Review: Omalizumab added to corticosteroids reduces exacerbations and corticosteroid use in adults and children with asthma

Rodrigo GJ, Neffen H, Castro-Rodriguez JA. ***Efficacy and safety of subcutaneous omalizumab vs placebo as add-on therapy to corticosteroids for children and adults with asthma: a systematic review.*** *Chest. 2011;139:28-35.*

Clinical impact ratings: GM ★★★★☆☆ A ★★★★★☆☆ PM ★★★★★☆☆

Question

In adults and children with moderate-to-severe, persistent, allergic asthma, is subcutaneous omalizumab safe and efficacious when added to corticosteroid therapy?

Review scope

Included studies compared subcutaneous omalizumab with placebo as add-on therapy to corticosteroids in children and adults with allergic asthma. Primary outcomes were reduction in corticosteroid use and asthma exacerbations; secondary outcomes included adverse events.

Review methods

MEDLINE, EMBASE/Excerpta Medica (to April 2010), Cochrane Controlled Trials Register (first quarter 2010), and Novartis and US Food and Drug Administration databases were searched for randomized, parallel, placebo-controlled trials. 8 trials (n = 3429) met the inclusion criteria. 6 trials included adolescents and adults only (> 12 y), and 2 also included children (≤ 12 y). All trials were sponsored by the pharmaceutical industry. Omalizumab, 0.016 mg/kg/IU/mL every 2 to 4 weeks, was given as add-on therapy to oral or inhaled corticosteroids for 12 to 28 weeks (stable-steroid phase); in 5 trials, this was followed by an 8- to 28-week steroid-reduction phase. 2 trials met ≥ 4 of 5 quality criteria (risk for bias).

Main results

Meta-analysis showed that patients allocated to omalizumab had lower rates of asthma exacerbations, including hospitalizations for asthma exacerbations, during both the stable-steroid and steroid-reduction phases (Table). Meta-analyses of trials that included a steroid-reduction phase showed that patients allocated to omalizumab were more likely to completely withdraw from corticosteroid therapy or to reduce the dose by > 50% (Table). The omalizumab and placebo groups did not differ for patients reporting serious adverse events (3.8% vs 5.3%, P = 0.14); however, the omalizumab group had higher rates of suspected treatment-related adverse events (5.0% vs 3.2%, P = 0.03), mainly injection-site reactions (20% vs 13%, P = 0.002)

Omalizumab (omal) vs placebo (plac) as add-on therapy to corticosteroids in adults and children with persistent, allergic asthma*

Outcomes	Steroid phase†	Number of trials (n)	Omal	Plac	RRR (95% CI)	NNT (CI)
≥ 1 exacerbation	Stable	8 (3429)	14%	24%	43% (34 to 52)	10 (7 to 13)
	Reduction	5 (2210‡)	17%	31%	45% (35 to 53)	8 (6 to 10)
Hospitalization for exacerbation	Stable	5 (2139‡)	1.7%	4.8%	56% (17 to 48)	33 (22 to 69)
	Reduction	3 (1405‡)	0.13%‡	2.03%‡	86% (34 to 97)	52 (34 to 206)‡
					RBI (CI)	NNT
Complete withdrawal from corticosteroids	Reduction	4 (529‡)	42%	21%	80% (42 to 128)	5 (4 to 6)
> 50% reduction in corticosteroid dose	Reduction	4 (1098‡)	76%	56%	34% (23 to 46)	5 (4 to 6)

**RRR, RBI, NNT, and CI defined in Glossary. All results based on a random-effects model.*

†Stable-steroid phase lasted 12 to 28 wk; in 5 trials, a subsequent steroid-reduction phase lasted 8 to 28 wk.

‡Information provided by author.

Conclusion

In adults and children with moderate-to-severe, persistent, allergic asthma, subcutaneous omalizumab added to corticosteroid therapy reduces exacerbations; patients allocated to omalizumab are more likely to completely withdraw from corticosteroid therapy.

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Commentary

Clinical asthma is heterogeneous in patterns of onset, triggers, natural history, and response to therapy. As a result, asthma is now regarded as several diseases that share a common clinical manifestation (1). The advent of biological treatments with monoclonal antibodies has enabled targeting of underlying, specific, pathogenetic mechanisms rather than just treating end-organ (airway smooth muscle) manifestations. The most promising therapies with this approach are anti-IgE (omalizumab) and anti-IL5 (mepolizumab).

Rodrigo and colleagues conducted a meta-analysis of 8 RCTs that included both children and adults and found omalizumab to be efficacious and safe. However, immunomodulation therapies have the potential to cause opportunistic infections or cancer, and the studies included in the meta-analysis all lasted ≤ 1 year. It is, however, encouraging that other, albeit small, studies have shown sustained and progressive benefit with up to 7 years of maintenance therapy (2). Prolonged clinical remissions for ≥ 3 years have also been reported, even after maintenance omalizumab has been stopped (3).

Although the findings on short-term use of omalizumab have been reassuring, wider and more prolonged use is needed to judge its longer-term safety. Further, because of heterogeneity in disease pathophysiology, the efficacy of omalizumab is likely to depend on asthma phenotype. Finally, although omalizumab may not dramatically improve measurable lung function, it represents an important therapeutic addition by reducing asthma exacerbations and improving quality of life in selected patients.

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References

1. **Anderson GP.** Endotyping asthma: new insights into key pathogenic mechanisms in a complex, heterogeneous disease. Lancet. 2008;372:1107-19.
2. **Pace E, Ferraro M, Bruno A, et al.** Clinical benefits of 7 years of treatment with omalizumab in severe uncontrolled asthmatics. J Asthma. 2011;Mar 11:[Epub ahead of print].
3. **Nopp A, Johansson SG, Adédoyin J, et al.** After 6 years with Xolair; a 3-year withdrawal follow-up. Allergy. 2010;65:56-60.