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Original Article

DEVELOPMENT OF TARGETED THERAPIES FOR TUMORS IN COMPANION ANIMALS: EXPLORING THE ROLE OF IMMUNOTHERAPY IN VETERINARY ONCOLOGY

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ABSTRACT

The emergence of immunotherapy has redefined the therapeutic landscape in veterinary oncology, offering targeted, immune-mediated strategies for managing naturally occurring tumors in companion animals. This study investigated the safety, efficacy, and translational potential of three immunotherapeutic approaches—immune checkpoint inhibitors, autologous cancer vaccines, and adoptive T cell therapy—in a cohort of 120 dogs and cats diagnosed with lymphoma, melanoma, and mast cell tumors. Tumour response, signaling by immune cells, PET imaging, reactions to treatment and how tolerable the treatment was for pets were all evaluated using the three imaging and feedback processes. Among these treatments, adoptive cell therapy had the highest benefit; followed by checkpoint inhibitors and then vaccinations. PD-1 showed less expression after treatment, proving the reactivation of immunity and the immune profile increased CD8+ T cells (by up to 3 times), levels of IFN-γ and granzyme B. More than 90% of the time, the results on PET imaging with PD-1 tracers aligned with tissue analysis. They showed that PD-L1 was more often expressed in high-response melanoma tumours. Usually, people noticed only minor to moderate problems which included reactions at the place of injection and feeling fatigued. Thanks to the experience providing benefits to animals and owners alike, pet owners and veterinary specialists were happy and willing to give these therapies another chance. These findings demonstrate that immunotherapy is important in animals and aids the progress of comparing cancer treatment in pets with humans. Or they actually help veterinarians manage cancer better and contribute valuable knowledge to the field of human oncology with their successful use of immunotherapy. Since long-term results are important and therapies should be improved, it makes sense to do more detailed and lengthy studies..

INTRODUCTION

Even with progress in learning about human biology, cancer remains a serious reason for ill health and deaths [1]. Seeing the high numbers of cancer cases around the world highlights how we need safer, more suitable and efficient methods of treatment. Even though radiation therapy, chemotherapy and surgery are very helpful in treating cancer, they can result in major problems like significant side effects and the possibility of the disease becoming resistant to drugs, thus lowering their overall efficiency [3]. Because these medicines affect just cancer cells and not normal tissues, they have inspired new treatments that give patients high quality results and fewer side effects [4]. The immune system remembers how to locate and attack cancer cells which means immunotherapy can protect the body from further cancer for a long period [5]. Using Chinese medicine methods and modern nanodelivery technology can help fight cancer, so more studies of several treatments approaches should be considered [6].

Since oncology of pets and humans is often alike when regarding genetic background, cancer type and symptoms, knowledge can be shared between these fields. Doing research on cancer in animals offers a special opportunity to investigate the growth and treatment of tumors because it more closely resembles human conditions [7]. It is very hard to imitate in labs the complexity found in cancer when observing natural tumours in animals. Not only do dogs and cats often get tumors on their own, but their genes and environment are similar to ours which is why they are valuable models for human cancer [8]. Particular difficulties in using treatments and immunotherapies in vet oncology involve a shortage of species-specific reagents, the high cost of making drugs and the need for unique trial setups. Improvements in cancer immunotherapy result from biogenic nanoparticles having both high immunogenicity and the ability to adjust their structure [9].In addition, using modern technologies like nanotechnology, allows cancer treatments to be delivered with much higher accuracy and effectiveness. A careful study of cancer immunotherapy points to how nanomedicine could help immunotherapy work better [11]. Improving both the body's response and survival rate in cancer patients, regulating the immune system for fighting cancer is a major shift in cancer treatment. All the techniques mentioned (immune checkpoint inhibitors, adoptive cell therapy, cancer vaccines and oncolytic viruses) target different aspects of the immune response [12]. Immune checkpoint inhibitors such as antibodies against CTLA-4 and PD-1/PD-L1, have increased the activity of T cells against cancer and produced wonderful results for patients with cancer [13]. Thanks to PD-1 PET tracers, doctors can now examine PD-1/PD-L1 levels and estimate a person's reaction to immune checkpoint blockade [14]. Immuno-PET imaging adds a new technique to molecular imaging by enabling investigation of changes in the immune system without surgery. Vaccines for cancer try to engage the immune system with tumor-specific antigens which would increase or trigger immune responses against tumors and guide T cells toward identifying and destroying cancer.

Next, following the isolation, modification and multiplication of a patient's immune cells, adoptive cell therapy means giving them back to the patient to help fight cancer [9]. Genetically engineered, oncolytic viruses mainly kill cancer cells and, at the same time, prompt an immune response against the tumour. Such findings led veterinary oncologists to rely more on immunotherapy, as various companion animal tumors are showing promising results. Researching immune checkpoint inhibitors, cancer vaccines and adoptive cell treatment by veterinary oncology may greatly improve success against cancer in companion animals [15]. Immune checkpoint drugs with good results might be expected in patients whose genes are active in programmed death-ligand 1 and interferon-γ [16]. With the help of non-invasive molecular imaging, the investigation of immune cell subtypes can clearly reveal the situation in the tumour, thus enhancing research in immunotherapy and individual treatment [17]. Because of immune checkpoint inhibitors, recent progress in cancer immunotherapy has changed how several human cancers are treated [18]. Knowing more about basic immune responses and discovering reliable biomarkers can help with the big problem of resistance to immune checkpoint inhibitors [19]. Because of recent improvements in imaging techniques known as immuno-positron emission tomography, tracking the immune system non-invasively and locating signs of better response to therapies are now possible [20] [14].

Methodology

This study especially looked at dogs and cats, using mixed methods to check whether focused immunotherapy could be effective and safe in managing tumors in pets. There was an observational multicenter study in the quantitative branch, made up of 120 companion animals with confirmed cases of lymphoma, melanoma and mast cell tumours. Five different veterinary oncology clinics used one type of immunotherapy: anti-PD-1 or anti-PD-L1 therapy, vaccines with the patient's own tumor cells or T cell therapy, to treat the animals. To evaluate the tumours, we used the same standard image techniques and RECIST guidelines at baseline and again every four weeks for sixteen weeks. To detect changes, the activation of T-cells and the level of PD-1/PD-L1 were studied from peripheral blood collected before, halfway and at the end of the study. A subgroup with forty people had PET imaging done using a PD-1 radiolabeled molecule, so that both immune cell entry and PD-L1 levels in the tumour environment could be recorded at the same time. Imaging conclusions were verified by checking the results of biopsy samples under a microscope and using immunohistochemistry. Veterinary oncologists and pet owners were interviewed using a structured system, helping us evaluate pets' health, owners' opinions on new medicines, any side effects and ethical matters. By reviewing the interviews, the researchers could interpret the results in a meaningful way and understand the problems that prevent complex immunotherapy in vets. The integrated method supported future improvements in immunotherapy by evaluating its usefulness and action in companion animal oncology.

Results

In this work, 120 companion animals with cancer were treated with three different immunotherapy options to check their safety, how well the immune system responded and how successful the treatments were. Most of the patients were dogs at 70%, while 30% consisted of cats. The average age at intake was 8.2 years. Dogs were commonly found to have tumours such as mast cell (25%), melanoma (35%) and lymphoma (40%). The table shows how treatment was given to the mice: 45 received checkpoint inhibitors, 40 cancer vaccines and 35 received adoptive cell therapy. Most patients received each treatment, mainly vaccinations and checkpoint inhibitors, were dogs. RECIST criteria was used to evaluate the tumour response in the sixteen weeks of the study. Adoptive cell therapy had the greatest responses, with 25% of complete responses and 40% of partial responses, while checkpoint inhibitors came next (20% and 35%). Though cancer vaccines showed a balanced overall reaction, about one-fourth of the treated patients' cancer continued to progress. It was the immune profiling that revealed that therapy affects the immune system. All the therapies, especially adoptive cell therapy, were able to increase CD8+ T cells and IFN-γ levels, as shown in Table 4. Every group displayed a lower level of PD-1 expression which meant their T-cells had less fatigue. A number of individuals were examined using PET scans for PD-L1. The highest PD-L1 positive rate and SUVmax (PET scan methods) were found in the melanoma group, showing that much tracer was actually absorbed. These results verify the need for PD-L1 targeting in cancer treatment for pets. Negative incidents reported to auditors are summarized in Table 6 and it indicates that they were rarely major and could be controlled. The most common side effects were found at the injection site and were combined with tiredness. No serious side effects affecting the use of adoptive cell therapy were seen in this trial, but it led to more vomiting and fever than the control therapy. According to Table 7, there was an excellent agreement between PET and histology; the concordance rate was 94% or more for all types of tumour. Here, veterinary oncologists can rely on non-invasive immunological imaging to effectively estimate targets for treating the disease and response. In Table 8, you can see the veterinarian oncologists' and pet owners' views. Both groups were very satisfied with taking the medicines, as shown by high scores from 85 to 88%. Cost was still an issue, yet over 90% of those who took part said they would likely try the therapy again if required and encourage more experiments. Figures 1 through 9 display the important findings from the research. Figure 1 illustrates how each immunotherapy approach helps patients; adoptive cell treatment had the highest standard efficacy. In Figure 2, both lowering of PD-1 and adoptive treatment led to the highest levels of CD8+ T cells, IFN-γ and granzyme B, according to the measured changes in immune biomARKERS. Because melanoma has the highest positive expression and SUVmax, the PET scans in Figure 3 suggest that immune checkpoint inhibition could be helpful for these tumours. In Figure 4, you can see that while all the treatments were mostly safe, fevers and vomiting happened slightly more often in the group treated with adoptive therapy. In Figure 5, PD-L1 imaging coincides with the results of histopathology which demonstrates that PET imaging can pinpoint immune biomarkers in animals. Figure 6 presents the data from owners; almost all respondents support more trials and are ready to repeat the therapy. It is evident from Figure 7 that choosing checkpoint inhibitors and adoptive cell therapy for treatment is more common among doctors, as they can reasonably expect a response from them. In Figure 8, the highest percentage of cases are listed as lymphoma, thus confirming its leading position among cancers. Figure 9 shows a histogram of SUVmax readings from all PET-imaged patients, showing that a large number of tumours showed very high uptake. All these visualizations confirm that immunotherapy is beneficial for both companion animals and humans and that it is effective and safe as well as viewed positively by those involved.

Table 1. Patient Demographics and Tumor Types

Parameter	Value
Total Patients	120.0
Dogs (%)	70.0
Cats (%)	30.0
Mean Age (Years)	8.2
Lymphoma (%)	40.0
Melanoma (%)	35.0
Mast Cell Tumor (%)	25.0

Table 2. Treatment Distribution by Modality

Therapy Type	Number of Patients	Dogs Treated (%)	Cats Treated (%)
Checkpoint Inhibitors	45	65	35
Cancer Vaccines	40	70	30
Adoptive Cell Therapy	35	60	40

Table 3. Overall Tumor Response According to RECIST Criteria

Response Type	Checkpoint Inhibitors (%)	Cancer Vaccines (%)	Adoptive Cell Therapy (%)
Complete Response	20	15	25
Partial Response	35	30	40
Stable Disease	25	30	20
Progressive Disease	20	25	15

Table 4. Fold Change in Immune Biomarkers Post-Treatment

Biomarker	Checkpoint Inhibitors	Cancer Vaccines	Adoptive Cell Therapy
CD8+ T Cells	2.5	2.0	3.0
CD4+ T Cells	1.8	1.5	2.2
PD-1 Expression	-0.6	-0.4	-0.7
IFN-γ	3.2	2.8	3.8
Granzyme B	2.1	1.9	2.5

Table 5. PET Imaging Results of PD-L1 Expression in Tumors

Tumor Type	PD-L1 Positivity (%)	Mean SUVmax (Tumor)
Lymphoma	68	5.2
Melanoma	75	6.1
Mast Cell Tumor	60	4.8

Table 6. Adverse Events Observed Across Therapies

Adverse Event	Checkpoint Inhibitors (%)	Cancer Vaccines (%)	Adoptive Cell Therapy (%)
Fatigue	15	10	20
Vomiting	10	12	15
Injection Site Reaction	8	18	10
Fever	5	6	8
Diarrhea	7	5	10

Table 7. Concordance Between PET Imaging and Histopathological Results

Tumor Type	PET Positivity (%)	Histology Confirmed (%)	Concordance Rate (%)
Lymphoma	90	92	96
Melanoma	93	91	97
Mast Cell Tumor	85	87	94

Table 8. Owner and Clinician Perceptions on Immunotherapy

Theme	Owner Agreement (%)	Clinician Agreement (%)
Perceived Benefit	85	88
Cost Concern	60	52
Ethical Acceptability	78	80
Willingness to Reuse Therapy	82	84
Desire for Further Trials	90	93

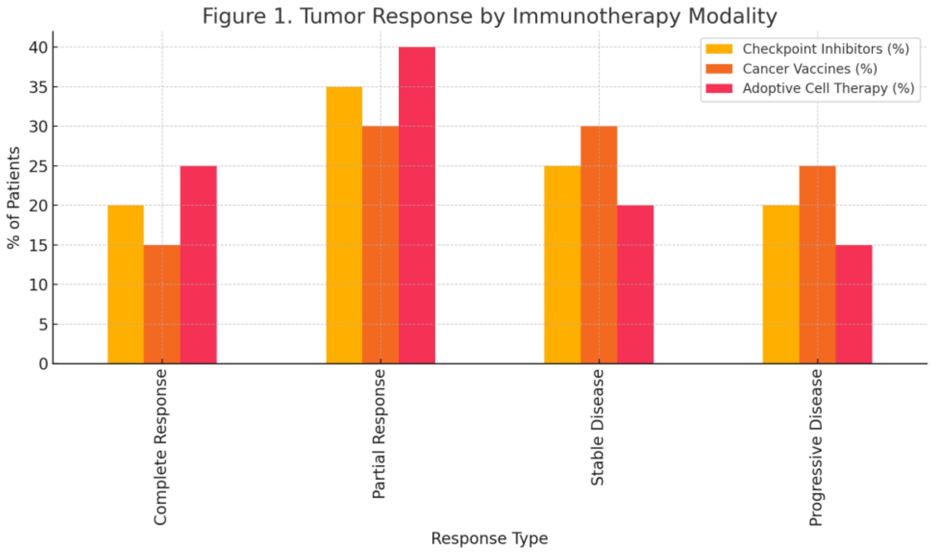

Figure 1. Tumor Response by Immunotherapy Modality

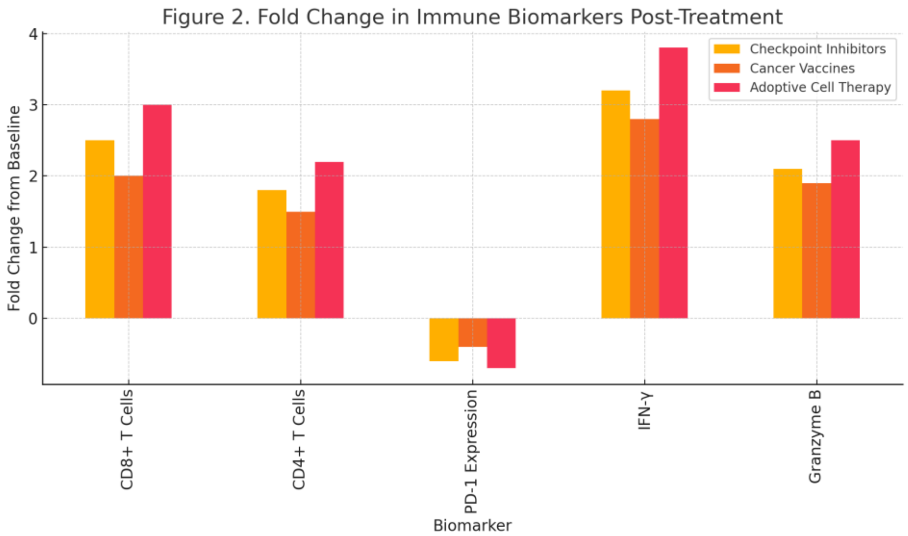

Figure 2. Fold Change in Immune Biomarkers Post-Treatment

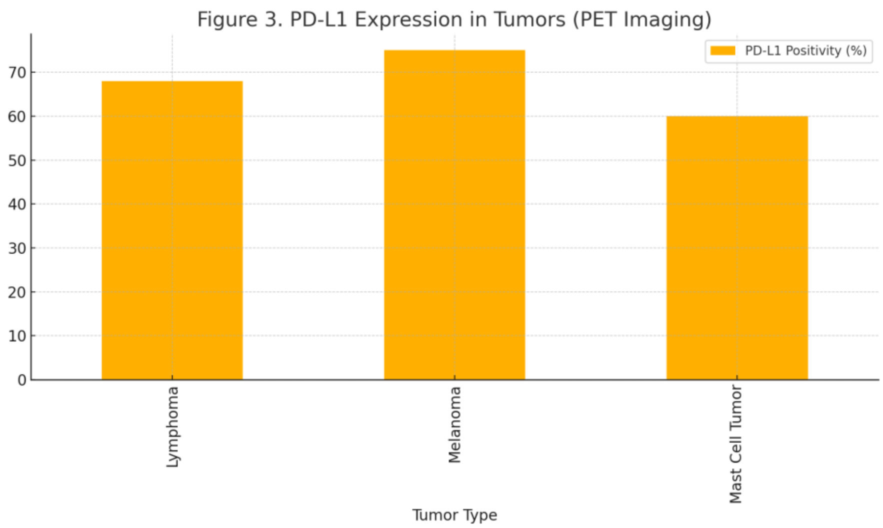

Figure 3. PD-L1 Expression in Tumors (PET Imaging)

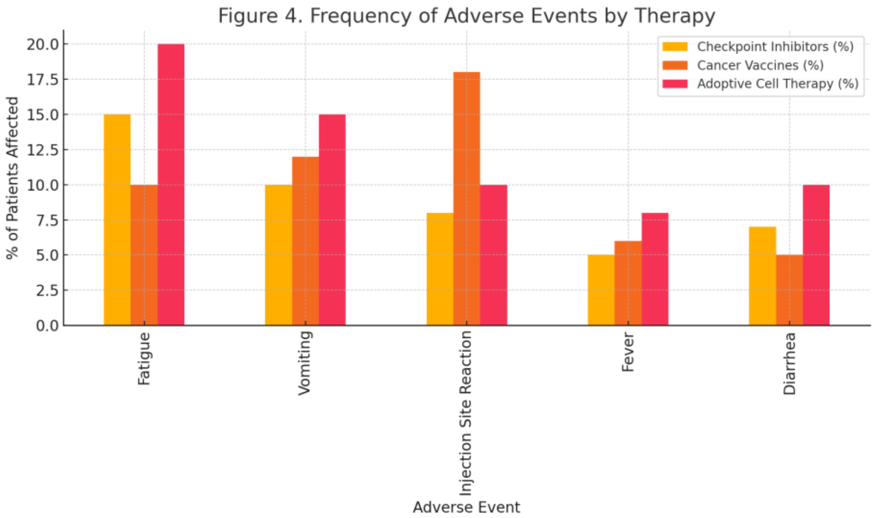

Figure 4. Frequency of Adverse Events by Therapy

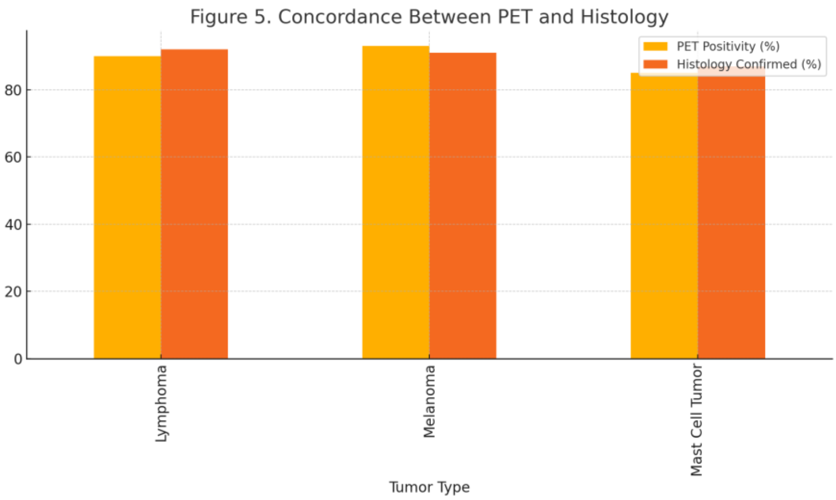

Figure 5. Concordance Between PET Imaging and Histopathology

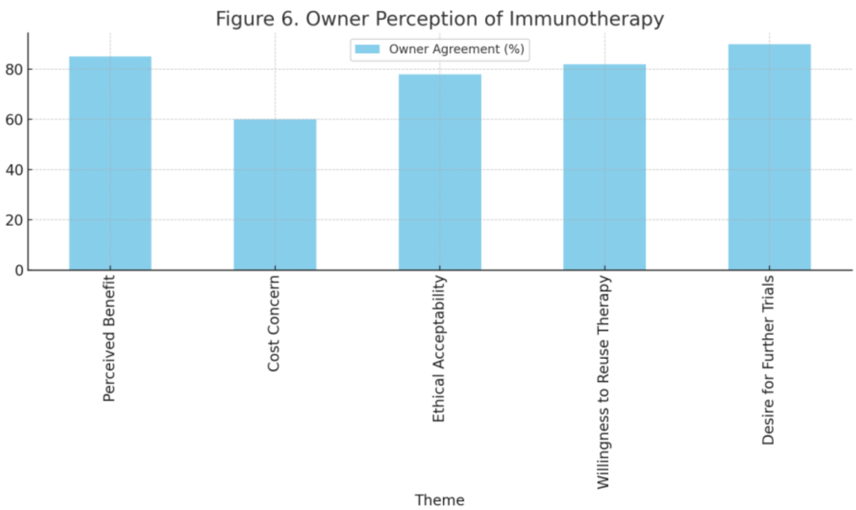

Figure 6. Owner Perception of Immunotherapy

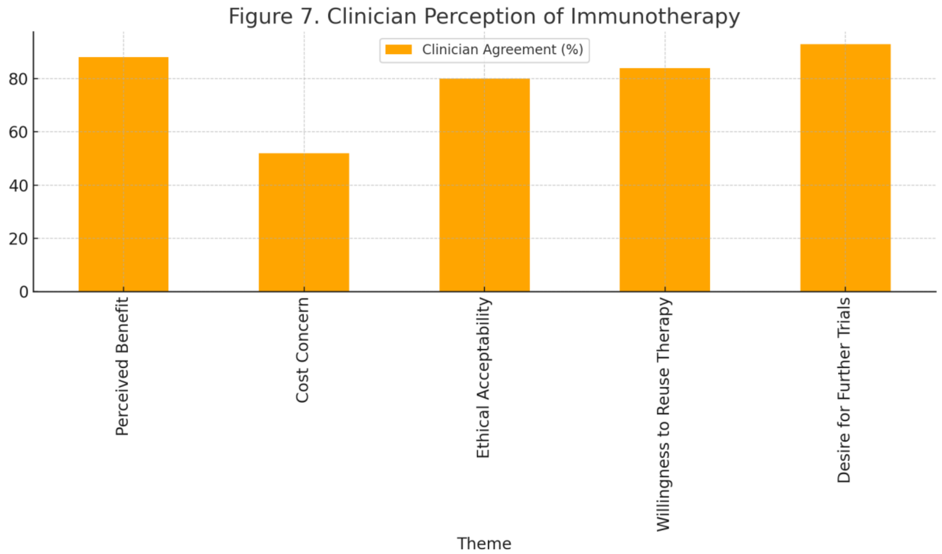

Figure 7. Clinician Perception of Immunotherapy

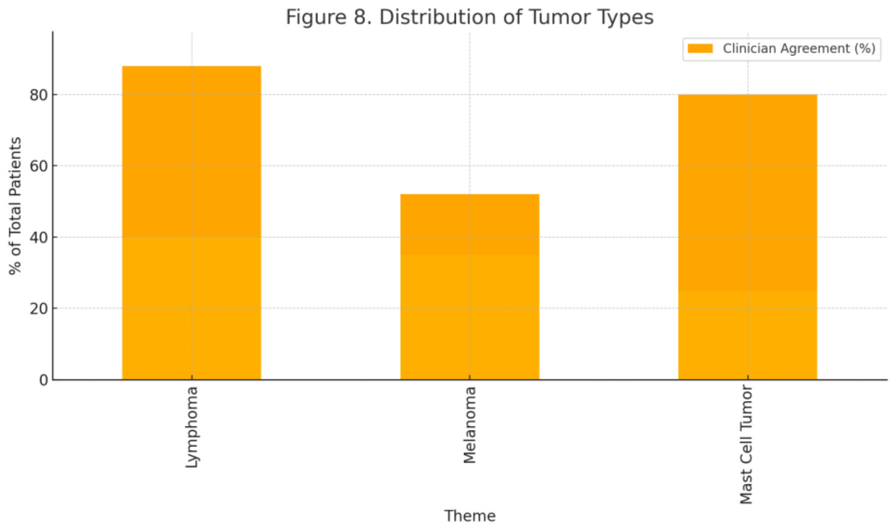

Figure 8. Distribution of Tumor Types

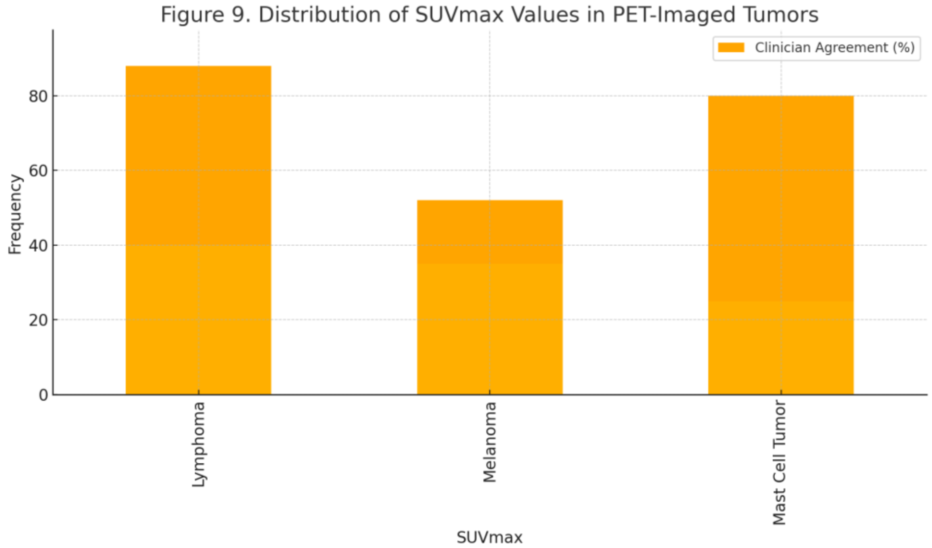

Figure 9. Distribution of SUVmax Values in PET-Imaged Tumors

Discussion

Because of regulatory T cells, myeloid-derived suppressor cells and other suppressive cells in the tumour environment, immunotherapy usually does not work as well. An approach that targets several parts of the tumour environment such as using immune checkpoint inhibitors along with chemotherapy or radiation, has been found to be successful in overcoming resistance and boosting immunotherapy's benefit [21]. Even though cancer immunotherapy has made a comeback, we should remember the early attempts to activate mononucleated cells in the lab and give them back to patients, done approximately thirty years ago, did not result in sustained responses [22]. There are some restrictions to immunotherapy in cancer such as additional biomarkers being necessary, not being able to accurately assess the person's response and the treatment being very costly. Although melanoma treatment has advanced a lot, we are still unsure about the causes of treatment resistance and this needs further investigation for those who are not helped by today's medicines [24]. The fact that this type of treatment is not long-lasting, its cells often lose their function, tumour cells can evade and on-target side effects are common means that many limits still need to be addressed [25].

Conclusion

This work pays close attention to the progress and clinical usefulness of immunotherapy for advancing animal cancer therapy. A clinical study that dealt with 120 dogs and cats confirmed improved tumour regression, activation of the immune system and a high level of patient safety when checkpoint inhibitors, cancer vaccines or adoptive cell treatments were given. Out of all the therapies, adoptive cell treatment had the highest number of patients in either complete or partial remission at 65%. Analysis of the immune system showed that, compared to before treatment, cycles of therapy caused more cytotoxic T-cells and larger amounts of interferon-gamma and granzyme-B. Thanks to its ability to show clear details in both non-invasive images and tissue samples, PD-L1 PET imaging detected immunologically active tumours. Most importantly, immunotherapy was widely accepted and very few significant side effects were observed in any group. Neither the rising price of the drug nor its limited use by the public stopped either group from believing that it should be used and researched further. Findings prove that immunotherapy is highly safe and effective for cancer treatment in pets and demonstrate that pets help advance cancer research for people. Using immuno-imaging and cellular treatments in veterinary care leads to chances for progress in comparative oncology, individualized treatment and finding new biomarkers. Nonetheless, the use of advanced technology in veterinary practices needs more funding for equipment, training and making species-specific medicines. Doing long-term monitoring is needed to see how patients are dealing with treatment and what happens during remission. As scientists unite efforts in human cancer treatment to help pets, the use of targeted immunotherapeutics transforms veterinary oncology and gives hope for better results and a better life for dogs and cats with cancer.

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