

### Similar response to omalizumab in children with allergic asthma from different racial backgrounds

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#### Clinical Implications

In this analysis, omalizumab reduced asthma exacerbations in children aged 6 years to younger than 12 years independent of racial background.

Racial and ethnic minority populations in the United States, especially Black children, endure an increased burden of asthma due to factors such as environmental exposure, access to health care, and genetics.<sup>1</sup> Compared with White children, Black children with asthma experience reduced quality of life, have more poorly controlled disease, require longer-term corticosteroid use, and are more frequently evaluated in emergency department visits.<sup>1</sup> In addition, Black children are 3 times as likely to be hospitalized and 7 times as likely to die from asthma as White children.<sup>2</sup> Despite these disparities, Black patients are often under-represented in clinical trials for asthma biologic therapies<sup>3</sup> and make up only 5% of all clinical trial participants.<sup>4</sup> Furthermore, studies suggest potential racial and ethnic differences in treatment response to asthma medications in children.<sup>5,6</sup>

Omalizumab is a humanized anti-IgE monoclonal antibody approved for the treatment of pediatric patients older than 6 years, adolescents, and adults with moderate-to-severe allergic asthma. Clinical outcomes after treatment with omalizumab in patients older than 12 years with moderate-to-severe allergic asthma are similar regardless of race.<sup>7</sup> However, potential racial differences have not been evaluated in pediatric patients younger than 12 years. In the pivotal pediatric trial IA05, omalizumab reduced the rate of severe exacerbations at 24 and 52 weeks and was generally well tolerated.<sup>8</sup> Given the racial diversity of the patient population in the IA05 trial, we assessed the response to omalizumab in children (aged 6 to <12 years) of different self-identified races.

The IA05 trial (NCT00079937) was a 52-week international, multicenter, randomized, double-blind, placebo-controlled, parallel-group study in children aged 6 years to younger than 12 years with a history of exacerbations and asthma symptoms despite inhaled corticosteroid use, conducted between April 2004 and January 2008. Patients were randomized 2:1, and omalizumab (75–375 mg) was administered (based on baseline IgE levels and weight) by subcutaneous injection once or twice a month. The study was conducted in accordance with Good Clinical Practice, local regulations, and the Declaration of Helsinki. The protocol was approved by institutional review boards

and/or ethics committees, and written, informed consent was obtained.

For this *post hoc* subgroup analysis, participants were categorized into 3 groups based on self-reported race at baseline: White (n = 325 [56.4%]; placebo, n = 113; omalizumab, n = 212), Black (n = 99 [17.2%]; placebo, n = 30; omalizumab, n = 69), and Asian/Other/Not reported (n = 152 [26.4%]; placebo, n = 49; omalizumab, n = 103) (as per the study protocol participants self-selected race from the options of White, Black, Oriental [Asian], or Other; for this analysis Asian [n = 2] and Other and Not reported [n = 150] have been combined). Clinically significant asthma exacerbations were defined as worsening of asthma symptoms requiring doubling of baseline inhaled corticosteroids and/or treatment with rescue systemic corticosteroids for at least 3 days. Severe asthma exacerbations were defined as clinically significant exacerbations that required treatment with systemic corticosteroids and where peak expiratory flow of forced expiratory volume in 1 second (FEV<sub>1</sub>) was less than 60% of personal best. A generalized Poisson regression model was used to evaluate asthma exacerbations and severe asthma exacerbations during the 52-week treatment period in each subgroup. High-level safety data are summarized for each racial subgroup, but no additional analysis was conducted.

Baseline demographics and clinical characteristics were generally similar across races (Table 1). However, a longer mean duration of asthma and a greater percentage of positive skin prick test for mold (though not other allergens) were found in Black patients relative to White and Asian/Other/Not reported patients. In addition, percent predicted FEV<sub>1</sub> was lower in Black patients (although FEV<sub>1</sub> [L] was similar between groups), and IgE levels were higher in Asian/Other/Not reported patients.

Placebo-corrected rate reductions in asthma exacerbations were greater in Black and Asian/Other/Not reported patients compared with White patients (Figure 1). Low numbers of severe exacerbations were recorded regardless of race and, when compared with placebo, a greater percentage of participants on omalizumab experienced no severe exacerbations regardless of race (White: placebo 87 of 113 [77.0%], omalizumab 185 of 212 [87.3%]; Black: placebo 23 of 30 [76.7%], omalizumab 58 of 69 [84.1%]; Asian/Other/Not reported: placebo 42 of 49 [85.7%], omalizumab 95 of 103 [92.2%]).

The incidence of treatment-emergent adverse events was similar between White, Black, and Asian/Other/Not reported patients (White: placebo 120 of 128 [93.8%], omalizumab 216 of 249 [86.7%]; Black: placebo 26 of 30 [86.7%], omalizumab 64 of 69 [92.8%]; Asian/Other/Not reported: placebo 48 of 49 [98.0%], omalizumab 100 of 103 [97.1%]), and the number of patients with serious adverse events was low across all groups (White: placebo 10 of 128 [7.8%], omalizumab 10 of 249 [4.0%]; Black: placebo 3 of 30 [10.0%], omalizumab 2 of 69 [2.9%]; Asian/Other/Not reported: placebo 4 of 49 [8.2%], omalizumab 5 of 103 [4.9%]). Overall safety findings were previously reported by Lanier et al.<sup>8</sup>

Although previous studies report a difference in the response to asthma treatments in people from different racial and ethnic

TABLE I. Baseline demographics and clinical characteristics

| Characteristic, mean (SD) unless stated               | Race and treatment |                      |                  |                     |                          |                      |
|-------------------------------------------------------|--------------------|----------------------|------------------|---------------------|--------------------------|----------------------|
|                                                       | White              |                      | Black            |                     | Asian/Other/Not reported |                      |
|                                                       | Placebo (n = 113)  | Omalizumab (n = 212) | Placebo (n = 30) | Omalizumab (n = 69) | Placebo (n = 39)         | Omalizumab (n = 103) |
| Age (y)                                               | 8.4 (1.7)          | 8.8 (1.8)            | 8.9 (1.6)        | 8.8 (1.7)           | 8.2 (1.7)                | 8.4 (1.7)            |
| Male, n (%)                                           | 72 (63.7)          | 132 (62.3)           | 21 (70.0)        | 55 (79.7)           | 36 (73.5)                | 72 (69.9)            |
| Weight, median (Q1, Q3) (kg)                          | 30.0 (25, 36)      | 31.5 (26, 39)        | 35.8 (29, 43)    | 37.7 (29, 48)       | 28.5 (24, 36)            | 28.0 (24, 34)        |
| BMI, median (Q1, Q3) (kg/m <sup>2</sup> )             | 16.9 (16, 20)      | 17.2 (16, 20)        | 18.7 (16, 21)    | 18.6 (17, 24)       | 17.1 (16, 19)            | 16.9 (15, 19)        |
| Percent predicted FEV <sub>1</sub> <sup>*</sup>       | 88.7 (16.8)        | 88.0 (17.6)          | 69.5 (17.9)      | 72.4 (12.1)         | 91.3 (17.4)              | 87.3 (17.3)          |
| FEV <sub>1</sub> (L)                                  | 1.6 (0.5)          | 1.7 (0.4)            | 1.4 (0.5)        | 1.5 (0.4)           | 1.6 (0.4)                | 1.5 (0.4)            |
| FEV <sub>1</sub> reversibility (%) <sup>†</sup>       | 23.3 (14.4)        | 24.6 (15.6)          | 31.9 (15.8)      | 28.1 (18.9)         | 21.4 (15.2)              | 27.6 (19.5)          |
| Historical reversibility (%) <sup>‡</sup>             | 20.9 (7.8)         | 24.3 (13.4)          | 27.2 (13.8)      | 25.2 (14.0)         | 23.4 (12.8)              | 24.0 (14.5)          |
| Serum total IgE (IU/mL)                               | 437.4 (340.9)      | 472.9 (351.4)        | 468.2 (276.4)    | 439.2 (304.0)       | 541.2 (365.0)            | 538.0 (342.1)        |
| Duration of allergic asthma (y)                       | 5.3 (2.6)          | 5.7 (2.7)            | 6.7 (2.5)        | 6.3 (2.7)           | 5.8 (2.3)                | 5.7 (2.5)            |
| Number of food or drug allergies, n (%)               |                    |                      |                  |                     |                          |                      |
| None                                                  | 79 (69.9)          | 165 (77.8)           | 18 (60.0)        | 45 (65.2)           | 35 (71.4)                | 81 (78.6)            |
| 1                                                     | 14 (12.4)          | 18 (8.5)             | 2 (6.7)          | 10 (14.5)           | 3 (6.1)                  | 14 (13.6)            |
| 2                                                     | 6 (5.3)            | 10 (4.7)             | 4 (13.3)         | 7 (10.1)            | 8 (16.3)                 | 3 (2.9)              |
| 3                                                     | 6 (5.3)            | 6 (2.8)              | 4 (13.3)         | 5 (7.2)             | 1 (2.0)                  | 1 (1.0)              |
| ≥4                                                    | 8 (7.1)            | 13 (6.1)             | 2 (6.7)          | 2 (2.9)             | 2 (4.1)                  | 4 (3.9)              |
| Omalizumab dose, median (Q1, Q3) (mg) <sup>§</sup>    | 255.0 (150, 300)   | 255.0 (150, 300)     | 262.5 (225, 300) | 225.0 (225, 300)    | 225.0 (225, 300)         | 225.0 (225, 300)     |
| Positive skin prick/RAST test, n (%)                  |                    |                      |                  |                     |                          |                      |
| Mold                                                  | 45 (39.8)          | 108 (50.9)           | 23 (76.7)        | 52 (75.4)           | 23 (46.9)                | 37 (35.9)            |
| House dust mite ( <i>Dermatophagoides pteronyss</i> ) | 85 (66.4)          | 178 (71.5)           | 20 (66.7)        | 46 (66.7)           | 37 (75.5)                | 76 (73.8)            |
| House dust mite ( <i>Dermatophagoides farinae</i> )   | 87 (68.0)          | 180 (72.3)           | 15 (50.0)        | 49 (71.0)           | 33 (67.3)                | 76 (73.8)            |
| Cat dander                                            | 56 (43.8)          | 125 (50.2)           | 16 (53.3)        | 45 (65.2)           | 18 (36.7)                | 26 (25.2)            |
| Dog dander                                            | 43 (33.6)          | 95 (38.2)            | 10 (33.3)        | 21 (30.4)           | 13 (26.5)                | 21 (20.4)            |
| Cockroaches                                           | 40 (31.3)          | 77 (65.9)            | 16 (53.3)        | 35 (50.7)           | 11 (22.4)                | 28 (27.2)            |

The numbers for the positive skin test for all allergens except for mold were White: n = 128 placebo, n = 249 omalizumab; Black: n = 30 placebo, n = 69 omalizumab; Asian/Other/Not reported: n = 49 placebo, n = 103 omalizumab. BMI, Body mass index; FEV<sub>1</sub>, forced expiratory volume in 1 second; Q, quarter; RAST, radioallergosorbent; SD, standard deviation.

<sup>\*</sup>Calculated using the Polgar spirometric reference equation.

<sup>†</sup>Percent increase in FEV<sub>1</sub> over baseline within 30 minutes of rescue medication (taken anytime between visits 1 and 6).

<sup>‡</sup>Historical reversibility within the last 12 months before entry. Note that due to a potential overlap in timing, historical reversibility and FEV<sub>1</sub> reversibility data are not mutually exclusive.

<sup>§</sup>Administered SQ every 2 or 4 weeks depending on the dose.

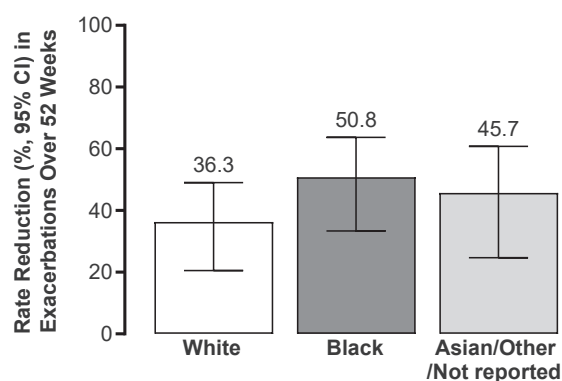


**FIGURE 1.** Placebo-corrected rate reduction in clinically significant asthma exacerbations. White  $n = 325$  (placebo,  $n = 113$ ; omalizumab,  $n = 212$ ), Black  $n = 99$  (placebo,  $n = 30$ ; omalizumab,  $n = 69$ ), and Asian/Other/Not reported  $n = 152$  (placebo,  $n = 49$ ; omalizumab,  $n = 103$ ). *CI*, Confidence interval.

backgrounds,<sup>5</sup> our findings suggest that response to omalizumab treatment in children aged 6 to younger than 12 years is likely independent of race. These findings are consistent with a previous investigation of racial differences in patients 12 years or older—in this study, omalizumab was found to reduce the frequency of asthma exacerbations and improve lung function and asthma-related quality of life in both White and Black patients with moderate-to-severe asthma.<sup>7</sup> However, our findings are limited by the *post hoc* nature of the analysis, the definitions of asthma exacerbation and severe exacerbation used in the original study (including the use of percent predicted FEV<sub>1</sub>, which differed between groups, in defining severe asthma exacerbations), self-report of race within the confines of the study protocol (which limits the interpretation of the findings from the Asian/Other/Not reported group), small patient numbers in some subgroups, and the applicability to recent practices. In addition, our findings have limited ability to show whether efficacy of omalizumab is associated with allergen sensitization.

In conclusion, this *post hoc* analysis of the IA05 trial suggests that omalizumab reduces asthma exacerbations in children aged 6 years to younger than 12 years regardless of self-reported race. These findings combined with previous findings in older patients suggest that response to omalizumab is likely independent of racial background, which may further incentivize current improvements in access to biologic treatments.<sup>9</sup>

### Data availability

Qualified researchers may request access to individual patient level data through the clinical study data request platform (<https://vivli.org/>). Further details on Roche's criteria for eligible studies are available here (<https://vivli.org/members/ourmembers/>). For further details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see here ([https://www.roche.com/research\\_and\\_development/who\\_we\\_are\\_how\\_we\\_work/clinical\\_trials/our\\_commitment\\_to\\_data\\_sharing.htm](https://www.roche.com/research_and_development/who_we_are_how_we_work/clinical_trials/our_commitment_to_data_sharing.htm)).

[com/research\\_and\\_development/who\\_we\\_are\\_how\\_we\\_work/clinical\\_trials/our\\_commitment\\_to\\_data\\_sharing.htm](https://www.roche.com/research_and_development/who_we_are_how_we_work/clinical_trials/our_commitment_to_data_sharing.htm)).

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Conflicts of interest: L. A. Millette, J. Ko, and P. Raut are employees of Genentech, Inc. and stockholders in Roche. C. T. J. Holweg is a former employee of Genentech, Inc. and stockholder in Roche. The rest of the authors declare that they have no relevant conflicts of interest.

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