A Prospective Pediatric Longitudinal Evaluation to Assess the Long-Term Safety of Tacrolimus Ointment for the Treatment of Atopic Dermatitis (APPLES™)

First published: 09/02/2016

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Study Finalised

Administrative details

EU PAS number

EUPAS12360

Study ID

36609

DARWIN EU® study

No

Study countries

Austria

Canada

France

Germany
Ireland
Netherlands
Poland
United Kingdom
United States

Study description

This is an observational study to assess the long-term safety of Protopic Ointment for the treatment of atopic dermatitis. Patients whose ages are/were < 16 years at the time of the first tacrolimus ointment exposure are eligible to participate. No drug is distributed during this observational trial.

Study status

Finalised

Research institutions and networks

Institutions

Multiple centres: 314 centres are involved in the study

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Henny Bang Jakobsen

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 03/01/2005

Actual: 03/01/2005

Study start date

Planned: 25/05/2005

Actual: 25/05/2005

Date of interim report, if expected

Actual: 26/10/2018

Date of final study report

Planned: 02/01/2023

Actual: 08/07/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

LEO Pharma A/S

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)

Other study registration identification numbers and links

ClinicalTrials.gov, registration number NCT00475605.

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

Data collection methods:

Primary data collection

Main study objective:

The APPLES Study is a large cohort study to assess the long-term safety of tacrolimus ointment 0.03% or 0.1% in the treatment of subjects with atopic dermatitis under actual use conditions, including the risk of developing cutaneous or systemic malignancies.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(D11AH01) tacrolimus

tacrolimus

Medical condition to be studied

Dermatitis atopic

Population studied

Short description of the study population

To be enrolled in the study subjects had to be diagnosed with atopic dermatitis (AD), had to have been exposed to tacrolimus ointment before the age of 16, and the subject o guardian had to have given written informed consent and assent (when relevant) to comply with the program requirements, including annual physical examinations, biennial dermatological examinations and direct contact twice a year for questionnaire completion.

Age groups

- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)

Estimated number of subjects

8000

Study design details

Outcomes

•Total systemic malignancies diagnosed more than 6 months after the initiation of tacrolimus ointment treatment.•Hodgkin and Non-Hodgkin lymphoma diagnosed more than 6 months after the initiation of tacrolimus ointment treatment.•Cutaneous malignancies (melanoma and non-melanoma skin cancer) diagnosed more than 6 months after initiation of tacrolimus ointment treatment.

Data analysis plan

Standardized Incidence Ratios and confidence intervals will be calculated for every outcome. The expected number of events are derived from available cancer registries covering the relevant countries of residence, taking into

account sex, age, and in the United States of America also race.

Documents

Study results

LP0156-1294 Clinical Trial Report - Synopsis -Redacted.pdf (150.72 KB)

Study publications

Paller AS, Folster-Holst R, Chen SC, Diepgen TL, Elmets C, Margolis DJ, Pollock...

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)

Other

Data sources (types), other

Prospective patient-based data collection

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