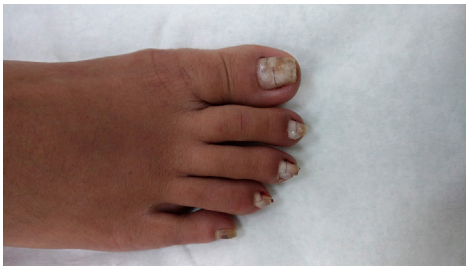

Fig 1. A patient with severe ingrown toenails. The patient received nail brace treatment for both sides of the big toenails and both sides of 3 lesser toenails.

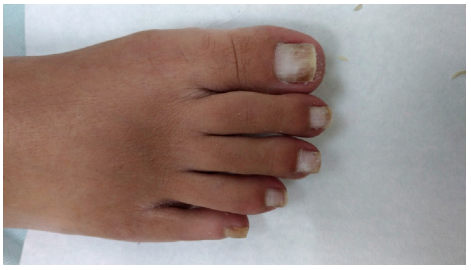

Fig 2. Ingrown toenails after treatment. The shapes of the ingrown toenails were restored after 6 months of nail brace treatment.

to 1 side of the nail rim, and the pad is glued onto the nail. The nail brace exerts a bending force via the restoring torque of the wire, facilitating correction of deformed nails.

We retrospectively collected the treatment data on patients with ingrown toenails of lesser toes who were treated at the Dermatology Clinic of Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan, between June 1, 2017, and May 31, 2018. This study was approved by the joint institutional review board of Taipei Medical University.

A total of 10 patients with 19 ingrown toenails (11 second toes, 4 third toes, and 4 fourth toes) and 28 affected sides (10 unilaterally and 9 bilaterally affected toes) were recruited. Of these 10 patients, 2 were men and 8 were women, and their mean age was 50.1 plus or minus 15.3 years (range, 27-80 years). All affected sides achieved at least 90% improvement based on the Physician's Global Assessment (Figs 1 and 2). The mean treatment duration and follow-up period (after nail brace removal) were 122.5 plus or minus 73.3 days (range, 30-259 days) and 174.5 plus or minus 100.8 days (range, 33-427 days), respectively. The treatment duration for unilaterally affected toes was much shorter than that for bilaterally affected toes (68.6 days vs 182.3 days). Bilaterally affected toes required a longer treatment duration because they were treated first on the 1 side and then on the other side because of limited space on the nail plates. No recurrence was noted during the entire follow-up period.

Compared with conventional 2-sided nail braces, the wire length of 1-sided nail braces can be more easily adjusted and the braces require less space on the nail plates, which is particularly useful for treating ingrown nails of lesser toes. In conclusion, this novel 1-sided nail brace was easily operated and showed good efficacy along with a low recurrence rate for treating ingrown toenails of lesser toes.

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Patients left behind: Rare dermatologic conditions miss the orphan drug development boom

To the Editor: Orphan drugs are those indicated for the treatment of uncommon conditions and are granted 7 years of exclusivity by the US Food and Drug Administration. As a result of this designation, there has been a considerable increase in rare disease research, pharmaceutical development, and market expenditures[1]; however, we hypothesize that rare dermatologic diseases have been relatively neglected.

We investigated the extent of clinical research for rare dermatologic diseases. First, we needed to create a list of these diseases because one does not exist due to the lack of tracking by analysts and professional organizations, the presence of multiple synonyms and subtype classifications, and because many of these rare dermatologic diseases are syndromic and overlap with other organ systems. The National Institutes of Health designates ~7000 rare diseases (https://globalgenes.org/rarelist); however, a subdivided list is unavailable. Therefore, we used the list of 586 rare dermatologic diseases from the Genetic and Rare Diseases Information Center, although inclusion does not serve as official National Institutes of Health recognition. Next, we grouped subtypes and syndromic variations according to their primary disease (for example, Waardenburg syndromes 1, 2, 3, and 4 were grouped as Waardenburg syndromes) and removed synonyms, resulting in a list of 428 rare dermatologic diseases. We then queried https://clinicaltrials.gov to identify trials registered for each of these rare dermatologic diseases. To avoid including trials that were not skin-related, studies whose endpoints were for nondermatologic outcomes were excluded. Of the 428 rare dermatologic diseases, 41 diseases (10%) were undergoing a total of 255 active clinical trials; 104 of these trials (41%) were industry-funded. Only 21 (5%) of the rare dermatologic diseases had treatments undergoing phase 2 or 3 clinical trials, suggesting that few rare dermatologic diseases were in late-stage clinical development or likely of reaching regulatory approval.

Our findings are supported by recent reports. In 2018, a total of 328 dermatologic medications were in development; however, most were for common diseases, such as skin cancer, psoriasis, acne, infections, eczema, and wounds.[2] In 2016, there were 566 orphan drugs in development with only 46 (8%) for skin conditions, of which approximately half were for burns, skin infections, cutaneous T-cell lymphoma, or advanced melanoma.[3] Market research also reflects relatively lower investment in dermatology. In 2017, orphan drug sales totaled $125 billion, representing 16% of the $663 billion of all prescription drug sales, yet global dermatology drugs sales were $21.5 billion (3%).[4,5]

Our study had several limitations. We searched just 1 major clinical trial database. In addition, similar investigations within different specialties are necessary to compare other areas of rare disease investment and research before definitive conclusions are made.

Lack of industry investment in rare dermatologic diseases might be attributed to perceptions of lower economic potential, regulatory challenges, and a limited understanding of skin disease pathophysiologies to be able to establish clinical and surrogate endpoints, making study design and demonstration of efficacy challenging. Further awareness, funding, patient support programs, and research are necessary to understand rare dermatologic disease natural history and develop validated, disease-specific endpoints for measuring patient outcomes, so these patients are not left behind.

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