Sanofi und Regeneron arbeiten gemeinsam an einem globalen Produktentwicklungsprogramm und an der Vermarktung von DUPIXENT®.

344553-MAT-DE-2104239-1.0-09/2021

Mit wegweisenden Therapien
komplexen Erkrankungen begegnen.

SANOFI GENZYME

WISSENSCHAFTLICHE INFORMATION

Baseline-Charakteristika von Patienten mit schwerem Asthma unter Dupilumab in der klinischen Praxis, in einer multinationalen, nicht-interventionellen, Real-World Studie

ProVENT

Lommatzsch M. et al., 2021

Präsentiert auf dem 31. Internationalen Kongress der European Respiratory Society (ERS). Virtueller Kongress, 5.-8. September 2021.

Mit wegweisenden Therapien
komplexen Erkrankungen begegnen.

SANOFI GENZYME

Real-World Characteristics of Patients Receiving Dupilumab in Routine Clinical Practice in a Multinational, Non-Interventional Study (ProVENT)

Marek Lommatzsch[1], Stephanie Korn[2], Olaf Schmidt[3], Hartmut Timmermann[4], Henrik Watz[5], Amr Radwan[6], Lucia de Prado-Gómez[7], Anne Atenhan[8], Sebastian Barbus[9], Mayank Thakur[8]

[1]Department of Pneumology, University of Rostock, Rostock, Germany; [2]Clinical Research Centre Respiratory Diseases IKF Pneumologie GmbH & Co. KG, Mainz, Germany; [3]Lungen- und Bronchialheilkunde, Koblenz, Germany; [4]Allergologie, Lungen- und Bronchialheilkunde, Hamburg, Germany; [5]Pulmonary Research Institute, LungenClinic Grosshansdorf, Airway Research Center North (ARCN), German Center for Lung Research (DZL), Grosshansdorf, Germany; [6]Regeneron Pharmaceuticals, Inc. Tarrytown, NY, USA; [7]Sanofi, Reading, UK; [8]Sanofi, Berlin, Germany; [9]Sanofi, Frankfurt, Germany

BACKGROUND

- Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4 and IL-13, key and central drivers of type 2-mediated inflammation in multiple diseases[1,2]
- In the EU, dupilumab is indicated as an add-on maintenance treatment in patients aged ≥ 12 years with severe asthma with type 2 inflammation characterized by raised blood eosinophils and/or raised fractional exhaled nitric oxide (FeNO) who are inadequately controlled with high-dose inhaled corticosteroid plus another medicinal product for maintenance treatment[3]
  - However, little is known about the characteristics of asthma patients who have been receiving dupilumab in routine clinical practice
- ProVENT is a non-interventional, real-world study enrolling patients in Germany, Switzerland, and Austria to assess the effectiveness, the pattern of use, and the subjective patient-reported outcomes (PROs) of dupilumab treatment under routine conditions in patients aged ≥ 12 years with severe uncontrolled asthma

OBJECTIVE

- **We assess the baseline characteristics for a pre-specified interim analysis of patients with type 2 asthma enrolled in this study, including demographics, effectiveness, asthma control, previous therapy, type 2 comorbidities, and biomarker levels (blood eosinophils, FeNO, and IgE)**

METHODS

Evaluation parameters

- ProVENT is enrolling patients aged ≥ 12 years with a baseline documentation of the following parameters:
  - Number of exacerbations in the past 24 months
  - Number of asthma-associated hospitalizations and emergency room visits
  - Values for forced expiratory volume in 1 second (FEV_1), peak expiratory flow (PEF), forced vital capacity (FVC), and maximal expiratory flow
  - Received ≥ 1 dose of dupilumab

METHODS (CONT.)

Study assessments

- This interim analysis pool includes the first 108 patients who enrolled in ProVENT since February 2020
  - N = 99 patients who had received ≥ 1 dose of dupilumab were analyzed in the final data set
  - The following characteristics were assessed: baseline characteristics (including socio-demographic and disease-related characteristics) of patients who receive dupilumab in a real-world setting, type 2 and other comorbidities, exacerbations and treatments in the 24 months prior to dupilumab treatment; asthma phenotype, baseline values of relevant biomarkers (blood eosinophil levels, total IgE, FeNO), concomitant therapies, and baseline values of the subjective PROs using pertinent questionnaires (e.g. 7-item Asthma Control Questionnaire [ACQ-7] and Standardized Asthma Quality of Life Questionnaire [AQLQ(S)])

RESULTS

Table 1. Baseline demographics, disease characteristics, and biomarker levels.

Characteristics	Population (N = 99)
Age, years	50.03 ± 16.14
Female sex, n (%)	58 (58.59)
Height, cm (n = 96)	171.33 ± 10.32
Weight, kg (n = 96)	83.73 ± 21.85
Smoker or ex-smoker, n (%)	30 (30.30)
Cigarettes per day, n	12.33 ± 7.21
OCS at study baseline, n (%)	15 (15.15)
Previously treated with other biologics, n (%)	17 (17.17)
Asthma relevant parameters	
Severe asthma exacerbations in the past 24 months, n (n = 98)	1.97 ± 3.22
… in patients with FeNO < 25 ppb, n (n = 22)	2.59 ± 4.71
… in patients with FeNO ≥ 25 ppb, n (n = 51)	1.86 ± 2.91
… in patients with FeNO ≥ 50 ppb, n (n = 25)	2.28 ± 3.34
… in patients with blood eosinophils ≥ 300 cells/µL, n (n = 26)	3.12 ± 4.61
… in patients with blood eosinophils ≥ 150 cells/µL, n (n = 34)	2.97 ± 4.08
… in patients with blood eosinophils < 150 cells/µL, n (n = 23)	1.95 ± 3.20
Pre-BD FEV_1, L (n = 82)	2.31 ± 0.83
Pre-BD FEV_1, % (n = 75)	70.81 ± 23.67
Biomarkers	
Blood eosinophils, cells/µL (n = 57)	474.70 ± 1,105.65
Blood eosinophils, median (Q1–Q3), cells/µL (n = 57)	184.00 (7.60–505.00)
FeNO, ppb (n = 74)	46.50 ± 35.61
FeNO, median (Q1–Q3), ppb (n = 74)	38.00 (23.00–64.00)
Total serum IgE, IU/mL (n = 65)	617.35 ± 1,032.02
Total serum IgE, median (Q1–Q3), IU/mL (n = 65)	181.00 (74.30–781.00)

All values are given in mean ± SD unless specified otherwise. BD, bronchodilator; IU, international unit; OCS, oral corticosteroid; ppb, parts per billion; Q1, 25% quantile; Q3, 75% quantile; SD, standard deviation.

RESULTS (CONT.)

Table 2. Baseline values of patient-reported outcomes.

Characteristics	Population (N = 99)	
	Mean ± SD	Median (Q1–Q3)
ACQ-5 score (n = 79)	2.49 ± 1.40	2.60 (1.20–3.40)
ACQ-7 score (n = 56)	2.51 ± 1.16	2.57 (1.57–3.43)
ACT score (n = 81)	15.48 ± 5.33	16.00 (11.00–20.00)
AQLQ(S) overall score (n = 79)	4.98 ± 1.46	5.00 (4.00–6.25)
AQLQ(S) emotional function score (n = 79)	4.59 ± 1.27	4.90 (3.64–5.50)
SNOT-22[a] score (n = 27)	46.48 ± 21.72	45.00 (30.00–63.00)
Separate SNOT score of the items identified as Important (n = 16)	18.44 ± 5.84	20.00 (16.00–22.00)
POEM[b] score (n = 15)	12.47 ± 8.25	12.00 (8.00–20.00)

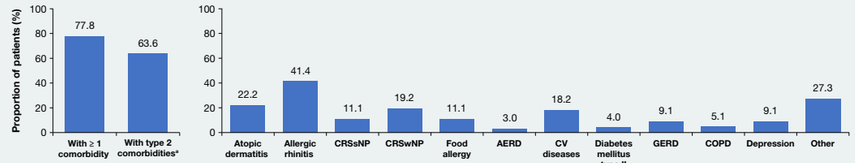
[a]SNOT-22 scores were only obtained for patients with comorbid CRSwNP. [b]POEM scores were only obtained for patients with comorbid AD.
ACQ-5, 5-item Asthma Control Questionnaire; ACT, Asthma Control Test; AD, atopic dermatitis; CRSwNP, chronic rhinosinusitis with/without nasal polyps; AQLQ(S), standardized asthma quality-of-life questionnaire; POEM, Patient-Oriented Eczema Measure; Q1, 25% quantile; Q3, 75% quantile; SNOT-22, 22-item Sino-Nasal Outcome Test; SD, standard deviation.

Table 3. Proportion of patients enrolled in ProVENT based on biomarker levels.

Characteristics	Population (N = 99)
FeNO category	
Patients with FeNO ≥ 50 ppb at baseline	26 (26.3)
Patients with FeNO ≥ 25 ppb at baseline	52 (52.5)
Patients with FeNO < 25 ppb at baseline	22 (22.2)
Patients with missing baseline measurement	25 (25.3)
Eosinophil category	
Patients with eosinophils ≥ 300 cells/µL at baseline	26 (26.3)
Patients with eosinophils ≥ 150 cells/µL at baseline	34 (34.3)
Patients with eosinophils < 150 cells/µL at baseline	23 (23.2)
Patients with missing baseline measurement	42 (42.4)
Type 2 asthma (eosinophils ≥ 150 cells/µL and/or FeNO ≥ 25 ppb at baseline)	
Patients with eosinophils ≥ 150 cells/µL and FeNO ≥ 25 ppb at baseline	17 (17.2)
Patients with eosinophils < 150 cells/µL and/or FeNO < 25 ppb at baseline	27 (27.3)
Patients with missing baseline measurement	55 (55.6)

All data are shown as n (%). FeNO, fractional exhaled nitric oxide; ppb, parts per million.

Figure 1. Patients with ongoing comorbidities.



*Type 2 comorbidites included: AD, allergic rhinitis, CRSw/sNP, AERD, EoE, food allergy. AERD, aspirin-exacerbated respiratory disease; COPD, chronic obstructive pulmonary disease; CRSsNP chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CV, cardiovascular; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease.

Figure 2. Asthma phenotype and allergen sensitivity in patients enrolled in ProVENT.

*Asthma phenotypes (mainly allergic, non-allergic, or mixed) were physician reported; mixed forms of asthma were defined according to classification of ICD-10 code for asthma bronchiale in Germany (https://www.icd-code.de/suche/icd/code/J45.-.html?sp=SAsthma). ICD, International Classification of Diseases.

Figure 3. Previous asthma therapies and therapies at baseline.

OCS, oral corticosteroids.

Table 4. Healthcare resource utilization and effects of disease in the past year by patients enrolled in ProVENT.

Characteristics	Population (N = 99)
Employment status, n (%)	
Full-time employed	36 (36.36)
Part-time employed	12 (12.12)
Unemployed	8 (8.08)
Retired	14 (14.14)
Missing	29 (29.29)
Student status (multiple answers possible), n (%)	
Full-time student	4 (4.04)
Part-time student	1 (1.01)
Secondary education (high school graduate)	1 (1.01)
Other education,	4 (4.04)
Medical consultations because of asthma in the past year (multiple answers possible), n (%)	
Family doctor	36 (36.36)
Internist	1 (1.01)
Lung specialist	63 (63.64)
Other specialist	12 (12.12)
Other	4 (4.04)
Number of sick days in the past 3 months…	
… due to asthma symptoms, mean ± SD (n = 34)	9.0 ± 9.5
… due to tiredness, mean ± SD (n = 10)	1.5 ± 3.4
… due to depression, mean ± SD (n = 9)	10.0 ± 30.0
Number of days without exercise or usual activities in the past 3 months…	
… due to anxiety, mean ± SD (n = 14)	5.4 ± 9.7
… due to asthma symptoms, mean ± SD (n = 51)	15.4 ± 20.0
… due to tiredness, mean ± SD (n = 20)	11.6 ± 19.1
… due to depression, mean ± SD (n = 15)	4.4 ± 10.5
… due to other reasons, mean ± SD (n = 7)	4.3 ± 11.3
Number of nights with sleep disturbances due to asthma symptoms in the past month, mean ± SD (n = 65)	7.4 ± 13.0

CONCLUSIONS

- **In this real-world study, a majority of asthma patients had elevated type 2 biomarkers, high exacerbation rates in the previous year, and poor quality of life**
- **Dupilumab was the first biologic agent as a therapy of choice for most of the patients with severe asthma**
  - **Only a few patients switched from other biologics to dupilumab in this patient cohort**
- **Only 64% of patients were treated by a pulmonologist in the past year due to asthma symptoms. 36% of patients consulted a primary care physician due to asthma, 12% a non-pulmonologist specialist**

References: 1. Gandhi NA, et al. Expert Rev Clin Immunol. 2017;13:425-37. 2. Le Floc'h et al. Allergy. 2020;75:1188-204. 3. DUPIXENT® (dupilumab). Summary of Product Characteristics. European Medicines Agency. Available from: https://ec.europa.eu/health/documents/community-register/2019/20190801145601/anx_145601_en.pdf. Accessed August, 2021.

Acknowledgments: Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. Medical writing/editorial assistance was provided by Martina Fuchsberger, PhD, of Excerpta Medica, and was funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc., according to the Good Publication Practice guideline.

Disclosures: Lommatzsch M: ALK, Allergopharma, AstraZeneca, Bencard Allergie, Berlin-Chemie, Boehringer Ingelheim, Bosch, Chiesi, Circassia, GSK, HAL Allergy, Janssen-Cilag, MSD, Mundipharma, Novartis, Nycomed/Takeda, Sanofi, Teva, UCB – honoraria for lectures and/or consultant fees; AstraZeneca, Novartis – reimbursement of attendance fees for conferences and educational events, and of travel and accommodation costs; AstraZeneca, DFG, GSK – research support; AstraZeneca, Sanofi – funding for performing clinical studies. **Korn S:** AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, Roche, Sanofi, Teva – honoraria for lectures and/or consultant fees; AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Roche, Sanofi – research support. **Schmidt O:** AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, Sanofi, Teva – honoraria for lectures and/or consultant fees; AstraZeneca, Boehringer Ingelheim, GSK, Novartis, Sanofi – research support. **Timmermann H:** AstraZeneca, Almirall, Astellas Pharma, Bayer, Boehringer Ingelheim, Berlin-Chemie, GSK, Leti Pharma, Meda, Mundipharma, Novartis, Nycomed, Pfizer, Sanofi, Takeda, Teva – consultant fees. **Watz H:** AstraZeneca, Bayer, Boehringer Ingelheim, Chiesi, GSK, Novartis, Sanofi, Takeda – consultant, travel, and speaker fees. **Radwan A**: Regeneron Pharmaceuticals, Inc. – employee and shareholder. **de Prado-Gómez L, Atenhan A, Barbus S, Thakur M:** Sanofi – employees, may hold stock and/or stock options in the company.

Presented at the 31st International Congress of the European Respiratory Society (ERS); Virtual Congress; September 5–8, 2021.