Benefits of Pneumocystis jirovecii pneumonia prevention among patients with autoimmune or inflammatory disease treated with prolonged high dose steroids. (PaRADISE)

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# Administrative details

#### Study description

Patients with inflammatory autoimmune diseases (IAD) are often severely immunocompromised and exposed to potentially serious infections. Pneumocystis jirovecii (P. jirovecii) is an opportunistic fungus responsible to Pneumocystis jirovecii pneumonia (PJP), especially in immunocompromised patients. PJP induces chronic or acute respiratory failure and can lead to intensive care unit admission and potentially death. Among IAD patients with PJP, rate of mortality is high, varying between 62% to 80%. Primary prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) for the majority of patients or aerosolized pentamidine or atovaquone used in case of TMP-SMX intolerance or allergy, is effective to prevent PJP occurrence and reduces its related mortality. Nevertheless, TMP-SMX exposes to potentially serious side effects such as toxidermia, drug-induced liver or renal injury, cytopenia or lupus induction. To date, except for HIV-infected patients, no clear recommendation exists about the use of PJP prophylaxis among patients with IAD. In 2019, prescription of TMP-SMX for PJP prevention among IAD patients remains highly dependent of local practice. This is a retrospective cohort study planned to assess the effect of PJP prophylaxis to prevent PJP among IAD patients treated with prolonged high dose steroids for IAD. Secondary aims are: To determine safety of PJP prophylaxis among patients with IAD and prolonged high dose steroids, globally and by IAD, To describe the use of PIP prevention in France in patients with IAD and prolonged high dose steroids, and factors associated with PJP prevention, To assess the incidence of PJP among patients with IAD and prolonged high dose steroids, by IAD, To identify risk factors for PJP development among patients with IAD and according to each IAD, To describe overall mortality rates and PJP mortality rates in IAD patients, globally and by IAD, To assess the incidence of hospitalizations (and their main cause) in incident IAD patients.

#### **Study status**

Ongoing

## Research institutions and networks

## **Institutions**

# Assistance Publique - Hôpitaux de Paris (AP-HP) France First published: 01/02/2024 Last updated: 01/02/2024 Institution Hospital/Clinic/Other health care facility

## Contact details

#### **Study institution contact**

Florence TUBACH florence.tubach@aphp.fr

Study contact

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## Primary lead investigator

Valérie POURCHER

**Primary lead investigator** 

# Study timelines

Date when funding contract was signed

Planned: 01/01/2020

Actual: 07/01/2020

#### Study start date

Planned: 31/12/2020

Actual: 01/12/2021

#### Data analysis start date

Planned: 31/12/2020 Actual: 01/12/2021

#### **Date of final study report**

Planned: 31/12/2023

## Sources of funding

Other

## More details on funding

French Ministry of Health

# Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

# Methodological aspects

Study type

Study type list

#### Study type:

Non-interventional study

#### Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Drug utilisation

Effectiveness study (incl. comparative)

#### Main study objective:

The main aim of this study is to assess the effect of Pneumocystis jirovecii pneumoniaprophylaxis (i.e. TMP-SMX or aerosolized pentamidine or atovaquone) to prevent PJP among IAD patients treated with prolonged high dose steroids.

## Study Design

#### Non-interventional study design

Cohort

# Study drug and medical condition

#### **Anatomical Therapeutic Chemical (ATC) code**

(J01EE01) sulfamethoxazole and trimethoprim sulfamethoxazole and trimethoprim (P01CX01) pentamidine isethionate pentamidine isethionate (P01AX06) atovaquone

atovaquone
(P01BB51) proguanil and atovaquone
proguanil and atovaquone
(H02AB) Glucocorticoids
Glucocorticoids

#### Medical condition to be studied

Autoinflammatory disease
Autoimmune disorder
Immune system disorder

#### Additional medical condition(s)

Vasculitis, Sarcoidosis, Autoimmune arthritis, Autoimmune colitis, Autoimmune endocrine disorder, Autoimmune hepatitis, Autoimmune lung disease, Autoimmune myocarditis, Autoimmune demyelinating disease, Autoimmune dermatitis, Autoimmune myositis, Autoimmune pancreatitis, Autoimmune pericarditis, Autoimmune uveitis, Immune-mediated neurological disorder, Immune-mediated renal disorder.

# Population studied

#### Age groups

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

#### **Special population of interest**

#### **Estimated number of subjects**

6700000

## Study design details

#### **Outcomes**

Time to Pneumocystis jirovecii pneumonia Diagnosis, Time to severe PJP prevention side effects (requiring hospitalization) for patients receiving PJP prophylaxis: - severe drug-induced cutaneous injury, - severe drug-induced liver or kidney injury, - lupus induction, - severe cytopenia, Time to death, in patients with PJP globally and by type of IAD, and in patients with incident IAD by type of IAD

#### Data analysis plan

PJP rates will be compared only within periods at risk of PJP (i.e. with high dose steroids greater than 20 mg daily (1 month or more) with or without PJP prophylaxis. We will make a dynamic matching on a time dependent propensity score. In order to have reasonable power in subgroup analysis by IAD, the matching will be stratified on the type of disease. Only the first line of high dose steroid treatment will be used in main analysis. Then a Cox model will be used, with time dependent confounding variables if needed. The propensity score will take into account known risk factors of PJP and confounding factors for the association of interest.

## Data management

## **ENCePP Seal**

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

#### Data sources

#### Data source(s), other

Système national des données de santé France

#### **Data sources (types)**

Administrative healthcare records (e.g., claims)

## Use of a Common Data Model (CDM)

#### **CDM** mapping

No

# Data quality specifications

#### **Check conformance**

Unknown

#### **Check completeness**

Unknown

#### **Check stability**

Unknown

## **Check logical consistency**

Unknown

# Data characterisation

#### **Data characterisation conducted**

No