Country Differences in the Clinical Manifestations and Treatment Patterns of Patients with Eosinophilic Granulomatosis with Polyangiitis (EGPA): A European Perspective

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Introduction

EGPA is a rare heterogeneous chronic disease characterised by the combination of small to medium vessel vasculitis, hypereosinophilia, eosinophilic tissue inflammation and the presence of asthma and/or chronic rhinosinusitis with/without nasal polyposis.[1–3]

Clinical manifestations of EGPA can affect multiple organ systems and can cause significant and, in some cases, life-threatening organ damage if untreated.[4,5]

OCS, immunosuppressants and more recently biologics are all included in EGPA treatment guidelines, but level of evidence for their use is low in most cases and little is known about real-world treatment patterns.[6]

Owing to the rarity of EGPA, published literature on the burden of EGPA in Europe is limited.[7]

This chart review study, describes differences in the real-world EGPA-related clinical manifestations, clinical outcomes and treatment patterns between 5 countries, using the largest European multi-country cohort of patients with EGPA.

Methods

Study design (GSK ID: 214661)

Real world | Retrospective | Chart review

Patient eligibility criteria
- ≥12 years of age
- Confirmed EGPA diagnosis
- ≥1 year of follow-up data from index*

N=407

Chart review conducted by 204 physicians† in 5 European countries: France, Germany, Italy, Spain, UK

Index date
First physician encounter after or at EGPA diagnosis: Jan 2015 to Dec 2019

EGPA diagnosis date → Patient history§ → Follow-up → End of follow-up‡

- Patient history§: Patient demographics; Disease characteristics; Comorbidities; Treatment patterns
- Follow-up: Clinical manifestations; Clinical outcomes

All outcomes assessed overall and by country

*Except where follow-up ended due to death; †recruited from targeted specialties of rheumatology (44%), pulmonology (37%), allergy (13%), and immunology (6%); ‡earliest of death, loss to follow-up or date of chart abstraction; §as available in the patient's chart

Results

Table 1. Patient demographics and clinical characteristics

	Overall (N=407)	France (N=81)	Germany (N=80)	Italy (N=80)	Spain (N=85)	UK (N=81)
Male, n (%)	231 (56.8)	51 (63.0)	44 (55.0)	47 (58.8)	42 (49.4)	47 (58.0)
Age at EGPA diagnosis, median (IQR), years	45 (33, 54)	49 (37, 57)	45 (30, 56)	40 (28, 50)	45 (35, 53)	45 (37, 53)
≥18 years of age, n (%)	383 (94.1)	78 (96.3)	73 (91.3)	74 (92.5)	78 (91.8)	80 (98.8)
Disease duration, median (IQR), years*	2.5 (1.8, 4.1)	2.1 (1.8, 2.9)	2.2 (1.7, 3.1)	3.7 (2.0, 5.9)	2.8 (1.9, 4.4)	2.3 (1.7, 3.5)
Length of follow-up, median (IQR), years	2.2 (1.7, 3.5)	2.0 (1.6, 2.6)	2.2 (1.6, 2.9)	2.9 (1.8, 4.2)	2.3 (1.7, 3.8)	2.1 (1.6, 3.3)
Proportion of patients with asthma,† n (%)	299 (73.5)	66 (81.5)	45 (56.3)	60 (75.0)	64 (75.3)	64 (79.0)
Patients with an asthma diagnosis prior to EGPA diagnosis, n (%)‡	160 (78.0)	39 (78.0)	24 (100.0)	36 (80.0)	33 (64.7)	28 (80.0)
Time from asthma diagnosis to EGPA diagnosis, median (IQR), years	1.8 (0.2, 5.6)	1.2 (0.3, 3.2)	4.4 (2.2, 7.3)	0.1 (0.0, 2.0)	2.9 (0.5, 8.1)	3.6 (0.9, 9.2)
Blood eosinophil count, n (%)	364 (89.4)	77 (95.1)	73 (91.3)	66 (82.5)	75 (88.2)	73 (90.1)
Median BEC (IQR), cells/μL§	1500 (600, 3300)	1500 (875, 2800)	2800 (1200, 4500)	1800 (900, 3000)	1400 (600, 4000)	800 (45, 3200)
Comorbidities and associated conditions, n (%)						
Vasculitis	197 (48.4)	37 (45.7)	35 (43.8)	44 (55.0)	42 (49.4)	39 (48.1)
Hypertension	163 (40.0)	28 (34.6)	32 (40.0)	41 (51.3)	31 (36.5)	31 (38.3)
Anxiety or depression	140 (34.4)	37 (45.7)	16 (20.0)	40 (50.0)	23 (27.1)	24 (29.6)
Lower respiratory disease‖	77 (18.9)	24 (29.6)	8 (10.0)	12 (15.0)	19 (22.4)	14 (17.3)
Osteoporosis	72 (17.7)	8 (9.9)	9 (11.3)	22 (27.5)	21 (24.7)	12 (14.8)
Glomerulonephritis	69 (17.0)	17 (21.0)	15 (18.8)	15 (18.8)	9 (10.6)	13 (16.0)
Obesity	68 (16.7)	8 (9.9)	15 (18.8)	11 (13.8)	21 (24.7)	13 (16.0)
Diabetes	35 (8.6)	4 (4.9)	8 (10.0)	4 (5.0)	11 (12.9)	8 (9.9)
Rheumatoid arthritis	20 (4.9)	10 (12.3)	2 (2.5)	3 (3.8)	4 (4.7)	1 (1.2)
Liver disease	11 (2.7)	0 (0.0)	3 (3.8)	0 (0.0)	6 (7.1)	2 (2.5)
Cancer (any)	8 (2.0)	2 (2.5)	0 (0.0)	1 (1.3)	3 (3.5)	2 (2.5)

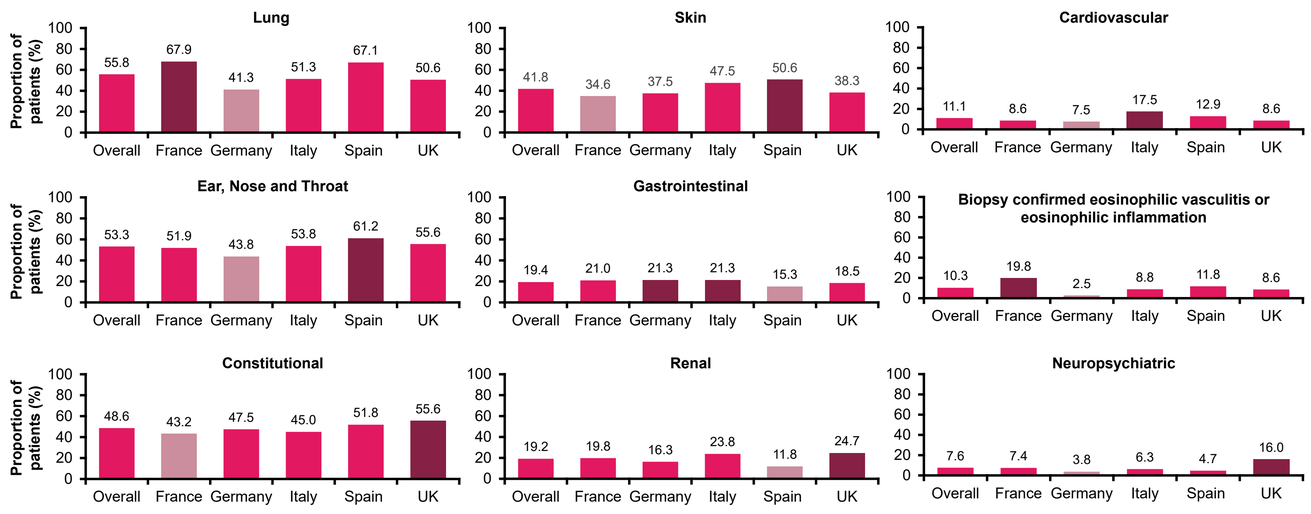
Highest and lowest values across the countries are indicated by the green and red shading, respectively. *Disease duration from diagnosis date to end of follow-up; †asthma assessed from birth to end of follow-up; ‡calculated from the total number of patients who had a reported diagnosis date for asthma: overall (n=205) France (n=50), Germany (n=24), Italy (n=45), Spain (n=51), and UK (n=35); §physicians reported the most recent value between diagnosis and index; ‖other than asthma and COPD

Conclusions

- While a high proportion of patients experienced multiple clinical manifestations across the 5 European countries, the organ systems most commonly affected varied by country, reinforcing the heterogeneity of this rare disease.
- There was also considerable country-by-country variation in clinical outcomes and treatments.
- In comparison to the other European countries, findings were most favourable in Germany with regards to manifestations and clinical outcomes.
  - Furthermore, Germany had the lowest number of distinct EGPA therapies used, potentially reflecting the benefit of consistency of care.
- Together, this study highlights the inconsistencies in treatment approach and outcomes for patients with EGPA across 5 large European countries and the need to optimise disease management to ensure that patients benefit from combined knowledge and consistent care in this rare and chronic disease.

Figure 1. Overall, 58.2% of patients had ≥3 distinct clinical manifestations. The most commonly affected organs varied by country including lungs in France (67.9%) and Spain (67.1%); ENT in the UK (55.6%) and Italy (53.8%); and constitutional in the UK (55.6%) and Germany (47.5%)

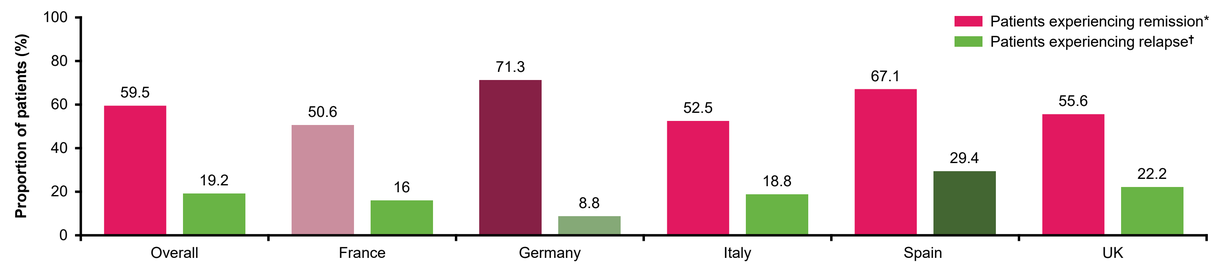
	Overall (n=407)	France (n=81)	Germany (n=80)	Italy (n=80)	Spain (n=85)	UK (n=81)
Number of distinct clinical manifestations						
Mean (SD)	4.0 (3.8)	4.0 (3.8)	3.1 (3.5)	4.1 (3.8)	4.3 (3.5)	4.4 (4.5)
Median (IQR)	3.0 (1.0, 6.0)	3.0 (1.0, 5.0)	2.0 (1.0, 4.0)	3.0 (1.0, 6.0)	3.0 (2.0, 6.0)	4.0 (1.0, 6.0)
Proportion of patients with ≥3 distinct clinical manifestations, n (%)	237 (58.2)	46 (56.8)	36 (45.0)	46 (57.5)	58 (68.2)	51 (63.0)



In the table, highest and lowest values across the countries are indicated by the green and red shading, respectively. In figure panels highest and lowest values across the countries are indicated by darker and lighter tones

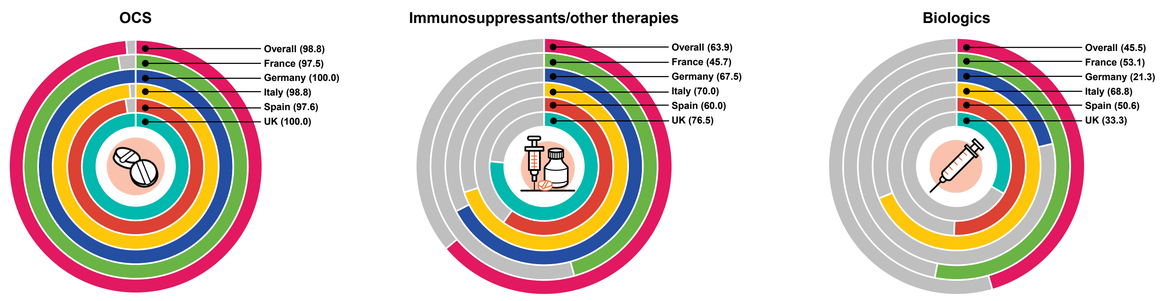
Figure 2. The proportion of patients who experienced remission was highest in Germany (71.3%) and lowest in France (50.6%); the proportion of patients who experienced relapse was lowest in Germany (8.8%) and highest in Spain (29.4%)

	Overall (n=407)	France (n=81)	Germany (n=80)	Italy (n=80)	Spain (n=85)	UK (n=81)
Duration of remission,‡ cumulative months, median (IQR)	12.0 (5.2, 22.2)	11.7 (3.9, 20.6)	15.7 (10.0, 27.8)	6.9 (2.3, 16.2)	8.3 (4.0, 20.0)	12.0 (7.4, 22.2)
Time from EGPA diagnosis to first remission, months, median (IQR)	14.5 (7.5, 26.9)	14.8 (6.9, 23.8)	8.1 (3.8, 14.0)	27.0 (17.9, 36.8)	19.1 (12.9, 37.0)	9.7 (6.9, 17.0)
Number of relapses,§ PPPY, mean (SD)	0.8 (1.0)	0.6 (0.3)	0.5 (0.4)	0.9 (0.4)	0.9 (0.8)	1.1 (1.9)



Remission or relapse occurring between index and the end of follow-up. In the table, highest and lowest values across the countries are indicated by the green and red shading, respectively. *Remissions (physician defined) reported for those patients who had ≥1 remission(s); †relapse was defined as a recurrence or worsening of EGPA symptoms requiring an increasing OCS dose, an increase/change in dose of immunosuppressive therapy, hospitalisation, or other definitions of relapse; ‡for patients who had >1 remission, the duration of remission was calculated as the sum of durations of remission for all reported remissions; §annualised relapse count calculated as relapses PPPY for those patients who experienced ≥1 relapse

Figure 3. OCS use was high in all countries, ranging between 97.5% in France to 100.0% in Germany and the UK; conversely, immunosuppressant and biologic use varied by country with immunosuppressants/other therapies ranging from 45.7% in France to 76.5% in the UK and biologic use ranging from 21.3% in Germany to 68.8% in Italy



	Overall	France	Germany	Italy	Spain	UK
Number of distinct EGPA therapies used						
Mean (SD)	3.9 (1.8)	3.9 (2.1)	3.3 (1.7)	4.4 (1.7)	4.2 (1.6)	3.8 (1.7)
Median (IQR)	4.0 (2.0, 5.0)	4.0 (2.0, 5.0)	3.0 (2.0, 4.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)
Maximum daily OCS dose, mg, mean (SD)*	30.2 (19.8)	35.8 (18.9)	28.8 (19.9)	19.9 (16.2)	34.0 (19.8)	31.6 (20.4)
Other treatments for EGPA-related clinical manifestations, n (%)†	302 (74.2)	54 (66.7)	50 (62.5)	73 (91.3)	69 (81.2)	56 (69.1)
Treatments related to the management of clinical conditions, n (%)‡	238 (58.5)	43 (53.1)	43 (53.8)	55 (68.8)	50 (58.8)	47 (58.0)

In the table, highest and lowest values across the countries are indicated by the green and red shading, respectively. *Receipt of ≥1 type of OCS was counted as a single therapy; †includes albuterol, analgesics, budesonide – formoterol, doxazosin, ipratropium bromide, levalbuterol, montelukast, ramipril, theophylline, tiotropium, valsartan, zafirlukast; ‡treatments related to the management of clinical conditions were assessed during the follow-up period. Included treatments: to improve bone mineral density and for: infections related to EGPA therapies; recovering cytopenia; haemorrhagic cystitis; hepatotoxicity; gastrointestinal toxicity, and thyroid hormone replacement therapy; insulin and folic acid supplements

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Abbreviations

BEC, blood eosinophil count; COPD, chronic obstructive pulmonary disease; EGPA, eosinophilic granulomatosis with polyangiitis; ENT, ear, nose and throat; IQR, interquartile range; OCS, oral corticosteroid; PPPY, per person per year; SD, standard deviation; UK, United Kingdom

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- **RWJ**, **JH**, **LB**, **RA-C** are employees of GSK and hold stocks/shares in GSK. **NK** was an employee of GSK at the time of the study and holds stocks/shares in GSK. **LH**, **AK** and **MSD** are employees of the Analysis Group, Inc., which received funding from GSK to conduct the study. **SD** was an employee of Analysis Group, Inc., at the time of the study, which received funding from GSK to conduct the study.
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