Treatment of port wine stains using Pulsed Dye Laser, Erbium Yag Laser and topical sirolimus in an open label pilot study (POLAR).

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Primary: to evaluate and compare the efficacy of:1) PDL treatment followed by topical sirolimus application after Er:Yag laser ablation of the stratum corneum in PWS 2) PDL treatment followed by topical sirolimus application without Er:Yag laser...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Skin vascular abnormalities
Study type	Interventional

Summary

ID

NL-OMON40605

Source
ToetsingOnline

Brief title
Acroniem: POLAR trial.
Verkorte titel: New treatment for port wine stains

Condition

- Skin vascular abnormalities

Synonym
Naevus flammeus, Port Wine Stain

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Erbium Yag Laser, Port Wine Stain, Pulsed Dye Laser, Sirolimus

Outcome measures

Primary outcome

Percentage clearance of the treated area assessed colorimetrically (Minolta

colorimeter).

Secondary outcome

- Percentage clearance of the treated area assessed by standardized digital

colour image analysis.

- Percentage clearance of the treated area assessed by photographic evaluation

by an expert panel.

- To evaluate the improvement in quality of life;

- Patient discomfort and pain experienced during and following treatment;

- Patient-reported symptoms and side-effects;

- Systemic sirolimus exposure;

- Treatment satisfaction.

Study description

Background summary

Pulsed Dye Laser (PDL) treatment is currently the gold standard for the treatment of Port Wine Stains (PWS). However, a protracted course of treatments is usually necessary to obtain a clinically significant degree of lesion

blanching. This appears to be (partly) due to neo-angiogenesis. We hypothesize that the efficacy of standard PDL treatment can be greatly enhanced by subsequent application of topical sirolimus (Rapamycin or RPM). The rationale for this combined treatment is that by application of sirolimus after PDL, neo-angiogenesis will be inhibited, which may attenuate the reformation and reperfusion of PWS blood vessels disrupted by laser photothermolysis. By using the Erbium Yag (Er:Yag) laser for ablation of the stratum corneum in addition, we could facilitate superior penetration and local skin distribution of sirolimus and possibly inhibit neo-angiogenesis in deeper parts of the dermis. This combined treatment may result in a higher therapeutic efficacy in terms of PWS blanching.

Study objective

Primary: to evaluate and compare the efficacy of:
1) PDL treatment followed by topical sirolimus application after Er:Yag laser ablation of the stratum corneum in PWS
2) PDL treatment followed by topical sirolimus application without Er:Yag laser ablation of the stratum corneum
3) PDL treatment only
4) Sirolimus application only

Secondary:
- To evaluate the improvement in quality of life;
- To evaluate patient discomfort and pain experienced during and following treatment;
- To evaluate patient-reported symptoms and side-effects;
- To assess systemic sirolimus exposure after local application by measuring serum concentrations;
- To evaluate treatment satisfaction.

Study design

Open label pilot study.

Intervention

In the first treatment period all patients will receive a total of five treatments with two week intervals. Every patient will receive the following four treatments (utilizing a template with separate squares of 1cm2): 1) PDL treatment followed by topical sirolimus application after Er:Yag laser ablation of the stratum corneum compared with 2) PDL treatment followed by topical sirolimus application without Er:Yag laser ablation of the stratum corneum, 3) PDL treatment only and 4) sirolimus application only. After the six months follow-up period, during the second treatment period, patients will receive an additional five treatments of the adjacent cosmetic unit of the treated part of

the PWS, employing the most successful of the four treatment modalities as evaluated after the first treatment period.

Study burden and risks

The whole treatment period will entail 16 visits to the outpatient department. Percentage clearence will be assesed colormetrically by using a Minolta Colorimeter. Digital photographs will be assessed by colour image analysis and by an expert panel. Patients will be asked to fill in questionnaires about discomfort and pain experienced during and following treatment (VAS scores). Patient satisfaction (0-100 scale) and quality of life (DLQI) will be evaluated. Blood samples will be taken regularly to assess safety. Also serum concentrations of sirolimus will be assessed in order to evaluate potential systemic exposure. We propose the use of a topical formulation of sirolimus (Rapamune®) to minimize the risks associated with systemic sirolimus exposure.

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

• Subject has provided informed consent;
• Subject is >= 18 years of age at time of screening;
• Subject has an extra-facial homogenous PWS;
• The PWS is large enough in size to fit one of the templates (at least 11 cm x 3 cm or 7 cm x 5 cm);
• Subject has not received any laser treatment of the PWS in the last 3 months (in the treatment area);
• The PWS has a minimal erythema grading score of 3 (on a 4 point scale) in the opinion of the investigator;
• Screening blood safety values are within normal parameters or regarded as not clinically significant in the opinion of the investigator.

Exclusion criteria

• PWS with a nodular/hypertrophic component in the treatment area;
• PWS on cosmetically unacceptable locations in the opinion of the investigator;
• For women: pregnant or breast feeding during the treatment period;
• Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using adequate contraceptive measures; Effective contraception is defined as either:
o Barrier method of contraception: Condom or Occlusive cap (diaphragm or cervical/vault caps) with spermicide.
The following methods are considered more effective than the barrier method and are also acceptable:
o Total abstinence (when this is in line with the preferred and usual lifestyle of the subject).
o Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy) or tubal ligation at least six weeks before participating in the study.
o Male sterilization (at least 6 months prior to screening). For female subjects on the study, the vasectomized male partner should be the sole partner for that subject.
o Use of oral, injected or implanted hormonal methods of contraception or other forms, intrauterine device (IUD) or intrauterine system (IUS)
NOTE: Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks ago.
• Subject is known to have immune deficiency, or is immune compromised (including immunosuppression induced by medication);
• Known allergy to sirolimus or other constituents of the study medication;
• Incapacitated subjects;
• Any medical or psychiatric condition which, in the investigator*s opinion, would preclude

the participant from adhering to the protocol or completing the study per protocol.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-08-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rapamune
Generic name:	Sirolimus
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	03-01-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	31-03-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2013-004834-14-NL
CCMO	NL47292.078.13