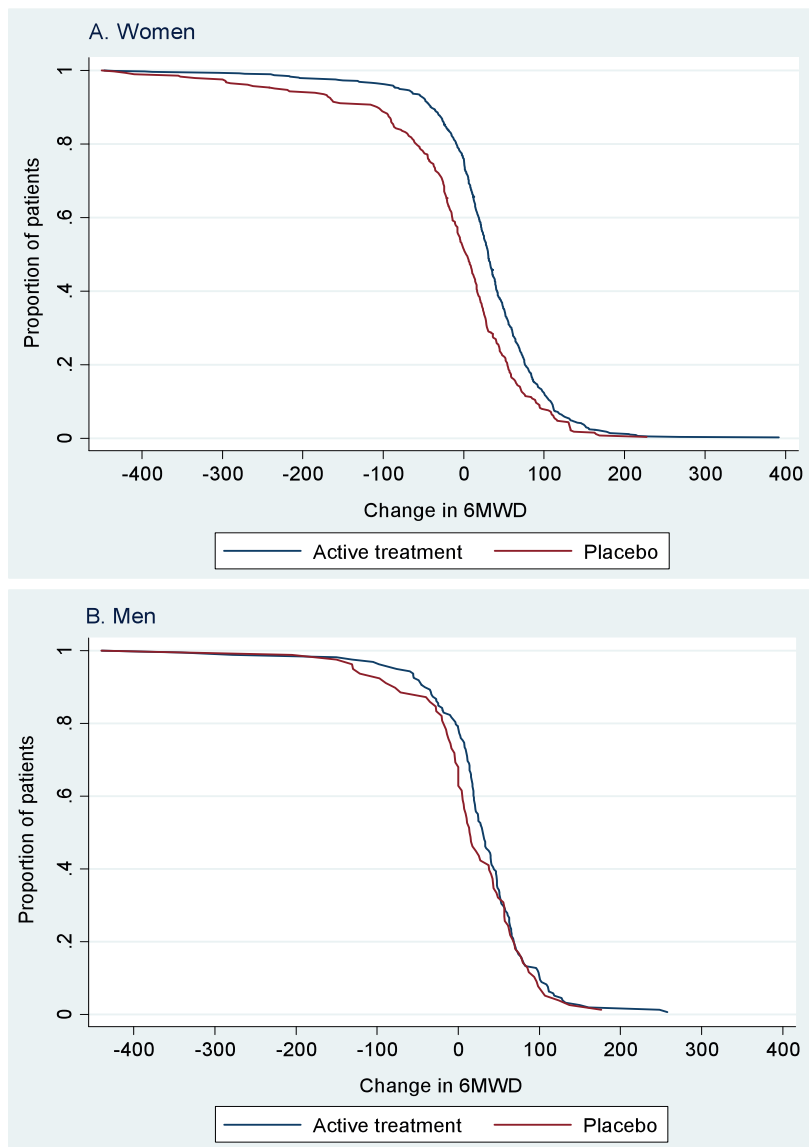




Race and Sex Differences in Response to Endothelin Receptor Antagonists for Pulmonary Arterial Hypertension

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e-Figure 1.

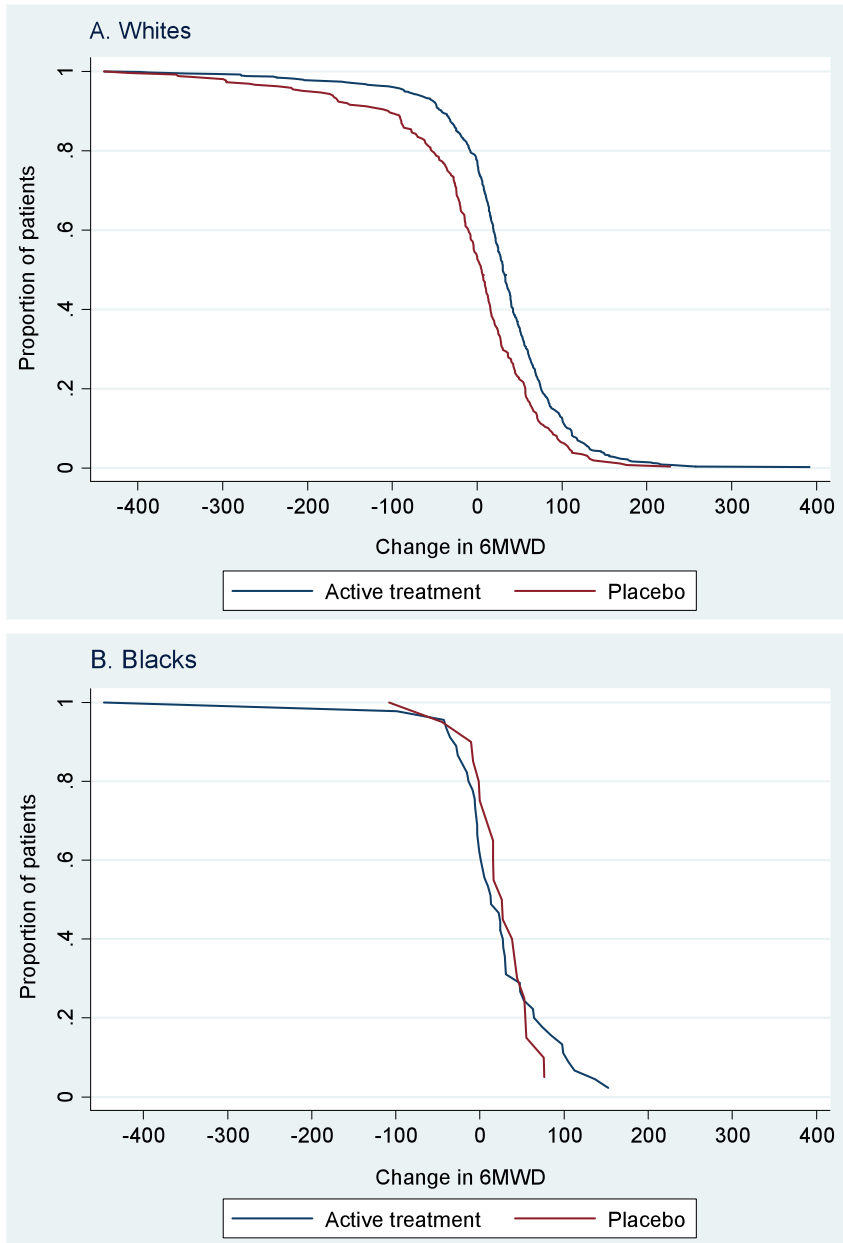


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e-Figure 2.



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e-Table 1. Characteristics of study participants by sex

| | Women | | Men | |
|------------------------------|----------------------|--------------------|----------------------|-------------------|
| | (n=894) | | (n=236) | |
| | Treatment (n=615) | Placebo (n=279) | Treatment (n=158) | Placebo (n=78) |
| Age, years | 50 (38-61) | 49 (35-60) | 51 (38-62) | 50 (40-65) |
| Race, n (%) | | | | |
| Black | 39 (6) | 16 (6) | 6 (4) | 4 (5) |
| White | 449 (73) | 195 (70) | 128 (81) | 64 (82) |
| Other | 127 (21) | 68 (24) | 24 (15) | 10 (13) |
| Height, cm | 160 (155-165) | 160 (155-165) | 173 (168-178) | 175 (170-180) |
| Weight, kg | 66 (58-77) | 67 (58-81) | 79 (68-90) | 80 (70-93) |
| BMI, kg/m ² | 26 (23-30) | 26 (23-31) | 26 (23-30) | 27 (24-30) |
| PAH Diagnosis, n (%) | | | | |
| Idiopathic | 362 (59) | 177 (64) | 116 (73) | 52 (67) |
| Connective tissue disease | 194 (32) | 73 (26) | 22 (14) | 13 (17) |
| HIV infection/Anorexigen Use | 13 (2) | 6 (2) | 10 (6) | 5 (6) |
| Congenital heart disease | 44 (7) | 22 (8) | 10 (6) | 8 (10) |
| NYHA functional class, n (%) | | | | |
| I-II | 205 (33) | 90 (32) | 51 (32) | 24 (31) |
| III-IV | 409 (67) | 189 (68) | 107 (68) | 54 (69) |
| Baseline Hemodynamics | | | | |
| Mean RAP, mmHg | 7.0 (5.0-10.0) | 7.0 (4.0-12.0) | 9.0 (5.0-14.0) | 8.0 (5.0-12.0) |
| Mean PAP, mmHg | 50 (40-60) | 53 (42-63) | 51 (42-62) | 49 (41-55) |
| Cardiac output, L/min | 4.1 (3.3-5.1) | 4.0 (3.3-5.2) | 4.4 (3.6-5.6) | 4.5 (3.8-5.4) |

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| | | | | |
|-------------------------------------|------------------|------------------|------------------|------------------|
| Cardiac index, L/min/m ² | 2.4 (1.9-2.9) | 2.3 (1.9-2.9) | 2.2 (1.9-2.8) | 2.2 (1.8-2.7) |
| PCWP, mmHg | 9.0 (7.0-12.0) | 10.0 (7.0-12.0) | 9.0 (7.0-12.0) | 10.0 (6.0-12.0) |
| PVR, Wood Units | 10.0 (6.9-14.9) | 10.8 (7.0-15.7) | 10.2 (6.2-13.9) | 8.5 (6.5-12.1) |
| Baseline laboratory values | | | | |
| Albumin, g/dL | 4.2 (3.9-4.4) | 4.2 (3.9-4.5) | 4.3 (4.0-4.6) | 4.2 (4.0-4.5) |
| Creatinine, mg/dL | 0.80 (0.71-0.88) | 0.80 (0.62-0.88) | 0.97 (0.84-1.06) | 0.99 (0.81-1.15) |
| Hemoglobin, g/dL | 14.4 (13.2-15.5) | 14.1 (12.9-15.5) | 16.2 (14.9-17.0) | 15.7 (13.9-17.2) |
| Sodium, mEq/L | 140 (138-142) | 140 (138-142) | 140 (139-142) | 141 (139-143) |
| Warfarin use, n (%) | 364 (59) | 182 (65) | 102 (65) | 48 (62) |
| Baseline 6MWD, m | 355 (285-410) | 358 (284-414) | 378 (314-427) | 393 (315-429) |
| Study, n (%) | | | | |
| ARIES-1 | 109 (18) | 59 (21) | 25 (16) | 8 (10) |
| ARIES-2 | 99 (16) | 44 (16) | 28 (18) | 21 (27) |
| BREATHE-1 | 114 (19) | 54 (19) | 31 (20) | 15 (19) |
| STRIDE-1 | 94 (15) | 47 (17) | 24 (15) | 13 (17) |
| STRIDE-2 | 145 (24) | 47 (17) | 40 (25) | 15 (19) |
| STRIDE-4 | 54 (19) | 28 (10) | 10 (6) | 6 (8) |

HIV indicates human immunodeficiency virus; BMI, body mass index; ARIES, Ambrisentan in Pulmonary

Arterial Hypertension, Randomized, Double-Blind, Placebo-Controlled, Multicenter, Efficacy Studies;

BREATHE, Bosentan: Randomized Trial of Endothelin receptor Antagonist Therapy; STRIDE, Sitaxsentan To Relieve Impaired Exercise.

Data shown as median (IQR) unless otherwise indicated.

e-Table 2. Characteristics of study participants by race

| | White | | Black | |
|-------------------------------------|----------------------|--------------------|---------------------|-------------------|
| | (n=836) | | (n=65) | |
| | Treatment (n=577) | Placebo (n=259) | Treatment (n=45) | Placebo (n=20) |
| Age, years | 54 (42-64) | 52 (41-64) | 45 (35-52) | 43 (36-57) |
| Sex (male), n (%) | 128 (22) | 64 (25) | 6 (13) | 4 (20) |
| Height, cm | 163 (158-170) | 164 (158-170) | 165 (160-170) | 168 (160-173) |
| Weight, kg | 70 (60-83) | 72 (61-87) | 77 (65-97) | 83 (73-94) |
| BMI, kg/m ² | 26 (23-31) | 26 (23-31) | 28 (24-35) | 30 (26-33) |
| PAH Diagnosis, n (%) | | | | |
| Idiopathic | 351 (61) | 167 (64) | 22 (49) | 12 (60) |
| Connective tissue disease | 171 (30) | 64 (25) | 17 (38) | 5 (25) |
| HIV infection/Anorexigen Use | 16 (3) | 8 (3) | 5 (11) | 2 (10) |
| Congenital heart disease | 37 (6) | 20 (8) | 1 (2) | 1 (5) |
| NYHA functional class, n (%) | | | | |
| I-II | 185 (32) | 74 (29) | 9 (20) | 9 (45) |
| III-IV | 391 (68) | 185 (71) | 36 (80) | 11 (55) |
| Baseline Hemodynamics | | | | |
| Mean RAP, mmHg | 7.5 (5.0-11.0) | 7.0 (4.0-12.0) | 7.3 (5.0-13.5) | 8.0 (6.0-11.0) |
| Mean PAP, mmHg | 50 (39-60) | 51 (40-60) | 46 (37-53) | 47 (35-55) |
| Cardiac output, L/min | 4.2 (3.4-5.2) | 4.2 (3.4-5.2) | 4.3 (3.4-5.5) | 4.6 (4.3-5.6) |
| Cardiac index, L/min/m ² | 2.3 (1.9-2.8) | 2.3 (1.9-2.8) | 2.3 (1.8-2.8) | 2.4 (2.2-2.9) |
| PCWP, mmHg | 9.0 (6.0-12.0) | 9.0 (7.0-12.0) | 9.0 (7.0-12.0) | 10.5 (7.5-13.0) |
| PVR, Wood Units | 10.0 (6.6-14.0) | 10.0 (6.6-14.0) | 8.7 (5.2-12.3) | 8.2 (4.8-11.0) |
| Baseline laboratory values | | | | |

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| | | | | |
|---------------------|------------------|------------------|------------------|------------------|
| Albumin, g/dL | 4.2 (3.9-4.5) | 4.2 (4.0-4.5) | 4.1 (3.8-4.3) | 3.9 (3.9-4.1) |
| Creatinine, mg/dL | 0.86 (0.71-0.97) | 0.86 (0.71-0.97) | 0.80 (0.71-0.97) | 0.76 (0.65-0.97) |
| Hemoglobin, g/dL | 14.7 (13.5-15.9) | 14.5 (13.2-15.7) | 13.5 (12.8-15.1) | 12.7 (11.7-14.9) |
| Sodium, mEq/L | 140 (138-142) | 141 (139-142) | 140 (138-141) | 140 (138-141) |
| Warfarin use, n (%) | 356 (62) | 169 (65) | 32 (71) | 14 (70) |
| Baseline 6MWD, m | 363 (287-415) | 367 (285-417) | 355 (292-420) | 351 (281-406) |
| Study, n (%) | | | | |
| ARIES-1 | 90 (16) | 49 (19) | 7 (16) | 4 (20) |
| ARIES-2 | 112 (19) | 51 (20) | 0 (0) | 0 (0) |
| BREATHE-1 | 112 (19) | 59 (23) | 12 (27) | 1 (5) |
| STRIDE-1 | 83 (14) | 42 (16) | 8 (18) | 3 (15) |
| STRIDE-2 | 150 (26) | 46 (18) | 18 (40) | 9 (45) |
| STRIDE-4 | 30 (5) | 12 (5) | 0 (0) | 3 (15) |

HIV indicates human immunodeficiency virus; BMI, body mass index; ARIES, Ambrisentan in Pulmonary

Arterial Hypertension, Randomized, Double-Blind, Placebo-Controlled, Multicenter, Efficacy Studies;

BREATHE, Bosentan: Randomized Trial of Endothelin receptor Antagonist Therapy; STRIDE, Sitaxsentan To Relieve Impaired Exercise.

Data shown as median (IQR) unless otherwise indicated.

e-Table 3. Sensitivity analysis results for change in 6MWD from baseline to 12-week follow-up by sex.

| | Women (n=894) | Men (n=236) | Difference-in-difference (95% CI) | p-value for interaction |
|--|------------------|----------------|--------------------------------------|----------------------------|
| <i>Walk distance subsequent to clinical event coded as 50 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 34.3 | 20.7 | | |
| Placebo | -6.7 | 3.9 | | |
| Δ (treatment-placebo) | 41.0 | 16.8 | 24.2 (0, 48.4) | 0.05 |
| Partially adjusted model[†]: | | | | |
| Treatment | 35.3 | 21.2 | | |
| Placebo | -6.9 | 5.6 | | |
| Δ (treatment-placebo) | 42.2 | 15.6 | 26.6 (2.5, 50.7) | 0.03 |
| <i>Walk distance subsequent to clinical event coded as 100 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 35.2 | 22.7 | | |
| Placebo | -2.8 | 5.8 | | |
| Δ (treatment-placebo) | 38.0 | 16.9 | 21.1 (-1.4, 43.6) | 0.07 |
| Partially adjusted model[†]: | | | | |
| Treatment | 35.0 | 22.1 | | |
| Placebo | -4.2 | 6.5 | | |
| Δ (treatment-placebo) | 39.2 | 15.6 | 23.6 (1.2, 46.0) | 0.04 |

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Walk distance subsequent to clinical event coded as 150 m
Base model*:

| | | | | |
|------------------------------|------|------|-------------------|------|
| Treatment | 36.1 | 24.6 | | |
| Placebo | 1.1 | 7.6 | | |
| Δ (treatment-placebo) | 35.0 | 17.0 | 18.0 (-3.1, 39.1) | 0.10 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|------|------|-------------------|-------|
| Treatment | 34.8 | 23.0 | | |
| Placebo | -1.5 | 7.5 | | |
| Δ (treatment-placebo) | 36.3 | 15.5 | 20.8 (-0.1, 41.7) | 0.053 |

Walk distance subsequent to clinical event coded as 275 m
Base model*:

| | | | | |
|------------------------------|------|------|-------------------|------|
| Treatment | 38.3 | 29.5 | | |
| Placebo | 11.0 | 12.2 | | |
| Δ (treatment-placebo) | 27.3 | 17.3 | 10.0 (-9.1, 29.1) | 0.31 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|------|------|-------------------|------|
| Treatment | 34.1 | 25.3 | | |
| Placebo | 5.4 | 9.7 | | |
| Δ (treatment-placebo) | 28.7 | 15.6 | 13.1 (-5.6, 31.8) | 0.17 |

* Adjusted for study, height, and baseline walk distance

[†] Adjusted for study, height, baseline walk distance, age, race, and diagnosis category

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e-Table 4. Sensitivity analysis results for absolute distance walked at 12-week follow-up by sex.

| | Women (n=894) | Men (n=236) | Difference-in- difference (95% CI) | p-value for interaction |
|--|------------------|----------------|---------------------------------------|----------------------------|
| <i>Walk distance subsequent to clinical event coded as 50 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 382.5 | 379.8 | | |
| Placebo | 341.5 | 363.2 | | |
| Δ (treatment-placebo) | 41.0 | 16.6 | 24.4 (-9.7, 58.5) | 0.16 |
| Partially adjusted model[†]: | | | | |
| Treatment | 373.1 | 371.5 | | |
| Placebo | 329.1 | 358.4 | | |
| Δ (treatment-placebo) | 44.0 | 13.1 | 30.9 (-2.0, 63.8) | 0.07 |
| Fully adjusted model[‡]: | | | | |
| Treatment | 369.6 | 363.7 | | |
| Placebo | 322.9 | 358.6 | | |
| Δ (treatment-placebo) | 46.7 | 5.1 | 41.6 (7.7, 75.5) | 0.02 |
| <i>Walk distance subsequent to clinical event coded as 100 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 383.4 | 381.5 | | |
| Placebo | 345.5 | 364.8 | | |
| Δ (treatment-placebo) | 37.9 | 16.7 | 21.2 (-11.5, 53.9) | 0.20 |

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Partially adjusted model[†]:

| | | | | |
|------------------------------|-------|-------|-------------------|------|
| Treatment | 373.1 | 372.4 | | |
| Placebo | 332.1 | 359.2 | | |
| Δ (treatment-placebo) | 41.0 | 13.2 | 27.8 (-3.6, 59.2) | 0.08 |

Fully adjusted model[‡]:

| | | | | |
|------------------------------|-------|-------|------------------|------|
| Treatment | 369.8 | 364.9 | | |
| Placebo | 326.3 | 359.7 | | |
| Δ (treatment-placebo) | 43.5 | 5.2 | 38.3 (6.1, 70.5) | 0.02 |

Walk distance subsequent to clinical event coded as 150 m

Base model*:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 384.3 | 383.3 | | |
| Placebo | 349.4 | 366.4 | | |
| Δ (treatment-placebo) | 34.9 | 16.9 | 18.0 (-13.4, 49.4) | 0.26 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|-------|-------|-------------------|------|
| Treatment | 373.0 | 373.3 | | |
| Placebo | 335.1 | 360 | | |
| Δ (treatment-placebo) | 37.9 | 13.3 | 24.6 (-5.4, 54.6) | 0.11 |

Fully adjusted model[‡]:

| | | | | |
|------------------------------|-------|-------|------------------|------|
| Treatment | 370.1 | 366.2 | | |
| Placebo | 329.7 | 360.9 | | |
| Δ (treatment-placebo) | 40.4 | 5.3 | 35.1 (4.3, 65.9) | 0.03 |

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Walk distance subsequent to clinical event coded as 275 m

Base model*:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 386.5 | 387.7 | | |
| Placebo | 359.3 | 370.6 | | |
| Δ (treatment-placebo) | 27.2 | 17.1 | 10.1 (-19.0, 39.2) | 0.50 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 373.0 | 375.5 | | |
| Placebo | 342.7 | 362.1 | | |
| Δ (treatment-placebo) | 30.3 | 13.4 | 16.9 (-10.7, 44.5) | 0.23 |

Fully adjusted model[‡]:

| | | | | |
|------------------------------|-------|-------|-------------------|------|
| Treatment | 370.7 | 369.3 | | |
| Placebo | 338.3 | 363.7 | | |
| Δ (treatment-placebo) | 32.4 | 5.6 | 26.8 (-1.5, 55.1) | 0.06 |

* Adjusted for study and height

[†] Adjusted for study, height, age, race, and diagnosis category

[‡] Adjusted for study, height, age, race, diagnosis category, cardiac index, and pulmonary capillary wedge pressure

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e-Table 5. Change in 6MWD from baseline to 12-week follow-up by sex for patients with idiopathic PAH

| | Women (n=539) | Men (n=168) | Difference-in-difference (95% CI) | p-value for interaction |
|--|------------------|----------------|--------------------------------------|----------------------------|
| Base model*: | | | | |
| Treatment | 40.3 | 20.5 | | |
| Placebo | -15.4 | -13.4 | | |
| Δ (treatment-placebo) | 55.7 | 33.9 | 21.8 (-11.4, 55.0) | 0.20 |
| Partially adjusted model[†]: | | | | |
| Treatment | 35.0 | 18.8 | | |
| Placebo | -20.4 | -13.8 | | |
| Δ (treatment-placebo) | 55.4 | 32.6 | 22.8 (-10.4, 56.0) | 0.18 |

* Adjusted for study, height, and baseline walk distance

[†] Adjusted for study, height, baseline walk distance, age, and race

e-Table 6. Sensitivity analysis results for change in 6MWD from baseline to 12-week follow-up by race.

| | White (n=894) | Black (n=65) | Difference-in-difference (95% CI) | p-value for interaction |
|--|------------------|-----------------|--------------------------------------|----------------------------|
| <i>Walk distance subsequent to clinical event coded as 50 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 32.9 | 16.0 | | |
| Placebo | -6.1 | 18.0 | | |
| Δ (treatment-placebo) | 39.0 | -2.0 | 41.0 (-3.0, 85.0) | 0.07 |
| Partially adjusted model[†]: | | | | |
| Treatment | 33.4 | 13.0 | | |
| Placebo | -6.3 | 12.8 | | |
| Δ (treatment-placebo) | 39.7 | 0.02 | 39.5 (-4.2, 83.2) | 0.08 |
| <i>Walk distance subsequent to clinical event coded as 100 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 34.1 | 17.7 | | |
| Placebo | -2.5 | 18.1 | | |
| Δ (treatment-placebo) | 36.6 | -0.4 | 37.0 (-4.1, 78.1) | 0.08 |
| Partially adjusted model[†]: | | | | |
| Treatment | 34.4 | 13.9 | | |
| Placebo | -2.9 | 12.2 | | |
| Δ (treatment-placebo) | 37.3 | 1.7 | 35.6 (-5.0, 76.2) | 0.09 |

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Walk distance subsequent to clinical event coded as 150 m

Base model*:

| | | | | |
|------------------------------|------|------|-------------------|------|
| Treatment | 35.3 | 19.3 | | |
| Placebo | 1.2 | 18.3 | | |
| Δ (treatment-placebo) | 34.1 | 1.0 | 33.1 (-5.5, 71.7) | 0.09 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|------|------|-------------------|------|
| Treatment | 35.3 | 14.9 | | |
| Placebo | 1.0 | 11.6 | | |
| Δ (treatment-placebo) | 34.3 | 3.3 | 31.0 (-7.1, 69.1) | 0.11 |

Walk distance subsequent to clinical event coded as 275 m

Base model*:

| | | | | |
|------------------------------|------|------|--------------------|------|
| Treatment | 38.2 | 23.4 | | |
| Placebo | 10.3 | 18.6 | | |
| Δ (treatment-placebo) | 27.9 | 4.8 | 23.1 (-12.2, 58.4) | 0.20 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|------|------|--------------------|------|
| Treatment | 37.7 | 17.2 | | |
| Placebo | 9.2 | 10.0 | | |
| Δ (treatment-placebo) | 28.5 | 7.2 | 21.3 (-13.2, 55.8) | 0.23 |

* Adjusted for study, height, and baseline walk distance

[†] Adjusted for study, height, baseline walk distance, age, sex, and diagnosis category

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e-Table 7. Sensitivity analysis results for absolute distance walked at 12-week follow-up by race.

| | White (n=836) | Black (n=65) | Difference-in-difference (95% CI) | p-value for interaction |
|--|------------------|-----------------|--------------------------------------|----------------------------|
| <i>Walk distance subsequent to clinical event coded as 50 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 385.2 | 369.5 | | |
| Placebo | 346.1 | 357.3 | | |
| Δ (treatment-placebo) | 39.1 | 12.2 | 26.9 (-36.3, 90.1) | 0.41 |
| Partially adjusted model[†]: | | | | |
| Treatment | 387.8 | 361.0 | | |
| Placebo | 347.5 | 344.7 | | |
| Δ (treatment-placebo) | 40.3 | 16.3 | 24.0 (-36.4, 84.4) | 0.44 |
| Fully adjusted model[‡]: | | | | |
| Treatment | 399.0 | 379.7 | | |
| Placebo | 359.9 | 351.5 | | |
| Δ (treatment-placebo) | 39.1 | 28.2 | 10.9 (-47.7, 69.5) | 0.72 |
| <i>Walk distance subsequent to clinical event coded as 100 m</i> | | | | |
| Base model*: | | | | |
| Treatment | 386.3 | 371.1 | | |
| Placebo | 349.7 | 357.6 | | |
| Δ (treatment-placebo) | 36.6 | 13.5 | 23.1 (-37.4, 83.6) | 0.45 |

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Partially adjusted model[†]:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 388.6 | 362.0 | | |
| Placebo | 350.8 | 344.5 | | |
| Δ (treatment-placebo) | 37.8 | 17.5 | 20.3 (-37.2, 77.8) | 0.49 |

Fully adjusted model[‡]:

| | | | | |
|------------------------------|-------|-------|-------------------|------|
| Treatment | 399.4 | 379.9 | | |
| Placebo | 362.8 | 351.0 | | |
| Δ (treatment-placebo) | 36.6 | 28.9 | 7.7 (-48.0, 63.4) | 0.79 |

Walk distance subsequent to clinical event coded as 150 m

Base model*:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 387.4 | 372.6 | | |
| Placebo | 353.3 | 357.9 | | |
| Δ (treatment-placebo) | 34.1 | 14.7 | 19.4 (-38.7, 77.5) | 0.51 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 389.4 | 363.0 | | |
| Placebo | 354.1 | 344.3 | | |
| Δ (treatment-placebo) | 35.3 | 18.7 | 16.6 (-38.4, 71.6) | 0.55 |

Fully adjusted model[‡]:

| | | | | |
|------------------------------|-------|-------|-------------------|------|
| Treatment | 399.8 | 380.2 | | |
| Placebo | 365.6 | 350.5 | | |
| Δ (treatment-placebo) | 34.2 | 29.7 | 4.5 (-48.8, 57.8) | 0.87 |

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Walk distance subsequent to clinical event coded as 275 m

Base model*:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 390.2 | 376.4 | | |
| Placebo | 362.2 | 358.8 | | |
| Δ (treatment-placebo) | 28.0 | 17.6 | 10.4 (-43.7, 64.5) | 0.71 |

Partially adjusted model[†]:

| | | | | |
|------------------------------|-------|-------|-------------------|------|
| Treatment | 391.5 | 365.4 | | |
| Placebo | 362.4 | 343.8 | | |
| Δ (treatment-placebo) | 29.1 | 21.6 | 7.5 (-43.1, 58.1) | 0.77 |

Fully adjusted model[‡]:

| | | | | |
|------------------------------|-------|-------|--------------------|------|
| Treatment | 400.7 | 380.8 | | |
| Placebo | 372.6 | 349.4 | | |
| Δ (treatment-placebo) | 28.1 | 31.4 | -3.3 (-52.4, 45.8) | 0.90 |

* Adjusted for study and height

† Adjusted for study, height, age, sex, and diagnosis category

‡ Adjusted for study, height, age, sex, diagnosis category, and New York Heart Association class

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e-Table 8. Change in 6MWD from baseline to 12-week follow-up by race for patients with idiopathic PAH.

| | White (n=518) | Black (n=34) | Difference-in-difference (95% CI) | p-value for interaction |
|--|------------------|-----------------|--------------------------------------|----------------------------|
| Base model*: | | | | |
| Treatment | 38.9 | 14.4 | | |
| Placebo | -16.6 | 20.6 | | |
| Δ (treatment-placebo) | 55.5 | -6.2 | 61.7 (-3.8, 127.2) | 0.06 |
| Partially adjusted model[†]: | | | | |
| Treatment | 37.7 | 6.4 | | |
| Placebo | -17.3 | 16.7 | | |
| Δ (treatment-placebo) | 55.0 | -10.3 | 65.3 (0.5, 130.6) | 0.05 |

* Adjusted for study, height, and baseline walk distance

[†] Adjusted for study, height, baseline walk distance, age, and sex.

e-Table 9. Regression output for model examining change in 6MWD from baseline to 12-week follow-up by sex.

| | Estimate | Standard Error | t-value | p-value |
|---------------------------|----------|----------------|---------|---------|
| Intercept | -78.73 | 61.11 | -1.29 | 0.20 |
| Treatment | 45.25 | 6.22 | 7.28 | <0.001 |
| Sex (male) | 14.41 | 21.21 | 1.18 | 0.24 |
| Study | | | | 0.009 |
| ARIES-1 | -16.01 | 11.05 | -1.45 | 0.14 |
| ARIES-2 | -25.25 | 11.20 | -2.25 | 0.02 |
| BREATHE -1 | -17.86 | 11.04 | -1.62 | 0.11 |
| STRIDE-1 | -38.80 | 11.32 | -3.43 | 0.001 |
| STRIDE-2 | -30.15 | 10.92 | -2.76 | 0.006 |
| Height | 0.92 | 0.36 | 2.53 | 0.01 |
| Baseline walk distance | -0.08 | 0.03 | -2.46 | 0.01 |
| Age | -0.55 | 0.20 | -2.82 | 0.005 |
| Race | | | | 0.50 |
| White | -4.32 | 14.79 | -0.29 | 0.77 |
| Black | -11.91 | 18.04 | -0.66 | 0.51 |
| Hispanic | -14.86 | 15.81 | -0.94 | 0.35 |
| Diagnosis | | | | 0.09 |
| Connective tissue disease | -11.81 | 6.10 | -1.93 | 0.05 |
| Congenital heart disease | 10.96 | 10.58 | 1.04 | 0.30 |
| HIV/Anorexigen Use | 6.60 | 15.39 | 0.43 | 0.67 |

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| | | | | |
|---------------|--------|-------|-------|------|
| Sex*Treatment | -29.66 | 13.27 | -2.24 | 0.03 |
|---------------|--------|-------|-------|------|

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e-Table 10. Regression output for model examining absolute distance walked at 12 week follow-up by sex.

| | Estimate | Standard Error | t-value | p-value |
|---------------------------|----------|----------------|---------|---------|
| Intercept | 135.23 | 84.40 | 1.60 | 0.11 |
| Treatment | 49.92 | 8.49 | 5.88 | <0.001 |
| Sex (male) | 38.02 | 16.61 | 2.29 | 0.02 |
| Study | | | | 0.03 |
| ARIES-1 | -4.78 | 15.26 | -0.31 | 0.75 |
| ARIES-2 | -12.98 | 15.43 | -0.84 | 0.40 |
| BREATHE -1 | -14.17 | 15.28 | -0.92 | 0.35 |
| STRIDE-1 | 18.15 | 15.30 | 1.19 | 0.24 |
| STRIDE-2 | -19.94 | 15.13 | -1.32 | 0.19 |
| Height | 1.48 | 0.50 | 2.95 | 0.003 |
| Age | -1.90 | 0.26 | -7.28 | <0.001 |
| Race | | | | 0.04 |
| White | 27.89 | 19.96 | 1.40 | 0.16 |
| Black | 11.69 | 24.38 | 0.48 | 0.63 |
| Hispanic | -0.55 | 21.35 | -0.03 | 0.98 |
| Diagnosis | | | | 0.01 |
| Connective tissue disease | -27.24 | 8.37 | -3.25 | 0.001 |
| Congenital heart disease | 2.70 | 14.91 | 0.18 | 0.86 |
| HIV/Anorexigen Use | -6.78 | 21.88 | -0.31 | 0.76 |
| Baseline cardiac index | 16.89 | 4.04 | 4.18 | <0.001 |

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| | | | | |
|---------------|--------|-------|-------|------|
| Baseline PCWP | -0.12 | 0.97 | -0.12 | 0.91 |
| Sex*Treatment | -44.93 | 18.22 | -2.47 | 0.01 |

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e-Table 11. Regression output for model examining change in 6MWD from baseline to 12-week follow-up by race.

| | Estimate | Standard Error | t-value | p-value |
|---------------------------|----------|----------------|---------|---------|
| Intercept | -94.22 | 67.50 | -1.40 | 0.16 |
| Treatment | 42.20 | 6.29 | 6.71 | <0.001 |
| Race (black) | 23.17 | 20.49 | 1.13 | 0.26 |
| Study | | | | 0.06 |
| ARIES-1 | -7.19 | 14.61 | -0.49 | 0.62 |
| ARIES-2 | -20.57 | 14.44 | -1.42 | 0.15 |
| BREATHE -1 | -5.55 | 14.35 | -0.38 | 0.70 |
| STRIDE-1 | -29.74 | 14.83 | -2.01 | 0.04 |
| STRIDE-2 | -22.63 | 14.02 | -1.61 | 0.11 |
| Height | 0.92 | 0.40 | 2.31 | 0.02 |
| Baseline walk distance | -0.06 | 0.03 | -1.70 | 0.09 |
| Age | -0.54 | 0.20 | -2.56 | 0.01 |
| Sex (male) | -6.59 | 8.60 | -0.77 | 0.44 |
| Diagnosis | | | | 0.16 |
| Connective tissue disease | -13.27 | 6.61 | -2.01 | 0.04 |
| Congenital heart disease | 9.65 | 12.24 | 0.79 | 0.43 |
| HIV/Anorexigen Use | 1.37 | 15.97 | 0.09 | 0.93 |
| Race*Treatment | -43.62 | 24.04 | -1.81 | 0.07 |

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e-Table 12. Regression output for model examining absolute distance walked at 12-week follow-up by race.

| | Estimate | Standard Error | t-value | p-value |
|---------------------------|----------|----------------|---------|---------|
| Intercept | 295.55 | 88.23 | 3.35 | 0.001 |
| Treatment | 41.54 | 8.27 | 5.02 | <0.001 |
| Race (black) | -5.21 | 26.77 | -0.19 | 0.85 |
| Study | | | | 0.002 |
| ARIES-1 | -6.90 | 19.23 | -0.36 | 0.72 |
| ARIES-2 | -20.93 | 18.94 | -1.10 | 0.27 |
| BREATHE -1 | 10.73 | 19.31 | 0.56 | 0.58 |
| STRIDE-1 | 20.46 | 19.33 | 1.06 | 0.29 |
| STRIDE-2 | -23.63 | 18.42 | -1.28 | 0.20 |
| Height | 1.18 | 0.53 | 2.25 | 0.02 |
| Age | -1.87 | 0.26 | -7.00 | <0.001 |
| Sex (male) | 12.74 | 11.34 | 1.12 | 0.26 |
| Diagnosis | | | | 0.01 |
| Connective tissue disease | -27.82 | 8.67 | -3.21 | 0.001 |
| Congenital heart disease | 7.90 | 16.06 | 0.49 | 0.62 |
| HIV/Anorexigen Use | -4.75 | 21.12 | -0.22 | 0.82 |
| NYHA class (III/IV) | -65.81 | 8.55 | -7.69 | <0.001 |
| Race*Treatment | -13.99 | 31.53 | -0.44 | 0.66 |

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