Phase I/II clinical trial of 2-difluoromethyl-ornithine (DFMO) and a novel polyamine transport inhibitor (MQT 1426) for feline oral squamous cell carcinoma

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Abstract

Polyamines are essential for cell proliferation. Their production is dysregulated in many cancers and polyamine depletion leads to tumour regression in mouse models of squamous cell carcinoma (SCC). The purpose of this study was to determine the maximally tolerated dose of the polyamine transport inhibitor, MQT 1426, when combined with the ornithine decarboxylase (ODC) inhibitor, DFMO, and to determine whether this therapy results in reduction in tumour polyamine levels. Thirteen cats with oral SCC received both drugs orally and serial tumour biopsies were obtained for polyamine measurement. Cats were monitored for response to therapy and toxicity. A maximum tolerated dose (MTD) of MQT 1426 when combined with DFMO was determined. Dose-limiting toxicity was vestibular in nature, but was fully reversible. Spermidine and total polyamine levels decreased significantly in tissues, two cats experienced objective tumour regression and six cats had stable disease. These results suggest that further study of polyamine depletion therapies is warranted.

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