Samcyprone™ (Diphenylcyclopropenone Ointment) for the Treatment of Common Warts

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Background

Diphenylcyclopropenone (DPCP) is a potent topical immunotherapy agent that has been used in a compounded form since the late 1970's by physicians for the treatment of common warts, alopecia areata, and cutaneous metastases of melanoma[1]. Although not approved by the FDA or EMA, physicians continue to use compounded DPCP because of its proven effects in these dermatologic conditions. The use of the drug as reported in the literature is not standardized and widely varying strengths have been suggested for the sensitization and challenge treatments with DPCP, resulting in inconsistent results from a safety and efficacy viewpoint.

Hypothesis

Treating common warts with a proprietary ointment formulation of DPCP (Samcyprone) consisting of a low sensitization (0.4% DPCP) dose followed by a standardized weekly treatment dose (0.04% DPCP) regimen, is safe and effective.

Methods

A phase 2a clinical study was conducted evaluating Samcyprone (DPCP Sensitization and Treatment Ointments) for the treatment of common warts. The study was a multi-center, multi-dose trial conducted in subjects with at least one cutaneous, plantar or periungual wart present for at least four weeks. In this trial, subjects were first treated with a sensitization dose (0.4% DPCP) on the inner arm and on one or more preselected wart lesions. Once the sensitization response was confirmed, subjects continued with weekly treatments for 10 weeks with 0.04% DPCP. Wart clearance was evaluated based on the Investigator's Global Assessment Score (IGAS) and wart measurements over time during the treatment period. Immunotherapeutic Skin Response Scores (ISRS) were also collected as a safety assessment of local reactions to be expected from a topical immunomodulator. Efficacy results below are for Per Protocol population.

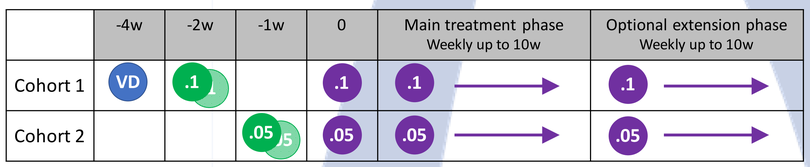

Figure 1: Dosing schedule for the 2 cohorts included in the study. Dosing with a vehicle ointment preceded dosing with the sensitization dose (solid green icons) in Cohort 1. Sensitization dose could be repeated once if the first dose did not result in a delayed-type hypersensitivity (DTH) reaction (shaded green icons). One week (Cohort 2) or two weeks (Cohort 1) after DTH, weekly treatment was started for up to 10 weeks. If warts were ≥50% cleared after the 10th treatment, subjects could be enrolled in the optional extension phase for up to 10 more weeks. Singular warts were treated with 0.1 ml doses in Cohort 1, and 0.05 ml doses in Cohort 2.

Score	ISRS
0	No skin reaction
1+	Erythema only
2+	Erythema and cutaneous induration
3+	Erythema, papules and small vesicles
4+	Large vesicles, bullae and severe local reaction besides erythema

Score	IGAS
0	Complete or partial eradication not achieved
1	Partial eradication: <50% reduction in the area of all treated warts
2	Partial eradication: ≥ 50% reduction in the area of all treated warts or complete eradication of at least half of the treated warts
3	Complete eradication: elimination of all treated warts and restoration of normal epidermal lines and markings.

Table 1 & 2: Immunotherapeutic Skin Response Score (left) and Investigator's Global Assessment Scores used to determine sensitization responses and wart clearance responses respectively.

Results

The Primary Objectives were to evaluate the effectiveness of Sensitizing DPCP Ointment (0.4%) in eliciting a sensitization response in generally healthy subjects with common warts and to determine the therapeutic response (wart clearance) after treatment with 0.04% DPCP Ointment.

Immunotherapeutic response:
Of the 88 subjects enrolled in the study, 85 received at least one sensitization dose of 0.4% DPCP ointment, and a DTH response was observed in all but 2 subjects (one in each cohort), overall resulting in a 97.7% success rate of 0.4% DPCP ointment in eliciting the required immunotherapeutic response. A higher proportion of subjects in Cohort 2 required a second sensitization dose however (Table 3).

	Cohort 1	Cohort 2
Overall sensitization rate	97.4%	97.9%
Subjects requiring a second sensitization dose	5.3%	46.8%

Table 3: Percentage of subjects in each cohort requiring a second sensitization dose to get a DTH response level of 2+ on the ISRS scale.

Wart response rate:
The total number of wart lesions in the per protocol population (PP) was 87. Already during the first 10 weeks of weekly treatments, a significant number of warts had a positive response to the treatment, i.e. displayed a ≥50% reduction in wart size (Figure 2). The overall wart response rate at that time was 70.1%, but is was substantially lower for plantar warts.

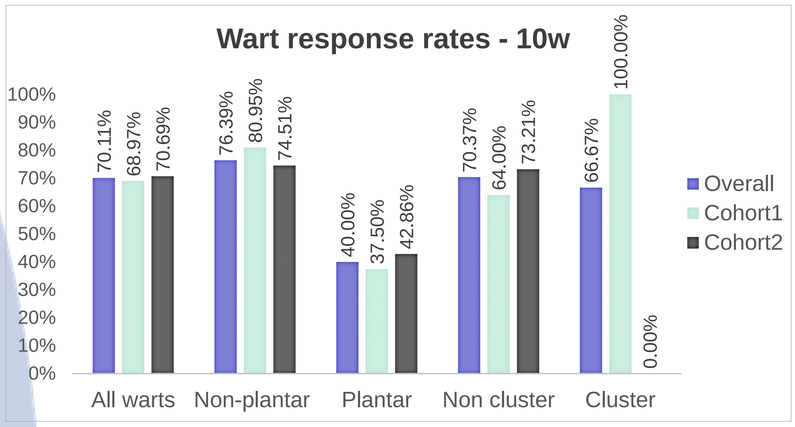

Figure 2: Wart response rates (≥ 50% reduction in wart size), as determined by wart measurements, after the first 10w of the study. A breakdown is shown by location (plantar or not) and type (cluster or not) and for each of the 2 cohorts. Cluster results to be interpreted with caution due to small sample size.

Wart clearance rate:
Complete clearance during the first 10 weeks of treatment was seen in 43.7% of all warts. Throughout the full course of the study, 47 warts (54.0%) achieved complete clearance (Figure 3). More non-plantar wart lesions, compared to plantar wart lesions, achieved complete clearance: Clearance rate of non-plantar warts lesions was the highest in Cohort 1 (57.1% during first 10 weeks, 71.4% after complete study). Similarly, more non-cluster lesions (singular warts), as compared to wart clusters, achieved complete clearance: Clearance rate of non-cluster lesions was the highest in Cohort 1 (52.0% during first 10 weeks, 60.0% after complete study).

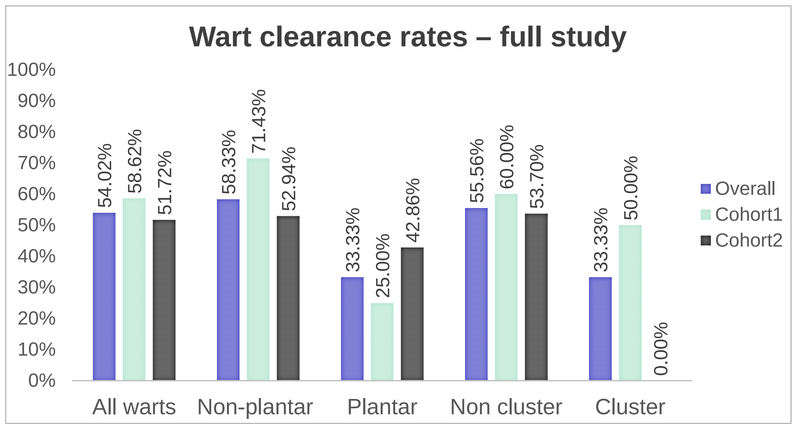

Figure 3: Wart clearance rates, as determined by wart measurements, throughout the full study duration. A breakdown is shown by location (plantar or not) and type (cluster or not) and for each of the 2 cohorts. Cluster results to be interpreted with caution due to small sample size.

Safety:
Drug-related adverse events reported in the study were mostly local reactions due to the sensitization and challenge responses in the skin which are to be expected for a topical immune response modifier such as DPCP. There were no drug related SAEs, and no Dose Limiting Toxicities.

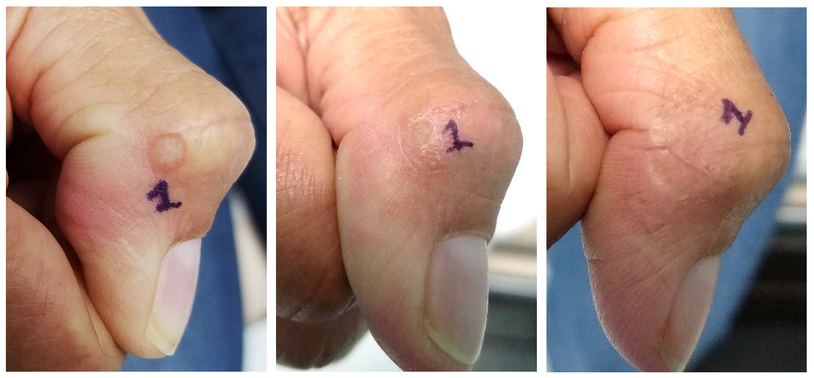

Figure 4: Example of wart clearance: prior to treatment (left), midway during treatment (mid) and after treatment (right).

Conclusions

- Treating common warts with Samcyprone is safe and effective.
- Response and treatment length is defined by wart type, with most warts requiring treatment for ≤10 weeks with once weekly dosing.
- Increased cure rates are expected with pretreatment (curettage or filing to pinpoint bleeding) and longer treatment duration for some wart types.

References

1. Holzer AM, Kaplan LL, Levis WR: Haptens as drugs: contact allergens are powerful topical immunomodulators. *J Drugs Dermatol* 2006; 5:410-6

Acknowledgements

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