NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Bimagrumab

Trial Indication(s)

Sarcopenia

Protocol Number

CBYM338E2202

Protocol Title

A 28 week, randomized, double-blind, placebo-controlled, two-part, multi-center, parallel group dose range finding study to assess the effect of monthly doses of bimagrumab 70, 210, and 700 mg on skeletal muscle strength and function in older adults with sarcopenia (InvestiGAIT)

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II

Study Start/End Dates

Study Start Date: December 2014 (Actual)
Primary Completion Date: June 2018 (Actual)
Study Completion Date: June 2018 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

Two-part, randomized, double-blind, placebo-controlled study design in older adults with sarcopenia assigned to one of four treatment groups

Centers

58 centers in 13 countries: Spain(4), United States(17), Taiwan(1), Japan(12), France(4), Switzerland(2), Germany(2), Denmark(2), Belgium(2), Australia(2), Korea, Republic of(3), Russia(4), Czech Republic(3)

Objectives:

Primary objective

- To assess the effect of 24 weeks of bimagrumab treatment on patient physical function, assessed by a change in the SPPB total score from baseline to week 25 relative to placebo in older adults with sarcopenia.

Secondary objectives

- To assess the effect of bimagrumab compared to placebo on the safety and tolerability of multiple doses of bimagrumab administered over 24 weeks as measured by vital signs, clinical laboratory values, electrocardiogram (ECG), echocardiogram (in a limited number of patients), and adverse events (AE) in older adults with sarcopenia.
- To assess the effect of bimagrumab compared to placebo on improvement in physical function as measured by a change from baseline to week 25 in the 6 minute walk test (6MWT) distance in older adults with sarcopenia.
- To assess the effect of bimagrumab compared to placebo on improvement in mobility as measured by change from baseline to week 25 in usual gait speed (GS) over 4 meters in older adults with sarcopenia.
- To assess the effect of bimagrumab on total lean body mass and appendicular skeletal muscle index (ASMI) measured by DXA, assessed by the change from baseline to week 25 compared to placebo in older adults with sarcopenia.

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

BYM338 was supplied as a 150 mg/mL concentrate for solution for intravenous (i.v.) infusion. BYM338 70 mg, 210 mg or 700 mg six i.v. administrations of study drug over the 24-week treatment period.

Statistical Methods

- Change from baseline SPPB total score at week 25 was analyzed using an analysis of covariance model (ANCOVA) with treatment and subgroup 1 (Japan / non-Japan) as fixed effects, and the baseline SPPB total score as a covariate. A 95% confidence interval (CI) was estimated for treatment vs. placebo comparison. To establish 'statistical significance', the lower confidence was required to be positive.
- Change from baseline SPPB total score at week 25 was analyzed using an analysis of covariance model (ANCOVA) with treatment and subgroup 1 (Japan / non-Japan) as fixed effects, and baseline SPPB total score as a covariate. In order to establish 'clinical significance', the point estimate of treatment vs. placebo was required to be more than one unit, which is the minimum clinically important difference (MCID) of the test.
- Change in gait speed from baseline at week 25 was analyzed using a mixed-effects model of repeated measures (MMRM) with treatment, visit, baseline, and subgroup 1 (Japan / non-Japan) as covariates. Treatment to placebo comparison (70 mg vs. placebo, 210 mg vs.placebo, and 700 mg vs. placebo) at each visit was estimated along with the 95% confidence interval, and a p-value to reflect the one-sided evaluation of treatment superiority over placebo was reported.
- Change in 6 minute walk test distance from baseline at Week 13 and Week 25 was analyzed in a similar manner to the gait speed.
- The ratio of baseline to Week 25 of total LBM and ASMI (DXA parameters) were analyzed with the MMRM. Data were transformed using natural logarithms, then analyzed using baseline, treatment, subgroup 1 (Japan / non-Japan), and visit as covariates. A saturated covariance structure was used for observations coming from the same patient. All results comparing treatment vs. placebo were back transformed to the original scale to present the adjusted geometric mean ratio with 95% CIs and a p-value to reflect the one-sided evaluation of treatment superiority over placebo was reported.
- Summary tables with the number, percentage, and severity of AEs were provided to assess safety per treatment group. The number and percentage of patients with AEs within each treatment group were tabulated by body system and preferred term. All data for vital signs, ECG evaluations, hematology, blood chemistry, urinalysis, immunogenicity data and other safety relevant data were listed for each patient and summarized by descriptive statistics per treatment group, and for visit/time interval where appropriate.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Low muscle mass as confirmed by DXA;
- Low gait speed <0.8 m/s
- SPPB score less than or equal to 9;
- Weigh at least 35 kg;
- Adequate dietary intake;

Exclusion Criteria:

- A lower limb fracture in the past 6 months or any impairment or disease severely affecting gait (e.g. stroke with hemiparesis, myasthenia gravis, Parkinson's disease, peripheral polyneuropathy, intermittent claudication in advanced peripheral vascular disease, spinal stenosis, or severe osteoarthritis of the knee or hip with ineffective pain management);
- Requires regular assistance from another person for general activities of daily living (e.g. bathing, dressing, toileting).
- Intraocular surgery and laser procedures for refractive correction within 6 months prior to screening;
- Any underlying muscle disease including active myopathy or muscular dytrophy;
- Confirmed diagnosis of heart failure classified as New York Heart Association Class III or IV (e.g. dilated cardiomyopathy);
- Type I diabetes or uncontrolled Type 2 diabetes;
- Chronic kidney disease [estimated glomerular filtration rate (GFR) < 30 mL/min];
- History of confirmed chronic obstructive pulmonary disease with a severity grade > 2 on the Medical Research Council Dyspnea Scale;
- Confirmed rheumatoid arthritis or other systemic autoimmune disease requiring immunosuppressive therapy or corticosteroids >10 mg/d prednisone equivalent;
- Known history or presence of severe active acute or chronic liver disease (e.g., cirrhosis);
- Myocardial infarction, coronary artery bypass graft surgery, percutaneous coronary intervention (e.g. angioplasty or stent placement), or deep vein thrombosis/pulmonary embolism within 12 weeks of screening;
- Active cancer (i.e., under current treatment), or cancer requiring treatment in the last 5 years excluding non-melanoma skin cancers or cancers with excellent prognosis (e.g., early stage prostate or breast cancer, carcinoma in situ of the uterine cervix);
- Any chronic active infection (e.g., HIV, Hepatitis B or C, tuberculosis, etc).

Participant Flow Table

Overall Study

	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo	Total
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion	
Started	19	18	113	67	217
Completed	17	12	95	64	188
Not Completed	2	6	18	3	29
Adverse Event	1	0	4	1	6
Death	0	0	2	0	2
Lost to Follow-up	0	0	1	0	1
Physician Decision	0	1	0	0	1
Protocol Deviation	0	3	2	1	6
Patient/Guardian Decision	1	2	9	1	13

Baseline Characteristics

	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo	Total
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion	
Number of Participants [units: participants]	19	18	113	67	217
Age Continuous (units: years) Mean ± Standard Deviation					
	79.3±5.89	78.0±6.38	79.5±5.46	78.3±5.03	79.0±5.45
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)					
Female	9	8	66	43	126
Male	10	10	47	24	91
Race (NIH/OMB) (units: participants) Count of Participants (Not Applicable)					
American Indian or Alaska Native	0	0	1	0	1
Asian	5	3	17	11	36
Native Hawaiian or Other Pacific Islander	0	0	1	0	1
Black or African American	3	0	0	1	4
White	11	14	93	54	172
More than one race	0	0	0	1	1
Unknown or Not Reported	0	1	1	0	2

Summary of Efficacy

Primary Outcome Result(s)

Change from Baseline in total Short Physical Performance Battery (SPPB) Score to week 25

(Time Frame: Baseline, week 25)

	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion
Number of Participants Analyzed [units: participants]	19	18	113	67
Change from Baseline in total Short Physical Performance Battery (SPPB) Score to week 25 (units: Score on a scale) Mean ± Standard Deviation				
Baseline	7.1 ± 2.12	7.3 ± 2.11	7.2 ± 1.63	7.3 ± 1.67
Week 25	8.5 ± 2.48	8.7 ± 1.64	8.7 ± 2.12	8.4 ± 2.25

Statistical Analysis

Groups	BYM338 70 mg, Placebo
P Value	0.274
Method	Mixed Models Analysis

Mean Difference (Final Values)	0.28
95 % Confidence Interval 2-Sided	-0.64 to 1.21

Statistical Analysis

Groups	BYM338 210 mg, Placebo
P Value	0.320
Method	Mixed Models Analysis
Mean Difference (Final Values)	0.26
95 % Confidence Interval 2-Sided	-0.83 to 1.35

Statistical Analysis

Groups	BYM338 700 mg, Placebo
P Value	0.134
Method	Mixed Models Analysis
Mean Difference (Final Values)	0.31
95 % Confidence Interval 2-Sided	-0.24 to 0.87

Secondary Outcome Result(s)

Change from Baseline at Week 25 in the 6 minute walk test (6MWT) distance

(Time Frame: Baseline, week 25)

	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion
Number of Participants Analyzed [units: participants]	19	18	113	67
Change from Baseline at Week 25 in the 6 minute walk test (6MWT) distance (units: meters) Mean ± Standard Deviation				
Baseline	293.30 ± 91.842	291.81 ± 82.527	294.30 ± 83.602	312.43 ± 93.924
Week 25	304.98 ± 102.934	340.71 ± 72.911	315.32 ± 97.020	322.71 ± 103.865

Statistical Analysis

Groups	BYM338 70 mg, Placebo
P Value	0.576
Method	Mixed Models Analysis
Mean Difference (Final Values)	-3.32
95 % Confidence Interval 2-Sided	-37.6 to 30.95

Statistical Analysis

Groups	BYM338 210 mg, Placebo
P Value	0.178
Method	Mixed Models Analysis
Mean Difference (Final Values)	19.60
95 % Confidence Interval 2-Sided	-22.2 to 61.41

Statistical Analysis

Groups	BYM338 700 mg, Placebo
P Value	0.163
Method	Mixed Models Analysis
Mean Difference (Final Values)	10.31
95 % Confidence Interval 2-Sided	-10.4 to 30.98

Change from Baseline to Week 25 in usual Gait speed (GS) over 4 meters

(Time Frame: baseline, week 25)

	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion

Number of Participants Analyzed [units: participants]	19	18	113	67
Change from Baseline to Week 25 in usual Gait speed (GS) over 4 meters (units: m/sec) Mean ± Standard Deviation				
Baseline	2.37 ± 0.684	2.72 ± 0.752	2.58 ± 0.624	2.70 ± 0.493
Week 25	3.12 ± 0.857	3.60 ± 0.699	3.30 ± 0.902	3.23 ± 0.838

Statistical Analysis

Groups	BYM338 70 mg, Placebo
P Value	0.488
Method	Mixed Models Analysis
Mean Difference (Net)	0.00
95 % Confidence Interval 2-Sided	-0.10 to 0.10

Statistical Analysis

Groups	BYM338 210 mg, Placebo
P Value	0.055
Method	Mixed Models Analysis
Mean Difference (Net)	0.10
95 % Confidence Interval 2-Sided	-0.02 to 0.22

Statistical Analysis

Groups	BYM338 700 mg, Placebo
P Value	0.161
Method	Mixed Models Analysis
Mean Difference (Net)	0.03
95 % Confidence Interval 2-Sided	-0.03 to 0.09

Percentage Change from Baseline to Week 25 on appendicular skeletal muscle index (ASMI) measured by Dual Energy X-ray Absorptiometry (DXA)

(Time Frame: baseline, week 25)

	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion
Number of Participants Analyzed [units: participants]	19	18	113	67
Percentage Change from Baseline to Week 25 on appendicular skeletal muscle index (ASMI) measured by Dual Energy X-ray Absorptiometry (DXA) (units: kg/m2) Mean ± Standard Deviation				
Baseline	5.99 ± 0.886	5.87 ± 0.795	5.70 ± 0.823	5.55 ± 0.753
Week 25	6.04 ± 0.947	6.42 ± 0.849	6.10 ± 0.836	5.60 ± 0.717

Statistical Analysis

Groups	BYM338 70 mg, Placebo
P Value	0.213
Method	Mixed Models Analysis
Mean Difference (Net)	1.01
95 % Confidence Interval 2-Sided	0.99 to 1.03

Statistical Analysis

Groups	BYM338 210 mg, Placebo
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	1.06
95 % Confidence Interval 2-Sided	1.03 to 1.09

Statistical Analysis

Groups	BYM338 700 mg, Placebo
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	1.06

95 % Confidence Interval 2-Sided	1.05 to 1.08

Percentage Change from Baseline to Week 25 on Total lean body mass measured by Dual Energy X-ray Absorptiometry (DXA)

(Time Frame: baseline, week 25)

	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion
Number of Participants Analyzed [units: participants]	19	18	113	67
Percentage Change from Baseline to Week 25 on Total lean body mass measured by Dual Energy X-ray Absorptiometry (DXA) (units: kg) Mean ± Standard Deviation				
Baseline	37.44 ± 8.507	35.84 ± 7.300	35.39 ± 8.891	33.65 ± 6.890
Week 25	38.26 ± 8.660	39.52 ± 8.343	37.86 ± 9.064	33.95 ± 6.921

Statistical Analysis

Groups	BYM338 70 mg, Placebo
P Value	0.458
Method	Mixed Models Analysis
Mean Difference (Net)	1.00

95 % Confidence Interval 2-Sided	0.98 to 1.02

Statistical Analysis

Groups	BYM338 210 mg, Placebo
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	1.05
95 % Confidence Interval 2-Sided	1.03 to 1.08

Statistical Analysis

Groups	BYM338 700 mg, Placebo
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	1.06
95 % Confidence Interval 2-Sided	1.04 to 1.07

Summary of Safety

Safety Results

All-Cause Mortality

	BYM338 70 mg N = 19	BYM338 210 mg N = 18	BYM338 700 mg N = 113	Placebo N = 67
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion
Total participants affected	0 (0.00%)	0 (0.00%)	2 (1.77%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Treatment-emergent adverse events
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment

	BYM338 70 mg N = 19	BYM338 210 mg N = 18	BYM338 700 mg N = 113	Placebo N = 67
Arm/Group Description	BYM338 70 mg intravenous infusion	BYM338 210 mg intravenous infusion	BYM338 700 mg intravenous infusion	Placebo intravenous infusion

Total participants affected	0 (0.00%)	3 (16.67%)	14 (12.39%)	5 (7.46%)
Cardiac disorders				
Atrial fibrillation	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Atrial flutter	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Cardiac failure congestive	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Cardio-respiratory arrest	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Myocardial infarction	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Pulseless electrical activity	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Gastrointestinal disorders				
Colitis ulcerative	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Gastrointestinal disorder	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
General disorders and administration site conditions				
Asthenia	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Immune system disorders				
Anaphylactic reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Infections and infestations				
Erysipelas	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Pneumonia	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)

Injury, poisoning and procedural complications				
Aortic injury	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Spinal fracture	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Investigations				
Blood alkaline phosphatase increased	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Hepatic enzyme increased	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Metabolism and nutrition disorders				
Decreased appetite	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Musculoskeletal and connective tissue disorders				
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Myalgia	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Neck pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Metastases to lung	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Renal neoplasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Nervous system disorders				
Aphasia	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Ischaemic stroke	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)

Subarachnoid haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Pulmonary oedema	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Respiratory arrest	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Vascular disorders				
Hypertension	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Hypertensive crisis	0 (0.00%)	0 (0.00%)	1 (0.88%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Treatment-emergent adverse events
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	3%

	BYM338 70 mg N = 19	**BYM338 210 mg N = 18**	**BYM338 700 mg N = 113**	**Placebo N = 67**
Arm/Group Description	BYM338 70 mg	BYM338 210 mg	BYM338 700 mg	Placebo intravenous infusion

	intravenous infusion	intravenous infusion	intravenous infusion	
Total participants affected	12 (63.16%)	13 (72.22%)	94 (83.19%)	41 (61.19%)
Blood and lymphatic system disorders				
Anaemia	0 (0.00%)	1 (5.56%)	3 (2.65%)	0 (0.00%)
Cardiac disorders				
Bradycardia	2 (10.53%)	0 (0.00%)	3 (2.65%)	0 (0.00%)
Palpitations	0 (0.00%)	1 (5.56%)	2 (1.77%)	0 (0.00%)
Ear and labyrinth disorders				
Vertigo	2 (10.53%)	0 (0.00%)	1 (0.88%)	2 (2.99%)
Endocrine disorders				
Androgen deficiency	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Eye disorders				
Trichiasis	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders				
Abdominal discomfort	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Constipation	0 (0.00%)	1 (5.56%)	6 (5.31%)	1 (1.49%)
Dental necrosis	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diarrhoea	1 (5.26%)	3 (16.67%)	22 (19.47%)	2 (2.99%)
Gastrooesophageal reflux disease	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Haemorrhoidal haemorrhage	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Nausea	0 (0.00%)	0 (0.00%)	8 (7.08%)	0 (0.00%)
Toothache	1 (5.26%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Vomiting	0 (0.00%)	0 (0.00%)	4 (3.54%)	0 (0.00%)
General disorders and administration site conditions				
Chest discomfort	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Fatigue	1 (5.26%)	1 (5.56%)	5 (4.42%)	0 (0.00%)
Infusion site swelling	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	0 (0.00%)	1 (5.56%)	1 (0.88%)	1 (1.49%)
Oedema	1 (5.26%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Peripheral swelling	1 (5.26%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Infections and infestations				
Bronchitis	1 (5.26%)	0 (0.00%)	6 (5.31%)	2 (2.99%)
Fungal skin infection	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gingivitis	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	3 (15.79%)	1 (5.56%)	5 (4.42%)	0 (0.00%)
Periodontitis	1 (5.26%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Sinusitis	0 (0.00%)	0 (0.00%)	4 (3.54%)	1 (1.49%)
Upper respiratory tract infection	1 (5.26%)	2 (11.11%)	5 (4.42%)	5 (7.46%)
Urinary tract infection	1 (5.26%)	0 (0.00%)	6 (5.31%)	1 (1.49%)
Vaginal infection	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Viral infection	0 (0.00%)	0 (0.00%)	5 (4.42%)	1 (1.49%)
Injury, poisoning and procedural complications				

Arthropod bite	0 (0.00%)	1 (5.56%)	1 (0.88%)	0 (0.00%)
Contusion	0 (0.00%)	1 (5.56%)	5 (4.42%)	7 (10.45%)
Fall	2 (10.53%)	3 (16.67%)	28 (24.78%)	24 (35.82%)
Muscle strain	0 (0.00%)	1 (5.56%)	2 (1.77%)	0 (0.00%)
Skin abrasion	1 (5.26%)	0 (0.00%)	1 (0.88%)	2 (2.99%)
Wound	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations				
Amylase increased	0 (0.00%)	0 (0.00%)	4 (3.54%)	0 (0.00%)
Blood creatine phosphokinase increased	1 (5.26%)	0 (0.00%)	3 (2.65%)	1 (1.49%)
C-reactive protein increased	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Lipase increased	0 (0.00%)	0 (0.00%)	6 (5.31%)	0 (0.00%)
Liver function test increased	0 (0.00%)	1 (5.56%)	1 (0.88%)	0 (0.00%)
Metabolism and nutrition disorders				
Decreased appetite	1 (5.26%)	1 (5.56%)	5 (4.42%)	0 (0.00%)
Hyperglycaemia	0 (0.00%)	1 (5.56%)	2 (1.77%)	0 (0.00%)
Musculoskeletal and connective tissue disorders				
Arthralgia	0 (0.00%)	1 (5.56%)	1 (0.88%)	2 (2.99%)
Back pain	1 (5.26%)	2 (11.11%)	5 (4.42%)	3 (4.48%)
Muscle spasms	4 (21.05%)	5 (27.78%)	37 (32.74%)	10 (14.93%)
Musculoskeletal pain	1 (5.26%)	0 (0.00%)	2 (1.77%)	1 (1.49%)
Myalgia	1 (5.26%)	1 (5.56%)	3 (2.65%)	2 (2.99%)

Osteoarthritis	0 (0.00%)	0 (0.00%)	4 (3.54%)	2 (2.99%)
Pain in extremity	0 (0.00%)	1 (5.56%)	6 (5.31%)	3 (4.48%)
Plantar fasciitis	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Nervous system disorders				
Dizziness	0 (0.00%)	0 (0.00%)	6 (5.31%)	0 (0.00%)
Dysgeusia	0 (0.00%)	1 (5.56%)	4 (3.54%)	0 (0.00%)
Headache	0 (0.00%)	0 (0.00%)	5 (4.42%)	3 (4.48%)
Hypoaesthesia	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Muscle contractions involuntary	1 (5.26%)	0 (0.00%)	3 (2.65%)	0 (0.00%)
Presyncope	1 (5.26%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Product issues				
Device dislocation	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders				
Insomnia	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders				
Lower urinary tract symptoms	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nocturia	1 (5.26%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders				
Cough	0 (0.00%)	0 (0.00%)	4 (3.54%)	0 (0.00%)
Productive cough	1 (5.26%)	0 (0.00%)	1 (0.88%)	0 (0.00%)
Skin and subcutaneous tissue disorders				

Acne	0 (0.00%)	3 (16.67%)	3 (2.65%)	0 (0.00%)
Actinic keratosis	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dermatitis contact	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Eczema	1 (5.26%)	0 (0.00%)	2 (1.77%)	0 (0.00%)
Eczema asteatotic	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (1.49%)
Pruritus	0 (0.00%)	1 (5.56%)	2 (1.77%)	0 (0.00%)
Rash	0 (0.00%)	0 (0.00%)	5 (4.42%)	0 (0.00%)
Seborrhoeic dermatitis	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)
Skin fissures	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urticaria	0 (0.00%)	1 (5.56%)	1 (0.88%)	0 (0.00%)
Vascular disorders				
Hypertension	0 (0.00%)	1 (5.56%)	9 (7.96%)	4 (5.97%)

Other Relevant Findings

Conclusion:

Twenty-four weeks of exposure to three dose levels of bimagrumab, up to 700 mg, was generally safe and well tolerated and demonstrated predictable pharmacokinetics and increase in lean body mass in older adults with sarcopenia. However, a sufficient, drug-related improvement over placebo was not observed in any assessment of functional performance, in the setting of optimal standard of care. Therefore, it was recommended to not move forward with bimagrumab in the indication of sarcopenia.
Results from this study demonstrate the effectiveness of an optimized standard of care to improve the functional performance and lean body mass of older men and women with sarcopenia. Clinically relevant improvements were observed in participants across the continuum of baseline functional status, in both men and women and from all study countries involved.

Date of Clinical Trial Report

11-Mar-2019