Omalizumab in patients with severe and refractory solar urticaria: A phase II multicentric study

To the Editor: Omalizumab is an anti-IgE antibody, approved for the treatment of chronic spontaneous urticaria (CSU).[1] Efficacy has also been reported in isolated cases of physical urticaria, including solar urticaria, with inconsistent results, potentially because of the use of different treatment schedules.[2-4]

We aimed to demonstrate the efficacy of the registered schedule of omalizumab in CSU in patients with solar urticaria by conducting a multicenter phase II study, approved by our institutional review board (Comité de Protection des Personnes Est-II no. 13/422; EudraCT no. 2013-004910-16; ClinicalTrials.gov NCT02262130).

Ten patients with solar urticaria refractory to antihistamines and a very large effect on quality of life (Dermatology Life Quality Index score >10) were recruited from 7 dermatology departments in France. A 300-mg subcutaneous dose of omalizumab was administered at intervals of 4 weeks, for a total of 8 weeks (3 administrations in total). Phototesting was performed at baseline and at weeks 12 and 20, as previously described.[5] The primary objective was to evaluate the efficacy of omalizumab by measuring at week 12 the proportion of patients without solar urticaria triggered by an ultraviolet dose greater than 10-fold the baseline minimal urticarial dose (Table I). The other efficacy end points included the proportion of patients showing a small effect on quality of life (Dermatology Life Quality Index score < 6), achieving 50% improvement from baseline in solar urticaria severity as measured on a visual analog scale, and being wheal-free (urticarial activity score over 7 days = 0) at week 12 and at week 20 to test for maintenance of efficacy.

Two patients reached the primary end point, corresponding to a response rate of 20% (95% confidence interval 2.52-55.6; $P = .2639$) (Table I). Overall, 40%, 40%, and 30% of patients achieved the secondary end points of Dermatology Life Quality Index score < 6, 50% improvement from baseline in solar urticaria severity as measured on a visual analog scale, and urticarial activity score over 7 days = 0, respectively (Table II). At week 12, 5 patients (50%) achieved at least 1 primary or secondary efficacy end point. At week 20, no patient showed a substantial increase in minimal urticarial dose or achieved a 50% improvement in baseline solar urticaria severity as measured on a visual analog scale (Tables I and II). During the 20-week study, no significant adverse events were observed.

Table I. Evolution of the minimal urticarial dose in patients receiving omalizumab for solar urticaria

Patient no.	Minimal urticarial dose		
	Baseline (action spectrum)	Wk 12	Wk 20
1	4 J/cm^2 (UVA)	5 J/cm^2	1 J/cm^2
2	3 J/cm^2 (UVA)	7 J/cm^2	3 J/cm^2
3	0.3 J/cm^2 (UVA)	0.5 J/cm^2	0.2 J/cm^2
	10 mJ/cm^2 (UVB)	10 mJ/cm^2	10 mJ/cm^2
4	2 J/cm^2 (UVA)	2 J/cm^2	2 J/cm^2
	250 mJ/cm^2 (polyC)	<250 mJ/cm^2	<250 mJ/cm^2
5	0.072 J/cm^2 (UVA)	0.144 J/cm^2	0.017 J/cm^2
	14 mJ/cm^2 (UVB)	417 mJ/cm^2	1.8 mJ/cm^2
6	0.5 J/cm^2 (UVA)	0.5 J/cm^2	ND
	61 mJ/cm^2 (polyC)	107 mJ/cm^2	
7	4 J/cm^2 (UVA)	>40 J/cm^2	0.5 J/cm^2
8	1 J/cm^2 (UVA)	1 J/cm^2	<1 J/cm^2
	60 mJ/cm^2 (UVB)	60 mJ/cm^2	1 mJ/cm^2
9	1 J/cm^2 (UVA)	3 J/cm^2	1.5 J/cm^2
10	0.6 J/cm^2 (UVA)	>6 J/cm^2	5 J/cm^2
	80 mJ/cm^2 (UVB)	>240 mJ/cm^2	40 mJ/cm^2

polyC, Polychromatic solar spectrum including 95% UVA and 5% UVB; *ND*, not determined; *UV*, ultraviolet radiation.

Table II. Proportion of patients achieving efficacy end points at weeks 12 and 20

Significant increase in MUD		DLQI < 6		VAS50		UAS7 = 0	
Wk 12	Wk 20	Wk 12	Wk 20	Wk 12	Wk 20	Wk 12	Wk 20
20%	0%	40%	11%	40%	0%	30%	11%

DLQI, Dermatology Life Quality Index; *MUD*, minimal urticarial dose; *UAS7*, urticarial activity score over 7 d; *VAS50*, 50% improvement from baseline in solar urticaria severity as measured on a visual analog scale.

The major strengths of the study are its prospective design and the use of a robust and measurable criterion (minimal urticarial dose); the major weaknesses are the lack of control placebo arm and the small number of patients included, owing to the rarity of the disease. Considering the primary efficacy criterion, our study failed to statistically demonstrate the efficacy of omalizumab, 300 mg every 4 weeks, for solar urticaria. Nevertheless, when considering patient-based outcomes and with the limited tools used to measure efficacy, the response rate could appear close to the mean proportion of patients with CSU achieving urticarial activity score over 7 days of 6 or less with the same dose of omalizumab (56.7%, pooled results).[1] Of note, similar to what is observed in

CSU, the improvement in solar urticaria was rapidly lost when omalizumab was stopped.

In conclusion, our data suggest that omalizumab may be a potentially interesting treatment for a certain subset of patients with severe and refractory solar urticaria.

We are indebted to Claire Thénié and Philippe Pinton from Novartis Pharma for their help in supporting this study; and to Dr Isabelle Madelaine (Pharmacie, Hôpital Saint-Louis, Paris), Dr Marie-Blanche Valnet-Rabier (Pharmacologie, Centre Hospitalier Régional Universitaire [CHRU] Besançon), Mrs Morgane Heberlé, Mrs Kristina Mouyabi, and Mr Béranger Martin (Délégation à la Recherche Clinique et à l'Innovation, CHRU Besançon) for their constant help and support in conducting the study.

François Aubin, MD, PhD,[a] Martine Avenel-Audran, MD,[b] Michel Jeanmougin, MD,[c] Henri Adamski, MD,[d] Jean-Louis Peyron, MD,[e] Marie-Claude Marguery, MD,[f] Fabienne Léonard, MD,[g] Marc Puyraveau, MSc,[b] and Manuelle Viguier, MD, PhD,[c] on behalf of the Société Française de Photodermatologie

Université de Franche Comté, EA3181, SFR4234, and Centre Hospitalier Universitaire, Service de Dermatologie, Besançon[a]; Service de Dermatologie, Centre Hospitalier Universitaire, Angers[b]; Université Paris Diderot, Assistance Publique Hôpitaux de Paris, Hôpital Saint-Louis, Service de Dermatologie, Paris[c]; Service de Dermatologie, Centre Hospitalier Universitaire Pontchaillou, Rennes[d]; Service de Dermatologie, Hôpital Saint-Eloi, Montpellier[e]; Hôpital Larrey, Service de Dermatologie, Centre Hospitalier Universitaire, Toulouse[f]; Service de Dermatologie, Centre Hospitalier Universitaire, Reims[g]; and Centre de Méthodologie Clinique, Centre Hospitalier Universitaire, Besançon,[b] France

Supported by a grant from Novartis Pharma. Omalizumab was provided free of charge by Novartis Pharma. The funders had no role in the study design or performance, manuscript writing, or decision to publish.

Disclosure: Dr Viguier received consulting fees, travel support, and payment for lectures from Novartis Pharma. Drs Aubin, Avenel-Audran, Adamski, and Marguery received travel support from Novartis Pharma. Drs Jeanmougin, Peyron, and Léonard, and Mr Puyraveau have no conflicts of interest to declare.

Presented as a poster in the European Academy of Dermatology and Venereology Meeting in Copenhagen, Denmark, October 7-11, 2015.

Correspondence to: Manuelle Viguier, MD, PhD, Service de dermatologie, Hôpital Saint-Louis, 1 avenue Claude Vellefaux 75475 Paris Cedex 10, France.

E-mail: manuelle.viguier@aphp.fr

REFERENCES

1. McCormark PL. Omalizumab: a review of its use in patients with chronic spontaneous urticaria. *Drugs*. 2014;74:1693-1699.
2. Guzelbey O, Ardelean E, Magerl M, Zuberbier T, Maurer M, Metz M. Successful treatment of solar urticaria with anti-immunoglobulin E therapy. *Allergy*. 2008;63:1563-1565.
3. Waibel KH, Reese DA, Hamilton RG, Devillez RL. Partial improvement of solar urticaria after omalizumab. *J Allergy Clin Immunol*. 2010;125:490-491.
4. Duchini G, Bäumler W, Bircher AJ, Scherer K. Failure of omalizumab (Xolair®) in the treatment of a case of solar urticaria caused by ultraviolet A and visible light. *Photodermatol Photoimmunol Photomed*. 2011;27:336-337.
5. Aubin F, Porcher R, Jeanmougin M, et al. Severe and refractory solar urticaria treated with intravenous immunoglobulins: a phase II multicenter study. *J Am Acad Dermatol*. 2014;71:948-953.

http://dx.doi.org/10.1016/j.jaad.2015.11.021

Persistence and failure rates of adalimumab monotherapy in biologic-naïve patients with psoriasis: A retrospective study

To the Editor: Pivotal controlled trials (CHAMPION, REVEAL)[1,2] have examined the efficacy of adalimumab therapy and contributed to its Food and Drug Administration approval for the treatment of severe psoriasis. It is important, however, to gather efficacy data in real-world settings to allow dermatologists to prescribe adalimumab with more confidence. The aim of this study was to determine the persistence rate, failure rate, and drug survival of monotherapy adalimumab under methods of common practice.

This retrospective chart review focused on patients with cutaneous psoriasis who presented to Kaiser Permanente Los Angeles Medical Center from 2008 to 2015 and did not have a change in insurance coverage. In all, 79 patients met inclusion criteria of at least 10% body surface area coverage, biologic-naïve status, and minimum 3-month adalimumab use. Thirteen patients had coexisting psoriatic arthritis, which increased the likelihood of adalimumab therapy. Failure was defined as the need to add a second therapy, either an oral medication (methotrexate, cyclosporine, acitretin) or phototherapy, or switch to a different oral or biologic agent (etanercept, infliximab, ustekinumab, or secukinumab). The date of failure was set as the start date of the new systemic agent or first phototherapy session.