Safety outcomes of Selective Serotonin Reuptake Inhibitors in Adolescent Attention-Deficit/Hyperactivity Disorder (The ASSURE study)

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Study Planned

Administrative details

EU PAS number

EUPAS44893

Study ID

44894

DARWIN EU® study

No

Study countries

☐ Korea, Republic of

Study description

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioral disorders of adolescents. In addition to ADHD, patients with ADHD also have many comorbidities such as anxiety disorder, depressive disorder, substance abuse, and autism spectrum disorder. Therefore, the American Academy of Pediatrics recommends that comorbidity evaluation be performed at least once when diagnosing ADHD as one of the key action statements in their 2019 clinical practice guideline. Especially, ADHD is closely related to depressive disorder. There are previous studies on high comorbidity rate, biological linkage or causality, and its clinical outcomes. When establishing a treatment strategy for ADHD patients with depression, the clinical hurdles for the use of antidepressants are concerns about changes in the patients' condition (i.e., suicidality, etc.) and an increase in adverse effects. Although the first-line treatment for adolescent ADHD and depressive disorder is recommended in different guidelines, the evidence for safety evaluation of concomitant use of those drugs is sparse. Therefore, in this study, we aimed to evaluate the safety of the co-use of selective serotonin reuptake inhibitors (SSRIs), the first recommended drug for adolescent depression, in ADHD patients (Adolescent ADHD and SSRI Use in Real-world data: ASSURE study). We also aimed to evaluate the safety outcome within the SSRI class as a head-to-head study.

Study status

Planned

Research institutions and networks

Institutions

Ajou University

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Institution

Contact details

Study institution contact

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Primary lead investigator

Shin Yunmi

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/07/2021

Study start date

Planned: 01/07/2021

Data analysis start date

Planned: 10/01/2022

Date of final study report
Planned: 31/07/2022

Sources of funding

- Other

More details on funding

Health Insurance Review & Assessment Service, Ministry of Health &Welfare, Republic of Korea (grant number: HR16C0001), Bio Industrial Strategic Technology Development Program (20003883) funded by Ministry of Trade, Industry & Energy (MOTIE, Korea) (grant : 20005021), Bio Industrial Strategic Technology Development Program (20003883) funded by Ministry of Trade, Industry & Energy (MOTIE, Korea) (grant : 20003883)

Study protocol

ASSURE_protocol_v1.0.pdf(374.48 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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Main study objective:

The primary objective is comparing the risk of safety outcomes which include neuropsychiatric events, cardiovascular events, and other events during concomitant use of methylphenidate and SSRI among adolescent ADHD patients.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

METHYLPHENIDATE

ATOMOXETINE

CLONIDINE

BUPROPION

Anatomical Therapeutic Chemical (ATC) code

(N06AB) Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors

Medical condition to be studied

Attention deficit hyperactivity disorder

Population studied

Age groups

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Estimated number of subjects

20000

Study design details

Outcomes

A primary outcome is a neuropsychiatric event that includes agitation, first-time psychosis, first-time tic disorder, mania, sleep disorder, suicidal event, and tremor. All conditions could be detected by diagnostic codes. Secondary outcomes are cardiovascular and other events. Cardiovascular events are including arrhythmia and hypertension. All conditions could be detected by diagnostic codes. Other events are including abdominal pain, constipation, headache, nausea/vomiting, seizure, and traumatic injury. All conditions could be detected by diagnostic codes.

Data analysis plan

In this study, we compare the treatment cohort with the comparator cohort for the hazards of outcome during the time-at-risk by applying a Cox proportional hazards model. The time-to-event of outcome among patients in the treatment and comparator cohorts is determined by calculating the number of days from

the start of the time-at-risk window (the cohort start date), until the earliest event among 1) the first occurrence of the outcome, 2) the end of the time-at-risk window and 3) the end of the observation period that spans the time-at-risk start. Propensity scores will be used as an analytic strategy to reduce potential confounding due to an imbalance between the target and comparator cohorts in baseline covariates. After estimating the PS, one-to-one matching will be performed.

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 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