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

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Study Ongoing

Administrative details

EU PAS number

EUPAS44554

Study ID

44555

DARWIN EU® study

No

Study countries

☐ France

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 PJP 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

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Institution | Hospital/Clinic/Other health care facility

Contact details

Study institution contact

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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

Immunocompromised

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

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