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

First published: 14/06/2023
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Study | Ongoing

Administrative details

PURI
https://redirect.ema.europa.eu/resource/105375

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 institution 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

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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
(R03DX10) benralizumab
(D11AH05) 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

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

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