ZaicaDerm

The future of Skin Cancer Treatment
Fully formulated cream that delivers Tea Tree Oil in a transdermal format

Using proprietary technology, ZaicaDerm, delivers 10% Tea Tree Oil below the skin, to treat and regress precancerous actinic keratosis

Based on established preclinical data, ZaicaDerm delivers a clinically effective quantity of TTO

Ref: JOURNAL OF DERMATOLOGICAL SCIENCE Topically applied Melaleuca alternifolia (tea tree) oil causes direct anti-cancer cytotoxicity in subcutaneous tumour bearing mice

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In 2010 Professor Manfred Beilharz and his team at The University of Western Australia conducted a preclinical trial and established that Tea Tree Oil (TTO) can significantly reduce the viability \textit{in vitro} of 2 murine tumor cell lines: AE17 and B16 in a dose and time dependent manner.

The \textit{in vivo} part of the study showed that 3% and 10% TTO can inhibit tumor growth in mice. 10% TTO in DMSO was able to cause regression of tumors. DMSO can enhance penetration of substances through skin (transdermal enhancer).

Unfortunately treatment with 10% TTO/DMSO was limited to 4 days due to development of severe irritation, allowing regrowth of the tumors.
The ZaicaDerm Alternative – Preclinical Testing

Pre trial test using one pair of mice with subcutaneous B16 melanoma
5 day treatment protocol:
ZaicaDerm versus No Treatment
Early stage pre-trial on B16 melanoma

Tumor was allowed to grow for 7 days before treatment began.

Photos were taken after the 5th daily treatment with cream-based TTO (ZaicaDerm)
Preclinical Trial #1 –

Evaluation of skin inflammation during topical treatment of tumor-bearing mice with Tea Tree Oil in a cream based formulation (ZaicaDerm)

Professor Don Cohen – University of Kentucky, USA

Primary Goal: Determine if inflammation in tumor-bearing mice is reduced with ZaicaDerm formulation compared to TTO/DMSO

Secondary Goal: Evaluate tumor growth inhibition by ZaicaDerm on an aggressive form of melanoma tumor.

(20 Albino C57Bl/6 mice were used in the study)
Tumor treatment with TTO cream does not cause dermal inflammation.
Tumor treatment with TTO cream does not cause dermal inflammation

Myeloperoxidase, a marker for inflammatory cells, was measured in skin of tumor-bearing mice.
TTO-cream inhibits growth of B16 melanoma in mice (10 mice/group)

(Fast growing tumor, clone F10)
5. Subcutaneous Tumor Weight – tumors of all mice per group were resected and weighed.

Comments: Weights of resected tumors bore out initial appearances. The average weight of tumors from mice treated with cream-based TTO was significantly smaller than tumors from mice treated with TTO in DMSO.
Anti-tumor activity of TTO cream is seen in multiple studies.
Preclinical Trial #3 –

Evaluation of anti tumor activity during topical treatment of tumor-bearing mice with Tea Tree Oil in a cream based formulation (ZaicaDerm)

*Professor Don Cohen – University of Kentucky, USA*

Primary Goal: Determine if TTO Cream Formulation (ZaicaDerm) inhibits growth of B16 melanoma tumors in the skin of mice.

(6 Albino C57Bl/6 mice were used in the study)
Three days after tumor inoculation, 3 mice were treated daily with TTO Cream (50 mg/treatment). 3 additional tumor-bearing mice remained untreated. Tumor volume was measured at the indicated time points.
Subcutaneous Tumor Size (group results)
Tumor size and weight are reduced by TTO cream

Skin inflammation was not observed at any point during TTO Cream treatment.
The target market

- Skin cancer is the most prevalent form of cancer in the United States and its incidence has increased over 300% during the last 20 years.
- Approximately 75,000 new cases of melanoma and nearly 2 million cases of non-melanoma skin cancer (NMSC) are diagnosed in the U.S. each year.
- The development of non-melanoma skin cancers, squamous cell carcinoma [SCC] and basal cell carcinoma [BCC], has been linked to repeated exposure to sun radiation over many years, whereas melanoma is also linked to the severity of sunburn.
- **Actinic keratosis** (AK) is a common precancerous condition of SCC that affects nearly **60 million** individuals in the United States. The presence of AK is also considered a marker for increased risk of developing BCC.
US Data: The direct cost of actinic keratosis management in the US was estimated at $US1.2 billion per year, with indirect costs totaling $US295 million – (year 2004 values)

According to the 2006 WHO data, more than 250 million people worldwide are living with actinic keratosis (also known as solar keratosis, AK or sun spots), a common skin condition which if not treated can lead to squamous cell carcinoma, a form of non-melanoma skin cancer.

Global Study highlights Physician preference for topical treatments for actinic keratosis with short term duration

- Actinic keratosis is a chronic condition which can be considered a form of early-stage skin cancer. Therefore it is important that physicians identify treatment options that will lead to improved adherence and ultimately improved outcomes for their patients to ensure satisfaction for patients over the longer term. These findings from over 400 physicians across eight countries provide us with a great insight into AK management and enable us to develop recommendations for improved practice."

- Ballerup, Denmark, 4 October 2013 - Over 90 per cent of physicians treating actinic keratosis (AK) prefer short duration treatment options with fast resolving local skin responses (LSRs),1 is the finding of a global study (‘Physician Perceptions and Experience of Current Treatment in Actinic Keratosis’) that was presented at the 22nd Congress of the European Academy of Dermatology and Venereology (EADV).

- This is the first study of its kind to look at physician treatment perceptions in actinic keratosis. Over 70 per cent of physicians have concerns about adherence and persistence of topical therapies being negatively influenced by long treatment durations, with local skin responses that may be severe and long lasting.1
Current Topical Treatment Options

**Imiquimod** *(tradename: Aldara)*

Imiquimod cream uses your immune system to attack cancers. It does this by releasing a number of chemicals called cytokines.

Use Rate: Once a day / 5 Days a week
Duration: 6 weeks
Effectiveness: 70% + success rate
Side Effects: Redness and soreness usually after 5 days. Itching and colour change of skin (which may be permanent)
Painful itchy eyes & mouth sores.

**5-fluorouracil** *(tradename: Efudex)*

Efudex (fluorouracil) topical is used to treat scaly overgrowths of skin (actinic or solar keratoses). It works by causing the death of cells that are growing fastest, such as abnormal skin cells.

Use Rate: Once or twice daily
Duration: 6 weeks
Side Effects: Skin irritation, burning, redness, dryness, pain, swelling, tenderness, or changes in skin color may occur at the site of application. Eye irritation (e.g., stinging, watering), trouble sleeping, irritability, temporary hair loss, or abnormal taste in the mouth may also occur.
ZaicaDerm is a topical cream used to treat scaly overgrowths of skin (actinic or solar keratosis). It may also be used in the treatment of superficial basal and squamous cell carcinoma.

ZaicaDerm (containing 10% Tea Tree Oil) induces an accumulation and activation of dendritic cells and an accumulation of T cells. The direct cytotoxicity of TTO \textit{in vivo} appears to be associated with TTO penetration.

Use Rate: Once or twice a day
Duration: 7 days, then as required (subject to final clinical data results)
Effectiveness: 85+ % (subject to final clinical data results)
Side Effects: None known at this point. Little or no skin irritation detected.
Grade II actinic keratosis on upper right hand of 64 year old male that had been continuously present for more than 12 months. Zaica Derm was applied twice per day for 14 days. All photos were taken under the same light source and at the same light intensity setting.
ZaicaDerm is manufactured using a patent pending technology, utilizing the unique vasodilation effects of natural vanilla extracts, in combination with maturation technology that provides a mild topical base with sub-cutaneous delivery potential.

Other potential uses for the ZaicaDerm technology include:

- Topical delivery of vaccines
- Topical delivery of insulin
- Topical delivery of peptides