Post-marketing study of ropinirole prolonged release tablets in Parkinson’s disease: Evaluation outcomes associated with long term use of Ropinirole-PR using the clinical practice research datalink (CPRD) (111981)

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Study Finalised

Administrative details

EU PAS number

EUPAS12518

Study ID

40748

DARWIN EU® study

No

Study countries

United Kingdom

Study description

Parkinson disease (PD) is a neurodegenerative condition resulting in the deficiency of dopamine, current available therapies aim to compensate for its deficiency. Ropinirole is non-ergot DA indicated for the treatment of PD. The immediate release formulation was approved over 15 years ago, a prolonged release formulation (ropinirole-PR) was more recently licensed in 2008. The proposed study is part of a post-marketing commitment to the MHRA to evaluate long term safety of ropinirole-PR. Specifically, it is proposed to estimate the incidence of dyskinesias, on-off phenomena (subject to feasibility) and impulse control disorders, in PD patients initiating ropinirole-PR monotherapy vs. initiators of immediate release DA monotherapy. This retrospective observational study will use longitudinal electronic medical records (EMR) from the UK- Clinical Practice Research Datalink (CPRD) supplemented with GP questionnaire data. Treatment persistence, adherence off-label use of ropinirole-PR will be also be evaluated. A propensity matched cohort design with adjustments for time varying covariates will be used.

Study status

Finalised

Research institutions and networks

Institutions

GlaxoSmithKline (GSK)

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Institution

Contact details

Study institution contact

GSK Clinical Disclosure Advisor GSK Clinical Disclosure Advisor Pharma.CDR@gsk.com

Study contact

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Primary lead investigator

GSK Clinical Disclosure Advisor GSK Clinical Disclosure Advisor

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 29/09/2015

Actual: 29/09/2015

Study start date

Planned: 31/03/2016

Actual: 07/04/2016

Date of final study report

Planned: 26/04/2018

Actual: 30/04/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

GlaxoSmithKline

Study protocol

gsk-111981-protocol-redact.pdf (1.57 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

To estimate, the incidence of dyskinesia in PD patients initiating ropinirole-PR monotherapy vs. immediate release dopamine agonist monotherapy. Other outcomes of interest are on-off phenomena (subject to feasibility) and impulse control disorders.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N04BC) Dopamine agonists

Dopamine agonists

Medical condition to be studied

Parkinson's disease

Population studied

Short description of the study population

The populations of interest comprised of individuals on the CPRD with a recorded Parkinson’s disease diagnosis that had initiated either ropinirole-PR monotherapy (ropinirole-PR) or an oral immediate release dopamine agonist (IR-DA) as monotherapy between 2008 and 2013.

Inclusion criteria:

Individuals were required to

- Meet the case definition of Parkinson’s disease
- Have initiated a dopamine agonist therapy between 2008-2013 and received at least two prescriptions for the therapy of interest.
- Have a minimum of 12 months of registration prior the date of initiation of the dopamine agonist therapy +30 days in order to collect information on disease, comorbidity, medical and prescription history.
- Belong to practices that are considered up to research standard at initiation of therapy.

Exclusion criteria

- Individuals in the immediate release dopamine agonist cohort that had previously been prescribed any prolonged release dopamine agonist (ropinirole-PR or

pramipexole-PR) were excluded.
- Individuals with evidence of adjunctive or prior history of levodopa use at time of initiating the dopamine agonist therapy were excluded, as were individuals with a history of dyskinesia or impulse control disorders prior to index date.
- Individuals with evidence of secondary or drug induced PD
- Aged <40 years at the time of PD diagnosis

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

Parkinson's disease patients

Estimated number of subjects

2.000

Study design details

Outcomes

Dyskinesia is the primary outcome. Additional outcomes are impulse control behaviors (ICD) and on-off phenomena. Dyskinesia and ICD will be identified using READ codes on the CPRD supplemented by GP questionnaire. On-off

phenomena will be identified solely byGP questionnaire, however, it may not be feasible or appropriate to evaluate this as an outcome should the GP response rate be low, Treatment persistence and adherence will be evaluated. Additionally time to levodopa initiation will be estimated. As levodopa is associated with dyskinesias, delay in its use may further reduce the risk of the development of motor complications, or reflect better control of PD symptoms by current therapy. The extent of off-label use of ropinirole-PR will be described.

Data analysis plan

The incidence of dyskinesia (and other outcomes of interest) will be calculated in the ropinirole-PR and propensity score matched IR-DA cohorts. Censoring occurs at the earliest of an outcome of interest, discontinuation of therapy+30days, end of a patient record or end of the study period. Crude incident rates per 1000 person years of follow-up for each outcome will be calculated. Incidence rates will be stratified by age group (at index date) and PD duration. Incidence rate ratios will be estimated between the exposure groups and adjusted for risk factors using multivariable Poisson regression. In addition, the incidence amongst switchers to ropinirole-PR and those initiating ropinirole-PR de novo will be estimated. A Cox proportional hazards regression model will be used to evaluate time to dyskinesias in individuals in both cohorts. Adjusted hazards ratios will be estimated, accounting for potential confounders and time varying covariates.

Documents

Study results

gsk-111981-clinical-study-report-redact.pdf (3.74 MB)

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)

Clinical Practice Research Datalink

Data sources (types)

Electronic healthcare records (EHR)

Other

Data sources (types), other

Data from CPRD will be supplemented by GP questionnaire data

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