantly greater in the group of vaccinated (349 days) in front of the no vaccinated (200 days). From Marconato (2015). *Enhanced therapeutic effect of APAVAC immunotherapy in combination with dose-intense chemotherapy in dogs with advanced indolent B-cell lymphoma*

#### Vaccine against the telomerase

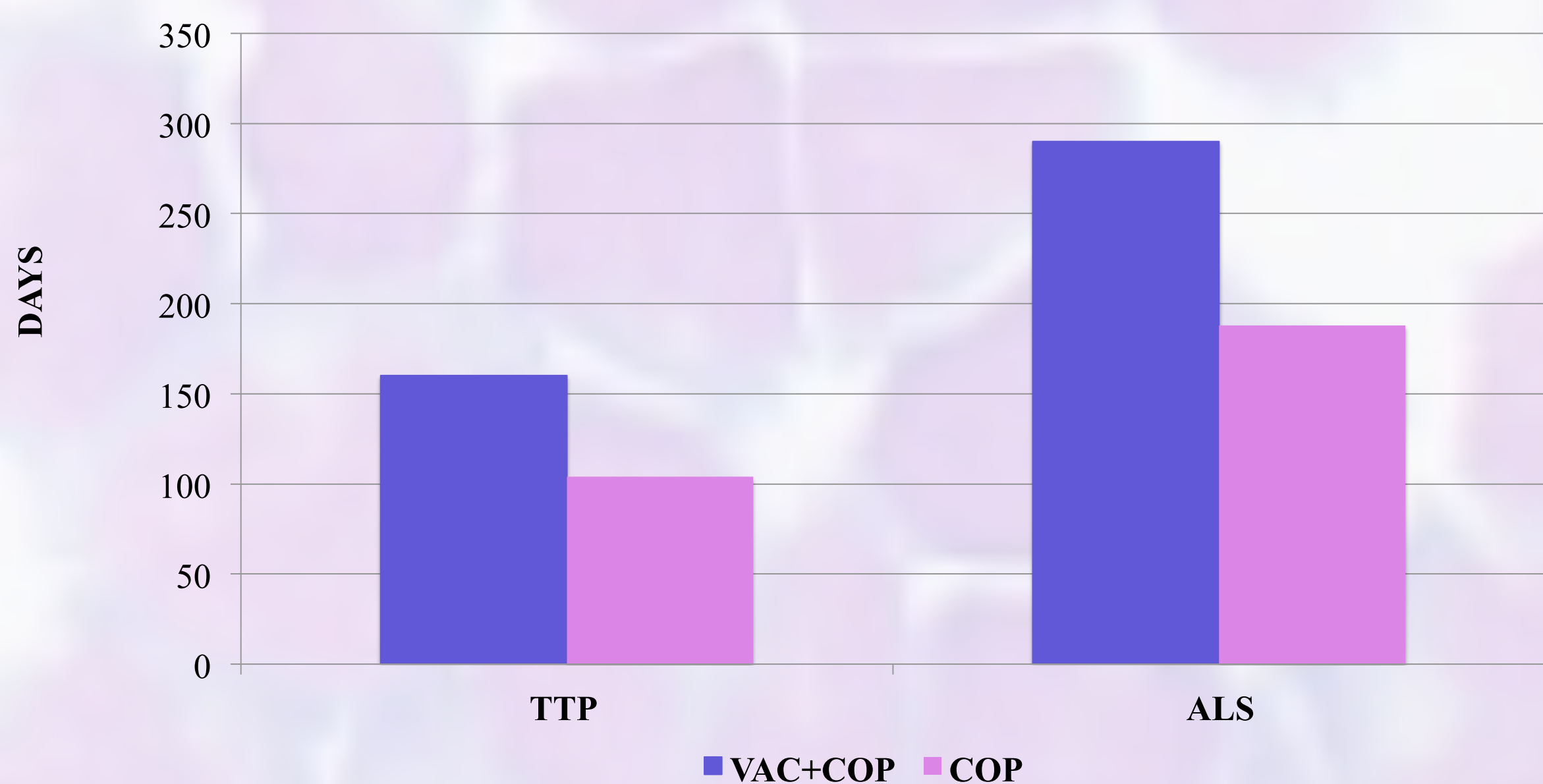


Fig. 3. TTP and AST of VAC+COP and COP. VAC+COP had a TTP longer in comparison with COP (160 and 104 days, respectively). The ALS was 290 and 188 days of average, respectively. From Peruzzi et al. (2010). *A vaccine targeting telomerase enhances survival of dogs affected by B-cell lymphoma*