Clinical trial results:
A randomized, placebo-controlled, double-blind trial evaluating the efficacy, tolerability and safety of ESO-101 in adult patients with active eosinophilic esophagitis

Summary

EudraCT number	2020-000082-16
Trial protocol	DE NL PL
Global end of trial date	09 October 2023

Results information

Result version number	v1 (current)
This version publication date	14 July 2024
First version publication date	14 July 2024

Trial information

Trial identification

Sponsor protocol code	ACESO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04849390
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	EsoCap AG
Sponsor organisation address	Malzgasse 9, Basel, Switzerland, 4052
Public contact	CEO, EsoCap AG, +43 69914950300, isabelle.racamier@esocapbiotech.com
Scientific contact	CEO, EsoCap AG, +43 69914950300, isabelle.racamier@esocapbiotech.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	09 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 October 2023
Global end of trial reached?	Yes
Global end of trial date	09 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy based on the histological response

Protection of trial subjects:

This trial was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki, independent ethics committee (IEC) informed consent regulations, and ICH GCP Guidelines. In addition, all national and local regulatory requirements were followed. Before any clinical trial-related activities were performed, the investigator (or authorized designee)
reviewed the informed consent form and explained the trial to potential trial patients. The investigator ensured that the patient was fully informed about the aims, procedures, potential risks, any discomforts, and expected benefits of the clinical trial.
Insurance coverage for all participating patients was guaranteed according to applicable legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 October 2020
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	Netherlands: 3
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Switzerland: 3
Worldwide total number of subjects	43
EEA total number of subjects	40

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)	42
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

59 patients were screened: 9 patients at 2 centers in Germany, 6 patients at 2 centers in The Netherlands, 3 patients at 1 center in Poland, 38 patients at 8 centers in Spain, and 3 patients at 1 center in Switzerland. 16 patients were screening failures (6 in Germany, 3 in The Netherlands, and 7 in Spain) and 43 patients were randomized.

Pre-assignment

Screening details:

Patients who met all inclusion and none of the exclusion criteria were eligible to participate in the trial.

Period 1

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

Blinding implementation details:

ESO-101 and placebo capsules were identical in appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	ESO-101

Arm description:

Dispersible polymer film (thin film) loaded with 800 µg mometasone furoate rolled in a hard gelatin capsule administered orally once-daily for 28 days.

Arm type	Experimental
Investigational medicinal product name	ESO-101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal film, Capsule, hard
Routes of administration	Oropharyngeal use

Dosage and administration details:

Patients took one oral capsule once daily in the evening at bedtime, ie, after eating dinner and after oral hygiene, for 28±2 consecutive days. Patients were not allowed to eat until they awoke the next morning and were not to drink for at least 2 hours after investigational medicinal product (IMP) intake.

Arm title	Placebo

Arm description:

Dispersible polymer film (thin film) without drug substance rolled in a hard gelatin capsule administered orally once-daily for 28 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal film, Capsule, hard
Routes of administration	Oropharyngeal use

Dosage and administration details:

Patients took one oral capsule once daily in the evening at bedtime, ie, after eating dinner and after oral hygiene, for 28±2 consecutive days. Patients were not allowed to eat until they awoke the next morning and were not to drink for at least 2 hours after IMP intake.

Number of subjects in period 1	ESO-101	Placebo
Started	28	15
Completed	27	13
Not completed	1	2
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	ESO-101
Reporting group description:	
Dispersible polymer film (thin film) loaded with 800 µg mometasone furoate rolled in a hard gelatin capsule administered orally once-daily for 28 days.	
Reporting group title	Placebo
Reporting group description:	
Dispersible polymer film (thin film) without drug substance rolled in a hard gelatin capsule administered orally once-daily for 28 days.	

Reporting group values	ESO-101	Placebo	Total
Number of subjects	28	15	43
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)	28	14	42
From 65-84 years	0	1	1
85 years and over	0	0	0
Age continuous			
Units: years			
median	38.5	47.0	
full range (min-max)	19 to 59	19 to 65	-
Gender categorical			
Units: Subjects			
Female	6	4	10
Male	22	11	33
Peak eosinophil count			
The number of eosinophils was normalized using a standard high-power field (hpf) size of 0.3 mm2.			
Units: 1/hpf			
arithmetic mean	86.95	84.65	
standard deviation	± 59.57	± 49.38	-

End points

End points reporting groups

Reporting group title	ESO-101
Reporting group description:	
Dispersible polymer film (thin film) loaded with 800 µg mometasone furoate rolled in a hard gelatin capsule administered orally once-daily for 28 days.	
Reporting group title	Placebo
Reporting group description:	
Dispersible polymer film (thin film) without drug substance rolled in a hard gelatin capsule administered orally once-daily for 28 days.	

Primary: Change in peak eosinophil count

End point title	Change in peak eosinophil count
End point description:	
For the assessment of the eosinophil count, 6 biopsy samples of the esophagus were taken (2 each from the proximal, mid, and distal segment of the esophagus) at Visit 2 (Baseline) and Visit 5 (end of treatment [EOT]). In general only one biopsy per segment was analyzed. If the data were not conclusive, the second biopsy was analyzed. In each analyzed biopsy sample, the peak eosinophil count was determined in 3 hpfs. For the analysis all analyzed hpfs were considered. The number of eosinophils was normalized using a standard hpf size of 0.3 mm^2.	
End point type	Primary
End point timeframe:	
Change from Baseline to EOT (Visit 5, Day 28)	

End point values	ESO-101	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	13		
Units: 1/hpf				
arithmetic mean (standard deviation)				
EOT	-49.11 (± 88.42)	6.63 (± 65.11)		

Statistical analyses

Statistical analysis title	Difference in change from Baseline
Statistical analysis description:	
The difference in the mean changes from Baseline between ESO-101 and placebo was tested using a 2-sided 2-sample t-test.	
Comparison groups	ESO-101 v Placebo

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	= 0.0318 [2]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-55.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-106.3
upper limit	-5.2

Notes:

[1] - The null hypothesis was defined as H0: μ1 = μ2 with μ1 being the mean absolute chanage from Baseline to EOT in overall peak eosinophil count in the ESO-101 group and μ2 the mean absolute chanage from Baseline to EOT in overall peak eosinophil count in the placebo group.

[2] - 5% confidence level

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From providing written informed consent until trial completion.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0
Reporting groups	
Reporting group title	ESO-101
Reporting group description: Dispersible polymer film (thin film) loaded with 800 µg mometasone furoate rolled in a hard gelatin capsule administered orally once-daily for 28 days.	
Reporting group title	Placebo
Reporting group description: Dispersible polymer film (thin film) without drug substance rolled in a hard gelatin capsule administered orally once-daily for 28 days.	

Serious adverse events	ESO-101	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	1 / 28 (3.57%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ESO-101	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 28 (64.29%)	9 / 15 (60.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	4 / 28 (14.29%)	3 / 15 (20.00%)	
occurrences (all)	16	6	
Somnolence			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Swelling face			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Dyspepsia			
subjects affected / exposed	5 / 28 (17.86%)	0 / 15 (0.00%)	
occurrences (all)	14	0	
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyperchlorhydria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Odynophagia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Oesophageal food impaction			

subjects affected / exposed	0 / 28 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Respiratory, thoracic and mediastinal disorders			
Dry throat			
subjects affected / exposed	0 / 28 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Throat irritation			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	
occurrences (all)	1	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 28 (3.57%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2021	Adaptation of 1 exclusion criterion for clarification and update of trial start and end dates

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported