Introduction

Distal subungual onychomycosis (DSO) is a fungal infection that results in thickening, discoloration and splitting of the fingernail plate, and lifting of the nail from the nail bed. The prevalence of DSO in Western adult populations is 2-14% (1) and incidence increases with age (2). Difficult to treat, DSO can significantly affect a patient's self esteem. The difficulty in treating DSO results from the deep-seated nature of the infection within the nail unit (nail plate, nail bed and surrounding tissue) and the inability of drugs to penetrate all sites effectively.

Although they are the most effective treatment for DSO, only 20-50% of patients respond to oral systemic drug therapy which can trigger adverse drug reactions and drug interactions.

MOB015B is a topical treatment for DSO that contains 10% terbinafine, a well known and highly effective antifungal agent. In vitro, it has been demonstrated that MOB015B can effectively penetrate the nail tissue and deliver terbinafine at sufficient efficacious concentrations into the nail and through the nail (3: data on file, Moberg Pharma).

We report here the clinical outcome data with MOB015B in a well designed, Phase IIa pilot study in patients with DSO. We also describe for the first time results from biopsies of nail and nail bed tissue to determine drug concentration from patients undergoing treatment for DSO.

Objectives

To evaluate the efficacy and safety of topical MOB015B in adults with DSO.

Methods

Study design: An open, single centre Phase IIa pilot study of 48 weeks of MOB015B topical treatment in adults ≥18 years with DSO. Diagnosis of DSO was confirmed by fungal culture positive for dermatophytes on a target great toenail with 25-75% nail involvement, and >2 mm of unaffected proximal nail. The study comprised a screening visit, baseline visit, five treatment period visits (4, 12, 24, 36 and 48 weeks) and one post treatment follow up visit/wash out period at 60 weeks. A control was not used as the primary efficacy variable was an objectively assessed parameter.

Treatment: MOB015B, in the form of a moderately viscous solution was applied once daily to affected nails at bedtime for 48 weeks.

Analysis: The primary analysis of the study was the proportion of patients with mycological cure defined as negative fungal culture and direct microscopy, at 60 weeks in the target nail. Secondary analyses included number of patients with negative fungal culture, negative direct potassium hydroxide (KOH) microscopy, and physician's global evaluation score [GES] ≥ 4 or 5; patient's subjective score; and terbinafine concentration in the nail and nail bed plasma.

Punch biopsies: A treated non target nail was carefully cleaned with alcohol and following local anaesthesia, a nail sample was obtained using a 4 mm punch biopsy. Following this, a 3 mm punch biopsy was introduced into the hole and a tissue biopsy was obtained from the nail bed.

Results

Patients’ baseline characteristics. Twenty five patients received at least one application of MOB015B and 24 (96%) completed the trial. All patients were male and Caucasian. The inclusion criteria allowed for target nails with 25-75% affected nail area, but post hoc analysis of the target nail photographs at baseline revealed that 17 (68%) patients had more than 50% affected nail area at inclusion.

Discussions

Myecological cure of DSO was achieved by 13 (52%) patients and was higher than those previously shown for topical onychomycosis treatments which have typically ranged from 29 to 35% (4, 5). Recently published data for tavaborole and efinaconazole show mycological cure rates of 36-55% (6). However, these studies included target nails with a lower degree of disease involvement than in this study (the majority of our patients had >50% disease involvement). In the case of efinaconazole, the mean area of target nail involvement was 36% (7).

Excellent clinical improvement or cure of the target nail, in conjunction with mycological cure, was observed in 7 (28%) patients. Notably, all patients had negative cultures at the follow up visit, 12 weeks post treatment (60 weeks).

We are the first to describe results from punch biopsies performed on patients undergoing treatment for DSO. High terbinafine concentrations were detected in both the nail plate and the nail bed, indicating effective MOB015B penetration into the nail unit with several orders of magnitude over the minimum inhibitory concentration for dermatophytes (0.001-0.1 µg/g). Low concentrations of terbinafine were detected in plasma, which were ~1000x lower than following orally administered terbinafine (8).

As might be expected for a topical treatment, two patients experienced transient irritation of the skin around the treated nails. This could be due to excessive application of MOB015B and leakage onto perungual skin. These convincing Phase II data warrant further investigation in randomised, controlled Phase III studies.

Conclusions

Daily topical administration of MOB015B was an efficacious treatment for DSO leading to mycological cure in over half the patients. Clinically significant improvement of the target nail in conjunction with mycological cure was observed in a high proportion of patients.

High terbinafine concentrations in nail and nail bed tissue and low plasma concentrations were observed.

MOB015B was safe and well tolerated.

References