



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of ESK-001 in Patients with Moderate to Severe Plaque Psoriasis

Summary

EudraCT number	2022-002633-34
Trial protocol	CZ PL
Global end of trial date	25 July 2023

Results information

Result version number	v1 (current)
This version publication date	16 November 2024
First version publication date	16 November 2024

Trial information

Trial identification

Sponsor protocol code	ESK-001-006
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05600036
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number : 159386

Notes:

Sponsors

Sponsor organisation name	Alumis Inc.
Sponsor organisation address	280 East Grand Avenue, South San Francisco, United States, 94080
Public contact	Clinical Trial Information Desk , Alumis Inc., 1 (650) 231-6625, info@alumis.com
Scientific contact	Clinical Trial Information Desk , Alumis Inc., 1 (650) 231-6625, info@alumis.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 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 June 2023
Global end of trial reached?	Yes
Global end of trial date	25 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the Psoriasis Area and Severity Index (PASI-75) between doses of ESK-001 and placebo after 12 weeks of treatment.

An independent Safety Monitoring Committee was utilized for monitoring the safety data in this study.

Protection of trial subjects:

This study was conducted in compliance with the Institutional Review Board (IRB) regulations stated in Title 21 of the United States Code of Federal Regulations (CFR), Part 56, Good Clinical Practice (GCP) regulations and guidelines, and all applicable local regulations. A waiver of the IRB requirements under 21 CFR Part 56 was granted for all foreign investigational studies conducted under IND 159386.

The clinical study protocol, the Investigator's Brochure, a sample informed consent form (ICF), and other study-related documents were reviewed and approved by the local or central IRBs of all study sites.

This study was conducted with the highest respect for the individual patients and in accordance with the Protocol, the ethical principles that have their origin in the Declaration of Helsinki, the informed consent regulations stated in Title 21 CFR, Part 50, International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) GCP (E6) §4.8, and all applicable local regulations.

This study was conducted in compliance with the informed consent regulations stated in Title 21 CFR, Part 50.

The Investigator explained the study and its objectives as well as potential risks and benefits to patients using the IRB-approved ICF. Each patient or their legal guardian/legally authorized representative signed and dated the ICF before any study-specific procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 157
Country: Number of subjects enrolled	Canada: 44
Country: Number of subjects enrolled	Czechia: 27
Worldwide total number of subjects	228
EEA total number of subjects	27

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)	206
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total, 312 patients were screened for study participation. Of the total 312 patients screened, 84 (26.9%) failed Screening primarily due to eligibility criteria not being met, and 2 patients were rescreened. Of the 228 patients randomized, a total of 227 patients (99.6%) were dosed and 209 patients (91.7%) completed treatment.

Pre-assignment

Screening details:

Screening was done per protocol inclusion/exclusion criteria.

Period 1

Period 1 title	Overall period (overall period)
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:

For this trial, study patients, Investigators, study center personnel, the Sponsor, or representatives on the clinical study team were all blinded to the treatment assignments. ESK-001 tablets and placebo-to-match ESK-001 tablets were matched for shape, size, and color.

Arms

Are arms mutually exclusive?	No
Arm title	10 mg QD

Arm description:

ESK-001 10 mg once a day.

Arm type	Experimental
Investigational medicinal product name	ESK-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg taken orally once a day.

Arm title	20 mg QD
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Arm description:

ESK-001 20 mg once a day.

Arm type	Experimental
Investigational medicinal product name	ESK-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg taken orally once a day.

Arm title	40 mg QD
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Arm description:

ESK-001 40 mg once a day.

Arm type	Experimental
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Investigational medicinal product name	ESK-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 40 mg taken orally once a day.	
Arm title	20 mg BID
Arm description: ESK-001 20 mg twice a day.	
Arm type	Experimental
Investigational medicinal product name	ESK-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 20 mg taken orally twice a day.	
Arm title	40 mg BID
Arm description: ESK-001 40 mg twice a day.	
Arm type	Experimental
Investigational medicinal product name	ESK-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 40 mg taken orally twice a day.	
Arm title	Placebo
Arm description: Placebo tablets for oral administration.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Placebo tablets for oral administration.	
Arm title	All active
Arm description: All active including QD (10, 20 and 40 mg) plus BID (20 and 40 mg)	
Arm type	Experimental
Investigational medicinal product name	ESK-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg QD or;
20 mg QD or;
40 mg QD or;
20 mg BID or;
40 mg BID

Number of subjects in period 1	10 mg QD	20 mg QD	40 mg QD
Started	36	36	39
Completed	36	30	33
Not completed	0	6	6
Consent withdrawn by subject	-	1	2
Adverse event, non-fatal	-	2	1
Other reasons	-	1	-
Lost to follow-up	-	2	1
Protocol deviation	-	-	2

Number of subjects in period 1	20 mg BID	40 mg BID	Placebo
Started	40	39	38
Completed	37	35	33
Not completed	3	4	5
Consent withdrawn by subject	-	3	5
Adverse event, non-fatal	-	1	-
Other reasons	2	-	-
Lost to follow-up	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	All active
Started	190
Completed	171
Not completed	19
Consent withdrawn by subject	6
Adverse event, non-fatal	4
Other reasons	3
Lost to follow-up	4
Protocol deviation	2

Baseline characteristics

Reporting groups

Reporting group title	10 mg QD
Reporting group description: ESK-001 10 mg once a day.	
Reporting group title	20 mg QD
Reporting group description: ESK-001 20 mg once a day.	
Reporting group title	40 mg QD
Reporting group description: ESK-001 40 mg once a day.	
Reporting group title	20 mg BID
Reporting group description: ESK-001 20 mg twice a day.	
Reporting group title	40 mg BID
Reporting group description: ESK-001 40 mg twice a day.	
Reporting group title	Placebo
Reporting group description: Placebo tablets for oral administration.	
Reporting group title	All active
Reporting group description: All active including QD (10, 20 and 40 mg) plus BID (20 and 40 mg)	

Reporting group values	10 mg QD	20 mg QD	40 mg QD
Number of subjects	36	36	39
Age categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
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)	33	33	37
From 65-84 years	3	3	2
85 years and over	0	0	0
Age continuous			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: years			
median	49.0	42.0	49.0
inter-quartile range (Q1-Q3)	40.0 to 61.0	37.0 to 49.0	44.0 to 56.0

Gender categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: Subjects			
Female	12	12	13
Male	24	24	26

Reporting group values	20 mg BID	40 mg BID	Placebo
Number of subjects	40	39	38
Age categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
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)	35	33	35
From 65-84 years	5	6	3
85 years and over	0	0	0
Age continuous			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: years			
median	49.5	45.0	50.5
inter-quartile range (Q1-Q3)	38.5 to 58.0	36.0 to 61.0	42.0 to 59.0
Gender categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: Subjects			
Female	17	13	7
Male	23	26	31

Reporting group values	All active	Total	
Number of subjects	190	228	
Age categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	171	206	
From 65-84 years	19	22	
85 years and over	0	0	

Age continuous			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: years			
median	47.0		
inter-quartile range (Q1-Q3)	38.0 to 57.0	-	
Gender categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: Subjects			
Female	67	74	
Male	123	154	

Subject analysis sets

Subject analysis set title	Intent-To-Treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients, regardless of whether they received study drug, with analyses conducted according to the assigned treatment.	
Subject analysis set title	Modified Intent-To-Treat
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized patients who received at least 1 dose of study drug, with analyses conducted according to the assigned treatment. This is the analysis population used for the primary efficacy analysis at Week 12.	
Subject analysis set title	Safety Analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients who received at least 1 dose of study drug with analyses conducted by actual treatment received.	

Reporting group values	Intent-To-Treat (ITT)	Modified Intent-To-Treat	Safety Analysis set
Number of subjects	228	227	227
Age categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
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)	206	205	205
From 65-84 years	22	22	22
85 years and over	0	0	0
Age continuous			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: years			
median	48		

inter-quartile range (Q1-Q3)	39 to 58		
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Gender categorical			
The reporting group includes a total of 228 Intent-to-treat participants. 38 participants received Placebo whereas 190 participants were assigned to active treatment at the dose levels described.			
Units: Subjects			
Female	74		
Male	154		

End points

End points reporting groups

Reporting group title	10 mg QD
Reporting group description: ESK-001 10 mg once a day.	
Reporting group title	20 mg QD
Reporting group description: ESK-001 20 mg once a day.	
Reporting group title	40 mg QD
Reporting group description: ESK-001 40 mg once a day.	
Reporting group title	20 mg BID
Reporting group description: ESK-001 20 mg twice a day.	
Reporting group title	40 mg BID
Reporting group description: ESK-001 40 mg twice a day.	
Reporting group title	Placebo
Reporting group description: Placebo tablets for oral administration.	
Reporting group title	All active
Reporting group description: All active including QD (10, 20 and 40 mg) plus BID (20 and 40 mg)	
Subject analysis set title	Intent-To-Treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized patients, regardless of whether they received study drug, with analyses conducted according to the assigned treatment.	
Subject analysis set title	Modified Intent-To-Treat
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All randomized patients who received at least 1 dose of study drug, with analyses conducted according to the assigned treatment. This is the analysis population used for the primary efficacy analysis at Week 12.	
Subject analysis set title	Safety Analysis set
Subject analysis set type	Safety analysis
Subject analysis set description: All randomized patients who received at least 1 dose of study drug with analyses conducted by actual treatment received.	

Primary: Proportion of patients with moderate to severe psoriasis achieving $\geq 75\%$ reduction in PASI score at 12 weeks.

End point title	Proportion of patients with moderate to severe psoriasis achieving $\geq 75\%$ reduction in PASI score at 12 weeks.
End point description: Efficacy endpoint analysis was done on the Modified Intent-to-Treat subset. Disease activity was assessed using Psoriasis Area and Severity Index (PASI), a grading system that derives a score for the severity of psoriatic lesions. The primary endpoint in this study was the proportion of patients achieving $\geq 75\%$ reduction in PASI (PASI-75) at Week 12. Data is presented here as the count of responders meeting the primary efficacy endpoint. The p-value is for comparison of the proportion of responders (Count of Responders/Number of participants) in each active group vs placebo using the CMH test adjusted for stratification factors.	
End point type	Primary

End point timeframe:

At week 12

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	39	39
Units: Participants	7	12	22	22

End point values	40 mg BID	Placebo	All active	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	38	189	
Units: Participants	25	0	88	

Statistical analyses

Statistical analysis title	ESK-001 10mg QD vs Placebo
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Statistical analysis description:

The p-value was comparing the proportion of responders in each active group vs placebo using the CMH test adjusted for stratification factors.

Comparison groups	10 mg QD v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0025
Method	Cochran-Mantel-Haenszel

Statistical analysis title	ESK-001 20mg QD vs Placebo
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Statistical analysis description:

The p-value was comparing the proportion of responders in each active group vs placebo using the CMH test adjusted for stratification factors.

Comparison groups	20 mg QD v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	ESK-001 40mg QD vs Placebo
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Statistical analysis description:

The p-value was comparing the proportion of responders in each active group vs placebo using the CMH test adjusted for stratification factors.

Comparison groups	Placebo v 40 mg QD
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	ESK-001 20mg BID vs Placebo
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Statistical analysis description:

The p-value was comparing the proportion of responders in each active group vs placebo using the CMH test adjusted for stratification factors.

Comparison groups	20 mg BID v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	ESK-001 40mg BID vs Placebo
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Statistical analysis description:

The p-value was comparing the proportion of responders in each active group vs placebo using the CMH test adjusted for stratification factors.

Comparison groups	40 mg BID v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	All active vs Placebo
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Statistical analysis description:

The p-value was comparing the proportion of responders in each active group vs placebo using the CMH test adjusted for stratification factors.

Comparison groups	All active v Placebo
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

Secondary: Incidence of treatment-emergent adverse events (TEAEs)

End point title	Incidence of treatment-emergent adverse events (TEAEs) ^[1]
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End point description:

TEAEs were defined as AEs occurring at any time point from first dose through the end of study (Week 16) for patients who complete the full Treatment Period of 12 weeks. If a patient discontinued study drug early, then the treatment-emergent period was first dose through 4 weeks after last dose.

End point type	Secondary
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End point timeframe:

Week 16 (4 weeks after last dose at week 12) or 4 weeks after early discontinuation.

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: Statistical analyses for all the arms is being reported only for the primary endpoint.

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	39	39
Units: Participants	19	14	19	18

End point values	40 mg BID	Placebo	Safety Analysis set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	39	38	227	
Units: Participants	25	15	110	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of serious adverse events (SAEs)

End point title	Incidence of serious adverse events (SAEs) ^[2]
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End point description:

The data presented here are Treatment-Emergent Adverse Events considered as Serious Adverse Events (any adverse event resulting in death, life-threatening emergency, prolonged hospitalization, or persistent and significant disability, regardless of expectedness and relatedness to the study drug or study procedures). The safety analysis dataset was used for this endpoint.

End point type	Secondary
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End point timeframe:

Week 16 (4 weeks after last dose at week 12) or 4 weeks after early discontinuation.

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: Statistical analyses for all the arms is being reported only for the primary endpoint.

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	39	39
Units: Participants	1	0	1	3

End point values	40 mg BID	Placebo	Safety Analysis set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	39	28	227	
Units: Participants	0	0	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients achieving an sPGA score of "0" ("cleared") or "1" ("minimal") after 12 weeks of ESK-001 treatment compared with placebo

End point title	Proportion of patients achieving an sPGA score of "0" ("cleared") or "1" ("minimal") after 12 weeks of ESK-001 treatment compared with placebo ^[3]
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End point description:

The number of patients that achieved an sPGA response (defined as a score of 0 ["cleared"] or 1 ["minimal"], sPGA-0/1) at week 12.

End point type	Secondary
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End point timeframe:

Week 12

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: Statistical analyses for all the arms is being reported only for the primary endpoint.

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	35	37
Units: Participants	6	14	21	19

End point values	40 mg BID	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Participants	23	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients achieving PASI-90 after 12 weeks of ESK-001 treatment compared with placebo

End point title	Proportion of patients achieving PASI-90 after 12 weeks of ESK-001 treatment compared with placebo ^[4]
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End point description:

This secondary endpoint measures the proportion of patients achieving $\geq 90\%$ reduction in PASI (PASI-90) at Week 12. Data is presented here as the count of responders meeting this secondary endpoint.

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[4] - 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: Statistical analyses for all the arms is being reported only for the primary endpoint.

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	39	39
Units: Participants	0	4	10	10

End point values	40 mg BID	Placebo	Modified Intent-To-Treat	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	39	38	227	
Units: Participants	15	0	39	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients achieving PASI-100 after 12 weeks of ESK-001 treatment compared with placebo

End point title	Proportion of patients achieving PASI-100 after 12 weeks of ESK-001 treatment compared with placebo ^[5]
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End point description:

This secondary endpoint measures the proportion of patients achieving 100% reduction in PASI (PASI-100) at Week 12. Data is presented here as the count of responders meeting this secondary endpoint.

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[5] - 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: Statistical analyses for all the arms is being reported only for the primary endpoint.

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	39	39
Units: Participants	0	0	3	4

End point values	40 mg BID	Placebo	Modified Intent-To-Treat	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	39	38	227	
Units: Participants	6	0	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in %BSA after 12 weeks of ESK-001 treatment compared with placebo.

End point title	Change from baseline in %BSA after 12 weeks of ESK-001 treatment compared with placebo. ^[6]
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End point description:

This secondary outcome reports the change in percent Body Surface Area (BSA) from baseline after 12 weeks of treatment. BSA is measure used to assess the severity of Psoriasis. Involvement of <3% BSA is considered mild, 3%-10% BSA is considered moderate and >10% of BSA is considered severe psoriasis.

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[6] - 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: Statistical analyses for all the arms is being reported only for the primary endpoint.

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	35	37
Units: Mean change from baseline				
arithmetic mean (standard deviation)	-6.86 (± 7.791)	-7.49 (± 8.082)	-14.63 (± 14.244)	-14.05 (± 12.895)

End point values	40 mg BID	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Mean change from baseline				
arithmetic mean (standard deviation)	-14.06 (± 12.102)	-3.24 (± 6.849)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in DLQI at Week 12 in ESK-001 compared with placebo

End point title	Change from baseline in DLQI at Week 12 in ESK-001 compared with placebo ^[7]
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End point description:

This secondary outcome reports the mean change in Dermatology Life Quality Index (DLQI) score after 12 weeks of treatment.

End point type	Secondary
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End point timeframe:

Week 12

Notes:

[7] - 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: Statistical analyses for all the arms is being reported only for the primary endpoint.

End point values	10 mg QD	20 mg QD	40 mg QD	20 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	34	33	37
Units: Mean change in DLQI score from baseline				
arithmetic mean (standard deviation)	-3.91 (± 5.878)	-4.97 (± 6.255)	-7.21 (± 7.066)	-7.24 (± 6.878)

End point values	40 mg BID	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	34		
Units: Mean change in DLQI score from baseline				
arithmetic mean (standard deviation)	-8.39 (± 6.538)	-0.68 (± 6.049)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Event data was collected from Screening through end of study (Week 16)

Adverse event reporting additional description:

The data presented here are Treatment-Emergent Serious Adverse Events (SAE's).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	10 mg QD
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Reporting group description:

ESK-001 10 mg once a day.

Reporting group title	20 mg QD
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Reporting group description:

ESK-001 20 mg once a day.

Reporting group title	40 mg QD
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Reporting group description:

ESK-001 40 mg once a day.

Reporting group title	20 mg BID
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Reporting group description:

ESK-001 20 mg twice a day.

Reporting group title	40 mg BID
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Reporting group description:

ESK-001 40 mg twice a day.

Reporting group title	Placebo
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Reporting group description:

Placebo tablets for oral administration.

Serious adverse events	10 mg QD	20 mg QD	40 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 39 (2.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Lower Limb Fracture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 39 (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
Tibia Fracture			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery occlusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	20 mg BID	40 mg BID	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 39 (7.69%)	0 / 39 (0.00%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Lower Limb Fracture			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia Fracture			

subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 38 (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
Cardiac disorders			
Coronary artery occlusion			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 38 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 38 (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
Enteritis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 38 (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
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	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	10 mg QD	20 mg QD	40 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 36 (22.22%)	4 / 36 (11.11%)	11 / 39 (28.21%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	4 / 39 (10.26%)
occurrences (all)	0	2	4
Dizziness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Dyspepsia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Dermatitis acneiform			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	2 / 39 (5.13%)
occurrences (all)	2	2	2
Nasopharyngitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
COVID-19			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Diabetes mellitus subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	0 / 36 (0.00%) 0	0 / 39 (0.00%) 0
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Non-serious adverse events	20 mg BID	40 mg BID	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 39 (46.15%)	18 / 39 (46.15%)	9 / 38 (23.68%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 39 (7.69%)	3 / 39 (7.69%)	2 / 38 (5.26%)
occurrences (all)	3	3	2
Dizziness			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 39 (2.56%)	2 / 39 (5.13%)	0 / 38 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	1 / 38 (2.63%)
occurrences (all)	2	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 39 (5.13%)	2 / 39 (5.13%)	0 / 38 (0.00%)
occurrences (all)	2	2	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	0 / 38 (0.00%)
occurrences (all)	0	2	0
Dermatitis acneiform			

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 39 (5.13%) 2	0 / 38 (0.00%) 0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 39 (2.56%)	3 / 39 (7.69%)	0 / 38 (0.00%)
occurrences (all)	1	3	0
Nasopharyngitis			
subjects affected / exposed	1 / 39 (2.56%)	3 / 39 (7.69%)	3 / 38 (7.89%)
occurrences (all)	1	3	3
COVID-19			
subjects affected / exposed	1 / 39 (2.56%)	1 / 39 (2.56%)	3 / 38 (7.89%)
occurrences (all)	1	1	3
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported