Comparative efficacy of omalizumab and ciclosporin for chronic spontaneous urticaria

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1 INTRODUCTION

- In Singapore, omalizumab and ciclosporin are used as add-on therapy for antihistamine-resistant chronic spontaneous urticaria (CSU) (Figure 1).

First line:
Second generation H_1-antihistamines

↓ If symptoms persist after 6-8 weeks

Increase dosage of second generation H_1-antihistamines up to four-fold registered dose

↓ If symptoms continue to persist

Second line:
Add-on to H_1-antihistamines: omalizumab or ciclosporin

Figure 1: Treatment algorithm of CSU in Singapore

- This analysis aims to evaluate the comparative efficacy of omalizumab and ciclosporin as add-on therapy for CSU to inform local treatment practices in Singapore.

2 METHODS

- PubMed and EMBASE.com electronic databases were searched up to October 2018 using defined criteria to identify RCTs of omalizumab or ciclosporin as add-on therapy to H_1-antihistamines for CSU.
- A key outcome considered was change in mean weekly Urticaria Activity Score (UAS7).
- Pairwise meta-analysis was conducted for this outcome. Due to differences in trial designs and patient characteristics across studies, a random effects model was employed.
- In the absence of head-to-head trials, Bucher's method of adjusted indirect comparison was used to estimate the comparative effectiveness between omalizumab and ciclosporin, with placebo as the common comparator.

3 RESULTS

- Mean change from baseline in UAS7 score at week 12 was reported in 5 omalizumab studies (Table 1). Only 1 ciclosporin trial reported UAS7 score, but at week 4.
- Pairwise meta-analysis for omalizumab trials were conducted with and without the GLACIAL trial in scenario analyses as the background therapy used in this study was dissimilar to the other trials.

Pairwise meta-analysis: Omalizumab 300mg every 4 weeks vs placebo; UAS7 score at week 12

- Pooled estimate for absolute mean change in UAS7 score at week 12 was statistically larger than placebo (Figure 2), however, clinical significance was uncertain (95% CI did not lie completely beyond the MCID of 9.5 for this outcome).
- Pooled results were similar with or without inclusion of the GLACIAL trial.

Grattan et al (2000): ciclosporin 4mg/kg/day vs placebo; UAS7 score at week 4

- Mean change in UAS7 score at week 4 was statistically larger in the ciclosporin arm compared with placebo, however, the 95% CI was wide, likely due to the small sample size.

Indirect comparison: omalizumab vs ciclosporin

- Results based on mean change in UAS7 score showed that there were no significant differences between the two treatments (Table 2).

Trial name	Background therapy
Omalizumab 300mg every 4 weeks vs placebo	
ASTERIA I (2015)[i]	Approved dose of H_1-antihistamine
ASTERIA II (2013)[ii]	Approved dose of H_1-antihistamine
POLARIS (2017)[iii]	Approved dose of H_1-antihistamine
X-ACT (2016)[iv]	2-4x approved dose of H_1-antihistamine
GLACIAL (2013)[v]	H_1-antihistamine (up to 4x approved dosage) plus H_2-antihistamine, leukotriene antagonist, or both.
Ciclosporin 4mg/kg daily vs placebo	
Grattan et al (2000)[vi]	2x approved dose of H_1-antihistamine

Table 1: Included trials which reported mean change from baseline in UAS7 score

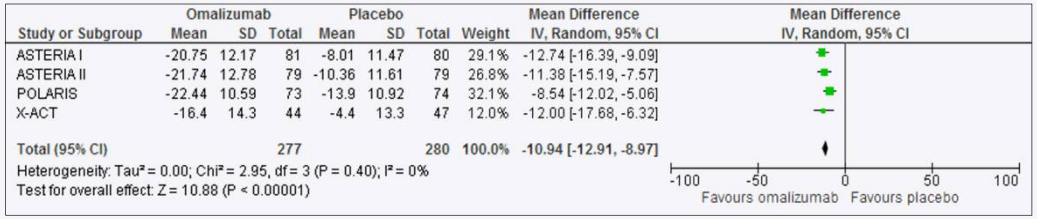

Figure 2: Forest plot of comparison for mean change in UAS7 score at wk 12, omalizumab 300mg vs placebo, excluding GLACIAL trial

Omalizumab 300mg vs placebo*			Ciclosporin vs placebo (from Grattan et al, 2000)			Indirect comparison Omalizumab vs ciclosporin	
N	Mean Change in UAS7	95%CI	N	Mean Change in UAS7	95%CI	Effect Size	95%CI
557	-10.94	-12.91, -8.97	30	-10.4	-17.99, -2.81	**-0.54**	**-8.28, 7.20**

**Results from pairwise meta-analysis of omalizumab trials (excluding GLACIAL trial)*

Table 2: Results of indirect comparison for mean change in UAS7 score

4 DISCUSSION AND CONCLUSION

- Due to differences in trial designs and patient characteristics between the omalizumab and ciclosporin studies, results of the indirect comparison should be interpreted with caution.
- On the basis of similar place in therapy, the results from our analysis, despite being informed by limited evidence, may be useful to confirm the clinical comparability of the drugs and inform local practice in Singapore.

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vi) Grattan C, Donnell BFO, Francis DM. Randomized double-blind study of cyclosporin in chronic 'idiopathic' urticaria. British Journal of Dermatology. 2000;143:365-72.