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

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## Administrative details

EU PAS number EUPAS1000000361	
<b>Study ID</b> 1000000361	
DARWIN EU® study	
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

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#### **Networks**

## Observational Health Data Sciences and Informatics (OHDSI) Network

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Network

### Contact details

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**Primary lead investigator** 

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## 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

 Determine and compare the incidence rate of previously known side effects of omalizumab and dupilumab, including eosinophilia, helminth infection, anaphylaxis, and conjunctivitis.

## 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

ΑII

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

#### Data sources

Data source(s), other

Severance Hospital, South Korea

#### Data sources (types)

Electronic healthcare records (EHR)

## Use of a Common Data Model (CDM)

No 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