A Multicenter, Randomized, Double blind, Vehicle-controlled, Phase 3 Efficacy and Safety Study of Patidegib Topical Gel, 2%, for the Reduction of Disease Burden of Persistently Developing Basal Cell Carcinomas (BCCs) in Subjects with Basal Cell Nevus Syndrome

Published: 05-11-2018
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Primary Objective:To assess the number of new BCCs in the 2 arms (Patidegib Topical Gel, 2%, and Vehicle (placebo)) when applied twice daily to the face of subjects with Gorlin Syndrome.Secondary Objective:To assess the safety and tolerability of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON55856

Source
ToetsingOnline

Brief title
PATIDEGIB study

Condition

- Skin and subcutaneous tissue disorders congenital
- Skin neoplasms malignant and unspecified
- Skin neoplasms malignant and unspecified

Synonym
skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: PellePharm, Inc.
Source(s) of monetary or material Support: PellePharm;Inc.

Intervention

Keyword: Basal cell carcinoma, Basal Cell Nevus Syndrome, Gorlin syndrome

Outcome measures

Primary outcome

The primary endpoint is the number of new BCCs per subject by Month 12.

Secondary outcome

Secondary Endpoints:

1. The number of nSEBs per subject by Month 12.

2. The proportion of subjects developing >=2 facial new BCCs by Month 12.

3. The proportion of subjects developing >=1 facial new BCCs by Month 12.

4. The number of qualifying new BCCs per subject by Month 9.

5. The number of qualifying new BCCs per subject by Month 6.

6. aBCCdex change in Lesion Symptoms scale score from Baseline to Month 12.

The exploratory endpoints are:

1. The proportion of SEBs that undergo clinical resolution at Month 12.

2. The number of BCC surgeries from Baseline to Month 12.

3. Change in aBCCdex Worry About Future Lesions scale score from Baseline to

Month 12.

4. Change in aBCCdex Mental Health scale score from Baseline to Month 12.

5. Change in aBCCdex Social/Relationships scale score from Baseline to Month 12.

6. Change in aBCCdex Life Impact scale score from Baseline to Month 12.

Study description

Background summary

Basal cell nevus (Gorlin) syndrome (BCNS) is a rare autosomal dominant heritable disease characterized by numerous phenotypic abnormalities, most prominent among which is the development of numerous basal cell carcinomas (BCCs) over a lifetime. Reports of its prevalence vary; the highest estimate is 1:31,000. The burden of BCCs varies among Gorlin Syndrome patients. In general, Gorlin Syndrome patients have their BCCs treated as they become problematic (i.e., at risk of invasion of vital structures such as eyes, nose, or ears, become large enough that scarring will be particularly noticeable if treatment is delayed, or become large enough off the face such that they are uncomfortable, bleed). Thus BCNS patients typically are never free of BCCs; in a trial of the effects of vismodegib vs. BCCs in Gorlin Syndrome patients, Gorlin Syndrome subjects had an average of 27 BCCs present at baseline. Although oral vismodegib can produce complete clinical clearing, once the drug is stopped the BCCs recur.
Several topically-applied drugs are used in the treatment of BCCs. Some of them can cure approximately 80% of the superficial subtype of BCCs, which generally occur off the face, but they generally are not useful vs. nodular BCCs, which are the more prevalent subtype, especially on the face. Prevention of BCCs so far has been limited to admonitions to avoid sunlight, advice which is followed infrequently by patients at risk of developing sporadic skin tumors, and which has not been shown to produce a statistically significant reduction in BCC incidence. Following identification of uncontrolled HH signaling as the driving molecular abnormality in all BCCs, several anti-HH drugs have been developed for oral treatment of BCCs. But because of annoying class-specific side effects, most patients discontinue their treatment, and most/all of the clinically and histologically cleared BCCs recur to the same size as before treatment. Patidegib is a semi-synthetic small molecule and when given orally has good therapeutic efficacy versus advanced BCCs but produces the same types of adverse effects as do other systemic HH inhibitors. Patidegib Topical Gel, 2%, is manufactured with excipients generally accepted as safe, is stable in the developed gel formulation, and can be applied to mini-pig skin without irritation. Application of Patidegib Topical Gel, 2%, significantly reduces

murine BCC tumor size in vivo and reduces GLI1 biomarker expression in vitro in human BCC tumor explants. PellePharm, Inc. is developing Patidegib Topical Gel, 2%, for the reduction of BCC burden in subjects with Gorlin Syndrome. This trial will evaluate the ability of Patidegib Topical Gel, 2%, to reduce new surgically eligible BCCs (SEBs) in subjects with Gorlin syndrome.

Study objective

Primary Objective:
To assess the number of new BCCs in the 2 arms (Patidegib Topical Gel, 2%, and Vehicle (placebo)) when applied twice daily to the face of subjects with Gorlin Syndrome.

Secondary Objective:
To assess the safety and tolerability of Patidegib Topical Gel, 2%, in subjects treated twice daily for 12 months

Study design

This is a global, multicenter, randomized, double-blind, stratified, vehicle-controlled study of the efficacy and safety of Patidegib Topical Gel, 2%, applied topically twice daily to the face of adult subjects with Gorlin Syndrome.
Subjects will be randomized (1:1) to receive either Patidegib Topical Gel, 2%, or Vehicle for 12 months.
The assignment of subjects to the two groups will be stratified by gender, age (>= or <60 years), and previous Hedgehog inhibitor (HHI) therapy.
Study duration is approximately 14 months: up to 45-day Screening period, 12 months active treatment, and 30-day safety follow up.
Number of subjects : Up to 150 subjects
All subjects who complete the Month 12/Exit Visit having demonstrated adequate compliance with application of the Investigational Product (IP) without major Protocol Deviations (PDs) during the study will be eligible for participation in the open-label extension study.

Intervention

Subjects will be randomized (1:1) to receive either Patidegib Topical Gel, 2%, or Vehicle for 12 months to assess the number of new BCCs in the 2 arms (Patidegib Topical Gel, 2%, and Vehicle) when applied twice daily to the face of subjects with Gorlin Syndrome and the safety and tolerability of Patidegib Topical Gel, 2%, in subjects treated twice daily for 12 months

Study burden and risks

In complete studies with the topical gel, the most common side effects were

muscle spasms and irritation at the application site (redness, itching, pain/burning/stinging and hair loss at the application site).

The following risks may be associated with patidegib topical gel:
• the skin may become itchy, red, and/or dry when using this study gel.
• there may bepain/burning/stinging at the application site.
• The study gel may affect the quality and quantity of hair in areas where it is applied.

The placebo may also cause side effects. The most important ones are:
• Itchy skin
• Red skin
• Dry skin

There is a risk of an allergic reaction:
• a rash
• a fast pulse
• sweating
• a feeling of dread
• swelling around the eyes and mouth
• swelling of the throat
• wheezing
• having a hard time breathing
• a sudden drop in blood pressure (making the patient feel dizzy or lightheaded)
• inability to breathe without assistance

Blood Draws
It may be painful when blood is drawn . Some people get dizzy or faint from a blood draw. The patient could also get an infection, which is rare, or have bleeding, redness, or bruising at the skin puncture.

Unknown Risks
Patidegib Topical Gel, 2% is an investigational treatment so there may be risks and side effects that are not yet known.
There may also be unknown risks to an unborn child.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Key Inclusion criteria:
1. The subject must be at least 18 years old at the Screening visit.
2. The subject must meet diagnostic criteria for BCNS (Inclusion Criteria 3).
3. The subject must have had at least 10 (with at least 3 on the face) clinically typical BCCs present within 24 months prior to Randomization (Baseline/Day 1). Additionally, the subject must have at least 2 BCCs with longest diameter <5 mm present on the face prior to randomization.
4. The subject must be willing to abstain from application of a non-study topical medication (prescription or over the counter) to facial skin for the duration of the trial.

Exclusion criteria

Key Exclusion criteria:
1. The subject has used topical treatment to the face or systemic therapies that might interfere with the evaluation of the study IP.
2. The subject is known to have a hypersensitivity to any of the ingredients in the IP.
3. The subject has uncontrolled systemic disease.
4. The subject has been treated for invasive cancer within the past 5 years

excluding non-melanoma skin cancer, Stage I cervical cancer, ductal carcinoma in situ of the breast, or chronic lymphocytic leukemia (CLL) Stage 0.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-05-2019
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Patidegib Topical Gel 2%
Generic name:	Patidegib Topical Gel 2%

Ethics review

Approved WMO

Date:	05-11-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	18-04-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-05-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-06-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-09-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-10-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-02-2020
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-02-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-03-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-03-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-07-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-07-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-11-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	

Date:	21-01-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-01-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2018-001462-42-NL
ClinicalTrials.gov	NCT03703310
CCMO	NL66329.068.18