UMKC IACUC POLICY

Humane Endpoints for Studies Involving Spontaneous and Induced Tumors

The UMKC IACUC is obligated to provide policies that notify and train personnel concerning the appropriate techniques, equipment, and agents for performing appropriate procedures to ensure humane care and use of laboratory animals.

Background

In cancer research, it is often necessary to propagate human or animal tumors (xenografts) in immuno-compromised animals in order to study the biology of the tumor or to determine if certain treatment regimens are effective. Additionally, various transgenic rodent models have now been created to study "naturally" occurring tumors in these animals. Such research can produce pain and discomfort in experimental animals. This policy includes guidelines that provide a rational approach to terminating a study while meeting the research objectives and minimizing pain and distress in the research subjects. These guidelines are intended to be general in nature and will not be applicable in every case. Most investigators are familiar with the biology of the tumors they induce or transplant. If the tumor is aggressive in their animal model, these guidelines will not be applicable and the humane endpoints specific to the tumor behavior will need to be developed by the PI and approved by the IACUC (see below). The IACUC and Attending Veterinarian are available for consultation to assist scientists in developing the specific humane endpoints for their study.

Policy

In all cases, humane endpoints are to be listed in an animal use protocol that is reviewed by the UMKC Institutional Animal Care and Use Committee. The minimization of animal pain and maximization of animal welfare is the intended goal. When efficacious and consistent with research goals, pain and distress should be alleviated using analgesics, tranquilizers or sedatives.

The study of tumors, spontaneous or induced, is not a time-based event. It is not acceptable to indicate a tumor will be followed for a specific amount of time. Tumors may develop at predictable rates but will not develop the same in every individual animal.

Investigators should choose the earliest endpoint that is compatible with the scientific objectives of the research, to minimize potential pain, distress or discomfort.

A system for frequent monitoring of animals for tumor development should be part of the experimental objective. Frequency of monitoring should be based on expected growth/metastatic properties of the tumor type in the animal model used, if known. If unknown, then a pilot study may be warranted, using 5-10 animals, to assess any adverse effects associated with tumor progression and enable humane endpoints to be established.

Limits of the tumor burden should be established and described in detail in the animal use protocol.

Limits on the severity of tumor-associated disease in the animal should be described based upon what is known or predicted about development of the tumor in the animal. This is important in metastatic disease, internal organ neoplasia, ascitic tumors, or cancers of the hemopoietic and lymphatic systems.

While it is recognized that each individual animal use protocol should be evaluated on the specifics of the animal model and the type of tumor induced, propagated or transplanted, the following guidelines are offered. Animals should be euthanized when:

I. In mice, measurable peripheral tumor burden (sum of all solid tumors) is equal to or more than 2.0 cm in diameter measured in any one direction or 4.2cm^3. In rats, peripheral tumor burden is equal to no more than 4.0 cm measured in any one direction or 33.5 cm^3 (based on 2019 Guidelines from the National Cancer Research Institute).

Tumor volume may be calculated using calipers and the formula $(L \times W^2)/2$. Smaller tumor burdens might be necessary, based on tumor location.

II. Tumor burden is equal to or more than 10% of the starting body weight or the expected weight of an animal of equal age and sex.
III. Tumor interferes with the normal activities of an animal such as walking, normal posture, eating or drinking.
IV. Tumor ulcerates the skin causing leakage of body fluids internally or externally.
V. A body condition score (BCS) ≤ 2
VI. Loss of 20% of body weight after the peripheral tumor burden is subtracted.
VII. Failure to eat or drink for 24-48 hours (species dependent).
VIII. Persistent hypothermia
IX. Unresponsive to stimuli or is moribund.

Other clinical signs that indicate tumor related disease when seen in combination or individually for more than 24-48 hours and should be considered humane endpoints include:

- Distension of the abdomen with fluid or palpable masses resembling the size of a pregnant animal.
- Abnormal activities, posture, movements, reluctance to move, limping or abnormal gait.
- Persistent self-induced trauma
- Any change in excretions such as constipation, diarrhea or other identifiable change in bowel or urinary activity.
- Rough hair coat or generalized loss of hair or fur.
- Nasal or ocular discharge, bleeding from any orifice.
- Abnormal vocalizations when touched or handled.
- Labored respiration
- Severe anemia (pale feet or ears or decreased Packed Cell Volume)

If there is a violation of this policy, the incident will be reviewed by the IACUC and in egregious cases the veterinarian will have the authority to suspend animal use under the protocol until IACUC review.

Reference

1. Endpoints in Animal Studies Proposals
https://oacu.oir.nih.gov/animal-research-advisory-committee-guidelines
updated 4/24/19