PN is often refractory to topical corticosteroids and calcineurin inhibitors, and many patients require systemic treatment. There are few studies to guide further therapy. In 1995, Berth-Jones et al observed that PN might respond to cyclosporine,[2] which was also observed in another study.[3] Treatment with cyclosporine has been associated with adverse events, including creatinine elevation, hypertension, gastric upset, muscle pains, angioedema, gingival hyperplasia, and neuropathy.[4] Siepmann et al published a report on a series of 14 patients treated with cyclosporine showing a significant response in 13 patients, 7 of whom experienced the aforementioned side effects.[5]

We present a retrospective chart review of PN patients seen in the academic medical center–based practices of 2 physicians (Drs Orlow and Cohen) from 2005-2015 that illustrates the rapid improvement cyclosporine can afford patients with PN.

We obtained institutional review board approval (S14-01982). A retrospective chart review was performed for patients with a diagnosis of PN or lichen simplex seen at the academic medical center–based practices of 2 attending physicians (Drs Orlow and Cohen) from 2005-2015. Patients treated with cyclosporine were included, and charts were reviewed to exclude those without clear diagnoses or treated with other therapies. Data regarding patient age, length of and dosing of cyclosporine treatment, side effects attributed to cyclosporine, whether or not remission was achieved, and time to remission were collected.

In all, 76 patient charts were reviewed; 8 patients qualified for inclusion, 5 of which were female (Table I). The average age was 57 years. With the pediatric patient excluded, the average age of included adults was 64 years.

Patients were counseled regarding possible side effects and the need for laboratory and blood pressure monitoring. The average dose of cyclosporine was 3.1 mg/kg, and the average time until improvement was ~3 weeks. Patients reported fewer new lesions, decreased pruritus, and resolution of existing lesions.

Four patients had complications attributed to cyclosporine, which included migraines, nausea, hypertension, dizziness, blurry vision, keratoacanthoma, hypercholesterolemia, and folliculitis. None had an elevation in creatinine. Six patients achieved remission, 1 was lost to follow-up, and the final patient reported significant improvement but not remission. No patients reported recurrence upon treatment discontinuation.

Limitations include the study's small sample size, retrospective nature, and the patient population being from 1 academic medical center. PN is difficult to treat, with many patients refractory to first-line topical or phototherapy. We suggest cyclosporine as a first-line systemic therapy for severe, recalcitrant disease, with the plan to transition to topical or phototherapy over the course of 3-6 months. Cyclosporine would not be recommended for PN patients with impaired renal function. Given the aforementioned side effect profile, patients must be appropriately selected and willing to undergo regular monitoring. In our experience, PN can rapidly improve with cyclosporine treatment.

Lauren E. Wiznia, MD, Shields W. Callahan, MD, David E. Cohen, MD, MPH, and Seth J. Orlow, MD, PhD

From The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, New York

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Correspondence to: Seth J. Orlow, MD, PhD, The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, 240 East 38th St, 11th Floor, New York, NY 10016

E-mail: seth.orlow@nyumc.org

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Efficacy and rapid activity of omalizumab retreatment in chronic spontaneous urticaria

To the Editor: The efficacy and safety of omalizumab for the adjunctive treatment of chronic spontaneous urticaria (CSU) is well documented.[1-4] However, many patients experience disease flare-ups at variable intervals after their last omalizumab dose, and

Table I. Patient demographics and clinical characteristics at baseline

Characteristics	Patients, N = 31
Age, y, mean ± SD	48.1 ± 13.4
Female, n (%)	22 (71)
Duration of CSU, mo, mean ± SD	17.1 ± 10.2
History of angioedema, n (%)	21 (67.7)
CSU medication history, n (%)	
H_1 antihistamines at the licensed dosage	31 (100)
H_1 antihistamines at high dosage	11 (35.5)
Leukotriene receptor antagonists	2 (6.5)
Systemic corticosteroids	12 (38.7)
Cyclosporine	1 (3.2)
Total IgE level, kU_A/L	
Mean ± SD	131.8 ± 106.6
Median (range)	100 (5-391.2)
Positive thyroid autoantibody test result, n (%)	6 (25.0)
Positive ASST, n (%)	14 (45.2)
In clinic UAS, mean ± SD*	4.8 ± 0.9
UAS7, mean ± SD†	23.5 ± 5.7
Weekly ISS, mean ± SD†	13 ± 4.3
Weekly hive score, mean ± SD†	10.4 ± 4.2
Presence of angioedema at baseline, n (%)†	4 (12.9)

ASST, Autologous serum skin test; *CSU*, chronic spontaneous urticaria; *ISS*, Itch Severity Score; *SD*, standard deviation; *UAS*, Urticaria Activity Score; *UAS7*, Urticaria Activity Score summed over 7 consecutive days.

*Defined as the highest value taken at the day-14 visit, day-7 visit, and day-1 visit.

†Based on data collected from a patient's daily diary during the 7 days before the first treatment date.

appropriate management of these patients remains unclear.

Our retrospective study included 31 patients with refractory CSU (Table I) who had achieved a complete response to a first course of treatment with omalizumab (ie, ≥90% improvement in symptoms)[2] and then received omalizumab retreatment after disease relapse. A third treatment course was administered to 16 patients who had a complete response to the second round of omalizumab. All patients were treated during September 2015-July 2017. The study protocol was approved by the ethics committee of Bari University Hospital, and informed consent was obtained from all participants.

On the basis of local labeling information,[5] subcutaneous omalizumab (300 mg) was given every 4 weeks for 24 weeks (first treatment course) and was administered again (second and third treatment course) at least 8 weeks after the end of the previous course, to patients with a Urticaria Activity Score 7 score similar to that in the pretreatment stage.

After the first treatment course, all patients obtained a complete response and experienced a relapse of disease with an intensity of symptoms similar to the pretreatment period within 5-20 weeks after their last omalizumab injection (Fig 1).

The rate of complete response after the second course of omalizumab was 93.5% (29/31). Of these 29 patients, 16 patients (55%) had increased symptom scores, which returned to baseline values within 5-16 weeks after their last omalizumab injection of the second treatment (Fig 1). All 16 of these patients started on a new 24-month course of omalizumab treatment; 15 of 16 patients (93.8%) achieved complete remission of symptoms. At the last follow-up, ≥8 weeks after the administration of the last dose of omalizumab, 11 of the 15 patients (68.7%) had experienced a relapse or CSU. The mean time to achieve complete therapeutic response was 4.9 weeks during the first treatment course, 3.8 weeks during the second course, and 1.8 weeks during the third, with a statistically significant difference between time to complete response with the first and third course ($P = .018$). All 3 omalizumab treatment courses were well tolerated.

Because >90% of patients experienced disease relapse after discontinuation of omalizumab,[3] and considering omalizumab is an expensive drug, it is rather important to know whether and when these patients can interrupt treatment with this medication or whether they have to be retreated in case of recurrence of symptoms after discontinuation of therapy.

Despite a relatively small sample size, to the best of our knowledge, this is the first real-life study reporting high safety and efficacy of omalizumab with 2 subsequent retreatments of relapsed patients, indicating those who achieve a complete response to a first treatment course with omalizumab might have a complete response to subsequent treatment cycles. In 2 previous studies[3,4] only 1 retreatment course was given. In our study, a third treatment course was given to some patients, and we found that the response to omalizumab was faster as the number of retreatments increased.

Eustachio Nettis, MD,[a] Elisabetta Di Leo, MD, PhD,[b] Caterina Foti, MD, PhD,[c] Luca Cegolon, MD, MSc, PhD,[d] and Angelo Vacca, MD, PhD[a]

From the Department of Biomedical Sciences and Human Oncology Unit of Internal Medicine G. Baccelli Aldo Moro University of Bari Medical School, Policlinico, Bari, Italy[a]; Section of Allergy and Clinical Immunology, Unit of Internal Medicine—F. Miulli Hospital, Acquaviva delle Fonti, Bari, Italy[b]; Department of Biomedical Science

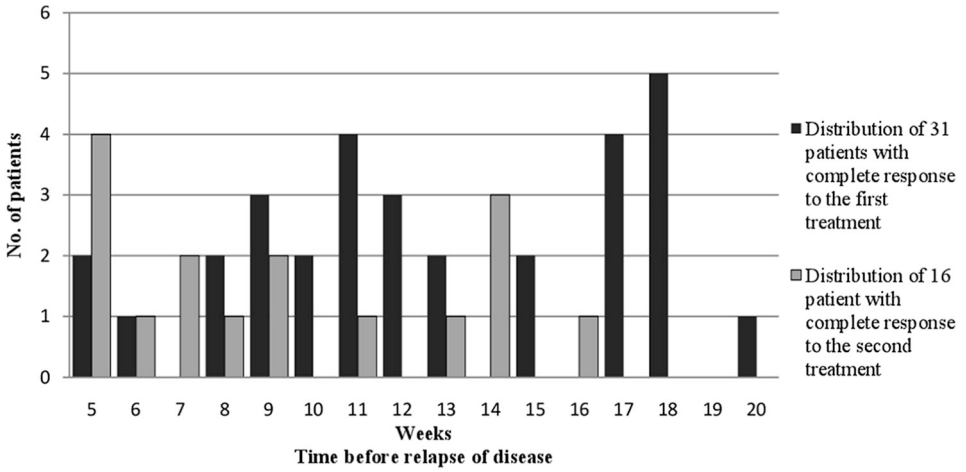

Fig 1. Distribution of occurrences of relapse of urticaria patients after first and second treatment with omalizumab. Patients who experienced relapse had an intensity of symptoms similar to the pretreatment period.

and Human Oncology, Dermatological Clinic, University of Bari, Bari, Italy[c]; and Scientific Directorate, Instituto di Ricovero e Cura a Carattere Scientifico Burlo Garofolo, Trieste, Italy[d]

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Correspondence to: Elisabetta Di Leo, MD, PhD, Section of Allergy and Clinical Immunology, Unit of Internal Medicine, F. Miulli Hospital, Strada Provinciale per Santeramo Km 4.100, Acquaviva delle Fonti, Bari, Italy

E-mail: elisabettadileo71@libero.it

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Occurrence of vismodegib-induced cramps (muscular spasms) in the treatment of basal cell carcinoma: A prospective study in 30 patients

To the Editor: Vismodegib is a hedgehog pathway inhibitor approved for treating locally advanced and metastatic basal cell carcinoma. Cramps (muscular spasms) are among vismodegib's major adverse effects (40%-80% of patients).[1,2] In the pivotal study of Sekulic et al, 72.1% of treatment discontinuation occured within the first year of follow-up.[2] A recent study shows that stretching muscles before going to sleep reduces both the frequency and severity of nighttime cramps.[3] Our objective was to characterize cramps and discuss an appropriate treatment.

We assessed the occurrence and evolution of cramps in all patients treated with vismodegib at Lille University Hospital (Supplementary Appendix; available at http://www.jaad.org), in a prospective study conducted during September 2014-November 2015. Patients completed a questionnaire that was developed in collaboration with a specialist in neuromuscular diseases to determine the characteristics of patient muscle spasms. We evaluated the benefits of hydration and muscle stretching performed by physiotherapists or by patients themselves following guidelines from a recent study.[3]

Thirty patients were included in this study; 72% experienced muscle spasms, with 14% categorized as grade III according to Common Terminology Criteria