Biologics for type 2 severe asthma: What is the evidence?

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Overview of key clinical trials evaluating biologics in patients with type 2 severe asthma

Drug[1]	Patient population in key clinical trials
Omalizumab[2] • Initial biologic approved for use in asthma • Binds to IgE	**Severe uncontrolled allergic asthma** • N=850 patients aged 12–75 years who had inadequately controlled severe allergic asthma despite treatment with high-dose ICS plus LABAs, with or without other controllers
Mepolizumab[3] • First anti-IL-5 antibody approved for use in asthma	**Severe uncontrolled eosinophilic asthma** • Patients (N=61) who had ≥2 severe exacerbations exacerbations in the previous year despite receiving high-dosage ICS, all subjects had markers of eosinophilic airway inflammation
Reslizumab[4] • Reslizumab uses a “cut-off” value for eosinophils of 400 cells/µl • Directed against IL-5	**Severe uncontrolled eosinophilic asthma** • N=953 patients aged 12–75 years with uncontrolled moderate-to-severe asthma who had ≥1 exacerbation in the previous year despite treatment with medium- or high-dose ICS and with blood eosinophil counts ≥400 cells/µl
Benralizumab[5] • Directed against the IL-5R	**Severe uncontrolled eosinophilic asthma** • N=1,306 patients aged 12–75 years with uncontrolled severe asthma with elevated blood eosinophil counts who had ≥2 exacerbations in the previous year despite receiving high dose ICS plus LABA
Dupilumab[6] • Directed against the IL-4R and also blocks IL-13 activation	**Severe uncontrolled eosinophilic asthma** • N=1,902 patients ≥12 years with uncontrolled moderate-to-severe asthma with elevated blood eosinophil counts who had ≥1 exacerbation in the previous year despite treatment with a medium- to high-dose ICS plus LABA/LTRA

ICS, inhaled corticosteroids; IgE, immunoglobulin-E; IL, interleukin; IL-4R, IL-4 receptor; IL-5R, IL-5 receptor; LABAs, long-acting beta agonists; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroids.

1. Busse WW. *Allergol Int.* 2019;68:158–66; 2. Hanania NA, et al. *Ann Intern Med.* 2011;154:573–82; 3. Haldar P, et al. *N Engl J Med.* 2009;360:973–84; 4. Castro M, et al. *Lancet Respir Med.* 2015;3:355–66; 5. FitzGerald JM et al. *Lancet*. 2016;388:2128–41; 6. Castro M et al. *N Engl J Med*. 2018;378:2486–96.

Overview of key efficacy findings

Drug[1]	Asthma exacerbation[1]	Lung function[1]	Corticosteroid weaning[1]
Omalizumab	Reduces by 25%	Minimal or equivocal improvement	Decreases use of ICS, but no data that it helps with OCS weaning
Mepolizumab	Reduces by ~50%	Inconsistent effect	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (14%)
Reslizumab	Reduces by ~50–60%	Improved	Has not been specifically evaluated for this indication
Benralizumab	Reduces by ~25–60%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)
Dupilumab	Reduces by ~50–70%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)

ICS, inhaled corticosteroids; OCS, oral corticosteroids.

1. Mc Gregor MC et al. *Am J Respir Crit Care Med.* 2019;199:433–45.

Overview of key efficacy and safety findings

Drug[1]	Asthma exacerbation[1]	Lung function[1]	Corticosteroid weaning[1]	Safety[2]
Omalizumab	Reduces by 25%	Minimal or equivocal improvement	Decreases use of ICS, but no data that it helps with OCS weaning	• Reactions at the site of injection are common, but minor • Anaphylaxis is rare
Mepolizumab	Reduces by ~50%	Inconsistent effect	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (14%)	• Headache and reactions at the site of injection are common, but minor
Reslizumab	Reduces by ~50–60%	Improved	Has not been specifically evaluated for this indication	• Headache and reactions at the site of injection are common, but minor
Benralizumab	Reduces by ~25–60%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)	• Headache and reactions at the site of injection are common, but minor
Dupilumab	Reduces by ~50–70%	Improved	Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)	• Reactions at the site of injection are common, but minor • Blood eosinophilia occurs in 4-13% of patients

ICS, inhaled corticosteroids; OCS, oral corticosteroids.

1. Mc Gregor MC et al. *Am J Respir Crit Care Med.* 2019;199:433–45. 2. Global Initiative for Asthma, 2019. Available at www.ginasthma.org (Accessed March 2020).

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Can patient characteristics help to inform treatment decisions?

- The use of patient characteristics to inform treatment decisions is still unclear

The 2019 GINA guidelines note that:

Anti-IgE	Anti-IL-5 or anti-IL-5R	Anti-IL-4R
• May be beneficial for those patients with **severe allergic asthma**	• May be beneficial for patients whose severe asthma is **predominantly mediated by eosinophils**	• May be beneficial for patients for whom luminal obstruction and severity may be driven by factors such as **mucus production, eosinophils, and smooth muscle contraction and remodelling**

Ig, immunoglobulin; IL:, interleukin; IL-4R, IL-4 receptor; IL-5-R; IL-5 receptor.
Global Initiative for Asthma, 2019. Available at www.ginasthma.org (Accessed March 2020).

Guidelines for managing patients with CRSwNP

- Patients with severe asthma and CRSwNP may have a worse prognosis[1]

2019 GINA guidelines for patients with evidence of type 2 inflammation and CRSwNP suggest:[2]

1. Consider non-biologic treatments

- Consider clinical type 2 phenotypes for which specific add-on treatment is available
- For CRSwNP, consider intensive intranasal corticosteroids; surgical advice may be needed

2. Consider add-on biologic type 2 targeted treatments

- Add-on treatment with anti-IL-5, mepolizumab, for severe eosinophilic asthma may improve CRSwNP
- CRSwNP is a factor that may predict good asthma response to anti-IL-5/anti-IL-5R therapy
- The anti-IL-4R, dupilumab, may be used to treat CRSwNP

CRSwNP, chronic rhinosinusitis with nasal polyps; GINA, Global Initiative for Asthma; IL, interleukin; IL-4R, IL-4 receptor; IL-5-R; IL-5 receptor.

1. Langdon C, Mullol J. *J Asthma Allergy.* 2016;9:45–53; 2. Global Initiative for Asthma, 2019. Available at www.ginasthma.org (Accessed March 2020).