Clinical trial results:
A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Cohort, Dose-Ranging Study Investigating the Effect of EDP1815 in the Treatment of Mild to Moderate Plaque Psoriasis

Summary

EudraCT number	2019-004901-28
Trial protocol	GB PL HU
Global end of trial date	10 November 2021

Results information

Result version number	v1 (current)
This version publication date	11 September 2022
First version publication date	11 September 2022

Trial information

Trial identification

Sponsor protocol code	EDP1815-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 19576

Notes:

Sponsors

Sponsor organisation name	Evelo Biosciences Inc.
Sponsor organisation address	620 Memorial Drive, Suite 500, Cambridge, United States, MA 02139
Public contact	Stuart Abel, Evelo Biosciences Inc., +44 (0)779 626 8347, clinicaltrials@evelobio.com
Scientific contact	Stuart Abel, Evelo Biosciences Inc., +44 (0)779 626 8347, clinicaltrials@evelobio.com

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	20 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2021
Global end of trial reached?	Yes
Global end of trial date	10 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the safety and efficacy of 3 different doses of EDP1815 for the treatment of psoriasis following daily dosing for 16 weeks.

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki, ICH GCP, and all applicable country and local regulations. A written informed consent was obtained from each participant before entering the study or performing any nonroutine procedure. Each prospective participant or his or her legal guardian was given a full explanation of the study, was allowed to read the approved ICF, and had any questions answered.

Background therapy:

There wasn’t any background therapy. All prior and concomitant medications were listed.

Evidence for comparator:

This was placebo-controlled study.

Actual start date of recruitment	21 September 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 23
Country: Number of subjects enrolled	Poland: 130
Country: Number of subjects enrolled	United Kingdom: 83
Country: Number of subjects enrolled	Hungary: 13
Worldwide total number of subjects	249
EEA total number of subjects	143

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)	235
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who met all of the inclusion and none of the exclusion criteria were enrolled into the study. A total of 249 subjects were randomly assigned in 1:1:1 ratio to one of the 3 parallel cohorts: Cohort 1: 0.8 × 10^11 cells of EDP1815 or placebo; Cohort 2: 3.2 × 10^11 cells of EDP1815 or placebo; Cohort 3: 8.0 × 10^11 cells of EDP1815 or placebo

Pre-assignment

Screening details:

Study comprised a screening period of up to 4 weeks. Participants were allowed into the study if they were between the ages of 18 and 70 years (inclusive) with a documented diagnosis of mild to moderate plaque psoriasis for ≥6 months and agreed to follow contraceptive guidance.

Period 1

Period 1 title	Treatment period - Week 20 (Part A)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This was a double-blind study.
Part A of the study comprised a screening period of up to 4 weeks, a baseline visit, a treatment period of 16 weeks (8 planned study site visits), and a follow-up visit at Week 20 (4 weeks after cessation of dosing).

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: EDP1815 1 Capsule

Arm description:

One capsule of EDP1815

Arm type	Experimental
Investigational medicinal product name	EDP1815 1 capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule EDP1815 self-administered orally once daily. EDP1815 PIC contained 0.8 x 10^11 cells of Prevotella histicola. 56 subjects were treated with the EDP1815 versus 28 subject treated with placebo.

Arm title	Cohort 2: EDP1815 4 Capsules

Arm description:

Four capsules of EDP1815

Arm type	Experimental
Investigational medicinal product name	EDP1815 4 capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

4 capsules EDP1815 self-administered orally once daily. Total daily dose was 3.2 x 10^11 cells of Prevotella histicola. 55 patients were treated with EDP1815 versus 27 were treated with placebo.

Arm title	Cohort 3: EDP1815 10 Capsules

Arm description:	
Ten capsules of EDP1815	
Arm type	Experimental
Investigational medicinal product name	EDP1815 10 capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
10 capsules EDP1815 self-administered orally once daily. Total daily dose was 8.0 x 10^11 cells of Prevotella histicola. 55 patients were treated with EDP1815 versus 28 treated with placebo.	
Arm title	Placebo
Arm description:	
EDP1815 matching placebo administered once daily as 1, 4 or 10 capsules.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
1, 4 or 10 capsules Placebo self-administered orally once daily. Placebo was identical in appearance to EDP1815 but did not contain Prevotella histicola or any other bacteria.	

Number of subjects in period 1	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules
Started	56	55	55
Completed	36	45	41
Not completed	20	10	14
Consent withdrawn by subject	4	3	4
Other	1	1	-
Pregnancy	-	1	-
Adverse event	2	1	-
Treatment failure removal by the investigator	4	2	3
Use of nonpermitted concurrent therapy	-	-	-
Lost to follow-up	1	-	3
Lack of efficacy	8	2	4

Number of subjects in period 1	Placebo
Started	83
Completed	64
Not completed	19
Consent withdrawn by subject	3
Other	-

Pregnancy	-
Adverse event	3
Treatment failure removal by the investigator	6
Use of nonpermitted concurrent therapy	1
Lost to follow-up	3
Lack of efficacy	3

Period 2

Period 2 title	Follow-up period - Week 40 (Part B)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This was double-blind study.
Part B of the study was designed to assess the durability of treatment response and incidence of rebound of psoriasis following cessation of dosing with follow-up to Week 40 (24 weeks after cessation of dosing). Participants who completed Part A of the study without confirmation of treatment failure or rebound were permitted to enter Part B of the study.
No treatment was conducted during part B.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: EDP1815 1 Capsule

Arm description:

One capsule of EDP1815 was administrated in Cohort 1.

Arm type	Experimental
Investigational medicinal product name	EDP1815 1 capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Part A dosage and administration: 1 capsule EDP1815 self-administered orally once daily. EDP1815 PIC contained 0.8 x 10*11 cells of Prevotella histicola.

Arm title	Cohort 2: EDP1815 4 Capsules

Arm description:

Four capsules of EDP1815 were administrated in Cohort 2.

Arm type	Experimental
Investigational medicinal product name	EDP1815 4 capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Part A dosage and administration: 4 capsules EDP1815 self-administered orally once daily. Total daily dose was 3.2 x 10*10 cells of Prevotella histicola.

Arm title	Cohort 3: EDP1815 10 Capsules

Arm description:

Ten capsules of EDP1815 were administrated in Cohort 3.

Arm type	Experimental
Investigational medicinal product name	EDP1815 10 capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Part A dosage and administration: 10 capsules EDP1815 self-administered orally once daily. Total daily dose was 8.0 x 10*10 cells of Prevotella histicola.

Arm title	Placebo

Arm description:

EDP1815 matching placebo administered once daily as 1, 4 or 10 capsules.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Part A dosage and administration: 1, 4 or 10 capsules Placebo self-administered orally once daily. Placebo was identical in appearance to EDP1815 but did not contain Prevotella histicola or any other bacteria.

Number of subjects in period 2[1]	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules
Started	23	31	29
Completed	22	25	25
Not completed	1	6	4
Consent withdrawn by subject	1	3	3
Other	-	1	-
Lost to follow-up	-	2	1

Number of subjects in period 2[1]	Placebo
Started	41
Completed	37
Not completed	4
Consent withdrawn by subject	2
Other	1
Lost to follow-up	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 249 subjects started Treatment period (Part A), 186 subjects completed Part A and 124 subjects entered into Follow up period (Part B).

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: EDP1815 1 Capsule
Reporting group description:	
One capsule of EDP1815	
Reporting group title	Cohort 2: EDP1815 4 Capsules
Reporting group description:	
Four capsules of EDP1815	
Reporting group title	Cohort 3: EDP1815 10 Capsules
Reporting group description:	
Ten capsules of EDP1815	
Reporting group title	Placebo
Reporting group description:	
EDP1815 matching placebo administered once daily as 1, 4 or 10 capsules.	

Reporting group values	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules
Number of subjects	56	55	55
Age categorical			
Units: Subjects			
Adults (18-64 years)	52	53	51
From 65-84 years	4	2	4
Age continuous			
Units: years			
median	44.0	42.0	44.0
full range (min-max)	18 to 69	19 to 67	23 to 70
Gender categorical			
Units: Subjects			
Female	22	24	13
Male	34	31	42

Reporting group values	Placebo	Total	
Number of subjects	83	249	
Age categorical			
Units: Subjects			
Adults (18-64 years)	79	235	
From 65-84 years	4	14	
Age continuous			
Units: years			
median	44.0		
full range (min-max)	19 to 68	-	
Gender categorical			
Units: Subjects			
Female	33	92	
Male	50	157	

Subject analysis sets

Subject analysis set title	mITT set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT set consisted of all participants who were randomized to treatment and who received at least 1 dose of study treatment. Participants who withdrew from the study before the end of Week 4 and were replaced were included in this analysis set. All analyses using the mITT grouped participants according to randomized treatment. The mITT set was the primary population of interest for the efficacy analyses.

Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set consisted of all participants who received any study drug. All analyses using the safety set grouped participants according to treatment received. If
participants received multiple treatments during the study, they were assigned to treatment group in the following manner:
• If a participant received both active EDP1815 and placebo treatments, they were assigned to the active treatment group.
• If a participant received 2 or more different active dose levels, they were assigned to the highest dose they received.
The safety set was used for all safety data presentations.

Reporting group values	mITT set	Safety set	
Number of subjects	249	249	
Age categorical Units: Subjects			
Adults (18-64 years)	237	237	
From 65-84 years	14	14	
Age continuous Units: years			
median	43.0	43.0	
full range (min-max)	18 to 70	18 to 70	
Gender categorical Units: Subjects			
Female	92	92	
Male	157	157	

End points

End points reporting groups

Reporting group title	Cohort 1: EDP1815 1 Capsule
Reporting group description:	
One capsule of EDP1815	
Reporting group title	Cohort 2: EDP1815 4 Capsules
Reporting group description:	
Four capsules of EDP1815	
Reporting group title	Cohort 3: EDP1815 10 Capsules
Reporting group description:	
Ten capsules of EDP1815	
Reporting group title	Placebo
Reporting group description:	
EDP1815 matching placebo administered once daily as 1, 4 or 10 capsules.	
Reporting group title	Cohort 1: EDP1815 1 Capsule
Reporting group description:	
One capsule of EDP1815 was administrated in Cohort 1.	
Reporting group title	Cohort 2: EDP1815 4 Capsules
Reporting group description:	
Four capsules of EDP1815 were administrated in Cohort 2.	
Reporting group title	Cohort 3: EDP1815 10 Capsules
Reporting group description:	
Ten capsules of EDP1815 were administrated in Cohort 3.	
Reporting group title	Placebo
Reporting group description:	
EDP1815 matching placebo administered once daily as 1, 4 or 10 capsules.	
Subject analysis set title	mITT set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The mITT set consisted of all participants who were randomized to treatment and who received at least 1 dose of study treatment. Participants who withdrew from the study before the end of Week 4 and were replaced were included in this analysis set. All analyses using the mITT grouped participants according to randomized treatment. The mITT set was the primary population of interest for the efficacy analyses.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety set consisted of all participants who received any study drug. All analyses using the safety set grouped participants according to treatment received. If participants received multiple treatments during the study, they were assigned to treatment group in the following manner: • If a participant received both active EDP1815 and placebo treatments, they were assigned to the active treatment group. • If a participant received 2 or more different active dose levels, they were assigned to the highest dose they received. The safety set was used for all safety data presentations.	

Primary: Analysis of Percentage Change from Baseline in PASI Score – Bayesian MMRM

End point title	Analysis of Percentage Change from Baseline in PASI Score – Bayesian MMRM
End point description:	
The primary efficacy endpoint was percentage change in PASI score from baseline at Week 16.	
End point type	Primary

End point timeframe:

At week 16

End point values	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	54	54	82
Units: percent				
number (confidence interval 95%)				
Percentage change from baseline (Posterior mean)	-20.37 (-31.65 to -9.47)	-22.73 (-33.08 to -11.88)	-23.49 (-34.18 to -12.12)	-14.39 (-22.66 to -5.52)

Statistical analyses

Statistical analysis title	Statistical Analysis - Cohort 1 vs Placebo

Statistical analysis description:

Performed using a Bayesian Mixed Model for Repeated Measures (MMRM) analysis with parameters for treatment*visit and baseline*visit and baseline BMI. Non-informative priors following a normal distribution with mean of 0 and a SD of 1000 were used for all parameters. After a burn-in of 10,000 samples, 100,000 MCMC samples were generated with a thin of 20 to leave 5000 retained samples for the analysis.

Comparison groups	Cohort 1: EDP1815 1 Capsule v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.799 [2]
Method	Bayesian MMRM
Parameter estimate	Posterior mean
Point estimate	-5.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.28
upper limit	7.12

Notes:

[1] - All post-baseline visits were included in the model but only the Week 16 results are shown here. All four treatment groups were included into the same model and pairwise treatment differences between each active treatment group and the pooled placebo group were estimated using the posterior mean difference and 95% credible interval.

[2] - Posterior probability of superiority over placebo.

Statistical analysis title	Statistical Analysis - Cohort 2 vs Placebo

Statistical analysis description:

Performed using a Bayesian Mixed Model for Repeated Measures (MMRM) analysis with parameters for treatment*visit and baseline*visit and baseline BMI. Non-informative priors following a normal distribution with mean of 0 and a SD of 1000 were used for all parameters. After a burn-in of 10,000 samples, 100,000 MCMC samples were generated with a thin of 20 to leave 5000 retained samples for the analysis.

Comparison groups	Placebo v Cohort 2: EDP1815 4 Capsules

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.887 [4]
Method	Bayesian MMRM
Parameter estimate	Posterior mean
Point estimate	-8.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.07
upper limit	5.04

Notes:

[3] - All post-baseline visits were included in the model but only the Week 16 results are shown here. All four treatment groups were included into the same model and pairwise treatment differences between each active treatment group and the pooled placebo group were estimated using the posterior mean difference and 95% credible interval.
[4] - Posterior probability of superiority over placebo.

Statistical analysis title	Statistical Analysis - Cohort 3 vs Placebo

Statistical analysis description:

Performed using a Bayesian Mixed Model for Repeated Measures (MMRM) analysis with parameters for treatment*visit and baseline*visit and baseline BMI. Non-informative priors following a normal distribution with mean of 0 and a SD of 1000 were used for all parameters. After a burn-in of 10,000 samples, 100,000 MCMC samples were generated with a thin of 20 to leave 5000 retained samples for the analysis.

Comparison groups	Placebo v Cohort 3: EDP1815 10 Capsules
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.897 [6]
Method	Bayesian MMRM
Parameter estimate	Posterior mean
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.22
upper limit	4.65

Notes:

[5] - All post-baseline visits were included in the model but only the Week 16 results are shown here. All four treatment groups were included into the same model and pairwise treatment differences between each active treatment group and the pooled placebo group were estimated using the posterior mean difference and 95% credible interval.
[6] - Posterior probability of superiority over placebo.

Secondary: Summary and Analysis of PASI-50 Response - GLMM

End point title	Summary and Analysis of PASI-50 Response - GLMM

End point description:

Analysis of treatment with EDP1815 (1 capsule and 4 capsules) in the proportion of participants achieving PASI-50 at Week 16 compared to placebo.

End point type	Secondary

End point timeframe:

At week 16

End point values	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	47	40	66
Units: percent				
number (confidence interval 95%)				
Responders (%)	29.7 (15.9 to 47.0)	31.9 (19.1 to 47.1)	25.0 (12.7 to 41.2)	12.1 (5.4 to 22.5)

Statistical analyses

Statistical analysis title	Statistical Analysis - Cohort 1 vs Placebo

Statistical analysis description:

Generalised linear mixed model (GLMM) with a logit link function. Treatment, visit, baseline PASI score, and baseline BMI terms included in the model as fixed effects together with treatment visit and baseline PASI score visit interactions. An unstructured covariance structure was used. All post-baseline visits were included in the model but only the Week 16 results are shown here.

Comparison groups	Cohort 1: EDP1815 1 Capsule v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.048
Method	Generalised linear mixed model (GLMM)
Parameter estimate	Odds ratio (OR)
Point estimate	2.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	6.94

Notes:

[7] - All four treatment groups were included into the same model and pairwise odds ratios for each active treatment group compared to placebo were estimated with 95% confidence interval.

Statistical analysis title	Statistical Analysis - Cohort 2 vs Placebo

Statistical analysis description:

Generalised linear mixed model (GLMM) with a logit link function. Treatment, visit, baseline PASI score, and baseline BMI terms included in the model as fixed effects together with treatment visit and baseline PASI score visit interactions. An unstructured covariance structure was used. All post-baseline visits were included in the model but only the Week 16 results are shown here.

Comparison groups	Placebo v Cohort 2: EDP1815 4 Capsules
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.022
Method	Generalised linear mixed model (GLMM)
Parameter estimate	Odds ratio (OR)
Point estimate	2.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	7.37

Notes:

[8] - All four treatment groups were included into the same model and pairwise odds ratios for each active treatment group compared to placebo were estimated with 95% confidence interval.

Statistical analysis title	Statistical Analysis - Cohort 3 vs Placebo

Statistical analysis description:

Generalised linear mixed model (GLMM) with a logit link function. Treatment, visit, baseline PASI score, and baseline BMI terms included in the model as fixed effects together with treatment visit and baseline PASI score visit interactions. An unstructured covariance structure was used. All post-baseline visits were included in the model but only the Week 16 results are shown here.

Comparison groups	Placebo v Cohort 3: EDP1815 10 Capsules
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.285
Method	Generalised linear mixed model (GLMM)
Parameter estimate	Odds ratio (OR)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	4.7

Notes:

[9] - All four treatment groups were included into the same model and pairwise odds ratios for each active treatment group compared to placebo were estimated with 95% confidence interval.

Secondary: Cumulative Incidence of Partial Relapse in the Week 16 Responders Population

End point title	Cumulative Incidence of Partial Relapse in the Week 16 Responders Population

End point description:

Cumulative Incidence of Partial Relapse was measured at week 20, 24, 28, 40. Partial relapse was the event of interest and was defined, after the Week 16 visit, as loss of PASI-50 response after cessation of study treatment or the participant began a new treatment for psoriasis.

End point type	Secondary

End point timeframe:

At week 20, 24, 28, 40

End point values	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	16	10	9
Units: percent				
number (confidence interval 95%)				

Incidence of participants with event – Week 20	16.7 (2.1 to 48.4)	33.3 (11.8 to 61.6)	0 (0 to 30.8)	11.1 (0.3 to 48.2)
Incidence of participants with event – Week 24	33.3 (9.9 to 65.1)	40.0 (16.3 to 67.7)	10.0 (0.3 to 44.5)	11.1 (0.3 to 48.2)
Incidence of participants with event – Week 28	33.3 (9.9 to 65.1)	53.3 (26.6 to 78.7)	20.0 (2.5 to 55.6)	33.3 (7.5 to 70.1)
Incidence of participants with event – Week 40	33.3 (9.9 to 65.1)	53.3 (26.6 to 78.7)	20.0 (2.5 to 55.6)	44.4 (13.7 to 78.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence of Relapse in the Week 16 Responders Population

End point title	Cumulative Incidence of Relapse in the Week 16 Responders Population

End point description:

Cumulative Incidence of Relapse was measured at week 20, 24, 28, 40. Relapse was the event of interest and was defined, after the Week 16 visit, as an increase in PASI score to the baseline value or greater or the participant began a new treatment for psoriasis.

End point type	Secondary

End point timeframe:

At week 20, 24, 28 and 40

End point values	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	16	10	9
Units: percent				
number (confidence interval 95%)				
Incidence of participants with event – Week 20	0 (0 to 26.5)	0 (0 to 21.8)	0 (0 to 30.8)	0 (0 to 33.6)
Incidence of participants with event – Week 24	0 (0 to 26.5)	6.7 (0.2 to 31.9)	10.0 (0.3 to 44.5)	0 (0 to 33.6)
Incidence of participants with event – Week 28	0 (0 to 26.5)	13.3 (1.7 to 40.5)	10.0 (0.3 to 44.5)	0 (0 to 33.6)
Incidence of participants with event – Week 40	8.3 (0.2 to 38.5)	13.3 (1.7 to 40.5)	10.0 (0.3 to 44.5)	0 (0 to 33.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Incidence of Rebound in the mITT Population

End point title	Cumulative Incidence of Rebound in the mITT Population

End point description:

Cumulative Incidence of Rebound has been measured on or before Week 20/Follow-up, at week 24 and

28 in the mITT Population. Rebound was the event of interest and was defined as an increase in PASI score to 125% of baseline value or above or onset of new pustular/erythrodermic psoriasis on or before the Week 28 visit.

End point type	Secondary

End point timeframe:

On or before Week 20, at week 24 and 28

End point values	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	31	29	41
Units: percent				
number (confidence interval 95%)				
Incidence of participants with event – Week 20	8.1 (1.7 to 21.9)	4.7 (0.6 to 15.8)	2.2 (0.1 to 11.8)	6.3 (1.7 to 15.2)
Incidence of participants with event – Week 24	13.5 (4.5 to 28.8)	4.7 (0.6 to 15.8)	2.2 (0.1 to 11.8)	7.8 (2.6 to 17.3)
Incidence of participants with event – Week 28	16.2 (6.2 to 32.0)	7.0 (1.5 to 19.1)	2.2 (0.1 to 11.8)	10.9 (4.5 to 21.2)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the whole study period.	
Adverse event reporting additional description:	
TEAE is defined as an adverse event with onset date and time on or after the date and time of the first dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Cohort 1: EDP1815 1 Capsule
Reporting group description:	
One capsule of EDP1815 was administrated in Cohort 1.	
Reporting group title	Cohort 2: EDP1815 4 Capsules
Reporting group description:	
Four capsules of EDP1815 were administrated in Cohort 2.	
Reporting group title	Cohort 3: EDP1815 10 Capsules
Reporting group description:	
Ten capsules of EDP1815 were administrated in Cohort 3.	
Reporting group title	Placebo
Reporting group description:	
EDP1815 matching placebo administered once daily as 1, 4 or 10 capsules.	

Serious adverse events	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	1 / 55 (1.82%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	0 / 55 (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

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 83 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1: EDP1815 1 Capsule	Cohort 2: EDP1815 4 Capsules	Cohort 3: EDP1815 10 Capsules
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 56 (37.50%)	21 / 55 (38.18%)	25 / 55 (45.45%)
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	2 / 56 (3.57%)	1 / 55 (1.82%)	5 / 55 (9.09%)
occurrences (all)	2	1	5
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 56 (12.50%)	3 / 55 (5.45%)	5 / 55 (9.09%)
occurrences (all)	20	5	8
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 56 (3.57%)	1 / 55 (1.82%)	4 / 55 (7.27%)
occurrences (all)	2	1	6
Abdominal pain			
subjects affected / exposed	1 / 56 (1.79%)	3 / 55 (5.45%)	2 / 55 (3.64%)
occurrences (all)	2	4	2
Dyspepsia			

subjects affected / exposed	0 / 56 (0.00%)	4 / 55 (7.27%)	2 / 55 (3.64%)
occurrences (all)	0	7	2
Flatulence			
subjects affected / exposed	0 / 56 (0.00%)	3 / 55 (5.45%)	1 / 55 (1.82%)
occurrences (all)	0	3	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	3
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 56 (3.57%)	3 / 55 (5.45%)	1 / 55 (1.82%)
occurrences (all)	2	3	1
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 56 (3.57%)	3 / 55 (5.45%)	1 / 55 (1.82%)
occurrences (all)	2	3	1
Upper respiratory tract infection			
subjects affected / exposed	4 / 56 (7.14%)	0 / 55 (0.00%)	1 / 55 (1.82%)
occurrences (all)	5	0	1

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 83 (31.33%)		
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	3 / 83 (3.61%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 83 (10.84%)		
occurrences (all)	15		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 83 (6.02%)		
occurrences (all)	6		
Abdominal pain			

subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	2 / 83 (2.41%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 83 (4.82%)		
occurrences (all)	4		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2020	The first participant was enrolled under Protocol Amendment 3, dated 26 May 2020.
17 November 2020	The following is a summary of the major changes implemented with Protocol Amendment 4, dated 17 Nov 2020: • Local Amendment 3.1 (Hungary specific) was included. • Post-treatment follow-up was extended for a maximum of up to 6 months. • One secondary and 1 exploratory objective were added. • Definitions of response, relapse, and rebound based on PASI score were added. • Statistical analyses, endpoints, and supportive analyses were updated. • Skin plaque biopsy description was added. • Instructions for participants on withholding emollients or moisturizers were added. • 1,25-dihydroxy vitamin D3 and its analogs were removed from exclusion criterion #8. • Exclusion criterion #21 was clarified. • Pre- and probiotic use was clarified. • Allowed and prohibited vaccines were updated. • Eligibility confirmation at baseline/Visit 2 was clarified to be based on screening laboratory results. • The maximum allowed dose (overdose management) was clarified. • Clarification on data blinding was added. • "On the morning of the visit" ECGs and vital signs were changed to "on the day of the visit" in footnotes of the SoA. • The ideal size of lesion area for digital photography was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported