4. Kwa L, Silverberg JI. Financial burden of emergency department visits for atopic dermatitis in the United States. *J Am Acad Dermatol*. 2018;79(3):443-447.
5. Kwatra SG. Breaking the itch-scratch cycle in prurigo nodularis. *N Engl J Med*. 2020;382(8):757-758.

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Efinaconazole 10% topical solution for the treatment of onychomycosis in pediatric patients: Open-label phase 4 study

To the Editor: Onychomycosis is a chronic fungal nail infection affecting an estimated 0.35% to 5.5% of children worldwide,[1] although parents and health care practitioners are hesitant to use long-term systemic treatments in children.[2] Efinaconazole 10% topical solution is an azole antifungal approved by the US Food and Drug Administration to treat onychomycosis in patients 6 years of age and older.[3,4] We report here a phase 4, open-label, multicenter study (NCT02812771) of efinaconazole in patients 6 to 16 years old with distal lateral subungual onychomycosis.

Efinaconazole was administered once daily for 48 weeks, with 4-week posttreatment follow-up at week 52. Participants had culture-positive mild to severe onychomycosis affecting 20% or more of at least 1 great toenail. The study was approved by institutional review boards and was conducted according to international scientific/ethical standards. All participants and/or legal guardians provided informed consent. The primary study objective was evaluation of tolerability and pharmacokinetics (PK).

Of 62 enrolled participants, 12 (19.4%) discontinued the study (withdrawal by parent/guardian, n = 6; lost to follow-up, n = 5; participant request, n = 1). For those who received the study drug (n = 60; safety population), the mean age was 13.4 years, 66.7% were male, and 88.3% were White. None of the treatment-emergent adverse events (TEAEs) led to study discontinuation (Table I). The only treatment-related TEAE was ingrown nail. No safety signals or trends associated with local skin reactions were observed. Adverse event findings and TEAE rates from this study were similar to those from two 52-week, phase 3 pivotal studies of efinaconazole 10% in adults.[3]

The PK population included 17 participants (12-16 years) with moderate to severe onychomycosis affecting 50% or more of each great toenail and onychomycosis in at least 4 additional toenails. The mean age was 14.1 years, 64.7% of patients were male, and 100% were White. In 15 participants with evaluable PK data at week 4, the concentration-time profile for efinaconazole was relatively stable during the 24-hour dosing interval. Systemic exposure to efinaconazole was low, with a mean area under the concentration-time curve (AUC_{0-24}) of 11.4 ng*h/mL and maximum plasma concentration (C_{max}) of 0.549 ng/mL. The median time to C_{max} was 12 hours. These results are comparable to those previously reported in adults (AUC_{0-24}, 12.15 ng*h/mL; C_{max}, 0.67 ng/mL).[4]

Beyond the favorable safety results and expected PK profile, this study showed that a substantial proportion of participants had positive treatment responses to efinaconazole (Fig 1). Rates for complete cure (40.0%) and mycologic cure (65.0%) were considerably higher in this pediatric study than those observed previously in two 1-year adult studies (complete cure: 15.2%-17.8%; mycologic cure: 53.4%-55.2%).[3,4] Higher cure rates in children may be due to faster nail growth, shorter nail length, and/or shorter duration of infection (potentially

Table I. Treatment-emergent adverse event summary in pediatric participants treated with efinaconazole (safety population)

TEAEs	Efinaconazole 10% topical solution (n = 60)
Number of TEAEs	99
Participants with ≥1 TEAE, n (%)	38 (63.3)
Participants with ≥1 treatment-emergent SAE, n (%)	1 (1.7)*
TEAEs by maximum severity, n (%)	
Mild	31 (51.7)
Moderate	7 (11.7)
Severe	0
Most common TEAEs (≥5% in safety population), n (%)	
Nasopharyngitis	18 (30.0)
Headache	6 (10.0)
Influenza	5 (8.3)
Tinea pedis†	4 (6.7)
Contusion	4 (6.7)
Nail injury	4 (6.7)
Ingrown nail	4 (6.7)
Food poisoning	3 (5.0)
Treatment-related TEAE, n (%)	
Ingrown nail	2 (3.3)‡

SAE, Serious adverse event; *TEAE,* treatment-emergent adverse event.
*The SAE of pneumonia was deemed unrelated to treatment; the moderate event resolved with hospitalization and did not require a change in study drug application.
†At screening or baseline, tinea pedis was not exclusionary (severe moccasin tinea pedis was exclusionary); a total of 8 participants (13.3%) had tinea pedis at baseline.
‡Eight total events in 2 participants.

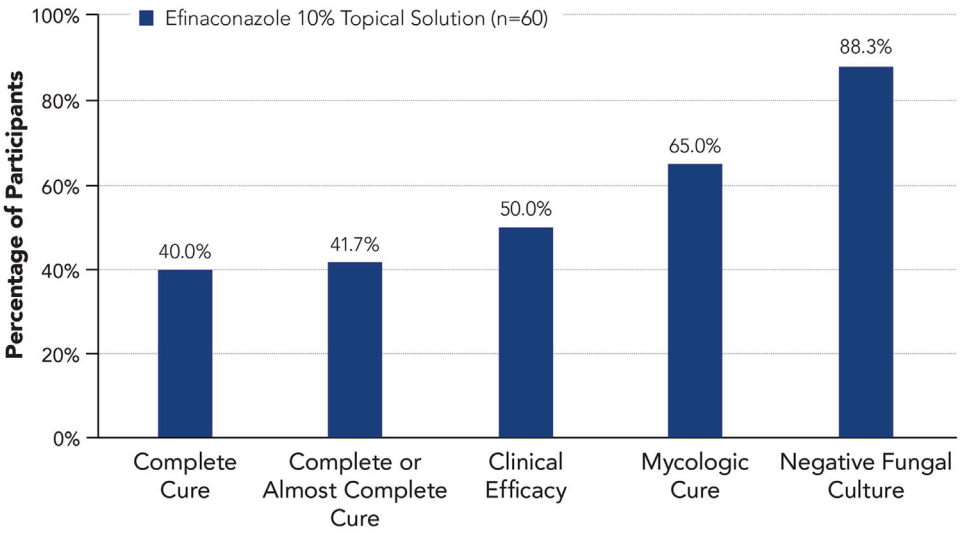

Fig 1. Onychomycosis efficacy after treatment with efinaconazole in pediatric participants (safety population, last observation carried forward). Data are shown for week 52 (4 weeks posttreatment). All assessments were based on the target great toenail sample. Mycologic cure was defined as negative potassium hydroxide examination findings and negative fungal culture results. Complete cure was defined as 0% clinical involvement of the target toenail and mycologic cure. Complete or almost complete cure was defined as 5% or less great toenail involvement and mycologic cure. Clinical efficacy was defined as affected target great toenail area of less than 10%.

reducing the risk of nail bed damage) versus adults. Additionally, complete and complete/almost complete cure rates at week 52 in this study (40.0% and 41.7%, respectively) were considerably higher than the 8.5% and 14.9% rates reported in a comparable phase 4, 1-year, open-label study of tavaborole 5% topical solution in patients 6 to 16 years old.[5]

Although this study may have been limited by the open-label design and lack of long-term follow-up, results indicate that efinaconazole 10% topical solution may be an appropriate treatment option in children and adolescents with mild to severe onychomycosis.

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REFERENCES

1. Gupta AK, Mays RR, Versteeg SG, et al. Onychomycosis in children: safety and efficacy of antifungal agents. *Pediatr Dermatol*. 2018;35(5):552-559.
2. Eichenfield LF, Friedlander SF. Pediatric onychomycosis: the emerging role of topical therapy. *J Drugs Dermatol*. 2017;16(2):105-109.
3. Elewski BE, Rich P, Pollak R, et al. Efinaconazole 10% solution in the treatment of toenail onychomycosis: two phase III multicenter, randomized, double-blind studies. *J Am Acad Dermatol*. 2013;68(4):600-608.
4. *JUBLIA (Efinaconazole) Topical Solution, 10% [package insert]*. Bridgewater, NJ: Ortho Dermatologics; 2016.
5. Rich P, Spellman M, Purohit V, et al. Tavaborole 5% topical solution for the treatment of toenail onychomycosis in pediatric patients: results from a phase 4 open-label study. *J Drugs Dermatol*. 2019;18(2):190-195.

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Variable clinical course of lichen planus following hepatitis C cure with direct-acting antivirals: A case series and literature review

To the Editor: Lichen planus (LP) is sometimes associated with hepatitis C virus (HCV).[1] No large studies have examined LP outcomes after HCV treatment with direct-acting antivirals (DAAs). Case reports and series chiefly describe oral LP (OLP) in Japan, where OLP has high prevalence and is strongly associated with HCV[2]; generalizability to other populations is unclear. Prior reports are also limited by reporting bias, describing primarily extreme outcomes (complete resolution or incident disease). To overcome these deficiencies, we performed a systematic electronic record search to identify patients with LP and DAA-treated HCV at 2 major medical centers in the United States and describe the clinical course of their LP after HCV cure.

We searched for patients with International Classification of Diseases, Ninth Revision and 10th Revision, codes for both LP and HCV at the University of California—San Francisco (UCSF), a tertiary referral academic medical center, and Zuckerberg San Francisco General Hospital (ZSFGH), an urban safety-net hospital affiliated with UCSF, and then manually reviewed cases to identify patients with successful DAA treatment of HCV, confirmed LP diagnosis, and adequate clinical description of LP outcome. We also systematically reviewed the literature for reported cases. This study was approved by the UCSF institutional review board. Methods and inclusion/exclusion criteria are available in the Supplemental Materials[3,4] (available via Mendeley at https://dx.doi.org/10.17632/wvyydpdwhp.2).

A literature search identified 6 case reports and 2 case series describing 16 patients with LP and DAA-cured HCV (Table I). Our series documents 6 additional patients (Table II). We analyzed LP distribution, LP outcome after DAA treatment of HCV (resolution, improvement, or exacerbation), and DAA received.

Of the 6 patients identified at UCSF/ZSFG, 3 (50%) had resolved LP after HCV cure, and 3 (50%) experienced persistent or worsened disease. No patients presented with purely oral LP.

Aggregate data of 22 patients from UCSF/ZSFGH and the literature review showed resolved/improved disease in 18 patients (81.8%) (resolved in 11 [50%]; improved in 7 [31.8%]) and persistent or worsened disease in 4 patients (18.1%). Of improved or resolved cases, 12 (66.7%) had oral-only disease. Cases of pure OLP were more likely to resolve ($\chi^2[1] = 5.02$; $P < .025$). Excluding 12 Japanese patients with pure OLP, the remaining 10 aggregate cases described 5 (50%) patients with improved or resolved disease and 5 (50%) with persistent relapsing/remitting or worsened disease.

Limitations of this study include the following: 1) it was a retrospective chart review, limited by