Topical Ionic Contra Viral Therapy (ICVT) as a novel treatment approach for cutaneous warts

T. van der Kolk[1], M.R. Dillingh[1], R. Rijneveld,[1] E.S. Klaassen,[1] M.N. de Koning[3], R.E. Genders,[4] J. N. Bouwes-Bavinck[4], G. Feiss,[2] R. Rissmann[1], J. Burggraaf[1]

[1]Centre for Human Drug Research, Leiden, the Netherlands, [2]Cutanea Life Science, Wayne, Pennsylvania, USA, [3] DDL Diagnostic Laboratory, Rijswijk, the Netherlands, [4]Department of Dermatology Leiden University Medical Centre, Leiden, the Netherlands

INTRODUCTION

ICVT comprised of digoxin and/or furosemide inhibits the K+ influx on which DNA viruses, such as the Human Papilloma Virus (HPV) rely for replication and is therefore a potential novel treatment for cutaneous warts. In vitro, this effect was most potent when digoxin and furosemide were combined [1].

OBJECTIVES

- To evaluate the systemic exposure of digoxin and furosemide after repeated topical application
- To assess the safety and tolerability profile of ICVT
- To explore the pharmacodynamic effects of topical application of ICVT on wart morphology and HPV viral load
- To validate HPV viral load quantitative PCR (qPCR) on relevant clinical material as preparation for subsequent studies

METHODS

- First in Human (FIH) phase I/II open-label study
- 12 male subjects
- ≥ 4 common warts
- 7 consecutive days of 980 mg topical application on lower back (safety)
- 7 consecutive days of topical application to 2 target warts (pharmacodynamics)
- 2 negative control target warts
- Standard safety assessments
- Therapeutic drug monitoring digoxin
- Clinical assessments, photography
- Genotyping of 23 cutaneous wart associated HPV types by surface swab [2]
- HPV viral load determination of HPV1, 2, 27, 57 when found by genotyping.

RESULTS

	Mean (SD)	Median	Min	Max
Age (years)	24.3 (5.3)	22.5	19	37
Height (cm)	180.1 (9.9)	182.2	162.9	191.1
Weight (kg)	73.3 (14.2)	70.1	59	111.1
BMI (kg/m2)	22.5 (3.0)	22.0	19.9	29.8

Table 1. Baseline characteristics

- Demographics / baseline characteristics comparable (table 1)
- 48 warts in total, 24 treated; 24 untreated
- HPV 2 and HPV 57 detected in swabs and biopsies (fig. 1)
- ICVT safe and well tolerated, no detectable systemic exposure
- Most frequent occurring AEs; headache (3/12), application site erythema and pruritus (both 2/12)
- Positive trend towards warts size reduction (table 2, fig.2)
- No clear trend in HPV load reduction in swab after 7 days of treatment (fig. 3)
- Significant correlation between HPV viral load by swab and biopsy, p = 0.0033 (fig. 4)

	Baseline	Day 7	Day 14
Wart diameter (mm) – mean (SD)	5.3	5.0	4.9
Wart height (mm) – mean (SD)	1.8	1.3	1.1
Wart volume (mm³) – mean (SD)	202.7	128.0	113.9

Table 2. Change in wart size from baseline to End of Study

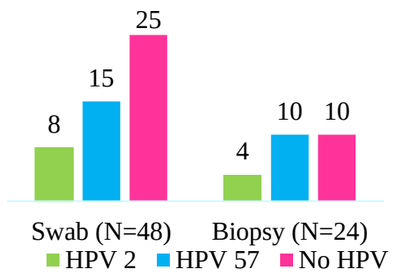

Figure 1. HPV detected in swab and biopsy

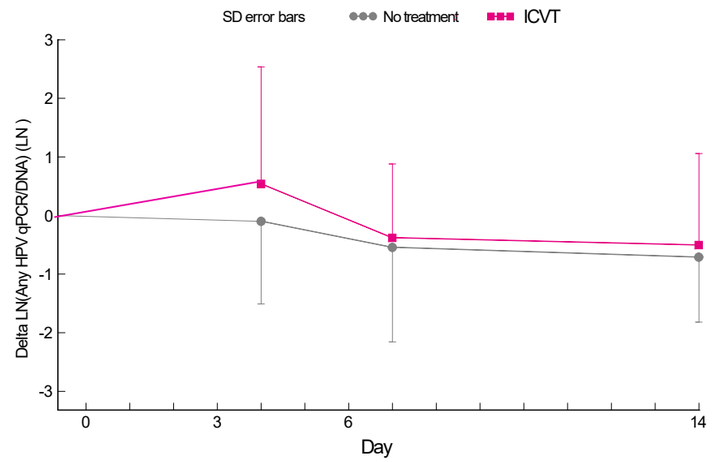

Figure 3. Viral load summary graph, any HPV type, log transformed (qPCR/DNA) (LN) change from baseline

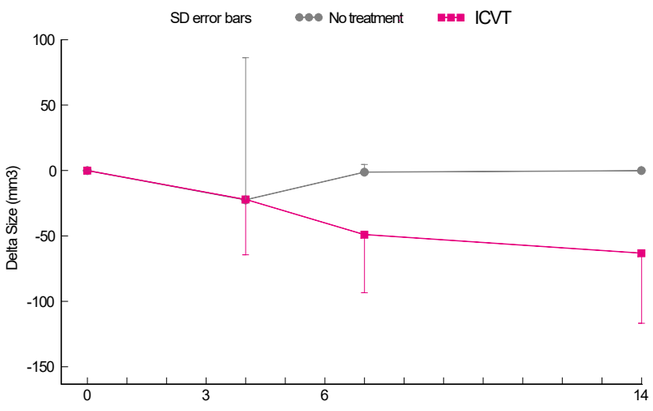

Figure 2. Summary graph of wart size per target lesion (change from baseline values)

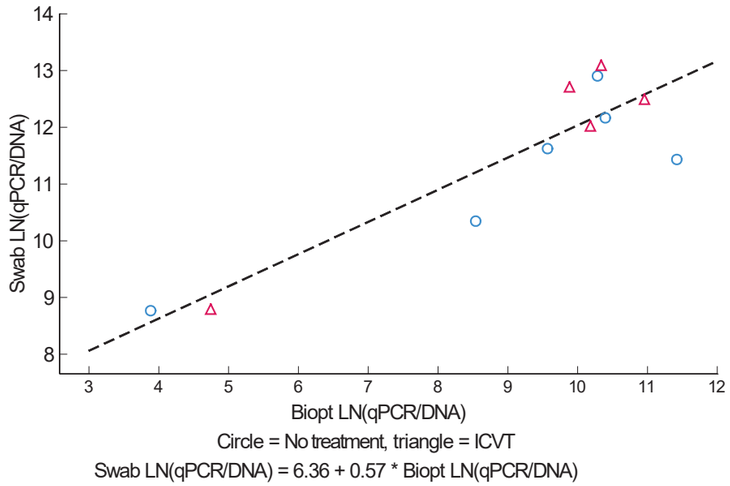

Figure 4. Linear regression model Swab versus Biopsy

CONCLUSIONS

- Safe for administration to humans
- Trend towards wart size reduction after 7 days of treatment, indicating pharmacological activity
- HPV viral load by swab valuable new biomarker
- A phase II, randomized, double-blind, trial with 80 patients will be conducted with longer treatment and follow-up period

References
[1] Hartley C, Hartley M, Pardoe I, Knight A: Ionic Contra-Viral Therapy (ICVT); a new approach to the treatment of DNA virus infections. Arch Virol 151:2495-2501 (2006).
[2] de Koning MN et al.: Evaluation of a novel broad-spectrum PCR-multiplex genotyping assay for identification of cutaneous wart-associated human papillomavirus types. J Clin Microbiol 48:1706-1711 (2010).

Centre for Human Drug Research | Zernikedreef 8 | 2333 CL Leiden | The Netherlands
Tel +31 71 52 46 400 | info@chdr.nl | www.chdr.nl