

Evaluating patient responses to omalizumab in solar urticaria

To the Editor,

Solar urticaria (SU) is characterised by intense pruritus or burning, erythematous flare and whealing, usually beginning within 5–10 min of sun exposure, with considerable impact on quality of life (QoL).¹ Action spectra commonly involve UVA/visible light, and SU may occur year-round or seasonally.¹ First-line management involves photoprotection and H1 antihistamines, but these frequently fail to control. Second-line options of phototherapy, plasmapheresis, immunosuppressive agents and intravenous immunoglobulins may be unsuitable, unavailable or entail prolonged immunosuppression in a chronic disorder or risks through derivation from pooled human plasma. Omalizumab (Xolair®, Novartis), recombinant IgE monoclonal antibody licensed for chronic spontaneous urticaria (CSU), exhibits benefit in refractory SU in small series/case reports (Table 1a). Omalizumab binds free IgE, which downregulates FcεRI receptors on mast cells and basophils, decreasing degranulation and inflammatory mediator production.²

Benefit of omalizumab in SU has been assessed mainly through the impact on minimal urticarial dose (MUD) on phototesting, with no measure routinely used for scoring clinical activity (Table 1a). However, a validated clinical scoring system is available for assessing severity of CSU, that is the Urticaria Activity Score (UAS7),³ and a validated disease-specific QoL tool, that is the Chronic Urticaria Quality of Life (CU-Q2oL) questionnaire, has been developed⁴; both tools are recommended by the EAACI/GA²LEN/EDF/WAO urticaria guideline.⁵ Here, we report severe SU successfully treated with omalizumab on a recurrent annual basis, where detailed quantitation of photobiological outcomes was accompanied by use of adapted CSU clinical activity and QoL tools, and review the literature.

A 30-year-old man had eight-month history of pruritic, erythematous plaques on photo-exposed sites, with nausea and fatigue, occurring within 10 min of sun exposure and resolving within 1–2 h. He was taking no relevant medication, and his porphyrin and connective tissue disease screens were negative. Monochromator phototesting showed urticarial responses (Figure 1A) through 320–500 nm. Broadband UVA (BBUVA, 320–400 nm) and solar-simulated radiation (SSR, 320–400 nm; Figure 1B) also provoked immediate urticarial response. Management involved UV/visible radiation filtering sunscreens and high-dose oral H1 antihistamines. A course of narrowband UVB (NBUVB) was given, but not repeated in view of only moderate benefit, alongside development of a basal cell carcinoma. He virtually stopped all outdoor activities, and totally covered his skin, including wearing a balaclava.

Following three of a 6-month course of monthly omalizumab 300 mg subcutaneous injections, he improved greatly and participated in outdoor surfing and mountain climbing. His MUD on monochromator phototesting improved substantially, no urticaria

provoked except at 400 nm (Table 1b), and broadband provocation was negative (Figure 1C). This was mirrored by improvement in his modified UAS7 (Appendix 1; Figure 1D), dermatology life quality index (DLQI) and modified CU-Q2oL (Appendix 2; Figure 1E). One month post-treatment symptoms recurred, and MUD returned to pre-treatment levels. He has been successfully treated in two further years, demonstrated by clinical activity and QoL scores (Figure 1D,E), with relapse 4–6 weeks post-treatment cessation. While scores correlated with phototest findings, serum total IgE did not (pre-treatment 160–188 KU/L, post-treatment 657 KU/L).

A 48-year-old female presented with seven-year history of recurrent eruption February–November, only 2 min of sun exposure causing immediate pruritus and erythema of exposed sites, duration 1–several hours. Symptoms were provoked through window glass, and she reported severe impact on daily activities. She was taking no relevant medication, and her porphyrin and connective tissue disease screens were negative. Monochromator phototesting to UVB, UVA and visible radiation showed urticarial response to UVA at 330–370 nm (Table 1b). Immediate wheal and flare were also provoked by BBUVA and SSR. Photoprotective measures including sunscreen, and combination of high-dose H1 antihistamines, gave no benefit. NBUVB was attempted; even with 30 mg oral prednisolone cover, discontinuation was necessary due to burning erythema. Following a 6-month course of monthly 300 mg omalizumab subcutaneous injections, she could tolerate 20–30 min of sun exposure to body and 10 min to face, without wheal or flare. Repeat phototesting demonstrated raised MUD (Table 1b) with no urticarial response at 370 nm. Her pre- and post-treatment total IgE was 43.5 and 180 KU/L, respectively. A further course of omalizumab again produced clinical benefit, reflected in improved QoL scores (Figure 1F). She participated in outdoor activities and tolerated sun exposure on sunny holiday abroad, contrasting with previous experience. Her QoL indicators assessed during winter (off omalizumab) did not return to pre-treatment levels, as symptoms were seasonal.

Our experience demonstrates life-changing response of SU to omalizumab, which does not diminish on repeated annual courses. This is reflected both objectively by repeat phototesting and subjectively through QoL and clinical activity scores. In accordance with our findings, a recent systematic review of all chronic inducible urticaria subtypes supported omalizumab treatment for refractory SU.⁶ However, specific aspects may benefit from consideration when assessing and treating SU that do not apply in CSU, particularly through its (a) differences in symptomatology and (b) provocation by sunlight. In the sole phase II study of omalizumab in SU, the unmodified UAS7 (maximum 7-day score 42) and a visual analogue scale were used to assess clinical activity but outcome is evaluated by % patients reaching designated

TABLE 1 (a) Summary of case reports and case series of omalizumab treatment in solar urticaria. (b) Minimal Urticarial Doses (MUD, J/cm²) to monochromator phototesting^a

Report	Patients	Refractory to anti-histamine therapy?	Total IgE pre-treatment	Omalizumab dose	Pre-treatment MUD	Post-treatment MUD
(a)						
R1. Guzelbey O, Ardelean E, Magerl M et al. Allergy. 2008;63:1563-5.	52-year female	Yes	22 KU/L	150 mg every 4 weeks	1.4 J/cm ² BB UVA (Saalmann-Multitester SBC LT 400)	Retested at 4 weeks: >6 J/cm ² BB UVA ↑
R2. Waibel KH, Reese DA, Hamilton RG et al. J Allergy Clin Immunol. 2010;125:490-1.	16-year male	Yes	578 IU/mL (free IgE)	400 mg every 2 weeks	<5 J/cm ² BB UVA <20 mJ/cm ² BB UVB	<5J/cm ² NC 40 mJ/cm ² ↑
R3. Duchini G, Baumlér W, Bircher AJ et al. Photo-dermatol Photoimmunol Photomed.2011;27:336-7.	24-year male	Yes	77.1 KU/L	150 mg every 4 weeks	BB UVA 6.3J/cm ² and "10 min VL" (slide projector with a 415 nm edge filter)	Retested at 12 weeks: NC
R4. Metz M, Altrichter S, Ardelean E et al. Int Arch Allergy Immunol.2011; 154:177-80.	1. 29-year male 2. 55-year female	Yes	322 KU/L 22 KU/L	300 mg/month 150 mg/every 2 weeks	2.4 J/cm ² BB UVA 1.1 J/cm ² BB UVA	>6 J/cm ² ↑ >6 J/cm ² ↑
R5. Metz M, Ohanyan T, Church MK, Maurer M. J Dermatol Sci. 2014;73:57-62	Retrospective study of 51 CSU and inducible urticaria patients, including 4 SU patients	Yes	Median 110 (range: 5-1667) kU/L (median of 44 un-specified patients)	1. 150 mg every 4 weeks 2. 150 mg every 4 weeks, increased to 300 mg every 4 weeks 3. 150 mg every 4 weeks, increased to 300 mg every 4 weeks 4. Not stated	BB UVA and UVB (Saalmann-Multitester SBC LT 400). MUD not stated	1-3 Complete response ↑ 4. Partial response (50% or more reduction in provocation threshold or >50% improvement of symptoms)
R6. Metz M, Ohanyan T, Church MK et al. JAMA Dermatology. 2014;150:288-90.	Retrospective case series of 25 CSU and inducible urticaria patients, including 1 SU patient	Yes	NRep	Dose range of 150 to 600 mg SC every 2-4 weeks (dose for SU patient not specified).	Tested with BB UVA and UVB sources. MUD not stated.	Retested after at least 3 months of treatment: SU patient showed CR. ↑

(Continues)

TABLE 1 (Continued)

Report	Patients	Refractory to anti-histamine therapy?	Total IgE pre-treatment	Omalizumab dose	Pre-treatment MUD	Post-treatment MUD
R7. Aubin F, Avenel-Audran M, Jeannouguin M et al. JAAD. 2016;74:574-5.	n = 10	Yes	NRep	300 mg every 4 weeks for 8 weeks	1. UVA 4 J/cm ² 2. UVA 3 J/cm ² 3. UVA 0.3 J/cm ² , UVB 10 mJ/cm ² 4. UVA 2 J/cm ² , polyC 250 mJ/cm ² 5. UVA 0.072 J/cm ² , UVB 14 mJ/cm ² 6. UVA 0.5 J/cm ² , polyC 61 J/cm ² 7. UVA 4 J/cm ² 8. UVA 1 J/cm ² , UVB 60 mJ/cm ² 9. UVA 1 J/cm ² 10. UVA 0.6 J/cm ² , UVB 80 mJ/cm ² (Solar simulator, slide projector, other UV lamps)	Retesting at 12 weeks 1. UVA 5 J/cm ² ↑ 2. UVA 7 J/cm ² ↑ 3. UVA 0.5 J/cm ² ↑, UVB 10 mJ/cm ² NC 4. UVA 2 J/cm ² , polyC <250 mJ/cm ² 5. UVA 0.144 J/cm ² , UVB 417 mJ/cm ² ↑ 6. UVA 0.5 J/cm ² NC, polyC 107 J/cm ² ↑ 7. UVA >40 J/cm ² ↑ 8. UVA 1 J/cm ² , UVB 60 mJ/cm ² NC 9. UVA 3 J/cm ² ↑ 10. UVA >6 J/cm ² , UVB >240 mJ/cm ² ↑
R8. Arasi S, Crisafulli G, Caminiti L et al. Pediatr Allergy Immunol 2015;26:583-5.	16-year female	Yes	228 IU/mL	375 mg every 2 weeks for 6 months, 300 mg in 7th month, 150 mg in 8th and 9th months	BB UVB 1.2 mJ/cm ² No response to BB UVA >5 J/cm ²	Retesting did not provoke a response ↑
R9. Levi A, Tal Y, Dranitzki Z et al. Pediatr Allergy Immunol 2015;26:588-90.	6-year child	Yes	2004 IU/mL	75 mg, then dose increased to 300 mg 2 weekly, then monthly	VL 30 mJ/cm ²	No response at 10 months ↑
R10. Sivaramakrishnan M, Morton C, Wong T et al. Br J Dermatol. 2015;173:91	1. 41-year male 2. 44-year female 3. 34-year female	Yes	137 KU/L 797 KU/L 179 KU/L	150 mg every 4-6 weeks, then 6-8 weekly 300 mg every 4 weeks 150 mg monthly for 2 months, then 300 mg monthly for 3 months	UVA 365 nm to VL 600 nm UVA 335-400 nm UVB 305 nm, UVA to visible light 460 nm	Good control at 3.5 years ↑ No response on provocation at 4 months ↑ No response to treatment NC
R11. Muller S, Schempp CM, Jakob T. JEADV. 2016;30:524-5	64-year female	Yes	12.6 KU/L	150 mg every 4 weeks	BB UVA1 (340-400 nm) <10J/cm ²	No response to treatment. NC
R12. Balue-Pique C, Peiro PA. JEADV. 2016;30:704-6.	1. 58-year female 2. 43-year female 3. 49-year female	Yes	2874 IU/mL 1500 IU/mL 980 IU/mL	450 mg per month 300 mg/month 300 mg/month	Negative to BB UVB and UVA (Waldmann UV800 & UV181) Negative to BB UVB and UVA Negative to BB UVB and UVA	Asymptomatic in daily life. ↑
R13. Brüning JH, Ziemer M, Pemler S, Simon JC et al. J Dtsch Derm Ges. 2016;14:936-7.	51-year male	Yes	NRep	300 mg 4 weekly for 3 months, increased to 450 mg monthly. 16-month course	BB UVA 2.2 J/cm ² BB UVB 2 mJ/cm ²	UVA 35.8 J/cm ² ↑ Minor response UVB

(Continues)

TABLE 1 (Continued)

Report	Patients	Refractory to anti-histamine therapy?	Total IgE pre-treatment	Omalizumab dose	Pre-treatment MUD	Post-treatment MUD
R14. de Dios-Velazquez A, Gonzalez de Arriba M, Beteta-Gorriti V et al. Ann Allergy Asthma Immunol. 2016;116:260-2	41-year male	Yes	186 KU/L	300 mg 4 weekly for 8 months (ongoing)	BB UVA 1 J/cm ² BB UVB no response (Waldmann 7001K)	Complete resolution of symptoms ↑
R15. Moncourrier M, Assikar S, Matei I et al. Photodermatol Photoimmunol Photomed. 2016 Sep;32:314-316.	1. 49-year female 2. 49-year male 3. 16-year female 4. 79-year female	Yes	NRep	300 mg every 2 weeks for 3 months 300 mg every 4 weeks for 3 months 150 mg every 2 weeks for 3 months 300 mg every 4 weeks for 3 months	VL: 2 min, UVA: 3 J/cm ² VL: 5 min, UVA: 5.65 J/cm ² , UVB: 30 sec VL: 15 min VL: 5 min	1. VL: 5 min, UVA 20 J/cm ² ↑ 2. UVA >20 J/cm ² ↑ 3. VL: no reaction ↑ 4. VL: no reaction ↑
R16. Terrani I, Bircher AJ, Scherer Hofmeier K. Clin Exp Dermatol. 2016;41:890-2.	53-year male	Yes	NR	300 mg every 4 weeks, reducing to every 8 weeks over 16 months	VL: positive provocation MUD not stated	Retesting did not provoke a response ↑
R17. Ghazanfar MN, et al. Br J Dermatol. 2016;175:404-6	1 patient, details NR	NRep	NRep	Initial dose 150 mg every 2 weeks or 300 mg every 4 weeks (specific details not given)	NR	
R18. Kowalzik L, Thiel W, Biefeld C, Ziegler H, Eickenscheidt L. Hautarzt. 2017 · 68:492-6	50-year female	Yes	NRep	300 mg single dose	UVB <0.001 J/cm ² UVA 0.1 J/cm ² UVA1 5 J/cm ² UAS7 score 30	UVB 0.02 J/cm ² ↑ UVA 0.4 J/cm ² ↑ UVA1 5 J/cm ² NC UAS7 score 14 (weeks 2, 3)
R19. Combalia A, Fernández-Sartorio C, Aguilera P. Actas Dermosifiliogr. 2017;108:593-594.	21-year female	Yes	294 kU/L	300 mg monthly (ongoing)	UVA 7 J/cm ² DLQI score 21	Retesting did not provoke a response ↑ DLQI score 0 at 24 hrs post-treatment
R20. Rodriguez-Jiménez P, Chicharro P, Pérez-Plaza A, de Argila D. Actas Dermosifiliogr. 2017 Oct;108:e53-e55.	1. 53-year female 2. 65-year female 3. 50-year female	Yes	502 IU/mL 17.2 IU/mL 1382 IU/mL	300 mg monthly for 12 months 300 mg monthly for 6 months 150 mg every 2 weeks for 1.5 months, then 300 mg monthly for 4 months	Wheal after 30 min VL Wheal after 30 min fluorescent radiation UVB, 10 mJ/cm ² UVA <0.6 mJ/cm ² SS <10 mJ/cm ²	Negative provocation test ↑ Partial clinical response Improved Skindex 29 scores following treatment (23% improvement QoL) No clinical or objective response NC

(Continues)

TABLE 1 (Continued)

Wavelength (half-maximum bandwidth), nm	Dose range, J/cm ²	MUD pre-omalizumab	MUD on omalizumab	MUD off omalizumab
(b)				
Patient 1				
300 (5)	1.8-80 (mJ/cm ²)	NR	NR	NR
320 (10)	0.13-4	2.5	NR	NR
330 (10)	0.31-14	5	NR	5
350 (20)	0.63-40	3.5	NR	3.5
370 (20)	1.8-57	3.5	NR	3.5
400 (20)	0.22-113	0.9	113	1.8
500 (20)	1.6-50	6.3	NR	6.3
600(20)	1.6-50	NR	NR	NR
Patient 2				
300 (5)	1.8-80 (mJ/cm ²)	NR	NR	NR
320 (10)	0.13-4	NR	NR	1
330 (10)	0.31-14	1.3	3.5	0.63
350 (20)	0.63-40	0.9	7	0.31
370 (20)	1.8-57	20	NR	NR
400 (20)	0.22-113	NR	NR	NR
500 (20)	1.6-50	NR	NR	NR
600 (20)	1.6-50	NR	NR	NR

BB, broadband; MUD, lowest dose at which a wheal or flare occurred; NC, no change; NR, no response; NRep, not reported; polyC, polychromatic solar spectrum including 95% UVA and 5% UVB; SS, solar simulator, VL, visible light; ↑ = complete or positive response.

^aPatients were exposed to narrowband UV and visible radiation using a xenon arc lamp and monochromator (Newport Spectra-Physics Ltd, Didcot, UK), and the irradiated sites were assessed for wheal and flare response. Irradiance was measured using a calibrated thermopile (Medical Physics, Dryburn Hospital Durham UK), digital voltmeter (Medical Physics, Royal Liverpool University Hospitals, Liverpool, UK) or calibrated spectrometer (STS-UV, Ocean Optics, Dunedin, Florida, USA).

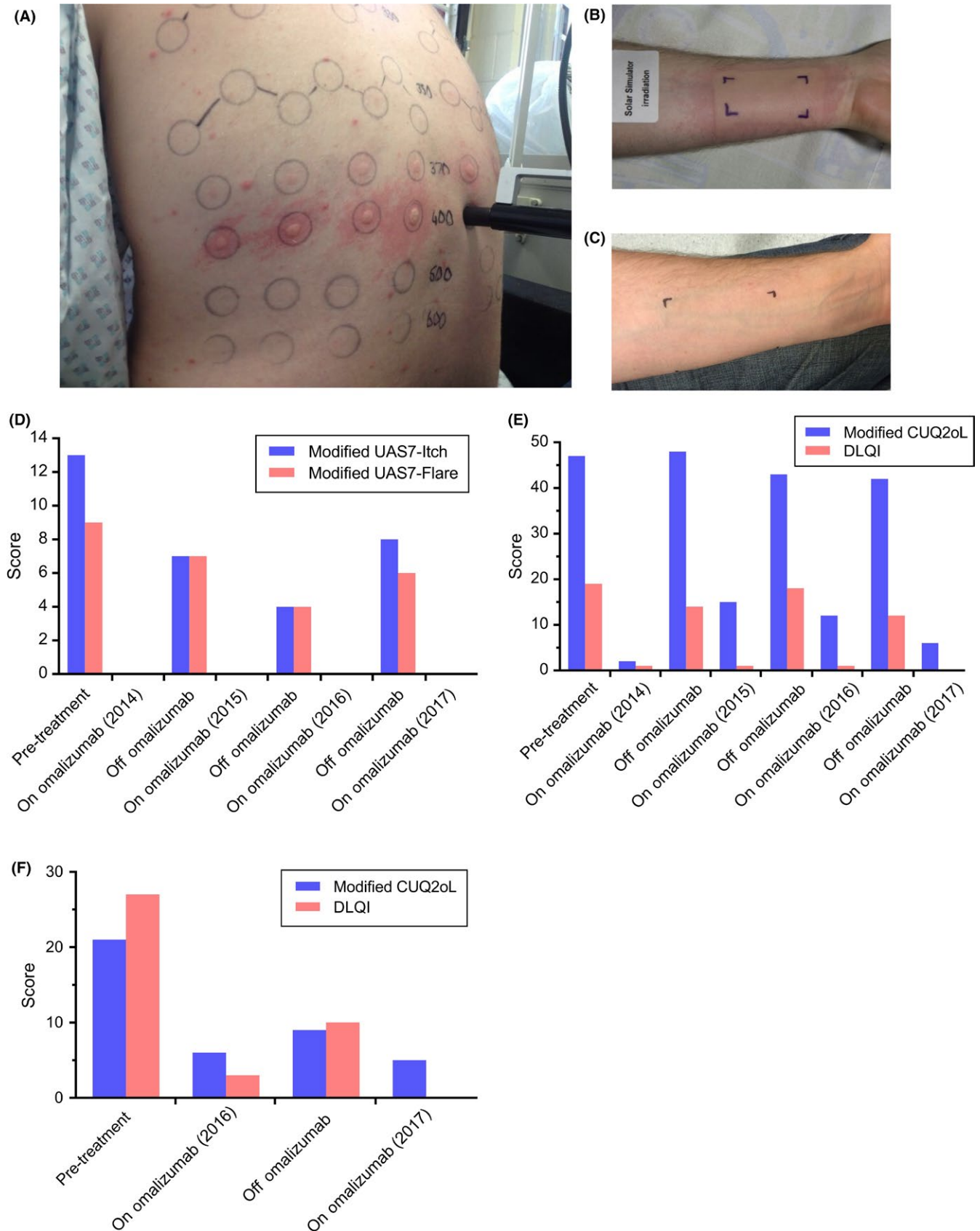


FIGURE 1 SU patients receiving omalizumab, showing clinical images of wheal and flare responses to monochromator phototesting. (A) positive photoprovocation response to solar simulated radiation pre-omalizumab (B) and negative on (C) omalizumab in patient 1, and scores for Modified Urticaria Activity (UAS7) for patient 1 (D) and Modified Chronic Urticaria Quality of Life (CU-Q2oL) and Dermatology Life Quality Index (DLQI) for patients 1 (E) and 2 (F)

targets, and individual scores are not presented⁷ (R7). In contrast, we adapted the UAS7 by including the extent of erythema (in addition to number of wheals/severity of pruritus) as this is usually a prominent feature in SU (Appendix 1). We also adapted the CU-Q2oL (23-item questionnaire, maximum score 115) by including erythema (additional to pruritus/wheel/angioedema); a free-text box also recorded systemic symptoms (eg, nausea and fatigue) (Appendix 2). The DLQI (10 questions, maximum score of 30), a validated measure in dermatology, not specifically adapted for urticaria or photosensitivity but employed in CSU trials,⁸ was used unchanged.

Case 1 in our report had a dramatic response to every omalizumab course, reflected by the modified UAS7 (score reduction to 0—both itch and flare), as well as by the modified CU-Q2oL and the DLQI (both showed pronounced reduction, the DLQI to 0). The scoring systems were not as useful in case 2 as case 1, because symptoms were absent during winter months (pre-omalizumab). This highlights the challenges of developing assessment tools for seasonal disorders, including the relevance of recording ambient radiation and personal sun exposure levels, and potentially the time to appearance of SU (shown although not utilised in Appendix 1), as well as objective phototesting, during clinical trials. The start and course length of omalizumab may also differ in SU from CSU, early springtime start appearing optimal and selected in our patients, to enhance patients' resistance before sunnier weather. Phototype could be influential, due to photoprotective effect of subsequent sun exposures, particularly in patients who tan easily.

Literature review reveals omalizumab benefits SU induced by UVB, UVA and visible radiation, with complete (28 cases) and partial (six cases) response reported (Table 1a, reports R1-10, R12-16, R18-20). Where a good or complete response was reported, this was usually evident within 4 weeks of commencing treatment. No effect was seen in seven cases, hinting at different underlying mechanism (Table 1a, reports R3, R7, R10, R11, R17, R20). Higher doses, that is omalizumab 300-450 mg monthly, may be more effective (R13) than 150 mg monthly (R3, R11). In the largest cohort (n = 10), a 20% response rate was reported to the primary end-point of no SU appearing with 10× baseline MUD⁷ (R7). However, repeat phototesting was performed 4 weeks postfinal dose. No relationship is evident between serum total IgE and clinical response (Table 1a), and it may be more relevant to assay free IgE.⁹ Information is limited but suggests efficacy may not relate to demonstration of circulating photoallergen (R3, R11, R13).

In conclusion, omalizumab is effective on a recurrent, annual basis for refractory SU and our exploration indicates responses to modified CSU assessment tools can reflect and complement objective phototesting outcomes. Optimised assessment measures could be used in future clinical trials in this challenging photodermatosis.¹

ACKNOWLEDGEMENT

This work was supported by the NIHR Manchester Biomedical Research Centre.

CONFLICT OF INTEREST

None declared.

ORCID

Lesley E. Rhodes  <http://orcid.org/0000-0002-9107-6654>

Liesel L. Griffin¹

Ann K. Haylett^{1,2}

Lesley E. Rhodes^{1,2} 

¹Centre for Dermatology, Salford Royal NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK

²Photobiology Unit, Centre for Dermatology Research, Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, School of Biological Sciences, The University of Manchester, Manchester, UK

Correspondence

Lesley E. Rhodes, Photobiology Unit, Centre for Dermatology Research, Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, School of Biological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Salford Royal NHS Foundation Trust, Manchester, UK.

Email: lesley.e.rhodes@manchester.ac.uk

All authors contributed equally to this work.

REFERENCES

- Haylett AK, Koumaki D, Rhodes LE. Solar urticaria in 145 patients: action spectra and impact on quality of life in adults and children. *Photodermatol Photoimmunol Photomed*. 2018;34:262-268.
- Chang TW, Chen C, Lin C-J, Metz M, Church MK, Maurer M. The potential pharmacologic mechanisms of omalizumab in patients with chronic spontaneous urticaria. *J Allergy Clin Immunol*. 2015;135(2):337-342.
- Mlynek A, Zalewska-Janowska A, Martus P, Staubach P, Zuberbier T, Maurer M. How to assess disease activity in patients with chronic urticaria? *Allergy*. 2008;63(6):777-780.
- Baiardini I, Pasquali M, Braido F, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). *Allergy*. 2005;60(8):1073-1078.
- Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. *Allergy*. 2014;69(7):868-887.
- Maurer M, Metz M, Brehler R, et al. Omalizumab in patients with chronic inducible urticaria: a systematic review. *J Allergy Clin Immunol*. 2018;141(2):638-649.
- Aubin F, Avenel-Audran M, Jeanmougin M, et al. Omalizumab in patients with severe and refractory solar urticaria: a phase II multicentric study. *J Am Acad Dermatol*. 2016;74(3):574-575.
- Maurer M, Rosen K, Hsieh HJ, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med*. 2013;368(10):924-935.
- Waibel KH, Reese DA, Hamilton RG, Devillez RL. Partial improvement of solar urticaria after omalizumab. *J Allergy Clin Immunol*. 2010;125(2):490-491.

APPENDIX 1

Urticaria Activity Score (UAS7) proforma—modified for Solar Urticaria^a

Please complete this score sheet every day.

	Pruritus (itching/burning sensation) 0 = none 1 = mild 2 = moderate 3 = severe	Number of hives 0 = none 1 = less than 20 2 = 20-50 3 = more than 50	Size of the largest hive (diameter)	Extent of the skin redness (flare) 0 = none 1 = mild 2 = moderate 3 = severe	Duration between sun exposure and appearance of rash (h/min)
Day 1					
Day 2					
Day 3					
Day 4					
Day 5					
Day 6					
Day 7					

^aAdaptations to the UAS7 for SU are shown in bold italics.

APPENDIX 2

Chronic Spontaneous Urticaria Quality of Life (CU-Q2oL) proforma—modified for Solar Urticaria^a

In the past 14 days, how much were you troubled by the following symptoms?

	Not at all (0)	A little (1)	Rather (2)	A lot (3)	V. much (4)
1	Itching/burning				
2	Wheals (hives)				
3	<i>Skin redness</i>				
4a	Swelling of your eyes				
4b	Swelling of your lips				
4c	<i>Other symptoms that you attribute to your solar urticaria (please specify)</i> 1..... 2..... 3..... 4.....				

Indicate how often you were limited by your hives (urticaria) in the past 14 days in the following areas of daily life

	Not at all (0)	A little (1)	Rather (2)	A lot (3)	V. much (4)
5	Work				
6	Physical activities				
7	Sleep				
8	Free time				
9	Social relationships				
10	Eating				

In the following questions, we would like to know more about the difficulties and problems that could be related to your hives (urticaria) (regarding the past 14 days)

	Never (0)	Rarely (1)	Sometimes (2)	Often (3)	V. often (4)
11	Do you have difficulties falling asleep?				
12	Do you wake up at night?				

(Continues)

APPENDIX 2 (Continued)

		Never (0)	Rarely (1)	Sometimes (2)	Often (3)	V. often (4)
13	Are you tired during the day, because you didn't sleep well at night?					
14	Do you have difficulties concentrating?					
15	Do you feel nervous?					
16	Do you feel miserable?					
17	Do you have to limit your food choices?					
18	Are you bothered by the symptoms of solar urticaria that appear on your body?					

In the following questions, we would like to know more about the difficulties and problems that could be related to your hives (urticaria) (regarding the past 14 days)

		Never (0)	Rarely (1)	Sometimes (2)	Often (3)	V. often (4)
19	Are you embarrassed to go to public places?					
20	Is it a problem for you to use cosmetics (eg, perfumes, creams, lotions, make up)?					
21	Do you have to limit your clothing choices?					
22	Are your sports activities limited because of your solar urticaria?					
23	Do you suffer side-effects from the medications you take for solar urticaria?					

^aAdaptations to the CU-Q2oL are shown in bold italics.