Clinical trial results:
A Phase 2a Study to Evaluate Safety, Tolerability, and Efficacy of PRCL-02 in Patients with Moderate to Severe Chronic Plaque Psoriasis

Summary

EudraCT number	2018-001216-29
Trial protocol	SK
Global end of trial date	08 July 2019

Results information

Result version number	v1 (current)
This version publication date	03 October 2021
First version publication date	03 October 2021

Trial information

Trial identification

Sponsor protocol code	PRCL-PoC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03614078
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PRCL Research Inc
Sponsor organisation address	1255 Robert-Bourassa #1610, Montreal, Canada, H3B 3X3
Public contact	Jurij Khrustalev, SanaClis TOV, +38 067504 36 00, jurij.khrustalev@sanaclis.eu
Scientific contact	Jurij Khrustalev, SanaClis TOV, +38 067504 36 00, jurij.khrustalev@sanaclis.eu

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	08 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2019
Global end of trial reached?	Yes
Global end of trial date	08 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of PRCL-02 after 12 weeks of once-daily oral dosing in subjects with moderate to severe chronic plaque psoriasis.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 September 2018
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	Slovakia: 36
Country: Number of subjects enrolled	Canada: 22
Country: Number of subjects enrolled	Ukraine: 34
Worldwide total number of subjects	92
EEA total number of subjects	36

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)	88
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 92 subjects who were randomly assigned to study treatment, 77 completed the study, and 15 did not complete the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	PRCL-02 25 milligrams (mg)

Arm description:

Loading dose of 150 mg followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks

Arm type	Experimental
Investigational medicinal product name	PRCL-02
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks

Arm title	PRCL-02 50 mg

Arm description:

Loading dose of 300 mg followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks

Arm type	Experimental
Investigational medicinal product name	PRCL-02
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks

Arm title	Placebo

Arm description:

Loading dose followed by a once daily maintenance dose at matching treatment levels, commencing on Day 2 and continuing for 12 weeks

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Loading dose followed by a once daily maintenance dose at matching treatment levels, commencing on Day 2 and continuing for 12 weeks

Number of subjects in period 1	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg	Placebo
Started	31	30	31
Completed	28	23	26
Not completed	3	7	5
Consent withdrawn by subject	2	2	3
High neutrophils	-	-	2
Participant did not return for visit	-	1	-
Adverse event, non-fatal	-	2	-
Dizziness and rash	-	1	-
Exacerbation of Psoriasis	-	1	-
Participant did not meet elgibility	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	PRCL-02 25 milligrams (mg)
Reporting group description:	
Loading dose of 150 mg followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks	
Reporting group title	PRCL-02 50 mg
Reporting group description:	
Loading dose of 300 mg followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Loading dose followed by a once daily maintenance dose at matching treatment levels, commencing on Day 2 and continuing for 12 weeks	

Reporting group values	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg	Placebo
Number of subjects	31	30	31
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	30	29	29
From 65-84 years	1	1	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	14	11	8
Male	17	19	23
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	31	30	31
Unknown or Not Reported	0	0	0
Race Units: Subjects			
Asian	1	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	27	29	31
More than one race	0	0	0
Unknown or Not Reported	2	0	0
American Indian or Alaska Native	1	0	0

Reporting group values	Total		
Number of subjects	92		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	88		
From 65-84 years	4		
85 years and over	0		
Gender categorical Units: Subjects			
Female	33		
Male	59		
Ethnicity Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	92		
Unknown or Not Reported	0		
Race Units: Subjects			
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	87		
More than one race	0		
Unknown or Not Reported	2		
American Indian or Alaska Native	1		

End points

End points reporting groups

Reporting group title	PRCL-02 25 milligrams (mg)
Reporting group description:	
Loading dose of 150 mg followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks	
Reporting group title	PRCL-02 50 mg
Reporting group description:	
Loading dose of 300 mg followed by a once daily maintenance dose commencing on Day 2 and continuing for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Loading dose followed by a once daily maintenance dose at matching treatment levels, commencing on Day 2 and continuing for 12 weeks	

Primary: Percentage of Subjects Achieving Psoriasis Area and Severity Index ≥75% (PASI 75) Improvement

End point title	Percentage of Subjects Achieving Psoriasis Area and Severity Index ≥75% (PASI 75) Improvement
End point description:	
Number of subjects is shown for each reporting group in lieu of percentage. Following 12 weeks of treatment. The Psoriasis Area and Severity Index (PASI) scores the severity of disease on a scale from 0 to 72 (where a score of 72 indicates extreme disease severity). PASI 75 indicates 75% improvement from baseline to Week 12 in the Psoriasis Area and Severity Index. Intent to treat population included all randomized subjects with moderate to severe chronic plaque psoriasis who took at least 1 dose of double-blind study treatment and at least the Week 1 post-baseline PASI assessment.	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

End point values	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	29	31	
Units: subjects	4	1	0	

Statistical analyses

Statistical analysis title	PRCL-02 25 mg vs placebo
Comparison groups	Placebo v PRCL-02 25 milligrams (mg)

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.053
Method	Fisher exact
Parameter estimate	lower 90% exact unconditional CI
Point estimate	13.3
Confidence interval	
level	90 %
sides	1-sided
lower limit	-3.4

Statistical analysis title	PRCL-02 50 mg vs Placebo
Comparison groups	PRCL-02 50 mg v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.483
Method	Fisher exact
Parameter estimate	Difference (90% lower confidence limit
Point estimate	3.4
Confidence interval	
level	90 %
sides	1-sided
lower limit	-13.6

Secondary: Number of Subjects With Any Treatment Emergent Adverse Event

End point title	Number of Subjects With Any Treatment Emergent Adverse Event

End point description:

End point type	Secondary

End point timeframe:

Baseline up to Week 18

End point values	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	30	31	
Units: Subjects	14	12	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve (AUC0-t)

End point title	Area Under the Concentration Time Curve (AUC0-t)[1]

End point description:

Pharmacokinetic (PK) analysis set included all randomized subjects who took at least 1 dose of double-blind study treatment and provide sufficient data for PK assessments.

End point type	Secondary

End point timeframe:

Pre-dose and 1, 2, 4, 8, 336, 672, 1008, 1344 hours post dose, on Day 84

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK endpoints were analyzed only in PRCL-02 25 mg and 50 mg dose groups.

End point values	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	165000 (± 627)	439000 (± 492)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Drug Concentration (Cmax)

End point title	Maximum Observed Drug Concentration (Cmax)[2]

End point description:

PK analysis set included all randomized subjects who took at least 1 dose of double-blind study treatment and provide sufficient data for PK assessments.

End point type	Secondary

End point timeframe:

Pre-dose and 1, 2, 4, 8, 336, 672, 1008, 1344 hours post dose, on Day 84

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK endpoints were analyzed only in PRCL-02 25 mg and 50 mg dose groups.

End point values	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	984 (± 200)	2220 (± 139)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Drug Concentration (Tmax)

End point title	Time to Reach Maximum Observed Drug Concentration

End point description:

PK analysis set included all randomized subjects who took at least 1 dose of double-blind study treatment and provide sufficient data for PK assessments.

End point type	Secondary

End point timeframe:

Pre-dose and 1, 2, 4, 8, 336, 672, 1008, 1344 hours post dose, on Day 84

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK endpoints were analyzed only in PRCL-02 25 mg and 50 mg dose groups.

End point values	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: Hours				
median (full range (min-max))	2.00 (0 to 8.12)	4.00 (0 to 358)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 20 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	PRCL-02 25 milligrams (mg)
Reporting group description: Loading dose of 150 mg followed by a once-daily maintenance dose commencing on Day 2 and continuing for 12 weeks.	
Reporting group title	PRCL-02 50 mg
Reporting group description: Loading dose followed by a once-daily maintenance dose commencing on Day 2 and continuing for 12 weeks.	
Reporting group title	Placebo
Reporting group description: Loading dose followed by a once-daily maintenance dose at matching treatment levels, commencing on Day 2 and continuing for 12 weeks.	

Serious adverse events	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	0 / 31 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Infections and infestations			
Measles			
subjects affected / exposed	1 / 31 (3.23%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	PRCL-02 25 milligrams (mg)	PRCL-02 50 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 31 (9.68%)	3 / 30 (10.00%)	4 / 31 (12.90%)
Nervous system disorders			

Dizziness			
subjects affected / exposed	2 / 31 (6.45%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 31 (3.23%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Psoriatric Arthritis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Recurrent Psoriatric Arthritis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2018	Amendment 1 -To indicate that male patients should avoid donating sperm while participating in this trial and for 4 months after stopping the study treatment. -To indicate that patients must withdraw from the study if they become pregnant. -Follicle Stimulating Hormone is now included in the Clinical Laboratory Tests, as this test may be used for assessment of patient eligibility for the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported