Evidence Table 13. Pharmacologic Therapy: Immunomodulators—Anti-Immunoglobulin E

Abbreviations used in table:

AE	**adverse event**
BDP	**beclomethasone dipropionate**
Der f	***Dermatophagoides farinae***
Der p	***Dermatophagoides pteronyssinus***
EAACI	**European Academy of Allergology and Clinical Immunology**
FEV_1	**forced expiratory volume in 1 sec**
HD	**high dose**
ICS	**inhaled corticosteroid**
IgE	**immunoglobulin E**
ITT	**intent-to-treat**
LABA	**long-acting beta-agonist**
NNT	**number needed to treat**
O	**omalizumab**
P	**placebo**
$PD_{20}FEV_1$	**cumulative dose of methacholine producing a 20% decrease in FEV_1**
PEF	**peak expiratory flow**
QoL	**quality of life**
SAE	**severe adverse event**
SD	**standard deviation**
SIT	**specific immunotherapy**

*** indicates primary outcome**

Evidence Table 13. Pharmacologic Therapy: Immunomodulators—Anti-Immunoglobulin E

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Taper/Decrease Steroids	Lung Function	Exacerbations/Symptoms	Other
Boulet et al. Inhibitory effects of an anti-IgE antibody E25 on allergen-induced early asthmatic response. Am J Respir Crit Care Med 1997;155(6): 1835–1840. (Genentech Inc.)	Multicenter, randomized, double-blind, parallel-group, placebo-controlled trial	To document safety and tolerance of rhuMAb-E25 and determine if it reduces the early asthmatic response of inhaled aeroallergens	20 (19—1 withdrawal from treatment group)	**Age** 21–44 yr; mean = 27.4 yr (SD=8.1) **Gender** 12 male, 8 female **Ethnicity** Not reported Highly positive allergy skin-prick test to at least 1 common aeroallergen and early asthmatic response on allergen inhalation in lab	Stable, mild, allergic asthma requiring only an inhaled beta$_2$-agonist on demand FEV_1 % pred. mean = 91.9 (SD=11.07)	**Arm 1** RhuMAb-E25 **Arm 2** Placebo	0.4 mL/kg on day 0; 0.2 mL/kg on days 7, 14, 28, 42, 56, and 70 (2.0 mg/kg IV)	10 weeks treatment, 1 week off-treatment followup			Mean serum-free IgE decreased 89% after rhuMAb-E25 ($p < 0.001$); no change occurred in placebo group. Allergen PC_{15} improved significantly after rhuMAb-E25 but not after placebo ($p < 0.002$). Median change of 2.7 doubling doses	*Safety: 1 withdrawal after first dose, probably related to study drug *High BDP dose (≥800 mcg/day), history of emergency asthma treatment in past year, and FEV_1 ≤65% pred. were predictive of greater probability of response.
Fahy et al. The effect of an anti-IgE monoclonal antibody on the early- and late-phase responses to allergen inhalation in asthmatic subjects. Am J Respir Crit Care Med 1997;155(6): 1828–1834. (Genentech Inc.)	Double-blind, placebo-controlled, randomized parallel group study	To examine the effects of neutralizing IgE on allergic airway responses	19 (18)	**Age** Mean = 31.5 yr Total serum IgE, mean = 142 IU/L	Mild asthma requiring only inhaled beta$_2$-agonists FEV_1 % pred., mean = 94	Arm 1 rhuMAb-E25 (n=10; 1 withdrawal) Arm 2 Placebo (n=9)	5 mg/mL by 5-min IV (0.1 mL/kg) 150 mM NaCl, 10 mM acetate, pH 5.2 by 5-min IV	9 weeks treatment, 1 week followup		*Trend was in favor of omalizumab for difference in FEV_1. RhuMAb-E25 significantly attenuated both early- and late-phase responses to airway challenge with allergen; reduced mean FEV_1 from 30% to 18.8% vs. 33% to 34% ($p=0.01$) during early phase and from 24% to 9% vs. 20% to 18% during late response ($p=0.047$)	PC_{20} for methacholine improved, but not significantly. Free IgE concentrations in serum decreased significantly in rhuMAb-E25 group as compared to placebo group ($p < 0.001$).	1 subject was withdrawn from rhuMAb-E25 treatment at 4 weeks because of asthma exacerbation.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline(If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Taper/ Decrease Steroids	Lung Function	Exacerbations/ Symptoms	Other
Milgrom et al. Treatment of allergic asthma with monoclonal anti-IgE antibody. N Engl J Med 1999;341(26): 1966–1973. (Genentech Inc.)	Multicenter, randomized, double-blind, placebo-controlled trial	To examine the efficacy of rhuMAb-E25 as a treatment for allergic asthma	317 (306)	Age 11–50 yr, mean = 30 yr (54 adolescents) Gender 42% male, 58% female Ethnicity Not reported Total serum IgE 17–1,957 IU/mL	Moderate-to-severe perennial allergic asthma FEV1 % pred., mean = 71; range, 29–129 Mean asthma symptom score = 4.0 (range, 1.5–6.5 out of 1–7) Daily use of beta2-agonist bronchodilator as rescue medication Median duration of asthma, 19 yr	Arm 1 High dose (HD) rhuMAb-E25 (n=106; 103 >4 weeks) Arm 2 Low dose (LD) rhuMAb-E25 (n=106; 103 >4 weeks) Arm 3 Placebo (n=105; 100 >4 weeks)	5.8 mcg/kg/ng IgE/mL 2.5 mcg/kg/ng IgE/mL	20 weeks: 12 weeks of continued ICS and half dose of treatment on days 0 and 4, full dose on day 7 and then once every 2 weeks; For 8 weeks, treatment continued and ICS was tapered. 10 weeks of followup	After 12 weeks, albuterol use reduced by 1.8 puffs/day in HD group (p=0.02) and by 1.2 puffs/day in LD group (p=0.24) vs. 0.8 puffs/day in placebo group. Decreases were maintained at 20 weeks.	PEF favored treatment at all points (p <0.01); FEV1 % pred. was significantly higher for treatment group between weeks 4 and 12 and between weeks 18 and 28. Morning PEF increased 30.7 L/min in HD group (p=0.007) and 18.6 L/min in LD group vs. 11.3 L/min in placebo group. At 20 weeks, increase from baseline was 29.9 L/min in HD group (p=0.02), 20.8 L/min LD group (p=0.046), and 10.2 L/min in placebo group.	30% HD (p=0.03) and 28% LD groups (p=0.01) had exacerbations vs. 45% of placebo group. *Asthma symptom score at 12 weeks: 2.8 for HD group and 2.8 for LD group vs. 3.1 for placebo group (p=0.008 and p=0.005, respectively)	3 HD, 3 LD, and 8 placebo subjects withdrew due to AE.
Busse et al. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. J Allergy Clin Immunol 2001; 108(2): 184–190. (Novartis Pharmaceuticals Corp. and Genentech, Inc.)	Multicenter, double-blind, placebo-controlled, randomized Phase III trial	To assess the efficacy and tolerability of subcutaneous omalizumab in adolescents and adults with severe allergic asthma whose disease was not adequately controlled with ICS	525 (525; 53 dropouts)	**Age** 12–74 yr; mean = 39.2 **Gender** 41% male, 59% female **Ethnicity** 89% Caucasian, 7% Black, 4% other Total serum IgE, 20–860 IU/mL (mean = 179)	Severe allergic asthma requiring daily ICS Duration 1–61 yr, mean = 21.6 yr FEV_1 % pred., mean = 68.0 BDP dose, 336–1008 mcg/day; mean = 569 mcg/day	**Arm 1** Omalizumab (n=268; 19 withdrawals) **Arm 2** Placebo (n=257; 34 withdrawals)	0.016 mg/kg IgE (IU/mL) every 4 weeks for 16 weeks; approximately 25% reduction every 2 weeks for weeks 16–28 Rescue albuterol, maximum of 8 puffs/day was allowed.	28 weeks (16-week stable phase, 12-week reduction phase)	Median reduction in ICS dose was greater in omalizumab group (75% vs. 50%, p <0.001). ≥50% reduction in BDP dose for 72.4% of omalizumab group vs. 54.9% of placebo group (p <0.001) BDP was discontinued in 39.6% of omalizumab and 19.1% of placebo group (p <0.001).		*Stable phase: 14.6% of intervention vs. 23.3% of placebo group experienced exacerbations (p=0.009), with mean of 0.28 vs. 0.54 (p=0.006) exacerbations, respectively. Reduction phase: 21.3% of intervention vs. 32.3% of placebo group experienced exacerbations (p=0.004), with average of 0.39 vs. 0.66 (p=0.003) exacerbations. Total IgE increased in treatment group and did not change in placebo group.	At 28 weeks, 60.6% of treatment vs. 28.1% of placebo patients rated treatment effectiveness as good or excellent (p <0.001).

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Taper/Decrease Steroids	Lung Function	Exacerbations/Symptoms	Other
Milgrom et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). Pediatrics 2001; 108(2):E36. (Genentech, Inc.; Novartis Pharmaceuticals Corp.)	Randomized, double-blind, placebo-controlled, parallel-group design	To evaluate the safety and steroid-sparing effect of omalizumab and its impact on asthma exacerbations in children with moderate to severe allergic asthma who require daily treatment with ICSs	334 (334)	**Age** 5–12 yr, mean = 9.4 yr **Gender** 69.2% male, 30.8% female **Ethnicity** White, 76.0%, Black, 15.6%, other, 8.4%	Moderate-to-severe allergic asthma Duration of allergic asthma: range, 1–12 yr; mean = 6.1 yr BDP dose: range, 168–672 mcg/day; mean = 278 mcg/day Serum total IgE: range, 20–1269 IU/mL; mean = 340 IU/mL FEV_1 % pred.: range, 43–129; mean = 84 FEV_1 reversibility, mean = 20.1% Morning PEF: range, 101–408 L/min; mean = 262 L/min Hospitalized for asthma in past year, 8.1% All children had minimal asthma symptoms, with mean rescue albuterol use <2 puffs/day.	**Arm 1** Omalizumab (O) (n=225; n=209 completers) **Arm 2** Placebo (P) (n=109; n=97 completers)	Subcutaneous dose, based on body weight and initial minimum of 0.016 mg/kg/IgE (IU/mL), per 4 weeks, was based on dosing chart for 16 weeks; dose was tapered approximately 25% of baseline dose every 2 weeks until elimination or worsening of asthma.	16-week stable-steroid phase and 12 weeks of steroid dose-reduction phase after 4- to 6-week run-in phase All children switched from ICS to equivalent dose of BDP for asthma control. Salbutamol 2 puffs (90 mcg/puff ex mouthpiece equal to 100 mcg/puff ex valve) was used as needed, with maximum 8 puffs/day, for rescue medication.	Greater proportion of O reduced ICS dose vs. P (p=0.001). Median reduction in dose was 100% in O vs. 66.7% in P. BDP withdrawal was completed in 55% of O group vs. 39% of P group (p=0.004).	Little change occurred in morning PEF, FEV_1, FVC, or $FEF_{25\%–75\%}$ during either phase, with minimal difference between groups.	During treatment phase, incidence of exacerbations was lower for O vs. P group (18.2% vs. 38.5%, p <0.001), and number of episodes/patient was lower for O vs. P group (0.42 vs. 2.72, p <0.001). Mean duration of episodes was similar in groups during both phases (range, 10–14 days). Fewer subjects in O vs. P group required urgent unscheduled physician visit (12.9% vs. 30.3%, p=0.001). At week 28, median number of puffs/day of rescue medication was 0 in O group and 0.46 in P group; change from baseline favored O treatment (p=0.004).	No treatment-related SAE occurred. Drug-related AEs were more frequent in O vs. P subjects (6.2% vs. 0.9%, p=0.029). Investigators' global evaluation of effectiveness favored O vs. P treatment (p <0.001): excellent for 31.5% of O group vs. 16.3% of P group and good for 44.7% of O group vs. 32.7% of P group. Fewer missed school days occurred for O vs. P subjects (0.65 vs. 1.21 days, p=0.040).
Soler et al. The anti-IgE antibody omalizumab reduces exacerbations and steroid requirement in allergic asthmatics. Eur Respir J 2001;18 (2):254–261. (Novartis Pharma AG and Genentech Inc.)	Multicenter, randomized, double-blind, placebo-controlled, parallel-group study	To evaluate the efficacy, safety, and corticosteroid-sparing effect of omalizumab administered subcutaneously in allergic asthma	546 (487)	**Age** 12–76 yr, mean = 39.5 yr **Gender** 49% male, 51% female **Ethnicity** Not reported Total serum IgE: range, 21–814 IU/mL, mean = 214.4 IU/mL	Moderate-to-severe allergic asthma, symptomatic despite ICS (500–1,200 mcg/day BDP) Mean duration of asthma, 19.7 yr; range, 1–68 yr	**Arm 1** Omalizumab (n=274; 19 withdrawals) **Arm 2** Placebo (n=232; 40 withdrawals)	0.016 mg/kg IU IgE/mL every 4 weeks Rescue salbutamol of 100 mcg/puff was allowed throughout the study.	28 weeks, after 4- to 6-week run-in 16-week stable steroid phase, then 8-week reduction phase, and lowest dose held for 4 weeks	Proportion able to reduce BDP dose was higher at end of steroid-reduction phase compared to stable-steroid phase higher in omalizumab group (p <0.001). Reduction in BDP ≥50% was achieved for 79% of omalizumab group and 55% of placebo group.	FEV_1 was significantly higher for omalizumab than placebo patients between weeks 18 and 28 (ITT analysis). PEF values favored omalizumab at all time points of the stable-steroid phase (ITT analysis).	*Omalizumab group had 58% fewer exacerbations per patient vs. placebo group during stable-steroid phase (p <0.001) and 52% fewer exacerbations during steroid-reduction phase (p <0.001).	Suspected drug-related AE events for 1.1% of omalizumab group; none were serious.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Taper/Decrease Steroids	Lung Function	Exacerbations/Symptoms	Other
Walker et al. Anti-IgE for chronic asthma. Cochrane Database Syst Rev 2002;(3): CD003559. (Garfield Weston Foundation UK ; NHS Research and Development UK ; The Thriplow Charitable Trust UK)	Meta-analysis of randomized, double-blind, parallel-group controlled trial Methodological quality as assessed by Jadad scale was fair to high (three scored 3, three scored 4, two scored 5).	To compare the clinical outcomes in studies that have compared anti-IgE monoclonal antibodies to placebo or other conventional therapy in the treatment of chronic asthma	8 trials; n=2,037	**Age** 6–12 yr (1 trial, n=334), ≥12 yr (7 trials, n=1,703)	Mild (3 trials), moderate to severe (4 trials), and severe asthma (1 trial)	**Arm 1** Omalizumab (O) **Arm 2** Placebo (P)	Intravenous route: 5.8 mcg/kg/ng IgE/mL, 2.5 mcg/kg/ng IgE/mL Inhaled route: 1 mg or 10 mg Subcutaneous route: 0.016 mg/kg/IU/mL	12–16 weeks (stable-steroid phase) followed by steroid-reduction phase Extension phase (2 trials)	*Subcutaneous O vs. P during steroid-reduction phase:* Achieving complete ICS withdrawal, OR 2.50, 95% CI 2.00 to 3.13 (4 trials, n=1,534); achieving >50% reduction in ICS usage, OR 2.50, 95% CI 2.02 to 3.10 (4 trials, n=1,645)	*Subcutaneous O vs. P during stable steroid phase:* No difference found in FEV_1 (2 trials, n=1,071) or PEF (4 trials, n=1,651). *Intravenous O vs. P*: No difference found in FEV_1 or PEF (2 trials, n=39).	*Subcutaneous O vs. P during stable-steroid phase:* Number with exacerbations, OR 0.46, 95% CI 0.35 to 0.61 (3 trials, n=1,405); asthma exacerbations/patient, diff. –0.19, 95% CI –0.29 to –0.09 (4 trials, n=1,651); rescue puffs/day, diff. –0.73, 95% CI –10.7 to –0.39 (2 trials, n=1,071); symptom scores diff. –0.48, 95% CI –0.67 to –0.28 (2 trials, n=1,071). *Subcutaneous O vs. P during steroid-reduction phase:* Number with exacerbation, OR 0.46, 95% CI 0.36 to 0.59 (3 trials, n=1,388); exacerbations requiring hospitalization, OR 0.11, 95% CI 0.03 to 0.48 (3 trials, n=1,405); exacerbations/patient, diff. –0.27, 95% CI –0.38 to –0.17 (4 trials, n=1,634); rescue puffs/day, diff. –0.73, 95% CI –1.06 to –0.40 (2 trials, n=1,071) *Intravenous O vs. P*: No difference in rescue medication use 1 week after end of treatment or in symptom scores (2 trials, n=39)	Reductions in serum free IgE ranged from 89% to 99% in all trials, despite different dosing regimens.
Berger et al. Evaluation of long-term safety of the anti-IgE antibody, omalizumab, in children with allergic asthma. Ann Allergy Asthma Immunol 2003;91(2): 182–188. (Novartis Pharmaceuticals Corp.)	Randomized, double-blind, placebo-controlled trial (only treatment group reported here)	To evaluate the long-term effects of the anti-IgE antibody omalizumab in children with asthma treated for full 52 weeks	225 (225)	**Age** 5–12 yr; mean = 9.4 **Gender** 70% male, 30% female **Ethnicity** 75% Caucasian, 17% Black, 8% other Total serum IgE: range, 30–1,300 IU/mL (mean = 348); body weight ≤90 kg 18% hospitalized for asthma in past year	204 moderate (FEV_1 % pred. >65%); 21 severe (FEV_1 % pred. ≤65%) Duration: range, 1–12 yr; mean = 6.1 yr Asthma well controlled ≥3 months with ICS doses equivalent to 168–420 mcg/day of BDP	**Arm 1** Omalizumab (n=225) **Arm 2** Placebo (not included in this report)	0.016 mg/kg/IgE (IU/mL) per 4 weeks	28-week treatment, 24-week open-label extension, 12 weeks off study drug.		FEV_1 remained stable	81.4% did not require other medication. No change occurred in mean BDP dosage No anti-omalizumab antibodies were detected; no clinically significant changes occurred in vital signs. Log_{10} methacholine PC_{20} was significant ($p < 0.05$) after treatment (change of 0.9 doubling doses); no change was found after placebo.	*Adverse events: 93% experienced AE unrelated to drug; 6.7% AE were suspected as related to drug (1 SAE resolved in 20 minutes).
Corren et al. Omalizumab, a recombinant humanized anti-IgE antibody, reduces asthma-related emergency room visits and hospitalizations in patients with allergic asthma. J Allergy Clin Immunol 2003; 111(1):87–90. (Novartis Pharma AG; Genentech, Inc.)	Pooled analysis of 3 multicenter, randomized, double-blind, placebo-controlled trials	To investigate the effect of omalizumab (Xolair) a recombinant humanized monoclonal anti-IgE antibody, on the rate of serious exacerbations during long-term therapy	1,405 (1,405)	**Age** ≥12 yr (2 studies, n=1,071); ages 6–12 yr (1 study, n=334) **Gender** Not reported **Ethnicity** Not reported	Moderate-to-severe allergic asthma Duration of asthma, ≥1 yr Total serum IgE level: range, 30–700 IU/mL (adolescents/adults) or 30–1,300 IU/mL (children) Required daily ICSs Positive skin-prick test to dust mite, cockroach, dog, or cat	**Arm 1** Omalizumab (O) (n=767) **Arm 2** Placebo (P) (n=638)	Subcutaneous injection every 2 or 4 weeks, dosed according to body weight and baseline IgE (≥0.016 mg/kg/IgE [IU/mL] every 4 weeks)	12 months. Dosages of BDP were stable over initial 16 weeks (steroid-stable phase) and reduced over 8 weeks (25% every 2 weeks), with lowest effective dose maintained for 4 weeks (steroid-reduction phase). Minimum effective dose was maintained for 24 weeks (extension phase).			*Incidence rate of unscheduled visits was lower for O group vs. P group (21.3 vs. 35.5 per 100 patient-yr; RR 0.60, 95% CI 0.44 to 0.81, p <0.01). *Incidence rate of ED treatment for exacerbation was lower for O vs. P group (1.8 vs. 3.8 per 100 patient-yr; RR 0.47, 95% CI 0.24 to 1.01, p=0.05). *Incidence rate of asthma-related hospitalization was 92% lower in O vs. P group (0.26 vs. 3.42 per 100 patient-yr, RR 0.08, 95% CI 0 to 0.25, p <0.01). Mean number of days per asthma-related hospitalization for O group was less than for P group (2.00 vs. 5.39, p=0.15).	

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Taper/Decrease Steroids	Lung Function	Exacerbations/Symptoms	Other
Ayres et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with poorly controlled (moderate-to-severe) allergic asthma. Allergy 2004;59(7): 701–708.	Multicenter, randomized, open-label, parallel-group study 49 centers in 5 European countries	To investigate the efficacy and tolerability of omalizumab in patients with poorly controlled allergic asthma in an open-label study in which omalizumab was added to and compared against best standard care (BSC) as defined by the NHLBI	312 (ITT analyses)	**Age** 12–73 yr, median 38 yr **Gender** 29% male, 71% female **Ethnicity** Not reported Serum IgE: range, 27–686 IU/mL; median, 167 IU/mL (treatment group only)	Poorly controlled, moderate-to-severe allergic asthma; receiving treatment at steps 3 and 4 of NHLBI guidelines 78% receiving LABA 91% with at least 1 emergency room visit in previous year FEV_1 % pred.: range, 15–139; median = 71 Mean Wasserfallen asthma symptom score = 17.3	**Arm 1** BSC with omalizumab (n=206) **Arm 2** BSC without omalizumab (n=106)	0.016 mg/kg/IgE (IU/mL) per 4 weeks Rescue salbutamol was permitted throughout the study.	52 weeks	Patients treated with omalizumab (n=173) reduced mean daily dose of ICS (–342 mcg/day), and those with BSC alone showed slight increase (+68 mcg/day), p <0.001.	Significant difference in FEV_1 of 2.48 L for omalizumab vs. 2.28 L for BSC alone, p=0.02	*Those treated with omalizumab experienced 4.84 fewer asthma deterioration-related incidents (ADRI) vs. those treated with BSC alone (49.6% reduction); 36.1% vs. 20.2%, respectively, remained ADRI-free during the study. Median time to first ADRI was 126 vs. 75 days, respectively (p=0.03). Lower annualized mean number of exacerbations with occurred with omalizumab than BSC alone (1.12 vs. 2.86, p <0.001). 49.5% omalizumab subjects vs. 26.4% BSC only were exacerbation free (p=0.001).	Percentage of AE was not significantly different between groups (p=0.116). 48 patients (16.5% of omalizumab group and 13.2% of BSC group) experienced SAE during study.
Bousquet et al. Predicting response to omalizumab, an anti-IgE antibody, in patients with allergic asthma. Chest 2004;125(4): 1378–1386. (Novartis Pharma AG and Genentech, Inc.)	Multicenter, double-blind, randomized, placebo-controlled Phase III study [combined data from Busse et al. (2001) and Solèr et al. (2001)]	To determine baseline characteristics predictive of best response to omalizumab therapy for allergic asthma, time to onset of response, and how long patients need to be treated before a response could be accurately predicted	1,070 (1,070)	**Age** 12–76 yr; mean = 39.4 **Gender** 43% male, 57% female **Ethnicity** Not reported Total serum IgE, 30–860 IU/mL (mean = 197); 41% with history of emergency asthma treatment in past year	Symptomatic allergic asthma with daily doses of BDP (200–2,000 mcg/day; mean = 725 mcg/day,) Duration,1–68 yr, mean = 20.6 yr FEV_1 % pred., mean = 69; 21.5% with FEV_1 ≤65% pred.	**Arm 1** Omalizumab (n=542) **Arm 2** Placebo (n=528)	0.016 mg/kg/IgE subcutaneously every 4 weeks in addition to stable BDP therapy Rescue BDP and albuterol were permitted.	16 weeks		Significant improvements in FEV_1 in the treatment group as compared to placebo group were maintained for the entire study (p values ranged from <0.001 to 0.019).	Time to exacerbation was longer for omalizumab patients (p <0.001). Probability of exacerbation by week 16 was 30% for placebo subjects and 16% for omalizumab subjects.	Odds of being responder were 2.25 times higher (95% CI, 1.68 to 3.01) with omalizumab than with placebo. 61% of responders at 16 weeks had responded at 4 weeks and 87% had responded by 12 weeks.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Taper/Decrease Steroids	Lung Function	Exacerbations/Symptoms	Other
Djukanovic et al. Effects of treatment with anti-immunoglobulin E antibody omalizumab on airway inflammation in allergic asthma. Am J Respir Crit Care Med 2004; 170(6): 583–593.	Multicenter, randomized, double-blind, placebo-controlled, parallel-group design (5 centers)	To determine whether omalizumab has anti-inflammatory effects in the airways of patients with allergic asthma	45 (42)	**Age** 19–48 yr, median = 26 yr **Gender** 47% male, 53% female **Ethnicity** Not reported	Stable asthma: 30 (66.7%) with mild asthma, 15 (33.3%) with moderately severe asthma Duration >1 yr Treatment with inhaled beta$_2$-agonists only No acute exacerbations for at least 6 weeks Positive skin-prick test for at least 1 of the following allergens: house- dust mite, cockroach, dog, or cat PC_{20} value, <8 mg/mL Sputum eosinophilia >2% or more of total nonsquamous cells	**Arm 1** Omalizumab (O) (n=22; n=21 completers) **Arm 2** Placebo (P) (n=23; n=22 completers)	150–300 mg every 4 weeks or 225–375 mg every 2 weeks on the basis of concentration of serum total IgE and body weight at baseline	16 weeks after run-in period of 3 weeks		No difference in change in airway responsiveness (p=0.14) was found between groups. In O group, PC_{20} changed from 1.01 to 0.73 mg/mL (p=0.47); in P group PC_{20} changed from 0.54 to 0.67 (p=0.26).	*Mean percent of eosinophils in induced sputum decreased from 6.6% to 1.7% for O group (p <0.001) and from 8.5% to 7.0% for P group (p >0.05). Difference in change between groups was –4.6% (p=0.05). Between-group differences for O vs. P for were: eosinophils in submucosa (p=0.03); IgE$^+$ cells in epithelium (p=.001) and submucosa (p <0.001); CD3$^+$ (p=0.01), CD4$^+$ (p=0.005), and CD8$^+$ (p=0.05); T lymphocytes and B lymphocytes (p=0.02).	
Holgate et al. Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma. Clin Exp Allergy 2004;34(4): 632–638. (Novartis Pharma AG and Genentech Inc.)	Multicenter, randomized, double-blind, placebo-controlled trial	To evaluate the ability of omalizumab to improve disease control to enable ICS reduction in patients with severe allergic asthma	246 (22 dropouts; ITT analysis)	**Age** 12–75 yr, mean = 40.8 yr **Gender** 39% male, 61% female **Ethnicity** Not reported Total serum IgE, 20–700 IU/mL	Severe asthma requiring ≥1,000 mcg/day fluticasone for symptom control and positive SPTs to aeroallergen/s FEV_1 % pred., mean = 64	**Arm 1** Omalizumab (n=126; 115 completed) **Arm 2** Placebo (n=120; 109 completed)	0.016 mg/kg/IgE (IU/mL) every 4 weeks Beta$_2$-agonists were allowed as needed.	32 weeks, after 6- to 10-week run-in period followed by 16-week corticosteroid-reduction phase	*Patients receiving omalizumab had greater mean reduction in fluticasone dose as compared to those receiving placebo (57.2% vs. 43.3%, p=0.003), with 73.8% vs. 50.8% achieving ≥50% dose reduction (p=0.001). Median reduction in prednisone was 50% in high dose (p=0.045) and 65% in low dose (p=0.11) groups vs. 0% in placebo. 21.4% vs. 15.0% with 100% reduction (p=0.198)	Trend in favor of omalizumab for FEV_1 throughout; trend was significant at weeks 4, 20, 28, and 30.	Difference in reduction of exacerbation rates did not reach statistical significance. 58% of omalizumab vs. 39% of placebo patients had improvement in asthma-related QoL (p <0.01).	1 omalizumab and 5 placebo patients had SAE not considered drug related. Completer rates were 91.3% for omalizumab and 90.8% for placebo group.

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Taper/Decrease Steroids	Lung Function	Exacerbations/Symptoms	Other
Noga et al. Immunological and clinical changes in allergic asthmatics following treatment with omalizumab. Int Arch Allergy Immunol 2004;131 (1): 46–52.	Substudy of a multicenter, randomized, double-blind, placebo-controlled, parallel-group trial	To strengthen previous findings by using more sensitive parameters of lung function and to define factors and mediators involved in immunological and cellular reactions in order to improve our understanding of the mode of action of omalizumab	35 (35)	**Age** 23–61 yr, mean = 37.5 yr **Gender** 54% male, 46% female **Ethnicity** Not reported	Moderate-to-severe allergic asthma Duration ≥1 yr FEV_1 % pred.: median = 79; range, 41–108 IgE mean = 165 IU/L All had positive skin-prick test to at least 1 of the tested allergens: house-dust mite, 76%; cat dander, 79%; dog dander, 57% ICS equivalent to BDP 500–1,000 mcg/day for at least 2 months Reversibility of >12% in FEV_1 over baseline within 30 min after taking 200 mcg of salbuterol	**Arm 1** Omalizumab (O) (n=18) **Arm 2** Placebo (P) (n=17)	Subcutaneous administration of at least 0.016 mg/kg/IgE every 4 weeks	16 weeks after 6-week run-in Stable dose of BMD 500–1,200 mcg/day		Eosinophils decreased in O vs. P subjects (6.1% to 1.3% vs. 3.5% to 6.0%; p <0.01). R_{aw} decreased in O v. P group (p <0.01) but returned to baseline 3 months after discontinuation of treatment. PC_{20} increased in O vs. P subjects (p <0.01), but after discontinuation of therapy there was no difference. No changes occurred in FEV_1 in either group. Free IgE levels decreased (p <0.01) to <10 IU/mL in all O subjects vs. no change in P subjects.		Interleukin-13 (IL-13) levels decreased in O vs. P subjects (9.4 to 7.0 pg/mL vs. 7.2 to 8.5 pg/mL; p <0.01). No difference was found for IL-6, IL-10, and s-ICAM levels. Decrease in IL-5 and IL-8 in the O group did not reach significance. Area of wheal reaction decreased in O group for all 3 allergens (p <0.001).
Vignola et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with concomitant allergic asthma and persistent allergic rhinitis: SOLAR. Allergy 2004;59(7): 709–717. (Novartis Pharma AG and Genentech Inc.)	Multicenter, randomized, double-blind, placebo-controlled, parallel-group trial	To evaluate the efficacy and safety of omalizumab in patients with concomitant asthma and persistent allergic rhinitis	405 (ITT analysis; 20 withdrew)	**Age** 12–74 yr, mean = 38.4 yr **Gender** 45% male, 55% female **Ethnicity** Not reported	Moderate-to-severe allergic asthma (GINA) and persistent allergic rhinitis; 90% severe persistent; ≥400 mcg/day budesonide 39% receiving LABA FEV_1 % pred., mean = 78.1	**Arm1** Omalizumab (n=209; 5 withdrawals) **Arm 2** Placebo (n=196; 15 withdrawals)	0.016 mg/kg IU IgE/mL every 4 weeks	28 weeks after 4-week run-in		Treatment group difference occurred in FEV_1 (73 mL, p=0.032), FVC (84 L, p=0.016), and PEF (11 L/min, p <0.001) compared with placebo.	*20.6% of omalizumab vs. 30.1% of placebo (p=0.02) experienced exacerbations (using imputed values), and 18.2% vs. 25.5% experienced exacerbations (p=0.055) without imputed values. Rate of exacerbations was 0.25 vs. 0.40 (p=0.02).	*Greater proportion treated with omalizumab had ≥1 point improvement in asthma QoL (57.5% vs. 40.6%, p <0.001). SAE rates were similar (1.4% vs. 1.5%) in the 2 groups.

Citation (Sponsor)	Study Design	Purpose/ Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (If Reported)	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/Off-Treatment Followup	Taper/Decrease Steroids	Lung Function	Exacerbations/Symptoms	Other
Humbert et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. Allergy 2005;60(3): 309–316.	Multicenter, randomized, double-blind, placebo-controlled study 18 centers in 14 countries	To evaluate the effect of add-on omalizumab on asthma exacerbations in patients with severe persistent asthma who were inadequately controlled despite GINA step 4 therapy	482 (419 for analysis; 52 withdrew)	**Age** 12–79 yr, mean = 43.3 yr **Gender** 34% male, 67% female **Ethnicity** 78% Caucasian, 7% Black, 15% other Serum IgE: range, 21–632 IU/mL; mean = 193 IU/mL	Severe persistent asthma FEV_1 % pred.: mean = 61, range 18–101 PEF: mean = 305; range, 93–635 Rescue medications: mean = 6.1 puffs/day ICD 900–8,000 mcg/day, mean = 2,330 mcg/day All receiving ICS plus LABA 67% at high risk for asthma mortality	**Arm 1** Omalizumab (n=209) **Arm 2** Placebo (n=210)	0.016 mg/kg/IgE (IU/mL) every 4 weeks	28 weeks after 8-week run-in phase (16-week followup phase not reported here)	Difference in rescue medication use was not significant.	Change from baseline in mean morning PEF was greater for omalizumab than for placebo (p=0.042). Improvement in FEV_1 was 190 mL for omalizumab and 96 mL for placebo (p=0.043).	*Exacerbation rate for omalizumab group was 0.68 vs. 0.91 for placebo group (p=0.042, rate ratio 0.738) after adjusting for baseline differences in history (NNT=2.2) Severe exacerbation rate was lower in omalizumab vs. placebo (0.24 vs. 0.48; p=0.002) (NNT=2.2). Mean change in symptom score was greater with omalizumab vs. placebo treatment (p=0.039).	Asthma QoL improvement from baseline of $\geq$0.5 points occurred for 60.8% of omalizumab group vs. 47.8% of placebo group (p=0.008).
Niebauer et al. Impact of omalizumab on quality-of-life outcomes in patients with moderate-to-severe allergic asthma. Ann Allergy Asthma Immunol 2006;96 (2):316–326. (Genentech, Inc.)	Meta-analysis of randomized clinical trials that measured asthma-related quality of life using the Juniper Asthma Quality of Life Questionnaire (AQLQ)	To summarize asthma-related QoL outcomes associated with omalizumab therapy in moderate-to-severe allergic asthma	5 trials, 2,056 subjects	**Age** 12–75 yr, mean = 39–42 yr (4 trials, n=1,722); 1 pediatric trial (n=334) mean = 9.4 yr **Gender** 70% male, 30% female in pediatric trial; 44% male, 56% female in 4 adolescent/adult trials **Ethnicity** Not reported	Moderate-to-severe allergic asthma (3 trials with adult and adolescent patients), allergic asthma (1 trial with n=334 children and adolescents), and asthma and allergic rhinitis (1 trial with adult and adolescent patients)	**Arm 1** Omalizumab (O) **Arm 2** Placebo (P)	Not reported Patients were permitted to use albuterol metered-dose inhaler as needed (5 trials), treated concomitantly with BDP (3 trials), used fluticasone (1 trial), or used budesonide Turbohaler (1 trial).	4- to 6-week run-in period, 16-week steroid-stabilization phase, 12- to 16-week steroid-reduction phase, and either an open-label or double-blind extension phase. 2 trials lasted 52 weeks, 1 lasted 32 weeks, and 2 lasted 28 weeks.	All results refer to Juniper Asthma Quality of Life Questionnaire (AQLQ) Overall effect sizes during steroid-reduction phase were 1.73 for O and 1.31 for P groups. *Change >0.5 in AQLQ for O vs. P:* steroid-stabilization phase, OR 1.35, 95% CI 1.11 to 1.64 (4 trials, n=1,649); steroid-reduction phase, OR 1.69, 95% CI 1.40 to 2.05 (5 trials, n=1,864); extension phase, OR 1.50, 95% CI 1.15 to 1.95 (3 trials, n=1,078) *Change >1.0 in AQLQ for O vs. P:* steroid-stabilization phase, OR=1.61, 95% CI 1.29 to 2.00 (4 trials, n=1,649); steroid-reduction phase, OR 2.03, 95% CI 1.66 to 2.47 (5 trials, n=1,864); extension phase, OR 1.25, 95% CI 0.97 to 1.59 (3 trials, n=1,078) with evidence of heterogeneity (p=0.01) *Change >1.5 in AQLQ for O vs. P:* steroid-stabilization phase, OR1.80, 95% CI 1.36 to 2.38 (4 trials, n=1,649); steroid-reduction phase, OR 2.11, 95% CI 1.68 to 2.65 (5 trials, n=1864); extension phase, OR 1.59, 95% CI 1.21 to 2.08 (3 trials, n=1,078) with evidence of heterogeneity (p=0.01)			