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Pharmacodynamics and pharmacokinetics of P-3074, a new finasteride topical solution, administered at four different doses

Submission date
18/12/2013

Recruitment status
No longer recruiting

Registration date
14/01/2014

Overall study status
Completed

Last Edited
14/01/2014

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Androgenetic alopecia in men is progressive hair loss that starts with shrinking of the hair follicles and reduction of the hair diameter. Although the mechanism of these changes has not been definitively established, male hair loss is known to depend on male sexual hormones (androgens), in particular on the androgen dihydrotestosterone (DHT), which is generated from testosterone. In fact, increased levels of DHT have been found in the scalps of men with androgenetic alopecia.
It has been proven that P-3074 (a topical solution containing finasteride 0.25%), applied directly on the scalp once a day for seven days, is able to penetrate the scalp skin and to act at the hair bulb level directly, blocking the local DHT more effectively and more consistently than oral finasteride.
The aim of this study is to find out the amount of topical finasteride which could be effective at the hair bulb level while reducing or avoiding the adverse effects known for oral finasteride.

Who can participate?
Thirty-two men aged between 18 and 65 years with androgenetic alopecia.

What does the study involve?
The volunteers will be randomly divided into four different cohorts (A, B, C and D).
Each cohort will be composed of eight subjects, and within each cohort six subjects will be randomly allocated to receive a once-daily topical treatment of the scalp skin area for 7 days with P-3074, and two subjects will receive a placebo (dummy) treatment. The different cohorts will be treated with different doses of finasteride.

What are the possible benefits and risks of participating?
No real potential benefits are foreseen to the volunteers participating in this study.
Potential risks of multiple dose oral administrations or topical applications of finasteride were expected to be limited. The known adverse reactions are decreased libido, reported in > 1% of men treated with finasteride 1 mg; erectile dysfunction and decreased volume of ejaculate. Other adverse reactions reported during clinical trials and/or post-marketing are the following:

hypersensitivity reactions, including rash, pruritus, urticaria and swelling of the lips and face; palpitation; increased hepatic enzymes; breast tenderness and enlargement; testicular pain and infertility. Breast cancer has been reported in men taking finasteride 5 mg during the post-marketing period in the UK but there have been no reported cases of male breast cancer associated with 1 mg finasteride use.

Where is the study run from?
The study will be conducted in the CROSS Research Phase I Unit located in Arzo, Switzerland.

When is the study starting and how long is it expected to run for?
The study will run from March 2014 until May 2014.

Who is funding the study?
Polichem SA, Switzerland.

Who is the main contact?
Dr Renata Palmieri (Contact for Polichem), renata.palmieri@polichem.com
Dr Milko Radicioni, Principal Investigator, clinic@croalliance.com

Contact information

Type(s)
Scientific

Contact name
Dr Milko Radicioni

Contact details
CROSS Research SA
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6864

Additional identifiers

Protocol serial number
PM1332

Study information

Scientific Title
Dose response, pharmacodynamic and pharmacokinetic study of P-3074, a new finasteride 0.25% topical solution, after 7-day multiple dose administration in male volunteers with androgenetic alopecia

Study objectives

To investigate the dose-response relationship, in terms of pharmacodynamic (PD) effects and pharmacokinetics (PK) of finasteride, after multiple topical applications of four doses of finasteride topical solution in male subjects with androgenetic alopecia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cantonal Ethics Committee (Comitato Etico Cantonale), Ticino, Switzerland, 10/12/2013, ref: CE2766

Study design
Single-center randomised placebo-controlled double-blind parallel-group dose-response pharmacodynamic and pharmacokinetic study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Androgenetic alopecia

Interventions
Thirty-two male volunteers will be randomly divided into four different cohorts (A, B, C and D). Each cohort will be composed of 8 subjects; within each cohort 6 subjects will be randomly allocated to receive a 7-day treatment of the scalp skin area with P-3074 (a new topical finasteride 0.25% formulation) and 2 subjects will receive placebo.

Cohort A: 100 microL of P-3074 (i.e., 0.2275 mg of finasteride) or placebo
Cohort B: 200 microL of P-3074 (i.e., 0.455 mg of finasteride) or placebo
Cohort C: 300 microL of P-3074 (i.e., 0.6825 mg of finasteride) or placebo
Cohort D: 400 microL of P-3074 (i.e., 0.91 mg of finasteride) or placebo

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
finasteride

Primary outcome(s)
Scalp and serum concentrations of dihydrotestosterone (DHT) at baseline and 6 ± 2 h after the last P-3074 or placebo dose (day 7). Two biopsies at each sampling time (baseline and 6 ± 2 h after last dose) will be taken. DHT in scalp and serum samples will be determined using validated analytical methods.

Key secondary outcome(s)
1. Plasma concentrations of finasteride at baseline and 6 ± 2 h after the last P-3074 or placebo dose (day 7) will be determined using validated analytical methods.
2. Scalp and serum concentrations of testosterone at baseline and 6 ± 2 h after the last P-3074 or placebo dose (day 7) will be determined using validated analytical methods.
3. Amount of finasteride per cm2 of adhesive tape strips - unabsorbed finasteride (2 tape strips per each time point will be applied and collected) at 12, 14, 16 and 16.5 h after the last dose of P-3074 or placebo (only for cohort D). The samples at 16.5 h will be collected after the shower.
4. Amount of finasteride per cm2 of adhesive tape strips - stratum corneum (20 tape strips per each time point will be applied and collected) at 12, 14 and 16 h after the last dose of P-3074 or placebo (only for cohort D).
5. Safety and tolerability: based on adverse events, physical examinations, vital signs, ECG and routine haematology, blood chemistry and urinalysis laboratory tests.

Completion date
31/05/2014

Eligibility

Key inclusion criteria
To be enrolled in this study, subjects must fulfil all of these criteria:
1. Informed consent: signed written informed consent before inclusion in the study
2. Sex and age: males, 18-65 years old inclusive
3. Androgenetic alopecia: recession of the frontal hairline and hair loss in the vertex or crown, or loss of hair over the frontal and vertex scalp regions, corresponding to at least stage 2 of the Hamilton-Norwood scale
4. Body mass index: 18.5-30 kg/m2 inclusive
5. Vital signs: systolic blood pressure 100-139 mmHg, diastolic blood pressure 50-89 mmHg, heart rate 50-90 bpm, measured after 5 min at rest in the sitting position
6. Full comprehension: ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to co-operate with the investigator and to comply with the requirements of the entire study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
Male

Key exclusion criteria
Subjects meeting any of these criteria will not be enrolled in the study:
1. ECG: clinically relevant abnormalities at ECG (12 leads)
2. Skin of the scalp: skin damage such as abrasion, hyperkeratosis or any abnormal findings in the scalp
3. Physical findings: clinically relevant abnormal physical findings
4. Laboratory analysis: clinically relevant abnormal laboratory values indicative of physical illness
5. Allergy: ascertained or presumptive hypersensitivity to the active principle and/or formulations' ingredients; history of anaphylaxis to drugs or allergic reactions in general, which the investigator considers may affect the outcome of the study
6. Diseases: relevant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, skin, haematological, endocrine or neurological diseases, that may interfere with the aim of the study
7. Medications: medications, including over the counter medications and herbal remedies, for 2 weeks before the start of the study (the anaesthetic used for the biopsies will be allowed; paracetamol and oral peri-operative antibiotic prophylaxis will be administered as needed)
8. Investigative drug studies: participation in the evaluation of any drug for 3 months starting from the first day of the month following the last visit in a previous study
9. Blood donations: blood donations for 3 months before this study
10. Drug, alcohol, caffeine, tobacco: history of drug, alcohol (>2 drinks/day, defined according to USDA Dietary Guidelines 2010), caffeine (>5 cups coffee/tea/day) or tobacco abuse (>10 cigarettes/day)
11. Diet: abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits within the past 4 weeks
12. Alcohol test: positive alcohol breath test before starting P-3074 administration
13. Drug abuse: positive abuse drug test at screening

Date of first enrolment
01/03/2014

Date of final enrolment
31/05/2014

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research SA
Arzo
Switzerland
6864

Sponsor information

Organisation
Polichem SA (Switzerland)

ROR
https://ror.org/05735qy63

Funder(s)

Funder type
Industry

Funder Name
Polichem SA (Switzerland)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration