Supplemental Online Content

Rooks D, Swan T, Goswami B, et al. Bimagrumab vs optimized standard of care for treatment of sarcopenia in community-dwelling older adults: a randomized clinical trial. *JAMA Netw Open*. 2020;3(10):e2020836. doi:10.1001/jamanetworkopen.2020.20836

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Supplementary Methods

The home-based exercise program was personalized to the participant's level of functional capability and performed independently two to three times each week with guidelines for the exercises to be performed at a mild to moderate intensity within a set range of repetitions. Exercises included basic single and multi-joint movements using body weight, common in a physiotherapy prescription, and were recorded in a diary by the participant. To ensure participants were above the minimum intake of dietary protein recommended to maintain muscle anabolism in older adults,[1] an established method of dietary assessment, including a three-day dietary food record or series of 24-hour recalls, was completed at screening and every one or two months during the 24-week treatment period. If a person qualified for the study except for the daily calorie or protein intake, counseling was provided on ways to increase intake during meals, and the person was reassessed after approximately four weeks. To support sufficient nutritional intake, a locally sourced (by country) oral nutritional supplement containing a minimum of 15 g protein was provided for daily consumption in addition to all regular meals. The few participants who chose not to consume an oral nutritional supplement received additional counseling to increase calorie and protein intake through their diet. Because vitamin D deficiency is common among older adults worldwide, an oral vitamin D3 supplement containing 800-2000 IU of vitamin D, also sourced locally, was also provided.[2]

eReferences

1. Bauer J, Biolo G, Cederholm T, et al. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. *J Am Med Dir Assoc*. 2013;14(8):542-559.
2. Roth DE, Abrams SA, Aloia J, et al. Global prevalence and disease burden of vitamin D deficiency: A roadmap for action in low- and middle-income countries. *Ann N Y Acad Sci*. 2018;1430(1):44-79.

eAppendix 2. Supplementary Results

ECG

In the majority of participants in all treatment dose groups, the ECGs performed at different time points in the study showed isolated values outside the reference range, but none were considered to be clinically significant by the investigator. Analyses show that changes within participants over time in those receiving bimagrumab were not significantly different than those receiving placebo.

Vital Signs

There were several isolated incidences of abnormal vital signs recorded at different time points during the study. However, all vital sign values returned to within normal range, at the subsequent assessment. The majority of these cases were not considered clinically significant by the investigators. Weight decrease was reported as an AE in four patients, all in the bimagrumab 700 mg treatment group. None of these AEs were considered related to the study drug by the investigators.

Falls

Although not powered for falls, the placebo group experienced a greater number of falls during the study (35.8% vs. 24.8%, $P<.007$), compared to the bimagrumab group. No difference in baseline characteristics or response to treatment was identified between fallers and non-fallers in either treatment group. Due to similar improvements in SPPB, 6MWD and gait speed and no change in strength in both the bimagrumab and placebo groups, the difference in fall rate between treatments may have occurred by chance.

eTable 1. Baseline Characteristics and Changes in Outcomes of All Participants Receiving Study Drug

Characteristics		Bimagrumab 70 mg (n=19)	Bimagrumab 210 mg (n=18)	Bimagrumab 700 mg (n=113)	Placebo (n=67)
Age, years	Mean (SD)	79.3 (5.89)	78 (6.38)	79.5 (5.46)	78.3 (5.03)
	Median	81.0	77.5	79	78
	Range	70–87	71–91	70–95	70–88
Gender, n (%)	Men	10 (52.6)	10 (55.6)	47 (41.6)	24 (35.8)
	Women	9 (47.4)	8 (44.4)	66 (58.4)	43 (64.2)
Race, n (%)	Caucasian	11 (58.0)	14 (78.0)	93 (82.3)	54 (80.6)
	Asian	5 (26.3)	3 (16.7)	17 (15.0)	11 (16.4)
	Other	NA	NA	0	1 (1.0)
Ethnicity, n (%)	Other	6 (31.6)	6 (33.3)	56 (49.6)	31 (46.3)
	Not Hispanic/ Latino	4 (21.1)	3 (16.7)	30 (26.5)	16 (23.9)
	Hispanic/ Latino	7 (36.8)	7 (38.9)	19 (16.8)	19 (28.4)
Height, cm	Mean (SD)	162.8 (8.97)	162.2 (8.42)	163.6 (12.50)	161.9 (9.55)
	Median	161.0	161.8	162	160
	Range	144–181	146–178	138–200	145–184
Weight, kg	Mean (SD)	64.1 (13.39)	66.5 (11.60)	65.6 (16.61)	62.3 (11.17)
	Median	62.8	68.5	63.4	62.8
	Range	41–100	43–83	36–111	42–94
BMI, kg/m^2	Mean (SD)	23.8 (2.57)	24.9 (2.92)	24 (3.55)	23.6 (2.84)
	Median	23.4	25.8	24	23.6

	Range	19–29	20–29	15–32	17–31
Total SPPB scores					
Baseline	Mean (SD)	7.1 (2.01)	7.6 (2.12)	7.1 (1.73)	7.3 (1.68)
Week 25	Mean (SD)	8.5 (2.48)	8.7 (1.64)	8.7 (2.12)	8.4 (2.25)
6-MWD, m					
Baseline	Mean (SD)	293.3 (91.84)	291.8(82.53)	294.3 (83.60)	312.4 (93.92)
Week 25	Mean (SD)	305.0 (102.93)	340.7 (72.91)	315.3 (97.02)	322.7 (103.9)
Gait speed, m/s					
Baseline	Mean (SD)	0.618 (0.1060)	0.679 (0.1456)	0.642 (0.1079)	0.656 (0.0836)
Week 25	Mean (SD)	0.74 (0.233)	0.86 (0.187)	0.81 (0.231)	0.79 (0.207)
Grip strength, kg					
Right hand					
Baseline	Mean (SD)	22.0 (7.02)	21.8 (8.32)	20.4 (7.79)	19.5 (7.36)
Week 25	Mean (SD)	23.4 (8.41)	24.4 (7.95)	22.1 (8.11)	20.5 (7.54)
Left hand					
Baseline	Mean (SD)	21.3 (6.65)	20.2 (7.80)	19.4 (7.63)	18.1 (7.09)
Week 25	Mean (SD)	22.9 (8.26)	22.9 (5.67)	20.7 (8.36)	19.3 (7.06)
LBM, kg					
Baseline	Mean (SD)	37.4 (8.51)	35.8 (7.30)	35.4 (8.89)	33.6 (6.89)
Week 25	Mean (SD)	38.3 (8.66)	39.5 (8.34)	37.9 (9.06)	33.9 (6.92)
FBM, kg					
Baseline	Mean (SD)	19.4 (6.21)	22.7 (6.48)	22.7 (8.74)	21.2 (7.5)
Week 25	Mean (SD)	18.9 (6.50)	21.4 (6.69)	20.1 (8.15)	22.1 (7.61)
ASMI, kg/m^2					

Baseline	Mean (SD)	6.0 (0.89)	5.9 (0.80)	5.7 (0.82)	5.5 (0.75)
Week 25	Mean (SD)	6.0 (0.95)	6.4 (0.85)	6.1 (0.83)	5.6 (0.72)
Daily protein intake, g/kg					
Baseline	Mean (SD)	1.49 (0.60)	1.49 (0.63)	1.41 (0.43)	1.61 (0.52)
Week 5	Mean (SD)	1.30 (0.42)	1.37 (0.51)	1.35 (0.51)	1.44 (0.48)
Week 9	Mean (SD)	1.32 (0.40)	1.46 (0.59)	1.48 (0.53)	1.60 (0.69)
Week 13	Mean (SD)	1.38 (0.52)	1.53 (0.57)	1.34 (0.41)	1.52 (0.56)
Week 17	Mean (SD)	1.33 (0.41)	1.54 (0.47)	1.37 (0.56)	1.53 (0.56)
Week 21	Mean (SD)	1.36 (0.49)	1.38 (0.35)	1.36 (0.38)	1.46 (0.44)
Week 25	Mean (SD)	1.45 (0.60)	1.50 (0.47)	1.35 (0.43)	1.45 (0.50)

6-MWD; 6-minute walk distance; ASMI, appendicular skeletal muscle index; BMI, body mass index; FBM, fat body mass; LBM, lean body mass; SD, standard deviation; SPPB, Short Physical Performance Battery

eTable 2. Baseline Characteristics for Responders and Nonresponders

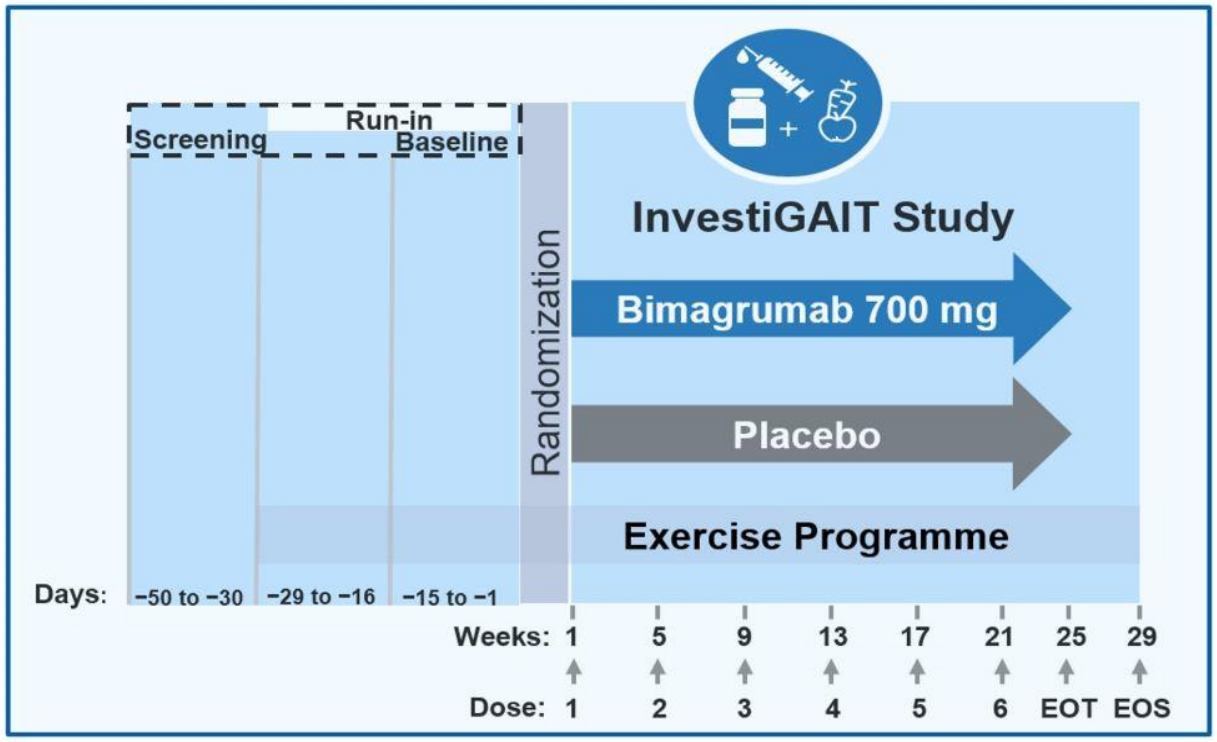
		Responder* **(n=153)**	**Non-responder** **(n=30)**
Age, years	Mean (SD)	78.4 (5.0)	80.9 (4.7)
	Median	78	80
	Range	70–91	70–91
Gender, n (%)	Male	71 (46.4)	9 (30)
	Female	82 (53.6)	21 (70)
BMI, kg/m^2	Mean (SD)	24.07 (3.19)	23.83 (3.36)
	Median	23.76	23.96
	Range	15.3–32.4	17–31.3
Total SPPB scores	Mean (SD)	7.29 (1.55)	6.93 (2.36)
	Median	8	7
	Range	2–11	1–11
Gait speed, m/s	Mean (SD)	0.65 (0.09)	0.63 (0.12)

	Median	0.66	0.64
	Range	0.3–0.8	0.4–0.9
6-MWD, m*	Mean (SD)	304.04 (82.68)	299.98 (118.87)
	Median	300	289.33
	Range	23–501	125–606
Balance scores	Mean (SD)	3.31 (0.93)	3.0 (1.15)
	Median	4	3
	Range	0–4	0–4
Chair rise time (for 5 stands), s	Mean (SD)	20.12 (6.76)	16.58 (4.48)
	Median	18.45	15.50
	Range	7.6–46.9	8.8–26.8

*Responder improved ≥1 point on SPPB score

6-MWD; 6-minute walk distance; BMI, body mass index; SD, standard deviation; SPPB, short physical performance

eFigure. Study Design



EOS, end of study (4 weeks after the EOT); EOT, end of treatment (4 weeks after the last dose)