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PRO54

Economic burden of Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) for ANCA-associated vasculatis (AAV) patients in France

INTRODUCTION

The two phenotypes of ANCA-associated vasculitis (AAV), Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) are a collection of relatively rare autoimmune diseases of unknown cause, characterized by inflammatory infiltration causing necrosis of blood vessels.

The annual incidences rates are 2.1-14.4 and 2.4-10.1 per million in Europe for GPA and MPA, respectively. These multisystem inflammatory diseases result in life-threatening or organ-threatening disease with an increased mortality ratio of 2.6.[(1)]

Currently used induction treatment (cyclophosphamide [CYC] or rituximab [RTX] with high-dose glucocorticoids [GCs]) has significantly improved outcome of AAV in terms of overall mortality but is associated with high toxicity. New therapies aim to target key pathophysiological mechanisms in AAV.

This study was set up to assess the therapeutic management of GPA and MPA patients and its associated economic burden in France from SNIIRAM data.

OBJECTIVES

PRIMARY OBJECTIVE

To describe the current therapeutic management of GPA and/or MPA patients and its evolution since the use of rituximab in both indications

SECONDARY OBJECTIVES

To describe the morbi-mortality events of GPA and/or MPA patients

To estimate the economic burden of patients with GPA and/or MPA

METHODS

STUDY OVERVIEW

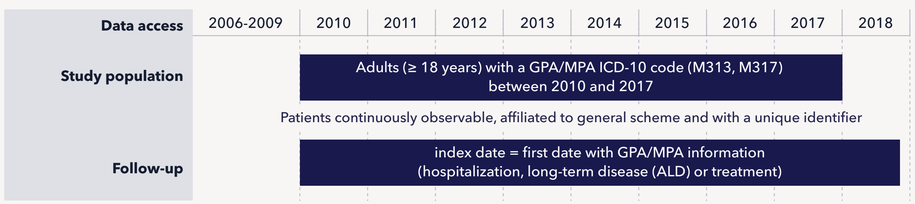
A retrospective cohort study was set up from French National Healthcare Database (Système National des Données de Santé - SNDS).

DATA SOURCES

The SNDS incorporates main French health public databases such as:

- SNIIRAM that records all reimbursed healthcare consumption in 2 databases:
  - DCIR with outpatient healthcare consumption data
  - PMSI with hospital healthcare consumption data
- CépiDC that records data on the medical causes of death

STUDY DESIGN



POPULATION AND OUTCOMES DEFINITION

INCIDENCE

Incident patients were defined as patients without any GPA or MPA information (hospitalizations for GPA or MPA or long-term disease (ALD) for GPA or MPA or treatment for GPA or MPA) during the 4 years prior to their index date. For patients who have a treatment of interest within 4 years prior to inclusion, if the date of initiation of that treatment occurs after January 1, 2010, patients were defined as incidents from that date of initiation of treatment.

The following patients were excluded from incident patients:

- Patients without treatment within 4 months of inclusion
- Patients who have only one GCS delivery with no further treatment during follow-up
- Patients who have only refractory specific treatment deliveries (IMG and IFX) with no other treatment during follow-up
- Patients who have only one GCS delivery with refractory specific treatment deliveries (IMG and IFX) without any other treatment during follow-up

INDUCTION PHASE

Induction phases were defined through a delivery of GCs with a dose ≥15mg/day, a delivery of CYC, a plasmatic exchange (PLEX) or a delivery of RTX with 3 or more deliveries per 3-month period

MAINTENANCE PHASE

Maintenance phases were defined through a delivery of GCs with a dose <15mg/day, a delivery of Mycophenolate mofetil (MMF) without a combined delivery within 30 days of GCs, a delivery of azathioprine (AZA) without a combined delivery within 30 days of GCs, a delivery of Methotrexate (MTX) without a combined delivery within 30 days of GCs or a delivery of RTX with less than 2 deliveries per 3 month-period. To note that if any of the above criteria was associated with a CYC administration or PLEX procedure; then, it was not considered as a criterion for identifying a maintenance phase.

OFF DRUG PHASE

A patient was defined as no longer on treatment if there was no delivery of any treatment for 60 days after the last delivery. This delay was extended to 180 days when 2 maintenance phases were following one each other.

COSTING

All directly or indirectly healthcare-related consumption of resources (associated or not to the management of GPA/MPA) were taken into account and notably medicines, consultations, laboratory test, medical devices, medical procedures, invalidity, daily allowance, transport, other non-hospital care, hospital care, external consultations in public hospital. Costing was carried out from the perspective of the French National Health Insurance.

CONCLUSION

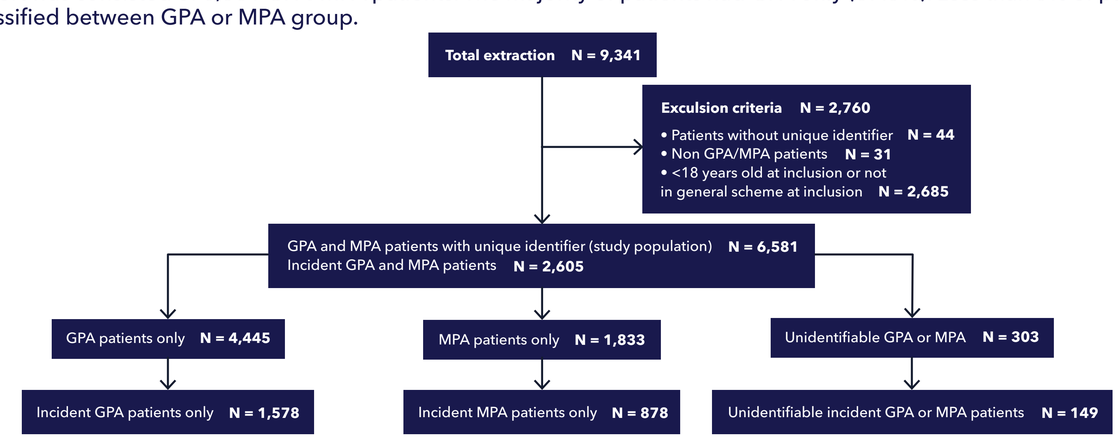
This study assessed the incidence and characteristics of GPA and MPA patients in France during a large period of time and described the evolution of therapeutic management of patients and its associated costs. The GPA patients showed to be predominant among the GPA/MPA population (68%).

Thus, given the associated major burden and the therapeutic management related events, there is a need for new innovative treatments to lower morbidity, mortality and cost.

RESULTS

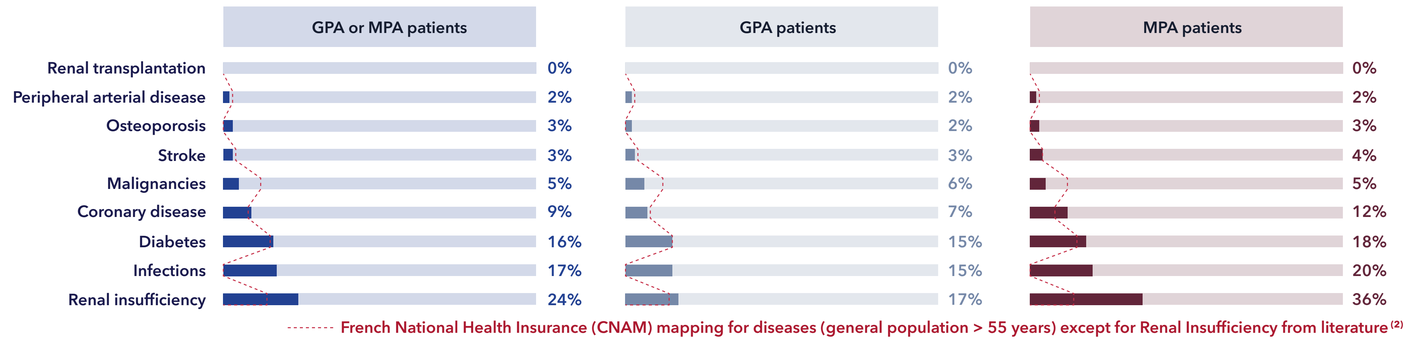
STUDY POPULATION

The study cohort was consisted of 6,581 GPA/MPA patients. The majority of patients had GPA only (67.5%). Less than 5% of patients were not able to be classified between GPA or MPA group.



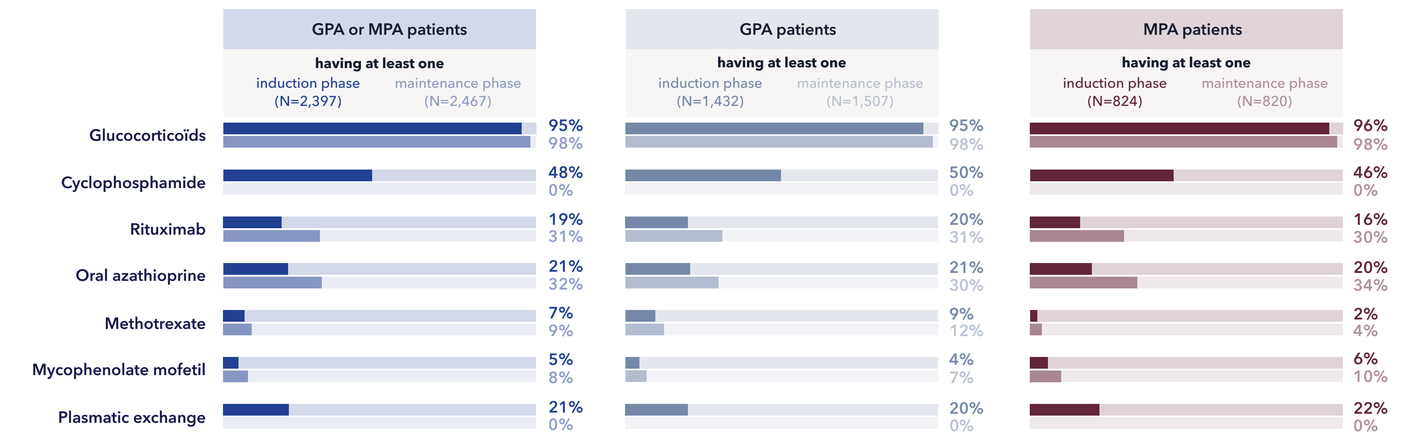
PATIENTS CHARACTERISTICS

GPA and MPA patients were aged 65 years old in median and 54.3% were men. 4.3% of patients were affiliated to Universal Health Insurance (CMUc) and 3.6% beneficiated of GPA-MPA related long-term disease (ALD). The most common comorbidities retrieved among GPA and MPA patients were quite closed to the ones retrieved in the French population aged 55 and over, except for cancer (5% vs 12%).



THERAPEUTIC MANAGEMENT

GPA and MPA patients had on average 1.82+/-1.15 induction phases, associated to a median duration of 3.0 months and 2.19+/-1.18 maintenance phases associated to a median duration of 3.8 months. Main treatments during induction and maintenance phases were glucocorticoids, cyclophosphamide, rituximab, oral azathioprine and plasmatic exchange.



MORTALITY

The standardized mortality rate ranged between 2 and 2.7 for 1,000 persons-years for our entire study population. The causes of mortality most often found were cardiovascular (16%), renal (11%), pulmonary (9%) and cancer (9%).

MORBIDITY EVENTS

The onset of main morbidity events found for the population during the 1st year were infections (37%), osteoporosis (18%), malignancies (8%) and diabetes (7%).

ECONOMIC BURDEN

Over the entire follow-up period for incident GPA and MPA patients, the average annual cost per patient was 26,560.23±53,427.99€, ranging from 24,569.90±50,667.59€ for patients with a GPA only to 30,463.81±60,783.32€ for patients with a MPA only. The cost breakdown per item of expenditure showed that the most important cost was hospitalizations (60%) followed by medicines (9%).

STRENGTHS AND LIMITATIONS

STRENGTHS

The main strength of the study was to be able to study almost the entire French population using two comprehensive databases, the DCIR and the PMSI.

Another strength of the study is the long duration of follow-up which allowed some patients to be followed up to almost 6 years.

LIMITATIONS

As the SNIIRAM is a claims database, it does not make it possible to know the indication of the medicines dispensed. Thus, certain treatments given in the management of GPA-MPA are not exclusive to this pathology, and GCs or immunosuppressants could have been dispensed for the treatment of another pathology. However, the selection of our populations based on reliable medical criteria allows us to be confident that the patients included are really suffering from GPA-MPA, limiting the bias of having dispensing of these drugs for another reason than the pathology of interest.

The phase identification criterion (i.e. induction or maintenance) is mainly dependent on the doses of GCs which was calculated based on assumptions, as the databases used do not make it possible to know the dosage prescribed by the clinician. However, discussions with experts validated the results.

(1) Watts et al. Classification, epidemiology and clinical subgrouping of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. avr 2015;30 Suppl 1:i14-22.
(2) Stengel et al. Epidemiology and prognostic significance of chronic kidney disease in the elderly–the Three-City prospective cohort study. Nephrology Dialysis Transplantation. oct 2011;26(10):3286-95.

SNIIRAM study registered with the INDS on Dec 13, 2018 and authorised by the CNIL on Jan 10, 2019. (DR-2019-009 (request 918434)) - CNAM agreement signed on June 21, 2019