Comparative Effectiveness and Safety of Selective Serotonin Reuptake Inhibitors in Adult Attention-Deficit/Hyperactivity Disorder and comorbid depression (ASSURE-Extend)

First published: 02/03/2023
Last updated: 31/05/2023

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/105096

EU PAS number
EUPAS103757

Study ID
105096

DARWIN EU® study
No

Study countries
Korea, Republic of

Study description
Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioral disorders. Recently, more and more cases of ADHD persisting into adulthood or new-onset ADHD at adulthood suggest that a new approach is needed to manage ADHD. Unlike children, adults can have many deficits in higher-level executive functioning and emotional control and have many comorbid diseases due to diverse environmental exposures. Establishing treatment strategies according to comorbidities in ADHD patients is important, but the related evidence is weak. Most of Adult with ADHD also have many comorbidities

such as anxiety disorder, depressive disorder, substance abuse, and autism spectrum disorder. 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.16 Although the first-line treatment for ADHD and depressive disorder is recommended in different guidelines, the evidence for effectiveness and safety evaluation of concomitant use of those drugs is sparse. Therefore, in this study, we aimed to evaluate the real-world evidence for comparative effectiveness and safety of the co-use of selective serotonin reuptake inhibitors (SSRIs), the fist recommended drug for depression, in ADHD patients (Adolescent ADHD and SSRI Use in Real-world Data – Extend to Adult: ASSURE Extend study). We also aimed to evaluate the outcome systemically through comparison between user vs non-user, between SSRI ingredient level as head-to-head study.

Study status
Finalised

Research institution and networks

Institutions

Ajou University
First published: 01/02/2024
Last updated 01/02/2024
Institution

Contact details

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Study timelines

Date when funding contract was signed
Planned:
01/02/2023
Actual:
01/02/2023

Study start date
Planned:
01/02/2023
Actual:
15/02/2023

Data analysis start date
Planned:
01/02/2023
Actual:
28/02/2023

Date of final study report
Planned:
30/04/2023
Actual:
30/05/2023

Sources of funding

- Other

More details on funding

Health Insurance Assessment and Review Services

Study protocol

Protocol_v1.pdf(843.33 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 list

Study topic:
Human medicinal product
Disease /health condition

Study type:
Non-interventional study

Scope of the study:
Assessment of risk minimisation measure implementation or effectiveness
Effectiveness study (incl. comparative)

Data collection methods:
Secondary data collection

Main study objective:
We aimed to conduct comparative effectiveness research to establish real-world evidence for the safety of MPH and SSRIs in patients with ADHD.

Study Design

Non-interventional study design
Cohort
Other

Non-interventional study design, other
Retrospective, observational study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
(N06AB) Selective serotonin reuptake inhibitors
(N06AB10) escitalopram
(N06AB03) fluoxetine
(N06AB06) sertraline
(N06AB05) paroxetine
(N06BA04) methylphenidate
(N06BA09) atomoxetine

Medical condition to be studied
Attention deficit hyperactivity disorder

Population studied

Short description of the study population
Adult patients aged 18 years or older who had prescribed with methylphenidate (MPH) for attention deficit hyperactivity disorder (ADHD) and selective serotonin reuptake inhibitor (SSRI) for depressive disorder identified from national claims database from the Health Insurance Review and Assessment Service of South Korea.
Inclusion criteria:
? Adolescents who prescribed MPH for ADHD and have depressive disorder
- ?18 years old adults
- ADHD diagnosis for the first time in the patient’s history on or before the index date
- Depressive disorder diagnosis for the first time in the patient’s history on or before the index date
- At least 365 days of observation time prior to the index date
- No other ADHD medications such as atomoxetine, clonidine, or bupropion

? Adults who prescribed MPH for ADHD and prescribed any SSRI for depressive disorder.
- ?18 years old adults
- ADHD diagnosis for the first time in the patient’s history on or before the index date
- Depressive disorder diagnosis for the first time in the patient’s history on or before the index date
- At least 365 days of observation time prior to the index date
- No other ADHD medications such as atomoxetine, clonidine, and bupropion
- No other antidepressant drugs except the target ingredient before the index date

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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)

Special population of interest
Other

Special population of interest, other
Patients with attention deficit hyperactivity disorder

Estimated number of subjects
8000

Study design details

Outcomes
The primary outcomes are neuropsychiatric events that include anxiety, extrapyramidal symptoms, mania, hospitalization related to ADHD or schizophrenia. The secondary outcomes are safety events including cardiovascular, gastrointestinal, and other events.

Data analysis plan
• Primary analyses: As-treated risk window • Sensitivity analyses: Intention-to-treat risk window Risk window starts from 1 day to last observation after the index date. • Preventing bias from left censoring of data In order to prevent bias in the first visit and first prescription due to left censoring, the patients diagnosed and prescribed for the first year of the data period will not be used. • Preventing bias from time-related settings In order to reduce time-related bias, sensitivity analysis will be additionally performed in addition to the main analysis. Sensitivity analyses according to time-at-risk setting (As-treated or Intention-to-treat) and different gap durations between the concomitant drugs will be performed (e.g. between MPH and SSRI: 30 days, 0 days). • Preventing bias from reverse causality To avoid reverse causality due to outcome variables, additional sensitivity analysis will be conducted in which symptomatic patients are removed.

Documents

Study publications
Kim C, Lee DY, Park J, Yang SJ, Tan EH, Prieto-Alhambra D, Lee YH, Lee S, Kim S…

Data management

Data sources

Data sources (types)
Administrative data (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