Response to Omalizumab in Allergic Asthma Patients From Different Racial Backgrounds

Stanley J. Szefler,[1] Elina Jerschow,[2] Bongin Yoo,[3] Pranathi Janampally,[3] Hooman Pazwash,[3] Cecile T.J. Holweg,[3] Golda Hudes[2]

[1]Pediatric Asthma Research Program, Breathing Institute, Children's Hospital Colorado, and University of Colorado School of Medicine, Aurora, CO, USA; [2]Albert Einstein College of Medicine, Bronx, NY, USA; [3]Genentech, Inc., South San Francisco, CA, USA

Background

- Patients from racial minorities frequently experience an increased asthma burden compared with white patients.[1]
- Racial/ethnic minorities are frequently underrepresented in clinical research[2,3]; only 6% of clinical trial participants are African American or Hispanic, despite representing 30% of the US general population.[2]
- Enhanced understanding of different responses to medication is necessary to improve patient management.

Objective

- To estimate the effect of omalizumab in patients with allergic asthma from different racial backgrounds.

Methods

Study Design and Patients

- Post hoc analysis of 2 prospective US-based studies evaluating omalizumab in adolescent and adult allergic asthma: the placebo-controlled EXTRA and single-armed PROSPERO studies.
- EXTRA (NCT00314574)[4] was a multicenter, randomized, double-blind, placebo-controlled, 48-week study of omalizumab in patients 12–75 years of age with uncontrolled allergic asthma despite high-dose inhaled corticosteroids and long-acting beta-agonists ± other controllers:
  - Baseline prebronchodilator forced expiratory volume in 1 second (FEV_1) 40–80% of predicted
  - No requirement for bronchodilator reversibility
  - Exacerbations and safety were assessed throughout the study; lung function was assessed every 4 weeks; and Asthma Quality of Life Questionnaire (AQLQ) was assessed at baseline and Weeks 16, 32, and 48.
- PROSPERO (NCT01922037)[5] was a multicenter, prospective, single-armed, 48-week study of omalizumab in patients ≥12 years of age who initiated omalizumab based on physician assessment of need.
  - Exacerbations and safety were assessed throughout the study; lung function and AQLQ were assessed at baseline, 6 months, and end of study/early termination.

Racial Groups

- Patients were categorized into groups by race (self-reported) as either white, black/African American, or other.
  - Other racial groups were not reported in this analysis because only 41/848 (5%) of modified intention-to-treat (ITT) patients in EXTRA and 104/801 (13%) of omalizumab-treated patients in PROSPERO identified as "other" race and the "other" racial group consisted of patients from several different races.

Statistical Analyses

- Exacerbation rates were examined using a Poisson regression model, including treatment, dosing schedule, concomitant asthma medications, and number of exacerbations in the prior year (EXTRA) and race and number of exacerbations in the past year (PROSPERO).
  - Data were normalized by subject-time on study medication at risk for both studies.
- Changes in FEV_1 and AQLQ score were estimated using an analysis of covariance model including baseline value for FEV_1 or AQLQ and treatment and their interaction (EXTRA) and race (PROSPERO).
- Safety data for racial subgroups were summarized according to reporting requirements per protocol for each study.
  - Because of low numbers in some subgroups, only overall safety events are provided.
- Due to the post hoc nature of the analysis, *P* values were not calculated.

Results

Baseline Demographics and Clinical Characteristics

EXTRA

- Of 848 modified ITT patients in EXTRA, 807 patients (white, n=631; black/African American, n=176) were included.
- Baseline characteristics were generally similar across treatment arms and races, with a few exceptions (**Table 1, bold text**).

Table 1. Baseline Demographic and Clinical Characteristics in White and Black/African American Patients From EXTRA

	White			Black/African American		
Characteristic	Placebo n=318	Omalizumab n=313	Overall n=631	Placebo n=86	Omalizumab n=90	Overall n=176
Age, y, mean (SD)	46.2 (13.6)	44.0 (14.4)	45.1 (14.0)	40.9 (15.0)	41.5 (14.5)	41.2 (14.4)
Male, n (%)	99 (31.1)	128 **(40.9)**	227 (36.0)	23 (26.7)	25 (27.8)	48 (27.3)
BMI, kg/m², mean (SD)	31.5 (7.1)	32.2 (7.9)	31.9 (7.5)	32.4 (8.0)	32.1 (8.0)	32.2 (8.0)
Eosinophil level, cells/µL, median (Q1, Q3)	260.0 (150.0, 430.0)	270.0 (170.0, 430.0)	270 (160.0, 430.0)	260.0 (190.0, 550.0)	220.0 (130.0, 405.0)	240 (140.0, 440.0)
Total IgE, IU/mL, median (Q1, Q3)	127.0 (63.0, 231.0)	136.0 (75.0, 249.0)	132 (15.0, 692.0)	**178.5** (95.0, 299.0)	139.0 (89.0, 240.0)	159.0 (89.5, 283.5)
FeNO, ppb, mean (SD)	26.9 (26.6)	25.0 (22.4)	25.9 (24.4)	**36.7** (38.5)	**44.2** (40.3)	39.9 (39.2)
Reversibility, %, mean (SD)	10.9 (15.6)	12.5 (16.6)	11.7 (16.1)	15.2 (15.7)	12.6 (17.1)	13.9 (16.4)
$ppFEV_1$, %, mean (SD)	65.8 (13.9)	66.5 (14.5)	66.2 (14.2)	60.1 (13.4)	60.7 (14.9)	60.4 (14.1)
Exacerbation history, events/y, mean (SD)	1.9 (1.3)	1.9 (1.5)	1.9 (1.4)	**2.2** (1.9)	**2.4** (3.9)	2.3 (3.1)
Asthma duration, y, mean (SD)	25.1 (15.8)	23.7 (15.5)	24.4 (15.7)	24.0 (15.8)	20.7 (14.9)	22.3 (15.4)

BMI, body mass index; FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E; $ppFEV_1$, percent predicted forced expiratory volume in 1 second; Q1, first (lower) quartile; Q3, third (upper) quartile.

PROSPERO

- Of 801 omalizumab-treated patients in PROSPERO, 697 patients (white, n=567; black/African American, n=130) were included.
- Baseline demographic and clinical characteristics were generally similar between white and black/African American patients in PROSPERO, with a few exceptions (**Table 2, bold text**).

Table 2. Baseline Demographic and Clinical Characteristics in White and Black/African American Patients From PROSPERO

Characteristic	White n=567	Black/African American n=130
Age, y, mean (SD)	**49.1** (17.2)	**40.0** (16.7)
Male, n (%)	221 **(39.0)**	41 **(31.5)**
BMI, kg/m², mean (SD)	30.5 (8.1)	32.8 (9.6)
Eosinophil level, cells/µL, median (Q1, Q3)	230.0 (130.0, 390.0)	215.0 (130.0, 365.0)
IgE, IU/mL, median (Q1, Q3)	**164.6** (69.9, 397.1)	**308.5** (106.8, 793.1)
FeNO, ppb, mean (SD)	34.4 (34.8)	34.3 (29.2)
Reversibility, %, mean (SD)	7.4 (11.6)	8.4 (13.6)
$ppFEV_1$, %, mean (SD)	75.3 (20.7)	77.1 (20.1)
Exacerbation history, events/y, mean (SD)	2.9 (3.3)	2.9 (2.7)

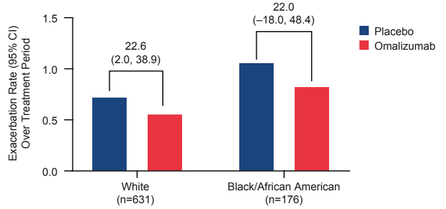
BMI, body mass index; FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin ppFEV$_1$, percent predicted forced expiratory volume in 1 second; Q1, first (lower) quartile; Q3, third (upper) quartile.

Exacerbation Rate

EXTRA

- In EXTRA, the exacerbation rate during the study was lower with omalizumab versus placebo in both racial groups.
- A similar placebo-corrected exacerbation rate reduction (relative change [95% CI]) was observed for white and black/African American patients (**Figure 1**).

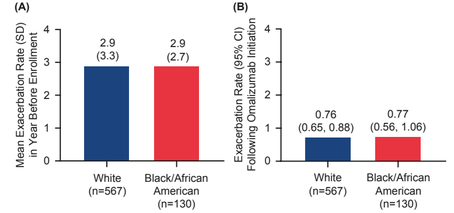
Figure 1. Exacerbation Rate During 48-Week Study Period in EXTRA by Racial Group



PROSPERO

- In PROSPERO, exacerbation rates in the year before enrollment were similar for white and black/African American patients (**Figure 2A**).
- Following omalizumab initiation, rates were lower in both groups and similar between racial groups (**Figure 2B**).

Figure 2. Exacerbation Rate (A) in the Year Before Enrollment and (B) Following Omalizumab Initiation in PROSPERO by Racial Group



Lung Function Changes

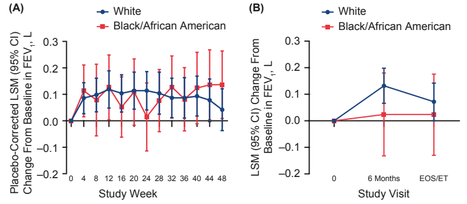
EXTRA

- Despite low reversibility at baseline, lung function improvements occurred in both racial groups.
- Placebo-corrected improvements were similar for white and black/African American patients (95% CIs highly overlapped; **Figure 3A**).

PROSPERO

- Despite low reversibility, FEV_1 improvements occurred in all patients at Month 6 and at end of study/early termination.
- Mean FEV_1 improvements were greater in white versus black/African American patients at each time point; however, 95% CIs overlapped substantially (**Figure 3B**).

Figure 3. LSM Differences for FEV_1 by Racial Group in (A) EXTRA and (B) PROSPERO



EOS/ET, end of study/early termination; FEV_1, forced expiratory volume in 1 second; LSM, least squares mean.

AQLQ Score Improvements

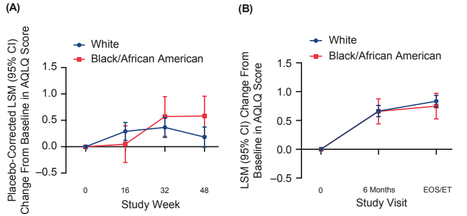
EXTRA

- In EXTRA, AQLQ score improvements were observed in both patient populations.
- Black/African American patients tended to experience greater mean AQLQ score improvements than white patients at Week 48; however, 95% CIs overlapped substantially (**Figure 4A**).

PROSPERO

- In PROSPERO, similar and minimally clinically important improvements (0.5 points[6]) in AQLQ scores from baseline at 6 months and end of study/early termination were observed for both white and black/African American patients (**Figure 4B**).

Figure 4. LSM Differences for AQLQ Scores by Racial Group in (A) EXTRA and (B) PROSPERO



AQLQ, Asthma Quality of Life Questionnaire; EOS/ET, end of study/early termination; LSM, least squares mean.

Safety

EXTRA

- The percentage of patients with any adverse event (AE) was similar across racial and treatment groups.
- The percentage of patients with an AE leading to drug discontinuation was similar across racial and treatment groups.
- A higher percentage of black/African American versus white patients experienced a serious AE (SAE) in both treatment groups (**Table 3**).

Table 3. AEs Reported by White and Black/African American Patients From EXTRA

	White		Black/African American	
	Placebo n=318	Omalizumab n=313	Placebo n=86	Omalizumab n=90
Patients with any AE, n (%)	259 (81.4)	254 (81.2)	62 (72.1)	72 (80.0)
Patients with AEs leading to drug discontinuation, n (%)	11 (3.5)	13 (4.2)	2 (2.3)	4 (4.4)
Patients with any SAE, n (%)	28 (8.8)	27 (8.6)	15 (17.4)	10 (11.1)

AE, adverse event; SAE, serious adverse event.

PROSPERO

- A slightly higher percentage of black/African American versus white patients experienced an SAE; however, no placebo arm was available for comparison (**Table 4**).

Table 4. AEs Reported by White and Black/African American Patients From PROSPERO

	White n=567	Black/African American n=130
Patients with any causality-related AE, n (%)	15 (2.6)	2 (1.5)
Patients with AE with causality unknown, n (%)	17 (3.0)	2 (1.5)
Patients with any SAE, n (%)	59 (10.4)	20 (15.4)

AE, adverse event; SAE, serious adverse event.

Limitations

- Limitations included those inherent to post hoc subgroup analyses, and a lack of comparison with patients from other minority racial backgrounds.
- Additionally, outcomes in EXTRA and PROSPERO cannot be compared directly because EXTRA was placebo controlled and PROSPERO was single armed.

Conclusions

- Black/African American and white patients with moderate-to-severe allergic asthma had a similar response to omalizumab in terms of exacerbation rate and FEV_1 and AQLQ score improvements in this analysis.
- AE profiles were similar between racial groups, with slightly higher SAEs in black/African American patients in PROSPERO. However, no placebo arm was available for comparison.

References **1.** Guilbert T, et al. *J Allergy Clin Immunol Pract.* 2019;7:568–77. **2.** Konkel L. *Environ Health Perspect.* 2015;123:A297–302. **3.** Akenroye A, Keet C. *J Allergy Clin Immunol Pract.* 2020;8:739–41.e6. **4.** Hanania NA, et al. *Ann Intern Med.* 2011;154:573–82. **5.** Casale TB, et al. *J Allergy Clin Immunol Pract.* 2019;7:156–64.e1. **6.** Juniper EF, et al. *J Clin Epidemiol.* 1994;47:81–7.

Disclosures **SJS:** advisory panel member for Aerocrine, AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo, Genentech, Inc., GlaxoSmithKline, Merck, Novartis, Regeneron, Roche, Sanofi, and Teva; research grant from GlaxoSmithKline. **EJ:** advisory panel member for Genentech, Inc., GlaxoSmithKline, Novartis, Regeneron, and Sanofi; research grant from Cumberland; United States Medical Licensing Examination committee member for the National Board of Medical Examiners. **BY, PJ, HP, CTJH:** employees of Genentech, Inc.; stockholders in Roche. **GH:** research grant support from AstraZeneca, Genentech, Inc., and Merck; advisory board member for AstraZeneca and GlaxoSmithKline.

Acknowledgments This study was funded by Genentech, Inc., a member of the Roche Group, and Novartis Pharma AG. Third-party writing assistance was provided by Nicole Tom, PhD, of Envision Pharma Inc., and funded by Genentech, Inc., a member of the Roche Group, and Novartis Pharmaceuticals Corporation.

Presented at the American Academy of Allergy, Asthma & Immunology (AAAAI) 2020 Annual Meeting, March 13–16, 2020, Philadelphia, PA