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Early and Visible Improvements after Application of K101 in the Appearance of Nails Discoloured and Deformed by Onychomycosis

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ABSTRACT

Onychomycosis is a fungal infection of the nails of the fingers and toes and is difficult to cure. A previous 24*-week, placebo-controlled study demonstrated that a solution containing propylene glycol, urea and lactic acid* (*K*101) *was well-tolerated and effective in the treatment of onychomycosis. Patients who received K*101 *judged that their condition had improved from Week* 2 *of treatment onwards. The aim of the current study was to further evaluate and document early visible effects on nail appearance after application of topical K*101 *in an 8-week baseline-controlled study in* 75 *patients. Patients graded the appearance of their nail compared with baseline using a four-point scale. Compared with baseline,* 91.8% (67/73; 95% *confidence interval* (*CI*): 83.0%, 96.9%) *of the patients experienced at least some improvement in their target nail after 8 weeks of treatment. At Week* 2, *the proportion showing some improvement was* 76.7% (56/73; 95% *CI*: 65.4%, 85.8%) *with this number increasing to* 87.7% (64/73; 95% *CI*: 77.9%, 94.2%) *at Week* 4. *Proportions of patients reporting less thickened, less discoloured, less brittle and softer nails increased over the course of the study. No safety issues were identified. In conclusion, K*101 *provided early visible improvements in nails affected by onychomycosis.*

Keywords*: *K*101, *Onychomycosis, Early Effects, Topical

1. Introduction

Onychomycosis is a fungal infection that affects the nails of the hand and foot. Infection rates in Western adult populations range from 2% to 14%, although onychomycosis may affect up to 50% of people over 70 years of age [1]. Prevalence of onychomycosis is also higher in the immuno-compromised, children with Down's syndrome and patients with diseases that affect the peripheral circulation, such as diabetes mellitus [2,3]. Onychomycosis is often associated with pain and discomfort coupled with a significant negative impact on emotional health and social image [4,5].

Onychomycosis can be treated pharmacologically with both systemic and topical agents [6]. Systemic antifungal drugs such as terbinafine and itraconazole are effective treatments; although their use must be balanced against the risk of unpleasant side-effects that include gastrointestinal disorders, skin rashes and headache [5,7]. Serious side-effects occur in less than 1% of patients, but these can include fatal liver toxicity [8]. Topical agents are usually formulated as lacquers that adhere to the nail plate and include antifungal drugs such as amorolfine, tioconazole and ciclopirox 8% [5,7]. Topical application allows targeted delivery to infected areas, minimising the risk of secondary effects related to systemic exposure.

K101, a topical treatment for onychomycosis, is a combination of propylene glycol, urea and lactic acid. The concept of using propylene glycol solutions of urea and lactic acid to treat onychomycosis was investigated in a study of 23 patients who applied a test solution twice daily for 2 - 6 months. The solution was effective in 21 of the 23 patients treated [9]. The efficacy of K101 was confirmed in a placebo-controlled study that documented the efficacy and tolerability of K101 versus placebo in 493 patients with onychomycosis. A greater number of patients who received K101 experienced mycological cure after 26 weeks of treatment (27% versus 10%) [10]. Also, almost half the patients who received K101 con-

patients were male (63.5%) and Caucasian (97.3%). Three patients were discontinued from the study: one due to protocol non-compliance and two due to non-attendance at follow-up visits. All patients had abnormal finger and/or toenails and 22 (29.7%) had abnormal skin on hands and feet as a result of fungal infection. Overall, mean (standard deviation) adherence was 99.45 (2.3) % (full analysis set).

3.2. Efficacy Results

The proportion of patients experiencing at least some improvement of the target nail at 8 weeks, compared with baseline, was 91.8% (67/73 patients; 95% CI; 83.0, 96.9) (**Table 1**. full analysis set). After 2 weeks of treatment, 76.7% (56/73) of patients experienced at least some improvement of the target nail; this proportion increased to 87.7% (64/73) after 4 weeks. Similar results were obtained for the per protocol data set. During the treatment period, the number (%) of patients reporting clear/very good improvement of the target nail increased from nine (12.4%) at Week 2 to 38 (52.0%) at Week 8 (**Table 2**).

Over the 8 weeks of the study, increasing proportions of patients reported that, compared with baseline, their target nails were less thickened (from 32.9% at Week 2 to 75.3% at Week 8), less discoloured (from 60.3% to 67.1%), less brittle (from 15.1% to 45.2%) and softened (from 35.6% to 71.2%) (**Table 3**). Visible improvements in the condition of the target nails from baseline to Week 8 are presented in **Figure 1** for a patient with infection of moderate baseline intensity and in **Figure 2** for a patient with infection of severe baseline intensity. In the course of treatment, visible signs of fungal infection regressed

Table 1. Improvement in target nail (defined as a score ≥ 2 on the Global Assessment Scale).

Time	Full analysis set (*N* = 73)		Per protocol set (*N* = 71)	
	n (%)	95% CI	*n* (%)	95% CI
Week 2	56 (76.7)	65.4, 85.8	55 (77.5)	66.0, 86.5
Week 4	64 (87.7)	77.9, 94.2	63 (88.7)	79.0, 95.0
Week 8	67 (91.8)	83.0, 96.9	66 (93.0)	84.3, 97.7

CI: confidence interval

Table 2. Patient experience of target nail appearance compared with baseline (full analysis set; *N* = 73)

	Week 2	Week 4	Week 8
	n (%)	*n* (%)	*n* (%)
No improvement	17 (23.3)	9 (12.3)	6 (8.2)
Some improvement	47 (64.4)	41 (56.2)	29 (39.7)
Clear improvement	8 (11.0)	21 (28.8)	29 (39.7)
Very good improvement	1 (1.4)	2 (2.7)	9 (12.3)

Table 3. Patient assessment of individual nail attributes (full analysis set; *N* = 73).

	Week 2		Week 4		Week 8	
	n (%)	95% CI	*n* (%)	95% CI	*n* (%)	95% CI
Less thickened	24 (32.9)	(22.3, 44.9)	44 (60.3)	(48.1, 71.5)	55 (75.3)	(63.9, 84.7)
Less discoloured	44 (60.3)	(48.1, 71.5)	52 (71.2)	(59.4, 81.2)	49 (67.1)	(55.1, 77.7)
Less brittle	11 (15.1)	(7.8, 25.4)	25 (34.2)	(23.5, 46.3)	33 (45.2)	(33.5, 57.3)
Softened	26 (35.6)	(24.7, 47.7)	41 (56.2)	(44.1, 67.8)	52 (71.2)	(59.4, 81.2)

CI: confidence interval.

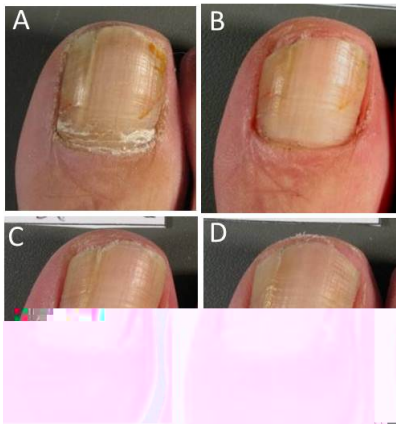

Figure 1. Photographic sequence showing target nail appearance at baseline (Panel A), at Week 2 (Panel B), Week 4 (Panel C) and Week 8 (Panel D) for a patient with onychomycosis of moderate intensity at baseline.

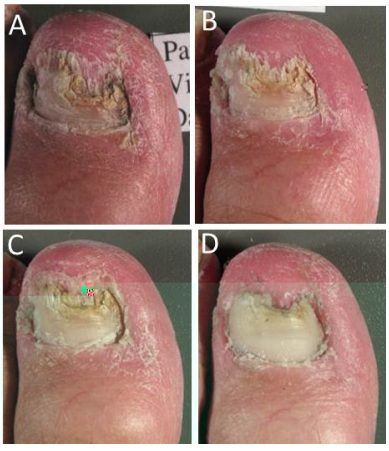

Figure 2. Photographic sequence showing target nail appearance at baseline (Panel A), at Week 2 (Panel B), Week 4 (Panel C) and Week 8 (Panel D) for a patient with onychomycosis of severe intensity at baseline.

and in general, a more uniform and smooth appearance was observed throughout the nail.

3.3. Safety and Tolerability

Eight patients (10.8%) experienced nine adverse event episodes; none of these was judged to be related to K101 by the Investigator. Seven of the events were considered to be mild and two were moderate in intensity. The most frequently reported adverse event was rhinorrhoea (*n* = 4).

4. Discussion

This 8-week, open-label study was designed to evaluate the early clinical effects of treatment with K101 in patients with onychomycosis. Efficacy was assessed in terms of improvement from baseline in nail appearance. Standardised photographic techniques were used to doaois 8-wsepl appea 60.(76(ug]TJ7)6(d%ve)9(h)5(d)-2(e)6h 1(ed)4nai)4(l)5(u)5provemb

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