Impact of Body Mass Index on Omalizumab Response in Adults With Moderate-to-Severe Allergic Asthma

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Background

- Obesity is associated with increased asthma severity,[1] poorer asthma control,[1,2] and inadequate response to conventional medications.[3,4]
- Several biologics are currently approved for treatment-resistant asthma, based on either fixed- or adjustable-dosing regimens.[5,6]
- Some studies suggest that response to biologics in patients with higher body mass index (BMI) may be diminished.[6]
- The reasons for this are unclear, but may relate to fixed-dosing regimens.

Objective

- To estimate the effect of omalizumab by BMI classification in patients with moderate-to-severe allergic asthma.

Methods

Study Design

- Pooled data from adults ≥18 years of age with moderate-to-severe allergic asthma enrolled in the pivotal 008/009 studies (16-week steroid-stable phase) were analyzed by the following BMI categories[7]:
  - <25 kg/m^2 (normal/underweight [n=397])
  - 25–29 kg/m^2 (overweight [n=330])
  - ≥30 kg/m^2 (obese [n=268]).
- Response to omalizumab within each BMI category was assessed for:
  - Relative reduction in exacerbation rate
  - Change from baseline in forced expiratory volume in 1 second (FEV_1), total asthma symptom score (TASS), and Asthma Quality of Life Questionnaire (AQLQ) score.

Statistical Analysis

- Exacerbation rate reduction was assessed using a Poisson regression model, with study and treatment group as independent variables, normalized by time at risk in the steroid-stable phase.
- Change from baseline in FEV_1, TASS, and AQLQ score was assessed using an analysis of covariance model with baseline value, treatment, and their interaction as covariates.

Results

Baseline Demographics and Clinical Characteristics

- Baseline demographics and clinical characteristics were generally similar across treatment groups and BMI subgroups (**Table**).
  - However, compared with normal and overweight patients, obese patients tended to have:
    - Lower mean immunoglobulin E (IgE) levels, worse mean symptom scores, and poorer quality of life at baseline.

Table. Baseline Demographics and Clinical Characteristics by BMI Classification

	BMI Classification, kg/m^2					
	<25		25–29		≥30	
Characteristic	OMA n=203	PBO n=194	OMA n=161	PBO n=169	OMA n=140	PBO n=128
Age, y, mean (SD)	40.0 (13.3)	38.6 (13.1)	43.4 (12.1)	41.3 (12.4)	41.9 (10.9)	44.1 (10.1)
Female, n (%)	125 (61.6)	115 (59.3)	70 (43.5)	75 (44.4)	90 (64.3)	91 (71.1)
Race, n (%)						
White	192 (94.6)	178 (91.8)	142 (88.2)	155 (91.7)	125 (89.3)	107 (83.6)
Other/unknown	11 (5.4)	16 (8.2)	19 (11.8)	14 (8.3)	15 (10.7)	21 (16.4)
BMI, kg/m^2, mean (SD)	22.6 (1.9)	22.5 (1.8)	27.3 (1.4)	27.2 (1.3)	35.4 (5.1)	35.7 (4.9)
Never smoker, n (%)	158 (77.8)	148 (76.3)	119 (73.9)	116 (68.6)	102 (72.9)	86 (67.2)
$ppFEV_1$, mean (SD)	70.8 (14.2)	71.1 (13.9)	66.6 (14.4)	69.2 (13.5)	70.1 (15.0)	66.1 (16.3)
FEV_1 reversibility, %, mean (SD)	26.8 (16.0)	25.8 (14.0)	25.5 (14.1)	25.1 (13.0)	27.2 (14.3)	26.6 (14.3)
Serum total IgE, IU/mL, mean (SD)	211.8 (178.8)	219.0 (174.0)	186.1 (141.7)	194.4 (140.4)	168.7 (125.3)	150.4 (112.1)
Blood eosinophils, cells/μL, mean (SD)	296.9 (176.0)	339.2 (207.7)	294.1 (202.4)	321.9 (199.6)	280.8 (165.5)	287.2 (185.2)
TASS (range, 0–9), mean (SD)	4.0 (1.3)	4.1 (1.4)	4.0 (1.1)	4.1 (1.2)	4.3 (1.4)	4.3 (1.2)
AQLQ score (range, 1–7), mean (SD)	4.5 (1.0)	4.3 (1.0)	4.3 (0.9)	4.4 (1.0)	4.0 (1.0)	4.0 (1.1)

AQLQ, Asthma Quality of Life Questionnaire; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; IgE, immunoglobulin E; OMA, omalizumab; PBO, placebo; $ppFEV_1$, percent predicted forced expiratory volume in 1 second; TASS, total asthma symptom score.

Asthma Exacerbation Rate by BMI Category

- Compared with the placebo group, asthma exacerbation rates were consistently lower across all BMI categories in patients receiving omalizumab (**Figure 1A**).
- The asthma adjusted exacerbation rate in the placebo group increased with increasing BMI (**Figure 1A**).
- This resulted in larger placebo-adjusted relative reduction in exacerbation rate (95% CI) with increasing BMI (**Figure 1B**).

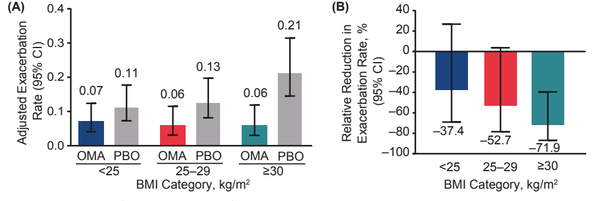
Change in FEV_1 by BMI Category

- Improvements in FEV_1 were observed across all BMI categories in patients receiving omalizumab compared with placebo (**Figure 2**).
- No consistent difference in change in FEV_1 was observed between patients with normal BMI versus overweight or obese patients.

Change in TASS by BMI Category

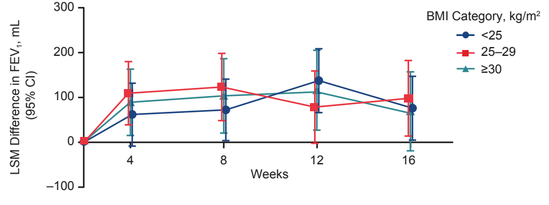
- Improvements in TASS were observed across all BMI categories in patients receiving omalizumab compared with placebo (**Figure 3**).
- There was a trend towards slightly greater improvements in normal BMI and overweight patients compared with obese patients; however, 95% CIs largely overlapped.

Figure 1. Adjusted (A) Exacerbation Rate (95% CI) and (B) Relative Rate Reduction During the 16-Week Steroid-Stable Period for Omalizumab Versus Placebo by BMI Category



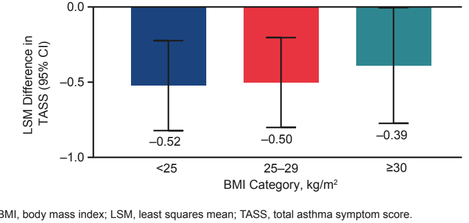
BMI, body mass index; OMA, omalizumab; PBO, placebo.

Figure 2. LSM Difference in Change From Baseline in FEV_1 (95% CI) During the 16-Week Steroid-Stable Period for Omalizumab Versus Placebo by BMI Category



BMI, body mass index; FEV_1, forced expiratory volume in 1 second; LSM, least squares mean.

Figure 3. LSM Difference in Change From Baseline to Week 16 in TASS (95% CI) for Omalizumab Versus Placebo by BMI Category

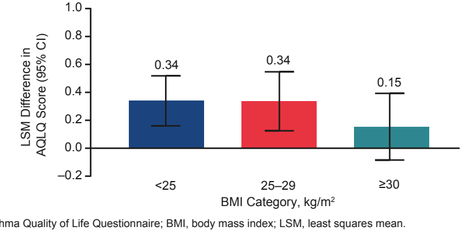


BMI, body mass index; LSM, least squares mean; TASS, total asthma symptom score.

Change in AQLQ Score by BMI Category

- Improvements in AQLQ score were observed across all BMI categories in patients receiving omalizumab compared with placebo (**Figure 4**).
- There was a trend towards slightly greater improvements in normal BMI and overweight patients compared with obese patients.

Figure 4. LSM Difference in Change From Baseline to Week 16 in AQLQ Score (95% CI) for Omalizumab Versus Placebo by BMI Category



AQLQ, Asthma Quality of Life Questionnaire; BMI, body mass index; LSM, least squares mean.

Safety

- Safety for the subgroups presented has not been evaluated. Safety results from the overall study population have been published in Busse et al[8] and Solèr et al.[9]

Conclusions

- Omalizumab reduced asthma exacerbations and improved FEV_1, TASS, and asthma-related quality of life across all BMI groups compared with placebo.
- Lung function improvements were similar across BMI categories.
- Reductions in asthma exacerbations were greater in obese patients versus nonobese patients, whereas improvements in TASS and AQLQ scores tended to be greater in nonobese patients.
- These findings suggest that omalizumab may provide clinical benefit irrespective of BMI.
- Limitations were inherent to the post hoc nature of the analyses.

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Disclosures **BG:** consultant for Genentech, Inc. and Novartis; speaker for Regeneron and Sanofi. **AED:** no conflict of interest to disclose. **BY, PJ, RCL, CTJH:** employees of Genentech, Inc.; stockholders in Roche. **TH:** former consultant for Genentech, Inc. and Novartis Pharmaceuticals Corporation. **NJ:** honoraria from AstraZeneca, GlaxoSmithKline, and Teva.

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