

**Abstract N°: 6411****Comparative Efficacy of Omalizumab, Dupilumab, and Remibrutinib in Chronic Spontaneous Urticaria: A Network Meta-Analysis of Randomized Control Trials**

Grace Xiong^{*1}, Daniel Rayner², Lauren Kim¹, Susheen Mahmood¹, Tiffany Yu³, Mohannad Abu Hilal⁴

¹McMaster University, Michael G. DeGroote School of Medicine, Hamilton, Canada

²University of Western Ontario, Schulich School of Medicine, London, Canada

³University of Ottawa, Faculty of Medicine, Ottawa, Canada

⁴McMaster University, Division of Dermatology,, Hamilton, Canada

Introduction & Objectives:

Chronic spontaneous urticaria (CSU) is a challenging dermatologic condition characterized by persistent hives and angioedema that significantly impairs quality of life. While omalizumab remains the standard treatment for patients with CSU who have failed antihistamines, emerging therapies have shown promise in randomized control trials (RCTs). However, a lack of direct comparative trials presents challenges in treatment selection. This study aims to compare the relative efficacy of omalizumab, dupilumab, and remibrutinib in CSU through a network meta-analysis (NMA).

Materials & Methods:

Four databases were searched through March 2025 for RCTs evaluating omalizumab (75/150/300 mg Q4W), dupilumab (300 mg Q2W), or remibrutinib (25 mg BID) in CSU. A frequentist random-effects NMA was conducted in R to assess the following outcomes at weeks 12/24: change in 7-day Urticaria Activity Score (UAS7), 7-day Itch Severity Score (ISS7), Dermatology Life Quality Index (DLQI), disease control (UAS7 $\leq$ 6), symptom remission (UAS7 = 0), and no quality-of-life impact (DLQI 0/1).

Results:

Fifteen trials with 4,913 (76.8% female) patients were included. Patients had severe disease activity (mean UAS7: 30.3) and significant itch (ISS7: 14.3) at baseline. CSU also had a very large impact on patient's quality of life at baseline, with a mean DLQI of 13.4.

NMA revealed that Omalizumab 300 mg Q4W consistently demonstrated the greatest effect sizes at efficacy endpoints. It yielded the largest reductions in UAS7 at both 12 weeks (MD -10.04; 95% CI -11.15 to -8.94) and 24 weeks (MD -10.38; 95% CI -14.24 to -6.52). Omalizumab 300 mg Q4W also had the highest odds of achieving symptom remission [ORs: 9.23; 95% CI 6.38-13.35 (week 12), 6.50; 95% CI 2.94-14.37 (week 24)], and disease control [ORs: 7.14; 95% CI 5.17-9.85 (week 12), 6.73; 95% CI 1.84-24.28 (week 24)] at both timepoints. Regarding patient-reported outcomes, omalizumab 300 mg Q4W showed the highest relative ISS7 reductions (week 12 MD -4.14; 95% CI -4.68 to -3.60, week 24 MD -4.53; 95% CI -5.66 to -3.41) and second highest DLQI improvement.

Remibrutinib 25 BID showed the highest DLQI improvement (MD -4.59) and second most favourable reduction in UAS7 (MD -7.48; 95% CI -9.01 to -5.84) and symptom remission (OR: 4.46; 95%CI 2.91-6.84) at 12 weeks. Dupilumab 300 mg Q2W demonstrated good itch control (MD -3.68; 95% CI -5.61 to -1.75) and the second most favourable reduction in UAS7 (MD -7.43; 95% CI -11.25 to -3.60) at 24 weeks, but mixed results in efficacy otherwise. Omalizumab 150mg and 75mg Q4W generally exhibited good efficacy at 12 weeks, but results were not sustained through 24 weeks.

Conclusion: Omalizumab 300 mg Q4W demonstrated the most consistent and durable improvements in disease activity, symptom remission, itch control. Remibrutinib showed promising effects on efficacy and quality of life at 12 weeks, and may be a useful option for patients refractory to omalizumab. These results emphasize the importance of individualized therapy based on patient response and CSU endotype, and highlight omalizumab's continued role as a first-line therapy. Newer options such as remibrutinib and dupilumab appear generally effective, offering promising tools which may help address unmet needs in CSU patients who fail standard treatments. Future studies are warranted to better characterize the role of emerging therapies in patients with CSU who exhibit an inadequate response to higher doses of omalizumab.

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