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Statistical Analysis Plan
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EXPLORATORY STUDY TO EVALUATE THE SAFETY AND EFFICACY OF CD10367 IN SUBJECTS WITH PSORIASIS

STATISTICAL ANALYSIS PLAN
RD.03.SPR.112075
Project 315
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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviations	Terms
AEs	Adverse events
ATC	Anatomical Therapeutic Chemical
AUC	Area Under Curve
BLQ	Below Limit of Quantification
CV	Coefficient of variation
EGFR	Epidermal Growth Factor Receptor
ERK	Extracellular signal – Regulated Kinases
ET	Early Termination
FU	Follow Up
IHC	Immuno Histo Chemistry
ITT	Intent-To-Treat
Ln	Logarithmic
LOCF	Last Observation Carried Forward
LOQ	Limit Of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
N	Number
NA	Not Applicable
CCI	[redacted]
PK	PharmacoKinetic
PP	Per protocol
PT	Preferred Term
R&D	Research & Development
SAEs	Serious Adverse Events
SAS	Statistical Analyses System
SD	Standard deviation
SOC	System Organ Class
TSS	Total Sum Score
WHO	World Health Organization

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1. STUDY OBJECTIVES

The primary objective is to evaluate, in a modified Dumas-Scoltz psoriasis mini-zone test, the safety and efficacy of CD10367 solution at 1% and 3% after a three weeks treatment period of once daily application.

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2. STUDY DESIGN

Phase IIa.

This is an exploratory, single-centre (France), investigator blinded, randomized, controlled, intra-individual study (Dumas-scholtz design).
Approximately 40 male or female of at least 18 and up to 70 years old suffering from stable plaque psoriasis vulgaris will be screened to randomize 24 subjects.
The subjects will be screened within 3 weeks prior to the pre-treatment period of up to 2 weeks, followed by a treatment period of 3 weeks and a follow-up period of 1 week.
During the pre-treatment period, the subject will apply a keratolytic product at home twice a day on the selected plaques defined by the investigator. CCI [redacted] extreme cream from PPD [redacted] (tube 50ml) with 50% of urea and 2% of salicylic acid (other components: serine, histidine, glycenin, protease, fragrance free and paraben free) will be used as the keratolytic agent. On these target areas, the desquamation will be controlled by the dermatologist and if the scaling's score is 0 or 1 (none or mild), the subject will be enrolled.

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A final visit at Day 19 (or early termination visit if any) will be performed to evaluate safety and efficacy of the treatments, CCI [redacted] .

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The study is expected to last approximately 5 months from the first subject included in the study to the last visit of the last subject. The total maximum study duration for one subject will be 9 weeks.

3. EFFICACY AND SAFETY ASSESSMENT

	Screening period	Pre-treatment period	Treatment Period											Follow-up period
	Up to 3 weeks before pre-treatment period	1 or 2 weeks [a] before treatment period	Week 1				Week 2				Week 3			Week 4 to 5
			D1	D2 &D3	D4	D5	D8	D9 & D10	D11	D12	D15	D16&D17&D18	Final visit D19 /ET	D26 +/- 2
Informed Consent Form	X													
Demographics and Medical history	X													
Previous treatments and procedures	X													
Physical examination	X												X	
Vital signs	X		X										X	
ECG	X [b]												X	
Ophthalmic examination	X [b]												X	
Inclusion Criteria and Exclusion Criteria	X		X											
Selection of target sites	X		X											
Urinalysis	X												X	
Safety tests Blood sampling	X												X	
Randomization			X											
Local Tolerance [c]				D2 only	X		X		X		X		X	
Individual clinical scores	X		X		X		X		X		X		X	
Clearing score					X		X		X		X		X	
Keratolytic product application of selected plaque at home daily		X												
Products application			X	X	X	X	X	X	X	X	X	X		
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PK blood sampling						X							X	X
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Concomitant treatments and Procedures	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events [d]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Exit form [e]													X [f]	X

a. if the scaling score did not reach 0 or 1 after 1 week of pre-treatment, the pre-treatment period can be extended to 2 weeks, otherwise the subjects will start D1 visit immediately. b ECG and ophthalmic exams should be done as close as possible to baseline visit. c Local tolerance CCI of the concerned zone must be taken at any visit in case of AE in a treatment zone. d Adverse Events have to be collected from the ICF signature. e Exit form should be signed after subject data collection has been completed. f Exit form should be completed at ET visit only if no follow-up visit is planned (discontinuation)

4. EFFICACY AND SAFETY VARIABLES

4.1. Efficacy variables

Primary clinically efficacy criteria

Area Under the Curve (AUC) from Day 1 to Day 19 of Total Sum Score (TSS) (sum of erythema, scaling and induration scores).

Secondary clinically efficacy criteria

- AUC of individual clinical scores (erythema, scaling and induration) from Day 1 to Day 19.

Erythema is scored on the following 5-point scale:

0	**None**	No detectable erythema.
1	**Mild**	Slight pinkness present
2	**Moderate**	Definite redness, easily recognized.
3	**Severe**	Intense redness
4	**Very Severe**	Very intense redness

Scaling is scored on the following 5-point scale:

0	**None**	No shedding
1	**Mild**	Barely perceptible shedding, noticeable only on light scratching or rubbing.
2	**Moderate**	Obvious but not profuse shedding
3	**Severe**	Heavy scale production
4	**Very Severe**	Very thick scales

Induration is scored on the following 5-point scale:

0	**None**	Normal skin thickness. No elevation of skin
1	**Mild**	Barely perceptible elevation (by touching) of the psoriasis plaques.
2	**Moderate**	Obvious elevation above the normal skin level; moderate thickening
3	**Severe**	Definite thick elevation above normal skin level
4	**Very Severe**	Very thick elevation

- TSS at each visit (screening, end of pre-treatment period for Z1 and Z2, day 1, day 4, day 8, day 11, day 15 and day 19) and TSS percent change from baseline;
- Erythema, scaling and induration score at each visit: screening, end of pre-treatment period for Z1 and Z2, day 1, day 4, day 8, day 11, day 15 and day 19) and their change from day 1;
- Success rate (defined as a clearing score of 0 or 1) at each evaluation visit (day 4, day 8, day 11, day 15 and day 19) and the time to first success.

The clearing score is defined as:

0	Complete clearing	No scaling and no infiltration even on palpation. Post inflammatory hypo- or hyperpigmentation may be present.
1	Almost clear	Residual erythema with some induration/ infiltration (not clinically visible but palpable) without scaling, or residual erythema and residual scaling with no infiltration.
2	Unchanged	Unchanged or less than almost clear.

The time to partial clearing (clearing score of 0 or 1) is defined as:

0	No Success at any day
1	Success at Day 19 and not before
2	Success at Day 15 and not before
3	Success at Day 11 and not before
4	Success at Day 8 and not before
5	Success at Day 4 and not before

Only the earliest day of success will be considered in defining the time to partial clearing, independently of the subsequent days.

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4.2. Safety variables

- Local tolerance (irritation, stinging/burning, pruritus) twice weekly using a 4-point scale for each mini-zone:

Irritation	**Skin irritation Assessment**	
0	None:	No signs of irritation
1	Mild:	Slight signs of irritation
2	Moderate:	Moderate signs of irritation: Obvious increase in redness as compared to the non-treated surrounding area
3	Severe:	Severe signs of irritation
Stinging/ Burning	**Prickling pain sensation**	
0	None:	No stinging/burning
1	Mild:	Slight warm, tingling/stinging sensation; not really bothersome
2	Moderate:	Definite warm, tingling/stinging sensation that is somewhat bothersome
3	Severe:	Hot, tingling/stinging sensation that causes severe discomfort
Pruritus	**Itch sensation**	
0	None:	No itching
1	Mild:	Itching is noticeable but not really bothersome

2	Moderate:	Definite itching that is somewhat bothersome
3	Severe:	Marked itching, urge to scratch and causes definite discomfort

- Incidence and multiplicity of Adverse Events (from informed consent signature to the end of the study);
- Ophtalmic examination at screening and day 19/ET
- Physical examination at screening and day 19/ET;
- Vital signs performed after 5 minutes rest in the sitting position (systolic blood pressure, diastolic blood pressure, pulse rate, vital signs evaluation) at screening, baseline and day 19/ET;
- 12-lead electrocardiogram during the screening period and at day 19/ET;
- Blood samplings for laboratory safety tests (haematology and blood chemistry) at screening and day 19/ET (Virology will be performed only at screening);
- Urinalysis at screening and day 19/ET;

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5. POPULATIONS ANALYZED

5.1. The Intent-to-treat (ITT) population

The ITT Population is defined as comprising all subjects who are randomized.

5.2. The Per-Protocol (PP) efficacy population

This population will consist of ITT subjects, except some subjects considered as not evaluable due to major deviations from protocol.

Major deviations will be defined after data entry and before breaking the treatment blind, and may include: inclusion criteria not respected, interfering therapy, protocol deviation, poor compliance to study treatment administration or protocol requirements, unblinding. The decision on determining whether a subject is excluded from the per-protocol (PP) population will be made during the blind review meeting.

If no patient has a major deviation, PP efficacy population will be the same as ITT population, and results will be presented on the ITT population only.

5.3. The Safety population

Safety population corresponds to all subjects who received at least once the study treatment during the treatment period.

In case of identical populations, only one safety population will be used for the analysis.

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7. STATISTICAL METHODS AND DATA CONSIDERATIONS

SAS® version 9.3 will be used for the analysis. Graphics will be performed on SAS.

The categorical variables will be summarized by frequency and percentage for each response category (N, %). The continuous variables will be summarized using means, medians, minimum, maximum, and standard deviations.

7.1. Study subjects

7.1.1. Disposition of subjects

Subject disposition will be summarized in the ITT population.
Normal completion as well as early discontinuation will be summarized using frequency distribution (n, %). All early discontinuations will be detailed in a subject-by-subject listing.

7.1.2. Protocol deviations

All protocol deviations, including the decisions regarding major/minor protocol deviations, will be documented in the blind data review meeting and entered into a dataset.
Subjects with major protocol deviations will be excluded from the PP population.
Major protocol deviations will be summarized using frequency distribution (n, %) and will be detailed in a subject-by-subject listing.

7.2. Efficacy analysis

7.2.1. Data sets analyzed

Number of subjects included in each population (ITT population, PP population, safety population, CCI [redacted]) will be summarized.

7.2.2. Demographic characteristics

Frequency distribution (n, %), for qualitative criteria, will be used.
Usual descriptive statistics (n, mean, standard deviation, median, min, max), for quantitative criteria, will be used.
Analysis will be performed on ITT population and PP population (if the number of patients is too different).

7.2.3. Medical history, previous and concomitant therapies, medical and surgical procedures

Medical history will be defined as any disease present before the Screening visit.
Frequency distribution of subjects with previous or/and concomitant disease(s) will be tabulated.
Previous and concomitant therapies will be coded using the World Health Organization (WHO) Drug Dictionary (version v032015).
Previous therapies are defined as therapies stopped within the 6 months preceding the screening visit. Frequency distribution of subjects with at least one previous therapy will be tabulated by Anatomical Therapeutic Chemical (ATC) classification.
Concomitant therapies are defined as any ongoing therapies at the time of the screening visit, and any new therapies started or changed since the screening visit.
Frequency distribution of subjects with at least one concomitant therapy will be tabulated by ATC classification.
Previous and concomitant procedures will be coded using the Medical Dictionary for Regulatory Activities (MedDRA version 18.0).
Previous procedures are defined as procedures stopped within 6 months preceding the screening visit.

Frequency distribution of subjects with at least one previous procedure will be tabulated (n, %) by preferred term.
Concomitant procedures are defined as any ongoing procedures at the time of the screening visit, and any new procedures started or changed since the screening visit.
Frequency distribution of subjects with at least one concomitant procedure will be tabulated (n, %) by preferred term.

7.2.4. Compliance

CCI extreme cream will be applied at home by the subject twice daily, up to 2 weeks before the treatment period upon the judgment of the dermatologist. The scaling score should be 0 or 1 when the subject is enrolled.
All applications during the treatment period will be performed by a person from the investigational team at the study centre, once daily during 3 weeks, 5 days a week except for the third week, for a total of 14 applications.
Subjects with a low compliance will be excluded from PP population during the data review.

7.2.5. Efficacy analysis

7.2.5.1 Primary and secondary efficacy analysis

Descriptive statistics will be done on observed cases for PP and ITT populations.
The Area Under the Curve (AUC) will be calculated from Day 1 (before application) to Day 19 by subject and by treatment/pre-treatment on the Z1-Z6 mini-zone, using the trapezoidal rule on ITT and PP population.
Dates of theorical visit will be used to perform AUC.
AUC of TSS will be submitted to an analysis of variance including subject and treatment/pre-treatment as factors in the model, CCI
AUC of individual clinical scores (erythema, scaling and induration) will be submitted to the same variance analysis.
TSS and TSS percent change from day 1 will be descriptively summarized by visit, as the individual score of erythema, scaling and induration and their respective change from day 1. The analysis will be performed on PP population and ITT population (baseline and Endpoint/LOCF)
Success will be presented in frequency tables (N,%) by treatment/pre-treatment and by visit.
The time to first success will be summarized by treatment/pre-treatment.
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7.2.6. Statistical and analytical issues

7.2.6.1 Adjustment for covariates

Adjustments to baseline value, i.e., day 1 will be considered in the calculation of change and percent change.

7.2.6.2 Handling of dropouts or missing data

For evaluation by visit, on ITT population, a last visit named "Endpoint/LOCF" containing the last observation carried forward (LOCF) will be created.

For Area Under the Curves (of the TSS or for each individual clinical score), no imputation for missing assessment will be done and calculations will be done on observed data, nevertheless for the subjects who terminated earlier, the Final Visit will be imputed to the closest theoretical visit of the protocol.

For patients who have individual score assessments on unscheduled day, closest theoretical visit of the protocol will be used, for each evaluation overtime and AUC.

7.2.6.3 Interim analyses and data monitoring

Not Applicable (NA)

7.2.6.4 Multicenter studies

NA

7.2.6.5 Multiple comparison/multiplicity

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7.2.6.6 Use of an efficacy subset of patients

NA

7.2.6.7 Active-Control studies intended to show equivalence

NA

7.2.6.8 Examination of Subgroups

NA

7.3. Safety analysis

All safety data will be summarized based on the safety population.

7.3.1. Extent of exposure

Number of days of keratolytic during the pre-treatment period in zone 1 and 2 will be summarized.
Study product application will be presented by treatment/pre-treatment and by visit.
Number of study products applications will be summarized by treatment/pre-treatment.

7.3.2. Local tolerance

Local individual signs/symptoms (irritation, skinging/burning, pruritus) in term of frequency distribution and in quantitative description and the worst score (from Day 2 to Day 19/ET) over time of each individual sign/symptom will be calculated by study product.

7.3.3. Adverse events

Adverse Events will be tabulated by study treatment/pre-treatment and in overall.
Occurrence of adverse events will be separated in two periods: the pre-treatment period from the beginning of the pre-treatment period to day 1 excluded, and the treatment period from the date of first application of study drugs to the end of the study.
For the pre-treatment period, only a table with the overview of the adverse events and a listing of the adverse events during this period will be performed.
For the treatment period, Adverse Events (AE) will be tabulated in frequency tables by System Organ Class (SOC) and Preferred Term (PT) based on MedDRA version 18.0. Additional summary tables will be provided for Adverse Events that are considered serious (SAEs), related to study product, related to protocol procedure, related to the study (study product and/or protocol procedure), Adverse Events of special interest, and Adverse Events leading to discontinuation.

Due to the intra-individual study design and whenever possible (known from CRF) AE will be imputed to the treated area, when not possible then the AE will be imputed to all treated zones.

AEs with an onset prior to the pre-treatment period will be listed separately.

7.3.4. Physical examination, vital signs

Physical examination and vital signs evaluation will be summarized by visit using frequency tables (Normal/Abnormal and not clinically significant/Abnormal and clinically significant).
Shift table will be tabulated.
Systolic blood pressure, diastolic blood pressure and pulse rate will be summarized by visit in quantitative manner. Change from baseline will be calculated.

7.3.5. Ophthalmic examination

Ophthalmic examination will be summarized by visit using frequency tables (Normal/Abnormal and not clinically significant/Abnormal and clinically significant).

Shift table will be tabulated.

7.3.6. 12-lead electrocardiogram

Results of 12-lead electrocardiogram will be summarized by visit using frequency tables (Normal/Abnormal and not clinically significant/Abnormal and clinically significant).
Shift table will be tabulated.
QTc interval and change from screening will be also summarized by visit.

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7.3.8. Laboratory parameters

Each hematology and biochemistry parameter will be subject to quantitative and qualitative analyses at screening and at day 19/ET.
Quantitative values in standard units will be summarized at screening and at Day 19/ET, as well as change from screening.
Frequency of subjects with low, normal, high values with respect to normal range will be summarized at screening and at day 19/ET.
Shift tables will be displayed presenting data at screening and at day 19/ET.
Each urinalysis parameter will be subject to qualitative analyses at screening and at day 19/ET.
Shift tables will also be displayed.
In case of urinalysis parameter in quantitative manner, results will be presented by summary statistics.

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7.4.1. Plasma concentration

Raw values of concentration of CD10367 will be summarized with geometric mean, arithmetic mean, standard deviation (SD), coefficient of variation (CV), median, minimum and maximum values by visit (day 5; day 19/ET and day 26).
Logarithmic values (ln) of concentration of CD10367 will be summarized with mean, standard deviation, median, minimum and maximum value by visit.

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[redacted]

7.5. Analysis visit definition

NA

8. CHANGES FROM THE PROTOCOL ANALYSIS PLAN

NA

9. TABLES, FIGURES AND GRAPHS

9.1. Study subjects

Table. Enrollment by Center

Table. Subjects who discontinued treatment and reason for discontinuation

Table. Major protocol deviations

9.2. Efficacy analyses

9.2.1. Subjects characteristics

Table. Data sets analyzed

Table. Demographic data – ITT population
Including age (as quantitative data and by class 18-64, 65-84 and >=85), gender, race, phototype, subject of childbearing potential.

Table. Medical history – ITT population
Including duration of psoriasis and relevant or major illnesses present before the screening visit.

Table. Previous therapies by ATC term – ITT population

Table. Previous procedures by preferred term – ITT population

Table. Concomitant therapies by ATC term – ITT population

Table. Concomitant procedures by preferred term – ITT population

9.2.2. Baseline characteristics

Table. Target location – ITT population

	CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	CD10367 1%	CD10367 3%	Betneval 0.1%	Overall
N							
Elbows	n(%)						
Knees	n(%)						
…							

Table. Target location – PP population

Table. Pre-treatment clinical scores in mini-zones Z1 and Z2 – ITT population

		CD10367 placebo pre-treated	CD10367 3% pre-treated	Overall
Erythema	N			
	2			
	3			
	4			
	Mean			
	SD			
	Median			
	(Min,Max)			
Scaling	N			
	0			
	1			
	Mean			
	SD			
	Median			
	(Min,Max)			
Induration…	…			
TSS	…			

Table. Pre-treatment clinical scores in mini-zones Z1 and Z2 – PP population

Table. Baseline clinical scores in mini-zones Z1 to Z6 – ITT population

Baseline corresponds to week 1 day 1.

Table. Baseline clinical scores in mini-zones Z1 to Z6 – PP population

Baseline corresponds to week 1 day 1.

9.2.3. Primary and secondary efficacy criteria

Table. AUC of TSS – Treatment period - PP and ITT population

		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	CD10367 1%	CD10367 3%	Betneval 0.1%
AUC of TSS (PP)	N						
	Mean						
	SD						
	Median						
	(Min,Max)						
AUC of TSS (ITT)	N						
	Mean						
	SD						
	Median						
	(Min,Max)						

Table. Analysis of variance for AUC of TSS – Treatment period - PP population

		LSmean(SE)	p-value*
Model Effects	Patient	-	
Treatment	CD10367 placebo pre-treated		
Treatment	CD10367 3% pre-treated		
	…		
Contrast	CD10367 placebo – Betneval		
	…		

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Table. AUC of erythema – Treatment period - PP and ITT population

Table. Analysis of variance for AUC of erythema – Treatment period - PP population

Table. AUC of scaling – Treatment period - PP and ITT population

Table. Analysis of variance for AUC of scaling – Treatment period - PP population

Table. AUC of induration – Treatment period - PP and ITT population

Table. Analysis of variance for AUC of induration – Treatment period - PP population

Table. TSS and TSS percent change from day 1 – PP population

TSS		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	CD10367 1%	CD10367 3%	Betneval 0.1%
Screening	N						
	Mean						
	SD						
	Median						
	(Min,Max)						
End of pre-treatment period*							
Day 1, Day 4	N						
	Mean						
	SD						
	Median						
	(Min,Max)						
Percent change from Day 1 at Day 4	N						
	Mean						
	SD						
	Median						
	(Min,Max)						
Day 8, Day 11, Day 15, Day 19	N						
	…						
Percent change from Day 1 at Day 8, Day 11, Day 15, Day 19	N						
	…						

*performed only in Z1 and Z2

Table. TSS and TSS percent change from day 1 – ITT population

ITT population and with only 2 visits: Day 1 and Endpoint/LOCF

Table. Erythema and change from day 1 – PP population

Table. Erythema and change from day 1 – ITT population

Table. Scaling and change from day 1 –PP population

Table. Scaling and change from day 1 –ITT population

Table. Induration and change from day 1 – PP population

Table. Induration and change from day 1 – ITT population

Table. Clearing score by visit – Treatment period - PP population

Clearing score		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	…	…
Day 4	N					
	0					
	1					
	2					
	Mean					
	SD					
	Median					
	(Min,Max)					
Day 8, Day 11, Day 15, Day 19	…					

Table. Clearing score by visit – Treatment period - ITT population

Same table as above but on ITT population and with the additional visit Endpoint/LOCF

Table. Success by visit – Treatment period - PP population

Success		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	…	…
Day 4	N					
	No					
	Yes					
Day 8, Day 11, Day 15, Day 19	N					
	No					
	Yes					

Table. Success by visit – Treatment period - ITT population

Table. Time to first success – Treatment period - PP and ITT population

Time to first success		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	…	…
PP	N					
	No success at any day					
	Success at Day 19 and not before					
	Success at Day 15 and not before					
	Success at Day 11 and not before					
	Success at Day 8 and not before					
	Success at Day 4 and not before					
	Mean					
	SD					
	Median					
	(Min,Max)					
ITT	…					

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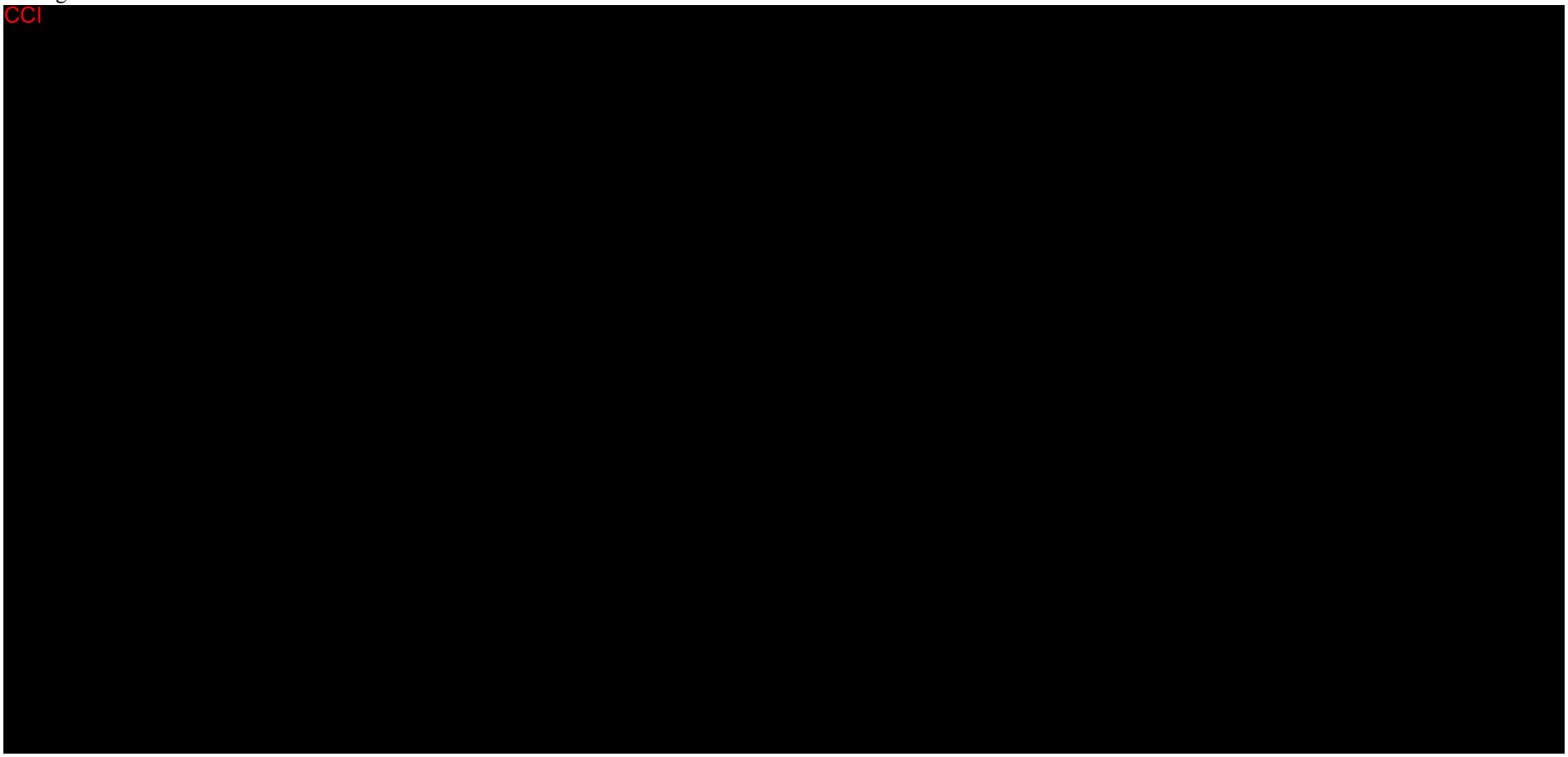

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9.3. Safety analyses

9.3.1. Extent of exposure

Table. Pre-treatment duration of keratolytic product – Safety population

		CD10367 placebo pre-treated	CD10367 3% pre-treated
Number of days of keratolytic product applications	N 4 5 6 7 N Mean SD Median (Min,Max)		

Table. Study drug applications during the treatment period on mini-zones Z1 to Z6 – Safety population

		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	…	…
Day 1	N					
	No					
	Yes					
Day 2, 3 4, 5, 8, 9, 10, 11, 12, 15, 16, 17,18	N					
	No					
	Yes					
Day 2: reason for not applied	N					
	Temporarily discontinued due to irritation					
	Permanent discontinuation due to irritation					
	Other					
…						

Table. Number of applications during the treatment period on mini-zones Z1 to Z6 – Safety population

	CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	…	…
N					
11					
12					
13					
Mean					
SD					
Median					
(Min,Max)					

9.3.2. Local tolerance

Table. Irritation in term of continuous data

Irritation		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	…	…	…
Day 2							
	N	xx	xx	xx	xx	xx	xx
	Mean±sd	xx.x±xx.x	xx.x±xx.x	xx.x±xx.x	xx.x±xx.x	xx.x±xx.x	xx.x±xx.x
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(Min,Max)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Day 3…							
…							
Day 19							
Day 19/ET							
Follow-up							

0= None – 1=Mild – 2=Moderate – 3=Severe

Table. Irritation in term of frequency distribution

Irritation		CD10367 placebo pre-treated	CD10367 3% pre-treated	CD10367 placebo	…
Day 2	N				
	0- None				
	1- Mild				
	2- Moderate				
	3 – Severe				
Day 2 …					

Table. Stinging /Burning in term of continuous data
Table. Stinging /Burning in term of frequency distribution
Table. Pruritus in term of continuous data
Table. Pruritus in term of frequency distribution
Table. Worst Score in term of frequency distribution

9.3.3. Adverse events

Table. Overview of adverse events during the pre-treatment period – Safety population

Table. Listing of adverse events during the pre-treatment period – Safety population

Table. Listing of adverse events prior the pre-treatment period – Safety population

†Or listing if few AE.

Table. Overview of adverse events during the treatment period – Safety population

Table †. Summary of adverse events by Preferred Term – Safety population

Table †. Summary of adverse events Related to the study drug by Preferred Term – Safety population

Table †. Summary of adverse events Related to the protocol procedure by Preferred Term – Safety population

Table †. Summary of adverse events Related to the study by Preferred Term – Safety population

Table . Summary of adverse events by System Organ Class and Preferred term – Safety population

Table †. Summary of adverse events Related to the study drug by System Organ Class and Preferred term – Safety population

Table †. Summary of adverse events Related to the protocol procedure by System Organ Class and Preferred term – Safety population

Table †. Summary of adverse events Related to the study by System Organ Class and Preferred term – Safety population

Table †. Summary of adverse events by severity by System Organ Class and by Preferred term – Safety population

Table †. Summary of adverse events Related to the study drug by severity by System Organ Class and by Preferred term – Safety population

Table †. Summary of adverse events Related to the protocol procedure by severity by System Organ Class and by Preferred term – Safety population

Table †. Summary of adverse events Related to the study by severity by System Organ Class and by Preferred term – Safety population

Table †. Summary of serious adverse events by System Organ Class and by Preferred term – Safety population

Table †. Summary of adverse events leading to discontinuation by System Organ Class and by Preferred term – Safety population

Table †. Summary of AESIs by System Organ Class and by Preferred term – Safety population

9.3.4. Vital Signs, Physical Findings

Table. Physical examination – Safety population

		Screening	DAY 19/ET
Physical examination	N		
	Normal		
	Abnormal and Not clinically significant		
	Abnormal and Clinically significant		

Table. Shift table of Physical examination – Safety population

	Day 19/ET		
Screening	Normal	Abnormal and not clinically significant	Abnormal and clinically signficant
Normal			
Abnormal and not clinically significant			
Abnormal and clinically signficant			

Table. Vital signs – Safety population

		Screening	Baseline	D19/ET	Change from baseline
Systolic blood pressure (mmHg)	N				
	Mean				
	SD				
	Median				
	(Min,Max)				
Diastolic blood pressure (mmHg)	…				
Pulse rate (bpm)	…				
Vital signs evaluation	N				
	Normal				
	Abnormal and Not clinically significant				
	Abnormal and Clinically significant				

Table. Shift table of vital signs evaluation – Safety population

	Day 19/ET		
Baseline	Normal	Abnormal and not clinically significant	Abnormal and clinically signficant
Normal			
Abnormal and not clinically significant			
Abnormal and clinically signficant			

Table. Ophthalmic examination – Safety population

Table. Shift table of ophthalmic examination – Safety population

Table. 12-lead ECG – Safety population

		Screening	DAY 19/ET
ECG	N		
	Normal		
	Abnormal and Not clinically significant		
	Abnormal and Clinically significant		
QTC (ms)	N		
	Mean		
	SD		
	Median		
	(Min,Max)		
QTC > 500 ms	N		
	No		
	Yes		
Change in QTC (ms)	N		
	Mean …		
Change > 60 ms	N No Yes		

Table. Shift table for 12-lead ECG – Safety population

CCI

[redacted]

9.3.5. Laboratory Parameters

Table. Haematology – Summary statistics – Safety population

		Screening	D19/ET	Change from Screening
White blood cells (Giga/L)	N			
	Mean			
	SD			
	Median			
	(Min,Max)			
…				

Table. Haematology – Distribution by normality level – Safety population

Table. Haematology – Shift table – Safety population

Table. Blood chemistry – Summary statistics – Safety population

Table. Blood chemistry – Distribution by normality level – Safety population

Table. Blood chemistry – Shift table – Safety population

Table. Virology at screening – Safety population

Table. Urinalysis *– Summary statistics – Safety population

*: only for data in quantitative manner (like pH for exemple)

Table. Urinalysis – Distribution by normality level – Safety population

Table. Urinalysis – Shift table – Safety population

9.4. Graphs

Graph. Mean TSS versus time per treatment -PP population

Graph. Median TSS percent change from day 1 by visit and by treatment -PP population

Graph. Mean Erythema versus time per treatment -PP population

Graph. Mean Erythema change from day 1 by visit and by treatment -PP population

Graph. Mean Scaling versus time per treatment -PP population

Graph. Mean Scaling change from day 1 by visit and by treatment -PP population

Graph. Mean Induration versus time per treatment -PP population

Graph. Mean Induration change from day 1 by visit and by treatment -PP population

Graph. Success by visit -PP population

CCI [redacted]

Graph. Mean Irritation versus time per treatment -Safety population

Graph. Mean Stinging/burning versus time per treatment -Safety population

Graph. Mean Pruritus versus time per treatment -Safety population

CCI [redacted]

Some other descriptive graphics could be performed upon request.

CCI [redacted]

CCI

CCI [redacted]