Feline injection-site sarcoma in translational oncology

Prof. Dr. Johannes Hirschberger
Clinic of Small Animal Medicine
Centre for Clinical Veterinary Medicine, Faculty of Veterinary Medicine, LMU Munich

Coinvestigators

Prof. Dr. Gerhard Wess	Clinic of Small Animal Medicine, LMU Munich
Dr. René Dörfelt	Clinic of Small Animal Medicine, LMU Munich
Prof. Dr. Andrea Meyer-Lindenberg	Clinic of Small Animal Surgery & Reproduction, LMU Munich
Dr. Andreas Brühschwein,	Clinic of Small Animal Surgery & Reproduction, LMU Munich
Prof. Dr. Markus Schwaiger	Nuclear Medicine, Klinikum Rechts der Isar, TUM Munich
Christine Baumgartner	Center for Preclinical Research, Klinikum Rechts der Isar, TUM Munich
Prof. Dr. Lars Lindner	Department of Internal Medicine III, LMU Munich

Summary for Lay Reader

Soft tissue sarcomas are special tumours with very infiltrative growth and relatively low metastasis rate. These tumours occur in all species – including humans, dogs, and cats.
In human medicine, there are strict regulations for diagnosis and treatment of different neoplasias. However, in veterinary medicine, diagnostic and treatment options are not so high developed. New scientific approaches can be performed because there is no standard alternative.
We have a model for soft tissue sarcomas – the feline injection-site sarcoma, mostly fibrosarcomas. These tumours behave biologically like human fibrosarcomas. Our goal is to establish nuclear radiological diagnostic procedures to describe the tumour growth plus metabolism and to develop treatment procedures by combining regional hyperthermia and chemotherapy with thermosensitive liposomes.

Research Objectives

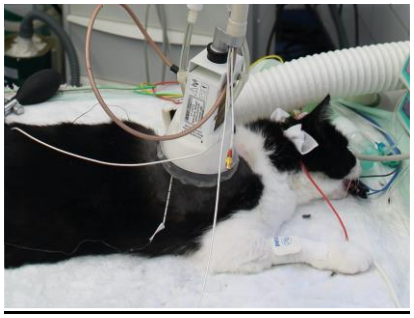
Clinical studies in human medicine are time consuming, and the process of development and approval of new anti-cancer drugs can take a long time. Veterinary practitioners have limited access to safe and effective chemotherapeutic treatments that have been tested in a clinical research environment. In veterinary medicine, unlike human medicine, scientific trials with new drugs or methods can be legally performed as the first line therapy, and not only in advanced stages of a disease. The results of clinical studies and trials in larger mammals such as dogs and cats can be used to improve the design of similar trials in human beings, and can reduce needed resources toward next steps in the human medicine treatment approval process. Therefore, by engaging in companion animal clinical trials, pharmaceutical companies can use their resources more economically and efficiently, thus saving both time and money. This is a win-win situation for the client/pharmaceutical company and for the animal patient. All animal studies have to be approved by an ethics committee, and are conducted under strict ethical guidelines. The translational oncology program at LMU Centre for Clinical Medicine is aiming to fill the gap between syngenic mice and human cancer patients by using companion animals with spontaneously occurring neoplastic diseases as animal models for clinical trials with distinct advantages. Companion animals are a large, genetically heterogeneous group that share the same environment as humans, and more than 30% of dogs and cats develop malignant neoplasms spontaneously. Thus companion animal models are very suitable for the development of human anti-neoplastic drugs.

For more than 20 years, the Clinic of Small Animal Medicine of the Ludwig Maximilian University in Munich has been performing clinical trials in dogs and cats with spontaneously occurring neoplastic diseases.
Project for diagnosing tumour biology (Prof. Dr. Markus Schwaiger): Evaluation of 2-Deoxy-2-[18F]fluoro-D-glucose (FDG) Positron Emission Tomography/Computed Tomography (PET/CT) for the Staging of Dogs with Malignant Tumors. (Prof. Dr. Franz Schilling): multimodal functional CEST-MRI (Chemical Exchange Saturation Transfer Magnetic Resonance Imaging), HP-MRI (Hyperpolarized Magnetic Resonance Imaging), [18F]-FMISO-PET (18F-Misonidazole), [18F]-FDG-PET (Fluorodeoxiglucose Positron Emission Tomography) Imaging in vivo to analyze heterogeneity of solid tumours.
Project for sarcoma treatment (Prof. Dr. Lars Lindner): Intravascularly releasing doxorubicin-containing thermosensitive liposomes with simultaneous hyperthermia in advanced spontaneous feline soft tissue sarcomas.

Key Findings

Nuclear imaging can well describe the tumour metabolism. Tumour response to treatment can be demonstrated in regular intervals.
Regional hyperthermia with thermosensitive liposomes containing doxorubicin is effective and well tolerated in the treatment of feline injection-site sarcomas up to a dose of 1 mg/kg every 2 weeks.

Figures



Cat with sarcoma on the shoulder. Regional Hyperthermia performed with clinical head-and-neck radiofrequency applicator.

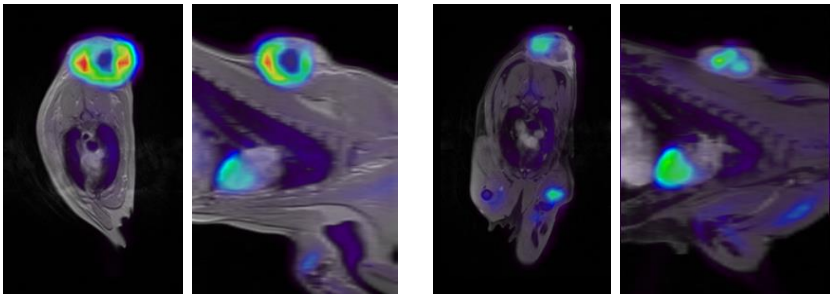


Figure: Prof. Dr. Markus Schwaiger

PET-MRI demonstration of tumour remission and tumour metabolism. Reduction after regional hyperthermia and intravenous therapy with Doxorubicin containing thermosensitive liposomes in a cat with soft tissue sarcoma after 2 treatment cycles.

Selected publications

1. Hossann M, Hirschberger J, Schmidt R, Baumgartner Ch, Zimmermann K, Baer S, Ratzlaff Ch, Peller M, Troedson K, Limmer S, Brühschwein A, Dörfelt R, Kreutzmann N, Wess G, Knösel Th, Schagon O, Fischer J, Grüll H, Willerding L, Schmidt M, Meyer-Lindenberg A, Issels R, Schwaiger M, Eggermont A, ten Hagen T, Lindner L. Optimized thermosensitive doxorubicin liposomes for neoadjuvant treatment of locally advanced soft tissue sarcoma. Clinical Cancer Research submitted 2020.
2. Lars Lindner. Heat mediated drug delivery with temperature sensitive liposomes – a synergistic approach. ICONAN Munich, Oct 16-18, 2019.
3. Holtermann N, Kiupel M, Hirschberger J. The tyrosine kinase inhibitor toceranib in feline injection site sarcoma: efficacy and side effects. Vet Comp Oncol. 2017; 15(2): 632-640. doi: 10.1111/vco.12207.
4. Zimmermann K, Hossann M, Hirschberger J, Troedson K, Peller M, Schneider M, Brühschwein A, Meyer-Lindenberg A, Wess G, Wergin M, Dörfelt R, Knösel T, Schwaiger M, Baumgartner C, Brandl J, Schwamberger S, Lindner L. A pilot trial of doxorubicin containing phosphatidyldiglycerol based thermosensitive liposomes in spontaneous feline soft tissue sarcoma. International Journal of Hyperthermia, 2017; 33(2): 178-190.
5. Seiler, SM. Baumgartner, C. Hirschberger, J. Ambros, J. Beer, J. Brühschwein, A. Kreutzmann, N. Laberke, S. Wergin, M. Meyer-Lindenberg, A. Brandl, J. von Thadden, A-K. Farrell, E. Schwaiger, M. Comparative Oncology: Evaluation of 2-Deoxy-2-[18F]fluoro-D-glucose (FDG) Positron Emission Tomography/Computed Tomography (PET/CT) for the Staging of Dogs with Malignant Tumors. PloS One, 2015; 10.

Funding

Funder	Project title	Start date	End date
Pharmaceutical company	Canine model of diffuse large cell B-cell lymphoma: a molecular therapy	2016	2019