Clinical trial results:
A Phase 2b, Randomized, Multicenter, Double-Blind, Placebo-Controlled, Multiple-Dose Study to Evaluate the Efficacy, Safety, and Tolerability of NDI-034858 in Subjects with Active Psoriatic Arthritis

Summary

EudraCT number	2021-005888-52
Trial protocol	CZ
Global end of trial date	02 June 2023

Results information

Result version number	v1 (current)
This version publication date	19 May 2024
First version publication date	19 May 2024

Trial information

Trial identification

Sponsor protocol code	4858-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05153148
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.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	02 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to assess the effect of TAK-279 at different doses on the rheumatological signs, symptoms, and function in participants with active psoriatic arthritis (PsA).

Protection of trial subjects:

Each participant signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 58
Country: Number of subjects enrolled	Poland: 167
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Czechia: 40
Worldwide total number of subjects	290
EEA total number of subjects	232

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)	255
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 45 investigative sites in the United States (US), Germany, Poland, and the Czech Republic from 6 January 2022 to 2 June 2023.

Pre-assignment

Screening details:

A total of 305 participants with a diagnosis of psoriatic arthritis were enrolled in a 1:1:1:1 ratio to receive either one of the 3 doses of NDI-034858 or placebo.

Pre-assignment period milestones

Number of subjects started	305[1]
Number of subjects completed	290

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Withdrawal by Subject: 8
Reason: Number of subjects	Other: 3
Reason: Number of subjects	Randomized Without Dosing due to Ineligibility: 2
Reason: Number of subjects	Lost to Follow-up: 1
Reason: Number of subjects	Coronavirus Disease 2019 (COVID-19): 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: Of the 305 subjects, only 290 were randomized and received at least one dose of the study drug.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo capsules, orally, once daily (QD) for 12 weeks.

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

Dosage and administration details:

NDI-034858 placebo-matching oral capsules

Arm title	NDI-034858 Low Dose

Arm description:

Participants received low dose of NDI-034858, capsules, orally, QD for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	NDI-034858
Investigational medicinal product code	
Other name	TAK-279
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
NDI-034858 oral capsules

Arm title	NDI-034858 Medium Dose

Arm description:
Participants received medium dose of NDI-034858, capsules, orally, QD for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	NDI-034858
Investigational medicinal product code	
Other name	TAK-279
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
NDI-034858 oral capsules

Arm title	NDI-034858 High Dose

Arm description:
Participants received high dose of NDI-034858, capsules, orally, QD for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	NDI-034858
Investigational medicinal product code	
Other name	TAK-279
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
NDI-034858 oral capsules

Number of subjects in period 1	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose
Started	72	71	75
Completed	64	61	62
Not completed	8	10	13
Adverse Event	4	6	7
Other	-	-	-
Withdrawal by Subject	3	4	4
Lost to follow-up	1	-	2

Number of subjects in period 1	NDI-034858 High Dose
Started	72
Completed	58
Not completed	14
Adverse Event	9
Other	1

Withdrawal by Subject	4
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo capsules, orally, once daily (QD) for 12 weeks.	
Reporting group title	NDI-034858 Low Dose
Reporting group description:	
Participants received low dose of NDI-034858, capsules, orally, QD for 12 weeks.	
Reporting group title	NDI-034858 Medium Dose
Reporting group description:	
Participants received medium dose of NDI-034858, capsules, orally, QD for 12 weeks.	
Reporting group title	NDI-034858 High Dose
Reporting group description:	
Participants received high dose of NDI-034858, capsules, orally, QD for 12 weeks.	

Reporting group values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose
Number of subjects	72	71	75
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	49.7	48.3	52.5
standard deviation	± 11.83	± 10.43	± 12.15
Gender categorical Units: Subjects			
Female	37	40	46
Male	35	31	29
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	1	4
Not Hispanic or Latino	70	69	71
Unknown or Not Reported	0	1	0
Race/Ethnicity, Customized Units: Subjects			
White White	69	66	71
Non-white Non-white	1	3	4
Missing Missing	2	2	0
Height Units: centimeters (cm)			
arithmetic mean	170.3	170.1	169.0
standard deviation	± 10.65	± 8.67	± 9.04
Body Mass Index (BMI)			
BMI = weight (kg)/[height (m)^2]			
Units: kilograms per meter square (kg/m^2)			
arithmetic mean	29.48	29.78	30.04
standard deviation	± 6.865	± 8.153	± 7.937

Weight			
Units: kilograms (kg)			
arithmetic mean	86.26	86.97	85.85
standard deviation	± 25.307	± 26.611	± 22.048

Reporting group values	NDI-034858 High Dose	Total	
Number of subjects	72	290	
Age Categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	49.0		
standard deviation	± 11.51	-	
Gender categorical			
Units: Subjects			
Female	43	166	
Male	29	124	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	9	
Not Hispanic or Latino	70	280	
Unknown or Not Reported	0	1	
Race/Ethnicity, Customized			
Units: Subjects			
White White	69	275	
Non-white Non-white	3	11	
Missing Missing	0	4	
Height			
Units: centimeters (cm)			
arithmetic mean	170.4		
standard deviation	± 9.06	-	
Body Mass Index (BMI)			
BMI = weight (kg)/[height (m)^2]			
Units: kilograms per meter square (kg/m^2)			
arithmetic mean	30.15		
standard deviation	± 6.610	-	
Weight			
Units: kilograms (kg)			
arithmetic mean	87.74		
standard deviation	± 20.152	-	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo capsules, orally, once daily (QD) for 12 weeks.	
Reporting group title	NDI-034858 Low Dose
Reporting group description:	
Participants received low dose of NDI-034858, capsules, orally, QD for 12 weeks.	
Reporting group title	NDI-034858 Medium Dose
Reporting group description:	
Participants received medium dose of NDI-034858, capsules, orally, QD for 12 weeks.	
Reporting group title	NDI-034858 High Dose
Reporting group description:	
Participants received high dose of NDI-034858, capsules, orally, QD for 12 weeks.	

Primary: Percentage of Participants who Achieved at Least an American College of Rheumatology 20 (ACR20) Response at Week 12

End point title	Percentage of Participants who Achieved at Least an American College of Rheumatology 20 (ACR20) Response at Week 12

End point description:

ACR20 is composite measure defined as improvement of 20 percent(%) from baseline in both number of tender (68) & number of swollen (66) joints & a 20% improvement in at least 3 of following 5 criteria: patient global assessment of psoriatic arthritis (PGA-PsA) [visual analog scale (VAS) where, 0=very good, no symptoms & 100=very poor, severe symptoms], physician global assessment of psoriatic arthritis (PhGA-PsA) [(VAS) where 0=no disease activity & 100=maximum disease activity], patient global assessment of psoriatic arthritis pain (PGAAP) [(VAS) where 0=no pain & 100=most severe pain], disability history questionnaire i.e., Health Assessment Questionnaire-Disability Index [HAQ-DI] (20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip & activities, 0=without difficulty to 3=unable to do) & acute phase reactant like high sensitivity C-reactive protein [hsCRP]). Percentages are rounded off to the nearest decimal.

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	71	75	72
Units: percentage of participants				
number (confidence interval 95%)	29.2 (18.7 to 39.7)	35.2 (24.1 to 46.3)	53.3 (42.0 to 64.6)	54.2 (42.7 to 65.7)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.446
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	21.1

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	9
upper limit	39.9

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.6
upper limit	39.6

Secondary: Percentage of Participants who Achieved at Least an ACR-50 Response at Week 12

End point title	Percentage of Participants who Achieved at Least an ACR-50 Response at Week 12

End point description:

The ACR-50 is a composite measure defined as improvement of 50% from baseline in both the number of tender (68) and number of swollen (66) joints, and a 50% improvement in at least three of the following five criteria: PGA-PsA (VAS where, 0 is 'very good, no symptoms' and 100 is 'very poor, severe symptoms'), PhGA-PsA [(VAS) where 0=no disease activity and 100=maximum disease activity], PGAAP [(VAS) where 0=no pain & 100=most severe pain], disability history questionnaire (i.e., HAQ-DI) [20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do] and an acute phase reactant [i.e., erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)]. Percentages are rounded off to the nearest decimal. Full Analysis Set included all randomised participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	71	75	72
Units: percentage of participants				
number (confidence interval 95%)	9.7 (2.9 to 16.6)	15.5 (7.1 to 23.9)	26.7 (16.7 to 36.7)	26.4 (16.2 to 36.6)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.312
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	16.6

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	28.6

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	29.1

Secondary: Percentage of Participants who Achieved at Least an ACR-70 Response at Week 12

End point title	Percentage of Participants who Achieved at Least an ACR-70 Response at Week 12

End point description:

The ACR-70 is a composite measure defined as improvement of 70% from baseline in both the number of tender (68) and number of swollen (66) joints, and a 70% improvement in at least three of the following five criteria: PGA-PsA (VAS where, 0 is 'very good, no symptoms' and 100 is 'very poor, severe symptoms'), PhGA-PsA [(VAS) where 0=no disease activity and 100=maximum disease activity], PGAAP [(VAS) where 0=no pain & 100=most severe pain], disability history questionnaire (i.e., HAQ-DI) [20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities, 0=without difficulty to 3=unable to do] and an acute phase reactant (i.e., ESR or CRP). Percentages are rounded off to the nearest decimal. Full Analysis Set included all randomised participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	71	75	72
Units: percentage of participants				
number (confidence interval 95%)	5.6 (1.5 to 13.6)	8.5 (2.0 to 14.9)	14.7 (6.7 to 22.7)	13.9 (5.9 to 21.9)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.532
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	12.7

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.158
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	19.4

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo

Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.101
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	20.1

Secondary: Change From Baseline in Tender Joint Count (TJC) at Week 12

End point title	Change From Baseline in Tender Joint Count (TJC) at Week 12

End point description:

The TJC 68 is a total score of points assigned for the presence of tenderness in the 68 joints in the upper body and upper/lower extremity. The response to tenderness for each joint was evaluated using the following scale: 'Present' was assigned a score of 1 whereas, 'Absent', 'Not Done', 'Not Applicable', or joints with missing response were assigned a score of 0. The sum of all tender joints was derived. The overall tender joint count ranged from 0 to 68, with a higher score indicating a greater degree of tenderness. A negative change from baseline indicates improvement. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	64	63
Units: tender joints				
least squares mean (standard error)	-5.9 (± 1.12)	-7.6 (± 1.12)	-8.9 (± 1.12)	-8.3 (± 1.15)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.268
Method	Mixed Model Repeated Measure (MMRM)
Parameter estimate	Treatment Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	1.3

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	0.6

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	0

Secondary: Change From Baseline in Swollen Joint Count (SJC) at Week 12

End point title	Change From Baseline in Swollen Joint Count (SJC) at Week 12

End point description:

The SJC 66 (TJC 68 joint assessment minus hip joints, which cannot be assessed for swelling) is a total score of points assigned for presence of swelling in the 66 joints in the upper body and upper/lower extremity. The response to swelling for each joint was evaluated using the following scale: 'Present' was assigned a score of 1 whereas, 'Absent', 'Not Done', 'Not Applicable', or joints with missing response were assigned a score of 0. The sum of all swollen joints was derived. The overall swollen joint count ranged from 0 to 66, with a higher score indicating a greater degree of swelling. A negative change from baseline indicates improvement. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	64	63
Units: swollen joints				
least squares mean (standard error)	-3.9 (± 0.57)	-4.8 (± 0.58)	-5.0 (± 0.58)	-5.0 (± 0.59)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.7

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.177
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.5

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.196
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.5

Secondary: Change From Baseline in PGA-PsA at Week 12

End point title	Change From Baseline in PGA-PsA at Week 12

End point description:

Participants assessed their overall disease status based on symptoms of psoriasis and psoriatic arthritis at the time of the visit using the PGA-PsA VAS of 100 millimeters (mm) which ranges from 0 (very good, no symptoms) to 100 (very poor, severe symptoms). A negative change from Baseline indicates improvement in symptoms. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	65	63	62
Units: mm				
least squares mean (standard error)	-11.1 (± 2.85)	-12.9 (± 2.84)	-20.2 (± 2.85)	-19.8 (± 2.92)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.637
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	5.9

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.5
upper limit	-0.9

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17
upper limit	-1.4

Secondary: Change From Baseline in PGAAP at Week 12

End point title	Change From Baseline in PGAAP at Week 12

End point description:

Participants assessed their overall psoriatic arthritis-related pain at the time of the visit using the PGAAP VAS of 100 mm which ranges from 0 (no pain) to 100 (most severe pain). A negative change from Baseline indicates improvement in pain. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	65	63	62
Units: mm				
least squares mean (standard error)	-12.1 (± 2.75)	-13.0 (± 2.74)	-18.8 (± 2.75)	-18.4 (± 2.82)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.812
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	6.6

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.102
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	1.3

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.079
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.2
upper limit	0.8

Secondary: Change From Baseline in PhGA-PsA at Week 12

End point title	Change From Baseline in PhGA-PsA at Week 12

End point description:

The participants' overall disease status was assessed, taking into account signs, symptoms, and function, of all components of joint and skin affected at the time of the visit and this overall status was rated by the investigator using the PhGA-PsA VAS of 100 mm where 0 is 'very good, asymptomatic, and no limitation of normal activities' and 100 is 'very poor, very severe symptoms which are intolerable, and inability to carry out all normal activities'. A negative change from Baseline indicates improvement in symptoms. Full Analysis Set included all randomised participants who received at least one dose of

study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary
End point timeframe: Baseline, Week 12	

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	66	64	63
Units: mm				
least squares mean (standard error)	-20.7 (± 2.66)	-29.6 (± 2.65)	-31.3 (± 2.65)	-31.6 (± 2.73)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-8.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.2
upper limit	-1.7

Statistical analysis title	NDI-034858 High Dose vs Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	-3.6

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-10.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.8
upper limit	-3.4

Secondary: Change From Baseline in HAQ-DI Total Score at Week 12

End point title	Change From Baseline in HAQ-DI Total Score at Week 12

End point description:

The HAQ-DI consists of 20 questions referring to 8 domains consisting of dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. Each item is scored from 0 (without any difficulty) to 3 (unable to do). The worst score within each domain will be used as domain score (i.e., if score for 1 question is 1 and 2 for other, then worst score for the domain is 2). The HAQ-DI total score is calculated by dividing the sum of the domain scores by the number of non-missing domains. The total score indicates the patient's self-assessed level of functional ability and higher scores indicate worse functional ability. The HAQ-DI total score ranges from 0 to 3. A higher score indicates worse function and greater disability. A negative change from Baseline indicates improved function. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	64	63
Units: score on a scale				
least squares mean (standard error)	-0.22 (± 0.053)	-0.29 (± 0.053)	-0.32 (± 0.053)	-0.28 (± 0.055)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.357
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.08

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.467
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.09

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.195
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.05

Secondary: Change From Baseline in Dactylitis Count (DC) at Week 12

End point title	Change From Baseline in Dactylitis Count (DC) at Week 12

End point description:

Tender score (0 = no tenderness, 1 = tender, 2 = tender and wince, 3 = tender and withdraw) is collected for Dactylitis Assessments on the Dactylitis Score Sheet that is used for calculation of total score. DC equals the number of tender fingers and toes (tender score >0). For participants with dactylitis status absent for all the fingers and toes, the DC is set as 0. The total score range of DC is from 0 to 60, higher scores indicate greater presence of dactylitis. A negative change from baseline indicates improvement. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	12	14
Units: dactylitis count				
least squares mean (standard error)	-2.1 (± 0.39)	-0.8 (± 0.41)	-2.0 (± 0.47)	-1.9 (± 0.41)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	2.4

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.3

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.758
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.3

Secondary: Change From Baseline in Leeds Enthesitis Index (LEI) at Week 12

End point title	Change From Baseline in Leeds Enthesitis Index (LEI) at Week 12

End point description:

Enthesitis is assessed using LEI. The enthesitis examination by LEI evaluates the presence or absence of pain by applying local pressure on 6 anatomical sites: medial femoral condyle (left and right), lateral epicondyle (left and right), and the achilles tendon insertion (left and right). Enthesitis at each site is scored as 0 (enthesitis absent) and 1 (enthesitis present). LEI is derived as the sum of the enthesitis score over the 6 sites, divided by the number of sites with non-missing score. The total score ranges from 0 to 6, higher scores indicate greater degree of enthesitis. A negative change from baseline indicates improvement. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants who had a baseline LEI score of ≥1 and with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	33	34	31
Units: score on a scale				
least squares mean (standard error)	-0.9 (± 0.24)	-1.4 (± 0.24)	-1.6 (± 0.24)	-1.0 (± 0.25)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.131
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.2

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.687
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.5

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.043
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0

Secondary: Percentage of Participants With Minimal Disease Activity (MDA) Response at Week 12

End point title	Percentage of Participants With Minimal Disease Activity (MDA) Response at Week 12

End point description:

MDA is a measure to indicate a state of minimal disease activity, and is a composite score of 7 domains. A participant is considered as having achieved the MDA if the participant fulfills at least 5 of the following 7 criteria: TJC 68 ≤1; SJC 66 ≤1; Psoriasis area and severity index (PASI) score ≤1 [The total score ranges from 0 (no disease) to 72 (maximal disease)] or body surface area (BSA) ≤3%; PGAAP ≤15 [using VAS on a scale of 0 (no pain) to 100 (serious pain)]; PGA-PsA ≤20 [using VAS on a scale of 0 (very well) to 100 (very poor)]; HAQ-DI score ≤0.5; LEI score ≤1. Percentages are rounded off to the nearest decimal. Full Analysis Set included all randomised participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	71	75	72
Units: percentage of participants				
number (confidence interval 95%)	12.5 (4.9 to 20.1)	18.3 (9.3 to 27.3)	28.0 (17.8 to 38.2)	29.2 (18.7 to 39.7)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose

Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.349
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	17.4

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	29.3

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	15.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	28.3

Secondary: Change From Baseline in Disease Activity Index for Psoriatic Arthritis

(DAPSA) at Week 12	
End point title	Change From Baseline in Disease Activity Index for Psoriatic Arthritis (DAPSA) at Week 12

End point description:

The DAPSA score is a composite score and was calculated using: TJC68, SJC66, PGA-PsA, PGAAP, and hsCRP level (milligram per deciliter [mg/dL]). DAPSA scores 0-4 = remission, 5-14 = low disease activity, 15-28 = moderate disease activity, and >28 = high disease activity. The DAPSA score has a lower bound of 0 and has no upper bound. A higher DAPSA score indicated more active disease activity. A negative change from baseline indicates improvement. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	64	63	62
Units: score on a scale				
least squares mean (standard error)	-11.56 (± 1.948)	-15.30 (± 1.946)	-17.99 (± 1.943)	-16.79 (± 1.989)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.167
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-3.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.04
upper limit	1.57

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose

Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-6.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.73
upper limit	-1.13

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.056
Method	MMRM
Parameter estimate	Treatment Difference
Point estimate	-5.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.59
upper limit	0.13

Secondary: Percentage of Participants Who Achieved PASI-75 Response at Week 12

End point title	Percentage of Participants Who Achieved PASI-75 Response at Week 12

End point description:

PASI-75 is assessed in participants with psoriasis involvement for ≥3% of BSA at Baseline & assesses extent of involvement & severity of psoriasis. To calculate PASI, the body is divided into 4 regions: head & neck, trunk, upper limbs, & lower limbs. Each of these areas are assessed separately for percentage of area involved & for erythema, induration, & scaling, which are each rated on a scale of 0-4, which translates to numeric score that ranges from 0 (indicates no involvement) to 6 (90% to 100% involvement). PASI produces numeric score that can range from 0 (no disease) to 72 (maximal disease). For PASI-75, improvement threshold from baseline in PASI score is 75%. Higher score indicates more severe disease. Percentages are rounded off to nearest decimal. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analysed is number of participants with psoriasis covering ≥ 3% of BSA at Baseline and with available data.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	46	46
Units: percentage of participants				
number (confidence interval 95%)	15.4 (4.1 to 26.7)	25.6 (11.9 to 39.3)	28.3 (15.2 to 41.3)	45.7 (31.3 to 60.0)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.186
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	29.4

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.5
upper limit	47.6

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.101
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	32.1

Secondary: Percentage of Participants Who Achieved a Physician Global Assessment of Psoriasis (PhGA-PsO) of 0 or 1 and at Least a 2-point Improvement at Week 12

End point title	Percentage of Participants Who Achieved a Physician Global Assessment of Psoriasis (PhGA-PsO) of 0 or 1 and at Least a 2-point Improvement at Week 12

End point description:

PhGA-PsO responder is defined as participants 1) who had PhGA-PsO score of 0 or 1 at any given post-baseline visit; and 2) who had at least 2-point improvement from baseline. The PhGA-PsO is measured using a 0 to 4 scale with a 0 meaning clear or a 4 meaning severe. The proportion of participants achieving PhGA-PsO response at Week 12 was calculated and analyzed for participants with a score of at least 2 at baseline. Percentages are rounded off to the nearest decimal. Full Analysis Set included all randomised participants who received at least one dose of study drug. Number of subjects analyzed is the number of participants with PhGA-PSO ≥2 at Baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	54	63	58
Units: percentage of participants				
number (confidence interval 95%)	15.8 (6.3 to 25.3)	20.4 (9.6 to 31.1)	20.6 (10.6 to 30.6)	32.8 (20.7 to 44.8)

Statistical analyses

Statistical analysis title	NDI-034858 Low Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Low Dose

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.54
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	19

Statistical analysis title	NDI-034858 High Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 High Dose
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.034
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	31.3

Statistical analysis title	NDI-034858 Medium Dose vs. Placebo
Comparison groups	Placebo v NDI-034858 Medium Dose
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.466
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	19.3

Secondary: Number of Participants With Treatment-Emergent Adverse Events

(TEAEs), Serious Adverse Events (SAEs) and Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Adverse Events of Special Interest (AESIs)

End point description:

Adverse Event(AE)=medical occurrence that does not necessarily have a causal relationship with this drug also including clinically meaningful findings in laboratory safety tests,vital signs,weight,and electrocardiogram(ECG).TEAEs=AEs occurring at time of or post study drug dosing until study end.SAE=any medical occurrence at any dose that resulted in death,was life-threatening,required inpatient hospitalization/prolongation of existing hospitalization,resulted in persistent or significant disability/incapacity,was a congenital abnormality/birth defect,an important medical event.AESIs included Common Terminology Criteria for Adverse Events(CTCAE)Grade≥2 cytopenia,CTCAE Grade≥3 elevation of creatine phosphokinase(CPK)[clinically significant or not]defined as CPK>5xupper limit of normal(ULN),infections,adverse events of abnormal liver function tests,adverse events of renal dysfunction,major adverse cardiovascular events,thromboembolic events,gastrointestinal perforation,and malignancies.

End point type	Secondary

End point timeframe:

From first dose of study drug up to end of study (up to Week 16)

End point values	Placebo	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	71	75	72
Units: participants				
TEAEs	39	42	45	56
SAEs	4	4	3	2
AESIs	19	33	22	38

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of NDI-034858

End point title	Plasma Concentration of NDI-034858[1]

End point description:

Plasma concentration of NDI-034858 was measured in participants who received low, medium, or high dose of NDI-034858. Pharmacokinetic (PK) Analysis Set included all participants in the Safety Analysis Set with at least one evaluable post-dose PK assessment. Number analysed is the number of participants with data available for analysis at the specified time point.

End point type	Secondary

End point timeframe:

Pre-dose, 1 hour post-dose on Day 1 and Week 4, 4 hours post-dose at Week 4, Pre-dose at Week 8, and anytime at Week 12

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for NDI-034858 arms only.

End point values	NDI-034858 Low Dose	NDI-034858 Medium Dose	NDI-034858 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	75	72	
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (n=66,75,71)	0.000 (± 0.000)	0.000 (± 0.000)	0.000 (± 0.000)	
Day 1: 1 hour (n=71,74,72)	5.860 (± 7.251)	25.43 (± 37.21)	38.32 (± 59.74)	
Week 4: Pre-dose (n=67,66,65)	25.26 (± 17.95)	82.11 (± 74.46)	187.5 (± 140.9)	
Week 4: 1 hour (n=64,61,62)	33.03 (± 24.05)	112.8 (± 81.19)	245.3 (± 184.6)	
Week 4: 4 Hours (n=64,61,61)	46.68 (± 25.85)	149.5 (± 90.56)	370.1 (± 178.4)	
Week 8: Pre-dose (n=67,67,62)	26.99 (± 21.00)	78.29 (± 69.37)	209.4 (± 182.0)	
Week 12: Any Time (n=61,61,58)	24.85 (± 20.58)	66.17 (± 51.81)	178.2 (± 149.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug up to end of study (up to Week 16)	
Adverse event reporting additional description:	
All-cause Mortality: all enrolled participants. SAEs and Other AEs: Safety Analysis Set included all randomized participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo capsules, orally, QD for 12 weeks.	
Reporting group title	NDI-034858 High Dose
Reporting group description:	
Participants received high dose of NDI-034858, capsules, orally, QD for 12 weeks.	
Reporting group title	NDI-034858 Medium Dose
Reporting group description:	
Participants received medium dose of NDI-034858, capsules, orally, QD for 12 weeks.	
Reporting group title	NDI-034858 Low Dose
Reporting group description:	
Participants received low dose of NDI-034858, capsules, orally, QD for 12 weeks.	

Serious adverse events	Placebo	NDI-034858 High Dose	NDI-034858 Medium Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 72 (5.56%)	2 / 72 (2.78%)	3 / 75 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal adenocarcinoma			
subjects affected / exposed	1 / 72 (1.39%)	0 / 72 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 72 (0.00%)	0 / 72 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Coronary artery disease			
subjects affected / exposed	0 / 72 (0.00%)	0 / 72 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 72 (0.00%)	1 / 72 (1.39%)	0 / 75 (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
Gastrointestinal disorders			
Gastrointestinal inflammation			
subjects affected / exposed	0 / 72 (0.00%)	0 / 72 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 72 (0.00%)	0 / 72 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	1 / 72 (1.39%)	0 / 72 (0.00%)	0 / 75 (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
Osteoarthritis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 72 (0.00%)	0 / 75 (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
Arthritis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 72 (0.00%)	0 / 75 (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
Infections and infestations			
Cellulitis			

subjects affected / exposed	0 / 72 (0.00%)	0 / 72 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 72 (1.39%)	0 / 75 (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 tract infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 72 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	NDI-034858 Low Dose		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 71 (5.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Bell's palsy			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal inflammation			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	NDI-034858 High Dose	NDI-034858 Medium Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 72 (18.06%)	35 / 72 (48.61%)	27 / 75 (36.00%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 72 (4.17%)	1 / 72 (1.39%)	4 / 75 (5.33%)
occurrences (all)	3	1	4
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 72 (4.17%)	4 / 72 (5.56%)	6 / 75 (8.00%)
occurrences (all)	3	6	6
Gastrointestinal disorders			
Aphthous ulcer			
subjects affected / exposed	0 / 72 (0.00%)	6 / 72 (8.33%)	1 / 75 (1.33%)
occurrences (all)	0	7	1
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 72 (0.00%)	6 / 72 (8.33%)	2 / 75 (2.67%)
occurrences (all)	0	7	4
Dermatitis allergic			
subjects affected / exposed	0 / 72 (0.00%)	4 / 72 (5.56%)	1 / 75 (1.33%)
occurrences (all)	0	5	1
Rash			
subjects affected / exposed	0 / 72 (0.00%)	4 / 72 (5.56%)	6 / 75 (8.00%)
occurrences (all)	0	4	6
Rash maculo-papular			

subjects affected / exposed	0 / 72 (0.00%)	4 / 72 (5.56%)	2 / 75 (2.67%)
occurrences (all)	0	5	4
Rash papular			
subjects affected / exposed	0 / 72 (0.00%)	4 / 72 (5.56%)	3 / 75 (4.00%)
occurrences (all)	0	4	3
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	4 / 72 (5.56%)	1 / 72 (1.39%)	2 / 75 (2.67%)
occurrences (all)	5	1	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 72 (4.17%)	7 / 72 (9.72%)	7 / 75 (9.33%)
occurrences (all)	4	7	7
Upper respiratory tract infection			
subjects affected / exposed	2 / 72 (2.78%)	7 / 72 (9.72%)	3 / 75 (4.00%)
occurrences (all)	3	7	4

Non-serious adverse events	NDI-034858 Low Dose		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 71 (26.76%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	3		
Gastrointestinal disorders			
Aphthous ulcer			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	4		
Rash maculo-papular			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Rash papular			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	6		
Upper respiratory tract infection			
subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2021	The following changes were made as per Amendment 1: 1) Participants with SAEs or severe AEs could be discontinued from study drug regardless of relationship to drug. 2) Added homeopathic medications to the concomitant medications recorded. 3) Clarified that ESRs would be performed at the clinical sites, not the central laboratory. 4) PGA and functional assessment of chronic illness-fatigue (FACIT-F) were described for clarity. 5) Revised stopping rules for potential hepatic laboratory abnormalities.
06 April 2022	The following changes were made as per Amendment 2: 1) Revised statistical analysis methods to include estimand of interest, clarifications for definition of analysis data sets, use of the MH stratum-weighted test. 2) Clarified and defined study objectives and endpoints. 3) Updated inclusion criteria. 4) Updated exclusion criteria. 5) Added footnotes to schedule of activities clarifying the timing of each visit was based on Day 1, allowance for use of a T-Spot. tuberculosis (TB) test (TBT), and timing for AE collection based on Day 1 dosing time. 6) Added information to define the formulation of NDI-034858 used in this study.
05 May 2023	The following changes were made as per Amendment 3: 1) Updated the Sponsor change of address. 2) Updated that NDI-034858 is now also known as TAK-279. 3) Clarified "ACR-50 or ACR-70" secondary endpoints by separating into 2 statements.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported