Patients and Methods

A summary is provided in Figure 1.

An open-label single-arm 8-week postmarketing clinical investigation of K101-03 in patients with onychomycosis or nail psoriasis was conducted at 8 sites in Italy in 2016. K101-03 is a nonsterile viscous solution containing propylene glycol, urea, lactic acid, glycerol, sodium hydroxide, and disodium EDTA.

The clinical investigation plan (dated February 16, 2016) was approved, in writing, by the independent ethics committees for the different study sites between April 14, 2016, and June 28, 2016, before the first patient was enrolled at the respective sites. The study was conducted in accordance with the Declaration of Helsinki, ICH E6 Good Clinical Practice, ISO 14155:2011, MEDDEV guidelines, and Italian regulations.

Male and female subjects who fulfilled the following inclusion criteria were invited to participate in the study: (i) age ≥18 years, (ii) psoriatic nail dystrophy or 25–75% of a big toenail or thumbnail affected by onychomycosis (confirmed by KOH microscopy), and (iii) willingness and ability to provide signed written informed consent. The following exclusion criteria were applied: (i) proximal subungual onychomycosis, (ii) psoriatic nail dystrophy with involvement of the nail matrix, (iii) other nonmycotic/nonpsoriatic conditions known to cause an abnormal nail appearance, (iv) topical treatment of the nail with an antifungal medication or systemic use of an antifungal treatment in the previous month, (v) topical therapy for nail psoriasis in the previous month, (vi) initiation or alteration of systemic therapy for psoriasis in the previous month, (vii) initiation or alteration of systemic therapy for psoriasis with infliximab in the previous 6 weeks or with ustekinumab in the previous 3 months, (viii) participation in another clinical study of an investigational drug or device during the previous 4 weeks, and (ix) known allergy to any of the ingredients in the study treatment.

Patients were assessed for eligibility at an initial screening visit, during which they underwent

a physical examination of their hands and feet. Demographics, medical history, and prior and concomitant medications were recorded. Patients judged eligible to participate in the study were invited to attend a second visit (baseline visit) a maximum of 2 weeks later. At this visit, patient eligibility was confirmed, and a "target" nail (disease-affected big toenail or thumbnail) was selected. Each patient was given a 10-mL tube of K101-03 and was shown how to use it. Patients were instructed to apply K101-03 to all of their affected nails once daily just before bedtime for 8 weeks.

The patients attended further visits after 1, 2, 4, and 8 weeks of K101-03 treatment. At each visit, treatment compliance was assessed with the question "On average, how many days per week have you applied the investigational device since the last visit?" Patients were asked to rate the appearance of the target nail compared to baseline on a 4-point global assessment scale: 1 = no improvement, 2 = some improvement, 3 = clear improvement, and 4 = very good improvement. They were also asked whether, compared to baseline, the target nail had become (i) less thickened, (ii) less discolored, (iii) less brittle, and (iv) softer (yes/no/cannot determine). Images of target nails were captured by standardized photography at the baseline visit and at the visits after 1, 2, 4, and 8 weeks of K101-03 treatment.

The primary endpoint was the proportion of patients who reported at least some improvement in the target nail (a score of ≥ 2 on the global assessment scale) after 8 weeks of K101-03 treatment. The secondary endpoints included the proportions of patients who reported (i) at least some improvement in the target nail after 1, 2, and 4 weeks of treatment and (ii) improvements in thickening, discoloration, brittleness, and softness after 1, 2, 4, and 8 weeks of treatment. Other secondary endpoints were percentage treatment compliance and the occurrence of AEs between the first application of K101-03 and the end of the 8-week treatment period. AEs were recorded at each study visit and were classified according to severity, seriousness, and relationship to K101-03.

The safety set comprises all patients who used K101-03 at least once; patients who also

assessed the target nail at least once after baseline using the global assessment scale are included in the full analysis set. The per-protocol set comprises patients with (i) ≥80% treatment compliance during the 8-week study period, (ii) no major protocol deviations, and (iii) data for the primary endpoint. The primary efficacy analysis is based on the full analysis set. Missing values for the global assessment scale were imputed by the last observation carried forward method.

Statistical analyses were performed using SAS®. Patient age and treatment compliance are presented as the mean, standard deviation, median, and range. Categorical data are presented as the frequency (number) and percentage. Two-sided 95% confidence intervals were calculated based on the normal approximation to the binomial distribution. No adjustments were made for multiple comparisons or for possible differences according to study site.