Evaluating Necrosis and Ulceration in Tumors and Determining Humane End-Point

Ofra Benny

Introduction

Subcutaneous or intradermal tumors may grow rapidly and some are prone to developing haemorrhagic areas, which can cause rapid expansion and ulceration (e.g., human A2780 ovarian carcinoma and AR42J pancreatic carcinoma xenografts). Ulceration is a lesion typified by necrosis of superficial tissues, which may be dry, suppurating or exudative. Tissue necrosis or ulceration of the skin overlying the developing tumor may occur. Ulceration or necrosis may result in loss of body fluids and/or infection, requiring euthanasia. Some tumors, such as those grown in sensitive sites or that develop extensive necrosis, may be painful, although objective criteria are lacking for mice.

Some treatments as chemotherapies, anti-angiogenic drugs and irradiation can accelerate tumor necrosis and thus show ulceration that may reflect tumor response to the therapy.

Justification for maintaining mice with ulcerated lesions

In general tumor ulceration should be set as a humane end-point. However in some cases, when it is well justified in the protocol submission, it can be asked to monitored and not be considered automatically as and end point.

These cases includes:

- Cases where the formation of necrosis and ulcerations are expected as part as the treatment.
- If the necrosis and ulceration appear as part of the natural growth pattern of the Subcutaneous or intradermal tumors, below the 1.5cm length which is considered as a general end point.

How to monitor the necrotic and ulcerated lesions:

- Necrotic lesions resulting in skin breakdown or exudation (fluid or blood accumulation) persisting beyond 48-72 h without closure of the "wound" are generally ground for termination: from 48 h should be discussed with the veterinary stuff.
- Signs for infections and systemic sickness (reduced mobility, weight loss) should be set as end-points.
- It is possible to provide a supporting treatment when necrosis and ulceration appear in the form of fluid injection and topical antibiotics to prevent injection. If the treatment prevents infection, mice can be kept alive while monitored.

References:

Guidelines for the welfare and use of animals in cancer research.
P Workman et al. Br J Cancer, 2010. 102 (11) 1555-1577

Guidelines for Maintenance of Tumors and Hybridomas in Rodents. IOWA State University. Institutional Animal Care and Use Committee. Revised: Sept 13, 2010