Anti-IL-5/5R versus anti-IL4R switching strategies for uncontrolled severe asthma treated by anti-IL5/5R : A target trial emulation (RAMSES-Switch)

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Study Ongoing

Administrative details

EU PAS number

EUPAS105374

Study ID

105375

DARWIN EU® study

No

Study countries

☐ France

Study description

Severe asthma, affects for 5 to 10% of asthma patients.Biologic therapies have emerged as effective treatments for severe asthma, and five monoclonal antibodies (mAbs) are now available in France to target different subtypes of severe asthma. Intensity of clinical response varies from patient to patient: therefore, for patients with insufficient response, a switch to another drug is possible, since most of the biologics target similar populations of patients with severe asthma. Although response to a biologic given as a second or third line of treatment has been documented, the best strategy to switch from a molecule to another one has not been evaluated yet. In case of failure of anti-IL5 or anti IL5R drugs, two main strategies are used: switching to dupilumab, an anti IL4/13R mAb that also targets eosinophilic asthma or switching to another anti IL5 drug. This study aimed to compare the efficacy of the two switching strategies on asthma control in patients with severe eosinophilic asthma with insufficient clinical response to a first-line anti-IL5/5R mAb treatment. We planned an emuation of a target trial using the data of the Research on severe asthma cohort (RAMSES-cohort). We planned to use a propensity score framework to deal with potential cofounders to the observational nature of the data.

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

yon-HC de Lyon - La Croix Rousse (9) Clamart-HIA Percy (33)Colmar-Hôpitaux Civils de Colmar (4) Paris-APHP - Cochin (16)-Saint-Denis-Centre Cardiologique du Nord - Moulins Gémeaux (25) Antony-Hôpital Privé d'Antony (47)andoeuvre-lès-Nancy-CHRU de Nancy - Brabois (53)Brest-CHU de Brest, Paris-APHP - Bichat (1) Montfermeil-GHI Le Raincy Montfermeil (10), Lille-CHRU de Lille - Albert Calmette (8) Reims-CHU de Reims - Maison Blanche (21), Montpellier-CHU de Montpellier - Arnaud de Villeneuve (11) Orléans-CHR d'Orléans - La Source (15), Marseille-APHM - Nord (37) Pierre-Bénite-HC de Lyon - Sud (19), Dijon-CHRU de Dijon - François Mitterrand (34) Pringy-CHR d'Annecy (20), Créteil-CHI Créteil (5) Suresnes-Hôpital Foch

(57), La Tronche-CHU de Grenoble - La Tronche (6) Caen-CHU de Caen - Côte de Nacre (3), Le Kremlin-Bicêtre-APHP - Bicêtre (7 Amiens-CHU d'Amiens Sud (46), Besançon-CHU de Besançon - Jean Minjoz (39) Paris-GH Paris Saint Joseph (51

Networks

RAMSES Study Group, CRISALIS (Clinical Research Initiative in Severe Asthma : a Lever for Innovation & Science)

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Candice Estellat

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 10/12/2018

Study start date
Planned: 01/09/2019

Actual: 30/09/2022

Data analysis start date
Planned: 01/03/2023

Actual: 01/05/2023

Date of final study report
Planned: 15/09/2023

Sources of funding

- Pharmaceutical company and other private sector
- Other

More details on funding

Astrazeneca, GlaxoSmithKLine, Sanofi, Boston Scientific, Novartis, French Society of Pneumology

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:

Effectiveness study (incl. comparative)

Main study objective:

In severe asthma patients after first failure of an anti-IL5/anti-IL-5R (mepolizumab or benralizumab), we aim to compare the variation of asthma control, measured by ACT, of two switching strategies : switching from anti-IL5/anti-IL-5R to an anti-IL4R (dupilumab) vs. switching from anti IL5/anti-IL-5R to another anti-IL5/anti-IL-5R.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(R03DX09) mepolizumab

mepolizumab

(R03DX10) benralizumab

benralizumab

(D11AH05) dupilumab

dupilumab

Medical condition to be studied

Asthma

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)

Estimated number of subjects

200

Study design details

Outcomes

Change in Asthma Control Test (ACT). Time Frame 6 months. ACT >20 (n,%)

Time frame 6 mo for all outcomes Change in Annual asthma exacerbation rate,

in Annual asthma severe exacerbation rate,in maintenance oral corticosteroids dose, in Forced expiratory volume in one second, Asthma Quality of Life Questionnaire, inSino-nasal Outcome Test 22, in Blood eosinophil count Maintenance of treatment at time of switch +Exploratory outcomes

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Data analysis plan

Patient characteristics will be described .Use of Target trial emulation framework and propensity score framework for potential cofounders. Marginal effect will be estimated via linear regression model, adjusted on the propensity score applying IPTW (ATE). Bootstrap will be performed to estimate robust variances. Secondary endpoints analysis will involve logistic regression for binary variables, linear regression for continue variables in the weighted populations. Kaplan-Meier estimator is used to estimate survival probabilities over time. Missing data on covariates and outcomes will be managed by multiple imputations assuming data will be missing at random. Causal contrasts : modified intention-to-treat analysis. 3 Subgroups analysis according to history of chronic rhinosinusitis, treatment before the switch, and history of treatment by omalizumab. Sensitivity analysis, restriction to switches after 2020 and using an IPTW to get an ATT.

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

Research on Severe Asthma (RAMSES), French nationwide cohort of severe asthma patients registered on ClinicalTrials.gov (NCT04077528) France

Data sources (types)

Other

Data sources (types), other

Prospective patient-based data collection

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