Comparative effectiveness and safety of omalizumab and dupilumab in children with asthma

First published: 13/11/2024

Last updated: 03/04/2025

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000361

Study ID

1000000361

DARWIN EU® study

No

Study countries

☐ Korea, Republic of

Study description

This study is a cohort study which aims to:
1) Compare the effectiveness of omalizumab and dupilumab in pediatric asthma patients.
2) Compare the incidence of previously known side effects of omalizumab and dupilumab in pediatric asthma patients.

AIM 1) Comparative Effectiveness
- Determine and compare the incidence rate of asthma exacerbation in asthma patients on either omalizumab or dupilumab.
- Compare how much reduction of steroid use was achieved in asthma patients on either omalizumab or dupilumab.

AIM 2) Comparative Safety
- Determine and compare the incidence rate of previously known side effects of omalizumab and dupilumab, including eosinophilia, helminth infection, anaphylaxis, and conjunctivitis.

Study status
Ongoing

Research institutions and networks

Institutions

Yonsei University

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Networks

Observational Health Data Sciences and Informatics (OHDSI) Network

First published: 01/02/2024

Last updated: 01/02/2024

Network

Contact details

Study institution contact

Chang Hoon Han paul9567@yuhs.ac

Study contact

paul9567@yuhs.ac

Primary lead investigator

Seng Chan You 0000-0002-5052-6399

Primary lead investigator

ORCID number:

0000-0002-5052-6399

Study timelines

Date when funding contract was signed
Planned: 01/03/2024

Actual: 01/03/2024

Study start date
Planned: 08/05/2024

Actual: 08/05/2024

Date of final study report
Planned: 17/04/2025

Sources of funding

More details on funding

This research was supported by a grant of the MD-Phd/Medical Scientist Training Program through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea.

Study protocol

BiologicsCDM_Research Protocol_202401031.pdf (352.98 KB)

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 topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

This is a retrospective cohort study, comparing effectiveness outcomes and side effect incidence. Data sources will be electronic health record (EHR) data in Observational Medical Outcomes Partnership Common Data Model (OMOP-CDM) format, across the OHDSI network.

Main study objective:

This study is a cohort study which aims to:
1) Compare the effectiveness of omalizumab and dupilumab in pediatric asthma patients.
2) Compare the incidence of previously known side effects of omalizumab and dupilumab in pediatric asthma patients.

AIM 1) Comparative Effectiveness
• Determine and compare the incidence rate of asthma exacerbation in asthma patients on either omalizumab or dupilumab.

• Compare how much reduction of steroid use was achieved in asthma patients on either omalizumab or dupilumab.

AIM 2) Comparative Safety
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Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name
DUPILUMAB
OMALIZUMAB

Anatomical Therapeutic Chemical (ATC) code
(D11AH05) dupilumab
dupilumab
(R03DX05) omalizumab
omalizumab

Medical condition to be studied
Asthma

Population studied

Short description of the study population

The primary study population includes patients under the age of 18 diagnosed with asthma, either administered with omalizumab or dupilumab. Additionally, a secondary analysis will be done to include patients of all ages diagnosed with asthma.

Age groups

- **Paediatric Population (< 18 years)**
  - Preterm newborn infants (0 – 27 days)
  - Term newborn infants (0 – 27 days)
  - Children (2 to < 12 years)
  - Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Special population of interest

Other

Special population of interest, other

Patients diagnosed with asthma

Study design details

Setting

The target group consists of patients who were initiated with omalizumab and who meet the criteria below. The comparator group consists of patients who were initiated with dupilumab and who meet the criteria below.

As primary analysis, intention-to-treat design will be applied to derive 1-year outcomes.
As sensitivity analysis, on-treatment design will be applied. The cohort exit rule described below will be applied.

Index rule defining the index date:
• First exposure to one of the agents of interest from 2018-11-01 and after.
• Under the age of 18 at the index date.
• With continuous observation of at least 180 days before the event index date.

Inclusion rules based on the index date:
• At least 1 occurrence of asthma between 30 days before and 7 days after the index date.
• None of exposure to the drug of the other group in the observation period before the index date.

Exit rules defining the cohort end date (on-treatment):
• Event will persist until end of a continuous drug exposure of interest.
• Allowance for 60-day gaps between exposure records of the drug of interest.
• Add 30 days to the end of the last exposure record as an additional period of surveillance.
• Censored with an exposure of the drug of the other group.

Comparators

Target drug: omalizumab

Comparator drug: dupilumab

Outcomes

1) Primary Outcome - Effectiveness

– Asthma Exacerbation

Asthma exacerbation outcome is operationally defined as ER or inpatient visit due to asthma.

– Steroid Dose Reduction

Steroid dose reduction outcome is defined as reduction in total steroid use, comparing certain time periods before and after index date. 3 months before and after index date for 3-month total steroid dose reduction outcome, and 6 months before and after index date for 6-month steroid dose reduction outcome.

Total cumulative dose of each steroid ingredient is calculated within the designated time periods. Total steroid use is then calculated from summation of total cumulative dose of all included agents, converted to prednisolone equivalent doses. Conversion is done with approximate equivalent dose based on relative glucocorticoid activity.

Steroid dose reduction outcome is expressed using two different methods, as steroid dose percentage and steroid dose reduction groups, defined as below.

Steroid dose percentage: (Total steroid use after index date) / (Total steroid use before index date) × 100 (%)

Steroid dose reduction groups:

• Stop use

• Reduction of 75% or more

• Reduction of 50% or more, below 75%

• Reduction of 25% or more, below 50%

• Reduction below 25%

• No change or increased use

2) Secondary Outcome - Safety

– Eosinophilia

Three eosinophilia outcome cohorts based on severity are defined. (Eosinophil count above 500, 1500 and 3000 per microliter of blood)

– Helminth Infection

– Anaphylaxis

– Conjunctivitis

Data analysis plan

<Covariates for Propensity scores>

• Demographics

- Gender

- Age groups (5-year bands)

- Race

- Ethnicity

- Index Year/Month

• Condition Aggregation

- In prior 30d or365d

• Drug Aggregation

- In prior 30d or 365d

• Procedure

- In prior 30d or 365d

• Device

- In prior 30d or 365d

• Measurement

- In prior 30d or 365d

- Range Group in prior 365d
• Observation
- In prior 30d or 365d

<Definition of Time at Risk>
Primary analysis: Intention-to-treat (1 year)
Sensitivity analysis: On-treatment
Minimum time at risk: 1day

<Statistical Model Specification>
We compare the target cohort with the comparator cohort for the hazards of outcome during the time-at-risk by applying a Cox proportional hazards model. Incidence rates will be computed for each outcome in each exposure group. Propensity score adjustment will be:
• PS stratification: The target cohort and comparator cohorts will be stratified into 5 stratums of the PS distribution.

<Analysis to Perform>
• One comparison:
- New users of omalizumab with asthma (Target) vs. new users of dupilumab with asthma (Comparator)
• 2 populations:
- Age under 18
- All ages
• 7 outcomes:
- Asthma exacerbation
- Eosinophilia (Greater than 500/1500/3000)
- Helminth infection
- Anaphylaxis
- Conjunctivitis

• 2 time-at-risk:

- Intention-to-treat (1-year)

- On-treatment

• One model: Cox-regression after PS stratification

For steroid dose reduction outcome, the difference between the target and the comparator will be shown for both as steroid dose percentage and steroid dose reduction groups. The statistical method is as follows.

For steroid dose percentage:

• Wilcoxon rank sum test.

For steroid dose reduction groups:

• Fisher’s exact test will be used if any of the expected frequencies is <5.

• Chi-squared test will be used if all the expected frequencies are 5 or higher.

Documents

https://github.com/dr-you-group/BiologicsCDM

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

Severance Hospital, South Korea

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

CDM version

v5.4

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Not applicable

Procedures

Procedure of results generation

https://github.com/dr-you-group/BiologicsCDM