

## Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

Medwave 2015;15(6):e6346 doi: 10.5867/medwave.2015.6346

# What are the effects of omalizumab in refractory chronic spontaneous urticaria?

**Authors:** Mario López[1,3], Lucas Navajas-Galimany[1,2,3]

**Affiliation:**

[1] Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

[2] Departamento de Dermatología, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

**E-mail:** [fnavaja@uc.cl](mailto:fnavaja@uc.cl)

**Citation:** López M, Navajas-Galimany L. What are the effects of omalizumab in refractory chronic spontaneous urticaria?. *Medwave* 2015;15(6):e6346 doi: 10.5867/medwave.2015.6346

**Publication date:** 24/12/2015

### Abstract

Chronic spontaneous urticaria is a disorder mediated by mast cells, characterized by the development of wheals, angioedema or both, lasting six weeks or more, with or without a known trigger agent. First and second line treatment are antihistamines, but some refractory cases require other alternatives, such as omalizumab. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified four systematic reviews including five pertinent randomized controlled trials overall. We combined the evidence using meta-analysis and generated a summary of findings following the GRADE approach. We concluded omalizumab reduces symptoms and improves quality of life in patients with chronic spontaneous urticaria.

### Problem

Chronic spontaneous urticaria is a disorder mediated by mast cells, characterized by wheals, angioedema or both, lasting six weeks or more. Usual treatment is based on H1 antihistamines, but some patients do not achieve an optimal clinical response even with maximal doses. Different alternatives have emerged for second and third line treatment of this condition, such as omalizumab, a monoclonal antibody that selectively binds to IgE. It has been postulated that omalizumab would improve symptoms and quality of life. The main potential adverse effects are headache, abdominal pain and injection site reaction.

### Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information, we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

#### Key messages

- Omalizumab improves symptoms and quality of life in patients with chronic spontaneous urticaria.
- The findings of this summary are consistent with the systematic reviews identified and the recommendations of the main guidelines.

### About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found four systematic reviews [1],[2],[3],[4] that include five primary studies [5],[6],[7],[8],[9], all of which correspond to randomized controlled trials.</p>
<p>What types of patients were included</p>	<p>Five studies included adults with chronic spontaneous urticaria defined by increased itching or hives lasting for 6-8 weeks despite treatment with antihistamines. Three studies included patients with UAS7 (Urticaria Activity Score) &gt; 16 points [5],[6],[7], one study with UAS &gt; 4 points [8] and one study with UAS7 &gt; 10 points [9].</p>
<p>What types of interventions were included</p>	<p>The intervention was omalizumab versus placebo in all the studies, maintaining the antihistamine baseline treatment. One study used omalizumab 300 mg/day[5], one study used 75-375 mg/day [9], two studies used doses of 75, 150 and 300 mg/day [6],[7], and one study used doses of 75, 300 and 600 mg/day [8]. The treatment period with omalizumab lasted 24 weeks in three studies [5],[6],[9], 12 weeks in one study [7] and 4 weeks in one study [8].</p>
<p>What types of outcomes were measured</p>	<p>The outcomes measured were the change in the index of disease and quality of life. Index of disease was measured with UAS7, which evaluates itching and hives for seven days with a scale of 0-6 points per day, with a minimum of 0 points and a maximum of 42 points. Quality of life was evaluated with CU-Q2oL (Chronic Urticaria Quality of Life Questionnaire) which evaluates 23 factors ranging from 0 to 5 points, with a minimum of 0 points and a maximum of 115.</p>

### Summary of findings

The information on the effects of omalizumab is based on five randomized studies including 1117 patients. All studies measured improvement with UAS7 scale and four studies measured improvement with Q2oL [5],[6],[7],[8],[9].

- Omalizumab decreases disease activity in patients with chronic spontaneous urticaria refractory to antihistamines. The certainty of the evidence is high.
- Omalizumab improves quality of life of patients with chronic spontaneous urticaria refractory to antihistamines. The certainty of the evidence is high.

Omalizumab para la urticaria crónica espontánea refractaria a antihistamínicos				
<b>Pacientes</b>	Urticaria crónica espontánea			
<b>Intervención</b>	Omalizumab			
<b>Comparación</b>	Placebo			
Desenlaces	Efecto absoluto*		Efecto relativo (IC 95%)	Certeza de la evidencia (GRADE)
	SIN omalizumab	CON omalizumab		
	Diferencia: pacientes por 1000			
<b>Actividad de enfermedad</b> (Escala UAS7: de 0 a 42 puntos)	En promedio mejoraron en 8,4 puntos	En promedio mejoraron en 20 puntos	DM -11,58 (-13,39 a -9,77)	⊕⊕⊕⊕ Alta
	Diferencia: 11,6 puntos mejor con omalizumab (Margen de error: 9,77 a 13,39 mejor)			
<b>Calidad de vida</b> (Escala Q2oL: de 0 a 115 puntos)	En promedio mejoraron en 16,9 puntos	En promedio mejoraron en 30 puntos	DM -13,12 (-16,30 a -9,95)	⊕⊕⊕⊕ Alta
	Diferencia: 13,1 puntos mejor con omalizumab (Margen de error: 9,95 a 16,30 puntos mejor)			

Margen de error = Intervalo de confianza del 95%.  
DM: Diferencia de medias.  
GRADE: grados de evidencia del GRADE Working Group (ver más adelante).

\*Los riesgos **SIN OMALIZUMAB** están basados en los riesgos del grupo control en los estudios. El riesgo **CON OMALIZUMAB** (y su margen de error) está calculado a partir del efecto relativo (y su margen de error).

### About the certainty of the evidence (GRADE)\*

⊕⊕⊕⊕

**High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

**Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

**Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

**Very low:** This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

\*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

---

## Other considerations for decision-making

---

### To whom this evidence does and does not apply

---

- This evidence applies to adult patients with chronic spontaneous urticaria refractory to standard management with anti H1 antihistamines.
  - It does not apply to other types of chronic and acute urticaria.
- 

### About the outcomes included in this summary

---

- The outcomes selected for the summary of findings are those considered critical for decision making by the authors of this summary.
- 

### Balance between benefits and risks, and certainty of the evidence

---

- The benefits of omalizumab outweigh the risks, with a high certainty of evidence.
  - Omalizumab appears to be a safe drug when used in the short and medium term.
  - The likelihood of recurrence of symptoms is an element to consider when trying to reduce dose or to discontinue, requiring reinitiating the drug in some cases [10].
- 

### Resource considerations

---

- Omalizumab is expensive (approximated cost for 150 mg/ml and 300 mg/ml = £ 256 and £ 512) [11]. In Chile, the price of a 150 mg vial is around \$ 450,000 (Xolair®).
  - This factor would be a critical determinant of the decision to use this intervention, from both an individual or health system perspective.
- 

### Differences between this summary and other sources

---

- The conclusions of this summary agree with those of the systematic reviews identified.
  - The conclusions of this summary are consistent with the recommendations of the joint guidelines 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) [12].
- 

### Could this evidence change in the future?

---

- The probability of future evidence changing the conclusions of this summary is very low because of the certainty of the evidence.
-

## How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.

	Saini SS 2015	Kaplan A 2013	Maurer M 2013	Saini S 2011	Maurer M 2011
Mitchell S 2015					
Urgert MC 2015					
Carrillo DC 2014					
HSC, NIHR 2012					

Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database. The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question. The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies. The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Omalizumab versus placebo for chronic spontaneous urticaria](#)

## Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database ([www.epistemonikos.org](http://www.epistemonikos.org)).

These summaries follow a rigorous process of internal peer review.

## Conflicts of interest

The authors do not have relevant interests to declare.

## References

1. Mitchell S, Balp MM, Samuel M, McBride D, Maurer M. Systematic review of treatments for chronic spontaneous urticaria with inadequate response to licensed first-line treatments. *Int J Dermatol*. 2015 Sep;54(9):1088-104. | [CrossRef](#) | [PubMed](#) |
2. Carrillo DC, Borges MS, García E, Egea E, Serrano CD. Omalizumab vs. placebo in the management of chronic idiopathic urticaria: a systematic review. *World Allergy Organ J*. 2014 Dec 31;7(1):72. | [CrossRef](#) | [PubMed](#) |
3. Urgert MC, van den Elzen MT, Knulst AC, Fedorowicz Z, van Zuuren EJ. Omalizumab in patients with chronic spontaneous urticaria: a systematic review and GRADE assessment. *Br J Dermatol*. 2015 Aug;173(2):404-15. | [CrossRef](#) | [PubMed](#) |
4. HSC, NIHR. Omalizumab for chronic spontaneous urticaria- second line. Birmingham NIHR Horizon Scanning Centre (NIHR HSC) 2012. | [Link](#) |
5. Kaplan A, Ledford D, Ashby M, Canvin J, Zazzali JL, Conner E, et al. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. *J Allergy Clin Immunol*. 2013 Jul;132(1):101-9. | [CrossRef](#) | [PubMed](#) |

6. Saini SS, Bindslev-Jensen C, Maurer M, Grob JJ, Bülbül Baskan E, Bradley MS, et al. Efficacy and safety of omalizumab in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H1 antihistamines: a randomized, placebo-controlled study. *J Invest Dermatol.* 2015 Jan;135(1):67-75. | [CrossRef](#) | [PubMed](#) |
7. Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Giménez-Arnau A, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med.* 2013 Mar 7;368(10):924-35. | [CrossRef](#) | [PubMed](#) |
8. Saini S, Rosen KE, Hsieh HJ, Wong DA, Conner E, Kaplan A, et al. A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H1-antihistamine-refractory chronic idiopathic urticaria. *J Allergy Clin Immunol.* 2011 Sep;128(3):567-73.e1. | [CrossRef](#) | [PubMed](#) |
9. Maurer M, Altrichter S, Bieber T, Biedermann T, Bräutigam M, Seyfried S, et al. Efficacy and safety of omalizumab in patients with chronic urticaria who exhibit IgE against thyroperoxidase. *J Allergy Clin Immunol.* 2011 Jul;128(1):202-209.e5. | [CrossRef](#) | [PubMed](#) |
10. Har D, Patel S, Khan DA. Outcomes of using omalizumab for more than 1 year in refractory chronic urticaria. *Ann Allergy Asthma Immunol.* 2015 Aug;115(2):126-9. | [CrossRef](#) | [PubMed](#) |
11. British Medical Association and Royal Pharmaceutical Company of Great Britain. *British National Formulary. BNF 63.* London: BMJ Group and RPS Publishing; 2012.
12. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, 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 Jul;69(7):868-87. | [CrossRef](#) | [PubMed](#) |

13.

**Author address:**

[1] Facultad de Medicina  
Pontificia Universidad Católica de Chile  
Lira 63  
Santiago Centro  
Chile



Esta obra de Medwave está bajo una licencia Creative Commons Atribución-No Comercial 3.0 Unported. Esta licencia permite el uso, distribución y reproducción del artículo en cualquier medio, siempre y cuando se otorgue el crédito correspondiente al autor del artículo y al medio en que se publica, en este caso, Medwave.