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Tigilanol tiglate (EBC-46), a new tool in the anti-solid surface tumours tool box?

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Abstract

Tigilanol tiglate (EBC-46) is a small diterpene ester extracted from the seed of a native Australian rainforest plant, *Fontainea picrosperma* (family Euphorbiaceae), which has shown significant potential as a local intratumoural treatment for non-metastatic skin mast cell tumours (MCT) and skin soft tissue sarcoma in dogs.

Research to date demonstrates that tigilanol tiglate is a potent activator of Protein Kinase C (PKC) with drug action resulting in rapid hemorrhagic necrosis of tumours through a combination of direct disruption of tumour vasculature, initiation of acute but highly localized, pro-inflammatory responses, and local recruitment and activation of neutrophils (Boyle, *et al* 2014).

The manufacturing development, preclinical and clinical development of tigilanol tiglate injection for the treatment of non-metastatic skin MCT is well advanced. More than 30 pharmacokinetic, pharmacodynamic, metabolism, toxicology and target animal safety studies have been completed. Tigilanol tiglate Injection is currently being evaluated under an Investigational New Animal Drug (INAD) with the Food and Drug Administration - Centre for Veterinary Medicine (FDA-CVM) in the US where a pivotal randomized controlled field efficacy trial treating MCT in dogs is underway.

Canine MCT is a common neoplastic disease in dogs accounting for 16-21% of all cutaneous neoplasms (Bostock, 1986; Rothwell *et al.* 1987). Canine cutaneous MCT originate in the dermis and may extend into the subcutis, but there is also a subcutaneous MCT subset completely surrounded by adipose tissue with no follicular or epidermal involvement (Thompson *et al*, 2011). The current therapy of choice for skin and subcutis MCT is wide surgical resection (Pratschke, 2015). When this is not possible, one or a combination of, chemotherapy, radiotherapy or cytoreductive surgery is undertaken (Withrow and Vail, 2007). These therapeutic modalities often are costly, labour and time-intensive, and may not be readily available to dogs because of client preferences or lack of access to certain treatment modalities. Tigilanol tiglate offers much as a potential new approach within the range of treatment paradigms currently available for the management of canine MCT.

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