Clinical trial results:
A Phase II pilot safety and tolerability study of ILB in patients with Motor Neurone Disease (MND)/Amyotrophic Lateral Sclerosis (ALS)

Summary

EudraCT number	2018-000668-28
Trial protocol	GB
Global end of trial date	28 July 2021

Results information

Result version number	v1 (current)
This version publication date	29 March 2025
First version publication date	29 March 2025

Trial information

Trial identification

Sponsor protocol code	RG_17-250

Additional study identifiers

ISRCTN number	ISRCTN83738603
ClinicalTrials.gov id (NCT number)	NCT03705390
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor number: RG_17-250

Notes:

Sponsors

Sponsor organisation name	University of Birmingham
Sponsor organisation address	Mindelsohn Way, Birmingham, United Kingdom,
Public contact	Mr Darren Barton, University of Birmingham, D3B Team, Cancer Research UK Clinical Trials Unit, ALS@trials.bham.ac.uk
Scientific contact	Mr Darren Barton, University of Birmingham, D3B Team, Cancer Research UK Clinical Trials Unit, ALS@trials.bham.ac.uk

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	28 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2021
Global end of trial reached?	Yes
Global end of trial date	28 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The Primary Objective is:

To determine the safety and acceptability of ILB in ALS patients

Protection of trial subjects:

The trial was designed with input from the clinical and pre-clinical teams from the University of Birmingham and The Queen Elizabeth Hospital to allow quick and effective achievement of the clinical trial objectives to minimise the burden on patients

Background therapy:

None

Evidence for comparator:

Not applicable

Actual start date of recruitment	11 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	11
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	9
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Prior to screening- informed consent obtained and patients taking Riluzole had to discontinue 28 days prior to starting ILB treatment

Pre-assignment

Screening details:

Prior to starting treatment, patients completed a baseline screening assessment

Period 1

Period 1 title	Recruited
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	ILB® arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	ILB®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use, Solution for injection

Dosage and administration details:

ILB® subcutaneous injection at a dose of 2mg/kg once per week for up to a maximum of 48 weeks

Number of subjects in period 1	ILB® arm
Started	11
Completed	11

Period 2

Period 2 title	Treated patients
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Number of patients who underwent treatment

Arms

Arm title	ILB Treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	ILB®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use, Solution for injection

Dosage and administration details:

ILB® subcutaneous injection at a dose of 2mg/kg once per week for up to a maximum of 48 weeks

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is the recruitment period, whereas period 2 describes the analysis population

Number of subjects in period 2	ILB Treatment
Started	11
Completed	9
Not completed	2
Trial suspended for COVID-19	2

Baseline characteristics

Reporting groups	
Reporting group title	ILB Treatment

Reporting group description: -

Reporting group values	ILB Treatment	Total	
Number of subjects	11	11	
Age categorical 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)	9	9	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
median	57		
inter-quartile range (Q1-Q3)	53 to 62	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	7	7	
Family history of Motor Neurone Disease Units: Subjects			
No	10	10	
Yes	1	1	
Family history of fronto-temporal dementia Units: Subjects			
No	11	11	
Yes	0	0	
Time from ALS diagnosis to trial entry Units: months			
median	4.69		
inter-quartile range (Q1-Q3)	3.58 to 11.63	-	

End points

End points reporting groups

Reporting group title	ILB® arm
Reporting group description: -	
Reporting group title	ILB Treatment
Reporting group description: -	

Primary: Safety Assessed by SAEs - Measured by Incidence

End point title	Safety Assessed by SAEs - Measured by Incidence[1]
End point description:	
Measured by the incidence of serious adverse events (SAEs) and adverse events (AEs) using CTCAE grading v4.0	
End point type	Primary
End point timeframe:	
From informed consent up to 30 days after last administration of trial treatment	
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: Trial is single arm in nature, therefore all analysis is descriptive	

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of SAEs	1			

Statistical analyses

No statistical analyses for this end point

Primary: Safety Assessed by AEs - Measured by Incidence

End point title	Safety Assessed by AEs - Measured by Incidence[2]
End point description:	
Measured by the incidence of adverse events (AEs) using CTCAE grading v4.0.	
End point type	Primary
End point timeframe:	
From informed consent up to 30 days after last administration of trial treatment	
Notes:	
[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Trial is single arm in nature, therefore all analysis is descriptive	

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of AEs	270			

Statistical analyses

No statistical analyses for this end point

Primary: Safety Assessed by AEs - Measured by Grade

End point title	Safety Assessed by AEs - Measured by Grade[3]

End point description:

Measured by the incidence of adverse events (AEs) using CTCAE grading v4.0.

End point type	Primary

End point timeframe:

From informed consent up to 30 days after last administration of trial treatment

Notes:

[3] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of AEs				
Grade 1	265			
Grade 2	4			
Grade 3	1			
Grade 4	0			
Grade 5	0			

Statistical analyses

No statistical analyses for this end point

Primary: Safety Assessed by AEs - Summarised by Causality

End point title	Safety Assessed by AEs - Summarised by Causality[4]

End point description:

Relatedness categories: 1 = unrelated, 2 = unlikely to be related, 3 = possibly related, 4 = probably related, 5 =
definitely related

End point type	Primary

End point timeframe:

From informed consent up to 30 days after last administration of trial treatment

Notes:

[4] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of AEs				
Unrelated	127			
Unlikely to be related	45			
Possibly related	4			
Probably related	1			
Definitely related	93			

Statistical analyses

No statistical analyses for this end point

Primary: Safety Assessed by SAEs - Summarised by Admitting Event Grade

End point title	Safety Assessed by SAEs - Summarised by Admitting Event Grade[5]

End point description:

Grade refers to the severity of the admitting event as follows:
Grade 1 - Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2 - Moderate; minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental activities
of daily living.
Grade 3 - Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of
hospitalization indicated; disabling; limiting self care activities of daily living.
Grade 4 - Life-threatening consequences; urgent intervention indicated. Grade 5 - Death related to AE.

End point type	Primary

End point timeframe:

From informed consent up to 30 days after last administration of trial treatment

Notes:

[5] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of AEs				
Grade 1	0			
Grade 2	0			
Grade 3	1			
Grade 4	0			
Grade 5	0			

Statistical analyses

No statistical analyses for this end point

Primary: Safety Assessed by SAEs - Summarised by Admitting Event Relatedness

End point title	Safety Assessed by SAEs - Summarised by Admitting Event Relatedness[6]

End point description:

Relatedness categories: 1 = unrelated, 2 = unlikely to be related, 3 = possibly related, 4 = probably related, 5 = definitely related

End point type	Primary

End point timeframe:

From informed consent up to 30 days after last administration of trial treatment

Notes:

[6] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of SAEs				
Unrelated	1			
Unlikely to be related	0			
Possibly related	0			
Probably related	0			
Definitely related	0			

Statistical analyses

No statistical analyses for this end point

Primary: Safety Assessed by SAEs - Summarised by Admitting Event Type

End point title	Safety Assessed by SAEs - Summarised by Admitting Event Type[7]

End point description:

From informed consent up to 30 days after last administration of trial treatment

End point type	Primary

End point timeframe:

Description of the event type at admission

Notes:

[7] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of SAEs				
Generalised muscle weakness	1			
Other admitting event types	0			

Statistical analyses

No statistical analyses for this end point

Primary: Safety Assessed by SAEs - Summarised by Sequelae

End point title	Safety Assessed by SAEs - Summarised by Sequelae[8]

End point description:

Outcome of serious adverse events only: Resolved with sequelae or Resolved without sequelae

End point type	Primary

End point timeframe:

From informed consent up to 30 days after last administration of trial treatment

Notes:

[8] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of SAEs				
Resolved with Sequelae	0			
Resolved without Sequelae	1			

Statistical analyses

No statistical analyses for this end point

Primary: Tolerability Assessed by the Incidence of Intolerable Adverse Events

End point title	Tolerability Assessed by the Incidence of Intolerable Adverse Events[9]

End point description:

An intolerable adverse event will satisfy all of the following criteria:
1. Associated with a serious adverse event or a drug discontinuation of greater than three weeks;
2. Grade 3, 4 or 5 in severity according to CTCAE version 4;
3. In the opinion of the Investigator is i) definitely related or ii) probably related or iii) possibly related to the study
drug treatment.
Adverse events which are considered unrelated or probably not related will not be classed as intolerable events

End point type	Primary

End point timeframe:

From informed consent up to 30 days after last administration of trial treatment

Notes:

[9] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of intolerable adverse events	0			

Statistical analyses

No statistical analyses for this end point

Primary: Quantity of Study Drug Administered - Total Drug Administered

End point title	Quantity of Study Drug Administered - Total Drug

End point description:

Total drug administered over the study period (measured in milligrams)

End point type	Primary

End point timeframe:

From baseline to final treatment visit

Notes:

[10] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mg				
median (inter-quartile range (Q1-Q3))	4200 (1902 to 5754)			

Statistical analyses

No statistical analyses for this end point

Primary: Quantity of Study Drug Administered - Number of Administrations

End point title	Quantity of Study Drug Administered - Number of Administrations[11]

End point description:

Numerical count of the number of study drug injections given whilst on the trial

End point type	Primary

End point timeframe:

From baseline to final treatment visit

Notes:

[11] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of drug administrations				
median (inter-quartile range (Q1-Q3))	24 (14 to 35)			

Statistical analyses

No statistical analyses for this end point

Primary: Quantity of Study Drug Administered - Number of Interruptions

End point title	Quantity of Study Drug Administered - Number of

End point description:

Numerical count of the number of study drug injections missed whilst on the trial

End point type	Primary

End point timeframe:

From baseline to final treatment visit

Notes:

[12] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of interruptions				
median (inter-quartile range (Q1-Q3))	1.0 (0 to 3)			

Statistical analyses

No statistical analyses for this end point

Primary: Quantity of Study Drug Administered - Duration of Interruptions

End point title	Quantity of Study Drug Administered - Duration of Interruptions[13]

End point description:

Length of interruptions in weeks between study drug injections for those participants that experienced a treatment
interruption whilst on the trial

End point type	Primary

End point timeframe:

From baseline to final treatment visit

Notes:

[13] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: weeks				
median (inter-quartile range (Q1-Q3))	1.5 (1 to 2)			

Statistical analyses

No statistical analyses for this end point

Primary: Quantity of Study Drug Administered - Number of Discontinuations

End point title	Quantity of Study Drug Administered - Number of Discontinuations[14]

End point description:

numerical count of patients who discontinued study drug treatment

End point type	Primary

End point timeframe:

From baseline to final treatment visit

Notes:

[14] - 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: Trial is single arm in nature, therefore all analysis is descriptive

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: number of treatment discontinuations				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Revised Amyotrophic Lateral Sclerosis Functional Rating Scale Revised (ALSFRS-R) Change

End point title	Revised Amyotrophic Lateral Sclerosis Functional Rating Scale Revised (ALSFRS-R) Change

End point description:

A functional rating scale including assessments of communication, mobility, feeding, dressing and respiration. The total

score range is 0 - 40; with 0 being the best outcome and 40 being the worst. Change from baseline to final treatment
visit

End point type	Secondary

End point timeframe:

From baseline to final treatment visit

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Change in ALSFRS-R score from baseline				
median (inter-quartile range (Q1-Q3))	2.0 (0.5 to 3.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40) Score Change

End point title	Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40) Score Change

End point description:

This patient-reported outcome measures the subjective well-being of patients. There are 5 scales which are calculated
and scored: physical mobility, independence, eating and drinking, communication, emotional functioning. For
ALSAQ-40, an improved condition is represented by a decreasing sub-scale score.
The scales are as follows:
0 - 19: Never or very rarely experience problems 20 - 19: Rarely experience problems 40 - 59: Sometimes experience
problems 60 - 79: Often experience 80 - 100: Problems (nearly) always or unable to do at all

End point type	Secondary

End point timeframe:

From baseline to final treatment visit

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: change in ALSAQ-40 score from baseline				
median (inter-quartile range (Q1-Q3))				
Physical mobility	-5.0 (-15.0 to -3.8)			
Activities of daily living	-2.5 (-17.5 to 2.5)			
Eating and drinking	0 (-12.5 to 0)			

Communication	0 (-8.9 to 0)			
Emotional functioning	-7.5 (-18.5 to -5.0)			
Summary index score	-6.2 (-15.0 to -1.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Urinary p75ECD Change

End point title	Urinary p75ECD Change

End point description:

Urinary p75 extracellular domain (p75ECD) is a biological fluid-based biomarker of ALS disease progression

End point type	Secondary

End point timeframe:

From baseline to final treatment visit

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: ng/mmol creatinine				
median (inter-quartile range (Q1-Q3))	-0.62 (-0.98 to 0.22)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK; Amount of Detectable Drug) of ILB® in Plasma Following Administration

End point title	Pharmacokinetics (PK; Amount of Detectable Drug) of ILB® in Plasma Following Administration

End point description:

This outcome measure quantifies the amount of drug detectable in the blood after administration over time

End point type	Secondary

End point timeframe:

0.5 to 6 hours after ILB® administration

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	6[15]			
Units: µg/mL				
arithmetic mean (standard deviation)				
0.5 hours	3.73 (± 1.41)			
1 hour	4.86 (± 1.18)			
2 hours	5.56 (± 1.45)			
2.5 hours	5.66 (± 1.5)			
3.0 hours	5.4 (± 1.03)			
4.0 hours	4.76 (± 1.17)			
6.0 hours	3.72 (± 0.76)			

Notes:

[15] - Not all patient samples were of sufficient quality for reporting

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK; Tmax) Statistics of ILB® in Plasma Following Administration

End point title	Pharmacokinetics (PK; Tmax) Statistics of ILB® in Plasma Following Administration

End point description:

Tmax (the time the peak concentration occurred) was calculated to characterise the kinetic profile of ILB® in plasma post-administration

End point type	Secondary

End point timeframe:

0.5 hours to 6 hours after ILB® administration

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	6[16]			
Units: hours				
arithmetic mean (standard deviation)	2.42 (± 0.38)			

Notes:

[16] - Not all patient samples were of sufficient quality for reporting

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK; Cmax) Statistics of ILB® in Plasma Following Administration

End point title	Pharmacokinetics (PK; Cmax) Statistics of ILB® in Plasma Following Administration

End point description:

Cmax (peak concentration of ILB® in plasma post-administration) was calculated to characterise the kinetic profile of ILB® in plasma post-administration

End point type	Secondary

End point timeframe:

0.5 hours to 6 hours after ILB® administration

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	6[17]			
Units: µg/mL				
arithmetic mean (standard deviation)	6.03 (± 1.16)			

Notes:

[17] - Not all patient samples were of sufficient quality for reporting

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK; AUC0-last) Statistics of ILB® in Plasma Following Administration

End point title	Pharmacokinetics (PK; AUC0-last) Statistics of ILB® in Plasma Following Administration

End point description:

AUC0−last (area under the curve time 0 (time of administration) to the last value above the limit of quantification) was calculated to characterise the kinetic profile of ILB® in plasma post-administration

End point type	Secondary

End point timeframe:

0.5 hours to 6 hours after ILB® administration

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	6[18]			
Units: µg*h/mL				
arithmetic mean (standard deviation)	27.18 (± 5.62)			

Notes:

[18] - Not all patient samples were of sufficient quality for reporting

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK; t1/2) Statistics of ILB® in Plasma Following Administration

End point title	Pharmacokinetics (PK; t1/2) Statistics of ILB® in Plasma Following Administration

End point description:

t1/2 (terminal half-life of ILB® in plasma post-administration) was calculated to characterise the kinetic profile of ILB® in plasma post-administration

End point type	Secondary

End point timeframe:

0.5 hours to 6 hours after ILB® administration

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	3[19]			
Units: hours				
arithmetic mean (standard deviation)	3.74 (± 1.63)			

Notes:

[19] - Not all patient samples were of sufficient quality for reporting

Statistical analyses

No statistical analyses for this end point

Secondary: NfL in Plasma Change

End point title	NfL in Plasma Change

End point description:

Plasma neurofilament light chain (NfL) is a blood-based biomarker for neurodegeneration

End point type	Secondary

End point timeframe:

from baseline to final treatment visit

End point values	ILB Treatment			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: ng/L				
median (inter-quartile range (Q1-Q3))	1.5 (-3.0 to 4.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Details of all Adverse Events (AEs) were documented and reported from the signing of the informed consent and included the collection of all baseline AEs. AE collection continued until 30 days after the end of treatment visit.

Adverse event reporting additional description:

All AEs, either observed by the Investigator or reported by the subject, were recorded by the Investigator (on an adverse event form) and evaluated. AEs were reviewed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	ILB® arm

Reporting group description: -

Serious adverse events	ILB® arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Musculoskeletal and connective tissue disorders			
Generalised muscle weakness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ILB® arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Investigations			
Abnormal CRP blood results			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Abnormal eosinophil blood results			

subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Abnormal glucose levels (3.1, normal results 3.5-11.0)				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Abnormal hdl level, clinically insignificant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Abnormal mean cell haemoglobin level, clinically insignificant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Abnormal platelet distribution width result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Abnormal ptt blood result (elevated)				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Abnormal redcell distribution levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Abnormal red cell distribution levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Activated partial thromboplastin time prolonged				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Alanine aminotransferase increased				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	3			
Alkaline phosphatase increased				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Aspartate aminotransferase increased				

subjects affected / exposed	3 / 11 (27.27%)			
occurrences (all)	6			
Blood bilirubin increased				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	4			
CRP increased				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Cholesterol high				
subjects affected / exposed	5 / 11 (45.45%)			
occurrences (all)	8			
Creatinine level decreased				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased aptt result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased basophil count				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased basophil level				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Decreased basophil results				
subjects affected / exposed	4 / 11 (36.36%)			
occurrences (all)	4			
Decreased creatinine				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased creatinine levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	2			
Decreased creatinine result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased creatinine value - not				

clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased haematocrit value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased haemoglobin value				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased hdl cholesterol result				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Decreased hdl cholesterol value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased hdl cholesterol value -not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased hdl value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased igm result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased monocyte result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased potassium level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased rbc dist width				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased rbc distribution width				

subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Decreased red blood cell value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Decreased sodium levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated aptt ratio				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	2			
Elevated ast blood level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated c- reactive protein blood results				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated calcim level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated calcium level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated ck levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated creatine kinase result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated crp result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated crp value - not clinically significant				

subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated eosinophil result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated haematocrit blood level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated hdl cholesterol blood levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated mean cell haemoglobin				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated mean cell hb concentration				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated mean cell hb level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated mean cell hb result				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	2			
Elevated monocyte result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated red blood cell count				
subjects affected / exposed	3 / 11 (27.27%)			
occurrences (all)	4			
Elevated sodium levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Elevated total protein result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Hdl cholesterol levels high				

subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Hemoglobin increased				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased ck value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased crp level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased eosinophils count - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased esr value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased iga value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased monocyte count - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased neutrophil count - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	2			
Increased platelet dist width				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased platelet dist. width				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased rbc distribution width				

subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Increased white blood cell value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Low albumin level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Low haematocrit				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Low sodium				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Lymphocyte count decreased				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Mean cell hb concentration level elevated				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Neutrophil count decreased				
subjects affected / exposed	2 / 11 (18.18%)			
occurrences (all)	3			
Prolonged pr interval on ecg				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised ast blood levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	2			
Raised ast levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised blood glucose level				

subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised crp result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised eosinophil count				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised eosinophils				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised hdl cholesterol blood levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised sodium level				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Raised total protein result				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Reduced aptt ratio value - not clinically significant				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Reduced free thyroxine levels				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
White blood cell decreased				
subjects affected / exposed	3 / 11 (27.27%)			
occurrences (all)	5			
Fractured nasal bone following fall				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			
Reduced basophil count				
subjects affected / exposed	1 / 11 (9.09%)			
occurrences (all)	1			

Injury, poisoning and procedural complications			
Bruising			
subjects affected / exposed	9 / 11 (81.82%)		
occurrences (all)	92		
Bruising to right hip from fall			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Bruising to right shoulder following fall			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Bruising to the face following fall			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	5 / 11 (45.45%)		
occurrences (all)	9		
Fall up the stairs leading to flat due to increasing leg weakness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Fall while getting out of bed, due to increase in leg weakness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Not clinically significant abnormal blood creatinine			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Not clinically significant creatinine kinase, 286, (normal range 30-200)			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Not clinically significant monocyte count, 0.9, (normal range 0.2 - 0.8)			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Not clinically significant raised red cell distribution, 14.8 (normal range 11-14)			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chesty cough			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Cold chills down left arm			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Cramps in the chest and abdomen			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Discomfort at injection site when touched			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Patient fell faint			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Eye disorders			
'Sticky' left eye			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Rectal bleeding			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Allergic rhinitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Sore throat			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash on abdomen around injection site			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Rash on both feet			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Increased leg weakness leading to inability to stand resulting in admission to hospital			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Muscle spasm in legs			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Occasional spasm in neck when yawning			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Painful left shoulder blade			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Right hip pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Infections and infestations			
Bilateral ear infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Chest infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Common cold			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	4		
Patient visited the dentist and had a filling			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2019	Section 4.0 eligibility criteria amended to update the lung function assessments inclusion criteria (inclusion criteria 4), changes to the homeostasis markers (inclusion criteria 6) and clarification to exclusion criteria 10. Amendment to schedule of assessments, section 7.3.1 Myoglobin has been removed from the biochemistry sample analysis
26 June 2019	Clinical coordinator added Time frame for primary objective removed Eligibility criteria to continue onto the treatment extension added. Trial duration amended depending on if patients continue onto treatment extension Trial Schema updated based on treatment extension Pregnancy testing to be completed at screening and prior to Day 1 treatment. Additional schedule of events added for patients who go onto the treatment extension after 10 weeks. Patient process to re-consent to treatment extension 'Maximum of 2 weeks without treatment' removed. This is reviewed at clinicians discretion.
16 January 2020	Schedule of events updated with option to extend treatment to a maximum of up to 48 weeks based on clinical assessments and a discussion between the patient and clinician. Week 11 lung function tests moved to week 9. Week 11 intensive visit moved to week 10. Trial Schema updated to reflect the possible further treatment period of up to a maximum of 48 weeks. Thyroid and troponin tests removed from clinical assessments post week 24 in order to reduce treatment costs Dynamometer test introduced in order to assess the muscle strength using a hand-held device.
24 November 2020	Trial Synopsis updated to include single point long-term remote follow up visit starting in Q1 2021; Amended secondary outcome measures and exploratory outcome measures; list of biomarkers to be analysed; Updated trial duration Schedule of assessments updated to include single point long-term remote follow up visit and collection of ALSFRS-R. ALSAQ-40, concomitant and current medication Trial Schema updated to include single point long-term remote follow up visit Secondary Outcome Measures updated to include PK analysis Exploratory Outcome Measures updated with list of all biomarkers to be analysed Trial Design updated to include single point long-term remote follow up visit Added electronic re-consent for the single point long-term remote follow up visit to consent form Updated Quality of life to include the collection of QoL data in the form of ALSAQ-40 in single point long-term remote follow up visit Sample collection amended throughout to reflect planned analysis, sample storage and laboratories involved Patient Follow Up updated to include single point follow-up visit Serious Adverse Events updated to reflect e-mail reporting procedure. End of Trial Definition amended to coincide with updated timelines; final summary of clinical trial report and addendum including data from single point long-term remote follow up visits

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 March 2020	At the end of March 2020 all ALS trial research activity was suspended at the participating centre due to the escalation of the COVID-19 Pandemic. This meant that all on-site visits ended with the last visit on 26th March 2020 as this particular patient group were categorised as High Risk and susceptible to COVID-19 complications. A formal decision to halt recruitment and any further treatment visits, due to the ongoing COVID-19 pandemic and IMP expiry date, was made by the sponsor in October 2020. A protocol amendment was submitted and approved on 11th January 2021 which allowed for quality of life data collection from those patients already enrolled who consented to this visit. This data is to be included in the final clinical study report.	11 January 2021

Notes:

Limitations and caveats

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

Early termination due to the COVID-19 pandemic meant that both recruitment and further treatment was suspended after 11 patients had been recruited. As a result, patients were treated with interrupted and varying numbers of weekly ILB® treatments.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/38990927