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Sponsor Novartis
Generic Drug Name Not applicable
Therapeutic Area of Trial Rosacea
Approved Indication Investigational
Protocol Number CBFH772A2203
Title A Proof of Concept (PoC) Study to Evaluate the Safety, Tolerability, and Efficacy of 12 Week Administration of BFH772 Ointment in Rosacea Patients
Study Phase Phase 2
Study Start/End Dates 20 Sep 2011 to 15 Feb 2012
Study Design/Methodology This was a multicenter, randomized, blinded, comparator- and vehicle-controlled study in patients with rosacea. Enrolling patients must have had facial erythema consistent with erythematotelangiectatic rosacea (ETR). Patients were enrolled and randomized to either BFH772 1% ointment, BFH772 vehicle, or metronidazole 1% cream. The study consisted of up to a 3-week Screening period, a 12 week Treatment period, during which visits occurred every 2 weeks (plus an additional Week 1 visit to further enhance protocol adherence and study drug compliance), and a Follow–up period of 2 weeks after the last treatment application.
Centers 5 centers located in US

Publication

None

Test Product (s), Dose(s), and Mode(s) of Administration

BFH772 1% ointment, metronidazole 1% cream, vehicle to BFH772

Statistical Methods

The primary efficacy variable was the change from baseline in facial erythema score on the 10-point scale at Week 12. A positive sign of efficacy for the primary variable was considered to be a difference between BFH772 1% ointment and BFH772 vehicle of at least 2.25 with at least 70% level of proof. This criterion was evaluated by estimating posterior probabilities using Bayesian analysis in SAS. The primary analysis also considered the change from baseline at week 12 including baseline as a covariate. The primary comparison was between BFH772 1% ointment and BFH772 vehicle, although the change from baseline for the metronidazole arm was also determined and summarized in a similar way. For comparison, the equivalent posterior probability for the difference between metronidazole 1% cream and BFH772 vehicle was presented. Additional analyses were performed fitting a linear model to data from all available time points.

Secondary variables included: Investigator's global assessment of rosacea, Investigator's assessment of facial telangiectasia, inflammatory lesion count, patient's assessment of flushing frequency, and patient's assessment of facial redness. Secondary variables were summarized by treatment group and time. Differences between BFH772 1% ointment and BFH772 vehicle and between metronidazole 1% cream and BFH772 vehicle were calculated, together with 95% confidence intervals. All other data was summarized by treatment.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria

1. Male and female (women of non-child bearing potential only) patients, 18 to 65 years of age inclusive.
2. Have persistent facial erythema consistent with ETR on the cheeks with an Investigator's assessment of facial erythema of at least moderate severity as determined by clinical evaluation.

Exclusion criteria

1. Have ocular, phymatous or other types of specific rosacea (other than subtype 1 and 2) requiring treatment.
2. Have more than 12 inflammatory lesions on the face.
3. Have any other facial dermatosis that may interfere with the assessments on the face such as seborrheic dermatosis, acne vulgaris, perioral dermatitis, Morbihan's disease, cutaneous sarcoid or lupus erythematosus and /or flushing diseases, such as climacteric flushing, mastocytosis, carcinoid syndrome or phaechromocytosis.

Other standard entry criteria applied.

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Participant Flow

Patient disposition (Safety Population)

	BFH772 N=12 n (%)	BFH772 vehicle N=12 n (%)	Metronidazole N=12 n (%)	Total N=36 n (%)
Patients				
Completed	11 (91.7)	11 (91.7)	10 (83.3)	32 (88.9)
Discontinued	1 (8.3)	1 (8.3)	2 (16.7)	4 (11.1)
Main cause of discontinuation				
Subject withdrew consent	1 (8.3)	1 (8.3)	1 (8.3)	3 (8.3)
Lost to follow-up	0 (0.0)	0 (0.0)	1 (8.3)	1 (2.8)

Baseline Characteristics

Demographic summary by treatment group (Safety Population)

		BFH772 N=12	BFH772 vehicle N=12 (%)	Metronidazole N=12 (%)	Total N=36 (%)
Age (years)	Mean	50.2	49.2	42.9	47.4
	SD	11.1	10.5	12.9	11.7
	Median	52.5	54.0	48.0	51.5
	Range	24-62	30-64	23-58	23-64
Gender – n (%)	Male	3 (25.0)	4 (33.3)	5 (41.7)	12 (33.3)
	Female	9 (75.0)	8 (66.7)	7 (58.3)	24 (66.7)
Predominant Race – n (%)	Caucasian	12 (100.0)	12 (100.0)	12 (100.0)	36 (100.0)

Outcome measures

Primary Outcome Result(s)

The number of participants with adverse events used to assess Safety and Tolerability

See Safety Results

Change from Baseline in facial erythema score

				Difference (BFH772 vehicle – BFH772 /Metronidazole)		
Visit	**Treatment**	**n**	**LS mean**	**LS mean**	**S.E.**	**95% CI**
W12 /EOT	BFH772 vehicle	11	-1.5			
	BFH772	12	-0.8	-0.7	0.6	(-1.9, 0.4)
	Metronidazole	10	-1.2	-0.3	0.5	(-1.3, 0.7)

EOT = End of Treatment

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Secondary Outcome Results

Summary of mean patient's assessment of flushing frequency

	BFH772 N=12 n (%)	BFH772 vehicle N=12 n (%)	Metronidazole N=12 n (%)
Week 12	-0.2 (0.8)	-0.7 (1.1)	-0.3 (0.5)

Summary of change in mean patient's assessment of facial redness

	BFH772 N=12 N (SD)	BFH772 vehicle N=12 N (SD)	Metronidazole N=12 N (SD)
Week 12	0.0 (0.7)	-0.5 (0.9)	-0.5 (0.8)

Summary of change in mean investigator's global assessment of rosacea

	BFH772 N=12 n (SD)	BFH772 vehicle N=12 n (SD)	Metronidazole N=12 n (SD)
Week 1	-0.1 (0.5)	-0.2 (0.4)	-0.1 (0.3)
Week 2	-0.2 (0.4)	-0.3 (0.6)	-0.2 (0.4)
Week 4	-0.2 (0.4)	-0.4 (0.5)	-0.3 (0.5)
Week 6	-0.2 (0.4)	-0.7 (0.5)	-0.3 (0.5)
Week 8	-0.3 (0.5)	-0.5 (0.7)	-0.3 (0.5)
Week 10	-0.4 (0.5)	-0.5 (0.5)	-0.4 (0.5)
Week 12	-0.4 (0.5)	-0.5 (0.7)	-0.5 (0.5)

Summary of change in mean investigator's global assessment of facial telangiectasia

	BFH772 N=12 n (SD)	BFH772 vehicle N=12 n (SD)	Metronidazole 1% cream N=12 n (SD)
Week 1	0.1 (0.3)	0.3 (0.7)	0.1 (0.5)
Week 2	0.1 (0.3)	0.5 (0.5)	0.2 (0.6)
Week 4	-0.1 (0.4)	0.0 (0.4)	0.6 (0.7)
Week 6	0.0 (0.4)	0.3 (0.8)	0.1 (0.9)
Week 8	-0.1 (0.5)	0.2 (0.6)	0.4 (1.1)
Week 10	0.1 (0.3)	0.3 (0.3)	0.4 (1.3)
Week 12	-0.2 (0.4)	0.1 (0.6)	0.4 (1.2)

Summary of change in mean inflammatory lesion count

	BFH772 N=12 n (SD)	BFH772 vehicle N=12 n (SD)	Metronidazole 1% cream N=12 n (SD)
Week 1	0.0 (0.3)	0.0 (0.1)	-0.3 (0.9)
Week 2	0.0 (0.2)	-0.1 (0.2)	-0.1 (0.8)
Week 4	0.2 (0.6)	0.0 (0.4)	0.1 (2.5)
Week 6	0.3 (0.5)	-0.1 (0.2)	-0.5 (1.2)
Week 8	0.3 (0.8)	0.0 (0.4)	-0.5 (1.0)
Week 10	0.5 (1.4)	0.0 (0.4)	-0.8 (1.9)
Week 12	0.5 (1.0)	0.1 (0.4)	-0.5 (1.4)

Summary statistics of BFH772 plasma concentration (trough levels, PK population)

Statistics	Week 1	Week 4	Week 8	Week 12
N	12	11	11	11
Mean (SD)	103 (76.5)	138 (86.0)	103 (77.8)	82.0 (90.9)
CV (%)	74.6	62.4	75.4	111.0
Median	99.0	159.0	90.3	51.7

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Safety Results

Incidence of AEs by primary system organ class (Safety population)

	BFH772	BFH772 vehicle	Metronidazole	Total
	N=12	N=12	N=12	N=36
	n (%)	n (%)	n (%)	n (%)
Patients with at least one AE	6 (50.0)	4 (33.3)	4 (33.3)	14 (38.9)
Primary system organ class				
Eye disorders	1 (8.3)	2 (16.7)	1 (8.3)	4 (11.1)
Gastrointestinal disorders	1 (8.3)	0 (0.0)	2 (16.7)	3 (8.3)
Infections & infestations	1 (8.3)	1 (8.3)	1 (8.3)	3 (8.3)
Musculoskeletal & connective tissue disorders	1 (8.3)	0 (0.0)	1 (8.3)	2 (5.6)
Nervous system disorders	0 (0.0)	0 (0.0)	1 (8.3)	1 (2.8)
General disorders & administration site conditions	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.8)
Injury, poisoning and procedural complications	0 (0.0)	1 (8.3)	0 (0.0)	1 (2.8)
Psychiatric disorders	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.8)
Skin & subcutaneous tissue disorders	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.8)
Respiratory, thoracic & mediastinal disorders	0 (0.0)	0 (0.0)	1 (8.3)	1 (2.8)

Serious Adverse Events and Deaths

None

Other Relevant Findings

None

Date of Clinical Trial Report

20 Dec 2012

Date Inclusion on Novartis Clinical Trial Results Database

05 Feb 2013

Date of Latest Update