A study to explore the safety and acceptability of a treatment called ILB® in patients with Amyotrophic Lateral Sclerosis (ALS)

Basic Results Summary

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Participant Flow

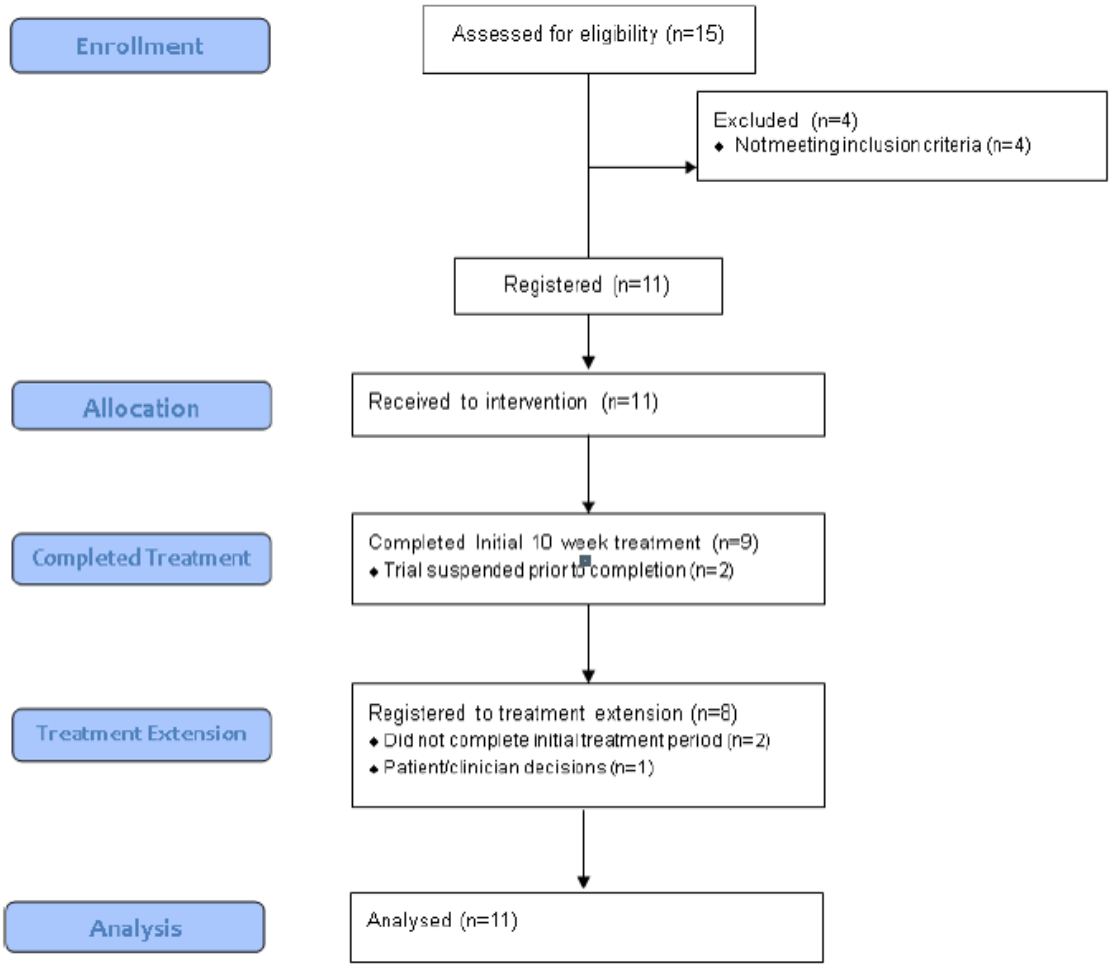

Figure 1. CONSORT diagram

Baseline Characteristics

Table 1: Summary baseline characteristics for all evaluable patients.

		Pooled (N=11)
Sex (n(%))		
	Female	4 (36.36%)
	Male	7 (63.64%)
Age (years)		
	n	11
	Mean (sd)	58 (8.77)
	Median	57
	IQR	(53, 62)
	Range	(44, 77)
Time from ALS diagnosis to trial entry (months)		
	n	11
	Mean (sd)	7.27 (5.34)
	Median	4.69
	IQR	(3.58, 11.63)
	Range	(1.61, 18)
Family history of motor neurone disease (n(%))		
	No	10 (90.91%)
	Yes	1 (9.09%)
Family history of fronto-temporal dementia (n(%))		
	No	11 (100.00%)
	Yes	0 (0.00%)

Table 2: Summary of age category distribution of evaluable patients.

Age Category	**n(%)**
Adults (18-64 years)	9 (81.82%)
From 65-84 years	2 (18.18%)
Total	**11 (100.00%)**

Table 3: Summary of patients enrolled to treatment extension following 10 weeks of initial treatment.

Enrolled to Treatment Extension	**n(%)**
Yes	8 (72.73%)
No	1 (9.09%)
Not applicable	2 (18.18%)
Total	**11 (100.00%)**

Table 4: Summary of patients taking Riluzole at screening visit.

Currently taking Riluzole	**n(%)**
No	10 (90.91%)
Yes	1 (9.09%)
Total	**11 (100.00%)**

Table 5: Summary of patients who have previously taken Riluzole.

Previously taking Riluzole	**n(%)**
No	3 (30.00%)
Yes	7 (70.00%0
Total	**10 (100.00%)**

Table 6: Summary of length of time between Riluzole discontinuation and screening visit in patients who reported previous consumption.

	Time since Riluzole discontinuation (months)
n	7
Mean (sd)	2.27 (5.68)
Median	0.03
IQR	(0, 0.35)
Range	(0, 15.13)

Table 7: Summary of whether reason for Riluzole discontinuation was attributable to trial in patients who reported previous consumption.

Reason for Riluzole discontinuation attributable to trial	**n(%)**
No	1 (14.29%)
Yes	6 (85.71%)
Total	**7 (100.00%)**

Outcome Measures

Primary outcome measures

1. **Safety parameters measured by the incidence of Serious Adverse Events (SAEs) and Adverse Events (AEs) using Common Terminology Criteria for Adverse Events (CTCAE) v4.0**

Table 8: Detailed summary of SAEs reported during the trial.

		n (%; N=1)
SAE Reason		
	Hospitalisation; Disability;	1 (100.00%)
	Congenital defect	0 (0.00%)
	Death	0 (0.00%)
	Hospitalisation	0 (0.00%)
	Life-threatening	0 (0.00%)
	Other	0 (0.00%)
SAE Categorisation		
	Unrelated SAE	1 (100.00%)
	SAR	0 (0.00%)
	Non fatal/life-threatening SUSAR	0 (0.00%)
	Fatal/life-threatening SUSAR	0 (0.00%)
SAE Outcome		
	Resolved - no sequelae	1 (100.00%)
	Resolved - with sequelae	0 (0.00%)
	Unresolved	0 (0.00%)
	Death	0 (0.00%)
Admitting Event Relatedness		
	Unrelated	1 (100.00%)
	Unlikely to be related	0 (0.00%)
	Possibly related	0 (0.00%)
	Probably related	0 (0.00%)
	Definitely related	0 (0.00%)
Admitting Event		
Musculoskeletal and connective tissue disorder - Other, specify: generalised muscle weakness		1 (100.00%)
Admitting Event Grade		
	Grade 1	0 (0.00%)
	Grade 2	0 (0.00%)
	Grade 3	1 (100.00%)
	Grade 4	0 (0.00%)
	Grade 5	0 (0.00%)

Table 9: Summary of AEs reported during the trial and number of patients affected.

	Incidence (n(%) (N=270))	Affected (n(%) (N=11))
AE Grade		
Grade 1	265 (98.15%)	11 (100%)
Grade 2	4 (1.48%)	3 (27.27%)
Grade 3	1 (0.37%)	1 (9.09%)
Grade 4	0 (0.00%)	0 (0%)
Grade 5	0 (0.00%)	0 (0%)
AE Relatedness		
Unrelated	127 (47.04%)	10 (90.91%)
Unlikely to be related	45 (16.67%)	10 (90.91%)
Possibly related	4 (1.48%)	1 (9.09%)
Probably related	1 (0.37%)	1 (9.09%)
Definitely related	93 (34.44%)	9 (81.82%)

2. Tolerability parameters measured by the incidence of intolerable adverse events.

Table 10. Number of intolerable events reported during the trial

Number of intolerable events reported during the trial
0

3. Quantity of drug administered.

Table 11: Quantity of drug administered during the trial.

Total number of treatment administrations	Average Weight (kg)	Average Dose (mg)	Cumulative Dose (mg)	Interruptions
37	90.10811	180.2162	6668	1
38	86.20263	172.3947	6551	0
34	72.07647	143.6176	4883	2
35	88.89714	177.7714	6222	1
35	75.62286	151.0571	5287	0
24	87.45417	175	4200	2
21	66.42857	132.8095	2789	0
21	70.63333	141.2857	2967	1
7	59.57143	119.1429	834	3
6	84.8	169.3333	1016	0
4	93.2	186.25	745	0

Secondary outcome measures

1. Revised ALS Functional Rating Scale (ALSFRS-R)

Table 12: ALSFRS-R total scores over study period, per patient

	Treatment Week (W)																		Follow up Week (W)		
Screening	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W15**	**W16**	**W19**	**W24**	**W25**	**W29**	**W33**	**W38**	**W12**	**W16**	**W26**
38	34	36	35	36	38	36	36	37	38	35	34	36		33	33	34	34	37	36	35	33	35
38	39	37	39	38	38	38	38	38	38	38	39	39		37	39	35	36	31	32	38	38	
29	29		32	32	31	31	31	31	31	31	31		30	32	32		33	28				
44	44	43	43	43	43	43	43	43	43	43	43	42		44	42		42	41				
41	39	39	39	39	39	39	39	39	39	39	39	38		39	38		37	38				
42	40	39	39	41	40	38	36	36	36	39	35	36		41	34							
38	40	39	40	38	37	37	38	37	38	38	37	39		39								
38	38	38	38	39	39		37	37	37	37	37	35		38								
35	33	34	34	32				33	35	33										33	30	
44	42	44	44	43	43	42																
36	40	38	38	37																		

2. ALS Assessment Questionnaire (ALSAQ-40)

Table 13: ALSAQ-40 total scores over study period, per patient

	Treatment Week (W)																		Follow up Week (W)		
Screening	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**	**W9**	**W10**	**W11**	**W15**	**W16**	**W19**	**W24**	**W25**	**W29**	**W33**	**W38**	**W12**	**W16**	**W26**
34.38	41.25	37.5	36.25	28.12	29.38	29.38	28.75	28.75	31.88	30	44.38	46.25		45.62	44.38	45	41.88	44.38	52.5	31.88	37.5	46.25
30.62	30.62	30.62	34.38	36.25	32.5	31.25	30	29.38	35	33.75	33.75	34.38		40.62	33.75	43.12	36.25	43.75	42.5	39.38	34.38	
38.75	38.12		31.88	31.25	20	24.38	16.88	13.12	13.12	12.5			20	22.5	27.5		30	42.5				
24.38	24.38	25.62	26.88	30	28.12	28.12	28.12	27.5	28.12	30	26.88	31.88		29.38	28.75		33.12	30.62				
23.12	30	26.25	20.62	21.88	20	18.75	18.75	22.5	20.62	20	19.38	20.62		23.75	23.12		21.25	26.25				
20.62	23.75	15.62	13.12	12.5	15	21.88	21.25	20.62	22.5	20	18.75	21.25		25.62	43.12							
35.62	33.75	26.88	31.88	29.38	32.5	30.62	26.25	28.75	33.75	30.62	33.12	33.75		30								
23.75	15.62	13.12	13.75	13.75	13.75		15.62	16.88	10.62	15	15	21.88		23.75								
36.88	41.88	55	47.5	45				56.25	52.5	53.12										57.5	51.88	
20	23.12	15.62	15	16.25	21.25	20.62																
23.12	33.75	34.38	35	36.88																		

3. Urinary $p75^{ECD}$

Table 14: Urinary $p75^{ECD}$ (ng/mmol creatinine) over treatment and follow-up weeks.

Week 1	Week 3	Week 5	Week 11	Week 12 (Follow-up)	Week 24	Week 25	Week 26 (Follow-up)
5.58		7.85	7.38	11.63	11.53	2.75	2.38
	6.53	4.14	6.5	3.55		3.08	
3.67		2.97	3.28		6.35		
1.67		2.02	0.71		1.05		
3.91		4.19	2.65		2.93		
2.98		7.02	4.95		5.49		
2.87		3.09					
8.07		7.43					
3.62							
0.97		1.17					

4. Pharmacokinetic (PK) ILB® in plasma following administration

Table 15: Summary of ILB® in plasma (µg/mL) post IMP administration.

	0.5hours	1.0hours	2.0hours	2.5hours	3.0hours	4.0hours	6.0hours
n	6	6	6	6	6	6	6
Mean (sd)	3.73 (1.41)	4.86 (1.18)	5.56 (1.45)	5.66 (1.5)	5.4 (1.03)	4.76 (1.17)	3.72 (0.76)
Median	3.32	4.67	5.7	5.79	5.24	4.56	3.87
IQR	(2.95, 4.03)	(4.23, 5.14)	(4.42, 6.87)	(4.79, 6.91)	(4.69, 6.25)	(4.15, 4.77)	(3.19, 4.25)
Range	(2.33, 6.28)	(3.49, 6.94)	(3.71, 7.03)	(3.44, 7.2)	(4.16, 6.67)	(3.62, 6.98)	(2.62, 4.59)

5. Neurofilament Light Chain (NfL) in plasma

Table 16: NfL concentration (µg/L) over treatment period and follow-ups, per patient

Week 1	Week 5	Week 11	Week 12 (follow-up)	Week 24	Week 25	Week 26 (follow-up)	Week 38
24	21	22	24	24	29	26	27
16	13	18	14	14	29		18
65	54	65		62			
37	33	34		49			
53	50	49		46			
40	38	41		35			
26	24	22					
55	51	56					
61			68				
44	41						
45							

Adverse Events

Table 17: Line listing of all 270 reported Adverse Events during the trial, ordered by category and toxicity.

Category	Toxicity	Exposed	Affected	Occurrences	Related	% Patients Affected
Blood and lymphatic system disorders	Blood and lymphatic system disorders - Other, specify: Not clinically significant abnormal blood creatinine	11	1	1	0	9.09
	Blood and lymphatic system disorders - Other, specify: Not clinically significant creatinine kinase, 286, (normal range 30-200)	11	1	1	0	9.09
	Blood and lymphatic system disorders - Other, specify: Not clinically significant monocyte count, 0.9, (normal range 0.2 - 0.8)	11	1	1	0	9.09
	Blood and lymphatic system disorders - Other, specify: Not clinically significant raised red cell distribution, 14.8 (normal range 11-14)	11	1	1	0	9.09
Eye disorders	Eye disorders - Other, specify: 'Sticky' left eye	11	1	1	0	9.09
Gastrointestinal disorders	Constipation	11	1	1	0	9.09
	Diarrhea	11	1	1	0	9.09
	Gastrointestinal disorders - Other, specify: Rectal bleeding	11	1	1	0	9.09
General disorders and administration site conditions	General disorders and administration site conditions - Other, specify: Chesty cough	11	1	1	0	9.09
	General disorders and administration site conditions - Other, specify: Cold chills down left arm	11	1	1	0	9.09
	General disorders and administration site conditions - Other, specify: Cramps in the chest and abdomen	11	1	1	0	9.09
	General disorders and administration site conditions - Other, specify: Discomfort at injection site when touched	11	1	1	1	9.09
	General disorders and administration site conditions - Other, specify: Patient felt faint	11	1	1	0	9.09
Infections and infestations	Infections and infestations - Other, specify: Bilateral ear infection	11	1	1	0	9.09
	Infections and infestations - Other, specify: Chest infection	11	1	1	0	9.09
	Infections and infestations - Other, specify: Common cold	11	3	4	0	27.27
	Infections and infestations - Other, specify: Patient visited the dentist and had a filling.	11	1	1	0	9.09
Injury, poisoning and procedural complications	Bruising	11	9	92	92	81.82
	Fall	11	5	9	0	45.45
	Injury, poisoning and procedural complications - Other, specify: Bruising to right hip from fall	11	1	1	0	9.09
	Injury, poisoning and procedural complications - Other, specify: Bruising to right shoulder following fall.	11	1	1	0	9.09
	Injury, poisoning and procedural complications - Other, specify: Bruising to the face following fall.	11	1	1	0	9.09
	Injury, poisoning and procedural complications - Other, specify: Fall up the stairs leading to flat, due to increasing leg weakness	11	1	1	0	9.09

Category	Toxicity	Exposed	Affected	Occurrences	Related	% Patients Affected
	Injury, poisoning and procedural complications - Other, specify: Fall while getting out of bed, due to increase in leg weakness	11	1	1	0	9.09
	Activated partial thromboplastin time prolonged	11	1	1	0	9.09
	Alanine aminotransferase increased	11	2	3	1	18.18
	Alkaline phosphatase increased	11	2	2	1	18.18
	Aspartate aminotransferase increased	11	3	6	1	27.27
	Blood bilirubin increased	11	1	4	0	9.09
	Cholesterol high	11	5	8	0	45.45
	Hemoglobin increased	11	1	1	0	9.09
	Investigations - Other, specify: Abnormal crp blood results	11	1	1	0	9.09
	Investigations - Other, specify: Abnormal eosinophil blood results	11	1	1	0	9.09
	Investigations - Other, specify: Abnormal glucose levels (3.1, normal results 3.5-11.0)	11	1	1	0	9.09
	Investigations - Other, specify: Abnormal hdl level, clinically insignificant.	11	1	1	0	9.09
	Investigations - Other, specify: Abnormal mean cell haemoglobin level, clinically insignificant.	11	1	1	0	9.09
	Investigations - Other, specify: Abnormal platelet distribution width result	11	1	1	0	9.09
Investigations	Investigations - Other, specify: Abnormal ptt blood result (elevated)	11	1	1	1	9.09
	Investigations - Other, specify: Abnormal red cell distribution levels	11	1	1	0	9.09
	Investigations - Other, specify: Abnormal red cell distribution levels.	11	1	1	0	9.09
	Investigations - Other, specify: Creatinine level decreased	11	1	1	0	9.09
	Investigations - Other, specify: Crp increased	11	1	1	0	9.09
	Investigations - Other, specify: Decreased aptt result	11	1	1	0	9.09
	Investigations - Other, specify: Decreased basophil count	11	1	1	0	9.09
	Investigations - Other, specify: Decreased basophil level	11	2	2	0	18.18
	Investigations - Other, specify: Decreased basophil result	11	4	4	0	36.36
	Investigations - Other, specify: Decreased creatinine	11	1	1	0	9.09
	Investigations - Other, specify: Decreased creatinine levels	11	1	2	0	9.09
	Investigations - Other, specify: Decreased creatinine result	11	1	1	0	9.09
	Investigations - Other, specify: Decreased creatinine value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Decreased haematocrit value - not clinically significant	11	1	1	0	9.09

Category	Toxicity	Exposed	Affected	Occurrences	Related	% Patients Affected
	Investigations - Other, specify: Decreased haemoglobin value	11	1	1	0	9.09
	Investigations - Other, specify: Decreased hdl cholesterol result	11	2	2	0	18.18
	Investigations - Other, specify: Decreased hdl cholesterol value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Decreased hdl cholesterol value -not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Decreased hdl value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Decreased igm result	11	1	1	0	9.09
	Investigations - Other, specify: Decreased monocyte result	11	1	1	0	9.09
	Investigations - Other, specify: Decreased potassium level	11	1	1	0	9.09
	Investigations - Other, specify: Decreased rbc dist width	11	1	1	0	9.09
	Investigations - Other, specify: Decreased rbc distribution width	11	2	2	0	18.18
	Investigations - Other, specify: Decreased red blood cell value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Decreased sodium levels	11	1	1	0	9.09
	Investigations - Other, specify: Elevated aptt ratio	11	1	2	0	9.09
	Investigations - Other, specify: Elevated ast blood level	11	1	1	0	9.09
	Investigations - Other, specify: Elevated c- reactive protein blood results	11	1	1	0	9.09
	Investigations - Other, specify: Elevated calcim level	11	1	1	0	9.09
	Investigations - Other, specify: Elevated calcium level	11	1	1	0	9.09
	Investigations - Other, specify: Elevated ck levels	11	1	1	0	9.09
	Investigations - Other, specify: Elevated creatine kinase result	11	1	1	0	9.09
	Investigations - Other, specify: Elevated crp result	11	1	1	0	9.09
	Investigations - Other, specify: Elevated crp value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Elevated eosinophil result	11	1	1	0	9.09
	Investigations - Other, specify: Elevated haematocrit blood level	11	1	1	0	9.09
	Investigations - Other, specify: Elevated hdl cholesterol blood levels.	11	1	1	0	9.09
	Investigations - Other, specify: Elevated mean cell haemoglobin	11	1	1	0	9.09
	Investigations - Other, specify: Elevated mean cell hb concentration	11	1	1	0	9.09
	Investigations - Other, specify: Elevated mean cell hb level	11	1	1	0	9.09
	Investigations - Other, specify: Elevated mean cell hb result	11	2	2	0	18.18
	Investigations - Other, specify: Elevated monocyte result	11	1	1	0	9.09

Category	Toxicity	Exposed	Affected	Occurrences	Related	% Patients Affected
	Investigations - Other, specify: Elevated red blood cell count	11	3	4	0	27.27
	Investigations - Other, specify: Elevated sodium levels	11	1	1	0	9.09
	Investigations - Other, specify: Elevated total protein result	11	1	1	0	9.09
	Investigations - Other, specify: Hdl cholesterol levels high	11	1	1	0	9.09
	Investigations - Other, specify: Increased ck value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Increased crp level	11	1	1	0	9.09
	Investigations - Other, specify: Increased eosinophils count - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Increased esr value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Increased iga value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Increased monocyte count - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Increased neutrophil count - not clinically significant	11	1	2	0	9.09
	Investigations - Other, specify: Increased platelet dist width	11	1	1	0	9.09
	Investigations - Other, specify: Increased platelet dist. width	11	1	1	0	9.09
	Investigations - Other, specify: Increased rbc distribution width	11	1	1	0	9.09
	Investigations - Other, specify: Increased white blood cell value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Low albumin level	11	1	1	0	9.09
	Investigations - Other, specify: Low haematocrit	11	1	1	0	9.09
	Investigations - Other, specify: Low sodium	11	1	1	0	9.09
	Investigations - Other, specify: Mean cell hb concentration level elevated	11	1	1	0	9.09
	Investigations - Other, specify: Prolonged pr interval on ecg	11	1	1	0	9.09
	Investigations - Other, specify: Raised ast blood levels	11	1	2	0	9.09
	Investigations - Other, specify: Raised ast levels	11	1	1	0	9.09
	Investigations - Other, specify: Raised blood glucose level	11	1	1	0	9.09
	Investigations - Other, specify: Raised crp result	11	1	1	0	9.09
	Investigations - Other, specify: Raised eosinophil count	11	1	1	0	9.09
	Investigations - Other, specify: Raised eosinophils	11	1	1	0	9.09
	Investigations - Other, specify: Raised hdl cholesterol blood levels.	11	1	1	0	9.09
	Investigations - Other, specify: Raised sodium level	11	1	1	0	9.09
	Investigations - Other, specify: Raised total protein result	11	1	1	0	9.09

Category	Toxicity	Exposed	Affected	Occurrences	Related	% Patients Affected
	Investigations - Other, specify: Reduced aptt ratio value - not clinically significant	11	1	1	0	9.09
	Investigations - Other, specify: Reduced basophil count	11	1	1	0	9.09
	Investigations - Other, specify: Reduced free thyroxine levels	11	1	1	0	9.09
	Lymphocyte count decreased	11	1	1	0	9.09
	Neutrophil count decreased	11	2	3	0	18.18
	White blood cell decreased	11	3	5	0	27.27
Musculoskeletal and connective tissue disorders	Back pain	11	1	1	0	9.09
	Musculoskeletal and connective tissue disorder - Other, specify: Fractured nasal bone following fall.	11	1	1	0	9.09
	Musculoskeletal and connective tissue disorder - Other, specify: Increased leg weakness leading to inability to st and resulting in admission to hospital	11	1	1	0	9.09
	Musculoskeletal and connective tissue disorder - Other, specify: Muscle spasm in legs	11	1	1	0	9.09
	Musculoskeletal and connective tissue disorder - Other, specify: Occasional spasm in neck when yawning	11	1	1	0	9.09
	Musculoskeletal and connective tissue disorder - Other, specify: Painful left shoulder blade.	11	1	1	0	9.09
	Musculoskeletal and connective tissue disorder - Other, specify: Right hip pain	11	1	1	0	9.09
Nervous system disorders	Headache	11	1	1	0	9.09
Psychiatric disorders	Insomnia	11	1	1	0	9.09
Respiratory, thoracic and mediastinal disorders	Allergic rhinitis	11	1	1	0	9.09
	Respiratory, thoracic and mediastinal disorders - Other, specify: Pneumonia	11	1	1	0	9.09
	Sore throat	11	1	1	0	9.09
Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders - Other, specify: Eczema	11	1	1	0	9.09
	Skin and subcutaneous tissue disorders - Other, specify: Rash on abdomen around injection site	11	1	1	1	9.09
	Skin and subcutaneous tissue disorders - Other, specify: Rash on both feet	11	1	1	0	9.09

Serious Adverse Events

Table 18: Line listing of Serious Adverse Events reporting during the trial.

Time from onset to Entry (Days)	SAE Reason	Reason Other Specify	SAE Category	Event	Other Events	Other Event Specify	Grade	Grades of Other Events	Relatedness	Outcome	Sequelae	Duration of Event (Days)
223	Hospitalisation		Unrelated SAE	Musculoskeletal and connective tissue disorder - Other, specify		generalised muscle weakness	3		Unrelated	Resolved - no sequelae		3

Table 19: Summary of Serious Adverse Events reporting during the trial.

Category	Toxicity	Number of Patients Exposed	Number of Patients Affected	Number of Occurrences	Number of Fatal Occurrences	Number of Events Related to ILB	Number Related and Fatal
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorder - Other, specify: Increased leg weakness leading to inability to stand resulting in admission to hospital	11	1	1	0	0	0