Network of Excellence

Educational Slides: Guideline on urticaria

Torsten Zuberbier

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Supporting and Promoting Excellence in Allergy and Asthma

Latest News

The EAACI/GA²LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update

This Guideline is the result of a systematic literature review using the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) methodology and a structured consensus conference held on 28 and 29 November 2012, in Berlin. It is 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) with the participation of delegates of 21 national and international societies. Urticaria is a frequent, mast cell-driven disease, presenting with wheals, angioedema, or both. The life-time prevalence for acute urticaria is approximately 20%. Chronic spontaneous urticaria and other chronic forms of urticaria do not only cause a decrease in quality of life, but also affect performance at work and school and, as such, are members of the group of severe allergic diseases. This guideline covers the definition and classification of urticaria, taking into account the recent progress in identifying its causes, eliciting factors and pathomechanisms. In addition, it outlines evidence-based diagnostic and therapeutic approaches for the different subtypes of urticaria. This guideline was acknowledged and accepted by the European Union of Medical Specialists (UEMS).

The Methods report describes the process of guideline development in detail. It is the result of a systematic literature review using the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) methodology and a structured consensus conference held on 28 and 29 November 2012, in Berlin.
A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-Q2oL)

**Background:** Health-related quality of Life in patients with chronic urticaria is evaluated by means of generic instruments or questionnaire designed for skin diseases. No disease-specific tool is now available for the assessment of chronic urticaria impact from patients’ viewpoint.

**Objective:** The aim of our study is to develop and validate a new questionnaire specifically designed for the assessment of quality of life in chronic urticaria (Chronic Urticaria Quality of Life Questionnaire – CU-Q2oL).

**Methods:** In the development phase of CU-Q2oL an initial list of items of 37 items was compiled and given to 80 patients with chronic urticaria; the 23 most significant items were selected and converted into questions evaluating the answers on a Likert scale of five steps. The validation procedure involved 125 patients (86 F and 39 M) (age 42.17 ± 9.24 years).

**Results:** Following a statistical analysis, CU-Q2oL showed a six-dimensional structure and good levels of internal consistency for the extracted factors: Pruritus (0.79), Swelling (0.65), Impact on life activities (0.83), Sleep problems (0.77), Looks (0.83) and Limits (0.74). In stable conditions CU-Q2oL showed a good reliability, ranged between 0.64 and 0.92. Responsiveness to clinical changes was accomplished.

**Discussion:** These results provide evidence that CU-Q2oL has specificity enough for being a valid tool for detecting the relative burden of CU on subjective wellbeing, and for obtaining a global evaluation both of CU impact and of treatments, taking into account the patient’s point of view. The CU-Q2oL was easily and quickly filled up and well accepted by the patients.

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Key words: disease specific questionnaire; quality of life; urticaria; validation.

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Italy

Accepted for publication 27 January 2005
<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
<th>SD</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urticaria interferes with my eating behaviour</td>
<td>69.74</td>
<td>3.01</td>
<td>2.10</td>
</tr>
<tr>
<td>Urticaria interferes with my social relationship</td>
<td>67.11</td>
<td>2.59</td>
<td>1.74</td>
</tr>
<tr>
<td>Difficulties in falling asleep</td>
<td>78.95</td>
<td>2.12</td>
<td>1.67</td>
</tr>
<tr>
<td>I feel embarrassed by urticaria signs on my body</td>
<td>84.21</td>
<td>2.73</td>
<td>2.29</td>
</tr>
<tr>
<td>Difficulties in being concentrated</td>
<td>61.84</td>
<td>2.53</td>
<td>1.56</td>
</tr>
<tr>
<td>Urticaria interferes with my work</td>
<td>69.74</td>
<td>2.73</td>
<td>1.90</td>
</tr>
<tr>
<td>Urticaria interferes with my sleep</td>
<td>71.10</td>
<td>2.93</td>
<td>2.12</td>
</tr>
<tr>
<td>I feel nervous</td>
<td>76.31</td>
<td>2.95</td>
<td>2.25</td>
</tr>
<tr>
<td>Urticaria interferes with my sport activities</td>
<td>57.89</td>
<td>3.06</td>
<td>1.77</td>
</tr>
<tr>
<td>I wake up during the night</td>
<td>61.84</td>
<td>2.83</td>
<td>1.75</td>
</tr>
</tbody>
</table>

Baiardini I et al. Allergy 2009
3rd International Consensus Meeting on Urticaria

Urticaria 2008

EAACI/GA²LEN/EDF/WAO
URTICARIA 2012

4th International Consensus Meeting on Urticaria

Berlin
Charité – Universitätsmedizin
Langenbeck-Virchow-Hall
Luisenstraße 58/59
10117 Berlin

28 – 29 November 2012
Societies involved in the Urticaria Guideline

AAAAI, American Academy of Allergy, Asthma & Immunology (see Acknowledgments); AEDV, Spanish Academy of Dermatology and Venereology; ASBAI, Brazilian Association of Allergy and Immunopathology; CDA, Chinese Dermatologist Association; CSACI, Canadian Society of Allergy and Clinical Immunology; DDG, German Society of Dermatology; DGAKI, German Society of Allergology and Clinical Immunology; EAACI, European Academy of Allergy and Clinical Immunology; EDF, European Dermatology Forum; ESCD, European Society of Contact Dermatitis; GA²LEN, Global Allergy and Asthma European Network; IAACI, Israel Association of Allergy and Clinical Immunology; IADVL, Indian Association of Dermatologists, Venereologists and Leprologists; JDA, Japanese Dermatological Association; ÖGDV, Austrian Society for Dermatology; SDF, French Society of Dermatology; SGDV, Swiss Society for Dermatology and Venereology; SPDV, Portuguese Society of Dermatology and Venereology; MSAI, Malaysian Society of Allergy and Immunology; UNEV, Urticaria Network; WAO, World Allergy Organization.
Risks and benefits were weighed out using a modified version of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.
GRADE

H. Schünemann et al, Am J Respir Crit Care Med 2006

- Clarity of risk/benefit
- Quality of supporting evidence
- Implications
- Factors that may decrease the quality of evidence
  - Small size studies
  - Poor quality of planning, randomization
  - Biases
  - Inconsistency of results
- Factors that may increase the quality of evidence
  - Large magnitude of effect
  - Dose-dependent gradient
URTICARIA 2012

4th International Consensus Meeting on Urticaria
URTICARIA 2012

4th International Consensus Meeting on Urticaria
This guideline, together with its sister guideline on the classification of urticaria (Zuberbier T, Asero R, Bindslev-Jensen C, Canonica GW, Church MK, Gómez-Aruma AM et al. EAACI/GA²LEN/EDF/WAO Guideline: definition, classification and diagnosis of urticaria. Allergy 2009;64: 1417–1426), is the result of a consensus reached during a panel discussion at the Third International Consensus Meeting on Urticaria, Utrecht 2008, a joint initiative of the Dermatology Section of the European Academy of Allergology 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). As members of the panel, the authors had prepared their suggestions regarding management of urticaria before the meeting. The draft of the guideline took into account all available evidence in the literature (including Medline and Embase searches and hand searches of abstracts at international allergy congresses in 2004–2008) and was based on the existing consensus reports of the first and the second symposium in 2000 and 2004. These suggestions were then discussed in detail among the panel members and with the over 300 international specialists of the meeting to achieve a consensus using a simple voting system where appropriate. Urticaria has a profound impact on the quality of life and effective treatment is, therefore, required. The recommended first-line treatment is new generation, non-sedating H1-antihistamines. If standard dosing is not effective, increasing the dosage up to four-fold is recommended. For patients who do not respond to a four-fold increase in dosage of non-sedating H1-antihistamines, it is recommended that second-line therapies should be added to the antihistamine treatment. In the choice of second-line treatment, both their costs and risk/benefit profiles are most important to consider. Corticosteroids are not recommended for long-term treatment due to their unavoidable severe adverse effects. This guideline was acknowledged and accepted by the European Union of Medical Specialists (UEMS).
URTICARIA 2012

4th International Consensus Meeting on Urticaria

POSITION PAPER

The EAACI/GA²LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update


Abstract

This guideline is the result of a systematic literature review using the ‘Grading of Recommendations Assessment, Development and Evaluation’ (GRADE) methodology and a structured consensus conference held on November 28 and 29, 2012, in Berlin. It is a joint initiative of the Dermatology Section of the European Academy of Allergology 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) with the participation of delegates of 21 national and international socie-
## Version 2008
### Classification for clinical use

<table>
<thead>
<tr>
<th>Group</th>
<th>Subgroup</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous urticaria</td>
<td>Acute spontaneous urticaria</td>
<td>spontaneous wheals &lt; 6 weeks</td>
</tr>
<tr>
<td></td>
<td>Chronic spontaneous urticaria</td>
<td>spontaneous wheals &gt; 6 weeks</td>
</tr>
</tbody>
</table>
### Version 2008
### Classification for clinical use

<table>
<thead>
<tr>
<th>Group</th>
<th>Subgroup</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical urticaria</td>
<td>Cold contact urticaria</td>
<td>eliciting factor: cold objects/air/fluids/wind</td>
</tr>
<tr>
<td></td>
<td>Delayed pressure urticaria</td>
<td>eliciting factor: vertical pressure (wheals arising with a 3 – 12 h latency)</td>
</tr>
<tr>
<td></td>
<td>Heat contact urticaria</td>
<td>eliciting factor: localized heat</td>
</tr>
<tr>
<td></td>
<td>Solar urticaria</td>
<td>eliciting factor: UV and/or visible light</td>
</tr>
<tr>
<td></td>
<td>Urticaria factitia /</td>
<td>eliciting factor: mechanical shearing forces</td>
</tr>
<tr>
<td></td>
<td>dermatographic urticaria</td>
<td>(wheals arising after 1 – 5 min)</td>
</tr>
<tr>
<td></td>
<td>Vibratory urticaria /</td>
<td>eliciting factor: vibratory forces, e.g. pneumatic hammer</td>
</tr>
<tr>
<td></td>
<td>angioedema</td>
<td></td>
</tr>
</tbody>
</table>
# 2013 revision an update: Classification for clinical use

## Table 2 Classification of chronic urticaria subtypes (presenting with wheals, angioedema, or both)

<table>
<thead>
<tr>
<th>Chronic urticaria subtypes</th>
<th>Inducible urticaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic spontaneous urticaria</td>
<td>Symptomatic dermographism*</td>
</tr>
<tr>
<td>Spontaneous appearance of wheals, angioedema, or both ≥6 weeks due to known or unknown causes</td>
<td>Cold urticaria†</td>
</tr>
<tr>
<td></td>
<td>Delayed pressure urticaria‡</td>
</tr>
<tr>
<td></td>
<td>Solar urticaria</td>
</tr>
<tr>
<td></td>
<td>Heat urticaria§</td>
</tr>
<tr>
<td></td>
<td>Vibratory angioedema</td>
</tr>
<tr>
<td></td>
<td>Cholinergic urticaria</td>
</tr>
<tr>
<td></td>
<td>Contact urticaria</td>
</tr>
<tr>
<td></td>
<td>Aquagenic urticaria</td>
</tr>
</tbody>
</table>

*also called *urticaria factitia*, dermographic urticaria; †also called cold contact urticaria; ‡also called pressure urticaria; §also called heat contact urticaria.
Assessment of disease activity in urticaria patients

<table>
<thead>
<tr>
<th>Score</th>
<th>Wheals</th>
<th>Pruritus</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Mild (&lt;20 wheals/24 h)</td>
<td>Mild (present but not annoying or troublesome)</td>
</tr>
<tr>
<td>2</td>
<td>Moderate (20–50 wheals/24 h)</td>
<td>Moderate (troublesome but does not interfere with normal daily activity or sleep)</td>
</tr>
<tr>
<td>3</td>
<td>Intense (&gt;50 wheals/24 h or large confluent areas of wheals)</td>
<td>Intense (severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep)</td>
</tr>
</tbody>
</table>

Sum of score: 0–6 for each day is summarized over one week (maximum 42).

Guidelines for Diagnosis of Urticaria

Wheals
- Recurrent unexplained fever? Joint/bone pain? Melenie?
  - Yes
  - No

  - Auto-inflammatory disease suspected??
  - Average wheal duration > 24h?
    - Yes
    - No
      - Signs of vasculitis in biopsy??
        - Yes
        - No
          - Acquired/ hereditary AE??
        - No
          - Urticarial vasculitis
            - Chronic spontaneous Urticaria
              - Chronic inducible Urticaria
                - HAE I-III
                - ACE-Ih induced AE

Angioedema
- ACE inhibitor treatment??
  - Yes
  - No
    - Remission after stop??
      - Yes
      - No

Interleukin-1
Histamine and other Mast Cell Mediators
Bradykinin

AE: angioedema; AH: Antihistamine; AID: Auto-inflammatory disease; HAE: Hereditary angioedema; IL-1: Interleukin-1.
## Diagnosis

**Spontaneous urticaria**
- **Acute spontaneous urticaria**
- **Chronic spontaneous urticaria**

<table>
<thead>
<tr>
<th>Subtypes</th>
<th>Routine diagnostic tests (recommended)</th>
<th>Extended diagnostic program* (suggested based on history only) for identification of underlying causes or eliciting factors and for ruling out possible differential diagnoses if indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Differential blood count. ESR or CRP</td>
<td>Test for (in no preferred order): (i) infectious diseases (e.g., Helicobacter pylori), (ii) type I allergy, (iii) functional autoantibodies, (iv) thyroid hormones and autoantibodies, (v) skin tests including physical tests, (vi) pseudosensitization-free diet for 3 weeks, (vii) tryptase, (viii) autologous serum skin test, and (ix) lesional skin biopsy</td>
</tr>
</tbody>
</table>

**Inducible urticaria**
- **Cold urticaria**
- **Delayed pressure urticaria**
- **Heat urticaria**
- **Solar urticaria**

<table>
<thead>
<tr>
<th>Subtypes</th>
<th>Routine diagnostic tests (recommended)</th>
<th>Differential blood count and ESR or CRP cryoproteins rule out other diseases, especially infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold provocative test (ice cube, cold water, cold wind)</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Pressure test and threshold test</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Heat provocaiton and threshold test</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>UV and visible light of different wavelengths and threshold test</td>
<td>None</td>
<td>Rule out other light-induced dermatoses</td>
</tr>
</tbody>
</table>

**Symptomatic demographism**
- **Vibratory Angioedema**
- **Aquagenic urticaria**
- **Cholinergic urticaria**
- **Contact urticaria**

<table>
<thead>
<tr>
<th>Subtypes</th>
<th>Routine diagnostic tests (recommended)</th>
<th>Differential blood count, ESR or CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elicit demographism and threshold test (dermographometer) Test with, for example, vortex</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Wet cloths at body temperature applied for 20 min</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Exercise and hot bath provocaiton cutaneous provocation test. Skin tests with immediate readings, for example prick test</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

*ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.
*Depending on suspected cause.
†Unless strongly suggested by patient history, for example allergy.
†As indication of severe systemic disease.

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Management
## 2008 Guidelines:

<table>
<thead>
<tr>
<th>First Line</th>
<th>very low (&lt; 1 €/d)</th>
<th>very low</th>
<th>new-generation H1-antihistamine (where available)</th>
<th>2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second Line</td>
<td>low (&lt; 5 €/d)</td>
<td>very low</td>
<td>Increased dosage up to fourfold</td>
<td>1-4 weeks</td>
</tr>
<tr>
<td>Third Line</td>
<td>low</td>
<td>very low</td>
<td>possiblyAlternative non-sedating antihistamine</td>
<td>1-4 weeks</td>
</tr>
<tr>
<td></td>
<td>low</td>
<td>very low</td>
<td>Add on: leukotriene receptor antagonist</td>
<td>1-4 weeks</td>
</tr>
<tr>
<td></td>
<td>medium (&lt;10 €/d)</td>
<td>medium</td>
<td>Systemic corticosteroid (only 3-7 days short course!)</td>
<td>3-7 days</td>
</tr>
<tr>
<td>Fourth Line</td>
<td>very low</td>
<td>very low</td>
<td>H2-antihistamine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>medium</td>
<td>medium</td>
<td>Cyclosporin A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>very low</td>
<td>medium</td>
<td>Dapsone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>high (&gt;10 €/d)</td>
<td>very low</td>
<td>Omalizumab</td>
<td></td>
</tr>
</tbody>
</table>
2013 revision and update – treatment algorithm

**First line:**
Modern second generation antihistamines

*If symptoms persist after 2 weeks*

**Second line:**
Increase dosage up to fourfold of modern second generation antihistamines

*If symptoms persist after 1–4 further weeks*

**Third line:**
Add on to second line*: Omalizumab or Ciclosporin A or Montelukast

*Short course (max 10 days) of corticosteroids may also be used at all times if exacerbations demand this*

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**Figure 2** Recommended treatment algorithm for urticaria. *The order of third-line treatments does not reflect preference. First line = High-quality evidence: Low cost and worldwide availability (e.g., modern second-generation antihistamines exist also in developing countries mostly cheaper than old sedating Antihistamines), per daily dose as the half-life time is much longer, very good safety profile, good efficacy. Second line = high-quality evidence: Low cost, good safety profile, good efficacy. Third line as add-on to AH. Ciclosporin A = High-quality evidence: Medium to high cost, moderate safety profile, good efficacy. Omalizumab = High-quality evidence: High cost, very good safety profile, very good efficacy. Montelukast = Low quality evidence: Low cost, good safety, low efficacy. Short course of corticosteroids = Low quality evidence: Low cost, worldwide availability, good safety profile (for short course only), good efficacy during intake, but very low for lasting efficacy.

Questions addressed by the 2012 revision and update of the urticaria guideline based on the GRADE principle
We recommend:

for ✓ or against x

We suggest:

for (✓) or against (x)
Question 1: Should the current classification be maintained in urticaria?

We recommend the use of this updated version of the classification of the 2013 revision (strong recommendation/clinical consensus)

100 % (voting result)
Question 2: Should the current activity score (UAS7) be maintained for assessing severity in urticaria?

We recommend the use of UAS7 to assess severity (strong recommendation/clinical consensus)
Question 3: Should routine diagnostic measures be performed in acute urticaria?

We recommend against routine diagnostic measures in acute urticaria (strong recommendation/clinical consensus)

100 % (voting result)
Question 4: Should routine diagnostic measures be performed in chronic spontaneous urticaria?

We recommend for only very limited routine diagnostic measures in chronic spontaneous urticaria (strong recommendation/clinical consensus)

100% (voting result)
Question 5: Should extended diagnostic measures be performed in chronic spontaneous urticaria?

We recommend for only limited extended diagnostic measures in chronic spontaneous urticaria based on patient history (strong recommendation/clinical consensus)

100 % (voting result)
Question 6: Should routine diagnostic measures be performed in inducible, non-spontaneous subtypes of urticaria?

We recommend limiting routine diagnostic measures to determining the threshold of eliciting factors in inducible urticaria subtypes (strong recommendation/clinical consensus)

100 % (voting result)
Question 7: Which instrument should be used to measure QoL in urticaria?

We recommend using the validated CU-Q2oL and AE-QoL instruments for assessing QoL impairment and to monitor disease activity (strong recommendation/clinical consensus)

100 % (voting result)
Question 8: Should patients with an allergic sensitization (positive specific IgE/skin prick test) avoid certain food items?

We recommend that patients with a known allergic sensitization based on specific IgE to food should only avoid these food items if there is relevant information, e.g. double blind oral provocation test or a clear history, to prove that the sensitization has a clinical relevance for urticaria (strong recommendation/high level of evidence)

100 % (voting result)
We recommend aiming for complete symptom control in urticaria as safely as possible (strong recommendation/clinical consensus following the WHO constitution in conformity with the Charter of the United Nations)
Question 10: Are modern second generation H1-antihistamines to be preferred over first generation H1-antihistamines in treatment of urticaria?

We recommend that modern second generation H1-antihistamines are to be preferred over first generation H1-antihistamines in the treatment of urticaria (strong recommendation/high level of evidence)

95 % (voting result)
Question 11: Are modern second generation antihistamines first line treatment in urticaria and to be preferred against other licensed medication?

We recommend that modern second generation H1-antihistamines are to be used as first line treatment of urticaria (strong recommendation/high level of evidence)

100 % (voting result)
REM Sleep delayed and reduced

Awake

Asleep

REM Sleep

Night

Day

Night

Day

First Generation Antihistamine

Question 12: Is an increase in the dose to fourfold of modern second generation H1-antihistaminines useful as second line treatment and to be preferred over other treatments in urticaria?

We recommend a trial of up to fourfold dose of modern second generation H-1 antihistaminines as second-line in the algorithm of treatment

98 % (voting result)
Question 13: Are H2-antihistamines useful in the treatment of urticaria as third line therapy?

We suggest the use of H2-antihistamines as add on therapy to modern second generation H-1 antihistamines as possible alternative treatment but not as first, second or third-line in the algorithm of treatment of urticaria (low recommendation/low level of evidence)

88 % (voting result)
Question 14: Is ciclosporin A useful as add on treatment in patients unresponsive to high doses of H1-antihistamines as third line treatment?

We recommend a trial of ciclosporin A as add on therapy to modern second generation H-1 antihistamines as third-line in the algorithm of treatment of urticaria (strong recommendation/high level of evidence)

100 % (voting result)
Question 15: Is omalizumab useful in the treatment of patients unresponsive to high doses of H1-antihistamines as third line treatment?

We recommend a trial of omalizumab as add on therapy to Modern second generation H-1 antihistamines as third-line in the algorithm of treatment of urticaria (strong recommendation/high level of evidence)

100 % (voting result)
Xolair is indicated as add-on therapy for the treatment of chronic spontaneous urticaria in adult and adolescent (12 years and above) patients with inadequate response to H1-antihistamine treatment (EMA approval in 2’2014, FDA approval in 4’2014)
Xolair is indicated as add-on therapy for the treatment of chronic spontaneous urticaria in adult and adolescent (12 years and above) patients with inadequate response to H1-antihistamine treatment (EMA approval in 2’2014, FDA approval in 4’2014)
Question 16: Should oral corticosteroids be used in the treatment of urticaria?

We recommend against the long-term use of systemic corticosteroids in urticaria (strong recommendation/high level of evidence)

and (✓) We suggest a trial of a short course of systemic corticosteroids in urticaria as third line therapy or as an option for acute exacerbation (weak recommendation/low level of evidence)

88 % (voting result)

99 % (voting result)
Question 17: Should leukotriene antagonists be used in the third line treatment of urticaria?

(✓)

We suggest a trial of montelukast as add on therapy to modern second generation H-1 antihistamines as third-line in the treatment of urticaria

(weak recommendation/low level of evidence)

99 % (voting result)
Question 18: Is Dapsone useful in the treatment of urticaria as third line therapy?

(✓) + (✗)

At the present time it is not possible to give a recommendation for or against treatment with dapsone

97% (voting result)
Question 19: Should the same treatment algorithm be used in children?

We suggest the same treatment algorithm to be used in children with chronic urticaria (weak recommendation/clinical consensus)

100 % (voting result)
Question 20: Should the same treatment algorithm be used in pregnant women and during lactation?

We suggest the same treatment algorithm be used in pregnant women and during lactation in urticaria (weak recommendation/clinical consensus)

97% (voting result)
Question 21: Are pseudoallergen-free diets useful in the extended diagnostic program of chronic spontaneous urticaria?

We recommend the use of pseudoallergen (non-allergic hypersensitivity reaction causing agents) free diets in the extended diagnostic program of chronic spontaneous urticaria in patients with daily or almost daily symptoms only (strong recommendation/high-quality evidence)

and

We suggest to use it in the management program only for those patients Responding to the diet (weak recommendation/high-quality evidence)

100 % (voting result)

89 % (voting result)
**Pseudoallergy in chronic urticaria: double blind, placebo controlled studies**

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Disease studied</th>
<th>Number of patients</th>
<th>Positive reactions to food additives</th>
<th>Improvement on diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kirchhof et al., 1982</td>
<td>chronic intermittent urticaria</td>
<td>100</td>
<td>39%</td>
<td>44%(^1)</td>
</tr>
<tr>
<td>Supramaniam &amp; Warner, 1986</td>
<td>urticaria and angio-edema in 74.4%</td>
<td>43</td>
<td>24%</td>
<td>87.5%(^1)</td>
</tr>
<tr>
<td>Zuberbier et al., 1995</td>
<td>Chronic urticaria and/ or angioedema</td>
<td>67</td>
<td>19 %</td>
<td>73% of all patients</td>
</tr>
<tr>
<td>Pigatto, Valsecchi,2000</td>
<td>chronic urticaria</td>
<td>202 of 348</td>
<td>37.3 %</td>
<td>62.4% improvement 17.3% no improvement 20.3% disrupted diet of all patients</td>
</tr>
</tbody>
</table>

\(^1\) after positive provocation
<table>
<thead>
<tr>
<th>General category</th>
<th>n (%)</th>
<th>Specific category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefited</td>
<td>48 (34)</td>
<td>Strong responders</td>
<td>20 (14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Partial responders</td>
<td>19 (14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Natural-coping subjects</td>
<td>9 (6)</td>
</tr>
<tr>
<td>Neutral</td>
<td>70 (50)</td>
<td>Disqualified</td>
<td>4 (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonresponders</td>
<td>64 (46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unknown</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Deteriorated</td>
<td>22 (16)</td>
<td>Addictive subjects</td>
<td>10 (7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sick-role subjects</td>
<td>5 (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative responders</td>
<td>7 (5)</td>
</tr>
</tbody>
</table>
Question 22: Should modern second generation antihistamines be taken regularly or as needed?

We recommend modern second generation oral H1-antihistamines be taken continuously in the Lowest necessary dose rather than on demand (strong recommendation/high-quality evidence)

98% (voting result)
Question 23: Should different H1-antihistamines be used at the same time?

We recommend preferably to updose modern second generation oral H1-antihistamines that do not cause sedation up to four fold (strong recommendation/high-quality evidence) instead of combining different H1-antihistamines at the same time (strong recommendation/low quality evidence)

100 % (voting result)
Question 24: If there’s no improvement, should higher than fourfold doses of H1-antihistamines be used?

We recommend preferably up-dosing with modern second generation H1-antihistamines that do not cause sedation up to fourfold (strong recommendation/high-quality evidence) and not to further increase the dose

99 % (voting result)