Clinical trial results:
An Open-Label Non-Randomized, Multi-Center Phase-2 Study of Convection-Enhanced Delivery (CED) of MDNA55 in Adults with Recurrent or Progressive Glioblastoma

Summary

EudraCT number	2016-003841-27
Trial protocol	PL
Global end of trial date	31 October 2019

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022
Summary attachment (see zip file)	MDNA55-05 - Synopsis (synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	MDNA-55-05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02858895
WHO universal trial number (UTN)	-
Other trial identifiers	BB IND: 007004

Notes:

Sponsors

Sponsor organisation name	Medicenna Therapeutics Inc
Sponsor organisation address	2 Bloor Street West, Suite 700, Toronto, ON , Canada, M4W 3E2
Public contact	Rosemina Merchant Chief Development Officer , Medicenna Therapeutics Inc., 001 +1 604 340 3081, nmerchant@medicenna.com
Scientific contact	Rosemina Merchant Chief Development Officer , Medicenna Therapeutics Inc., 001 +1 604 340 3081, nmerchant@medicenna.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	05 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 September 2019
Global end of trial reached?	Yes
Global end of trial date	31 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was designed to test the hypothesis that median overall survival (mOS) is improved to a clinically significant degree with MDNA55 administered via CED, as compared to current available treatments for rGBM. The design was based on a null hypothesis that mOS was 8 months (based on a clinically weighted average of published studies of FDA-approved therapies) versus an alternative hypothesis of 11.5 months following MDNA55 treatment.

Protection of trial subjects:

Conduct of the Clinical Investigation
The Investigator will ensure that this study is conducted in full conformance with the principles of the "Declaration of Helsinki" and its amendments, or with the laws and regulations of the locality in which the research is conducted, whichever affords the greater protection to the individual.

Background therapy:

All patients enrolled in the study would have received first line treatment for GBM including surgery and radiotherapy with or without chemotherapy (according to local practice; Stupp protocol, Stupp et al., 2005)

Evidence for comparator:

Not applicable; single arm study

Actual start date of recruitment	23 March 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	21 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	United States: 42
Worldwide total number of subjects	47
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	36
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study Initiation Date: First Subject First Visit: 23 Mar 2017
Study Completion Date: Last Subject Last Visit: 12 Sept 2019

Pre-assignment

Screening details:

Male/ female ≥ 18 yrs; primary (de novo) GB (recurred/progressed per RANO criteria), life expectancy > 12 weeks, KPS ≥ 70; tumor diameter ≥ 1cm x ≥ 1cm (minimum) to 4cm in any direction and no features which make the tumor a poor target for CED (e.g. significant liquefaction or geometric features not conducive to CED).

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	MDNA55

Arm description:

Single infusion of MDNA55 via convection enhanced delivery (CED)

Arm type	Experimental
Investigational medicinal product name	cpIL-4PE
Investigational medicinal product code	MDNA55
Other name	NBI-3001, PRX321
Pharmaceutical forms	Solution for infusion
Routes of administration	Intratumoral use

Dosage and administration details:

Single treatment (CED infusion) at doses of either 1.5, 3, 6, or 9 µg/mL and infusion volumes of up to 66 mL (according to tumor size) with a total dose ranging from 18 to 240 µg (within the established MTD of 240 µg)

Number of subjects in period 1	MDNA55
Started	47
Completed	8
Not completed	39
Consent withdrawn by subject	3
Disease progression	31
Adverse event, non-fatal	1
Death	2
hospice	1
did not receive drug due to catheters misplaced	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	47	47	
Age categorical			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	36	36	
From 65-84 years	11	11	
85 years and over	0	0	
Age continuous			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: years			
median	56		
full range (min-max)	34 to 78	-	
Gender categorical			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
Female	17	17	
Male	30	30	
Karnofsky Performance Score			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
70	3	3	
80	20	20	
90	19	19	
100	5	5	
MGMT Status			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
Methylated	18	18	
Unmethylated	24	24	
Not Available	5	5	
Steroid Use			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
Yes	19	19	

No	13	13	
Not applicable	14	14	
Missing	1	1	
GBM Grade			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
WHO Grade 4	47	47	
Number of prior relapses			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
1 relapse	37	37	
2 relapses	10	10	
Race			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	2	
Black or African American	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
White	41	41	
Other	3	3	
Height			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm			
median	173		
full range (min-max)	152 to 190.5	-	
Weight			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: kg			
arithmetic mean	78.67		
standard deviation	± 16.911	-	
Initial Diagnosis to 1st Relapse			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: months			
arithmetic mean	12.98		
standard deviation	± 7.673	-	
Initial Diagnosis to start of MDNA55 treatment			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: months			
arithmetic mean	15.594		
standard deviation	± 9.1340	-	
Max tumor diameter at initial diagnosis			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm			
arithmetic mean	3.331		
standard deviation	± 1.4310	-	
Max tumor diameter at baseline			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm			
arithmetic mean	3.160		

standard deviation	± 1.1736	-	
Tumor volume at baseline			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm3			
arithmetic mean	10.543		
standard deviation	± 11.0621	-	
Lymphocyte count			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: 10^9 cells/L			
arithmetic mean	0.991		
standard deviation	± 0.3839	-	

Subject analysis sets

Subject analysis set title	Intent to Treat / Safety Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent-to-Treat and Safety: ITT and Safety populations were identical and consisted of all subjects who signed an informed consent form and received any amount of study drug.

Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol

Subject analysis set description:

Per-Protocol Population: PP population consisted of all subjects in the mITT Population who had no major protocol violation during the study. Efficacy analyses were conducted on this population in support of the primary efficacy results.

Subject analysis set title	Modified Intent to Treat Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

mITT population was used for secondary response analyses and consisted of all subjects who received any amount of study drug, had adequate imaging (at least 1 post-treatment scan), and had sufficient clinical data for ORR analysis.

Reporting group values	Intent to Treat / Safety Population	Per protocol population	Modified Intent to Treat Population
Number of subjects	47	44	43
Age categorical			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	36		
From 65-84 years	11		
85 years and over	0		
Age continuous			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: years			
median	56	55.5	
full range (min-max)	34 to 78	34 to 77	

Gender categorical			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
Female	17	17	
Male	30	27	
Karnofsky Performance Score			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
70	3	3	
80	20	19	
90	19	19	
100	5	3	
MGMT Status			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
Methylated	18	17	
Unmethylated	24	23	
Not Available	5	4	
Steroid Use			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
Yes	19	19	
No	13	13	
Not applicable	14	11	
Missing	1	1	
GBM Grade			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
WHO Grade 4	47	44	
Number of prior relapses			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
1 relapse	37	35	
2 relapses	10	9	
Race			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	2	
Black or African American	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
White	41	38	
Other	3	3	
Height			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm			
median	173	172.36	
full range (min-max)	152 to 190.5	152 to 190.5	
Weight			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: kg			

arithmetic mean	78.67	78.46	
standard deviation	± 16.911	± 17.398	±
Initial Diagnosis to 1st Relapse			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: months			
arithmetic mean	12.98	13.14	
standard deviation	± 7.673	± 7.486	±
Initial Diagnosis to start of MDNA55 treatment			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: months			
arithmetic mean	15.594	15.711	
standard deviation	± 9.1340	± 9.1496	±
Max tumor diameter at initial diagnosis			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm			
arithmetic mean	3.331	3.213	
standard deviation	± 1.4310	± 1.3987	±
Max tumor diameter at baseline			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm			
arithmetic mean	3.160	3.056	
standard deviation	± 1.1736	± 1.0818	±
Tumor volume at baseline			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: cm3			
arithmetic mean	10.543	10.005	
standard deviation	± 11.0621	± 10.9851	±
Lymphocyte count			
Baseline and demographic characteristics will be summarized and presented descriptively.			
Units: 10^9 cells/L			
arithmetic mean	0.991	0.986	
standard deviation	± 0.3839	± 0.3949	±

End points

End points reporting groups

Reporting group title	MDNA55

Reporting group description:

Single infusion of MDNA55 via convection enhanced delivery (CED)

Subject analysis set title	Intent to Treat / Safety Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent-to-Treat and Safety: ITT and Safety populations were identical and consisted of all subjects who signed an informed consent form and received any amount of study drug.

Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol

Subject analysis set description:

Per-Protocol Population: PP population consisted of all subjects in the mITT Population who had no major protocol violation during the study. Efficacy analyses were conducted on this population in support of the primary efficacy results.

Subject analysis set title	Modified Intent to Treat Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

mITT population was used for secondary response analyses and consisted of all subjects who received any amount of study drug, had adequate imaging (at least 1 post-treatment scan), and had sufficient clinical data for ORR analysis.

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)[1]

End point description:

Primary endpoint analysis was based on the ITT population. The null hypothesis was mOS of 8.0 months, based on a clinically-weighted average of published studies of FDA-approved therapies versus the alternative hypothesis of 11.5 months.

End point type	Primary

End point timeframe:

From start of treatment until date of death from any cause. Subjects who were not known to have died at the time of the analysis were to be censored at the date of last contact.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics (number of subjects [n], mean, standard deviation [SD], minimum, maximum, and median) used to summarize continuous variables. Categorical variables were summarized using frequencies and percentage of subjects within each category. Summaries were provided for overall treatment. Baseline value defined as last non-missing assessment prior to catheter placement. Primary efficacy analysis was to be performed at 0.05 level of significance. No adjustments made for multiplicity.

End point values	Intent to Treat / Safety Population	Per protocol population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47	44		
Units: months				
median (confidence interval 80%)	10.2 (8.39 to 12.75)	11.64 (8.62 to 15.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

ORR, determined by independent central review (per RANO-based criteria)
Complete Response - Disappearance of all enhancing measurable and non-measurable disease sustained for at least 4 weeks.
Partial Response - ≥50% decrease in sum of products of perpendicular diameters or ≥65% decrease in total volume of all measurable enhancing lesions compared with baseline, sustained for at least 4 weeks
Progressive Disease - At least two sequential scans separated by at ≥4 weeks both exhibiting ≥25% increase in sum of products of perpendicular diameters or ≥40% increase in total volume of enhancing lesions.
Stable Disease - Does not qualify for CR, PR, or PD as defined above

End point type	Secondary

End point timeframe:

12 months

End point values	Modified Intent to Treat Population			
Subject group type	Subject analysis set			
Number of subjects analysed	41[2]			
Units: participants				
number (not applicable)	1			

Notes:

[2] - Two subjects were not evaluable and excluded from analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS, time from treatment until disease progression (per RANO-based criteria) or death Progressive Disease per RANO - At least two sequential scans separated by at ≥4 weeks both exhibiting ≥25% increase in sum of products of perpendicular diameters or ≥40% increase in total volume of enhancing lesions

End point type	Secondary

End point timeframe:

12 months

End point values	Modified Intent to Treat Population			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: months				
median (confidence interval 80%)	3.61 (2.79 to 5.08)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from catheter placement through 12 months post treatment or early withdrawal and followed until resolution, stabilization, data cut-off, or death. For subjects that withdraw from the study, SAEs that occur < 30 days collected.

Adverse event reporting additional description:

All patients were included in the in the ITT / Safety Population (N=47) for "MDNA55 (Overall)"; there is one patient that underwent catheter placement but did not receive the study drug; the infusion did not proceed due to catheter misplacement. Therefore, this participant is not included in the individual MDNA55 infusion arms (N=46)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	MDNA55 (Overall)

Reporting group description:

Intent-to-Treat/ Safety: ITT/ Safety populations identical and consist of all subjects who signed an informed consent form and received any amount of study drug.

Reporting group title	MDNA55 (1.5 mcg/mL)

Reporting group description:

Intent-to-Treat/ Safety: ITT/ Safety populations identical and consist of all subjects who signed an informed consent form and received any amount of study drug.

Reporting group title	MDNA55 (3.0 mcg/mL)

Reporting group description:

Intent-to-Treat/ Safety: ITT/ Safety populations identical and consist of all subjects who signed an informed consent form and received any amount of study drug.

Reporting group title	MDNA55 (6.0 mcg/mL)

Reporting group description: -

Reporting group title	MDNA55 (9.0 mcg/mL)

Reporting group description:

Intent-to-Treat/ Safety: ITT/ Safety populations identical and consist of all subjects who signed an informed consent form and received any amount of study drug.

Serious adverse events	MDNA55 (Overall)	MDNA55 (1.5 mcg/mL)	MDNA55 (3.0 mcg/mL)
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 47 (51.06%)	6 / 18 (33.33%)	2 / 9 (22.22%)
number of deaths (all causes)	36	16	8
number of deaths resulting from adverse events	8	2	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peritumoral Oedema			
subjects affected / exposed	0 / 47 (0.00%)	1 / 18 (5.56%)	0 / 9 (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

Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 47 (2.13%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	3 / 47 (6.38%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral Haemorrhage			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cerebrovascular Accident			
subjects affected / exposed	1 / 47 (2.13%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemorrhage Intracranial			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolic Encephalopathy			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (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
Neurological Decompensation			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	1 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Neurological Symptom			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Partial seizures			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (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
Seizure			
subjects affected / exposed	8 / 47 (17.02%)	4 / 18 (22.22%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	7 / 9	3 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status Epilepticus			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	2 / 9 (22.22%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (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

Complication of device insertion			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (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
Disease progression			
subjects affected / exposed	3 / 47 (6.38%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 47 (2.13%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (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
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (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			
Pneumonia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (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
Septic shock			
subjects affected / exposed	1 / 47 (2.13%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 47 (4.26%)	2 / 18 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MDNA55 (6.0 mcg/mL)	MDNA55 (9.0 mcg/mL)	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	9 / 13 (69.23%)	
number of deaths (all causes)	3	8	
number of deaths resulting from adverse events	2	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peritumoral Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cerebrovascular Accident			

subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhage Intracranial			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic Encephalopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological Decompensation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological Symptom			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			

subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 6 (33.33%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status Epilepticus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication of device insertion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MDNA55 (Overall)	MDNA55 (1.5 mcg/mL)	MDNA55 (3.0 mcg/mL)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 47 (97.87%)	18 / 18 (100.00%)	9 / 9 (100.00%)

Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Hypotension			
subjects affected / exposed	4 / 47 (8.51%)	3 / 18 (16.67%)	1 / 9 (11.11%)
occurrences (all)	4	3	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 47 (40.43%)	8 / 18 (44.44%)	3 / 9 (33.33%)
occurrences (all)	23	9	5
Gait disturbance			
subjects affected / exposed	7 / 47 (14.89%)	0 / 18 (0.00%)	3 / 9 (33.33%)
occurrences (all)	10	0	3
Oedema peripheral			
subjects affected / exposed	3 / 47 (6.38%)	2 / 18 (11.11%)	0 / 9 (0.00%)
occurrences (all)	3	2	0
Pain			
subjects affected / exposed	3 / 47 (6.38%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	3	1	1
Peripheral swelling			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	2	1	1
Respiratory, thoracic and mediastinal disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Dysphonia			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
Agitation			

subjects affected / exposed	4 / 47 (8.51%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	4	1	1
Anxiety			
subjects affected / exposed	5 / 47 (10.64%)	2 / 18 (11.11%)	1 / 9 (11.11%)
occurrences (all)	5	2	1
Confusion			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Confusional state			
subjects affected / exposed	7 / 47 (14.89%)	4 / 18 (22.22%)	2 / 9 (22.22%)
occurrences (all)	7	4	2
Depression			
subjects affected / exposed	5 / 47 (10.64%)	0 / 18 (0.00%)	2 / 9 (22.22%)
occurrences (all)	5	0	2
Insomnia			
subjects affected / exposed	12 / 47 (25.53%)	1 / 18 (5.56%)	4 / 9 (44.44%)
occurrences (all)	13	1	4
Irritability			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 47 (8.51%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	6	1	0
Blood albumin decreased			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	5	4	1
Blood bilirubin increased			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	5	3	0
Blood calcium decreased			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	4	3	1
Blood lactate dehydrogenase increased			

subjects affected / exposed	4 / 47 (8.51%)	2 / 18 (11.11%)	0 / 9 (0.00%)
occurrences (all)	4	2	0
Lymphocyte count decreased			
subjects affected / exposed	5 / 47 (10.64%)	3 / 18 (16.67%)	1 / 9 (11.11%)
occurrences (all)	13	10	2
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 47 (10.64%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	5	1	1
Skin abrasion			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
Aphasia			
subjects affected / exposed	12 / 47 (25.53%)	4 / 18 (22.22%)	3 / 9 (33.33%)
occurrences (all)	18	4	4
Brain oedema			
subjects affected / exposed	5 / 47 (10.64%)	1 / 18 (5.56%)	3 / 9 (33.33%)
occurrences (all)	6	1	3
Cognitive disorder			
subjects affected / exposed	4 / 47 (8.51%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Dizziness			
subjects affected / exposed	4 / 47 (8.51%)	2 / 18 (11.11%)	2 / 9 (22.22%)
occurrences (all)	5	2	3
Dysarthria			
subjects affected / exposed	4 / 47 (8.51%)	2 / 18 (11.11%)	1 / 9 (11.11%)
occurrences (all)	6	3	1
Epilepsy			
subjects affected / exposed	2 / 47 (4.26%)	2 / 18 (11.11%)	0 / 9 (0.00%)
occurrences (all)	3	3	0
Extensor plantar response			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	2	1	1
Facial paralysis			

subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences (all)	4	0	1
Facial paresis			
subjects affected / exposed	7 / 47 (14.89%)	2 / 18 (11.11%)	2 / 9 (22.22%)
occurrences (all)	7	2	2
Headache			
subjects affected / exposed	18 / 47 (38.30%)	10 / 18 (55.56%)	2 / 9 (22.22%)
occurrences (all)	35	10	7
Hemiparesis			
subjects affected / exposed	12 / 47 (25.53%)	4 / 18 (22.22%)	2 / 9 (22.22%)
occurrences (all)	17	4	2
Hypoaesthesia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences (all)	5	0	4
Memory impairment			
subjects affected / exposed	5 / 47 (10.64%)	0 / 18 (0.00%)	1 / 9 (11.11%)
occurrences (all)	6	0	1
Paraesthesia			
subjects affected / exposed	7 / 47 (14.89%)	2 / 18 (11.11%)	2 / 9 (22.22%)
occurrences (all)	7	2	2
Partial seizures			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Pyramidal tract syndrome			
subjects affected / exposed	8 / 47 (17.02%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	17	2	1
Seizure			
subjects affected / exposed	14 / 47 (29.79%)	4 / 18 (22.22%)	2 / 9 (22.22%)
occurrences (all)	17	5	2
Simple partial seizure			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	2	1	1
Tremor			
subjects affected / exposed	3 / 47 (6.38%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	3	1	0
Blood and lymphatic system disorders			

Thrombocytopenia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	6 / 47 (12.77%)	2 / 18 (11.11%)	1 / 9 (11.11%)
occurrences (all)	6	2	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	8 / 47 (17.02%)	3 / 18 (16.67%)	1 / 9 (11.11%)
occurrences (all)	8	3	1
Diarrhoea			
subjects affected / exposed	4 / 47 (8.51%)	2 / 18 (11.11%)	1 / 9 (11.11%)
occurrences (all)	5	2	1
Nausea			
subjects affected / exposed	8 / 47 (17.02%)	3 / 18 (16.67%)	2 / 9 (22.22%)
occurrences (all)	10	3	3
Vomiting			
subjects affected / exposed	6 / 47 (12.77%)	2 / 18 (11.11%)	2 / 9 (22.22%)
occurrences (all)	8	2	3
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 47 (4.26%)	0 / 18 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	3 / 47 (6.38%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	4	2	1
Urinary incontinence			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	5 / 47 (10.64%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	6	2	1
Muscular weakness			
subjects affected / exposed	15 / 47 (31.91%)	8 / 18 (44.44%)	1 / 9 (11.11%)
occurrences (all)	18	9	1
Pain in extremity			
subjects affected / exposed	3 / 47 (6.38%)	1 / 18 (5.56%)	1 / 9 (11.11%)
occurrences (all)	3	1	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	7 / 47 (14.89%)	3 / 18 (16.67%)	0 / 9 (0.00%)
occurrences (all)	7	3	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 47 (12.77%)	2 / 18 (11.11%)	0 / 9 (0.00%)
occurrences (all)	6	2	0
Dehydration			
subjects affected / exposed	2 / 47 (4.26%)	1 / 18 (5.56%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Hyperglycaemia			
subjects affected / exposed	3 / 47 (6.38%)	2 / 18 (11.11%)	1 / 9 (11.11%)
occurrences (all)	5	2	3
Hypokalaemia			
subjects affected / exposed	7 / 47 (14.89%)	3 / 18 (16.67%)	1 / 9 (11.11%)
occurrences (all)	7	3	1

Non-serious adverse events	MDNA55 (6.0 mcg/mL)	MDNA55 (9.0 mcg/mL)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	13 / 13 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	5 / 13 (38.46%)	
occurrences (all)	4	5	
Gait disturbance			
subjects affected / exposed	1 / 6 (16.67%)	3 / 13 (23.08%)	
occurrences (all)	4	3	
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Dysphonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Confusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	

Confusional state			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 6 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	3	
Insomnia			
subjects affected / exposed	4 / 6 (66.67%)	3 / 13 (23.08%)	
occurrences (all)	5	3	
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences (all)	2	3	
Blood albumin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Blood calcium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Skin abrasion			

subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Aphasia			
subjects affected / exposed	2 / 6 (33.33%)	3 / 13 (23.08%)	
occurrences (all)	5	5	
Brain oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Cognitive disorder			
subjects affected / exposed	3 / 6 (50.00%)	1 / 13 (7.69%)	
occurrences (all)	3	1	
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Dysarthria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Epilepsy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Extensor plantar response			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Facial paralysis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Facial paresis			
subjects affected / exposed	0 / 6 (0.00%)	3 / 13 (23.08%)	
occurrences (all)	0	3	
Headache			
subjects affected / exposed	4 / 6 (66.67%)	2 / 13 (15.38%)	
occurrences (all)	13	5	
Hemiparesis			
subjects affected / exposed	1 / 6 (16.67%)	5 / 13 (38.46%)	
occurrences (all)	4	7	

Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Memory impairment			
subjects affected / exposed	2 / 6 (33.33%)	2 / 13 (15.38%)	
occurrences (all)	3	2	
Paraesthesia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Partial seizures			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pyramidal tract syndrome			
subjects affected / exposed	3 / 6 (50.00%)	3 / 13 (23.08%)	
occurrences (all)	9	5	
Seizure			
subjects affected / exposed	5 / 6 (83.33%)	3 / 13 (23.08%)	
occurrences (all)	7	3	
Simple partial seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	1 / 6 (16.67%)	1 / 13 (7.69%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Diarrhoea			

subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Muscular weakness			
subjects affected / exposed	1 / 6 (16.67%)	5 / 13 (38.46%)	
occurrences (all)	2	6	
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	1 / 6 (16.67%)	3 / 13 (23.08%)	
occurrences (all)	1	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	3 / 13 (23.08%)	
occurrences (all)	1	3	
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 13 (15.38%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2017	Amendment 1 (dated 26 Apr 2017, Protocol Version 2.0) The reason for this amendment was to update protocol and inclusion criteria to reflect current treatment practices and disease assessment tools and refining the guidance for study drug administration.
14 August 2017	Amendment 2 (dated 14 Aug 2017, Protocol Version 3.0) The reason for this amendment was to include key changes to infusion parameters to enhance drug delivery and increase drug concentration; shift to a fixed dose approach with 180 µg administered via four catheters; clarifications and refinements to inclusion criteria and simplify study procedures; and provision to recruit additional subjects for preplanned analysis to retain power under new dosing regimen.
18 December 2017	Amendment 3 (dated 18 Dec 2017, Protocol Version 4.0) The overall reason for this amendment was to incorporate further changes advised on precautionary basis to infusion parameters (due to neurotoxicity events at a single site) and to clarify the reduction in dose concentration of both MDNA55 and Gd-DTPA.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33863808

http://www.ncbi.nlm.nih.gov/pubmed/34345478

http://www.ncbi.nlm.nih.gov/pubmed/34592195