Flat-coated Retriever Report for AGM, March 2018

Dr Jane Dobson, University of Cambridge

Cause of Death Register

At December 2017 the number of entries into the Cause of Death Register stood at 558 with 509 cases having complete information to allow further analysis. The key findings are:

- The median age at death was 9 years (range 1-16 years).
- The most common causes of death were "cancer" (n=336, 66%), "old age" (n=37, 7%) and cardiac and kidney conditions (n=22 and 19, 4% each).
- Within tumor related death "sarcoma, soft tissue" was the most common together with "sarcoma, histiocytic" (n=78, 23% and n=65, 19% respectively).
- "Cardiomyopathy, dilated" accounted for 50% (n=11) of the cardiac causes of death.

With respect to sex and neutering status:

Female: 191 neutered, 74 entire

Male: 147 neutered, 146 entire

Colour: 50 Liver, 497 remainder Black

Cause of death, entries, general category

cause of death	Number	percentage
Gastrointestinal disease	8	2
Haematological	11	2
Heart disease, Cardiac	22	4
Kidney disease	19	4
Liver disease	4	1
Musculoskeletal	7	1
Neurological	13	3
Old Age - age related	37	7
Other	27	5
Respiratory disease	2	0
Trauma / Accident	6	1
Tumour or Cancer related	336	66
Unknown	17	3
total	509	

The number of tumour / cancer-related deaths is still 66%, soft tissue and histiocytic sarcoma remain the most common tumour types (23% and 19% of all tumours respectively)

Tumour related cause of Death - all cases

Tumour type	Number	Percent
carcinoma NOS	15	4%
carcinoma, adenocarcinoma	9	3%
carcinoma, squamous cell	1	0%
carcinoma, transitional	4	1%
leukaemia	1	0%
lymphoma	24	7%
mast cell tumour	13	4%
melanoma	4	1%
sarcoma, fibrosarcoma	1	0%
sarcoma, haemangiopericytoma	3	1%
sarcoma, haemangiosarcoma	47	14%
sarcoma, histiocytic	65	19%
sarcoma, osteosarcoma	36	11%
sarcoma, soft tissue	78	23%
neoplasia unspecified	33	10%
Total	334	

Over 500 owners have kindly offered precious information for the good of the breed when grieving the loss of their beloved pet. Many people contributed a lot of detail of their dog's illness which Chiara Talamonti summarised for publication in a recent Newsletter. The contribution made by these owners has been very much appreciated by everyone involved in the project.

Other News.

In April 2017 we appointed Chiara Talamonti to undertake a 12 month project funded by Petsavers (BSAVA) entitled " Evaluation of the microenvironment and immune function in Histiocytic Sarcoma, a tumour of dendritic cells". We are very grateful to Liz Branscombe and Jane Alexander in helping us secure samples of blood and tumours for this work. The project is nearing completion, we are hoping to publish some of the findings in due course, there follows a summary of Chiara's achievements.

Previous histological investigation into the tumour microenvironment showed the presence of regulatory T lymphocytes (T_{regs}). The hypothesis is that these T_{regs} may be acting to impede the immune system's response to growth and spread of the tumour.

Using flow cytometry, the frequency of T_{regs} in peripheral blood of 8 flatcoated retrievers bearing histiocytic sarcoma was assessed using a validated panel of antibodies. Samples from 11 non-diseased flatcoated retrievers over the age of 8 were used as controls. No evidence of increased frequencies of

CD4+ T_{regs} was seen systemically in the affected animals. Suggesting the increased presence of T_{regs} is connected to changes within the tumour microenvironment.

To investigate further mechanisms by which the tumour may be evading the immune system response a further study was conducted on archived samples of histiocytic sarcomas previously collected during post-mortem examination or as biopsies for diagnostic procedures. Immunolabelling with antibodies to CD3, MHC II, E-cadherin, FoxP3 and IL-10 and PD-L1 was performed on 28 localised HS tumours. CD3, MHC II and E-cadherin findings confirmed the suspected origin of histiocytic sarcoma, mature dendritic cells. IL-10 was negative on almost all samples, except for 4 samples which expressed a low level of positivity, suggesting this molecule does not play a major role in the down-regulation of the immune system. FoxP3 expression on an average of 10% of infiltrating immune cells confirmed the presence of T_{regs} within the tumour themselves. However, this increase percentage was lost in peripheral blood. PD-L1 expression was found on all tumour samples analysed. PD-L1 (programmed death ligand 1) is a potential target for novel chemotherapeutic approaches to cancer therapy currently undergoing clinical development. Recently a canine clinical trial has been conducted on dogs with oral malignant melanoma, and two cases of undifferentiated sarcoma. So perhaps this offers some hope for the future management of histiocytic sarcoma in the breed.

Although Chiara's project is nearing completion we are still interested to hear of dogs affected by histiocytic sarcoma but do not require fresh blood or tissue samples at present.

Please pass our thanks to all members of the Breed Society for their continued support of our work.

Jane Dobson & Chiara Talamonti

8 March 2018