Clinical trial results:
Evaluation of the protection activity of microfine Ti02, pigmentary Ti02 and bisoctrizole and their combinations in voluntary patients with idiopathic solar urticaria (SU): phase II photoprovocation test.

Summary

EudraCT number	2007-000911-27
Trial protocol	GB
Global end of trial date	22 April 2008

Results information

Result version number	v2 (current)
This version publication date	17 August 2016
First version publication date	18 June 2015
Version creation reason	• New data added to full data set As the study was linked to a PIP, and despite PIP removal, replacement of the clinical study report synopsis by the study data sets.

Trial information

Trial identification

Sponsor protocol code	V00096 CR 205 (ORF)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Orfagen
Sponsor organisation address	3, avenue Hubert Curien, Toulouse CEDEX 1, France,
Public contact	Clinical project manager, Orfagen, info@orfagen.com
Scientific contact	Clinical project manager, Orfagen, info@orfagen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000585-PIP01-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 March 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 April 2008
Global end of trial reached?	Yes
Global end of trial date	22 April 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, Tinosorb MBBT) and their respective combinations.

Protection of trial subjects:

Patients benefit from thorough clinical examination. Local and systemic adverse effects were searched and monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	15
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After check of compliance with inclusion / non inclusion criteria, and after a wash-out period for patients who received potientally interfering treatments, patients were included in the study period (eg. 2 days for emolliant on back; 7 days for topical corticosteroids; 4 weeks for immunosuppressive agents;2 days for antihistaminiques) .

Period 1

Period 1 title	Study Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Investigator, Monitor, Data analyst, Assessor[2]

Blinding implementation details:

Because the test materials were not matched in appearance, a double-blind procedure cannot be applied . Accordingly, the assessment parameters (e.g. reading) were evaluated by the investigator who was masked to the test allocation sites.

Arms

Are arms mutually exclusive?	No
Arm title	V0096 CR vehicle

Arm description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Placebo
Investigational medicinal product name	V0096 CR vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a solar simulator.

Arm title	Ti02 microfine 12.15% alone

Arm description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Experimental
Investigational medicinal product name	Ti02 microfine 12.15% alone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a solar simulator.

Arm title	Ti02 pigmentary 3% alone

Arm description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Experimental
Investigational medicinal product name	Ti02 pigmentary 3% alone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a solar simulator.

Arm title	Bisoctrizole 10% alone

Arm description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Experimental
Investigational medicinal product name	Bisoctrizole 10% alone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a solar simulator.

Arm title	Combination of Ti02 microfine 12.15% + Ti02 pigmentary 3%

Arm description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Experimental
Investigational medicinal product name	Combination of Ti02 microfine 12.15% + Ti02 pigmentary 3%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a solar simulator.

Arm title	Combination of Ti02 microfine 12.15% + bisoctrizole 10%

Arm description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Experimental
Investigational medicinal product name	Combination of Ti02 microfine 12.15% + bisoctrizole 10%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a

solar simulator.

Arm title	Combination of Ti02 pigmentary 3% + bisoctrizole 10%

Arm description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Experimental
Investigational medicinal product name	Combination of Ti02 pigmentary 3% + bisoctrizole 10%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a solar simulator.

Arm title	V0096: Test product

Arm description:

The test product is a combination of Ti02 microfine 12.15% + Ti02 pigmentary 3% + bisoctrizole 10% . In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Arm type	Experimental
Investigational medicinal product name	Test product
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

2mg/cm2. Single application of the test materials (total of 8 treated sites) prior to irradiation using a solar simulator.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: because the test materials containing TiO2 microfine alone, TiO2 pigmentary alone, bisoctrizole alone, and their combinations are not matched in appearance, a double-blind procedure cannot be applied. Accordingly, the assessment parameters will be evaluated by the investigator who will be masked to the test allocation sites
[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: because the test materials containing TiO2 microfine alone, TiO2 pigmentary alone, bisoctrizole alone, and their combinations are not matched in appearance, a double-blind procedure cannot be applied. Accordingly, the assessment parameters will be evaluated by the investigator who will be masked to the test allocation sites

Number of subjects in period 1	V0096 CR vehicle	Ti02 microfine 12.15% alone	Ti02 pigmentary 3% alone
Started	15	15	15
Completed	14	14	14
Not completed	1	1	1
Consent withdrawn by subject	1	1	1

Number of subjects in period 1	Bisoctrizole 10% alone	Combination of Ti02 microfine 12.15% + Ti02 pigmentary 3%	Combination of Ti02 microfine 12.15% + bisoctrizole 10%
Started	15	15	15
Completed	14	14	14
Not completed	1	1	1
Consent withdrawn by subject	1	1	1

Number of subjects in period 1	Combination of Ti02 pigmentary 3% + bisoctrizole 10%	V0096: Test product
Started	15	15
Completed	14	14
Not completed	1	1
Consent withdrawn by subject	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Study Period
Reporting group description: Total population	

Reporting group values	Study Period	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Adults (18-64 years)	12	12	
From 65-84 years	3	3	
Gender categorical Units: Subjects			
Female	8	8	
Male	7	7	

End points

End points reporting groups

Reporting group title	V0096 CR vehicle

Reporting group description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Reporting group title	Ti02 microfine 12.15% alone

Reporting group description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Reporting group title	Ti02 pigmentary 3% alone

Reporting group description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Reporting group title	Bisoctrizole 10% alone

Reporting group description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Reporting group title	Combination of Ti02 microfine 12.15% + Ti02 pigmentary 3%

Reporting group description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Reporting group title	Combination of Ti02 microfine 12.15% + bisoctrizole 10%

Reporting group description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Reporting group title	Combination of Ti02 pigmentary 3% + bisoctrizole 10%

Reporting group description:

In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Reporting group title	V0096: Test product

Reporting group description:

The test product is a combination of Ti02 microfine 12.15% + Ti02 pigmentary 3% + bisoctrizole 10% . In order to compare the photoprotection activity of the 3 active ingredients alone (microfine TiO2, pigmentary TiO2, bisoctrizole) of the test and their respective combinations, each product was applied on randomised test areas before exposition to 1 Minimal Urticarial Dose (MUD), 3 MUD, 5 MUD, 7 MUD.

Primary: Photodermatosis Protection Factor (PPF)

End point title	Photodermatosis Protection Factor (PPF)[1]

End point description:

The PPF for each test product was calculated by dividing the MUD of the protected skin by the MUD of the unprotected skin, in each treatment group.

End point type	Primary

End point timeframe:

MUD reading 30 min after test product removal.
(Application of test product => 15 min later: phototesting with 1 MUD, 3 MUD, 5 MUD or 7 MUD =>

removal of test product => 30 min later: reading of the MUD)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: 8 different products applied on different test areas.

End point values	V0096 CR vehicle	Ti02 microfine 12.15% alone	Ti02 pigmentary 3% alone	Bisoctrizole 10% alone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	15	15
Units: PPF				
arithmetic mean (standard error)	1.93 (± 0.27)	3.27 (± 0.7)	2.33 (± 0.42)	3.53 (± 0.72)

End point values	Combination of Ti02 microfine 12.15% + Ti02 pigmentary 3%	Combination of Ti02 microfine 12.15% + bisoctrizole 10%	Combination of Ti02 pigmentary 3% + bisoctrizole 10%	V0096: Test product
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	15	15
Units: PPF				
arithmetic mean (standard error)	3.67 (± 0.69)	3.8 (± 0.75)	3.93 (± 0.75)	4.33 (± 0.64)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Whole study duration	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups	
Reporting group title	Randomised patients

Reporting group description: -

Serious adverse events	Randomised patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Randomised patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)		
Skin and subcutaneous tissue disorders			
Urticaria thermal			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported