FASE-CPHG study: a panoramic snapshot of difficult-to-treat, severe asthma in French nonacademic hospitals

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ABSTRACT

Background: Real-world data describing management of patients with severe asthma are limited. To address this issue, we conducted FASE-CPHG (France Asthme Sevère – Collège des Pneumologues des Hôpitaux Généraux), a descriptive, multicentric, and observational cross-sectional study.

Methods: French pulmonologists from nonacademic hospitals completed questionnaires on patient characteristics and ongoing asthma treatment for severe asthmatic patients observed during the inclusion period. In addition, we collected data from patients via self-assessment questionnaires.

Findings: 104 physicians recruited 1502 patients within 1 year. The mean age of the 1465 patients analysed was 54.4±16.1 years. Severe asthmatic patients were more frequently female (63%), with a history of atopy (65%). Most patients remained poorly controlled or uncontrolled, with an important difference between physicians’ opinion and the Global Initiative for Asthma criteria (63% versus 96%). The most common comorbidities included ear, nose and throat diseases (59% of cases); anxiety (40%); and gastro-oesophageal reflux disease (39%). Allergic sensitisation tests and/or blood eosinophil count evaluation, and spirometry were performed in 92% and 98% of patients, respectively. The mean eosinophil count and total serum IgE were 437 cells·mm−3 and 546 UI·L−1, respectively. In addition to high doses of inhaled corticosteroids plus long-acting β2-agonists, patients were receiving leukotriene receptor antagonists (52%), anticholinergic drugs (34%), anti IgE (27%) and oral corticosteroids (17%); 65% adhered to their treatment.

Interpretation: This study provides insight into the characteristics and management of severe asthma in France and may help improve knowledge on this pathology, which represents a high burden to healthcare.

@ERSpublications
This is a large study of severe asthma, with >1500 patients included, that gives new insights into epidemiological data, patients’ characteristics and disease management http://bit.ly/2K9NqMT

Cite this article as: Portel L, Parrat E, Nocent-Ejnaini C, et al. FASE-CPHG study: a panoramic snapshot of difficult-to-treat, severe asthma in French nonacademic hospitals. ERJ Open Res 2019; 5: 00069-2019 [https://doi.org/10.1183/23120541.00069-2019].

This article has supplementary material available from openres.ersjournals.com

Received: 13 March 2019 | Accepted after revision: 30 July 2019

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Introduction

Asthma is an inflammatory chronic airway disease characterised by dyspnoea, wheeze, cough and chest tightness. It is a frequent disease that affects >300 million people worldwide [1] and ~5–10% of the general population in France, according to Santé Publique France, the French national public health agency. However, epidemiological data regarding severe asthma in real life are scarce. Estimations vary from 5–10% [2] to >10% [3]. Recently, the asthmaPOP survey estimated prevalence of severe asthma in France to be 3.8% [4].

The European Respiratory Society, the American Thoracic Society and local French guidelines have defined asthma as severe when it requires treatment with high dose of inhaled corticosteroids (ICS) plus long-acting β2-agonists (LABAs) together with an add-on treatment to prevent it from becoming “uncontrolled” or when it remains uncontrolled despite this therapy [5, 6].

Severe asthma cases represent the majority of health costs for asthma, which are mainly due to indirect costs (absenteeism, lack of productivity) rather than medical costs, like medication, even if new treatments are relatively expensive. The costs drastically increase as disease control decreases, with the cost being five times higher for uncontrolled asthma [7].

Furthermore, severe asthma has been identified as a heterogeneous disease with various clinical phenotypes of differing severity, which develop through distinct mechanisms [8, 9]. The identification and characterisation of asthma subtypes have already led to the development of new therapies, including monoclonal antibodies directed against immunoglobulin (Ig)E (omalizumab) [6] or against interleukin (IL)-5 (mepolizumab, reslizumab, benralizumab) [10, 11], and will be valuable for developing new drugs and defining better asthma management.

To date, severe asthma remains poorly understood, and the impact of recent therapeutic advances on the management of this disease has been insufficiently studied. The aim of our study was to describe the clinical characteristics of adults with severe asthma and their management in French nonacademic hospitals.

Research in context

Evidence before this study
Data on severe asthma in real life are scarce.

Added value of this study
Our study was based on >1500 patients with severe asthma. We report updated data on epidemiology and biology and major information on disease control and treatment adherence, which are key for appropriate management of asthma. Moreover, no previous studies have included such a large sample of adult patients with severe asthma. Thus, we believe our study provides a great contribution to the existing literature.

Implications of all the available evidence
This article will be of interest because our results can assist clinicians in patient characterisation and improve their daily practice. Moreover, in this era of new treatments based on biological findings, our data will be of great interest for ongoing research in the industry.

Methods

Study population
The Collège des Pneumologues des Hôpitaux Généraux (CPHG) is a collaborative group of pulmonologists working in nonacademic hospitals. This structure has long been invested in clinical research, especially focusing on lung cancer, and has conducted two large epidemiological studies, KBP 2000 and KBP 2010, including >12000 patients [12, 13].

We initiated FASE-CPHG (France Asthme Sévère – Collège des Pneumologues des Hôpitaux Généraux) in 2016 as a descriptive, multicentric and observational cross-sectional study conducted in general hospitals in France. The study was approved by the local ethics committee (Comité Consultatif sur le Traitement de l’Information en matière de Recherche dans le domaine de la Santé) and was conducted according to the French law and guidelines on epidemiological and descriptive studies.

Pulmonologists from an extensive list of practitioners were contacted to confirm their willingness to participate in the FASE-CPHG observational study. During the inclusion period, between May 2016 and July 2017, selected pulmonologists were asked to recruit all patients who met the eligibility criteria to ensure exhaustivity. For the same reason, patients who refused to participate in the study were logged in a noninclusion register.
Patients fulfilling all following criteria were included in the study: age >18 years and severe asthma diagnosis according to the physician and based on the Global Initiative for Asthma (GINA) [14]. The physician informed all subjects about the study during a regular visit and patients were encouraged to participate. Oral consent was obtained from all patients before entering this non-interventional study. Patients diagnosed with solid cancer or malignant haemopathy, as well as those who refused to participate in the study, were excluded.

**Patient data collection**

During a regular patient visit, physicians completed a secure electronic case report form (eCRF) on patients’ characteristics (sociodemographic data, potential asthma triggers, medical history, comorbidities, clinical parameters) and ongoing asthma treatment for all patients seen during the study period.

In addition, patients were required to fill in a paper self-assessment questionnaire comprising items on asthma control (Asthma Control Test (ACT)), anxiety and depression (Hospital Anxiety and Depression Scale (HADS)) and medication adherence (four-item Morisky Medication Adherence Assessment Scale (MMAS-4)).

**Data management**

Data were entered into databases managed by Kappa Santé (Paris, France). Duplicates were identified using indirectly nominative data (initial age and sex) and reviewed by the participating pulmonologists. In addition to the online control present on the eCRF, a scientific committee reviewed data before database freeze for other errors, omissions or inconsistencies.

Patients enrolled by participating physicians with no completed CRFs were removed from the analysis.

**Statistical analyses**

All statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC, USA). p-values <0.05 were regarded as statistically significant.

Qualitative variables are presented as raw values and frequencies, and the numbers of missing data are specified. Quantitative data are expressed as numbers of analysed values or mean±SD.

According to the GINA criteria, severe asthma is defined as asthma that requires step 4 or 5 treatment to prevent it from becoming “uncontrolled” or asthma that remains “uncontrolled” despite this treatment [14]. Uncontrolled patients administered with step 3 treatment were also considered as severe asthmatics, as the adjustment strategy in cases of uncontrolled asthma for 3 months would be to step-up treatment to step 4. After validation by the physicians, patients treated only with short-acting β2-agonists (SABA) were excluded from analyses, as they were considered to be nonsevere asthma patients according to the GINA criteria.

Asthma control was evaluated using the ACT, a five-item questionnaire on activity limitation, shortness of breath, night symptoms, use of rescue medication and self-perception of asthma control. Each parameter was scored from 1 (poorly controlled) to 5 (well controlled). The HADS was used to evaluate anxiety and depression symptoms in patients. This scale contains 14 items divided in two subscales: one for anxiety (HADS-A) and one for depression (HADS-D). A score ≥11 on either scale indicates a definitive case, whereas scores <7 generally indicate an absence of the issue. The MMAS-4 questionnaire was used to assess medication adherence [15–17].

**Role of the funding source**

The funding bodies had no role in the conception of this manuscript, and they did not participate in any way in the design of the study, analysis of results, writing or revision of the manuscript.

The corresponding author confirms that he had full access to all the data in the study and had final responsibility for the decision to submit for publication.

**Results**

**Participation of pulmonologists and patient recruitment**

Patients were enrolled between May 2016 and July 2017. Out of the 1502 patients initially recruited by 104 physicians, 1465 completed the questionnaires and had available data, and were therefore eligible for analysis (figure 1). In the entire study population, questionnaires were missing from 98 patients.

**Confirmation of severe asthma**

Among the 1465 patients analysed, 95% were confirmed as severe asthmatic patients according to the GINA classification. For 78 patients, severe asthma was not confirmed, mainly due to the very short
follow-up (<6 months) by the pulmonologist (in 94% of cases; table 1). Since results from the confirmed severe asthma population according to the GINA were coherent with those of the entire study population, the following analysis was performed on the 1465 patients.

**Patient characteristics**

Characteristics of patients are shown in table 2. Most of the patients were female (63%), with an overall mean age of 54.4 years. The mean body mass index was 27.6 kg·m$^{-2}$. 32% of the population were overweight and 30% were obese. Most patients were nonsmokers (60%). Active smokers represented 12% of patients, smoking an average of 18 packs per year, among smokers and ex-smokers. There was a high incidence of atopy history, with personal atopy observed in 65% of patients. Regarding environmental exposures, 42% of the population was exposed to domestic animals, and approximately half of the patients (48%) lived in an urban environment.

**Asthma control**

A significant difference in asthma control was observed between asthma assessment according to pulmonologists’ judgment and to the GINA criteria (p<0.0001; table 3). Physicians considered that asthma
was well controlled in 37.4% of patients, while this number was only 4% according to the GINA criteria. A 96.7% association was found between asthma control according to the physician and that according to the GINA criteria regarding uncontrolled patients. A significant association was found between well-controlled asthma and high adherence level ($p<0.0001$; supplementary table S1).

**Asthma history and clinical presentation**

The mean age at diagnosis was 26.9 years. Asthma occurred before the age of 12 years in 34% of patients, while in 37%, asthma onset was between 13 and 39 years of age. Approximately half of the patients (52%) had a history of acute severe asthma. Several patients (65%) had experienced frequent exacerbations in the previous year, with an average number of 2.5 severe exacerbations per patient per year. Exacerbations led to an average number of 35.3 sick days over the previous year (table 4).

The most frequent asthma-related conditions were ear, nose and throat (ENT) diseases (identified in 58.9% of the patients), atopic dermatitis (15.4%) and drug allergy (14.1%). Chronic rhinitis was the most common ENT disease (table 5).

The majority of patients had one or more comorbidities (table 5) with a high prevalence of anxiety (39.5%), gastro-oesophageal reflux disease (GORD; 39.1%), arterial hypertension (25.5%) and obstructive sleep apnoea syndrome (11%). Using the HADS, we identified anxiety and depression in 43.3% and 23.6%, respectively, of severe asthma patients, which was greatly consistent with the physician’s judgment. Aspirin sensitivity was present in 160 (10.9%) patients, and Widal syndrome was diagnosed in 101 (6.9%) patients (table 5).

Allergic sensitisation tests and/or blood eosinophils counts were performed for almost all patients (92.1%; table 6). Patients were mostly allergic to dust mites (77.5%) and pollens (57%). The blood eosinophil count was >300 cells·mm$^{-3}$ in 53.4% of patients, with a mean value of 436.8±466.4 cells·mm$^{-3}$. The total serum IgE test was performed in 62.2% patients; the mean total IgE was 546.1±1013.2 IU·L$^{-1}$.

Spirometry was conducted in 98.2% of severe asthmatic patients and was most often performed in a short period prior to the study (~90% patients had a spirometry test in the previous 6 months). Prebronchodilator forced expiratory volume in 1 s (FEV$_1$) and the ratio of FEV$_1$ to forced vital capacity were 72.1% predicted and 70.2% pred, respectively. The intake of $\beta_2$-agonists led to a minimum 10% increase of FEV$_1$ in 33.4% of patients, reflecting the persistence of a significant reversibility of bronchial obstruction (table 7).

Exhaled nitric oxide was measured in only 64 (4.4%) patients, whereas chest and ENT computed tomography scans were performed in 52% and 16% of patients, respectively (table 7).

**Therapeutic management**

Almost all patients (n=1443) with severe asthma received a long-term treatment in addition to SABA. ~90% of the patients received a combination of ICS and LABA. ICS/LABA therapy was mainly used at high doses, with 44.5% of patients receiving a dose >1001 μg·day$^{-1}$ (equivalent dose of beclomethasone dipropionate). In addition, use of antileukotriene drugs (52.2%), anticholinergic drugs (34%), anti-IgE (26.8%), continuous oral corticosteroids (16.8%) and theophylline (6.7%) was frequently observed. Among concomitant therapies, 45% patients received antihistamine treatment and 33.2% received a treatment for GORD (table 8).
Patients had a mean adherence score of 3.4 on the MMAS-4. Based on MMAS, 835 (65%) patients were adherent to their treatment. Based on physician opinion, 78.5% of patients were considered as highly adherent, and >20% were considered nonadherent to their treatment (with medium or low adherence; table 8). 94.6% of patients was considered to have good inhalation technique according to their pulmonologist.

**Discussion**

This very large study presents a new picture for the descriptive epidemiology of severe asthma in France. We summarised cross-sectional data of >1500 patients with severe asthma, managed in nonacademic

| TABLE 2 Patient characteristics |
|---------------------------------|
| **Subjects n**                  | 1465 |
| Female                          | 921 [63] |
| **Age years**                   | 54.4±16.1 |
| 18–39                           | 281 [19] |
| 40–59                           | 586 [40] |
| ⩾60                            | 598 [41] |
| **BMI kg·m⁻²**                  | 27.6±6.2 |
| <18                            | 45 [3] |
| 18–24.99                       | 512 [35] |
| 25–29.99                       | 473 [32] |
| ⩾30                            | 435 [30] |
| **Physical activity level**     |      |
| No activity                     | 440 [32] |
| Occasional                      | 528 [38] |
| Regular                         | 323 [23] |
| Common or at competition level  | 99 [7] |
| Missing data                    | 75 |
| **Educational level**           |      |
| Ongoing                         | 8 [1] |
| No diploma                      | 420 [32] |
| Certificate of general education (junior high school) | 413 [31] |
| Baccalaureate (high school)     | 200 [15] |
| Post-baccalaureate diplomas (bachelor and graduate) | 285 [21] |
| Missing data                    | 139 |
| **Professional status**         |      |
| Active                          | 596 [42] |
| Inactive                        | 311 [22] |
| Retired                         | 511 [36] |
| Missing data                    | 47 |
| **Smoking status**              |      |
| Current smokers                 | 170 [12] |
| Ex-smokers                      | 424 [29] |
| Non-smokers                     | 871 [60] |
| **Smoking history pack-years⁻¹**| 17.9±14.8 |
| **History of atopy**            |      |
| Personal atopy                  | 958 [65] |
| Familial atopy                  | 566 [39] |
| **Animal exposure**             |      |
| Domestic animals                | 610 [42] |
| Dogs                            | 385 [63] |
| Cats                            | 341 [56] |
| Others (rabbits, rodents, birds, …) | 64 [11] |
| Nondomestic animals             | 115 [8] |
| **Housing**                     |      |
| Urban                           | 697 [48] |
| Rural                           | 391 [27] |
| Semi-rural                      | 377 [26] |
| **Residence proximity to a pollution source** | 148 [10] |
| **Residence proximity to a trunk road** | 290 [20] |

Data are presented as n, n (%) or mean±SD. BMI: body mass index.
hospitals in 2016–2017 in France. We analysed patients’ characteristics, medical history and comorbidities, as well as the clinical presentation of asthma with a detailed description of patient management (medication, adherence to treatment and asthma control). Our data are consistent with the results of previous studies confirming the female preponderance and high occurrence of atopy in severe asthmatics [18]. Chronic rhinitis was the most common asthma-related condition, while GORD, high blood pressure and anxiety and depression were frequent in this population. These comorbidities are frequent in severe asthmatic patients, as demonstrated in previous epidemiological studies. Indeed, a recent meta-analysis based on 26 studies (cohort studies, experimental studies and severe asthma registries) conducted in severe asthma populations demonstrated that among extrapulmonary comorbidities, sinusitis, GORD, obesity and hypertension are the most frequent [18].

Furthermore, we found that tobacco use among adults with severe asthma is not rare (12% of active smokers), illustrating the requirement for future efforts to reduce this well-known risk factor. Moreover, we confirmed the involvement of obesity and overweight in asthma, as ~30% and 32% of the patients in our study were obese and overweight; respectively, indicating that these factors must be taken into consideration when addressing severe asthma.

Our analysis showed that blood eosinophils were not measured for 25% of the patients, while the serum IgE test was conducted in only 62% of patients. This may have contributed to undertreatment of patients when considering emerging therapies, such as anti-IL-5 and anti-IgE treatments [19]. Moreover, the mean blood eosinophil count was quite high at 437 cells-mm$^{-3}$, with half of patients having a count >300 cells-mm$^{-3}$, indicating the possibility of treating a large number of our population of French adults with

### TABLE 3 Asthma control

| Control assessed by the physician | Well controlled | Partially controlled | Uncontrolled | Missing data | Total | p-value |
|----------------------------------|----------------|---------------------|-------------|--------------|-------|---------|
| Well controlled                  | 50 (10.1)      | 229 (46.1)          | 217 (43.8)  | 11           | 507   | <0.0001 |
| Partially controlled             | 2 (0.3)        | 98 (17)             | 479 (82.7)  | 19           | 598   |         |
| Uncontrolled                     | 1 (0.4)        | 7 (2.9)             | 236 (46.7)  | 6            | 250   |         |
| Missing data                     | 0              | 0                   | 5           | 7            | 12    |         |
| Total                            | 53 (4)         | 334 (25.2)          | 937 (70.8)  | 43           | 1367  |         |

Data are presented as n (%) or n, unless otherwise stated. GINA: Global Initiative for Asthma.

### TABLE 4 Asthma history

| Subjects | 1465 |
|----------|------|
| Age at asthma onset years | 26.9±20.4 |
| ≤12 | 496 [34] |
| 13–39 | 544 [37] |
| ≥40 | 417 [29] |
| Missing data | 8 |
| Asthma duration years | 27.4±17.9 |
| Pulmonology follow-up duration years | 13.5±12.7 |
| History of acute severe asthma | 757 [52] |
| >2 exacerbations in the past year | 949 [65] |
| Exacerbation history in the past year | |
| Medical consultations | 2.6±3.1 |
| Hospitalisations for asthma | 0.5±1.3 |
| Visits to emergency room | 0.6±1.7 |
| Severe exacerbation | 2.5±3.1 |
| Absenteeism from work/school due to asthma in the past year days | 35.3±68.1 |

Data are presented as n, mean±SD or n (%).
severe asthma with anti-IL-5. Finally, the very high percentage of patients with skin tests, blood eosinophils and spirometry suggest a good quality of the approach to severe asthma with relevant objective measurements.

Lung function testing was conducted in almost all patients in our study population, with the last assessment conducted during the previous 6 months. This reflects the current recommendations for the management of severe asthma, as the periodical measurement of lung function is an integral part of control assessment [6]. Furthermore, and despite its well-known clinical utility, only half of the patients benefited from computed tomography. Since this examination is important in the diagnosis of asthma complications and associated conditions [20], its broader use could help improve management and increase control of the disease. As expected considering the guidelines for severe asthma management [6], we found that exhaled nitric oxide is poorly assessed in current practice, in <5% of patients.

In addition to SABA, a high proportion of severe asthmatics in France (90%) received a combination of ICS and LABA, with a mean dose of 1326 μg·day⁻¹ (beclomethasone dipropionate equivalent). These results are coherent with current GINA recommendations and previous studies conducted across the world [21–23]. Antileukotriene treatment was used in 52.2% of the French severe asthmatics, which is a slightly lower percentage than the 65% in the Belgian registry including 350 patients [23], but similar to that in the Italian registry including 493 patients [24]. The results of these two studies were overall similar to ours, but were conducted on smaller samples. For example, we found that the same proportion of French

| TABLE 5 Medical history and comorbidities |
|------------------------------------------|
| **Subjects**                             | 1465 |
| **Medical history**                      |     |
| Aspirin intolerance                      | 160  |
| Widal syndrome                           | 101  |
| Food allergy                             | 153  |
| Drug allergy                             | 207  |
| Atopic dermatitis                        | 225  |
| Allergic bronchopulmonary aspergillosis  | 40   |
| Churg–Strauss syndrome                   | 15   |
| ENT disease                              | 862  |
| Chronic rhinitis                         | 655  |
| Chronic rhinosinusitis                   | 358  |
| Polyposis                                | 265  |
| **Comorbidities (ENT disease excluded)** |     |
| No comorbidity                           | 387  |
| 1 comorbidity                            | 435  |
| 2 comorbidities                          | 290  |
| ≥3 comorbidities                         | 350  |
| Missing data                             | 3    |
| **Gastro-oesophageal reflux disease**    |     |
| Arterial hypertension                    | 372  |
| Diabetes                                 | 149  |
| Ischaemic cardiopathy                    | 72   |
| Sleep apnoea                             | 161  |
| Osteoporosis                             | 156  |
| Anxiety                                  | 579  |
| Depression                               | 208  |
| Other mental disorder                    | 32   |
| **Anxiety and depression determined with self-assessment questionnaires** | 1367 |
| Anxiety level (HADS-A)                   | 7.4±4.4 |
| Presence of anxiety [score ≥7]           | 583  |
| Absence of anxiety [score ≤7]            | 763  |
| Missing data                             | 21   |
| Depression level (HADS-D)                | 5.1±3.8 |
| Presence of depression [score ≥7]        | 320  |
| Absence of depression [score ≤7]         | 1038 |
| Missing data                             | 9    |

Data are presented as n, n [%] or mean±SD. ENT: ear, nose and throat; HADS: Hospital Anxiety and Depression Scale; A: anxiety; D: depression.
patients were treated with anticholinergic (34%) and anti-IgE therapies (27%) as in the Belgian registry. Maintenance oral corticosteroids (17%) and theophylline (7%) were found in similar frequencies as in the Italian registry (24%), but were lower than in the other registries [21–23, 25]. The values of baseline FEV1 were slightly different between the FASE-CPHG population (72% pred), the Belgian registry (68% pred) and the Italian registry (75%); however, these differences cannot explain differences in the add-on treatment prescription in the three studies, such as the high rate (64%) of Italian patients receiving anti-IgE treatment. Only 4% of the French severe asthmatics were well controlled according to the GINA guidelines, while 65% were adherent to treatment. Uncontrolled asthma was also observed in the COBRA study including a French population of severe asthmatics in which >60% of patients were uncontrolled [26]. Overall, our study shows that physicians tend to overestimate asthma control. Since poor control is a burden for patients and a risk factor for exacerbations, a good evaluation is required in order to better manage patients. Our results show that asthma control assessment during patient visits needs to be improved in France, and strategies for patients are required to improve compliance for better controlling asthma. We expect that exhaustive investigation of the disease will be performed in the future according to new treatments, which were not available at the time of this study.

Despite these interesting results, our study has some limitations. First, its cross-sectional design did not allow us to establish causal associations and descriptions of follow-up. However, our main objective was to produce a comprehensive update on the characteristics of severe asthmatic patients and on practice
regarding the latest scientific progress. A constitution of cohorts with longitudinal follow-up could help to better define the relationship between asthma severity, control and adherence, as well as in the development of efficient practice in the management of asthma in France. Second, the design of the questionnaires did not allow us to perform an exhaustive assessment of comorbidities. Indeed, we chose to focus on pathologies more known to be associated with asthma. Moreover, since these data are declarative and some of these pathologies are underdiagnosed, comorbidity results could be underestimated and should be interpreted with caution. Despite these limitations, this study offers a good geographic representation of the disease. Participating centres were equitably distributed throughout the national territory, and all French regions were represented. Moreover, the participating physicians were asked to include their patients in an exhaustive manner. Thus, our data can be considered to be representative of the current real-world management of severe asthmatic patients in France.

In summary, this FASE-CPHG study is the largest French study and one of the largest worldwide studies to describe severe asthma in adults, with 1502 patients included. Severe asthmatics included in this study have similar characteristics to those previously described across European and American populations. To our knowledge, this is the first study providing an important overview of recent practice in the management of severe asthmatics in nonacademic hospitals in France in such a large sample. Our data indicate that general hospitals in France provide high quality management to severe asthmatics which is in accordance with the current recommendations of the European Respiratory Society and American Thoracic Society, and the GINA guidelines [2, 14]. However, control assessment, optimisation of treatment, as well as adherence to treatment, could be improved, for example by using standardised monitoring procedures or by creating a French registry. These data on epidemiology, management and therapy choices for severe asthma will help pulmonologists in more efficient patient characterisation and

| TABLE 7 Biology and lung function tests |
|----------------------------------------|
| Subjects                                |
| α1-antitrypsin test                     |
| <0.8 g L⁻¹                             |
| 0.8–0.99 g L⁻¹                         |
| ≥1 g L⁻¹                               |
| Mean result g L⁻¹                      |
| Pulmonary function tests                |
| Time since last spirometry months      |
| ≤6 months                              |
| 6–12 months                            |
| >12 months                             |
| Missing data                           |
| Pre-bronchodilator FEV₁ % pred         |
| Post-bronchodilator FEV₁ % pred        |
| Pre-bronchodilator FEV₁/FVC % pred     |
| FEV₁/FVC <70% pred                     |
| FEV₁ evolution after β₂-agonists %     |
| No evolution                           |
| Increase <10%                          |
| Increase ≥10%                          |
| Missing data                           |
| Exhaled nitric oxide measurements      |
| Results ppb                            |
| Chest CT scan                          |
| Bronchiectasis                         |
| Bronchial wall thickening              |
| Emphysema                              |
| ENT CT scan                            |
| Absence of clinical signs              |
| Polyps                                 |
| Chronic sinusitis                      |
| Missing data                           |

Data are presented as n, n (%) or mean±sd. FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; CT: computed tomography; ENT: ear, nose and throat.
in making appropriate treatment decisions. This study could also be interesting for companies to better understand this form of asthma, in order to develop new treatments. Furthermore, improving knowledge on this pathology and its current management could lead to a reduction of the tremendous costs related to the disproportionate use of medical resources to manage frequent exacerbations, which are part of severe asthma when uncontrolled. Further studies are still needed to better characterise and understand severe asthma, to identify potential associated features and biomarkers, which can provide new specific treatments for this pathology. Additional analyses of FASE-CPHG data are underway to better understand this disease, particularly in terms of phenotype description and management.

Acknowledgements: The authors would like to thank Vanessa Cohignac, Hélène Le Cloarec, Mathilde Pouriel and Nathalie Texier from Kappa Santé (Paris, France), a contract research organisation, for the operational management of the study, data analysis and preparation of the study report and the present article. The authors would also like to share compassionate thoughts for Juliette Ostinelli.

| TABLE 8 Medications |
|----------------------|
| Subjects | 1465 |
| No LABA/ICS | 22 (1.5) |
| Inhaled corticosteroids only \^ | 136 (9.3) |
| <500 μg·day\^-1 | 21 (15.4) |
| 500–1000 μg·day\^-1 | 41 (30.1) |
| 1000–2000 μg·day\^-1 | 57 (41.9) |
| >2000 μg·day\^-1 | 15 (11) |
| LABAs only | 106 (7.2) |
| ICS/LABA combination \^ | 1326 (90.5) |
| <500 μg·day\^-1 | 62 (4.7) |
| 500–1000 μg·day\^-1 | 419 (31.6) |
| 1000–2000 μg·day\^-1 | 590 (44.5) |
| >2000 μg·day\^-1 | 253 (19.1) |
| Anticholinergic treatment | 498 (34) |
| Antileukotriene (montelukast) | 759 (52.2) |
| Long-term oral corticosteroid therapy | 245 (16.8) |
| Mean daily dose \^ | 19.4±34.2 |
| Anti-IgE (omalizumab) | 390 (26.8) |
| Dose mg | 347±155.3 |
| Frequency of treatment | 180 (46.9) |
| Every 2 weeks | 204 (53.1) |
| Every 4 weeks | 6 |
| Missing data | 3.1±2.6 |
| Duration of treatment years | 97 (4.7) |
| Theophylline | 97 (4.7) |
| Other therapies | 84 (5.6) |
| Long-term azithromycin | 655 (45) |
| Antihistamine | 121 (8.3) |
| Antidepressants | 26 (1.8) |
| β-blocker | 483 (33.2) |
| Anti-GORD | 14 (1.5) |
| Postmenopausal hormone therapy | 54 (3.7) |
| Desensitisation in the previous 5 years | 84 (5.8) |
| Alternative medicine | 97 (4.7) |
| Patient adherence level according to physician | 1063 (78.5) |
| High | 245 (18.1) |
| Medium | 47 (3.5) |
| Low | 3.4±1 |
| Adherence level MMAS-4 score | 835 (64.8) |
| Adherent patient (score=4) | 454 (35.2) |
| Non-adherent patients (score <4) | 78 |

Data are presented as n, n (%) or mean±SD. LABA: long-acting β\_2-agonist; ICS: inhaled corticosteroid; Ig: immunoglobulin; GORD: gastro-oesophageal reflux disease; MMAS-4: four-item Morisky Medication Adherence Assessment Scale. \^: doses are presented as equivalent beclomethasone dipropionate; \^: doses are presented as equivalent prednisolone.

https://doi.org/10.1183/23120541.00069-2019
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