VDA-1102: A NOVEL WELL-TOLERATED TREATMENT FOR ACTINIC KERATOSIS

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BACKGROUND

ACTINIC KERATOSIS

- Actinic Keratosis (AK) is a prevalent early-stage malignancy of the skin that can lead to cutaneous Squamous Cell Carcinoma (cSCC).
- Due to their mechanisms of action, current effective AK field treatments are irritating and painful, and cause unsightly skin eruptions.
- These side effects result in hesitancy by both patients and physicians to initiate therapy, patient compliance issues, and/or unwillingness to re-treat lesions in the same treatment field.
- Furthermore, large populations susceptible to multiple AKs (e.g. immunosuppressed, post-transplant, elderly patients) go untreated.
- Thus, an efficacious minimally-irritating topical treatment for AK is a pressing unmet medical need.

VDA-1102: MECHANISM OF ACTION

VDA-1102 is a novel small-molecule HK2-modulator that triggers apoptosis and blocks glycolysis in HK2-expressing malignant cells. Normal cells that do not express HK2 are unaffected by VDA-1102.

ACTINIC KERATOSIS

- In cancer cells, HK2 attaches to the outer mitochondrial membrane via interaction with the VDAC1 channel. VDAC1/HK2 association results in apoptosis prevention (i.e., cell longevity) and a high rate of glycolysis that addresses the transformed cell's demand for energy and building blocks.

IN VIVO EFFICACY

Efficacy on UVB-damaged Skin of Hairless SKH-1 Mice

- In hairless female mice were chronically exposed to UVB radiation for 14 weeks. By which time, lesions of non-developed at least one mouse followed by a 1-week treatment phase (2% (w/w) SAG, or vehicle control). A BLD score that a treatment group to the vehicle-treated, *p<0.05, **p<0.01, ***p<0.001.

Efficacy in AK and SCC cells

- AK2 levels are upregulated in AK and SCC cell lines. The increase is more pronounced in SCC cells compared to AK cells.

PHARMACOKINETICS

Pharmacokinetic analysis for the parent compound (VDA-1102) and for its major metabolite demonstrated no systemic exposure of either.

CONCLUSIONS

- VDA-1102 is a selective HK2-modulator that triggers apoptosis in HK2-expressing malignant cells such as AK and cSCC, without affecting the surrounding normal tissue.
- In a proof-of-concept Phase 2a clinical trial, VDA-1102 ointment (applied once-daily for 28 days) reduced the number of AK lesions on the face and scalp of adult subjects, while being very well-tolerated both locally (skin) and systemically.
- A Phase 2b dose-ranging trial with VDA-1102 ointment (applied for 3 months) is currently ongoing.


SAFETY

Composite Local Skin Reaction Score

- VDA-1102 was well tolerated with minimal irritations.

EFFICACY

Treatment

- Placebo (N = 20)
- VDA-1102 (N = 20)

Category

- Any TEAE
- Any TEAE Related to Treatment
- Any TEAE Related to Treatment
- Study Withdrawals
- Drug Adjustments

Study Day

- 0
- 5
- 12
- 24
- 48

The mean of the composite LSR score from all 2 cohorts was negligible (left panel).

LOCAL SKIN REACTION

- Dose: 20/50/100 mg/g for major metabolite, 10 mg/g for Placebo.

Efficacy in Facial AK Lesions

- 4-8 AK lesions (Grades 1-2) in a 25 cm² area on face or scalp

PHARMACOKINETICS

- VDA-1102 (mean tmax): 1 hour for 2% SAG, 5 hours for 5%.
- VDA-1102 (mean tmax): 14 days for 2% SAG, 5 days for 5%.

IN VIVO EFFICACY

- Efficacy on UVB-damaged Skin of Hairless SKH-1 Mice
- Placebo
- HK1 & HK2 Levels in UVB-damaged Mouse Skin

NON-ClinICAL DATA

Hk2 in Actinic Keratosis & SCC

- High HK2 levels in skin SCC vs. Low HK2 levels in normal skin
- High HK2 levels in human AK and SCC cells

CLINICAL PHASE 2A DATA

- Study Design
- Local Skin Reactions

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