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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

NIO752

Trial Indication(s)

Progressive Supranuclear Palsy (PSP)

Protocol Number

CNIO752A02101

Protocol Title

A Randomized, Participant, Investigator and Sponsor Blinded, Placebo-Controlled Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Multiple Ascending Doses of Intrathecally Administered NIO752 in Participants with Progressive Supranuclear Palsy

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase I

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Study Start/End Dates

Study Start Date: February 16, 2021 (Actual)
Primary Completion Date: October 17, 2024 (Actual)
Study Completion Date: October 17, 2024 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a phase 1, multi-center, double-blind, placebo-controlled, multiple dose escalation First in Human (FIH) study with NIO752 in PSP participants. A total of 59 PSP participants in 5 treatment groups were randomized to sequentially receive NIO752 or placebo treatment.

Centers

12 centers in 4 countries: Germany(6), Canada(2), United States(3), United Kingdom(1)

Objectives:

Primary objective of the trial was to evaluate the safety and tolerability of repeated intrathecal (IT) administration of NIO752 in participants diagnosed with “probable PSP”.

Secondary objective was to evaluate pharmacokinetics of NIO752 in plasma and cerebrospinal fluid (CSF) of PSP participants after repeated IT injections.

Test Product (s), Dose(s), and Mode(s) of Administration

Intrathecal injections of NIO752 at the following doses:

- Dose A 4x
- Dose B 4x

- Dose C 4x
- Dose D 4x
- Dose E1 4x
- Dose E2 4x

Statistical Methods

The analyses were performed by Novartis and carried out using the most updated SAS version in the GPS environment. For all analysis sets, participants were analyzed according to the study treatment(s) received. The safety analysis set included all participants who received any study drug. The PK analysis set included all participants with at least one available valid (i.e., not flagged for exclusion) PK concentration measurement, who received any study drug and had no protocol deviations that impacted PK data.

The endpoints analyzed for the primary objective included:

- All safety data, including vital signs, ECG parameters, safety laboratory measurements and adverse events.

Descriptive summaries are reported for all the safety endpoints with adverse events summarized as per SoC and PT, severity, seriousness and relatedness.

The endpoints analyzed for the secondary objectives included:

- PK parameters derived from concentrations in plasma
- Concentration in CSF

Dose proportionality was also assessed using the derived PK parameters along with descriptive summaries and related plots.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Signed informed consent

2. Between 40 to 75 years old (inclusive)

3. Have PSP diagnosed for less than 5 years with a current classification of probable PSP Richardson syndrome, a progressive supranuclear palsy rating scale (PSPRS) score < 40 and MOCA score >17 at screening

4. Be able to ambulate independently or able to take at least 5 steps with minimal assistance

5. At least a 12-month history of postural instability or falls within 3 years from disease onset as per medical history

6. Vertical supranuclear gaze palsy, or reduced velocity of vertical saccade

7. Able and willing to meet all study requirements including:

Have a study partner who is reliable, competent, and at least 18 years of age, and will be able to accompany the participant to study visits, be knowledgeable of the participant's ongoing condition during the study to provide study related information to study site when required both in person and via a phone

Reside in a proximity to the study site to allow a timely unscheduled visit if necessary (ideally less than 2 hours)

Able to undergo lumbar puncture (LP), CSF draws and blood draws

8. If the participant is receiving levodopa/carbidopa, levodopa/benserazide, a dopamine agonist, catechol-o-methyltransferase (COMT) inhibitor, rasagiline, CoQ10 or other Parkinson's medications, acetylcholinesterase inhibitors, antipsychotics, memantine, or other non-tau modifying Alzheimer's medication the dose must have been stable for at least 30 days prior to the screening visit and must remain stable for the duration of the study. No such medication can be initiated during the study.

Exclusion Criteria:

1. Live in a skilled nursing facility or dementia care facility

2. Evidence of motor neuron disease, or any other neurological disease that could explain symptoms

3. Clinically significant laboratory abnormality

4. Attempted suicide, suicidal ideation with a plan that required hospital admission within 12 months prior to Screening. In addition, patients deemed by the Investigator to be at significant risk of suicide, major depressive episode, psychosis, confusion state, or

violent behavior should be excluded.

5. A clear and robust benefit from levodopa by history

6. Use of lithium, methylene blue or other putative disease modifying drugs for PSP within 30 days of screening

7. Any previous use of experimental therapy within 30 days or 5 half-lives prior to Day 1, whichever is greater

8. Any condition that increases risk of meningitis unless participant is receiving appropriate prophylactic treatment

9. History of post-lumbar-puncture headache of moderate or severe intensity and/or blood patch

11. Hospitalization for any major medical or surgical procedure involving general anesthesia within 12 weeks of Screening or planned during the study

12. Unable to undergo magnetic resonance imaging (MRI) due to for example claustrophobia, or presents absolute contraindications to MRI (e.g., metallic implants, metallic foreign bodies, pacemaker, defibrillator)

13. Patients with other significant brain MRI abnormalities by history or at screening.

Participant Flow Table

Overall Study

	NIO752 dose A	NIO752 dose B	NIO752 dose C	NIO752 dose D	NIO752 dose E1	NIO752 Dose E2	Pooled Placebo	Total
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E1 via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of matching placebo via lumbar puncture	
Started	3	4	4	9	7	18	14	59
Completed	3	4	4	8	5	14	11	49
Not Completed	0	0	0	1	2	4	3	10

Adverse Event	0	0	0	0	1	1	0	2
Lost to Follow-up	0	0	0	1	0	0	0	1
Subject decision	0	0	0	0	0	3	2	5
Death	0	0	0	0	1	0	1	2

Baseline Characteristics

	NIO752 dose A	**NIO752 dose B**	**NIO752 dose C**	**NIO752 dose D**	**NIO752 dose E1**	**NIO752 Dose E2**	**Pooled Placebo**	**Total**
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E1 via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of matching placebo via lumbar puncture	
Number of Participants [units: participants]	3	4	4	9	7	18	14	59
Baseline Analysis Population Description								
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation								
	69.0±5.29	64.5±2.52	65.3±9.71	66.1±7.20	65.3±5.68	64.9±4.23	67.4±3.48	65.9±5.11
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)								

Female	1	3	2	5	1	9	7	28
Male	2	1	2	4	6	9	7	31
Race (NIH/OMB) (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)								
American Indian or Alaska Native	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	1	1
White	3	4	4	9	7	17	13	57
More than one race	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0
Ethnicity (NIH/OMB) (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)								
Hispanic or Latino	0	0	0	0	0	1	0	1
Not Hispanic or Latino	3	4	4	9	7	17	14	58
Unknown or Not Reported	0	0	0	0	0	0	0	0

Primary Outcome Result(s)

Number of participants with adverse events and serious adverse events

Description: Incidence of AEs and SAEs by treatment group including changes in laboratory values, vital signs, electrocardiograms (ECGs), suicidality ratings and cerebrospinal fluid infection indicators qualifying and reported as AEs. AE grades to characterize the severity of the AEs were

based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5. For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE.

Time Frame: Baseline up to approximately one year (3-month treatment plus 9-month follow-up or 9-month treatment plus 3-month follow-up)

Analysis Population Description: The safety analysis set included all participants that received any study drug.

	NIO752 dose A	NIO752 dose B	NIO752 dose C	NIO752 dose D	NIO752 dose E1	NIO752 Dose E2	Pooled Placebo
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E1 via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of matching placebo via lumbar puncture
Number of Participants Analyzed [units: participants]	3	4	4	9	7	18	14
Number of participants with adverse events and serious adverse events (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
AEs	3 (100%)	4 (100%)	3 (75%)	9 (100%)	7 (100%)	18 (100%)	14 (100%)
AEs of mild intensity	3 (100%)	4 (100%)	3 (75%)	8 (88.89%)	7 (100%)	16 (88.89%)	13 (92.86%)
AEs of moderate intensity	3 (100%)	2 (50%)	3 (75%)	8 (88.89%)	5 (71.43%)	14 (77.78%)	10 (71.43%)
AEs of severe intensity	1 (33.33%)	0 (%)	1 (25%)	6 (66.67%)	3 (42.86%)	4 (22.22%)	4 (28.57%)
Study drug-related AEs	0 (%)	0 (%)	2 (50%)	6 (66.67%)	6 (85.71%)	6 (33.33%)	3 (21.43%)
Serious AEs	1 (33.33%)	0 (%)	1 (25%)	5 (55.56%)	3 (42.86%)	5 (27.78%)	7 (50%)

Fatal AEs	0 (%)	0 (%)	0 (%)	0 (%)	1 (14.29%)	0 (%)	1 (7.14%)
AEs leading to treatment discontinuation	0 (%)	0 (%)	0 (%)	1 (11.11%)	1 (14.29%)	1 (5.56%)	0 (%)
Ae leading to dose adjustment/ interruption	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Secondary Outcome Result(s)

PK parameters: peak blood plasma concentration (Cmax)

Description	The maximum (peak) and trough observed plasma drug concentration after single dose administration (mass × volume-1) based on plasma concentrations of NIO752.
Time Frame	Treatment 1 day 1: Pre-dose and 0.5, 1, 2, 3, 4, 5, 6, 8, 12, 24 hours post IT injection.
Analysis Population Description	The Pharmacokinetics analysis set (PAS) included all participants with at least one available valid PK concentration measurement, who received any study drug and with no protocol deviations with relevant impact on PK data.

	NIO752 dose A	**NIO752 dose B**	**NIO752 dose C**	**NIO752 Dose E1**	**NIO752 dose D**	**NIO752 Dose E2**
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture
Number of Participants Analyzed [units: participants]	3	3	4	18	9	6
PK parameters: peak blood plasma concentration (Cmax) (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	70.9 ± 54.2	337 ± 275	296 ± 374	533 ± 475	1380 ± 901	748 ± 638

PK parameters: time to peak blood plasma concentration (Tmax)

Description	The time to reach maximum (peak) plasma drug concentration after single dose administration (time) based on plasma concentrations of NIO752.
Time Frame	Treatment 1 day 1: Pre-dose and 0.5, 1, 2, 3, 4, 5, 6, 8, 12, 24 hours post IT injection.
Analysis Population Description	The Pharmacokinetics analysis set (PAS) included all participants with at least one available valid PK concentration measurement, who received any study drug and with no protocol deviations with relevant impact on PK data.

	NIO752 dose A	NIO752 dose B	NIO752 dose C	NIO752 Dose E1	NIO752 dose D	NIO752 Dose E2
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture
Number of Participants Analyzed [units: participants]	3	3	4	18	9	6
PK parameters: time to peak blood plasma concentration (Tmax) (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	2.00 (1.02 to 2.08)	1.98 (1.80 to 4.03)	4.96 (1.08 to 23.4)	2.92 (1.02 to 6.15)	3.57 (2.03 to 8.02)	2.93 (2.03 to 24.2)

PK parameters: (AUCinf)

Description	The area under the concentration-time curve (AUC) from time zero to infinity (mass x time x volume-1) based on plasma concentrations of NIO752.
Time Frame	Treatment 1 day 1: Pre-dose and 0.5, 1, 2, 3, 4, 5, 6, 8, 12, 24 hours post IT injection. Day 29, 57, 85, 113, 169, 253, 337, 358.
Analysis Population Description	The Pharmacokinetics analysis set (PAS) included all participants with at least one available valid PK concentration measurement, who received any study drug and with no protocol deviations with relevant impact on PK data.

	NIO752 dose A	NIO752 dose B	NIO752 dose C	NIO752 Dose E1	NIO752 dose D	NIO752 Dose E2
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture
Number of Participants Analyzed [units: participants]	3	3	2	16	8	6
PK parameters: (AUCinf) (units: hours*ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	1440 ± 1320	3250 ± 300	5330 ± 3500	5480 ± 2140	20700 ± 15000	14200 ± 8520

PK parameters: (AUClast)

Description	The area under the concentration-time curve (AUC) from time zero to the last measurable concentration sampling time (tlast) (mass x time x volume-1) based on plasma concentration of NIO752
Time Frame	Treatment 1 day 1: Pre-dose and 0.5, 1, 2, 3, 4, 5, 6, 8, 12, 24 hours post IT injection. Day 29, 57, 85, 113, 169, 253, 337, 358.
Analysis Population Description	The Pharmacokinetics analysis set (PAS) included all participants with at least one available valid PK concentration measurement, who received any study drug and with no protocol deviations with relevant impact on PK data.

	NIO752 dose A	NIO752 dose B	NIO752 dose C	NIO752 Dose E1	NIO752 dose D	NIO752 Dose E2
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture

Number of Participants Analyzed [units: participants]	3	3	4	18	9	6
PK parameters: (AUClast) (units: hours*ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	489 ± 190	2610 ± 890	2900 ± 3060	3900 ± 2530	12000 ± 6320	6630 ± 2920

NIO752 plasma concentrations

Description	Concentrations of NIO752 in blood plasma. Measurements below the limit of quantitation were set to 0.
Time Frame	Treatment 1 day 1: Pre-dose and 0.5, 1, 2, 3, 4, 5, 6, 8, 12, 24 hours post IT injection. Day 14, 29, 57, 85, 113, 169, 253, 337, 358.
Analysis Population Description	The Pharmacokinetics analysis set (PAS) included all participants with at least one available valid PK concentration measurement, who received any study drug and with no protocol deviations with relevant impact on PK data.

	NIO752 dose A	**NIO752 dose B**	**NIO752 dose C**	**NIO752 Dose E1**	**NIO752 dose D**	**NIO752 Dose E2**
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture
Number of Participants Analyzed [units: participants]	3	3	4	18	9	6
NIO752 plasma concentrations (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
day 1 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
day 1 - 0.5h	37.8 ± 30.7	192 ± 248	104 ± 181	196 ± 223	510 ± 518	93.7 ± 82.5
day 1 - 1h	67.7 ± 52.1	250 ± 283	216 ± 292	351 ± 353	561 ± 425	234 ± 189
day 1 - 2h	63.7 ± 56.0	283 ± 313	271 ± 395	477 ± 456	1220 ± 989	544 ± 505

day 1 - 3h	108	236 ± 210	247 ± 389	460 ± 474	1090 ± 983	710 ± 667
day 1 - 4h	42.2 ± 39.7	232 ± 128	239 ± 389	369 ± 340	1190 ± 863	620 ± 515
day 1 - 5h	30.4 ± 24.4	204 ± 110	222 ± 351	285 ± 266	1060 ± 758	496 ± 401
day 1 - 6h	27.4 ± 13.8	182 ± 73.1	167 ± 203	251 ± 218	1040 ± 652	418 ± 316
day 1 - 8h	20.5 ± 5.63	140 ± 55.2	157 ± 144	191 ± 167	737 ± 443	309 ± 161
day 1 - 12h	13.4 ± 5.31	67.6 ± 34.8	94.7 ± 72.1	88.8 ± 42.5	306 ± 141	203 ± 81.3
day 1 - 24h	6.94 ± 6.51	35.9 ± 21.0	48.8 ± 12.3	54.4 ± 28.8	152 ± 53.7	170 ± 100
day 14 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
day 29 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00		0.00 ± 0.00	
day 57 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00		0.00 ± 0.00	
day 85 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
day 113 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00		0.00 ± 0.00	
day 169 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
day 253 - 0h				0.00 ± 0.00		0.00 ± 0.00
day 337 - 0h				0.00 ± 0.00		0.00 ± 0.00
day 358 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00		0.00 ± 0.00	

NIO752 CSF concentrations

Description	Concentrations of NIO752 in cerebrospinal fluid. Measurements below the limit of quantitation were set to 0.
Time Frame	Day 1, 29, 57, 85, 113, 169, 253, 337, 358.
Analysis Population Description	The Pharmacokinetics analysis set (PAS) included all participants with at least one available valid PK concentration measurement, who received any study drug and with no protocol deviations with relevant impact on PK data.

	NIO752 dose A	NIO752 dose B	NIO752 dose C	NIO752 Dose E1	NIO752 dose D	NIO752 Dose E2

Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture
Number of Participants Analyzed [units: participants]	3	3	4	18	9	6
NIO752 CSF concentrations (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
day 1 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
day 29 - 0h	1.25 ± 0.739	2.24 ± 1.95	4.82 ± 2.82		2.96 ± 1.55	
day 57 - 0h	1.79 ± 0.952	3.57 ± 2.23	4.90 ± 6.15		3.87 ± 3.28	
day 85 - 0h	1.69 ± 0.771	3.73 ± 2.86	7.02 ± 4.47	0.373 ± 0.521	3.80 ± 2.31	0.571 ± 0.480
day 113 - 0h	2.22 ± 1.03	4.45	7.73 ± 4.23		1.40 ± 1.86	
day 169 - 0h	0.00 ± 0.00	0.973 ± 0.0318	1.33 ± 0.411	0.541 ± 0.476	0.00 ± 0.00	0.368 ± 0.453
day 253 - 0h				0.716 ± 0.592		0.953 ± 0.329
day 337 - 0h				0.978 ± 0.509		0.682 ± 1.03
day 358 - 0h	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00		0.00 ± 0.00	

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

No data identified.

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Safety Results

Time Frame	Baseline up to approximately one year (3-month treatment plus 9-month follow-up or 9-month treatment plus 3-month follow-up)
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	NIO752 dose A N = 3	NIO752 dose B N = 4	NIO752 dose C N = 4	NIO752 dose D N = 9	NIO752 dose E1 N = 7	NIO752 Dose E2 N = 18	Pooled Placebo N = 14
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E1 via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of matching placebo via lumbar puncture
Total Number Affected	0	0	0	0	1	0	1
Total Number At Risk	3	4	4	9	7	18	14

Serious Adverse Events

Time Frame	Baseline up to approximately one year (3-month treatment plus 9-month follow-up or 9-month treatment plus 3-month follow-up)

Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

	NIO752 dose A N = 3	NIO752 dose B N = 4	NIO752 dose C N = 4	NIO752 dose D N = 9	NIO752 dose E1 N = 7	NIO752 Dose E2 N = 18	Pooled Placebo N = 14
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E1 via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of matching placebo via lumbar puncture
Total # Affected by any Serious Adverse Event	1	0	1	5	3	5	7
Total # at Risk by any Serious Adverse Event	3	4	4	9	7	18	14
Gastrointestinal disorders							
Inguinal hernia	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Upper gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Infections and infestations							
Appendicitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia aspiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)
Pyelonephritis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Injury, poisoning and procedural complications							
Ankle fracture	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Clavicle fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Femur fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Rib fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Skin laceration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Tibia fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Traumatic subarachnoid haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Metabolism and nutrition disorders							
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Lung adenocarcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Pancreatic carcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders							
Encephalopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Pleocytosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Progressive supranuclear palsy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Psychiatric disorders							
Confusional state	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Suicide attempt	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)

Respiratory, thoracic and mediastinal disorders							
Aspiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Surgical and medical procedures							
Assisted suicide	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (7.14%)
Vascular disorders							
Internal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Time Frame	Baseline up to approximately one year (3-month treatment plus 9-month follow-up or 9-month treatment plus 3-month follow-up)
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 0%

	NIO752 dose A N = 3	NIO752 dose B N = 4	NIO752 dose C N = 4	NIO752 dose D N = 9	NIO752 dose E1 N = 7	NIO752 Dose E2 N = 18	Pooled Placebo N = 14
Arm/Group Description	4 intrathecal injections of NIO752 Dose A via lumbar puncture	4 intrathecal injections of NIO752 Dose B via lumbar puncture	4 intrathecal injections of NIO752 Dose C via lumbar puncture	4 intrathecal injections of NIO752 Dose D via lumbar puncture	4 intrathecal injections of NIO752 Dose E1 via lumbar puncture	4 intrathecal injections of NIO752 Dose E2 via lumbar puncture	4 intrathecal injections of matching placebo via lumbar puncture
Total # Affected by any Other Adverse Event	3	4	3	9	7	18	14
Total # at Risk by any Other Adverse Event	3	4	4	9	7	18	14
Blood and lymphatic system disorders							
Anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders							
Arrhythmia supraventricular	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Atrial flutter	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bundle branch block right	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Supraventricular extrasystoles	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (5.56%)	0 (0.00%)
Ear and labyrinth disorders							
Vertigo	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Endocrine disorders							
Hyperparathyroidism secondary	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)

Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Eye disorders							
Asthenopia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Cataract	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Choroidal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Dry eye	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.11%)	1 (7.14%)
Eye irritation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	1 (7.14%)
Glaucoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Heterophoria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Ocular hyperaemia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Orbital haematoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Panophthalmitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Photophobia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (14.29%)	0 (0.00%)	1 (7.14%)
Vision blurred	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Visual acuity reduced	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Gastrointestinal disorders							
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Abdominal pain lower	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Anal incontinence	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Barrett's oesophagus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Constipation	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)
Diarrhoea	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	1 (7.14%)

Duodenal ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Dysphagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (5.56%)	0 (0.00%)
Faecaloma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Inguinal hernia	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Mouth ulceration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Nausea	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Noninfective gingivitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Salivary hypersecretion	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Toothache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
General disorders and administration site conditions							
Asthenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Catheter site irritation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Crying	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Fatigue	1 (33.33%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	2 (28.57%)	1 (5.56%)	0 (0.00%)
Feeling abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Feeling hot	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gait disturbance	0 (0.00%)	0 (0.00%)	1 (25.00%)	4 (44.44%)	1 (14.29%)	2 (11.11%)	2 (14.29%)
Hyperthermia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Injection site pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Puncture site pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Pyrexia	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Vessel puncture site haematoma	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders							
Drug hypersensitivity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Seasonal allergy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	1 (7.14%)
Infections and infestations							
Asymptomatic bacteriuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Clostridium difficile infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
COVID-19	0 (0.00%)	2 (50.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	3 (16.67%)	3 (21.43%)
Cystitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.11%)	0 (0.00%)
Eye infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Infectious mononucleosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Localised infection	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (14.29%)	3 (16.67%)	1 (7.14%)
Oral fungal infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Peritonitis bacterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (7.14%)
Post procedural infection	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyelonephritis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Tooth infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Urinary tract infection	0 (0.00%)	2 (50.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	2 (11.11%)	4 (28.57%)
Injury, poisoning and procedural complications							
Ankle fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Bone contusion	1 (33.33%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (14.29%)	1 (5.56%)	0 (0.00%)
Clavicle fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Contusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (33.33%)	0 (0.00%)	4 (22.22%)	2 (14.29%)
Eye contusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	1 (7.14%)
Fall	2 (66.67%)	1 (25.00%)	2 (50.00%)	4 (44.44%)	6 (85.71%)	4 (22.22%)	7 (50.00%)
Foot fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Haematuria traumatic	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hand fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Head injury	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.11%)	3 (21.43%)
Immunisation reaction	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Joint dislocation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Lip injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (5.56%)	0 (0.00%)
Post lumbar puncture syndrome	1 (33.33%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	2 (11.11%)	2 (14.29%)
Post procedural complication	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Procedural headache	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Procedural pain	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rib fracture	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Scapula fracture	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Skin abrasion	0 (0.00%)	1 (25.00%)	0 (0.00%)	4 (44.44%)	1 (14.29%)	3 (16.67%)	2 (14.29%)
Skin laceration	1 (33.33%)	2 (50.00%)	1 (25.00%)	4 (44.44%)	0 (0.00%)	5 (27.78%)	1 (7.14%)
Sunburn	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Traumatic haematoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Wound	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations							
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Amylase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Blood glucose increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Blood pressure increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	1 (7.14%)
Blood pressure systolic decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Blood thyroid stimulating hormone increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
C-reactive protein increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
CSF cell count increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
CSF protein increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (14.29%)	1 (5.56%)	0 (0.00%)
CSF white blood cell count increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Haemoglobin urine present	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Lipase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	2 (14.29%)

Lymphocyte morphology abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Oxygen saturation decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Protein urine present	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
SARS-CoV-2 test positive	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thyroxine free decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Urine bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Vitamin B12 decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Weight decreased	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
White blood cells urine positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Metabolism and nutrition disorders							
Diabetes mellitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vitamin B12 deficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Musculoskeletal and connective tissue disorders							
Arthralgia	1 (33.33%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	2 (14.29%)
Back pain	3 (100.00%)	1 (25.00%)	1 (25.00%)	1 (11.11%)	3 (42.86%)	0 (0.00%)	3 (21.43%)
Bursitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Chest wall haematoma	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Groin pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematoma muscle	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Limb discomfort	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mobility decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Muscle rigidity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)

Muscle spasms	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscle tightness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Muscular weakness	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Neck pain	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain in extremity	0 (0.00%)	0 (0.00%)	2 (50.00%)	0 (0.00%)	0 (0.00%)	3 (16.67%)	0 (0.00%)
Rhabdomyolysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Spinal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Torticollis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Basal cell carcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Blepharal papilloma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Metastases to liver	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metastases to peritoneum	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Squamous cell carcinoma of skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Nervous system disorders							
Akathisia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Akinesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Aphasia	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Areflexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.11%)	0 (0.00%)
Ataxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Balance disorder	0 (0.00%)	1 (25.00%)	1 (25.00%)	1 (11.11%)	3 (42.86%)	2 (11.11%)	0 (0.00%)
Carotid arteriosclerosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Dementia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	1 (5.56%)	4 (28.57%)
Drooling	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysarthria	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysstasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dystonia	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Freezing phenomenon	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Headache	2 (66.67%)	0 (0.00%)	1 (25.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	2 (14.29%)
Hypoaesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Motor dysfunction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscle contractions involuntary	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Nerve compression	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neurological symptom	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Paratonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Progressive supranuclear palsy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Psychomotor skills impaired	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Somnolence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (7.14%)
Speech disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Tremor	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)

Psychiatric disorders

Agitation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	0 (0.00%)	1 (7.14%)
Anxiety	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Binge eating	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Confusional state	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (14.29%)	1 (5.56%)	0 (0.00%)
Depression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)
Depression suicidal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Disorientation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (5.56%)	1 (7.14%)
Hallucination	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Hallucination, auditory	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Hallucination, visual	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Hypersexuality	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Insomnia	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Mental status changes	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Merycism	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychomotor retardation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Restlessness	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Sleep disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Sopor	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Suicidal ideation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Renal and urinary disorders							
Dysuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (42.86%)	0 (0.00%)	1 (7.14%)
Hypertensive nephropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Incontinence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	1 (7.14%)
Micturition urgency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Pollakiuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Renal failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary incontinence	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	1 (5.56%)	0 (0.00%)
Reproductive system and breast disorders							
Benign prostatic hyperplasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders							
Apnoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Bronchial haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chronic obstructive pulmonary disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Cough	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (5.56%)	0 (0.00%)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Epistaxis	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Hypoventilation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Increased bronchial secretion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Increased viscosity of upper respiratory secretion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinorrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Stridor	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tachypnoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders							

Actinic keratosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Blister	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Decubitus ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Dry skin	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ecchymosis	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Erythema	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)
Hyperhidrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Livedo reticularis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Miliaria	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Night sweats	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (7.14%)
Skin swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders							
Blood pressure fluctuation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)
Flushing	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	2 (11.11%)	0 (0.00%)
Haematoma	1 (33.33%)	1 (25.00%)	1 (25.00%)	2 (22.22%)	0 (0.00%)	4 (22.22%)	1 (7.14%)
Hypertension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Orthostatic hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral coldness	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Relevant Findings

NA

Conclusion:

A review of AEs, laboratory investigations, and other safety measures indicate that, consistent with the literature, the course of illness in PSP is characterized by frequent falls, head injuries, and other serious and non-serious AEs. Higher doses of NIO752 might be associated with more frequent cases of encephalopathy, which were observed to be transient events but some required hospitalization and treatment. Other treatment-related SAEs likely reflected class effects, such as CSF pleocytosis in the absence of an infectious process.

Dose E2 was considered safe and generally well tolerated compared to placebo. Although a higher dose level (DoseD) could be justified as part of the benefit/risk ratio, data suggests some patients may be more likely to experience treatment-related AEs on this higher dose level.

These safety and tolerability data coupled with PK findings support the future development of NIO752 in the PSP program.

Date of Clinical Trial Report

04 July 2025