(Figure 1). Their HAP scores gradually increased, and the hypotrichosis in the patient with TRPS1 did not improve (Figure 2A). Hair shaft diameters were increased in every participant with LIPH pathogenic variants (Figure 2B and C). There were no serious adverse events, but some mild adverse events were reported (dry skin on the scalp, trichiasis, and mild hypotrichosis on the entire body).

Discussion | Lysoosphatidic acids bind the P2Y5 receptor in the hair follicle epithelium and activate hair growth. In ARWH due to LIPH pathogenic variants, loss-of-function variants in LIPH lead to a deficiency of lysoosphatidic acids and insufficient activation of P2Y5. The present prospective intervention study suggests that minoxidil could be associated with improvements in hypotrichosis in ARWH owing to LIPH pathogenic variants. There appears to be a binary response to minoxidil, with one group responding better than the other. The data on causative pathogenic variants suggest that it is unrelated to the LIPH pathogenic variants. Among the 8 patients with ARWH due to LIPH pathogenic variants, 5 patients were unrelated, and the other 3 were from 1 family. All 3 members of the family were in the group responding better. Thus, we cannot exclude the possibility that the family had an unknown genetic modifying factor affecting the efficacy of minoxidil. We need to know more about the follicular pathology to understand the pharmacologic response to minoxidil.

Additional Contributions: We thank the patients and/or the patients’ family members for granting permission to publish this information.


Enanthem in Patients With COVID-19 and Skin Rash
Recalcati1 recently reported skin manifestations in 18 patients in Italy with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, or coronavirus disease 2019 (COVID-19), describing “erythematous rash,” “widespread urticaria,” and “chickenpox-like vesicles.” Additional reports have described other rashes, including petechial and purpuric changes, transient livedo reticularis, and acro-ischemic lesions. Whether these manifestations are directly related to COVID-19 remains unclear, since both viral infections and adverse drug reactions are frequent causes of exanthems. An important clue to distinguish between both entities is the presence of enanthem (oral cavity lesions). However, owing to safety concerns, many patients with suspected or confirmed COVID-19 do not have their oral cavity examined. Herein we describe variants of enanthem in a series of patients with COVID-19.

Methods | We included 21 consecutive patients from a tertiary care hospital who had skin rash and COVID-19, confirmed by real-time reverse transcriptase–polymerase chain reaction from a nasopharyngeal swab, and who required dermatology consultation from March 30 to April 8, 2020. The oral cavities of patients presenting with skin rash were systematically examined. Enanthems were classified into 4 categories: petechial, macular, macular with petechiae, or erythematovesicular. This study was approved by the institutional review board of Ramon y Cajal University Hospital in Madrid. Accordingly, informed consent was obtained verbally from all patients before examination, and they have been deidentified through omission of individual age and sex.

Results | Of 21 patients with COVID-19 and skin rash, 6 patients (29%) had enanthem. The age range of these patients was between 40 and 69 years, and 4 of the 6 (66%) were women. The morphology of the skin rash was papulovesicular, purpuric periflexural, and erythema multiforme–like in 1, 2, and 3 patients, respectively. The clinical and histologic findings of the erythema multiforme–like enanthem have been reported.
elsewhere. No enanthem was observed in patients with urticarial or typical maculopapular rashes. The enanthem was macular in 1 patient, petechial in 2 patients, and macular with petechiae in 3 patients, and was located in the palate in all patients (Figure). No patient presented with an erythematovesicular enanthem. The mean (range) time between the onset of COVID-19 symptoms and the appearance of mucocutaneous lesions was 12.3 days (range, −2 to 24 days). Interestingly, this latency was shorter in patients with petechial enanthem compared with those with a macular lesion with petechiae appearance. Drug intake and laboratory findings were not associated with any enanthem type (Table).

**Discussion** | The etiological diagnosis of exanthems can be challenging for dermatologists. Some useful clues are the rash morphology, the associated symptoms, and the presence of enanthem. Pustular morphology and dusky lesions are suggestive of drug etiology, while petechial or vesicular pattern, involvement of buttocks or acral sites, and enanthem suggest an infectious etiology, especially viral. In a large series of patients with atypical exanthems, only 9% of patients with enanthem had a drug reaction, whereas 88% had an infectious etiology, most frequently viral. Enanthems may present with petechiae, macules, papules, or vesicles in the mouth. Erythematovesicular and petechial patterns were most commonly associated with viral infections, the latter being more frequent in adults. This is consistent with the present series, in which 5 patients (83%) had petechiae as a main component of the enanthem. Furthermore, the 2 patients with a pure petechial enanthem developed these lesions 2 days before and 2 days after the onset of COVID-19 symptoms, making association with the drug intake unlikely.

This work describes preliminary observations and is limited by the small number of cases and the absence of a control group. Despite the increasing reports of skin rashes in patients with COVID-19, establishing an etiological diagnosis is challenging. However, the presence of enanthem is a strong

---

**Table. Clinical and Laboratory Findings of 6 Patients With COVID-19 and Enanthem**

<table>
<thead>
<tr>
<th>Patient, No.</th>
<th>Age, y</th>
<th>Exanthem type</th>
<th>Enanthem type</th>
<th>Time latency, d</th>
<th>Drug intake</th>
<th>Platelet count</th>
<th>D-dimer level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40s</td>
<td>Purpuric</td>
<td>M</td>
<td>12</td>
<td>LP, H</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>2</td>
<td>60s</td>
<td>Papulovesicular</td>
<td>P</td>
<td>−2</td>
<td>LP, H, A</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>3</td>
<td>60s</td>
<td>EM-like</td>
<td>MP</td>
<td>19</td>
<td>LP, H, A</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>4</td>
<td>50s</td>
<td>EM-like</td>
<td>MP</td>
<td>24</td>
<td>LP, H, A, T, C</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>5</td>
<td>40s</td>
<td>Purpuric</td>
<td>P</td>
<td>2</td>
<td>LP, H, A, T, C</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>6</td>
<td>60s</td>
<td>EM-like</td>
<td>MP</td>
<td>19</td>
<td>LP, H, A</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Abbreviations: A, azithromycin; C, corticosteroids; EM, erythema multiforme; H, hydroxychloroquine; LP, lopinavir/ritonavir; M, macular; MP, macular with petechiae; P, petechial; T, tocilizumab.

* Time latency is defined as days from the onset of coronavirus disease 2019 (COVID-19) symptoms to the appearance of mucocutaneous lesions. According to our center reference values, platelet count <140 × 10^3/μL was considered low, D-dimer level >0.5 μg/mL was considered high.
clue that suggests a viral etiology rather than a drug reaction, especially when a petechial pattern is observed.

Juan Jimenez-Cauhe, MD
Daniel Ortega-Quijano, MD
Dario de Perosanz-Lobo, MD
Patricia Burgos-Blasco, MD
Sergio Vaño-Galván, MD, PhD
Montse Fernandez-Guarino, MD, PhD
Diego Fernandez-Nieto, MD

Author Affiliations: Dermatology Department, Hospital Universitario Ramon y Cajal, IRYCS, Madrid, Spain.

Accepted for Publication: May 19, 2020.

Corresponding Author: Juan Jimenez-Cauhe, MD, Dermatology Department, Hospital Universitario Ramon y Cajal, Carretera Colmenar Viejo km 9/100, 28034 Madrid, Spain (jjimenezc92@gmail.com).

Published Online: July 15, 2020. doi:10.1001/jamadermatol.2020.2550

Author Contributions: Dr Jimenez-Cauhe had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Jimenez-Cauhe, Ortega-Quijano, de Perosanz-Lobo, Vaño-Galván, Fernández-Guarino.

Acquisition, analysis, or interpretation of data: Jimenez-Cauhe, Burgos-Blasco, Vaño-Galván, Fernández-Nieto.

Drafting of the manuscript: Jimenez-Cauhe, Ortega-Quijano, de Perosanz-Lobo, Fernández-Nieto.

Critical revision of the manuscript for important intellectual content: de Perosanz-Lobo, Burgos-Blasco, Vaño-Galván, Fernández-Guarino, Fernández-Nieto.


Administrative, technical, or material support: de Perosanz-Lobo, Burgos-Blasco, Vaño-Galván, Fernández-Guarino.


Conflict of Interest Disclosures: No reported.

Additional Contributions: We thank the pictured patient for granting permission to publish this information.


Trends in List and Net Prices of Self-administered Systemic Psoriasis Therapies Manufactured by US-Based Pharmaceutical Companies

Systemic psoriasis therapies are among the costliest drugs prescribed by dermatologists, and list prices of many of these drugs have increased over time.1 However, list price alone gives an incomplete picture of true treatment costs, as pharmaceutical companies provide discounts to payers (rebates) and other offsets, such as copay assistance, which affect the net price of these drugs. We describe 2009 to 2019 trends in list and net prices for self-administered psoriasis therapies manufactured by companies publicly traded in the United States.

Methods | We obtained 2007 to 2019 list and net price data from the investment firm SSR Health for self-administered psoriasis therapies available in the United States by January 1, 2019 (Table).2 This study was not subject to institutional review board review because no human data were used.

SSR Health estimates net prices for branded drugs manufactured by publicly traded companies using company-reported sales and number of units sold each quarter across the United States. Net prices account for all manufacturer discounts, including rebates to payers, coupon cards, 340B discounts (discounted prices to organizations caring for low-income and vulnerable patients), and any other concession accounted for in the reporting of sales. The robustness of SSR Health data in estimating net prices for prescription drugs has been demonstrated in peer-reviewed research.3 Net pricing for tildrakizumab was not available as it is manufactured by a nonpublicly traded manufacturer.

For each drug and year, we calculated average list (wholesale acquisition) and net costs of psoriasis treatment for the initial year of therapy for an 80-kg patient based on US Food and Drug Administration-approved recommended dosing. We adjusted prices by inflation using the consumer price index. All prices are shown adjusted to the value of the US dollar in 2009.

Results | For all drugs studied, list prices increased substantially over time, with the greatest increase observed for tumor necrosis factor inhibitors, which increased by approximately 200% from 2009 to 2019 (annual mean change for etanercept, 12%; adalimumab, 12%; and certolizumab, 10%). Although net prices steadily increased until 2016, they began to decrease for ustekinumab in 2016, secukinumab and guselkumab in 2017, and brodalumab, adalimumab, and certolizumab in 2018 (Figure).

As of 2019, there was a large (30%-59%) and widening gap between list and net prices because of increasing discounts. The list price was highest for certolizumab ($94379), followed by the interleukin (IL)-17A inhibitors secukinumab ($77883) and ixekizumab ($75848), and lowest for the oral phosphodiesterase-4 inhibitor apremilast ($34 543); net price was highest for the 3 tumor necrosis factor inhibitors (certolizumab, $48 193; etanercept, $43 910; and adalimumab, $39 751) and lowest for the IL-17-receptor inhibitor brodalumab ($17 692) (Table).

Discussion | We identified substantial price increases from 2009 to 2019 for self-administered psoriasis therapies. Even after accounting for inflation and discounts, the net price of some therapies more than doubled, highlighting the financial burden on payers and patients for these therapies.