



Clinical trial results:

An open-label, Phase IIa, multi-center, 12-week prospective study to evaluate the safety and efficacy of NOE-105 at a daily dose range of 2.5 mg to 15mg in adult and adolescent male patients with Tourette Syndrome (TS).

Summary

EudraCT number	2021-004424-15
Trial protocol	DE
Global end of trial date	03 November 2023

Results information

Result version number	v1 (current)
This version publication date	24 November 2024
First version publication date	24 November 2024

Trial information

Trial identification

Sponsor protocol code	NOE-TTS-211
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ANZCTR: ACTRN12621000319875

Notes:

Sponsors

Sponsor organisation name	Noema Pharma Australia Pty Ltd,
Sponsor organisation address	109 Pitt Street, Sydney, Australia,
Public contact	Clinical Trials, Noema Pharma, clinicaltrials@noemapharma.com
Scientific contact	Clinical Trials, Noema Pharma, clinicaltrials@noemapharma.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	13 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2023
Global end of trial reached?	Yes
Global end of trial date	03 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To identify the optimal dose range of NOE-105 that is associated with tic control in adult and adolescent patients with TS.

Protection of trial subjects:

Staggered recruitment of adolescent patients according to patient age, starting with a sentinel cohort of patients of at least 15 years of age.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2021
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	Australia: 11
Country: Number of subjects enrolled	Germany: 4
Worldwide total number of subjects	15
EEA total number of subjects	4

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)	2
Adults (18-64 years)	13
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects underwent screening and baseline assessments were recorded up to 28 days before dosing. A signed written ICF was obtained prior to all screening assessments.

Pre-assignment period milestones

Number of subjects started	16 ^[1]
Number of subjects completed	15

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
----------------------------	---------------------------------

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same. Justification: One patient was screened and signed an ICF, but did not meet the inclusion criterion 1 ("Ability and willingness to provide written informed consent and to comply with the study procedures")

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	NOE-105 Treatment
-----------	-------------------

Arm description:

Single arm of the study, dose escalation from 2.5 mg once daily to a maximum of 15 mg once daily.

Arm type	Experimental
Investigational medicinal product name	gemlapodect
Investigational medicinal product code	NOE-105
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Dosage escalation from 2.5 mg to 15 mg daily over the duration of the study.

Number of subjects in period 1	NOE-105 Treatment
Started	15
Completed	9
Not completed	6
Consent withdrawn by subject	4
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
-----------------------	---------------

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	13	13	
Gender categorical Units: Subjects			
Female	0	0	
Male	15	15	

End points

End points reporting groups

Reporting group title	NOE-105 Treatment
Reporting group description:	Single arm of the study, dose escalation from 2.5 mg once daily to a maximum of 15 mg once daily.

Primary: "Response" as assessed by the RAC, and reported using the 7-category TS-CGI-C scale.

End point title	"Response" as assessed by the RAC, and reported using the 7-category TS-CGI-C scale. ^[1]
-----------------	---

End point description:

Following the Week 12 End of study visit, patient data from those with at least on post treatment assessment were reviewed by the RAC to adjudicate the treatment response using the TS-CGI-C scale. In total, 8/14 (57.1%) patients were adjudicated by the RAC as responders to NOE-105 treatment, with scores of "Very Much Improved" reported in 2/14 (14.3%) patients, "Much Improved" reported in 4/14 (28.6%) patients, and "Minimally Improved" reported in 2/14 (14.3%) patients.

End point type	Primary
----------------	---------

End point timeframe:

Day 85

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The statistical methods focused primarily on descriptive statistics showing the changes over time in the efficacy endpoints.

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: %				
number (not applicable)				
Response	57.1			

Statistical analyses

No statistical analyses for this end point

Primary: Supplementary Measure to Primary Endpoint: "Response" as assessed by the Investigator using the TS-CGI-C scale

End point title	Supplementary Measure to Primary Endpoint: "Response" as assessed by the Investigator using the TS-CGI-C scale ^[2]
-----------------	---

End point description:

Investigators' assessment of "Response" using the TS-CGI-C scale (supplementary measure) with 8 responders (8/13, 61.5%).

End point type	Primary
----------------	---------

End point timeframe:

D85

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The statistical methods focused primarily on descriptive statistics showing the changes over time in the efficacy endpoints.

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: %				
number (not applicable)				
Response	61.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity of AEs. Laboratory and cardiovascular safety were also evaluated

End point title	Incidence and severity of AEs. Laboratory and cardiovascular safety were also evaluated
End point description:	
End point type	Secondary
End point timeframe:	Day 1, 8, 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85 and 28 days after last dose

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Adverse Events				
Mild	56			
Moderate	25			
Severe	2			
Laboratory and Cardiovascular Safety	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12/EoT in the YGTSS as measured by the TTS

End point title	Change from Baseline to Week 12/EoT in the YGTSS as measured by the TTS
-----------------	---

End point description:

End point type Secondary

End point timeframe:

From baseline to Day 85/EOT

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Change from Baseline				
arithmetic mean (standard deviation)				
TTS from baseline to Day 85	-7.8 (\pm 9.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed TS-CGI-S scale from Baseline to Week 12/EoT

End point title Investigator-assessed TS-CGI-S scale from Baseline to Week 12/EoT

End point description:

Investigator-assessed clinical global impression of change: the LS mean (95% CI) changes (reductions) from baseline in the Investigator-assessed TS-CGI-S scores

End point type Secondary

End point timeframe:

Day 85/EOT

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Change from Baseline				
least squares mean (confidence interval 95%)	-0.86 (-1.33 to -0.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12/EoT[2] in the YGTSS (completers only)

End point title Change from Baseline to Week 12/EoT[2] in the YGTSS

End point description:

A post-hoc analysis was performed of change from baseline to Day 85 (i.e., Week 12) in YGTSS TTS, including all patients who completed the full 12-week treatment period and attended the Day 85 study visit and reached a final dose between 10 and 15 mg.

End point type	Secondary
----------------	-----------

End point timeframe:

From baseline to Day 85/EOT

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Change from Baseline				
median (standard deviation)	-12.8 (± 7.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: PGI-C as completed by patients from Baseline to Week 12/EoT

End point title	PGI-C as completed by patients from Baseline to Week 12/EoT
-----------------	---

End point description:

Patients used an anchored-based assessment, in which, at the baseline visit, the patients were provided with a script and were requested to perform a voice recording. At W12/EoT, the patient was requested to listen to their baseline voice recording, and then rate the PGI-C comparing versus the baseline anchored with the voice recording

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline to Day 85/EoT

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: %				
number (not applicable)				
Very Much Improved	0			
Much Improved	46.2			
Minimally Improved	30.8			
No Change	7.7			
Minimally Worse	7.7			
Much Worse	7.7			
Very Much Worse	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient reported rating of the MSQ from Baseline to Week 12/EoT

End point title	Patient reported rating of the MSQ from Baseline to Week 12/EoT
-----------------	---

End point description:

The 7-point MSQ (from "extremely dissatisfied" to "extremely satisfied") was completed by the patient at the Day 85 visit.

The number and percentage of patients in each MSQ response category were presented, where the percentages were calculated from the number of patients completing the required 12 weeks of treatment.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline to Day 85/EoT

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: %				
number (not applicable)				
Extremely Satisfied	15.4			
Very Satisfied	23.1			
Somewhat Satisfied	7.7			
Neither Dissatisfied nor Satisfied	30.8			
Somewhat Dissatisfied	7.7			
Very Dissatisfied	0			
Extremely Dissatisfied	15.4			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Addendum to Primary Endpoint: Response to Study Treatment in Completers With A Final Dosing of NOE-105 Between 10 And 15 mg/Day

End point title	Addendum to Primary Endpoint: Response to Study Treatment in Completers With A Final Dosing of NOE-105 Between 10 And 15 mg/Day
-----------------	---

End point description:

End point type	Post-hoc
End point timeframe:	
Day 85	

End point values	NOE-105 Treatment			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: %				
number (not applicable)				
Response	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1, 8, 15, 22, 29, 36, 43, 50, 57, 64, 71, 78, 85 and 28 days after last dose

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.0
--------------------	------

Reporting groups

Reporting group title	NOE-105 Treatment
-----------------------	-------------------

Reporting group description:

Single arm of the study, dose escalation from 2.5 mg once daily to a maximum of 15 mg once daily (increased in 2.5 mg increments every week at discretion of the investigator). If intolerance occurred at any given dose, the daily dose of NOE-105 could be reduced by 2.5 mg.

Serious adverse events	NOE-105 Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	NOE-105 Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)		
Investigations			
Weight decreased			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	4		
Intraocular pressure decreased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		

Muscle strain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Nervous system disorders			
Dystonia subjects affected / exposed occurrences (all)	5 / 15 (33.33%) 10		
Tic subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 6		
Somnolence subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Akathisia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Dizziness subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Headache subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Initial insomnia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Sensory disturbance subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Tremor subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	6 / 15 (40.00%) 9		
Feeling abnormal			

<p>subjects affected / exposed occurrences (all)</p> <p>Pyrexia subjects affected / exposed occurrences (all)</p> <p>Thirst subjects affected / exposed occurrences (all)</p>	<p>1 / 15 (6.67%) 1</p> <p>1 / 15 (6.67%) 1</p> <p>1 / 15 (6.67%) 1</p>		
<p>Gastrointestinal disorders</p> <p>Diarrhoea subjects affected / exposed occurrences (all)</p> <p>Dysphagia subjects affected / exposed occurrences (all)</p> <p>Gastroesophageal reflux disease subjects affected / exposed occurrences (all)</p> <p>Loose tooth subjects affected / exposed occurrences (all)</p> <p>Nausea subjects affected / exposed occurrences (all)</p> <p>Salivary hypersecretion subjects affected / exposed occurrences (all)</p>	<p>2 / 15 (13.33%) 4</p> <p>1 / 15 (6.67%) 1</p> <p>1 / 15 (6.67%) 2</p> <p>1 / 15 (6.67%) 1</p> <p>1 / 15 (6.67%) 1</p> <p>1 / 15 (6.67%) 1</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough subjects affected / exposed occurrences (all)</p> <p>Dysphonia subjects affected / exposed occurrences (all)</p> <p>Sleep apnoea syndrome</p>	<p>1 / 15 (6.67%) 1</p> <p>1 / 15 (6.67%) 1</p>		

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Depression subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 3		
Conversion disorder subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Dissociation subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Disturbance in attention subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Panic attack subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Suicidal ideation subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Muscular weakness			

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Myalgia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Acarodermatitis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Helicobacter infection subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Sinusitis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	4 / 15 (26.67%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2020	To provide clarification on the study procedures: <ul style="list-style-type: none">- Baseline laboratory safety assessments- Study treatment compliance- PGI-C completion by patients
22 September 2021	<ul style="list-style-type: none">• To reduce the starting dose of NOE-105 from 5 mg to 2.5 mg to further improve tolerability, and specify that the IMP should be taken with the evening meal, since food has been shown to reduce C_{max}, in order to improve tolerability• To provide clarity on inclusion and exclusion criteria• To ensure that previous treatments for TS are captured
06 December 2021	<ul style="list-style-type: none">• To update the benefit/risk section of the Study Protocol and to add mitigation measures in case of study disruption due to public health crisis• To provide details on measures that would be put into place at times of study disruption during a civil crisis, natural disaster, or public health crisis (eg, from quarantines and resulting sites closures, regional travel restrictions, considerations if study site personnel or trial patients become infected with SARS-CoV-2) which would prevent patients from visiting study sites.
21 September 2022	<ul style="list-style-type: none">• To allow the recruitment of up to 5 adolescent patients with TS and to increase the number of patients from 10 to 18.• To exclude patients with positive urine drug screen for cannabinoids, cocaine, or nonprescribed opiates at screening.• To add PK assessments to inform the modelling of the PK of NOE-105 in adolescent patients
03 February 2023	<ul style="list-style-type: none">• To implement additional safety measures to monitor NOE-105 tolerability, as this was the first time that NOE-105 was to be administered to subjects < 18 years of age:<ul style="list-style-type: none">- A staggered recruitment was implemented as a prudent approach- It was added that patients had to remain in the clinic for 2 hours following the first dose of study treatment for safety monitoring- Newly included a DSMB- Provided adjusted instructions on the Investigator support to the patient in case of SIB emergence in adolescents• To update the table of risks

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported