Title: A survey of the treatment and management of patients with severe chronic spontaneous urticaria: A UK DCTN Trainee Group Initiative

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None: B. Ho1, K. Heelan2, L. Solman3, R. Jones4, J. Dua5, J.R. Ingram, C. Flohr
Chronic spontaneous urticaria (CSU) is characterized by the recurrent appearance of wheals, angioedema or both, occurring at least twice weekly for longer than 6 weeks (1), often managed with antihistamines, but occasionally requiring other systemic agents in recalcitrant cases.

A cross-sectional survey was conducted by means of an internet-based survey tool (Typeform). Participating consultants with a specialist interest in urticaria were identified and invited through the specialist registers of the British Society of Allergy and Clinical Immunology (BSACI), the Improving Quality in Allergy Services (IQAS) Group and the British Association of Dermatologists (BAD).

The survey content was based on current CSU treatment guidelines from EAACI/GA2LEN/EDF/WAO (2) and the British Society for Allergy and Clinical Immunology (BSACI) (3). The EAACI/GA2LEN/EDF/WAO guidelines are a joint initiative of the Dermatology Section of the European Academy of Allergy and Clinical Immunology (EAACI), the EU-funded network of excellence, the Global Allergy and Asthma European Network (GA2LEN), the European Dermatology Forum (EDF), and the World Allergy Organization (WAO). To standardise responses, all participants were presented with a case of recalcitrant CSU (failed on maximum dose non-sedating antihistamines and montelukast), requiring alternative systemic treatment. Questions covered usage of systemic treatments, routine disease severity assessments, adherence to treatment guidelines and perceived barriers to prescribing.

Responses (table 1) were received from 19 UK consultants (completion rate 73%), 15 of whom had greater than 10 years experience in the treatment of chronic spontaneous urticaria. The majority were allergy (58%) and dermatology consultants
(37%) and 56% provide a dedicated urticaria service. 37% treat adult and paediatric patients, and the majority (79%) use other systemic medications than antihistamines and montelukast. Omalizumab and ciclosporin were the most commonly used first line agents (47% and 27% respectively) (figure 1). 84% use validated measures to assess disease severity, including the urticaria activity score (UAS-7, 63%), the Physician Global Assessment (63%), the Patient Global Assessment (44%) and the Dermatology Quality of Life Index (DLQI, 38%). 89% use guidelines to direct their management of chronic spontaneous urticaria, with 50% using the EAACI/GA2LEN/EDF/WAO guideline (2), compared to 31% primarily using the BSACI one (3). The main perceived barriers to prescribing systemic medications were potential adverse effects (32% strongly agreed), potential long term toxicity (26% strongly agreed), cost of treatment (42% strongly agreed), and views expressed by patients and their family (37% agreed).

Our findings show variance between dermatology, allergy and immunology consultants with regard to the prescribing of systemic agents in CSU (figure 2). Our findings suggest allergists are more likely to prescribe omalizumab as first line treatment, while dermatologists more commonly prescribe ciclosporin, which is not in keeping with NICE guidance (5).

Drug-related adverse effects are the main perceived barrier for clinicians to prescribe systemic medications. Other barriers to prescribing are the cost of medications. The list price for 300mg Omalizumab monthly for 12 months is £6150 (4), excluding the cost of post-injection observations required in a secondary care setting, while ciclosporin (in generic formulation) costs £2660 for 300 mg/day for 12 months (4 mg/kg/day for 75 kg patient) (4), excluding the cost of renal function and blood pressure monitoring. The main limitation to our survey was the number of
respondents, as we chose to focus on consultant physicians with a specialist interest in urticaria.

In summary, our UK survey highlights the differences in management of CSU between dermatologists and other specialists, resulting in variation in the care provided for CSU patients. Although national and international treatment guidelines now recommend omalizumab as a first line agent for severe CSU not responding to antihistamine and montelukast treatment, these are based on placebo-controlled studies. The current lack of head-to-head comparisons between conventional systemics and biologic therapies may explain some of the variation in treatment approaches we observed and highlights the need for further research in this area, including a comprehensive health economic evaluation. (5,6).

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References
previously treated chronic spontaneous urticaria. NICE Technology appraisal guidance (TA339).

### Table 1: Summary of survey results

#### Section 1: Demographics

<table>
<thead>
<tr>
<th>Country of work</th>
<th>100% (19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital grade</td>
<td>Consultant</td>
</tr>
<tr>
<td>Specialty</td>
<td>Allergy</td>
</tr>
<tr>
<td></td>
<td>Dermatology 37% (7)</td>
</tr>
<tr>
<td></td>
<td>Immunology 5% (1)</td>
</tr>
<tr>
<td>Caseload</td>
<td>Adults only 42% (8)</td>
</tr>
<tr>
<td></td>
<td>Both Adults and Paediatrics 57% (11)</td>
</tr>
<tr>
<td></td>
<td>Paediatrics only 21% (4)</td>
</tr>
</tbody>
</table>

#### Number of years in specialty

- >20 years 53% (10)
- 10-20 years 26% (5)
- <10 years 21% (4)

#### Section 2: Use of systemic medications

**Do you use systemic medication for the management of chronic urticaria?**
- Yes 79% (15)
- No 21% (4)

**First line?**
- Omalizumab 47% (7)
- Ciclosporin 28% (4)
- Other 20% (3)
- Dapsone 7% (1)

**Second line?**
- Omalizumab 40% (6)
- Ciclosporin 35% (5)
- Mycophenolate Mofetil 13% (2)
- Other 13% (2)
- Dapsone 20% (3)
- Ciclosporin 13% (2)
- Methotrexate 13% (2)
- Mycophenolate Mofetil 13% (2)

**Third line?**
- Other 27% (4)
- Dapsone 20% (3)
- Ciclosporin 13% (2)
- Methotrexate 13% (2)
- Mycophenolate Mofetil 13% (2)
- Dapsone 60% (9)
- Ciclosporin 60% (9)
- Mycophenolate Mofetil 60% (9)
- Methotrexate 20% (3)

**If you use any of the listed treatments in children, which ones do you use?**
- Ciclosporin 80% (4)
- Omalizumab 80% (4)
- Azathioprine 60% (3)
- Dapsone 60% (3)
- Mycophenolate Mofetil 60% (3)
- Methotrexate 20% (1)

#### Section 3: Use of standardised measures

**Do you use standardised measures when assessing disease?**
- Yes 84% (16)
- No 16% (3)

**Physician global assessment**
- Most of the time 63% (10)
- Sometimes 13% (2)
- Never 25% (4)

**Patient global assessment**
- Most of the time 44% (7)
- Sometimes 25% (4)
- Rarely 6% (1)
- Never 25% (4)

**Urticaria activity score (UAS) ?**
- Most of the time 63% (10)
- Sometimes 38% (6)

**In-clinic UAS**
- Most of the time 25% (4)
- Sometimes 13% (2)
- Rarely 19% (3)
- Never 44% (7)

**Angioedema activity score**
- Sometimes 44% (7)
- Rarely 25% (4)
- Never 31% (5)

**Itch severity score**
- Most of the time 13% (2)
- Sometimes 19% (3)
- Rarely 31% (5)
- Never 38% (6)

**Weekly number of hives score**
- Most of the time 13% (2)
- Sometimes 25% (4)
- Rarely 19% (3)
- Never 44% (7)

**DLQI**
- Most of the time 38% (6)
- Sometimes 25% (4)
- Rarely 25% (4)
- Never 13% (2)

**Chronic Urticaria Quality of Life Questionnaire (CU-QoL)**
- Sometimes 25% (4)
- Rarely 25% (4)
- Never 50% (8)

**Angioedema Quality of Life Questionnaire (AE-QoL)**
- Sometimes 4% (1)
- Rarely 31% (5)
- Never 63% (10)

#### Section 4: Use of guidelines and perceived barriers

**Do you use guidelines to direct your management of urticaria?**
- Yes 89% (17)
- No 11% (2)

**Which guidelines do you refer to?**
- EACCI/GA2LEN/EDF/WAO 50% (8)
- Other 38% (6)
- Local guidelines 13% (2)

**Support services for patients**
- Access to nursing support 89% (16)
- Access to inpatient facilities 61% (11)
- Dedicated urticaria service 56% (10)
- Nurse prescribers 28% (5)

**Main perceived barriers to prescribing systemic medications**
- Cost
- Side Effect of treatments
- Views expressed by patient or family
- Long term toxicity
**Figure 1:** First-, second- and third-line systemic drug selection

![Bar chart showing first-, second- and third-line systemic drug selection.](chart1)

**Figure 2:** First-, second- and third-line systemic drug selection by specialty

![Bar chart showing first-, second- and third-line systemic drug selection by specialty.](chart2)