INTRATUMORALLY ADMINISTERED TIGILANOL TIGLATE (STELFONTA®) CAUSES HAEMORRHAGIC NECROSIS, RAPID TUMOUR CELL DEATH AND LOCAL CURE OF TUMOURS IN MOUSE MODELS

OBJECTIVES

Describe the mode of action of intratumorally administered tigilanol tiglate (also known as EBC-46) in destruction of target tumours in syngeneic and xenograft mouse models.

MATERIALS & METHODS

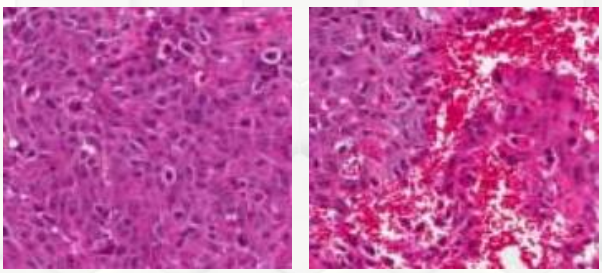
- **Preclinical mouse models of melanoma and squamous cell carcinoma to assess tumour response, systemic exposure in serum, and effects on injection into healthy tissue.**
- ***Ex vivo* studies of viability of tumour cells after tigilanol tiglate treatment.**
- ***In vitro* studies of sensitivity of cancer cell-lines and protein kinase C (PKC) activation profiles.**

RESULTS

- **The syngeneic and xenograft tumour mouse models showed that a single intratumoural injection of tigilanol tiglate caused:**
  - Rapid localised inflammation and influx of white blood cells into the tumour and immediate surrounds;
  - Loss of integrity of tumour vasculature within 1 hour of treatment (Figure 1); and
  - Rapid death of cancer cells in the treated tumours (no viable cells recovered by *ex vivo* culture 4 hours after treatment – Figure 2).
- **Activation of specific isoforms of protein kinase C (PKC) was shown to be responsible, at least in part, for the efficacy of tigilanol tiglate.**

CLINICAL INTEREST

A single intratumoral injection of tigilanol tiglate resulted in local cure of solid tumours in pre-clinical mouse models of cancer.



Excipient only **Tigilanol tiglate**

Figure 1: Vascular disruption and red cell extravasation is clearly evident in histopathology sections by 1 hour after treatment of squamous cell carcinoma xenografts on mice with tigilanol tiglate (right hand image) compared to tumours treated with excipient only (left hand image).

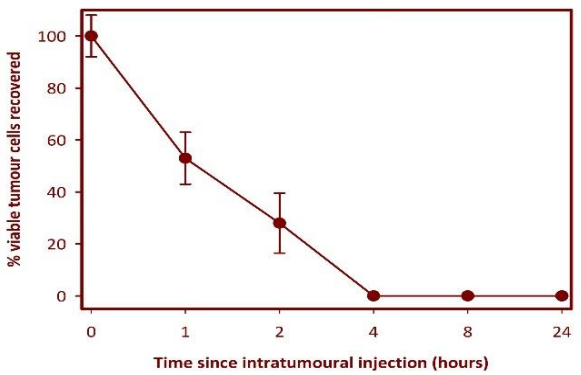


Figure 2: No viable tumour cells could be recovered in *ex vivo* culture from a xenograft mouse melanoma model by 4 hours after treatment with tigilanol tiglate.

REFERENCES

Boyle GM, D'Souza MMA, Pierce CJ, Adams RA, Cantor AS, Johns JP, et al. Intra-lesional injection of the novel PKC activator EBC-46 rapidly ablates tumours in mouse models. PLoS One. 2014;9(10):1–12.