Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Biological Activity, and PK of ND-L02-s0201 in Subjects with Idiopathic Pulmonary Fibrosis (IPF)

Summary

EudraCT number	2017-004919-39
Trial protocol	DE
Global end of trial date	24 August 2022

Results information

Result version number	v1 (current)
This version publication date	29 December 2023
First version publication date	29 December 2023

Trial information

Trial identification

Sponsor protocol code	ND-L02-s0201-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03538301
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nitto Denko Corporation
Sponsor organisation address	1-1-2, Shimohozumi, Ibaraki, Osaka, Japan, 567-8680
Public contact	Nitto Denko Corporation Study Director, Nitto Denko Corporation, clinicaltrialinfo005@nitto.com
Scientific contact	Nitto Denko Corporation Study Director, Nitto Denko Corporation, clinicaltrialinfo005@nitto.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	24 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 August 2022
Global end of trial reached?	Yes
Global end of trial date	24 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the safety and tolerability of ND-L02-s0201, administered at 2 dose levels, every 2 weeks over 24 weeks, versus placebo, in conjunction with standard of care (SOC)

Protection of trial subjects:

To ensure safety of the overall study an independent Data Monitoring Committee (DMC) was established. The DMC periodically reviewed the safety and tolerability of study treatment for the duration of the study. The DMC included a chairperson and pulmonologist who were experienced in idiopathic pulmonary fibrosis; all members were experienced with clinical trials and evaluating adverse events, and would not otherwise participate in the study. The DMC also included an independent statistician.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2018
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	Japan: 20
Country: Number of subjects enrolled	United States: 89
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	123
EEA total number of subjects	8

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)	27
From 65 to 84 years	96
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Diagnosis of idiopathic pulmonary fibrosis within 5 years before Visit 1a, confirmed by the Principal Investigator (PI) using American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin American Thoracic Association (ALAT) guidelines

Period 1

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

Blinding implementation details:

There was the potential for infusion-related reaction in a small percentage of participants receiving ND-L02-s0201 for Injection. Sites were expected to ensure the extent of unblinding did not go beyond the individuals who evaluated a participant with a possible infusion-related reaction or documented this information into the participant's casebook. Unblinded information should not have been documented in the participant's casebook.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Intravenous placebo infusion every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

Sodium Chloride 0.9% for Injection

Arm title	ND-L02-s0201 45 mg

Arm description:

ND-L02-s0201: 45 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.

Arm type	Experimental
Investigational medicinal product name	ND-L02-s0201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

45 mg ND-L02-s0201 for injection administered once every 2 weeks over a 24-week duration (a total of 12 doses).

Arm title	ND-L02-s0201 90 mg

Arm description:

ND-L02-s0201: 90 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for

Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.

Arm type	Experimental
Investigational medicinal product name	ND-L02-s0201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

90 mg ND-L02-s0201 for injection administered once every 2 weeks over a 24-week duration (a total of 12 doses).

Number of subjects in period 1	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg
Started	42	41	40
Completed	31	29	28
Not completed	11	12	12
Adverse event, serious fatal	1	1	-
Physician decision	-	1	-
Adverse event, non-fatal	1	4	4
Terminated Early due to COVID-19 impact	9	6	7
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Intravenous placebo infusion every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	
Reporting group title	ND-L02-s0201 45 mg
Reporting group description:	
ND-L02-s0201: 45 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	
Reporting group title	ND-L02-s0201 90 mg
Reporting group description:	
ND-L02-s0201: 90 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	

Reporting group values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg
Number of subjects	42	41	40
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age continuous Units: years			
arithmetic mean	68.7	68.9	69.2
standard deviation	± 6.16	± 6.22	± 6.53
Gender categorical Units: Subjects			
Female	5	7	6
Male	37	34	34
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	7	10	7
Black or African American	0	2	1
Native Hawaiian or Other Pacific Islander	0	0	0
White	34	29	31
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	5	2	4
Not Hispanic/Latino	37	39	36
Unknown	0	0	0
Smoking History Units: Subjects			
Yes - not active smoker	26	27	26
No	16	14	14
Background Standard of Care Units: Subjects			

Nintedanib	17	17	16
Pirfenidone	15	14	14
None	10	10	10
Body mass index group			
Category ranges are in kg/m2.			
Units: Subjects			
Normal (18.5 - 24.9)	12	11	10
Overweight (25 - 29.9)	15	17	22
Obese (30 and above)	15	13	8
Eligibility Criteria Based on high-resolution computed tomography			
Participants were staged based on the presence or absence of a usual interstitial pneumonia (UIP) pattern on chest HRCT scans assessments. The diagnosis of IPF was confirmed by the PI using ATS/ERS/JRS/ALAT consensus criteria (Raghu et al, 2011: https://www.atsjournals.org/doi/full/10.1164/rccm.2009-040GL).			
Units: Subjects			
Definite UIP	30	26	22
Consistent with UIP	6	10	11
Possible UIP	1	0	0
Inconsistent with UIP	5	5	7
GAP IPF Stage			
The GAP IPF stage for each subject was calculated by adding up the points assigned to categories I, II, and III, where stage I is the better and stage III is the worst. gender (G); age (A); baseline FVC,% predicted; and baseline DLco, % predicted Stage I: 0 to 3 points. This stage has the lowest risk of mortality Stage II: 4 to 5 points. This stage has a moderate risk of mortality Stage III: 6 to 8 points. This stage has the highest risk of mortality			
Units: Subjects			
Stage I	24	29	25
Stage II	17	11	15
Stage III	1	1	0
Height			
Units: centimetre			
arithmetic mean	172.399	172.316	171.519
standard deviation	± 6.5281	± 10.5278	± 9.2947
Weight			
Units: kilogram(s)			
arithmetic mean	85.579	84.234	82.255
standard deviation	± 15.4326	± 19.0174	± 17.6139
Body mass index			
Units: kilogram(s)/square metre			
arithmetic mean	28.765	28.093	27.780
standard deviation	± 4.7625	± 4.3072	± 4.5129
Baseline Pulse Oximetry			
Percentage of oxygen saturated hemoglobin is presented			
Units: percentage			
arithmetic mean	96.5	96.6	96.9
standard deviation	± 2.11	± 1.99	± 1.93
Baseline Forced Vital Capacity			
Units: litres			
arithmetic mean	2.861	3.012	2.890
standard deviation	± 0.7214	± 0.6866	± 0.7562

Baseline Percent Predicted Forced Vital Capacity			
Percentage of total normal FVC is presented			
Units: percentage			
arithmetic mean	73.943	79.319	76.658
standard deviation	± 17.0078	± 14.9940	± 18.1270
Baseline Forced Expiratory Volume in 1 second			
Units: litres			
arithmetic mean	2.270	2.380	2.274
standard deviation	± 0.5603	± 0.5345	± 0.5890
Baseline Percent Predicted Forced Expiratory Volume in 1 second			
Percentage of normal FEV is presented.			
Units: percent			
arithmetic mean	76.890	81.959	78.766
standard deviation	± 17.8868	± 14.8182	± 17.6653
Baseline ratio of Forced Expiratory Volume in 1 second/Forced Vital Capacity			
Units: ratio			
arithmetic mean	0.795	0.794	0.787
standard deviation	± 0.0501	± 0.0383	± 0.0450
Baseline Diffusion Capacity of the Lung for Carbon Monoxide Corrected for Hemoglobin			
Units: mL/min/mmHg			
arithmetic mean	12.574	12.972	12.391
standard deviation	± 3.9023	± 3.6453	± 3.3503
Duration of idiopathic pulmonary fibrosis			
Units: months			
arithmetic mean	28.227	24.678	27.272
standard deviation	± 17.4342	± 16.3543	± 15.7152
Risk of Mortality at 1-year			
The risk of mortality (1-, 2-, and 3-year risk) was derived based on baseline data at the start of the treatment period using the Gender, Age, and Physiology (GAP) methodology. Risk of mortality was derived using the algorithm listed in SAP- Appendix 1: GAP Algorithm for IPF Stage and Predicted Mortality.			
Units: risk ratio			
arithmetic mean	14.726	12.584	13.930
standard deviation	± 7.1570	± 4.9287	± 6.0984
Risk of Mortality at 2-year			
The risk of mortality (1-, 2-, and 3-year risk) was derived based on baseline data at the start of the treatment period using the Gender, Age, and Physiology (GAP) methodology. Risk of mortality was derived using the algorithm listed in SAP- Appendix 1: GAP Algorithm for IPF Stage and Predicted Mortality.			
Units: risk ratio			
arithmetic mean	28.505	24.922	27.233
standard deviation	± 12.5204	± 9.0103	± 11.0164
Risk of Mortality at 3-year			
The risk of mortality (1-, 2-, and 3-year risk) was derived based on baseline data at the start of the treatment period using the Gender, Age, and Physiology (GAP) methodology. Risk of mortality was derived using the algorithm listed in SAP- Appendix 1: GAP Algorithm for IPF Stage and Predicted Mortality.			
Units: risk ratio			
arithmetic mean	40.335	36.014	38.869

standard deviation	± 15.9727	± 11.9575	± 14.4372
Baseline Hemoglobin Corrected percent predicted DLCO			
Units: percentage of normal DLCO			
arithmetic mean	51.762	53.739	51.914
standard deviation	± 14.7970	± 13.1901	± 12.6957

Reporting group values	Total		
Number of subjects	123		
Age categorical			
Units: Subjects			
Adults (18-64 years)	0		
From 65-84 years	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	18		
Male	105		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	24		
Black or African American	3		
Native Hawaiian or Other Pacific Islander	0		
White	94		
Other	2		
Ethnicity			
Units: Subjects			
Hispanic or Latino	11		
Not Hispanic/Latino	112		
Unknown	0		
Smoking History			
Units: Subjects			
Yes - not active smoker	79		
No	44		
Background Standard of Care			
Units: Subjects			
Nintedanib	50		
Pirfenidone	43		
None	30		
Body mass index group			
Category ranges are in kg/m2.			
Units: Subjects			
Normal (18.5 - 24.9)	33		
Overweight (25 - 29.9)	54		
Obese (30 and above)	36		
Eligibility Criteria Based on high-resolution computed tomography			

Participants were staged based on the presence or absence of a usual interstitial pneumonia (UIP) pattern on chest HRCT scans assessments. The diagnosis of IPF was confirmed by the PI using ATS/ERS/JRS/ALAT consensus criteria (Raghu et al, 2011: https://www.atsjournals.org/doi/full/10.1164/rccm.2009-040GL).			
Units: Subjects			
Definite UIP	78		
Consistent with UIP	27		
Possible UIP	1		
Inconsistent with UIP	17		
GAP IPF Stage			
The GAP IPF stage for each subject was calculated by adding up the points assigned to categories I, II, and III, where stage I is the better and stage III is the worst. gender (G); age (A); baseline FVC,% predicted; and baseline DLco, % predicted Stage I: 0 to 3 points. This stage has the lowest risk of mortality Stage II: 4 to 5 points. This stage has a moderate risk of mortality Stage III: 6 to 8 points. This stage has the highest risk of mortality			
Units: Subjects			
Stage I	78		
Stage II	43		
Stage III	2		
Height Units: centimetre arithmetic mean standard deviation	- -		
Weight Units: kilogram(s) arithmetic mean standard deviation	- -		
Body mass index Units: kilogram(s)/square metre arithmetic mean standard deviation	- -		
Baseline Pulse Oximetry			
Percentage of oxygen saturated hemoglobin is presented			
Units: percentage arithmetic mean standard deviation	- -		
Baseline Forced Vital Capacity Units: litres arithmetic mean standard deviation	- -		
Baseline Percent Predicted Forced Vital Capacity			
Percentage of total normal FVC is presented			
Units: percentage arithmetic mean standard deviation	- -		
Baseline Forced Expiratory Volume in 1 second Units: litres arithmetic mean standard deviation	- -		

Baseline Percent Predicted Forced Expiratory Volume in 1 second			
Percentage of normal FEV is presented.			
Units: percent arithmetic mean standard deviation	- -		
Baseline ratio of Forced Expiratory Volume in 1 second/Forced Vital Capacity Units: ratio arithmetic mean standard deviation	- -		
Baseline Diffusion Capacity of the Lung for Carbon Monoxide Corrected for Hemoglobin Units: mL/min/mmHg arithmetic mean standard deviation	- -		
Duration of idiopathic pulmonary fibrosis Units: months arithmetic mean standard deviation	- -		
Risk of Mortality at 1-year			
The risk of mortality (1-, 2-, and 3-year risk) was derived based on baseline data at the start of the treatment period using the Gender, Age, and Physiology (GAP) methodology. Risk of mortality was derived using the algorithm listed in SAP- Appendix 1: GAP Algorithm for IPF Stage and Predicted Mortality.			
Units: risk ratio arithmetic mean standard deviation	- -		
Risk of Mortality at 2-year			
The risk of mortality (1-, 2-, and 3-year risk) was derived based on baseline data at the start of the treatment period using the Gender, Age, and Physiology (GAP) methodology. Risk of mortality was derived using the algorithm listed in SAP- Appendix 1: GAP Algorithm for IPF Stage and Predicted Mortality.			
Units: risk ratio arithmetic mean standard deviation	- -		
Risk of Mortality at 3-year			
The risk of mortality (1-, 2-, and 3-year risk) was derived based on baseline data at the start of the treatment period using the Gender, Age, and Physiology (GAP) methodology. Risk of mortality was derived using the algorithm listed in SAP- Appendix 1: GAP Algorithm for IPF Stage and Predicted Mortality.			
Units: risk ratio arithmetic mean standard deviation	- -		
Baseline Hemoglobin Corrected percent predicted DLCO Units: percentage of normal DLCO arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Intravenous placebo infusion every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	
Reporting group title	ND-L02-s0201 45 mg
Reporting group description:	
ND-L02-s0201: 45 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	
Reporting group title	ND-L02-s0201 90 mg
Reporting group description:	
ND-L02-s0201: 90 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	

Primary: Number of participants discontinuing study treatment due to TEAEs

End point title	Number of participants discontinuing study treatment due to TEAEs[1]
End point description:	
The number of participants with TEAEs leading to discontinuation from the study treatment. The Safety Population (including all participants who received at least one dose of study treatment) is presented. TEAE = treatment-emergent adverse event.	
End point type	Primary
End point timeframe:	
Change in the incidence and severity of adverse events related to study treatment from baseline to 24 weeks	
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: No statistical analysis required for this endpoint.	

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: Participants	1	3	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Decline in FVC from Baseline to Week 24

End point title	Rate of Decline in FVC from Baseline to Week 24
End point description:	
Slope in FVC from Baseline to Week 24 (measured in L/week). The intent-to-treat population (any randomized participants with treatment assignment according to the planned randomization) is presented. Slope and standard error are presented. The slope is approximated as least square mean/24 weeks.	

FVC = forced vital capacity

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: litres				
arithmetic mean (standard error)				
Slope in FVC (L/week)	-0.003366 (± 0.0014272)	-0.007519 (± 0.0015285)	-0.005478 (± 0.0015400)	

Statistical analyses

Statistical analysis title	Rate of Decline in FVC to Week 24: 45 mg v Placebo

Statistical analysis description:

Slope in FVC (L/week) in the 45 mg cohort versus placebo

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049
Method	random coefficient model
Parameter estimate	Slope Difference
Point estimate	-0.004153
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.008284
upper limit	-0.000021

Statistical analysis title	Rate of Decline in FVC to Week 24: 90 mg v Placebo

Statistical analysis description:

Slope in FVC (L/week) in the 90 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.316
Method	random coefficient model
Parameter estimate	Slope Difference
Point estimate	-0.002112

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.00626
upper limit	0.002036

Secondary: Absolute and Relative Change in FVC (L) from Baseline to Week 24

End point title	Absolute and Relative Change in FVC (L) from Baseline to Week 24

End point description:

Absolute and Relative Change in FVC (L) from Baseline to Week 24. The intent-to-treat population (any randomized participants with treatment assignment according to the planned randomization) is presented.
FVC = forced vital capacity

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: litres				
least squares mean (standard error)				
Baseline FVC (L)	2.8754 (± 0.11079)	3.0242 (± 0.11207)	2.9032 (± 0.11328)	
Week 24 FVC (L)	2.7946 (± 0.10946)	2.8438 (± 0.11144)	2.7717 (± 0.11253)	
Change from Baseline to Week 24 in FVC (L)	-0.0808 (± 0.03425)	-0.1805 (± 0.03668)	-0.1315 (± 0.03696)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 24 in FVC (L): 45mg

Statistical analysis description:

Change from Baseline to Week 24 in FVC (L) in the 45 mg cohort versus Placebo

Comparison groups	ND-L02-s0201 45 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049
Method	random coefficient model
Parameter estimate	Least Squares Mean Difference (Final)
Point estimate	-0.0997

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1988
upper limit	-0.0005

Statistical analysis title	Change from Baseline to Week 24 in FVC: 90 mg
Statistical analysis description:	
Change from Baseline to Week 24 in FVC (L) in the 90 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.316
Method	random coefficient model
Parameter estimate	Least Squares Mean Difference (Final)
Point estimate	-0.0507
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1502
upper limit	-0.0489

Secondary: Summary of Study Treatment Response of FVC

End point title	Summary of Study Treatment Response of FVC

End point description:

Proportion of participants with an FVC response defined as either having improvement or a decline by 0 to less than or equal to 5%, more than 5% to less than or equal to 10%, and more than 10% at Visit 14 (Day 169).

Participants with an FVC response were defined as improvement in FVC (ie, FVC value higher than baseline) or a decline of less than or equal to 10% from baseline.

The intent-to-treat population (any randomised participants with treatment assignment according to the planned randomisation) is presented.

FVC = forced vital capacity

End point type	Secondary

End point timeframe:

Baseline to Visit 14 (Day 169)

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: participants				
Improvement	9	7	5	
Decline ≥0% to ≤5%	10	6	10	
Decline >5% to ≤10%	8	6	6	
Decline >10%	3	7	4	
Test not done	12	15	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Study Treatment Response of ppFVC

End point title	Summary of Study Treatment Response of ppFVC

End point description:

Proportion of participants with an ppFVC response defined as either having improvement or a decline by 0 to less than or equal to 5%, greater than 5% to less than or equal to 10%, and greater than 10% at Visit 14 (Day 169).

Participants with a ppFVC response were defined as improvement in ppFVC (ie, ppFVC value higher than baseline) or a decline of less than or equal to 10% from baseline.

The intent-to-treat population (any randomised participants with treatment assignment according to the planned randomisation) is presented.

ppFVC = percent predicted forced vital capacity

End point type	Secondary

End point timeframe:

Baseline to Visit 14 (Day 169)

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: participants				
Improvement	9	7	5	
Decline ≥0% to ≤5%	10	6	10	
Decline >5% to ≤10%	8	6	6	
Decline >10%	3	7	4	
Test not done	12	15	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in DLCO and DLCO corrected for hemoglobin from Baseline to Week 24

End point title	Change in DLCO and DLCO corrected for hemoglobin from Baseline to Week 24

End point description:

Change in diffusion capacity of the lung for carbon monoxide (DLCO) and DLCO corrected for hemoglobin (mL/min/mmHg) from Baseline to Week 24.

The intent-to-treat population (any randomised participants with treatment assignment according to the planned randomisation) is presented.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: mL/min/mmHg				
least squares mean (standard error)				
Baseline DLCO Corrected for Hemoglobin	12.6709 (± 0.56489)	13.0723 (± 0.57141)	12.4800 (± 0.57759)	
Week 24 DLCO Corrected for Hemoglobin	11.7541 (± 0.58748)	12.3015 (± 0.59845)	12.2669 (± 0.60460)	
Change from Baseline to Week 24 in DLCO Corrected	-0.9169 (± 0.26950)	-0.7708 (± 0.28085)	-0.2131 (± 0.28408)	
Baseline DLCO Not Corrected for Hemoglobin	12.4411 (± 0.55897)	12.9860 (± 0.56543)	12.3792 (± 0.57155)	
Week 24 DLCO Not Corrected for Hemoglobin	11.5720 (± 0.57137)	12.2308 (± 0.58226)	12.0661 (± 0.58804)	
Change from Baseline to Week 24 in DLCO Not Correc	-0.8691 (± 0.26307)	-0.7551 (± 0.27406)	-0.3131 (± 0.27721)	

Statistical analyses

Statistical analysis title	DLCO Corrected: 45 mg cohort vs. Placebo

Statistical analysis description:

Change from Baseline to Week 24 in DLCO Corrected for Hemoglobin (mL/min/mmHg) in the 45 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.708
Method	random coefficient
Parameter estimate	Mean difference (final values)
Point estimate	0.146

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6226
upper limit	0.9147

Statistical analysis title	DLCO Corrected: 90 mg cohort vs. Placebo
Statistical analysis description:	
Change from Baseline to Week 24 in DLCO Corrected for Hemoglobin (mL/min/mmHg) in the 90 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074
Method	random coefficient
Parameter estimate	Mean difference (final values)
Point estimate	0.7038
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0695
upper limit	1.4771

Statistical analysis title	DLCO Not Corrected: 45 mg cohort vs. Placebo
Statistical analysis description:	
Change from Baseline to Week 24 in DLCO Not Corrected for Hemoglobin (mL/min/mmHg) in the 45 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.765
Method	random coefficient
Parameter estimate	Mean difference (final values)
Point estimate	0.114
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6362
upper limit	0.8641

Statistical analysis title	DLCO Not Corrected: 90 mg cohort vs. Placebo

Statistical analysis description:

Change from Baseline to Week 24 in DLCO Not Corrected for Hemoglobin (mL/min/mmHg) in the 90 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.148
Method	random coefficient
Parameter estimate	Mean difference (final values)
Point estimate	0.556
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1986
upper limit	1.3107

Secondary: Quantitative Changes of interstitial lung abnormalities as measured by HRCT

End point title	Quantitative Changes of interstitial lung abnormalities as measured by HRCT

End point description:

Changes of interstitial lung abnormalities as measured by high-resolution computed tomography (HRCT; ie, change in parenchymal feature [Baseline to Week 24), as determined by qualitative assessment (central radiologist) and quantitative analysis (Quantitative Lung Fibrosis – QLF analysis).

Quantitative HRCT parameters included the following:
• Quantitative Lung Fibrosis (QLF) score (% of whole lung field volume)
• Ground glass opacity (GGO) (% of whole lung field volume)
• Reticulation (% of whole lung field volume)
• Honeycombing (% of whole lung field volume)
• Normal lung (% of whole lung field volume)
• Emphysema (low attenuation area [LAA]; % of whole lung field volume)

The intent-to-treat population (any randomised participants with treatment assignment according to the planned randomisation) is presented.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: percentage of whole lung field volume				
least squares mean (standard error)				
Baseline Ground Glass Opacity	5.01 (± 0.357)	4.91 (± 0.399)	4.72 (± 0.367)	
Week 24 Ground Glass Opacity	4.77 (± 0.358)	4.49 (± 0.400)	4.52 (± 0.369)	
Change Baseline to Week 24 Ground Glass Opacity	-0.23 (± 0.177)	-0.41 (± 0.195)	-0.20 (± 0.182)	

Baseline Reticulation	27.46 (± 1.890)	23.69 (± 2.108)	24.03 (± 1.943)	
Week 24 Reticulation	28.13 (± 2.001)	24.97 (± 2.231)	26.34 (± 2.062)	
Change from Baseline to Week 24 in Reticulation	0.67 (± 0.964)	1.28 (± 1.069)	2.32 (± 1.010)	
Baseline Honeycombing	4.54 (± 0.861)	2.50 (± 0.961)	1.54 (± 0.886)	
Week 24 Honeycombing	6.36 (± 1.018)	3.11 (± 1.135)	2.37 (± 1.047)	
Change from Baseline to Week 24 Honeycombing	1.81 (± 0.542)	0.61 (± 0.604)	0.83 (± 0.558)	
Baseline Normal Lung	58.47 (± 2.281)	64.52 (± 2.544)	65.57 (± 2.343)	
Week 24 Normal Lung	56.42 (± 2.287)	63.35 (± 2.549)	62.68 (± 2.352)	
Change from Baseline to Week 24 in Normal Lung	-2.05 (± 1.027)	-1.17 (± 1.134)	-2.88 (± 1.057)	
Baseline Emphysema	9.62 (± 1.640)	10.66 (± 1.829)	8.14 (± 1.684)	
Week 24 Emphysema	12.08 (± 1.646)	9.54 (± 1.835)	8.45 (± 1.694)	
Change from Baseline to Week 24 in Emphysema	2.46 (± 0.936)	-1.12 (± 1.034)	0.31 (± 0.964)	
Baseline QLF Score	33.59 (± 2.189)	27.45 (± 2.441)	27.22 (± 2.249)	
Week 24 QLF Score	35.87 (± 2.195)	29.24 (± 2.447)	30.89 (± 2.258)	
Change from Baseline to Week 24 in QLF Score	2.28 (± 1.080)	1.79 (± 1.194)	3.67 (± 1.112)	

Statistical analyses

Statistical analysis title	Change from Baseline to Week 24 in QLF Score: 45mg
Statistical analysis description:	
Change from Baseline to Week 24 in QLF Score (% of whole lung field volume) in the 45 mg cohort versus Placebo	
Comparison groups	ND-L02-s0201 45 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.765
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.68
upper limit	2.71

Statistical analysis title	Change from Baseline to Week 24 in QLF Score: 90mg

Statistical analysis description:

Change from Baseline to Week 24 in QLF Score (% of whole lung field volume) in the 90 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	4.47

Statistical analysis title	Change from Baseline to Week 24 in GGO: 45mg

Statistical analysis description:

Change from Baseline to Week 24 in Ground Glass Opacity (% of whole lung field volume) in the 45 mg cohort versus Placebo.

GGO = Ground Glass Opacity

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.499
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.34

Statistical analysis title	Change from Baseline to Week 24 in GGO: 90mg

Statistical analysis description:

Change from Baseline to Week 24 in Ground Glass Opacity (% of whole lung field volume) in the 90 mg cohort versus Placebo.

GGO = Ground Glass Opacity

Comparison groups	Placebo v ND-L02-s0201 90 mg

Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.901
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.54

Statistical analysis title	Change from Baseline to Week 24 Reticulation: 45mg
Statistical analysis description:	
Change from Baseline to Week 24 in Reticulation (% of whole lung field volume) in the 45 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.676
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	3.46

Statistical analysis title	Change from Baseline to Week 24 Reticulation: 90mg
Statistical analysis description:	
Change from Baseline to Week 24 in Reticulation (% of whole lung field volume) in the 90 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.242
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	1.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.13
upper limit	4.42

Statistical analysis title	Change Baseline to Week 24 Honeycombing: 45 mg
Statistical analysis description:	
Change from Baseline to Week 24 in Honeycombing (% of whole lung field volume) in the 45 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.82
upper limit	0.4

Statistical analysis title	Change Baseline to Week 24 Honeycombing: 90mg
Statistical analysis description:	
Change from Baseline to Week 24 in Honeycombing (% of whole lung field volume) in the 90 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.211
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.53
upper limit	0.56

Statistical analysis title	Change Baseline to Week 24 Normal Lung: 45 mg

Statistical analysis description:

Change from Baseline to Week 24 in Normal Lung (% of whole lung field volume) in the 45 mg cohort versus Placebo

Comparison groups	ND-L02-s0201 45 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.568
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.16
upper limit	3.91

Statistical analysis title	Change Baseline to Week 24 Normal Lung: 90 mg

Statistical analysis description:

Change from Baseline to Week 24 in Normal Lung (% of whole lung field volume) in the 90 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.573
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.76
upper limit	2.09

Statistical analysis title	Change Baseline to Week 24 in Emphysema: 45 mg

Statistical analysis description:

Change from Baseline to Week 24 in Emphysema (% of whole lung field volume) in the 45 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	-3.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.35
upper limit	-0.81

Statistical analysis title	Change Baseline to Week 24 in Emphysema: 90 mg

Statistical analysis description:

Change from Baseline to Week 24 in Emphysema (% of whole lung field volume) in the 90 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112
Method	random coefficient model
Parameter estimate	Least squares mean difference (final)
Point estimate	-2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.82
upper limit	0.51

Secondary: Qualitative Changes of interstitial lung abnormalities as measured by HRCT

End point title	Qualitative Changes of interstitial lung abnormalities as measured by HRCT

End point description:

Changes of interstitial lung abnormalities as measured by high-resolution computed tomography (HRCT; ie, change in parenchymal feature [Baseline to Visit 14 (Day 169)]), as determined by qualitative assessment (central radiologist). The Likert scale values are included in the descriptions presented.

The intent-to-treat population (any randomised participants with treatment assignment according to the planned randomisation) with HRCT assessment at Visit 14/Early Termination is presented.

End point type	Secondary

End point timeframe:

Baseline to Visit 14 (Day 169)

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	30	34	
Units: participants				
Much Better (5)	0	0	0	
Better (4)	0	0	1	

Same (3)	28	26	28	
Worse (2)	6	3	3	
Much Worse (1)	3	1	2	
Unknown	0	0	0	

Statistical analyses

Statistical analysis title	ND-L02-s0201 45 mg versus Placebo
Comparison groups	ND-L02-s0201 45 mg v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.256 [2]
Method	Wilcoxon (Mann-Whitney)

Notes:

[2] - p-value vs. Placebo

Statistical analysis title	ND-L02-s0201 90 mg versus Placebo
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.241 [3]
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - p-value vs. Placebo

Secondary: Events of IPF Exacerbation or Death and Rate of First IPF Exacerbation

End point title	Events of IPF Exacerbation or Death and Rate of First IPF Exacerbation

End point description:

Total number of events of participants who experienced idiopathic pulmonary fibrosis (IPF) exacerbation (ie, an unexplained worsening of dyspnea, evidence of hypoxemia as defined by worsened or severely impaired gas exchange, new radiographic alveolar infiltrates, and an absence of an alternative explanation such as infection, pulmonary embolism, pneumothorax, or heart failure) or death (weeks).

End point type	Secondary

End point timeframe:

Baseline to study completion, up to Day 239

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: events	7	3	4	

Statistical analyses

Statistical analysis title	Log-Rank Test 45mg vs. Placebo p-value
Statistical analysis description:	
Time to First IPF Exacerbation or Death (weeks) in the 45 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.517 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.649
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.189
upper limit	2.225

Notes:

[4] - The p-value was calculated using a log-rank test stratified by standard of care.

Statistical analysis title	Log-Rank Test 90mg vs. Placebo p-value
Statistical analysis description:	
Time to First IPF Exacerbation or Death (weeks) in the 90 mg cohort versus Placebo	
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.506 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.678
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.198
upper limit	2.324

Notes:

[5] - The p-value was calculated using a log-rank test stratified by standard of care.

Statistical analysis title	Rate of First IPF Exacerbation (%): 45 mg

Statistical analysis description:

Rate of First IPF Exacerbation (%) in the 45 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.313 [6]
Method	Fisher exact
Parameter estimate	Proportion Difference (Final Values)
Point estimate	-9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.2
upper limit	5.5

Notes:

[6] - The p-value was based on Pearson's Chi-Square test. However, if any of the expected (not observed) cell counts are less than 5, a Fisher's Exact test was performed instead.

Statistical analysis title	Rate of First IPF Exacerbation (%): 90 mg

Statistical analysis description:

Rate of First IPF Exacerbation (%) in the 90 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.376
Method	Chi-squared
Parameter estimate	Proportion Difference (Final Values)
Point estimate	-6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.6
upper limit	9.2

Secondary: Events of Hospitalization for Respiratory Ailments or Death

End point title	Events of Hospitalization for Respiratory Ailments or Death

End point description:

Events (participants who experienced hospitalization for respiratory ailments or died) for respiratory ailments are presented.
The intent-to-treat population (any randomized participants with treatment assignment according to the planned randomization) is presented.

End point type	Secondary

End point timeframe:

Up to 12 weeks after the end of study treatment

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: events	5	3	3	

Statistical analyses

Statistical analysis title	Rate of Hospitalization Respiratory Ailments: 45mg

Statistical analysis description:

Rate of Hospitalization for Respiratory Ailments (%) in the 45 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.713
Method	Fisher exact
Parameter estimate	Proportion Difference (Final Values)
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.2
upper limit	9.6

Statistical analysis title	Rate of Hospitalization Respiratory Ailments: 90mg

Statistical analysis description:

Rate of Hospitalization for Respiratory Ailments (%) in the 90 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.713
Method	Fisher exact
Parameter estimate	Proportion Difference (Final Values)
Point estimate	-4.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.2
upper limit	10.7

Secondary: Total Events of Death Due to All Causes

End point title	Total Events of Death Due to All Causes

End point description:

Rate of mortality due to all causes is presented. Overall survival was defined as the time from start of study treatment to death due to any cause.

End point type	Secondary

End point timeframe:

Up to 12 weeks after the end of study treatment

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: participants	1	1	0	

Statistical analyses

Statistical analysis title	Overall Survival (weeks) in the 45 mg cohort

Statistical analysis description:

Overall Survival (weeks) in the 45 mg cohort versus Placebo

Comparison groups	ND-L02-s0201 45 mg v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.937
Method	Logrank

Statistical analysis title	Overall Survival (weeks) in the 90 mg cohort

Statistical analysis description:

Overall Survival (weeks) in the 45 mg cohort versus Placebo

Comparison groups	Placebo v ND-L02-s0201 90 mg

Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.414
Method	Logrank

Statistical analysis title	Rate of Mortality (%) in the 45 mg cohort

Statistical analysis description:
Rate of Mortality (%) in the 45 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Fisher exact
Parameter estimate	Proportion Difference (Final Values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.4
upper limit	10.9

Statistical analysis title	Rate of Mortality (%) in the 90 mg cohort

Statistical analysis description:
Rate of Mortality (%) in the 90 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Fisher exact
Parameter estimate	Proportion Difference (Final Values)
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.1
upper limit	6.8

Secondary: Events of Deterioration of IPF Resulting in Lung Transplantation or

Death and Rate of Deterioration of IPF Resulting in Lung Transplantation	
End point title	Events of Deterioration of IPF Resulting in Lung Transplantation or Death and Rate of Deterioration of IPF Resulting in Lung Transplantation

End point description:

Events of deterioration of Idiopathic Pulmonary Fibrosis (IPF) resulting in lung transplantation (LP; up to 12 weeks after the end of study treatment) or death (weeks) and rate of deterioration of IPF resulting in lung transplantation (up to 12 weeks after the end of study treatment) are presented.

Total events = Participants who experience deterioration of IPF resulting in LP (or died).

Rate of Deterioration = Rate of Deterioration of IPF Resulting in LP.

End point type	Secondary

End point timeframe:

Baseline to 12 weeks after end of study treatment

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: events				
Total events	3	1	0	
Rate of Deterioration	2	0	0	

Statistical analyses

Statistical analysis title	Rate of Deterioration of IPF: 45 mg vs. Placebo

Statistical analysis description:

Rate of Deterioration of IPF Resulting in Lung Transplantation (%) in the 45 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.494
Method	Fisher exact
Parameter estimate	Proportion Difference (Final Values)
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.6
upper limit	4.6

Statistical analysis title	Rate of Deterioration of IPF: 90 mg vs. Placebo

Statistical analysis description:

Rate of Deterioration of IPF Resulting in Lung Transplantation (%) in the 90 mg cohort versus Placebo.

The 95% CI for difference in proportions are based on the Chan-Zhang method.

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.494
Method	Fisher exact
Parameter estimate	Proportion Difference (Final Values)
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.2
upper limit	4.5

Secondary: Rate of Decline in ppFVC from Baseline to Week 24

End point title	Rate of Decline in ppFVC from Baseline to Week 24

End point description:

Slope in ppFVC from Baseline to Week 24 (measured in %/week). The intent-to-treat population (any randomized participants with treatment assignment according to the planned randomization) is presented.
Slope and standard error are presented. The slope is approximated as least square mean/24 weeks.
ppFVC = percent predicted forced vital capacity

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: %/week				
arithmetic mean (standard error)	-0.096455 (± 0.0373658)	-0.187694 (± 0.0400588)	-0.136051 (± 0.0403636)	

Statistical analyses

Statistical analysis title	Rate of Decline in ppFVC: 45 mg versus placebo
Comparison groups	Placebo v ND-L02-s0201 45 mg

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.098
Method	random coefficient model
Parameter estimate	Slope
Point estimate	-0.091238
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.199456
upper limit	0.016979

Statistical analysis title	Rate of Decline in ppFVC: 90 mg versus placebo
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.473
Method	random coefficient model
Parameter estimate	Slope
Point estimate	-0.039596
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.148248
upper limit	0.069056

Secondary: Percent Change in FVC From Baseline to Week 24

End point title	Percent Change in FVC From Baseline to Week 24

End point description:

Percent Change in FVC from Baseline to Week 24. The intent-to-treat population (any randomized participants with treatment assignment according to the planned randomization) is presented.
FVC = forced vital capacity

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: percent				
least squares mean (standard error)	-3.10 (± 4.793)	-5.64 (± 4.488)	-4.23 (± 4.723)	

Statistical analyses

Statistical analysis title	Placebo versus ND-L02-s0201 45 mg
Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.668
Method	random coefficient model
Parameter estimate	Median difference (final values)
Point estimate	-3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.59
upper limit	11.28

Statistical analysis title	Placebo versus ND-L02-s0201 90 mg
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.821
Method	random coefficient model
Parameter estimate	Median difference (final values)
Point estimate	-1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.57
upper limit	13.13

Secondary: Absolute and Relative Change in ppFVC (%) From Baseline to Week 24	
End point title	Absolute and Relative Change in ppFVC (%) From Baseline to Week 24

End point description:

Absolute and Relative Change in ppFVC (%) from Baseline to Week 24. The intent-to-treat population

(any randomized participants with treatment assignment according to the planned randomization) is presented.
ppFVC = percent predicted forced vital capacity

End point type	Secondary
End point timeframe:	
Baseline to Week 24	

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: percent				
least squares mean (standard error)				
Baseline ppFVC	74.5701 (± 2.54894)	79.8896 (± 2.57837)	77.2260 (± 2.60623)	
Week 24 ppFVC	72.2552 (± 2.58376)	75.3849 (± 2.63382)	73.9607 (± 2.65995)	
Change from Baseline to Week 24 in ppFVC	-2.3149 (± 0.89678)	-4.5046 (± 0.96141)	-3.2652 (± 0.96873)	

Statistical analyses

Statistical analysis title	Change from baseline to Week 24 in ppFVC: 45 mg
Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.098
Method	random coefficient model
Parameter estimate	Median difference (final values)
Point estimate	-2.1897
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7869
upper limit	0.4075

Statistical analysis title	Change from Baseline to Week 24 in ppFVC: 90 mg
Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.473
Method	random coefficient model
Parameter estimate	Median difference (final values)
Point estimate	-0.9503

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5579
upper limit	1.6573

Secondary: Percent Change in ppFVC From Baseline to Week 24

End point title	Percent Change in ppFVC From Baseline to Week 24
End point description:	
Percent Change in ppFVC from Baseline to Week 24. The intent-to-treat population (any randomized participants with treatment assignment according to the planned randomization) is presented. ppFVC = percent predicted forced vital capacity	
End point type	Secondary
End point timeframe:	
Baseline to Week 24	

End point values	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	41	40	
Units: percent				
least squares mean (standard error)	-3.10 (± 4.793)	-5.64 (± 4.488)	-4.23 (± 4.723)	

Statistical analyses

Statistical analysis title	Percent Change in ppFVC: 45mg versus placebo
Comparison groups	Placebo v ND-L02-s0201 45 mg
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7
Method	random coefficient model
Parameter estimate	Median difference (final values)
Point estimate	-2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.4
upper limit	10.34

Statistical analysis title	Percent Change in ppFVC: 90mg versus placebo

Comparison groups	Placebo v ND-L02-s0201 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.867
Method	random coefficient model
Parameter estimate	Median difference (final values)
Point estimate	-1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.31
upper limit	12.07

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Approximately 40 weeks (from screening to follow-up visit).	
Adverse event reporting additional description:	
The safety population includes all participants who received at least one dose of study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Intravenous placebo infusion every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	
Reporting group title	ND-L02-s0201 45 mg
Reporting group description:	
ND-L02-s0201: 45 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	
Reporting group title	ND-L02-s0201 90 mg
Reporting group description:	
ND-L02-s0201: 90 mg intravenous administration every 2 weeks (± 4 days for Visit 3 or ± 7 days for Visits 4 to 13, ensuring a minimum of 7 days between each dose) for a total of 12 doses.	

Serious adverse events	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 42 (21.43%)	4 / 41 (9.76%)	6 / 40 (15.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	0 / 40 (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
Prostate cancer			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Anastomotic haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	0 / 40 (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
Infusion related reaction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cervical radiculopathy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	0 / 40 (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
Encephalopathy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thalamic infarction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Vascular stent stenosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diverticulum			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Idiopathic pulmonary fibrosis			

subjects affected / exposed	4 / 42 (9.52%)	0 / 41 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	0 / 40 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 41 (2.44%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
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	Placebo	ND-L02-s0201 45 mg	ND-L02-s0201 90 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 42 (83.33%)	37 / 41 (90.24%)	37 / 40 (92.50%)
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Fatigue			
subjects affected / exposed	3 / 42 (7.14%)	3 / 41 (7.32%)	5 / 40 (12.50%)
occurrences (all)	3	3	5
Infusion site reaction			
subjects affected / exposed	1 / 42 (2.38%)	6 / 41 (14.63%)	2 / 40 (5.00%)
occurrences (all)	1	6	3
Oedema peripheral			
subjects affected / exposed	1 / 42 (2.38%)	1 / 41 (2.44%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Pain			
subjects affected / exposed	2 / 42 (4.76%)	0 / 41 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	2	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 42 (21.43%)	4 / 41 (9.76%)	6 / 40 (15.00%)
occurrences (all)	12	4	7
Dyspnoea			
subjects affected / exposed	5 / 42 (11.90%)	4 / 41 (9.76%)	3 / 40 (7.50%)
occurrences (all)	7	4	3
Hypoxia			
subjects affected / exposed	4 / 42 (9.52%)	0 / 41 (0.00%)	0 / 40 (0.00%)
occurrences (all)	6	0	0
Idiopathic pulmonary fibrosis			
subjects affected / exposed	4 / 42 (9.52%)	3 / 41 (7.32%)	4 / 40 (10.00%)
occurrences (all)	5	3	4
Rhinorrhoea			

subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	2 / 40 (5.00%)
occurrences (all)	0	1	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	3 / 40 (7.50%)
occurrences (all)	1	0	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	3 / 40 (7.50%)
occurrences (all)	0	1	3
Lipase increased			
subjects affected / exposed	0 / 42 (0.00%)	2 / 41 (4.88%)	1 / 40 (2.50%)
occurrences (all)	0	2	1
Weight decreased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 42 (0.00%)	2 / 41 (4.88%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	3 / 42 (7.14%)	0 / 41 (0.00%)	0 / 40 (0.00%)
occurrences (all)	4	0	0
Infusion related reaction			
subjects affected / exposed	3 / 42 (7.14%)	14 / 41 (34.15%)	19 / 40 (47.50%)
occurrences (all)	4	46	56
Nervous system disorders			
Dizziness			

subjects affected / exposed	2 / 42 (4.76%)	1 / 41 (2.44%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
Headache			
subjects affected / exposed	3 / 42 (7.14%)	4 / 41 (9.76%)	3 / 40 (7.50%)
occurrences (all)	3	7	3
Hypoaesthesia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Presyncope			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 42 (0.00%)	2 / 41 (4.88%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 42 (2.38%)	1 / 41 (2.44%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Diarrhoea			
subjects affected / exposed	2 / 42 (4.76%)	2 / 41 (4.88%)	1 / 40 (2.50%)
occurrences (all)	5	2	2
Nausea			
subjects affected / exposed	2 / 42 (4.76%)	4 / 41 (9.76%)	2 / 40 (5.00%)
occurrences (all)	2	4	2
Vomiting			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 42 (2.38%)	3 / 41 (7.32%)	1 / 40 (2.50%)
occurrences (all)	1	3	1
Rash			
subjects affected / exposed	2 / 42 (4.76%)	1 / 41 (2.44%)	3 / 40 (7.50%)
occurrences (all)	2	1	5
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 42 (4.76%)	1 / 41 (2.44%)	2 / 40 (5.00%)
occurrences (all)	3	1	2
Back pain			
subjects affected / exposed	5 / 42 (11.90%)	3 / 41 (7.32%)	3 / 40 (7.50%)
occurrences (all)	5	3	3
Muscle spasms			
subjects affected / exposed	2 / 42 (4.76%)	0 / 41 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	2 / 40 (5.00%)
occurrences (all)	0	1	2
COVID-19			
subjects affected / exposed	2 / 42 (4.76%)	1 / 41 (2.44%)	3 / 40 (7.50%)
occurrences (all)	2	1	3
Gastroenteritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	3 / 41 (7.32%)	1 / 40 (2.50%)
occurrences (all)	0	3	1
Sinusitis			
subjects affected / exposed	2 / 42 (4.76%)	0 / 41 (0.00%)	2 / 40 (5.00%)
occurrences (all)	2	0	2
Upper respiratory tract infection			
subjects affected / exposed	5 / 42 (11.90%)	2 / 41 (4.88%)	2 / 40 (5.00%)
occurrences (all)	5	2	2
Urinary tract infection			
subjects affected / exposed	2 / 42 (4.76%)	1 / 41 (2.44%)	0 / 40 (0.00%)
occurrences (all)	3	2	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 41 (4.88%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			

subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2	1 / 41 (2.44%) 1	0 / 40 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2018	Global Amendment: A combination toxicity study was completed in rats with ND-L02-s0201 and nintedanib. • The risk language was updated to include results from this study. Changes were incorporated based on feedback from the Sponsor and clinical team. • Updated exclusion criterion #12 to remove "full-dose anticoagulant therapy or high-dose antiplatelet therapy." • Clarified that the GAP staging assessment was a calculated factor that would be performed by the statistician. • Clarified the timing of the ECG collection at Visits 4 and 8. • Clarified that if a historical HRCT was available, it was to be submitted for overread to determine preliminary eligibility prior to the subject's Visit 1b HRCT. • Clarified that all subjects that met preliminary eligibility criteria were to have an HRCT scan at Visit 1b. • Added guidance for study staff on how to manage unblinding if a subject experienced an IRR. • Added RR to the list of ECG intervals. • Clarified that grading of AE severity was to use NCI CTCAE v5.0.
08 July 2019	Global Amendment: Updated based on comments received from FDA on 14 March 2018 and 20 April 2018. • Allowing dose adjustments or discontinuation of standard care as needed. • Allowing patients to start standard care after completing another treatment. • Adding ADA samples at Days 15 and 29. • Collecting a tryptase blood sample at the beginning. • Only allowing withdrawal if a subject withdraws consent. • Clarifying study withdrawal and data prevention steps. • Banking remaining ADA test samples. • Monitoring subjects with positive ADA until titers return to baseline.
18 September 2019	Global Amendment: Aligned the frequency of pregnancy tests with the CTFG guidelines and updated the protocol with respect to several minor issues. • Added urine pregnancy tests to Visits 4, 8, 12, and 15 (Days 29, 85, 141, and 197). • During treatment, pregnancy tests were performed every 4 weeks. After treatment, pregnancy tests were performed 2, 6, and 12 weeks after the last infusion. • Clarified when a second HRCT was required in the event of a rescreen. • Expanded the list of public clinical trial databases to include the US, Europe, and Japan.

17 June 2020	Global Amendment: Provided guidance to investigators regarding clinical trial conduct during outbreaks/pandemics resulting from SARS-CoV-2 infections. The guidance is based safety measures taken due to the COVID-19 pandemic. • Added cross references to Appendix F (Section 18.6) where guidance on clinical trial conduct relating COVID-19 was presented. • Clarified that the sample size of 40 subjects per treatment arm was approximate. • Added exclusion criterion for SARS-CoV-2 positive test. • Stated that additional sensitivity analyses were to be performed due to the COVID-19 pandemic in accordance with regulatory guidelines. • Stated that an HRCT was not required for subjects who terminated the study early and received <5 doses. • Stated that if a subject had an HRCT scan performed due to medical indication, the Investigator should consider whether to include it as an unscheduled scan or as the Visit 14/ET scan. • Changed the timing of the second and third scheduled DMC meetings to: o After 50% of subjects completed Visit 4 (Day 29) o After 75% of subjects completed Visit 8 (Day 85) • Indicated that subjects whose participation in the study was affected by restrictions relating to COVID-19, may be replaced. • Included guidance on how to conduct remote monitoring in accordance with the remote monitoring plan if onsite monitoring was not possible. • Added an appendix that provides guidelines for investigators for how to deal with restrictions relating to COVID-19.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported