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RESEARCH LETTER

Baseline Systemic Oral Corticosteroid Use in Patients with Asthma Initiating Dupilumab Treatment in the Real World: From the RAPID Global Registry

Nijra L Lugogo[1], Enrico Heffler[2,3], Vicente Plaza[4], Ole Hilberg[5], Changming Xia[6], Scott Nash[6], Nami Pandit[7], Juby A Jacob-Nara[7], Harry J Sacks[6], Paul J Rowe[7], Yamo Deniz[6], Megan Hardin[8], Xavier Soler[6]

[1]University of Michigan Medical School, Ann Arbor, MI, USA; [2]IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy; [3]Humanitas University, Pieve Emanuele, Milan, Italy; [4]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [5]Lillebaelt Hospital, Vejle, Denmark; [6]Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; [7]Sanofi, Bridgewater, NJ, USA; [8]Sanofi, Cambridge, MA, USA

Correspondence: Nijra L Lugogo, University of Michigan Medical School, 300 North Ingalls St, Suite 2C40, Ann Arbor, MI, 48109, USA, Email nlugogo@med.umich.edu

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Patients with uncontrolled, moderate-to-severe asthma are at a higher risk of impaired lung function and asthma exacerbations.[1] Oral corticosteroids (OCS) are commonly used for treating asthma exacerbations and as a chronic therapy if patients remain symptomatic. However, the potential and substantial detrimental effects of OCS are well known.[2] Dupilumab, a fully human VelocImmune®-derived monoclonal antibody,[3,4] blocks interleukin (IL)-4-alpha receptor, the shared receptor component for interleukin (IL)-4 and IL-13, which are key and central drivers of type 2 inflammation in multiple diseases.[5,6] In the Phase 3 LIBERTY ASTHMA QUEST (NCT02414854) and VENTURE (NCT02528214) studies, dupilumab significantly reduced the risk of severe exacerbations and improved lung function in adolescent and adult patients with uncontrolled, moderate-to-severe asthma, while reducing OCS use in patients with glucocorticoid-dependent severe asthma.[7,8] Improvements were sustained for up to two years in the long-term TRAVERSE extension study.[9] Dupilumab is approved in the USA for patients with OCS-dependent asthma.

The Registry of Asthma Patients Initiating DUPIXENT (RAPID; NCT04287621) is a global, prospective, observational register of a cohort of adolescents and adult patients with asthma who are initiating dupilumab treatment in a real-world setting. RAPID is being conducted in accordance with the Declaration of Helsinki, the International Conference on Harmonization Good Clinical Practice guidelines, and applicable regulatory requirements. The objective of the RAPID registry is to collect information on real-world use of asthma therapy and the long-term effectiveness and safety of dupilumab for asthma in the clinical setting. This analysis characterizes patients with asthma with and without a history of OCS use in the 3 months prior to enrollment in the real-world RAPID registry. A history of prior OCS use was defined as those patients taking controller medications at the start date, on or before the treatment start date and ongoing at treatment start date.

The RAPID registry is currently ongoing and has enrolled patients aged ≥12 years who initiate dupilumab for asthma as the primary indication according to country-specific prescribing information. The registry protocol was developed to permit standard-of-care treatment according to individual provider's normal clinical practice. The full design of the RAPID study has been previously published.[10] The initial approving ethics institution was Advarra, 6100 Merriweather Dr., Suite 600, Columbia, MD 21044 and in participating countries, the appropriate ethics committee approvals or institutional review boards were granted for RAPID and all patients provided written informed consent. Between March 6, 2020 and October 28, 2021, 205 patients were enrolled in the RAPID registry at 47 sites in Denmark, Sweden, and the USA, including Puerto Rico.

Of 205 enrolled patients, 52 (25%) reported using OCS medications in the 3 months prior to screening, with 21/52 (40.4%) patients reporting ongoing OCS use at the time of the first data cut. The most commonly used OCS medications were prednisone (46/52 [88%]), prednisolone (3/52 [6%]), and methylprednisolone (2/52 [3.8%]). Baseline demographics were similar in patients with and without a history of OCS use in the 3 months prior to enrollment (Table 1).

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Table 1 Baseline Demographic and Clinical Characteristics in the Overall Population and in Patients with and without a Prior History of OCS Use in the 3 Months Prior to Initiating Dupilumab for Asthma

	Total (N = 205)	With Prior OCS Use (n = 52)	Without Prior OCS Use (n = 153)
Age (years), mean (SD)	50.1 (17.41)	48.8 (16.78)	50.5 (17.65)
Age (years), median (range)	51 (12–85)	49 (13–83)	54 (12–85)
P-value			0.54
Female gender, n (%)	134 (65.4)	34 (65.4)	100 (65.4)
P-value			<0.0001
BMI (kg/m^2), mean (SD)	30.67 (7.96)	31.65 (8.75)	30.33 (7.68)
P-value			0.32
BMI group, n (%)			
< 25 kg/m^2	43 (21.0)	11 (21.2)	32 (20.9)
≥ 25 to <30 kg/m^2	63 (30.7)	10 (19.2)	53 (34.6)
≥ 30 kg/m^2	88 (42.9)	28 (53.8)	60 (39.2)
Missing	11 (5.4)	3 (5.8)	8 (5.2)
Race, n (%)			
White	152 (74.1)	35 (67.3)	117 (76.5)
Black or African American	27 (13.2)	8 (15.4)	19 (12.4)
Asian	2 (1.0)	0	2 (1.3)
Multiple	2 (1.0)	1 (1.9)	1 (0.7)
Other	6 (2.9)	3 (5.8)	3 (2.0)
Not reported	15 (7.3)	4 (7.7)	11 (7.2)
Missing	1 (0.5)	1 (1.9)	0
Age at diagnosis of asthma, years, mean (SD)	31.1 (21.91)	26.8 (21.83)	32.6 (21.81)
P-value			0.10
Diabetes, n (%)	25 (12.2)	9 (17.3)	16 (10.5)
P-value			<0.0001
Smoking status, n (%)			
Current	9 (4.4)	4 (7.7)	5 (3.3)
Former	41 (20.0)	10 (19.2)	31 (20.3)
Never	151 (73.7)	38 (73.1)	113 (73.9)
Unknown	4 (2.0)	0	4 (2.6)
P-value			<0.0001

(*Continued*)

Table 1 (Continued).

	Total (N = 205)	With Prior OCS Use (n = 52)	Without Prior OCS Use (n = 153)
Asthma controller medications, n (%)	199 (97.1)	50 (96.2)	124 (81.0)
ICS alone	17 (8.3)	13 (25.0)	10 (6.5)
ICS plus LABA	112 (54.6)	30 (57.7)	99 (64.7)
ICS plus LABA plus LAMA	23 (11.2)	10 (19.2)	16 (10.5)
P-value			<0.0001
FVC (L), mean (SD)	3.09 (1.08)	2.86 (1.11)	3.21 (1.0)
P-value			0.15
FVC pp (%), mean (SD)	80.2 (19.0)	80.7 (20.3)	80.0 (18.5)
P-value			0.87
FEV_1 (L), mean (SD)	2.29 (1.14)	2.27 (1.54)	2.31 (0.88)
P-value			0.90
FEV_1 pp (%), mean (SD)	70.3 (20.3)	66.6 (21.4)	72.4 (19.5)
P-value			0.17
$FEF_{25–75\%}$ pp (%), mean (SD)	56.7 (29.2)	45.3 (26.7)	62.6 (29.0)
P-value			0.008
PEF (L/min), mean (SD)	356.9 (169.83)	367.91 (203.62)	354.27 (162.90)
P-value			0.8
ACQ-6 score, mean (SD)	n = 193 2.4 (1.18)	n = 49 2.8 (1.41)	n = 144 2.2 (1.05)
P-value			0.01
AQLQ global score, mean (SD)	n = 192 4.1 (1.31)	n = 49 3.9 (1.34)	n = 143 4.1 (1.30)
Symptoms	4.1 (1.30)	3.9 (1.38)	4.1 (1.27)
Activity limitation	4.6 (1.46)	4.4 (1.52)	4.6 (1.44)
Emotional function	3.7 (1.71)	3.3 (1.65)	3.8 (1.71)
Environmental stimuli	3.8 (1.75)	3.7 (1.70)	3.8 (1.78)
P-value			0.257
Eosinophil count (cells/μL)			
Mean (SD)	0.493 (0.4435)	0.595 (0.5635)	0.461 (0.4015)
Median (Q1–Q3)	0.305 (0.200–0.695)	0.252 (0.200–0.960)	0.310 (0.200–0.600)
P-value			0.35

(*Continued*)

Table 1 (Continued).

	Total (N = 205)	With Prior OCS Use (n = 52)	Without Prior OCS Use (n = 153)
Eosinophil count (cells/μL) category, n/N1 (%)			
< 150	10/64 (15.6)	3/15 (20.0)	7/49 (14.3)
≥ 150 to < 300	15/64 (23.4)	5/15 (33.3)	10/49 (20.4)
≥ 300	39/64 (60.9)	7/15 (46.7)	32/49 (65.3)
P-value			<0.0001
FeNO (ppb), mean (SD)			
Mean (SD)	42.2 (34.83)	50.6 (34.81)	37.5 (34.37)
Median (Q1–Q3)	34.0 (16.0–56.0)	43.0 (26.0–63.0)	30.0 (13.0–56.0)
Range (ppb)	4–186	13–150	4–186
P-value			0.16
FeNO category, n/N1 (%)			
< 25 ppb	22/61 (36.1)	5/22 (22.7)	17/39 (43.6)
≥ 25 ppb	39/61 (63.9)	17/22 (77.3)	22/39 (56.4)
P-value			<0.0001

Notes: All *P*-values are comparisons between the prior OCS use and non-prior OCS use groups. *P*-value was calculated using *t*-test for continuous variables, and chi-square test for categorical variables.

Abbreviations: ACQ-6, 6-item asthma control questionnaire; AQLQ, Asthma Quality of Life Questionnaire; BMI, body mass index; $FEF_{25–75\%}$, forced expiratory flow between 25% and 75% of vital capacity; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; L, liters; LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroids; OCS, oral corticosteroids; PEF, peak expiratory flow; pp, percent predicted; ppb, parts per billion; Q, quartile; SD, standard deviation.

There was a higher incidence of diabetes in those patients with a history of OCS use compared with those without (17.3% vs 10.5%, P <0.0001) respectively), but numbers were small overall. Notably, the mean (standard deviation [SD]) body mass index was 31.7 (8.8) kg/m^2 and 30.3 (7.7) kg/m^2 for patient subgroups with and without prior OCS use, respectively. The mean (SD) age at asthma diagnosis was 26.8 (21.8) years and 32.6 (21.8) years, respectively, in patients with and without prior OCS use. The majority of patients had never smoked (73.1% and 73.9% [P < 0.0001], respectively) and never vaped (92.3% and 86.9% [P <0.0001], respectively).

Lung function was similar between the patients with and without OCS use before enrolling, with numerically lower values in the OCS group. In patients with a history of OCS use in the 3 months prior to enrollment, mean (SD) pre-bronchodilator forced expiratory volume in 1 second (FEV_1) (n = 30) was 2.3 (1.5) L, pre-bronchodilator percent predicted FEV_1 (n = 36) was 66.6% (21.4%), forced vital capacity (FVC) (n = 30) was 2.9 (1.1) L, percent predicted FVC (n = 33) was 80.7% (20.2%), peak expiratory flow (PEF) rate (n = 13) was 367.9 (203.6) L, and predicted forced expiratory flow between 25% and 75% of vital capacity ($FEF_{25–75\%}$) (n = 30) was 45.3% (26.7%). In patients without a history of OCS use in the 3 months prior to enrollment, mean (SD) pre-bronchodilator FEV_1 (n = 59) was 2.3 (0.9) L, pre-bronchodilator percent predicted FEV_1 (n = 64) was 72.4% (19.5%), FVC (n = 59) was 3.2 (1.0) L, percent predicted FVC (n = 63) was 80.0% (18.5%), PEF rate (n = 55) was 354.3 (162.9) L, and percent predicted $FEF_{25–75\%}$ (n = 59) was 62.6% (29.0%).

Blood eosinophil counts were available from 15 patients with a history of OCS in the 3 months prior to enrollment (mean: 0.595 [SD: 0.564; median: 0.252] 10^9/L), and from 49 patients without a history of OCS (mean: 0.461 [SD: 0.402; median: 0.310] 10^9/L). In patients with a history of OCS, 12/15 (80%) had baseline blood eosinophil counts of ≥150 cells/μL, compared with 42/49 (86%) of patients without a history of OCS. Baseline fractional exhaled nitric oxide (FeNO) levels were available from 22 patients with a history of OCS (mean: 50.6 [SD: 34.8; median: 43.0] parts

per billion [ppb]), and from 39 patients without a history of OCS (mean: 37.5 [SD: 34.4; median: 30.0] ppb). 17/22 (77%) patients with a history of OCS had FeNO levels ≥25 ppb, compared with 22/39 (56.4%, $P < 0.0001$) patients without a history of OCS.

In patients with a history of OCS use in the 3 months prior to enrollment, the mean (SD) 6-item Asthma Control Questionnaire (ACQ-6) score (n = 49) was 2.8 (1.4) and the mean (SD) Asthma Quality of Life Questionnaire (AQLQ) global score (n = 49) was 3.9 (1.3). In patients without a history of OCS use in the 3 months prior to enrollment, the mean (SD) ACQ-6 score (n = 144) was 2.2 (1.1), and the mean (SD) AQLQ global score (n = 143) was 4.1 (1.3). Individual AQLQ domain scores were also similar between groups.

Of the 52 patients with OCS use in the 3 months prior to enrollment, 50/52 (96%) were using asthma controller medications: 13/52 (25%) on inhaled corticosteroids (ICS) alone, 30/52 (58%) on ICS/long-acting beta agonists (LABA), and 10/52 (19%) on ICS/LABA/long-acting muscarinic antagonists (LAMA). Of the 153 patients with no history of OCS in the 3 months prior to enrollment, 124/153 (81%) were using asthma controller medications: 10/153 (7%) on ICS alone, 99/153 (65%) on ICS/LABA, and 16/153 (10%) on ICS/LABA/LAMA.

In this initial analysis of baseline characteristics of patients from RAPID initiating dupilumab for moderate-to-severe asthma in a real-world setting, 25% of the patients had received OCS in the 3 months prior to enrollment or were currently receiving OCS at enrollment. In the 3 months prior to enrollment, mean baseline FeNO levels were higher in the OCS patient group compared with the group without OCS, although the number of patients with available biomarker data is too small to draw meaningful conclusions. At the time of enrollment, patients with and without a history of recent OCS use presented with similarly impaired lung function, indicating a high unmet treatment need, regardless of prior OCS use. The finding that around a quarter of patients initiating dupilumab in RAPID had a recent history of or were receiving ongoing treatment with OCS indicates that, in this real-world asthma population, many patients are in need of add-on therapy to reduce OCS use.

Data Sharing Statement

Qualified researchers may request access to study documents (including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan) that support the methods and findings reported in this manuscript. Individual anonymized participant data will be considered for sharing once the indication has been approved by a regulatory body, if there is legal authority to share the data and there is not a reasonable likelihood of participant re-identification. Submit requests to https://vivli.org/.

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