

Phase 2/3 study of ulviprubart in inclusion body myositis: Study design, patient characteristics, and topline results

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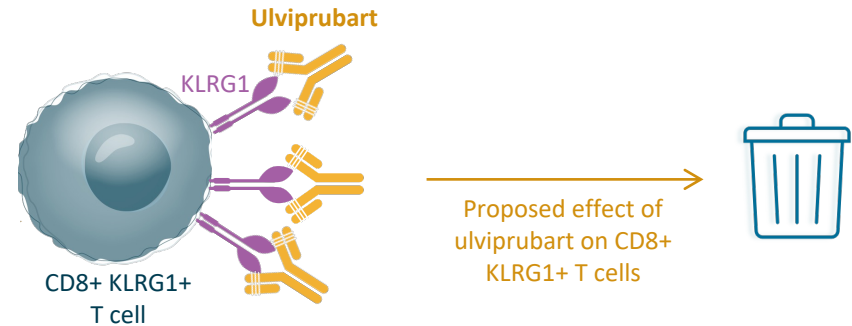
Disclosure Statement

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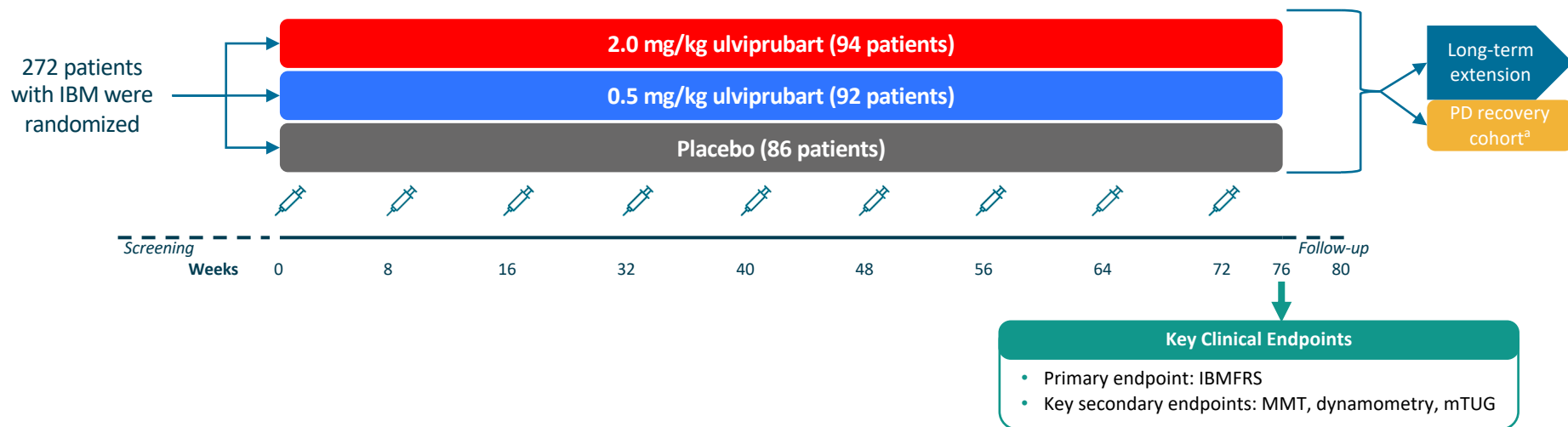
Introduction

- In patients with IBM, immune cells called T cells incorrectly attack and destroy muscles^{1,2}
- Most of these T cells are marked with proteins called CD8 and KLRG1^{3,4}
- Ulviprubart is a drug that was developed to recognize cells marked with KLRG1 and clear them from the body
- The goal of this clinical trial was to study whether ulviprubart could help the symptoms of IBM



The MUSCLE study: Objectives and design

- The goal of this phase 2/3 clinical trial was to study the efficacy, safety, and tolerability of subcutaneous (under the skin) injections of uliviprubart in patients with IBM
- The study was done at 45 sites in Australia, Belgium, Canada, France, Germany, the UK, and the US



Trial registration number: NCT05721573. All study medications are administered via subcutaneous injection. *To follow recovery of T cells in patients who prematurely discontinue; no study medications will be administered. IBM, inclusion body myositis; IBMFRS, Inclusion Body Myositis Functional Rating Scale; MMT, manual muscle testing; mTUG, modified Timed Up and Go; PD, pharmacodynamic; UK, United Kingdom; US, United States.



Characteristics of patients who could be included in the study

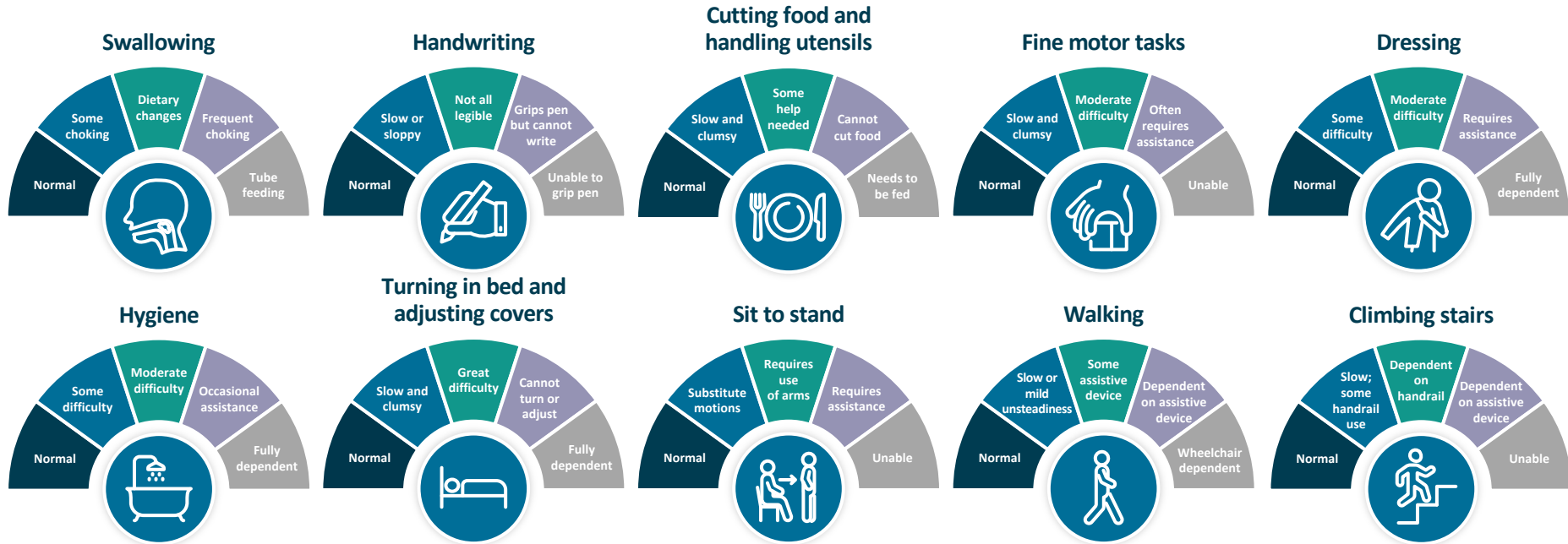


Patients could be included in the study if they

- Had an IBM diagnosis based on criteria from 2011¹
- Were 40 years old or older
- Were able to arise from a standard armchair with use of their arms but without support from another person or device
- Were able to walk 3 meters, turn around, walk back to the chair, and sit down, with or without an assistive device
- Weighed between 40 kg and 150 kg
- Did not have other forms of myositis or autoimmune disease (except Sjögren's or thyroid disease)

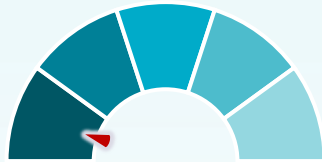
Primary endpoint: Change from study start in IBMFRS compared to placebo

IBMFRS is a 10-question, 40-point functional rating scale



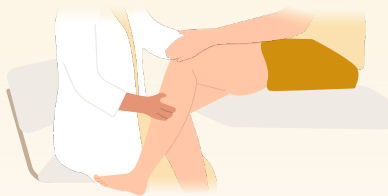
Measuring functional impact and changes in muscle strength in IBM

IBMFRS¹



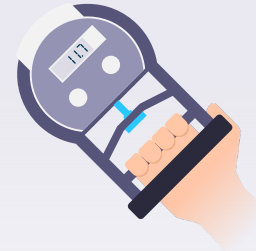
- 10-item **disease-specific functional scale** rated by a clinical evaluator
- Per-item score range, 0–4; total score range, 0–40
- **Higher** scores indicate **better functioning**

MMT²



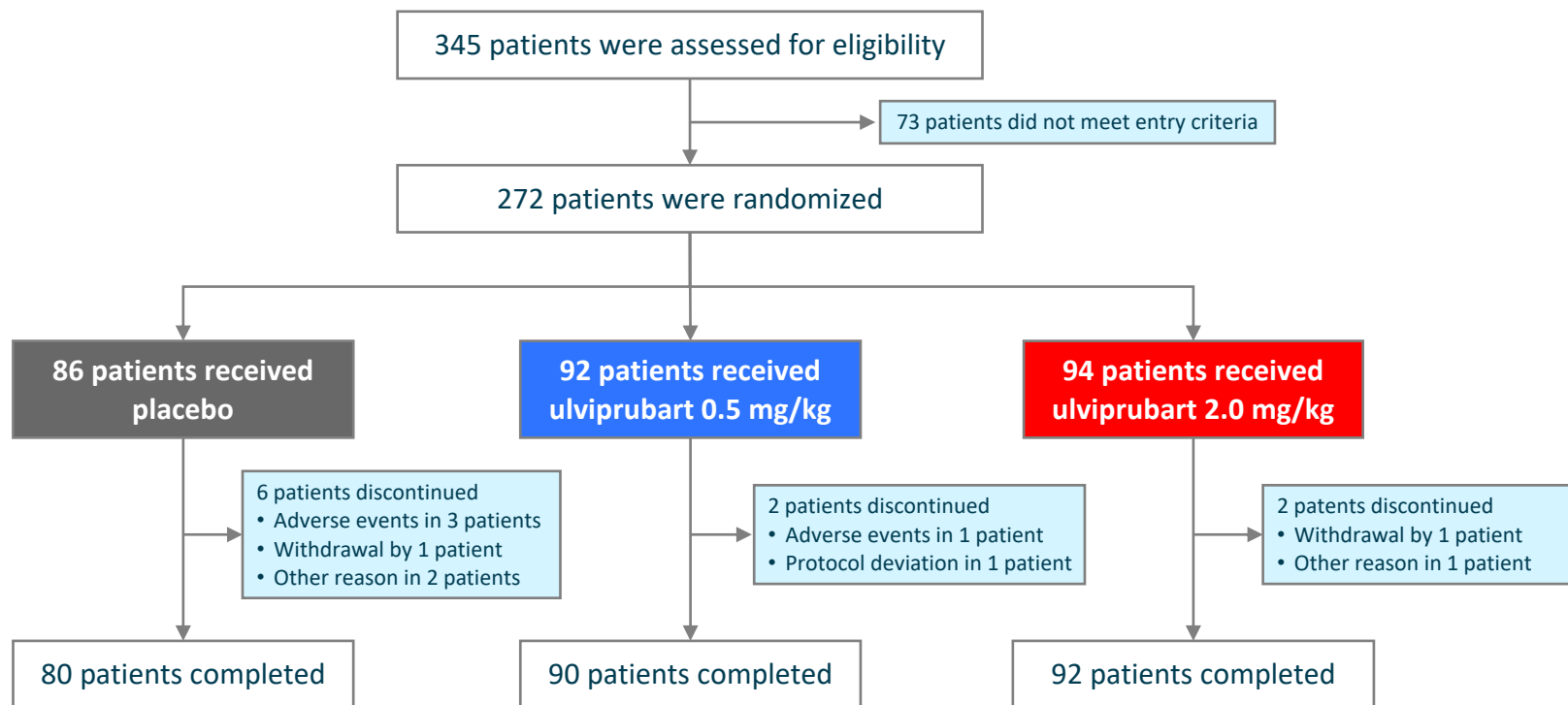
- Measures ability of muscles to move against gravity and resistance
- Assessed as part of a **physical examination** by a clinician
- **Higher** scores indicate **better muscle strength**

Dynamometry³



- Measurement via **medical device** of the force a muscle can exert
- Typically measured in the hand (grip strength) and quadriceps for IBM
- **Higher** values indicate **more force**

Patients in the MUSCLE study



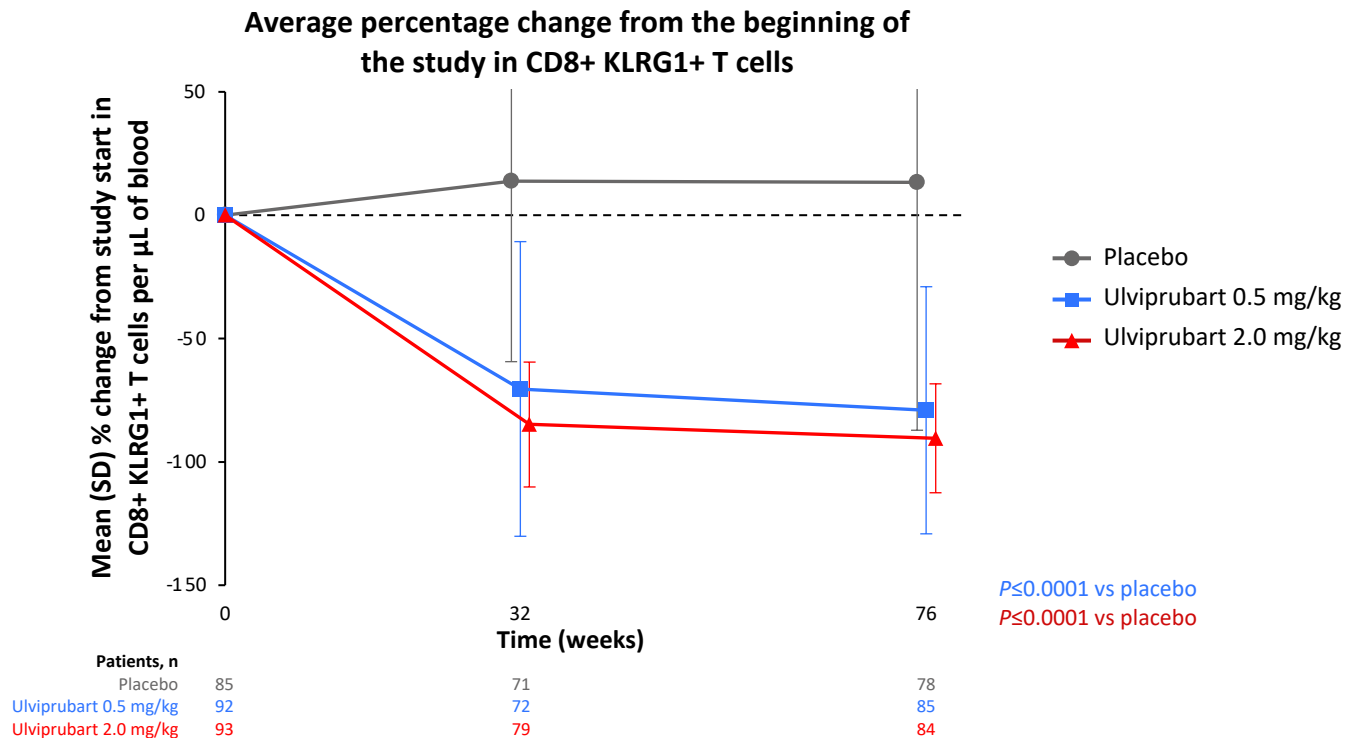
Characteristics of patients at the beginning of the study

- In this study, about 7 out of every 10 patients were 65 years old or older and most patients were male
- Patients in the study had some difficulties with daily functioning based on IBMFRS scores

Immune cells potentially involved in IBM

	Placebo (n=86)	Ulviprubart 0.5 mg/kg (n=92)	Ulviprubart 2.0 mg/kg (n=94)
Age, mean (SD), years	68.5 (7.6)	67.9 (7.0)	67.9 (8.7)
<65 years, n (%)	21 (24.4)	29 (31.5)	28 (29.8)
≥65 years, n (%)	65 (75.6)	63 (68.5)	66 (70.2)
Sex, male, n (%)	60 (69.8)	61 (66.3)	65 (69.1)
Race, White, n (%)	73 (84.9)	86 (93.5)	84 (89.4)
Weight, mean (SD), kg	82.5 (21.1)	83.2 (17.5)	84.8 (18.6)
BMI, mean (SD), kg/m ²	27.0 (5.1)	27.4 (5.0)	27.7 (4.6)
IBMFRS score, mean (SD)	27.8 (5.3)	27.1 (5.2)	27.0 (4.5)
Time from diagnosis, mean (SD), years	4.2 (3.8)	3.7 (2.9)	4.0 (3.1)
Time from symptom onset, mean (SD), years	8.7 (4.9)	8.9 (5.2)	9.2 (4.7)
CD8+ KLRG1+ T cells, cells/μL of blood, mean (SD)	324.3 (379.8)	327.4 (361.4)	335.5 (305.8)

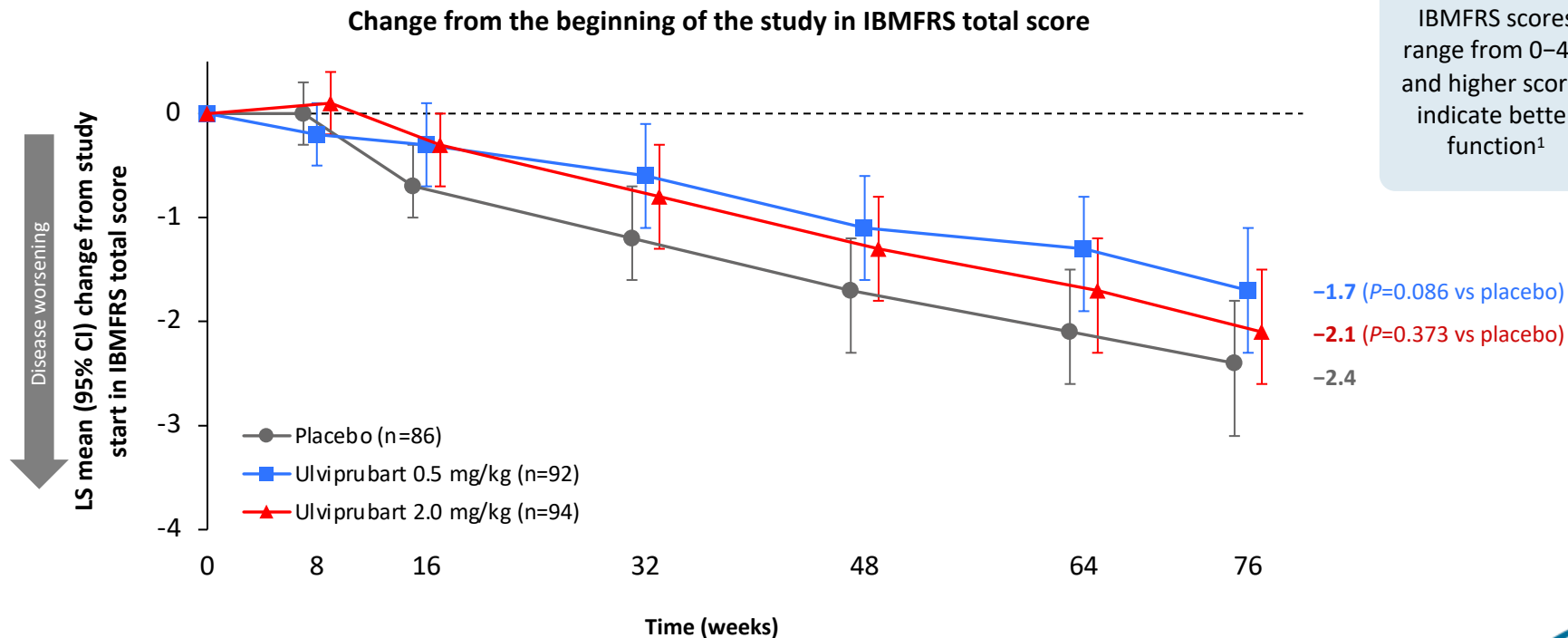
In patients who received either dose of ulviprubart, the levels of T cells marked with KLRG1 went down over time



Mean CD8+ KLRG1+ T cell levels were not significantly different between the ulviprubart 0.5 and 2.0 mg/kg groups. KLRG1, killer cell lectin-like receptor G1.



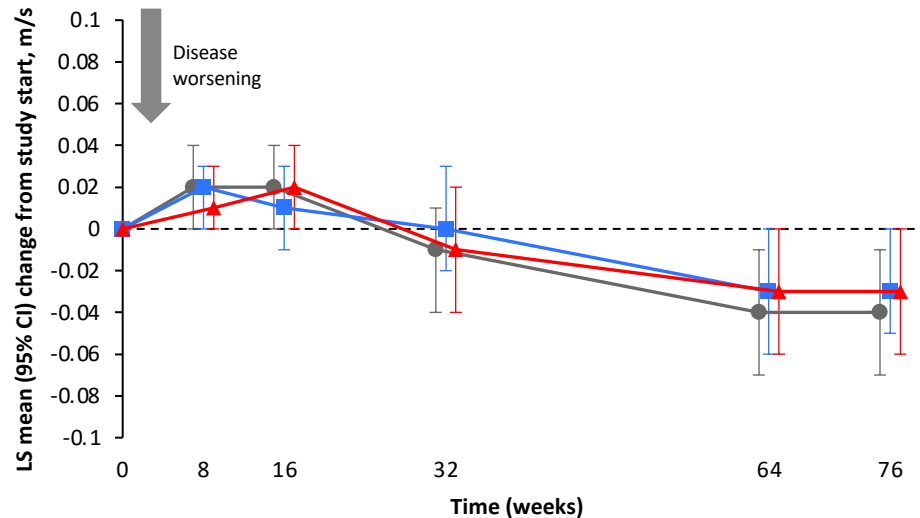
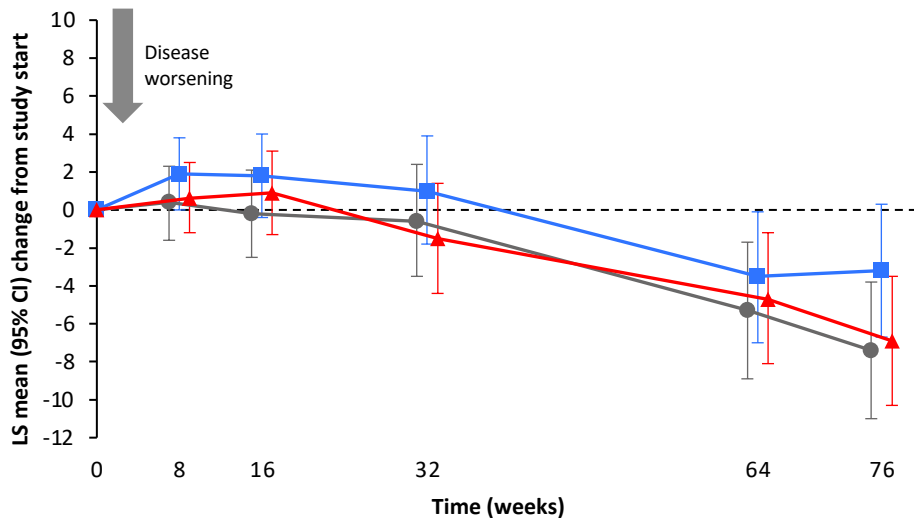
The primary endpoint was not met: At week 76, IBMFRS scores were not statistically different in patients treated with ulviprubarb compared with placebo



Changes in the MMT12 and mTUG assessments were also not significantly different with ulviprubart compared with placebo

Change in MMT12

Change in mTUG velocity (m/s)



● Placebo (n=86)

■ Ulviprubart 0.5 mg/kg (n=92)

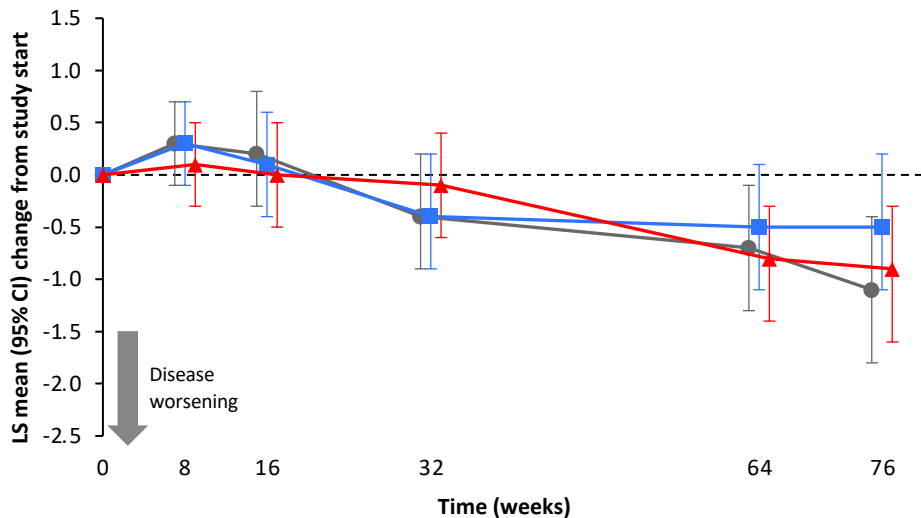
▲ Ulviprubart 2.0 mg/kg (n=94)

Changes from the beginning of the study with ulviprubart were not statistically significantly different vs placebo at any time point. LS, least squares; m/s, meters per second; MMT12, Manual Muscle Testing 12; mTUG, modified Timed Up and Go.

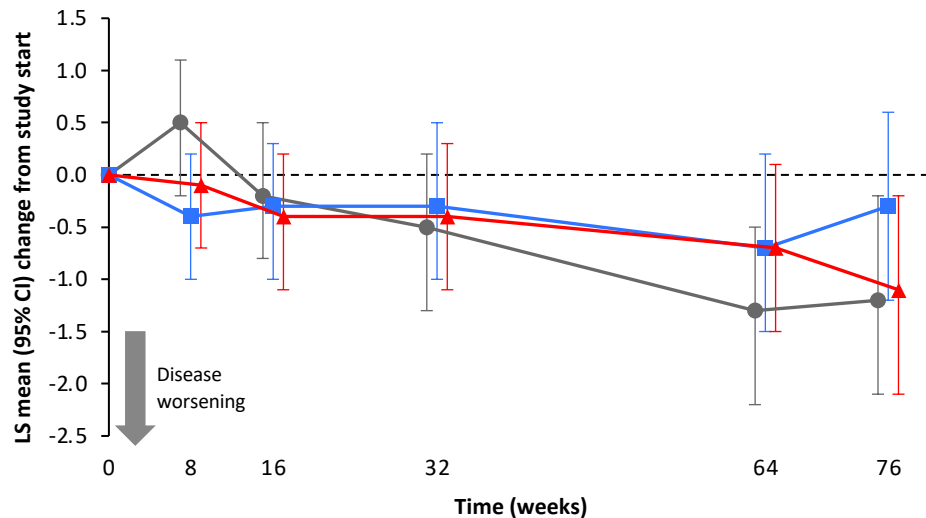


Changes in muscle strength were not significantly different with ulviprubart compared with placebo

Change in dynamometry grip strength for the dominant hand



Change in dynamometry quadriceps strength for the dominant leg



● Placebo (n=86^a)

■ Ulviprubart 0.5 mg/kg (n=92)

▲ Ulviprubart 2.0 mg/kg (n=94)

Changes from the beginning of the study with ulviprubart were not statistically significantly different vs placebo at any time point. ^an=85 for dominant quadriceps dynamometry. LS, least squares.



Additional analyses

Changes in IBMFRS were also studied in patients who:



Had less severe disease (IBMFRS scores of 29 or higher) or more severe disease (IBMFRS scores under 29) at the start of the study



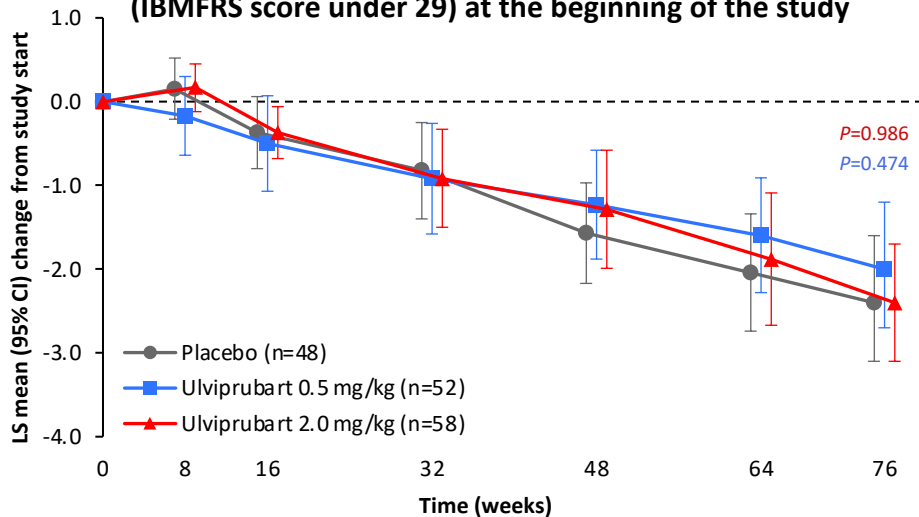
Had unique antibodies (anti-cN1A) in their blood or not



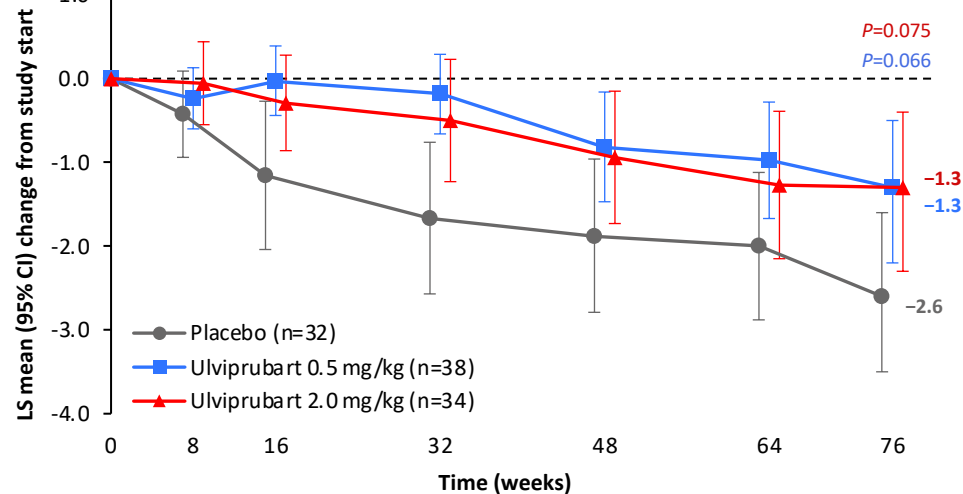
Were male versus female

Results suggest patients with less severe disease who received ulviprubart may have had a slower disease progression

Change in IBMFRS score in patients with more severe disease (IBMFRS score under 29) at the beginning of the study



Change in IBMFRS score in patients with less severe disease (IBMFRS score 29 or higher) at the beginning of the study



In patients with less severe disease

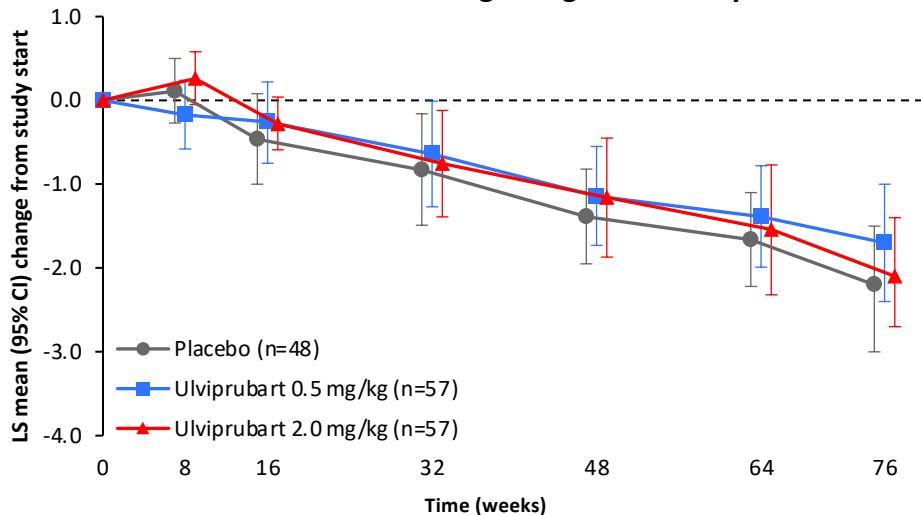
- There was a difference between ulviprubart and placebo at week 76 that represented a 50% slowing of disease progression
- The biggest differences occurred by week 16

Data for time points 8, 16, 32, 48, and 64 are mean estimates and remain to be validated. Patient numbers for changes from the beginning of the study at week 76 are shown. IBMFRS, Inclusion Body Myositis Functional Rating Scale; LS, least squares.

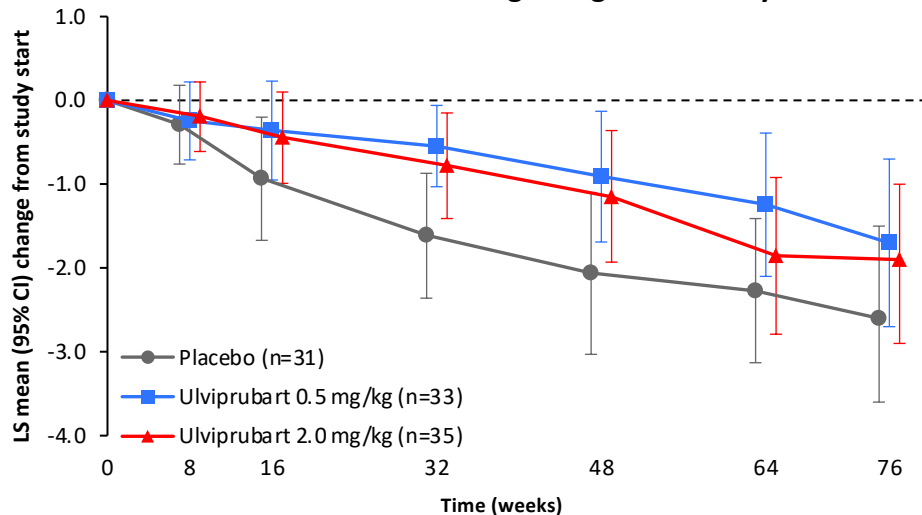


The presence of anti-cN1A antibodies in the blood did not affect IBMFRS score changes with ulviprubart or placebo

Change in IBMFRS score in patients with anti-cN1A antibodies at the beginning of the study^a



Change in IBMFRS score in patients without anti-cN1A antibodies at the beginning of the study



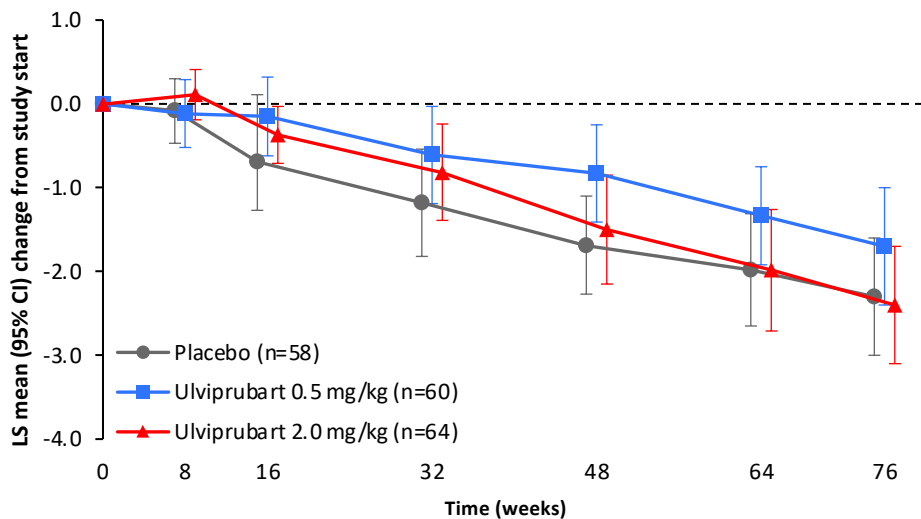
Antibodies against the cN1A protein have been found in the blood of patients with IBM. The presence of these antibodies can be used to help diagnose IBM¹

Data for time points 8, 16, 32, 48, and 64 are mean estimates and remain to be validated. Patient numbers for changes from the beginning of the study at week 76 are shown. ^aIncludes patients who were positive or borderline for anti-cN1A antibody at the beginning of the study. cN1A, cytosolic 5'-nucleotidase 1A; IBM, inclusion body myositis; IBMFRS, Inclusion Body Myositis Functional Rating Scale; LS, least squares. 1. Lilleker JB, et al. *Neuromuscul Disord.* 2024;37:36-51.

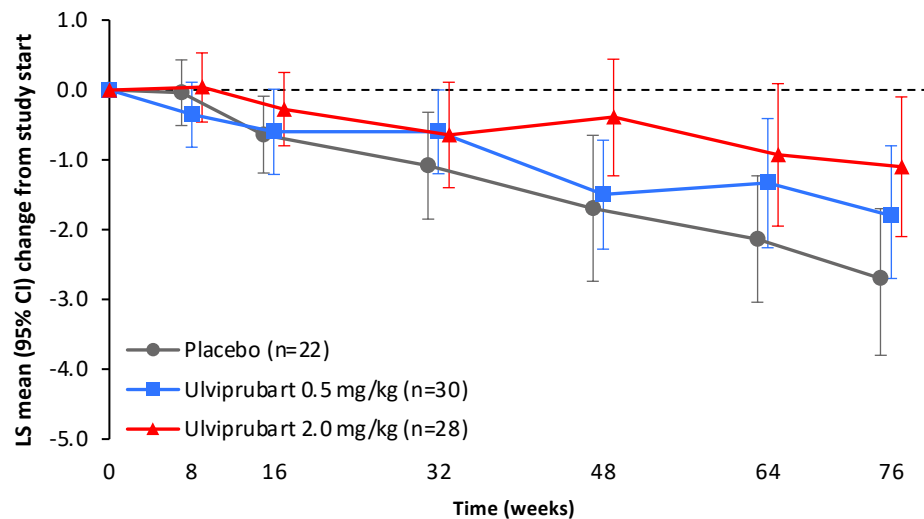


Changes in IBMFRS scores were similar in men and women who received ulviprubart or placebo

Change in IBMFRS score for male patients



Change in IBMFRS score for female patients



Data for time points 8, 16, 32, 48, and 64 are mean estimates and remain to be validated. Patient numbers for changes from the beginning of the study at week 76 are shown. IBMFRS, Inclusion Body Myositis Functional Rating Scale; LS, least squares.



Safety summary

- Most of the side effects in the trial were mild or moderate
- In general, ulviprubart had a favorable safety and tolerability profile compared with placebo

Patients, n (%)	Placebo (n=86)	Ulviprubart 0.5 mg/kg (n=92)	Ulviprubart 2.0 mg/kg (n=94)
Side effects	84 (97.7)	92 (100)	91 (96.8)
Side effects related to the study drug	31 (36.0)	54 (58.7)	64 (68.1)
Serious side effects	18 (20.9)	8 (8.7)	12 (12.8)
Serious side effects related to the study drug	0	0	0
Serious side effects leading to discontinuation ^a	1 (1.2)	0	0
Side effects leading to death ^b	2 (2.3)	0	1 (1.1)
Side effects of special interest ^c	57 (66.3)	70 (76.1)	78 (83.0)
Side effects of special interest related to the study drug	21 (24.4)	42 (45.7)	55 (58.5)
Side effects of special interest leading to discontinuation	1 (1.2)	0	0

^aEvents of pneumonia from regurgitated stomach contents and dehydration unrelated to treatment in 1 patient receiving placebo. ^bPlacebo: Events of metastatic malignant melanoma unrelated to treatment and rapid respiratory failure unrelated to treatment in 1 patient each; ulviprubart 2.0 mg/kg: Event of cerebral bleeding unrelated to treatment in 1 patient. ^cSide effects of special interest were infections or symptoms of systemic drug reactions (fever, chills, headache, cold-like symptoms).



Common side effects

- Falls were the most common side effects during the study
 - Falls happened at a similar rate in patients who were taking ulviprubart or placebo
- Common side effects reported during the study that occurred more often with ulviprubart than with placebo were chills, headache, fever, and cold-like symptoms

Patients, n (%)	Placebo (n=86)	Ulviprubart 0.5 mg/kg (n=92)	Ulviprubart 2.0 mg/kg (n=94)
Side effects that occurred in ≥10% of patients in any group			
Fall	44 (51.2)	48 (52.2)	52 (55.3)
Chills	3 (3.5)	21 (22.8)	30 (31.9)
Headache	9 (10.5)	27 (29.3)	22 (23.4)
Joint pain	20 (23.3)	20 (21.7)	19 (20.2)
Fever	2 (2.3)	12 (13.0)	17 (18.1)
COVID-19	9 (10.5)	15 (16.3)	16 (17.0)
Bruise	13 (15.1)	14 (15.2)	14 (14.9)
Nausea	9 (10.5)	9 (9.8)	13 (13.8)
Pain in extremity	11 (12.8)	13 (14.1)	12 (12.8)
Cold-like symptoms	2 (2.3)	11 (12.0)	12 (12.8)
Fatigue	8 (9.3)	11 (12.0)	11 (11.7)
Diarrhea	8 (9.3)	12 (13.0)	11 (11.7)
Ligament sprain	10 (11.6)	9 (9.8)	10 (10.6)
Skin abrasion	13 (15.1)	4 (4.3)	10 (10.6)
Urinary tract infection	10 (11.6)	13 (14.1)	9 (9.6)
Upper respiratory tract infection	12 (14.0)	12 (13.0)	8 (8.5)
Back pain	6 (7.0)	12 (13.0)	7 (7.4)
High blood pressure	10 (11.6)	4 (4.3)	7 (7.4)



Conclusions

- This clinical trial was designed to study whether a drug called ulviprubart could help people with IBM
 - The main way this was measured in the study was by evaluating changes in IBMFRS scores over time
- On average, the study did not show that ulviprubart was better than placebo: IBM got worse at a similar rate in patients receiving ulviprubart or placebo
- In the subgroup of patients with less severe disease, encouraging trends suggested that average IBMFRS scores decreased more slowly in patients treated with ulviprubart than in patients who received placebo
 - This represented a 50% slowing of disease progression with ulviprubart treatment
- In general, ulviprubart had a favorable safety profile compared with placebo

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