

Dokumentvorlage, Version vom 18.11.2025

**Dossier zur Nutzenbewertung
gemäß § 35a SGB V**

Sotatercept (Winrevair[®])

MSD Sharp & Dohme GmbH

Modul 4 A
Anhang 4-G

Pulmonale Arterielle Hypertonie

Medizinischer Nutzen und
medizinischer Zusatznutzen,
Patientengruppen mit therapeutisch
bedeutsamem Zusatznutzen

Stand: 16.02.2026

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Anhang 4-G1: Gesamtpopulation der Studie ZENITH

Im Folgenden wird ergänzend zu Abschnitt 4.3.1.3.1.1 die Gesamtpopulation der Studie ZENITH dargestellt

Die Ergebnisse beziehen sich auf den Database Cutoff Date vom 26. Juli 2024.

Tabelle 4G-1: Charakterisierung der Gesamtpopulation der Studie ZENITH – RCT mit dem zu bewertenden Arzneimittel

| Characteristic | Study: ZENITH (MK-7962-006) ^a | |
|---|--|-------------------------------|
| | Sotatercept N ^b =86 | Placebo N ^b =86 |
| Sex, n (%) | | |
| Male | 25 (29.1) | 15 (17.4) |
| Female | 61 (70.9) | 71 (82.6) |
| Age Group (Years), n (%) | | |
| <65 | 56 (65.1) | 66 (76.7) |
| ≥65 | 30 (34.9) | 20 (23.3) |
| Age (Years) | | |
| Mean (SD) | 55.3 (14.3) | 53.5 (14.3) |
| Median (Q1; Q3) | 58.0 (45.0; 67.0) | 57.0 (46.0; 64.0) |
| Min; Max | 19.0; 75.0 | 18.0; 75.0 |
| Race, n (%) | | |
| American Indian Or Alaska Native | 0 (0.0) | 1 (1.2) |
| Asian | 4 (4.7) | 3 (3.5) |
| Black Or African American | 5 (5.8) | 4 (4.7) |
| White | 73 (84.9) | 76 (88.4) |
| Other | 3 (3.5) | 2 (2.3) |
| Missing | 1 (1.2) | 0 (0.0) |
| Ethnicity, n (%) | | |
| Hispanic Or Latino | 6 (7.0) | 12 (14.0) |
| Not Hispanic Or Latino | 78 (90.7) | 73 (84.9) |
| Not Reported | 1 (1.2) | 1 (1.2) |
| Unknown | 1 (1.2) | 0 (0.0) |
| Region^c, n (%) | | |
| WHO Stratum A | 84 (97.7) | 80 (93.0) |
| Rest of the World | 2 (2.3) | 6 (7.0) |
| BMI (kg/m²) | | |
| Mean (SD) | 25.2 (5.8) | 25.8 (5.9) |
| Median (Q1; Q3) | 24.4 (22.1; 26.7) | 24.6 (21.4; 29.7) |
| Min; Max | 16.3; 49.5 | 16.8; 41.9 |
| REVEAL Lite 2.0 Risk Score^d, n (%) | | |
| 9 to 10 | 60 (69.8) | 60 (69.8) |
| ≥11 | 26 (30.2) | 26 (30.2) |
| WHO Diagnostic Pulmonary Hypertension Group I, PAH, n (%) | | |
| Drug or toxin-induced PAH | 6 (7.0) | 5 (5.8) |
| Heritable PAH | 11 (12.8) | 7 (8.1) |
| Idiopathic PAH | 42 (48.8) | 44 (51.2) |
| PAH associated with connective tissue disease | 22 (25.6) | 26 (30.2) |
| PAH associated with simple, congenital systemic-to-pulmonary shunts | 5 (5.8) | 4 (4.7) |

| Characteristic | Study: ZENITH (MK-7962-006) ^a | |
|---|--|-------------------------------|
| | Sotatercept N ^b =86 | Placebo N ^b =86 |
| at least 1 year following shunt repair | | |
| 6 Minute Walk Distance (m) | | |
| Mean (SD) | 270.3 (104.8) | 270.7 (99.9) |
| Median (Q1; Q3) | 292.6 (182.4; 343.0) | 282.5 (191.0; 350.0) |
| Min; Max | 11.0; 501.0 | 44.2; 493.0 |
| WHO Function Class, n (%) | | |
| III | 66 (76.7) | 62 (72.1) |
| IV | 20 (23.3) | 24 (27.9) |
| Combination Therapy, n (%) | | |
| Double Therapy | 21 (24.4) | 27 (31.4) |
| Triple Therapy | 65 (75.6) | 59 (68.6) |
| Prostacyclin Infusion Therapy, n (%) | | |
| Prostacyclin Infusion Therapy | 53 (61.6) | 49 (57.0) |
| Non-Prostacyclin Infusion Therapy | 33 (38.4) | 37 (43.0) |
| PAH Subtype, n (%) | | |
| CTD-associated | 22 (25.6) | 26 (30.2) |
| Not CTD-associated | 64 (74.4) | 60 (69.8) |
| PVR (dynes*sec/cm⁵) | | |
| Participants with data | 86 | 85 |
| Mean (SD) | 883.2 (410.9) | 874.7 (344.2) |
| Median (Q1; Q3) | 792.0 (584.0; 1104.0) | 792.0 (616.0; 1048.0) |
| Min; Max | 328.0; 2464.0 | 360.0; 1928.0 |
| Cardiac Output (L/min) | | |
| Mean (SD) | 4.7 (1.2) | 4.5 (1.4) |
| Median (Q1; Q3) | 4.5 (3.9; 5.6) | 4.4 (3.4; 5.4) |
| Min; Max | 2.2; 8.0 | 2.2; 9.6 |
| Cardiac Index (L/min/m²) | | |
| Mean (SD) | 2.6 (0.6) | 2.6 (0.8) |
| Median (Q1; Q3) | 2.5 (2.3; 3.0) | 2.3 (2.0; 3.1) |
| Min; Max | 1.4; 4.1 | 1.4; 4.4 |
| eGFR (ml/min/1.73m²) | | |
| Participants with data | 85 | 86 |
| Mean (SD) | 65.1 (24.6) | 73.5 (29.7) |
| Median (Q1; Q3) | 62.0 (46.0; 77.0) | 69.0 (50.0; 90.0) |
| Min; Max | 25.0; 136.0 | 23.0; 181.0 |
| NT-proBNP (pg/mL) | | |
| Mean (SD) | 3603.1 (4101.2) | 2687.3 (2771.2) |
| Median (Q1; Q3) | 1969.0 (1276.0; 3982.0) | 2123.5 (1113.0; 3799.0) |
| Min; Max | 184.0; 22752.0 | 18.5; 19519.0 |
| a: Database Cutoff Date: 26JUL2024 | | |
| b: Number of participants: full analysis set | | |
| c: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States | | |
| d: For participants with REVEAL Lite 2.0 risk score < 9 at screening, they are grouped under category 9 to 10 for the analyses | | |
| BMI: Body Mass Index; CTD: Connective Tissue Disease; eGFR: estimated Glomerular Filtration Rate; NT-proBNP: N-terminal pro B-type Natriuretic Peptide; PAH: Pulmonary Arterial Hypertension; PVR: Pulmonary Vascular Resistance; Q1: First Quartile; Q3: Third Quartile; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; SD: Standard Deviation; WHO: World Health Organization | | |

Tabelle 4G-2: Charakterisierung der Gesamtpopulation der Studie ZENITH
(Therapieabbrecher, Studienabbrecher) – RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006)^a | Sotatercept n (%) | Placebo n (%) |
|--|------------------------------|--------------------------|
| Participants in Population ^b | 86 | 86 |
| Status For Trial | | |
| Completed | 4 (4.7) | 30 (34.9) |
| Discontinued | 12 (14.0) | 18 (20.9) |
| Adverse Event | 0 (0.0) | 2 (2.3) |
| Death | 5 (5.8) | 10 (11.6) |
| More Than 3 Dose Delays Required Per Dose Adjustment Guidelines | 1 (1.2) | 0 (0.0) |
| Qtcf Above 500 Ms | 0 (0.0) | 1 (1.2) |
| Unwillingness Or Inability To Comply With Protocol | 1 (1.2) | 0 (0.0) |
| Withdrawal By Subject | 1 (1.2) | 4 (4.7) |
| Other | 4 (4.7) | 1 (1.2) |
| Ongoing | 70 (81.4) | 38 (44.2) |
| Status For Study Medication in Trial | | |
| Started ^c | 86 | 86 |
| Completed | 6 (7.0) | 33 (38.4) |
| Discontinued | 12 (14.0) | 19 (22.1) |
| Adverse Event | 0 (0.0) | 2 (2.3) |
| Death | 5 (5.8) | 10 (11.6) |
| More Than 3 Dose Delays Required Per Dose Adjustment Guidelines | 1 (1.2) | 0 (0.0) |
| Qtcf > 500 Ms During The Treatment Period | 0 (0.0) | 1 (1.2) |
| Unwillingness Or Inability To Comply With Protocol | 1 (1.2) | 0 (0.0) |
| Withdrawal By Subject | 1 (1.2) | 4 (4.7) |
| Other | 4 (4.7) | 2 (2.3) |
| Ongoing | 68 (79.1) | 34 (39.5) |
| <p>a: Database Cutoff Date: 26JUL2024</p> <p>b: Number of participants: full analysis set</p> <p>c: Number of participants: all participants as treated population</p> <p>Each participant is counted once for Trial Disposition based on the latest corresponding disposition record.</p> <p>Participants are considered to have completed the study if they experienced an event of PAH worsening-related hospitalization of ≥ 24 hours or lung transplantation.</p> <p>Ms: Milliseconds; PAH: Pulmonary Arterial Hypertension; QTcF: Fridericia's corrected QT interval; WHO: World Health Organization</p> | | |

Anhang 4-G2: Behandlungsdauer und Beobachtungsdauer

Im Folgenden werden die Behandlungs- und Beobachtungsdauer deskriptiv dargestellt.

Die Ergebnisse beziehen sich auf den Database Cutoff Date vom 26. Juli 2024.

Tabelle 4G-3: Behandlungsdauer und Beobachtungsdauer

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | Placebo |
|---|-------------------|-------------------|
| Duration of Treatment (Weeks)^b | | |
| N ^c | 20 | 24 |
| Mean (SD) | 52.5 (30.7) | 36.5 (19.2) |
| Median (Q1; Q3) | 49.5 (28.5; 75.4) | 32.1 (23.6; 49.3) |
| Min; Max | 3.0; 105.0 | 3.0; 90.0 |
| Observation Period | | |
| Overall Survival - Primary Analysis / Time to First Morbidity or Death (Weeks)^d | | |
| N ^c | 20 | 24 |
| Mean (SD) | 54.4 (30.6) | 35.9 (19.0) |
| Median (Q1; Q3) | 54.0 (33.4; 78.0) | 31.6 (23.8; 47.6) |
| Min; Max | 1.3; 104.6 | 7.3; 89.3 |
| Adverse Event / Serious Adverse Event (Weeks)^f | | |
| N ^c | 20 | 24 |
| Mean (SD) | 51.7 (30.2) | 35.8 (19.3) |
| Median (Q1; Q3) | 50.7 (30.3; 72.9) | 31.6 (23.8; 47.6) |
| Min; Max | 1.3; 104.6 | 3.1; 89.3 |
| 6-Minute Walk Distance (Weeks)^g | | |
| N ^c | 20 | 24 |
| Mean (SD) | 42.4 (29.5) | 31.4 (18.7) |
| Median (Q1; Q3) | 36.3 (18.9; 66.6) | 25.0 (23.2; 37.5) |
| Min; Max | 0.1; 96.1 | 0.1; 83.7 |
| Dyspnea Score (Pre-Vital Signs 6-Min Walk) Assessed by Borg CR10 (Weeks)^g | | |
| N ^c | 20 | 24 |
| Mean (SD) | 42.4 (29.5) | 31.4 (18.7) |
| Median (Q1; Q3) | 36.3 (18.9; 66.6) | 25.0 (23.2; 37.5) |
| Min; Max | 0.1; 96.1 | 0.1; 83.7 |
| EQ-5D-VAS (Weeks)^g | | |
| N ^c | 19 | 21 |
| Mean (SD) | 46.4 (25.7) | 29.3 (20.1) |
| Median (Q1; Q3) | 48.1 (36.0; 72.1) | 24.4 (23.6; 37.0) |
| Min; Max | 0.1; 96.1 | 0.1; 83.7 |
| a: Database Cutoff Date: 26JUL2024 b: Calculated from date of first dose until date of last dose + 3 weeks (dosing period) c: Number of participants: all participants as treated population, participants with WHO FC IV at baseline d: Calculated from date of randomization until date of death, date of last contact, or the database cutoff date if the participant is still alive e: Number of participants: full analysis set, participants with WHO FC IV at baseline f: Calculated from the date of first dose to the earliest of the date of last dose + planned safety follow-up time (up to 8 weeks after the date of last dose of treatment), date of death, date of last contact or the database cutoff date if the participant is still alive g: Calculated from date of randomization until date of last assessment CR10: 10 Point Category Ratio scale; EQ-5D: European Quality of Life 5 Dimensions; FC: Functional Class; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation; VAS: Visual Analog Scale; WHO: World Health Organization | | |

Anhang 4-G3: Sensitivitätsanalysen

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.1 die Sensitivitätsanalysen des primären Endpunktes der Studie ZENITH Zeit bis Tod jeglicher Ursache, Lungentransplantation oder Hospitalisierung von ≥ 24 Stunden aufgrund von PAH-Verschlechterung

Alle Ergebnisse beziehen sich auf den Database Cutoff Date vom 26. Juli 2024.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

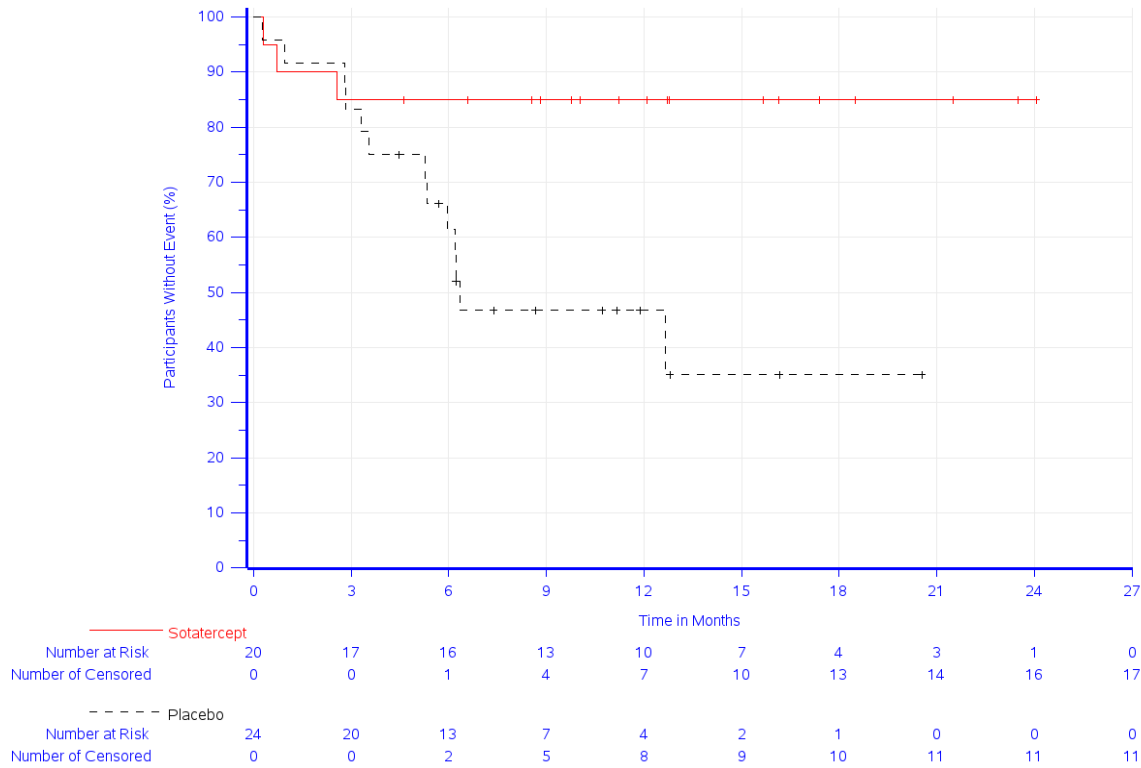
Tabelle 4G-4: Ergebnisse für den Endpunkt Zeit bis Tod jeglicher Ursache, Lungentransplantation oder Hospitalisierung von ≥ 24 Stunden aufgrund von PAH-Verschlechterung aus RCT mit dem zu bewertenden Arzneimittel - Sensitivitätsanalyse #1

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|---|----------------|-------------------------------|--|----------------|-------------------------------|--|-------------------------------------|------------------------|
| | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| All-cause Death, Lung Transplantation, or PAH Worsening-related Hospitalization of ≥ 24 Hours (Sensitivity Analysis - Include the Adjudicated Events Only) | 20 | 3 (15.0) | Not reached [-; -] | 24 | 13 (54.2) | 6.3 [5.3; -] | 0.22 [0.06; 0.79] | 0.020 |

^a Database Cutoff Date: 26JUL2024
^b Number of participants: full analysis set, participants with WHO FC IV at baseline
^c From product-limit (Kaplan-Meier) method for censored data
^d Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
^e Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

This table includes the first event of adjudication-confirmed PAH worsening-related hospitalization ≥ 24 hours, lung transplantation, or all-cause death prior to the cutoff date
CI: Confidence Interval; FC: Functional Class; PAH: Pulmonary Arterial Hypertension; WHO: World Health Organization

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 26JUL2024)
 All-cause Death, Lung Transplantation, or PAH Worsening-related Hospitalization of >=24 Hours (Sensitivity Analysis - Include the Adjudicated Events Only)
 This figure includes the first event of adjudication-confirmed PAH worsening-related hospitalization >=24 hours, lung transplantation, or all-cause death prior to the cutoff date

Abbildung 4G-1: Kaplan-Meier-Kurve für den Endpunkt Zeit bis zum Tod jeglicher Ursache, Lungentransplantation oder Hospitalisierung von ≥ 24 Stunden aufgrund von PAH-Verschlechterung der Studie ZENITH - Sensitivitätsanalyse #1

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Tabelle 4G-5: Ergebnisse für den Endpunkt Zeit bis Tod jeglicher Ursache, Lungentransplantation oder Hospitalisierung von ≥ 24 Stunden aufgrund von PAH-Verschlechterung aus RCT mit dem zu bewertenden Arzneimittel - Sensitivitätsanalyse #3 (Jump to Reference Methode)

| | Sotatercept (N=20) | Placebo (N=24) |
|--|-------------------------------|---------------------------|
| Number (%) of observed first events | 4 (20.0) | 13 (54.2) |
| All-cause death | 2 (10.0) | 0 (0.0) |
| Lung transplantation | 1 (5.0) | 0 (0.0) |
| PAH worsening-related hospitalization of ≥ 24 hours | 1 (5.0) | 13 (54.2) |
| Number (%) of participants missing follow-up time ^a | 1 (5.0) | 0 (0.0) |
| Total missing follow-up time ^b (months) | 10.6 | n.a. |
| Comparison vs. Placebo | | |
| Hazard Ratio (95% CI) ^c | 0.28 (0.09, 0.86) | |
| p-value ^d | 0.0177 | |
| Study: ZENITH (MK-7962-006) (Database Cutoff Date: 26JUL2024) | | |
| ^a Any participant who did not have a reported event prior to the database cutoff date and discontinued the study prior to the cutoff date will be considered as having missing follow-up. | | |
| ^b Lost follow-up time will be calculated as the time from the last visit with full assessment of efficacy endpoints to the data cutoff date. | | |
| ^c Based on Cox regression model with Efron's method of tie handling with treatment as a covariate. | | |
| ^d One-sided p-value based on the log-rank test. | | |
| This table includes the same events as the primary analysis. | | |
| CI: Confidence Interval; n.a.: not applicable; PAH: Pulmonary Arterial Hypertension | | |

Anhang 4-G4: Morbidität – Auswertungen über den Studienverlauf

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2 deskriptive Auswertungen über den Studienverlauf dargestellt. Hierzu werden zu jedem Erhebungszeitpunkt die Anzahl an verfügbaren Daten, der Mittelwert (inkl. Standardabweichung), der Median (inkl. Q1; Q3) und Minimum und Maximum zum jeweiligen Zeitpunkt tabellarisch dargestellt.

Alle Ergebnisse beziehen sich auf den Database Cutoff Date vom 26. Juli 2024.

Tabelle 4G-6: Auswertung über den Studienverlauf – 6MWD

| Deskriptive Zusammenfassung der 6MWD (in Metern) | Studie: ZENITH (MK-7962-006) ^a | |
|--|---|--------------------------------|
| | Sotatercept N ^b = 20 | Placebo N ^b = 24 |
| Baseline | | |
| N ^c | 20 | 24 |
| Mittelwert (SD) | 223,7 (138,5) | 240,7 (88,3) |
| Median (Q1; Q3) | 197,5 (122,9; 306,1) | 237,5 (173,5; 327,0) |
| Min, Max | 15,0; 528,0 | 42,7; 366,0 |
| Woche 3 | | |
| N ^c | 19 | 23 |
| Mittelwert (SD) | 268,9 (142,8) | 264,5 (82,8) |
| Median (Q1; Q3) | 296,0 (162,0; 332,2) | 295,5 (185,0; 334,0) |
| Min, Max | 25,0; 594,0 | 102,0; 365,8 |
| Woche 12 | | |
| N ^c | 18 | 23 |
| Mittelwert (SD) | 321,4 (143,5) | 264,3 (94,0) |
| Median (Q1; Q3) | 346,0 (200,0; 400,0) | 288,0 (192,0; 335,3) |
| Min, Max | 50,0; 563,0 | 75,0; 391,5 |
| Woche 24 | | |
| N ^c | 15 | 18 |
| Mittelwert (SD) | 349,2 (130,6) | 305,8 (112,1) |
| Median (Q1; Q3) | 375,0 (289,0; 427,0) | 324,5 (273,0; 370,0) |
| Min, Max | 100,0; 552,0 | 12,0; 450,0 |
| Woche 36 | | |
| N ^c | 11 | 11 |
| Mittelwert (SD) | 423,5 (92,7) | 288,6 (114,6) |
| Median (Q1; Q3) | 437,0 (350,0; 465,0) | 304,8 (184,0; 399,3) |
| Min, Max | 253,0; 589,0 | 72,0; 410,0 |
| Woche 48 | | |
| N ^c | 9 | 5 |
| Mittelwert (SD) | 426,2 (108,1) | 333,2 (90,2) |
| Median (Q1; Q3) | 446,0 (402,0; 488,0) | 307,8 (258,0; 390,0) |
| Min, Max | 202,0; 545,0 | 250,0; 460,0 |
| Woche 60 | | |
| N ^c | 7 | 3 |
| Mittelwert (SD) | 416,6 (110,9) | 304,7 (193,8) |
| Median (Q1; Q3) | 403,0 (332,0; 530,0) | 279,0 (125,0; 510,0) |
| Min, Max | 232,0; 540,0 | 125,0; 510,0 |
| Woche 72 | | |

| Deskriptive Zusammenfassung der 6MWD (in Metern) | Studie: ZENITH (MK-7962-006) ^a | |
|--|---|----------------------|
| | Sotatercept | Placebo |
| | N ^b = 20 | N ^b = 24 |
| N ^c | 5 | 1 |
| Mittelwert (SD) | 440,6 (141,7) | 262,0 (-) |
| Median (Q1; Q3) | 420,0 (415,0; 538,0) | 262,0 (262,0; 262,0) |
| Min, Max | 230,0; 600,0 | 262,0; 262,0 |
| Woche 84 | | |
| N ^c | 2 | 1 |
| Mittelwert (SD) | 474,0 (118,8) | 270,0 (-) |
| Median (Q1; Q3) | 474,0 (390,0; 558,0) | 270,0 (270,0; 270,0) |
| Min, Max | 390,0; 558,0 | 270,0; 270,0 |
| Woche 96 | | |
| N ^c | 2 | 0 |
| Mittelwert (SD) | 463,0 (134,4) | - (-) |
| Median (Q1; Q3) | 463,0 (368,0; 558,0) | - (-; -) |
| Min, Max | 368,0; 558,0 | -; - |
| a: Database cutoff date: 26. Juli 2024 | | |
| b: Anzahl der Patient:innen: Full-Analysis-Set Population; Patient:innen mit WHO FK IV zu Baseline | | |
| c: Anzahl der Patient:innen ohne fehlende Erhebung zur jeweiligen Visite | | |
| FK: Funktionsklasse; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung; WHO: World Health Organization | | |

Tabelle 4G-7: Auswertung über den Studienverlauf – Dyspnoe gemäß Borg CR10-Skala

| Pre-6MWD-Test Dyspnoe gemäß Borg-Skala | Studie: ZENITH (MK-7962-006) ^a | |
|--|---|---------------------|
| | Sotatercept | Placebo |
| | N ^b = 20 | N ^b = 24 |
| Baseline | | |
| N ^c | 20 | 24 |
| Mittelwert (SD) | 5,8 (4,3) | 4,3 (3,5) |
| Median (Q1; Q3) | 7,0 (1,0; 9,0) | 4,0 (1,0; 7,0) |
| Min, Max | 1,0; 14,0 | 1,0; 11,0 |
| Woche 3 | | |
| N ^c | 19 | 23 |
| Mittelwert (SD) | 4,7 (3,8) | 4,3 (3,3) |
| Median (Q1; Q3) | 5,0 (1,0; 9,0) | 5,0 (1,0; 7,0) |
| Min, Max | 1,0; 11,0 | 1,0; 9,0 |
| Woche 12 | | |
| N ^c | 18 | 23 |
| Mittelwert (SD) | 3,6 (3,8) | 4,5 (3,9) |
| Median (Q1; Q3) | 1,0 (1,0; 7,0) | 3,0 (1,0; 7,0) |
| Min, Max | 1,0; 10,0 | 1,0; 12,0 |
| Woche 24 | | |
| N ^c | 15 | 18 |
| Mittelwert (SD) | 4,2 (3,3) | 3,9 (3,6) |
| Median (Q1; Q3) | 3,0 (1,0; 7,0) | 1,0 (1,0; 7,0) |
| Min, Max | 1,0; 9,0 | 1,0; 9,0 |
| Woche 36 | | |
| N ^c | 11 | 11 |
| Mittelwert (SD) | 2,6 (3,7) | 3,5 (3,1) |

| Pre-6MWD-Test Dyspnoe gemäß Borg-Skala | Studie: ZENITH (MK-7962-006) ^a | |
|--|---|--------------------------------|
| | Sotatercept N ^b = 20 | Placebo N ^b = 24 |
| Median (Q1; Q3) | 1,0 (1,0; 1,0) | 3,0 (1,0; 7,0) |
| Min, Max | 1,0; 11,0 | 1,0; 9,0 |
| Woche 48 | | |
| N ^c | 9 | 5 |
| Mittelwert (SD) | 2,3 (2,6) | 4,6 (3,6) |
| Median (Q1; Q3) | 1,0 (1,0; 3,0) | 5,0 (1,0; 7,0) |
| Min, Max | 1,0; 9,0 | 1,0; 9,0 |
| Woche 60 | | |
| N ^c | 7 | 3 |
| Mittelwert (SD) | 2,9 (3,1) | 6,3 (1,2) |
| Median (Q1; Q3) | 1,0 (1,0; 5,0) | 7,0 (5,0; 7,0) |
| Min, Max | 1,0; 9,0 | 5,0; 7,0 |
| Woche 72 | | |
| N ^c | 5 | 1 |
| Mittelwert (SD) | 2,8 (4,0) | 11,0 (-) |
| Median (Q1; Q3) | 1,0 (1,0; 1,0) | 11,0 (11,0; 11,0) |
| Min, Max | 1,0; 10,0 | 11,0; 11,0 |
| Woche 84 | | |
| N ^c | 2 | 1 |
| Mittelwert (SD) | 1,0 (0,0) | 9,0 (-) |
| Median (Q1; Q3) | 1,0 (1,0; 1,0) | 9,0 (9,0; 9,0) |
| Min, Max | 1,0; 1,0 | 9,0; 9,0 |
| Woche 96 | | |
| N ^c | 2 | 0 |
| Mittelwert (SD) | 1,0 (0,0) | - (-) |
| Median (Q1; Q3) | 1,0 (1,0; 1,0) | - (-; -) |
| Min, Max | 1,0; 1,0 | -; - |
| a: Database cutoff date: 26. Juli 2024 | | |
| b: Anzahl der Patient:innen: Full-Analysis-Set Population; Patient:innen mit WHO FK IV zu Baseline | | |
| c: Anzahl der Patient:innen ohne fehlende Erhebung zur jeweiligen Visite | | |
| 6MWD: 6-Minuten Gehstrecke; CR10: 10 Punkte Category Ratio scale; FK: Funktionsklasse; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung; WHO: World Health Organization | | |

Tabelle 4G-8: Auswertung über den Studienverlauf – EQ-5D VAS

| EQ-5D VAS | Studie: ZENITH (MK-7962-006) ^a | |
|-----------------|---|-------------------------------|
| | Sotatercept N ^b =20 | Placebo N ^b =24 |
| Baseline | | |
| N ^c | 18 | 22 |
| Mean (SD) | 49.3 (23.0) | 55.9 (23.3) |
| Median (Q1; Q3) | 51.0 (36.0; 67.0) | 61.0 (42.0; 69.0) |
| Min; Max | 11.0; 97.0 | 4.0; 91.0 |
| Week 12 | | |
| N ^c | 14 | 16 |
| Mean (SD) | 68.9 (21.0) | 63.6 (17.8) |
| Median (Q1; Q3) | 75.0 (50.0; 82.0) | 64.0 (52.5; 74.5) |
| Min; Max | 29.0; 98.0 | 29.0; 94.0 |

| EQ-5D VAS | Study: ZENITH (MK-7962-006) ^a | |
|--|--|-------------------------------|
| | Sotatercept N ^b =20 | Placebo N ^b =24 |
| Week 24 | | |
| N ^c | 13 | 12 |
| Mean (SD) | 68.8 (21.6) | 73.8 (17.4) |
| Median (Q1; Q3) | 70.0 (65.0; 81.0) | 80.0 (63.0; 85.0) |
| Min; Max | 28.0; 99.0 | 36.0; 95.0 |
| Week 36 | | |
| N ^c | 12 | 6 |
| Mean (SD) | 60.6 (25.4) | 64.0 (19.5) |
| Median (Q1; Q3) | 67.5 (34.0; 79.5) | 53.0 (50.0; 86.0) |
| Min; Max | 19.0; 98.0 | 50.0; 92.0 |
| Week 48 | | |
| N ^c | 7 | 4 |
| Mean (SD) | 68.4 (21.9) | 69.5 (24.4) |
| Median (Q1; Q3) | 71.0 (45.0; 88.0) | 69.0 (48.5; 90.5) |
| Min; Max | 33.0; 92.0 | 47.0; 93.0 |
| Week 60 | | |
| N ^c | 5 | 1 |
| Mean (SD) | 81.0 (8.2) | 94.0 (-) |
| Median (Q1; Q3) | 75.0 (75.0; 89.0) | 94.0 (94.0; 94.0) |
| Min; Max | 75.0; 91.0 | 94.0; 94.0 |
| Week 72 | | |
| N ^c | 4 | 0 |
| Mean (SD) | 76.3 (26.8) | - (-) |
| Median (Q1; Q3) | 89.5 (62.5; 90.0) | - (-; -) |
| Min; Max | 36.0; 90.0 | -; - |
| Week 84 | | |
| N ^c | 1 | 1 |
| Mean (SD) | 40.0 (-) | 52.0 (-) |
| Median (Q1; Q3) | 40.0 (40.0; 40.0) | 52.0 (52.0; 52.0) |
| Min; Max | 40.0; 40.0 | 52.0; 52.0 |
| Week 96 | | |
| N ^c | 1 | 0 |
| Mean (SD) | 91.0 (-) | - (-) |
| Median (Q1; Q3) | 91.0 (91.0; 91.0) | - (-; -) |
| Min; Max | 91.0; 91.0 | -; - |
| a: Database Cutoff Date: 26JUL2024 | | |
| b: Number of participants: full analysis set population, participants with WHO FC IV at baseline | | |
| c: Number of participants with non-missing assessment at the given visit | | |
| EQ-5D: European Quality of Life 5 Dimensions; FC: Functional Class; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation; VAS: Visual Analog Scale; WHO: World Health Organization | | |

Anhang 4-G5: Unerwünschte Ereignisse Gesamtraten ohne erkrankungsbezogene Ereignisse

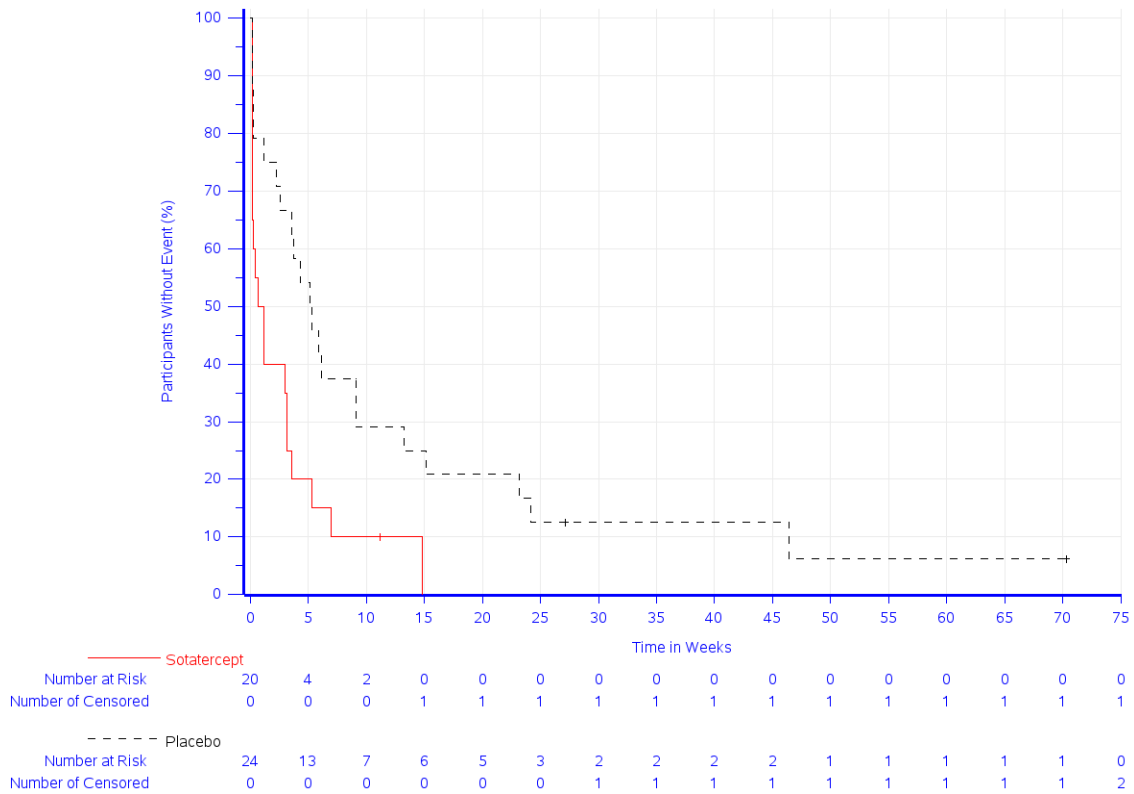
Für die Unerwünschten Ereignisse Gesamtraten ohne erkrankungsbezogene Ereignisse wurden die PTs Pulmonale Hypertonie und Pulmonale arterielle Hypertonie ausgeschlossen.

Alle Ergebnisse beziehen sich auf den Database Cutoff Date vom 26. Juli 2024.

Tabelle 4G-9: Unerwünschte Ereignisse Gesamtraten ohne erkrankungsbezogene Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

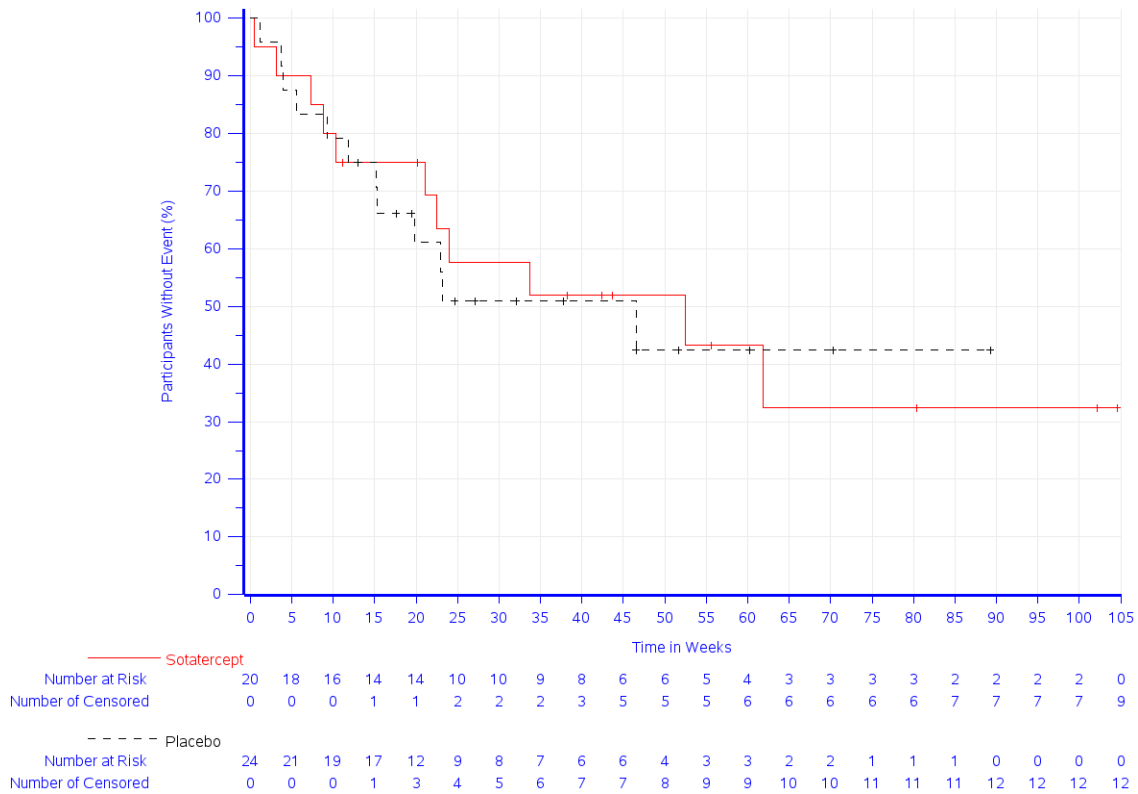
| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|---|----------------|-------------------------|-----------------------------------|----------------|-------------------------|-----------------------------------|-------------------------|------------------------|
| | N ^b | Participants with Event | Median Time ^c in weeks | N ^b | Participants with Event | Median Time ^c in weeks | Hazard Ratio | p-Value ^{d,e} |
| | | n (%) | [95 %-CI] | | n (%) | [95 %-CI] | | |
| Adverse Events excluding disease related AEs | 20 | 19 (95.0) | 0.93 [0.14; 3.14] | 24 | 22 (91.7) | 5.21 [2.29; 9.14] | 2.39 [1.23; 4.63] | 0.010 |
| Serious Adverse Events excluding disease related AEs | 20 | 11 (55.0) | 52.43 [10.29; -] | 24 | 12 (50.0) | 46.57 [15.14; -] | 0.94 [0.41; 2.15] | 0.887 |
| Severe Adverse Events excluding disease related AEs | 20 | 6 (30.0) | Not reached [35.29; -] | 24 | 10 (41.7) | Not reached [15.14; -] | 0.55 [0.20; 1.52] | 0.248 |
| Adverse Events Leading to Treatment Discontinuation excluding disease related AEs | 20 | 0 (0.0) | Not reached [-; -] | 24 | 1 (4.2) | Not reached [-; -] | n.a. [n.a.; n.a.] | 0.374 |

a: Database Cutoff Date: 26JUL2024
b: Number of participants: all participants as treated population excluding those who experienced only PAH related adverse events, participants with WHO FC IV at baseline
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
AE: Adverse Event; CI: Confidence Intervals; FC: Functional Class; n.a.: not applicable (when estimation not possible); WHO: World Health Organization



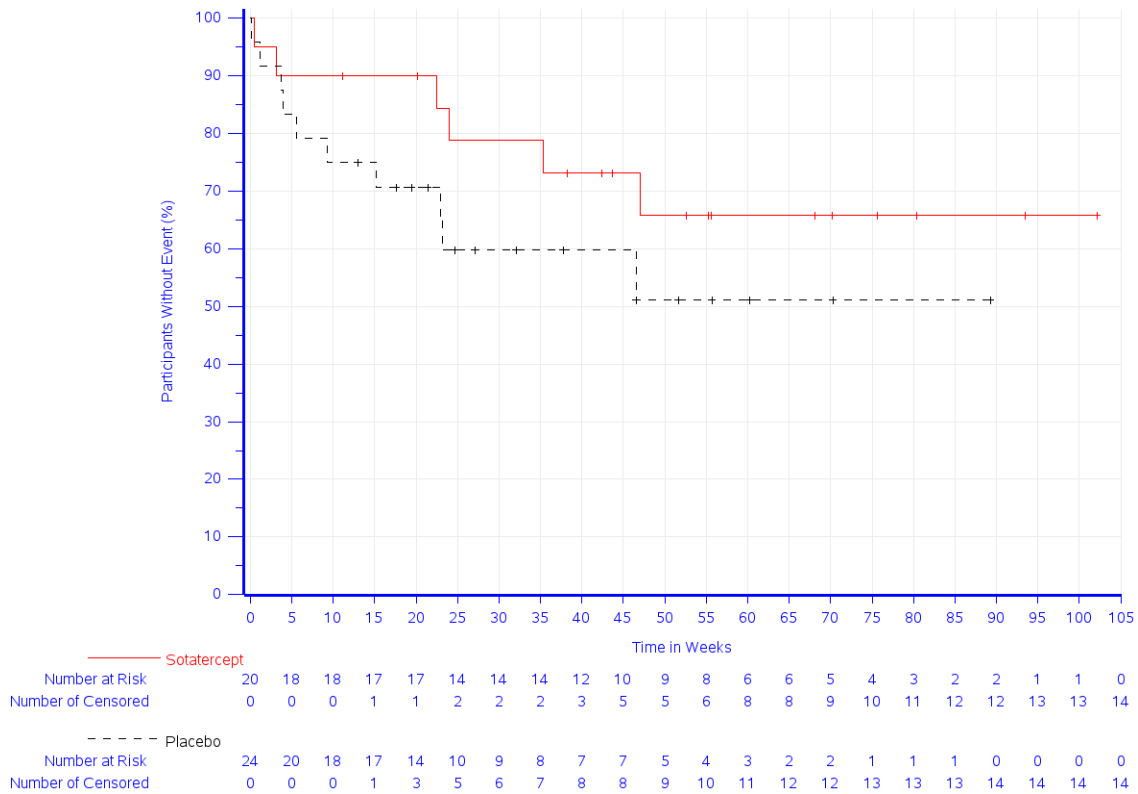
Study: ZENITH (MK-7962-006) (Database Cutoff Date: 26JUL2024)
 Adverse Events excluding PAH related AEs

Abbildung 4G-2: Zeit bis zum ersten Eintreten eines Ereignisses: Kaplan-Meier-Kurve für den Endpunkt Unerwünschte Ereignisse gesamt ohne erkrankungsbezogene Ereignisse der Studie ZENITH



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 26JUL2024)
 Serious Adverse Events excluding PAH related AEs

Abbildung 4G-3: Zeit bis zum ersten Eintreten eines Ereignisses: Kaplan-Meier-Kurve für den Endpunkt Schwerwiegende unerwünschte Ereignisse ohne erkrankungsbezogene Ereignisse der Studie ZENITH



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 26JUL2024)
Severe Adverse Events excluding PAH related AEs

Abbildung 4G-4: Zeit bis zum ersten Eintreten eines Ereignisses: Kaplan-Meier-Kurve für den Endpunkt Schwere unerwünschte Ereignisse ohne erkrankungsbezogene Ereignisse der Studie ZENITH



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 26JUL2024)
 Severe Adverse Events excluding PAH related AEs

Abbildung 4G-5: Zeit bis zum ersten Eintreten eines Ereignisses: Kaplan-Meier-Kurve für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse ohne erkrankungsbezogene Ereignisse der Studie ZENITH

Anhang 4-G6: Kaplan-Meier-Kurven der Subgruppen mit signifikantem Interaktionstest (p < 0,05)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Kaplan-Meier-Kurven der Subgruppenanalysen, für die ein signifikanter Interaktionstest (p < 0,05) vorliegt, dargestellt.

Alle Ergebnisse beziehen sich auf den Database Cutoff Date vom 26. Juli 2024

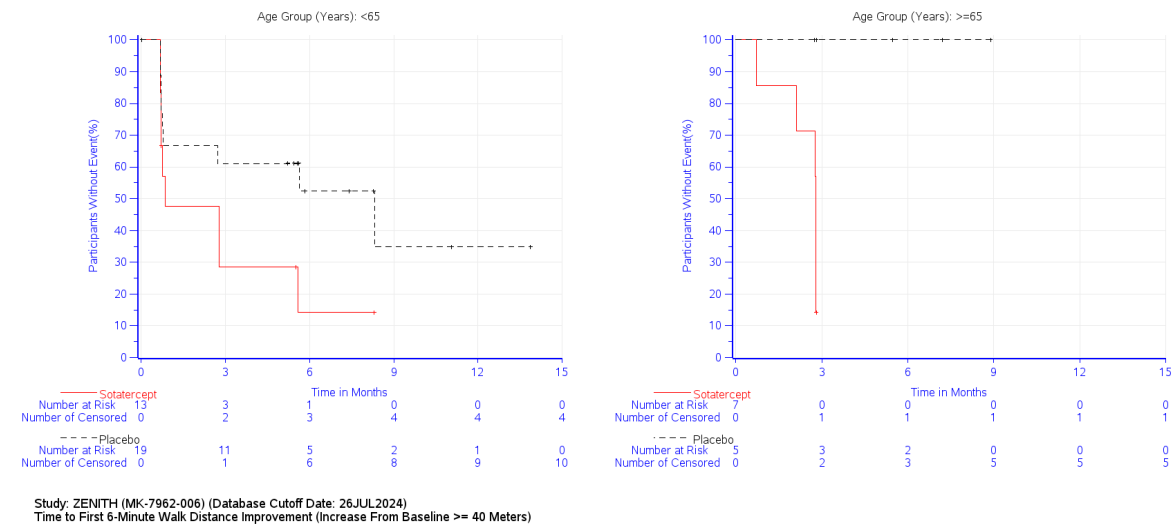


Abbildung 4G-6: Kaplan-Meier-Kurven für die Subgruppenanalyse nach Alter für den Endpunkt Zeit bis zur Verbesserung der 6MWD der Studie ZENITH

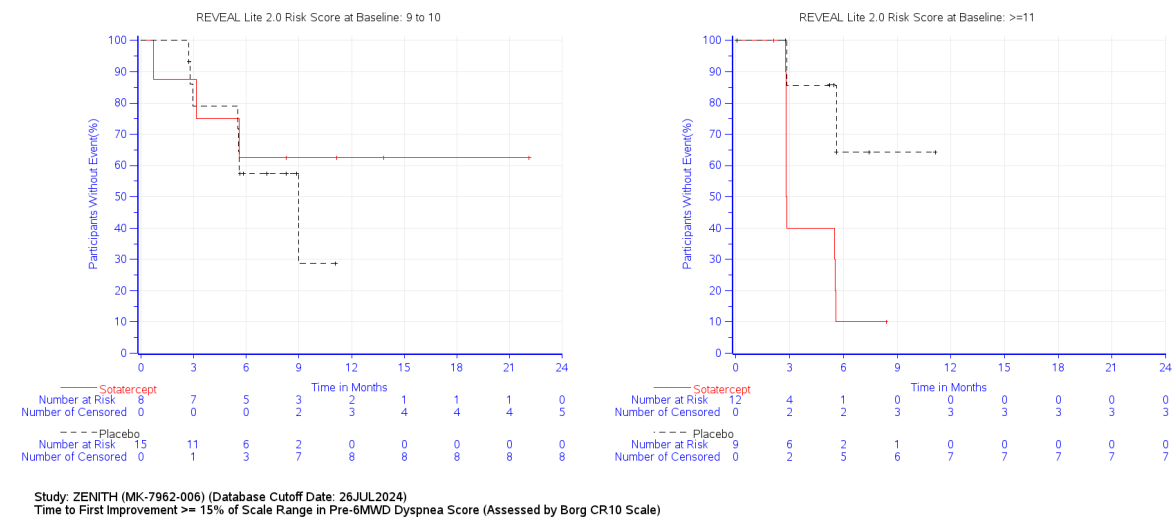


Abbildung 4G-7: Kaplan-Meier-Kurven für die Subgruppenanalyse nach REVEAL Lite 2.0 Risiko Score für den Endpunkt Zeit bis zur Verbesserung der Dyspnoe gemäß Borg Skala der Studie ZENITH

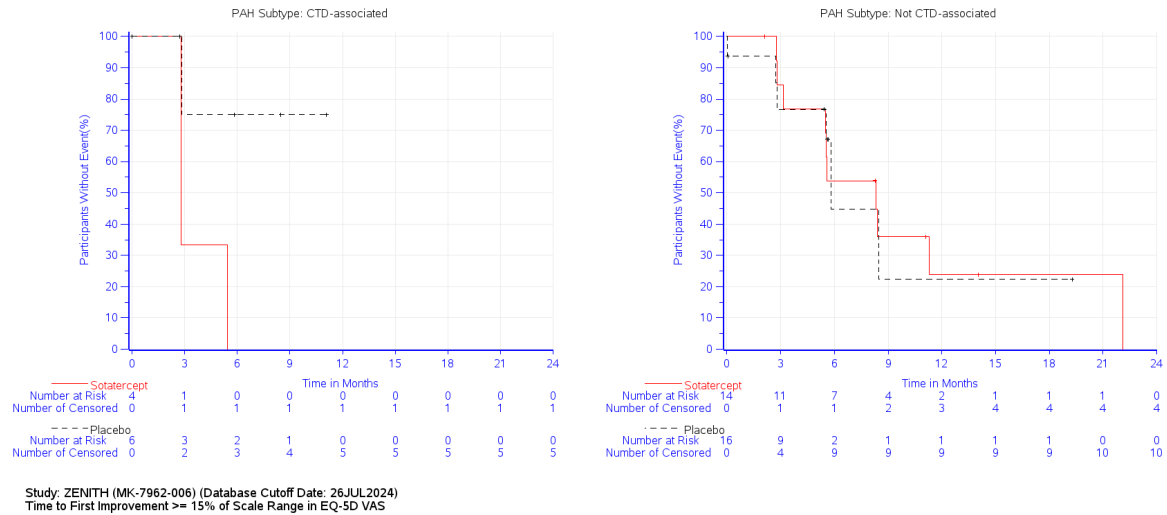


Abbildung 4G-8: Kaplan-Meier-Kurven für die Subgruppenanalyse nach PAH Subtyp für den Endpunkt Zeit bis zur Verbesserung der EQ-5D VAS der Studie ZENITH

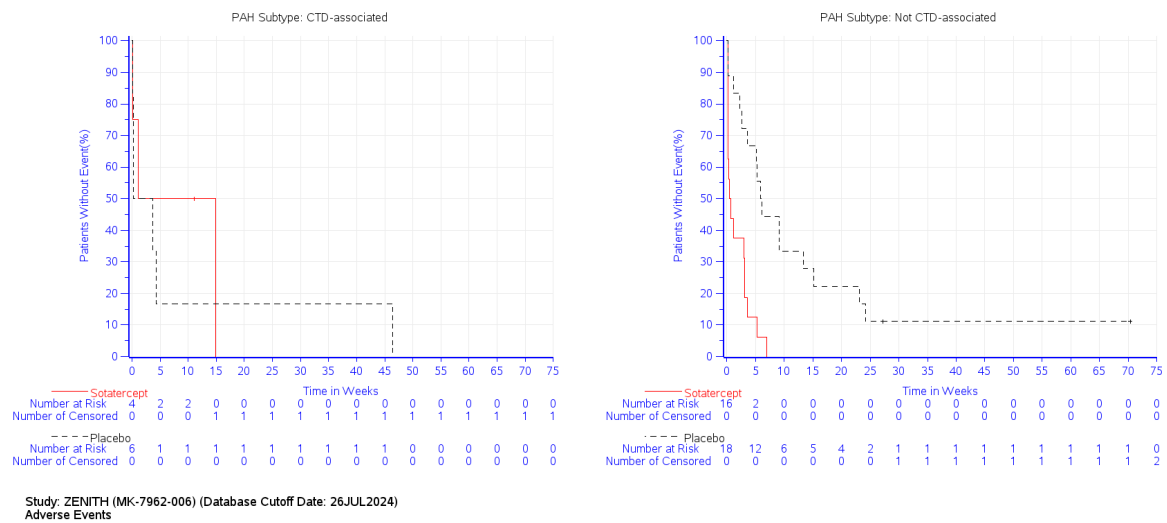


Abbildung 4G-9: Kaplan-Meier-Kurven für die Subgruppenanalyse nach PAH Subtyp für den Endpunkt Unerwünschte Ereignisse gesamt der Studie ZENITH

Anhang 4-G7: Ergebnisse der Subgruppen mit nicht signifikantem Interaktionstest ($p \geq 0,05$)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Ergebnisse der Subgruppenanalysen, für die ein nicht signifikanter Interaktionstest ($p \geq 0,05$) vorliegt, dargestellt.

Alle Ergebnisse beziehen sich auf den Database Cutoff Date vom 26. Juli 2024.

Mortalität

Gesamtüberleben

Tabelle 4G-10: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|---|---|--|---|---|--|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Overall Survival (Include All Deaths) | | | | | | | | | |
| Sex | | | | | | | | | |
| Male | 5 1 (20.0) | n.c. | | 3 0 (0.0) | n.c. | | n.c. | n.c. | n.c. |
| Female | 15 1 (6.7) | n.c. | | 21 5 (23.8) | n.c. | | n.c. | n.c. | |
| Age Group (Years) | | | | | | | | | |
| <65 | 13 1 (7.7) | n.c. | | 19 5 (26.3) | n.c. | | n.c. | n.c. | n.c. |
| ≥65 | 7 1 (14.3) | n.c. | | 5 0 (0.0) | n.c. | | n.c. | n.c. | |
| Region ^g | | | | | | | | | |
| WHO Stratum A | 19 2 (10.5) | n.c. | | 22 4 (18.2) | n.c. | | n.c. | n.c. | n.c. |
| Rest of the World | 1 0 (0.0) | n.c. | | 2 1 (50.0) | n.c. | | n.c. | n.c. | |
| REVEAL Lite 2.0 Risk Score at Baseline ^h | | | | | | | | | |
| 9 to 10 | 8 1 (12.5) | n.c. | | 15 1 (6.7) | n.c. | | n.c. | n.c. | n.c. |
| ≥11 | 12 1 (8.3) | n.c. | | 9 4 (44.4) | n.c. | | n.c. | n.c. | |
| PAH Subtype | | | | | | | | | |
| CTD-associated | 4 0 (0.0) | n.c. | | 6 2 (33.3) | n.c. | | n.c. | n.c. | n.c. |
| Not CTD-associated | 16 2 (12.5) | n.c. | | 18 3 (16.7) | n.c. | | n.c. | n.c. | |
| a: Database Cutoff Date: 26JUL2024 | | | | | | | | | |
| b: Number of participants: full analysis set, participants with WHO FC IV at baseline | | | | | | | | | |
| c: From product-limit (Kaplan-Meier) method for censored data | | | | | | | | | |
| d: Based on Cox regression model with treatment as a covariate using Wald confidence interval. Ties are handled using Efron's method | | | | | | | | | |
| e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) | | | | | | | | | |
| f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) | | | | | | | | | |
| g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United | | | | | | | | | |

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | Placebo | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|---|---|---|---|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| States | | | | | | | |
| h: For participants with REVEAL Lite 2.0 risk score < 9 at screening, they are grouped under category 9 to 10 for the analyses | | | | | | | |
| This table includes all-cause deaths up to the data cutoff date, including deaths after lung transplantation or after enrollment in SOTERIA | | | | | | | |
| CI: Confidence Interval; CTD: Connective Tissue Disease; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; WHO: World Health Organization | | | | | | | |

Morbidität

Tabelle 4G-11: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Zeit bis Tod jeglicher Ursache, Lungentransplantation oder Hospitalisierung von ≥ 24 Stunden aufgrund von PAH-Verschlechterung aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | Placebo | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|---|---|---|---|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| All-cause Death, Lung Transplantation, or PAH Worsening-related Hospitalization of ≥ 24 Hours | | | | | | | |
| Sex | | | | | | | |
| Male | 5 1 (20.0) | n.c. | 3 3 (100.0) | n.c. | n.c. | n.c. | n.c. |
| Female | 15 3 (20.0) | n.c. | 21 10 (47.6) | n.c. | n.c. | n.c. | n.c. |
| Age Group (Years) | | | | | | | |
| <65 | 13 2 (15.4) | Not reached [-; -] | 19 11 (57.9) | 6.3 [3.5; -] | 0.22 [0.05; 1.00] | 0.049 | 0.567 |
| ≥ 65 | 7 2 (28.6) | Not reached [0.7; -] | 5 2 (40.0) | Not reached [2.8; -] | 0.48 [0.06; 3.73] | 0.483 | |
| Region ^g | | | | | | | |
| WHO Stratum A | 19 4 (21.1) | n.c. | 22 12 (54.5) | n.c. | n.c. | n.c. | n.c. |
| Rest of the World | 1 0 (0.0) | n.c. | 2 1 (50.0) | n.c. | n.c. | n.c. | n.c. |
| REVEAL Lite 2.0 Risk Score at Baseline ^h | | | | | | | |
| 9 to 10 | 8 2 (25.0) | n.c. | 15 6 (40.0) | n.c. | n.c. | n.c. | n.c. |
| ≥ 11 | 12 2 (16.7) | n.c. | 9 7 (77.8) | n.c. | n.c. | n.c. | n.c. |
| PAH Subtype | | | | | | | |
| CTD-associated | 4 1 (25.0) | Not reached [2.6; -] | 6 4 (66.7) | 9.3 [3.3; -] | 0.36 [0.04; 3.25] | 0.362 | 0.855 |
| Not CTD-associated | 16 3 (18.8) | Not reached [12.1; -] | 18 9 (50.0) | 6.3 [5.3; -] | 0.28 [0.07; 1.05] | 0.060 | |
| a: Database Cutoff Date: 26JUL2024 | | | | | | | |
| b: Number of participants: full analysis set, participants with WHO FC IV at baseline | | | | | | | |
| c: From product-limit (Kaplan-Meier) method for censored data | | | | | | | |
| d: Based on Cox regression model with treatment as a covariate using Wald confidence interval. Ties are handled using Efron's method | | | | | | | |
| e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) | | | | | | | |

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|-------------------------|--|----------------|-------------------------|--|----------------|-------------------------------------|------------------------|---|
| | Participants with Event | Median Time ^e in Months [95 %-CI] | N ^b | Participants with Event | Median Time ^e in Months [95 %-CI] | N ^b | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| All-cause Death, Lung Transplantation, or PAH Worsening-related Hospitalization of ≥ 24 Hours | | | | | | | | | |
| f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) | | | | | | | | | |
| g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States | | | | | | | | | |
| h: For participants with REVEAL Lite 2.0 risk score < 9 at screening, they are grouped under category 9 to 10 for the analyses | | | | | | | | | |
| This table includes the first event of adjudication-confirmed PAH worsening-related hospitalization ≥ 24 hours, lung transplantation, or all-cause death prior to the cutoff date. All pre-cutoff deaths are included, regardless of adjudication and regardless of whether they occurred during or post ZENITH | | | | | | | | | |
| CI: Confidence Interval; CTD: Connective Tissue Disease; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; WHO: World Health Organization | | | | | | | | | |

Tabelle 4G-12: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Zeit bis zur Verbesserung der 6MWD aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|-------------------------|--|----------------------|-------------------------|--|----------------------|-------------------------------------|------------------------|---|
| | Participants with Event | Median Time ^e in Months [95 %-CI] | N ^b | Participants with Event | Median Time ^e in Months [95 %-CI] | N ^b | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Time to First 6-Minute Walk Distance Improvement (Increase From Baseline ≥ 40 Meters) | | | | | | | | | |
| Sex | | | | | | | | | |
| Male | 5 | 5 (100.0) | n.c. | 3 | 1 (33.3) | n.c. | n.c. | n.c. | n.c. |
| Female | 15 | 10 (66.7) | n.c. | 21 | 8 (38.1) | n.c. | n.c. | n.c. | n.c. |
| Region ^g | | | | | | | | | |
| WHO Stratum A | 19 | 14 (73.7) | n.c. | 22 | 8 (36.4) | n.c. | n.c. | n.c. | n.c. |
| Rest of the World | 1 | 1 (100.0) | n.c. | 2 | 1 (50.0) | n.c. | n.c. | n.c. | n.c. |
| REVEAL Lite 2.0 Risk Score at Baseline ^h | | | | | | | | | |
| 9 to 10 | 8 | 6 (75.0) | 2.8 [0.7; 5.6] | 15 | 5 (33.3) | Not reached [0.8; -] | 3.33 [0.99; 11.28] | 0.053 | 0.718 |
| ≥ 11 | 12 | 9 (75.0) | 2.1 [0.7; 2.8] | 9 | 4 (44.4) | Not reached [0.7; -] | 2.04 [0.63; 6.64] | 0.237 | |
| PAH Subtype | | | | | | | | | |
| CTD-associated | 4 | 1 (25.0) | Not reached [2.8; -] | 6 | 1 (16.7) | Not reached [0.7; -] | 1.58 [0.10; 25.30] | 0.746 | 0.822 |
| Not CTD-associated | 16 | 14 (87.5) | 2.1 [0.7; 2.8] | 18 | 8 (44.4) | 8.3 [0.8; -] | 3.01 [1.24; 7.31] | 0.015 | |
| a: Database Cutoff Date: 26JUL2024 | | | | | | | | | |
| b: Number of participants: full analysis set, participants with WHO FC IV at baseline | | | | | | | | | |
| c: From product-limit (Kaplan-Meier) method for censored data | | | | | | | | | |
| d: Based on Cox regression model with treatment as a covariate using Wald confidence interval. Ties are handled using Efron's method | | | | | | | | | |
| e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) | | | | | | | | | |
| f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) | | | | | | | | | |

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|---|---|--|---|---|--|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Time to First 6-Minute Walk Distance Improvement (Increase From Baseline \geq 40 Meters) | | | | | | | | | |

g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States

h: For participants with REVEAL Lite 2.0 risk score < 9 at screening, they are grouped under category 9 to 10 for the analyses

CI: Confidence Interval; CTD: Connective Tissue Disease; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; WHO: World Health Organization

Tabelle 4G-13: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Zeit bis zur Verbesserung der Dyspnoe gemäß Borg-Skala aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|---|---|-----------------|---|---|-------------------------|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Time to First Improvement \geq 15% of Scale Range in Pre-6MWD Dyspnea Score (Assessed by Borg CR10 Scale) | | | | | | | | | |
| Sex | | | | | | | | | |
| Male | 5 | 5 (100.0) | n.c. | 3 | 1 (33.3) | n.c. | n.c. | n.c. | n.c. |
| Female | 15 | 7 (46.7) | n.c. | 21 | 8 (38.1) | n.c. | n.c. | n.c. | |
| Age Group (Years) | | | | | | | | | |
| <65 | 13 | 7 (53.8) | 4.3 [2.8; -] | 19 | 8 (42.1) | 9.0 [5.5; -] | 1.66 [0.60; 4.60] | 0.327 | 0.571 |
| \geq 65 | 7 | 5 (71.4) | 5.6 [2.8; -] | 5 | 1 (20.0) | Not reached [2.8; -] | 3.36 [0.39; 28.99] | 0.270 | |
| Region ^g | | | | | | | | | |
| WHO Stratum A | 19 | 12 (63.2) | n.c. | 22 | 9 (40.9) | n.c. | n.c. | n.c. | n.c. |
| Rest of the World | 1 | 0 (0.0) | n.c. | 2 | 0 (0.0) | n.c. | n.c. | n.c. | |
| PAH Subtype | | | | | | | | | |
| CTD-associated | 4 | 3 (75.0) | 4.2 [0.7; -] | 6 | 3 (50.0) | 5.6 [2.7; -] | 2.03 [0.41; 10.16] | 0.389 | 0.918 |
| Not CTD-associated | 16 | 9 (56.3) | 5.6 [2.8; -] | 18 | 6 (33.3) | 9.0 [3.0; -] | 2.03 [0.72; 5.74] | 0.182 | |

a: Database Cutoff Date: 26JUL2024

b: Number of participants: full analysis set population, participants with WHO FC IV at baseline and without missing assessment at baseline and have at least one post-baseline assessment

c: From product-limit (Kaplan-Meier) method for censored data

d: Based on Cox regression model with treatment as a covariate using Wald confidence interval. Ties are handled using Efron's method

e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba,

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | Placebo | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|---|---|---|---|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States | | | | | | | |
| 6MWD: Six-Minute Walk Distance; CI: Confidence Interval; CR10: 10 Point Category Ratio scale; CTD: Connective Tissue Disease; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; WHO: World Health Organization | | | | | | | |

Tabelle 4G-14: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für für den Endpunkt Zeit bis zur Verbesserung der EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | Placebo | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|---|---|---|---|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Sex | | | | | | | |
| Male | 4 3 (75.0) | n.c. | 2 1 (50.0) | n.c. | n.c. | n.c. | n.c. |
| Female | 14 10 (71.4) | n.c. | 20 6 (30.0) | n.c. | n.c. | n.c. | n.c. |
| Age Group (Years) | | | | | | | |
| <65 | 12 9 (75.0) | 5.6 [2.8; -] | 18 5 (27.8) | Not reached [2.8; -] | 2.13 [0.69; 6.55] | 0.186 | 0.307 |
| ≥65 | 6 4 (66.7) | 5.6 [2.8; -] | 4 2 (50.0) | 5.8 [2.8; -] | 0.79 [0.13; 4.78] | 0.798 | |
| Region ^g | | | | | | | |
| WHO Stratum A | 17 12 (70.6) | n.c. | 20 5 (25.0) | n.c. | n.c. | n.c. | n.c. |
| Rest of the World | 1 1 (100.0) | n.c. | 2 2 (100.0) | n.c. | n.c. | n.c. | n.c. |
| REVEAL Lite 2.0 Risk Score at Baseline ^h | | | | | | | |
| 9 to 10 | 8 6 (75.0) | 5.6 [2.8; -] | 14 4 (28.6) | Not reached [2.8; -] | 3.95 [0.97; 16.00] | 0.055 | 0.068 |
| ≥11 | 10 7 (70.0) | 5.6 [2.8; -] | 8 3 (37.5) | 5.6 [0.0; -] | 0.74 [0.17; 3.14] | 0.682 | |
| a: Database Cutoff Date: 26JUL2024 | | | | | | | |
| b: Number of participants: full analysis set population, participants with WHO FC IV at baseline and without missing assessment at baseline and have at least one post-baseline assessment | | | | | | | |
| c: From product-limit (Kaplan-Meier) method for censored data | | | | | | | |
| d: Based on Cox regression model with treatment as a covariate using Wald confidence interval. Ties are handled using Efron's method | | | | | | | |
| e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) | | | | | | | |
| f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) | | | | | | | |
| g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States | | | | | | | |

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | Placebo | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|---|---|---|---|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Participants with Event N ^b n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Time to First Improvement \geq 15% of Scale Range in EQ-5D VAS | | | | | | | |
| h: For participants with REVEAL Lite 2.0 risk score < 9 at screening, they are grouped under category 9 to 10 for the analyses CI: Confidence Interval; EQ-5D VAS: European Quality of Life 5 Dimensions Visual Analogue Scale; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; WHO: World Health Organization | | | | | | | |

Nebenwirkungen***Unerwünschte Ereignisse***

Tabelle 4G-15: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|---|
| | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Adverse Events | | | | | | | | | |
| Sex | | | | | | | | | |
| Male | 5 | 5 (100.0) | n.c. | 3 | 3 (100.0) | n.c. | n.c. | n.c. | n.c. |
| Female | 15 | 14 (93.3) | n.c. | 21 | 19 (90.5) | n.c. | n.c. | n.c. | |
| Age Group (Years) | | | | | | | | | |
| <65 | 13 | 12 (92.3) | 0.4 [0.1; 1.1] | 19 | 17 (89.5) | 4.3 [0.3; 9.1] | 2.69 [1.20; 6.06] | 0.017 | 0.403 |
| ≥65 | 7 | 7 (100.0) | 3.1 [0.1; 7.0] | 5 | 5 (100.0) | 9.1 [2.6; -] | 2.23 [0.64; 7.84] | 0.210 | |
| Region ^e | | | | | | | | | |
| WHO Stratum A | 19 | 18 (94.7) | n.c. | 22 | 20 (90.9) | n.c. | n.c. | n.c. | n.c. |
| Rest of the World | 1 | 1 (100.0) | n.c. | 2 | 2 (100.0) | n.c. | n.c. | n.c. | |
| REVEAL Lite 2.0 Risk Score at Baseline | | | | | | | | | |
| 9 to 10 | 8 | 7 (87.5) | 1.6 [0.1; 3.6] | 15 | 13 (86.7) | 9.1 [0.3; 23.1] | 2.62 [0.94; 7.28] | 0.065 | 0.280 |
| ≥11 | 12 | 12 (100.0) | 0.9 [0.1; 5.3] | 9 | 9 (100.0) | 3.7 [0.1; 6.1] | 1.68 [0.68; 4.16] | 0.260 | |
| <p>a: Database Cutoff Date: 26JUL2024</p> <p>b: Number of participants: all participants as treated population, participants with WHO FC IV at baseline</p> <p>c: From product-limit (Kaplan-Meier) method for censored data</p> <p>d: Based on Cox regression model with treatment as a covariate using Wald confidence interval</p> <p>e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)</p> <p>f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)</p> | | | | | | | | | |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|---|
| | N ^b | Participants with Event n (%) | Median Time ^e in Weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^e in Weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Adverse Events | | | | | | | | | |
| g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States | | | | | | | | | |
| CI: Confidence Interval; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; WHO: World Health Organization | | | | | | | | | |

Tabelle 4G-16: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|---|
| | N ^b | Participants with Event n (%) | Median Time ^e in Weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^e in Weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Serious Adverse Events | | | | | | | | | |
| Sex | | | | | | | | | |
| Male | 5 | 3 (60.0) | n.c. | 3 | 3 (100.0) | n.c. | n.c. | n.c. | n.c. |
| Female | 15 | 8 (53.3) | n.c. | 21 | 13 (61.9) | n.c. | n.c. | n.c. | |
| Age Group (Years) | | | | | | | | | |
| <65 | 13 | 6 (46.2) | 52.4 [10.3; -] | 19 | 12 (63.2) | 23.0 [5.6; -] | 0.67 [0.25; 1.80] | 0.432 | 0.863 |
| ≥65 | 7 | 5 (71.4) | 33.7 [3.1; -] | 5 | 4 (80.0) | 23.1 [12.1; -] | 0.44 [0.09; 2.02] | 0.289 | |
| Region ^g | | | | | | | | | |
| WHO Stratum A | 19 | 11 (57.9) | n.c. | 22 | 15 (68.2) | n.c. | n.c. | n.c. | n.c. |
| Rest of the World | 1 | 0 (0.0) | n.c. | 2 | 1 (50.0) | n.c. | n.c. | n.c. | |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|---|
| | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| REVEAL Lite 2.0 Risk Score at Baseline | | | | | | | | | |
| 9 to 10 | 8 | 2 (25.0) | Not reached [10.3; -] | 15 | 8 (53.3) | 46.6 [11.9; -] | 0.44 [0.09; 2.10] | 0.305 | 0.940 |
| ≥11 | 12 | 9 (75.0) | 23.2 [3.1; 61.9] | 9 | 8 (88.9) | 12.3 [1.1; 23.6] | 0.48 [0.17; 1.34] | 0.160 | |
| PAH Subtype | | | | | | | | | |
| CTD-associated | 4 | 2 (50.0) | 22.4 [21.1; -] | 6 | 5 (83.3) | 29.2 [3.7; -] | 0.87 [0.14; 5.21] | 0.876 | 0.929 |
| Not CTD-associated | 16 | 9 (56.3) | 52.4 [8.9; -] | 18 | 11 (61.1) | 23.0 [12.1; -] | 0.74 [0.30; 1.82] | 0.512 | |
| a: Database Cutoff Date: 26JUL2024 b: Number of participants: all participants as treated population, participants with WHO FC IV at baseline c: From product-limit (Kaplan-Meier) method for censored data d: Based on Cox regression model with treatment as a covariate using Wald confidence interval e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States CI: Confidence Interval; CTD: Connective Tissue Disease; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; WHO: World Health Organization | | | | | | | | | |

Tabelle 4G-17: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|--|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|---|
| | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Sex | | | | | | | | | |
| Male | 5 | 1 | n.c. | 3 | 3 | n.c. | n.c. | n.c. | n.c. |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|---|
| | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Severe Adverse Events | | (20.0) | | | (100.0) | | | | |
| Female | 15 | 5 (33.3) | n.c. | 21 | 10 (47.6) | n.c. | n.c. | n.c. | |
| Age Group (Years) | | | | | | | | | |
| <65 | 13 | 3 (23.1) | Not reached [22.4; -] | 19 | 11 (57.9) | 23.0 [4.1; -] | 0.33 [0.09; 1.17] | 0.086 | 0.384 |
| ≥65 | 7 | 3 (42.9) | Not reached [3.1; -] | 5 | 2 (40.0) | Not reached [12.1; -] | 0.63 [0.10; 4.09] | 0.625 | |
| Region ^g | | | | | | | | | |
| WHO Stratum A | 19 | 6 (31.6) | n.c. | 22 | 12 (54.5) | n.c. | n.c. | n.c. | n.c. |
| Rest of the World | 1 | 0 (0.0) | n.c. | 2 | 1 (50.0) | n.c. | n.c. | n.c. | |
| REVEAL Lite 2.0 Risk Score at Baseline | | | | | | | | | |
| 9 to 10 | 8 | 2 (25.0) | Not reached [35.3; -] | 15 | 6 (40.0) | Not reached [5.6; -] | 0.54 [0.11; 2.67] | 0.447 | 0.452 |
| ≥11 | 12 | 4 (33.3) | Not reached [3.1; -] | 9 | 7 (77.8) | 12.3 [1.1; -] | 0.29 [0.08; 1.01] | 0.052 | |
| PAH Subtype | | | | | | | | | |
| CTD-associated | 4 | 1 (25.0) | Not reached [22.4; -] | 6 | 4 (66.7) | 26.1 [0.1; -] | 0.34 [0.04; 3.08] | 0.335 | 0.724 |
| Not CTD-associated | 16 | 5 (31.3) | Not reached [35.3; -] | 18 | 9 (50.0) | 23.1 [12.1; -] | 0.47 [0.15; 1.42] | 0.179 | |
| a: Database Cutoff Date: 26JUL2024 b: Number of participants: all participants as treated population, participants with WHO FC IV at baseline c: From product-limit (Kaplan-Meier) method for censored data d: Based on Cox regression model with treatment as a covariate using Wald confidence interval e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) g: Countries included in the WHO Stratum A category are Andorra, Australia, Austria, Belgium, Brunei Darussalam, Canada, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Netherlands, New Zealand, Norway, Portugal, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Kingdom and United States CI: Confidence Interval; CTD: Connective Tissue Disease; FC: Functional Class; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the | | | | | | | | | |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | Placebo | | Sotatercept vs. Placebo | | p-Value for Interaction Test ^f |
|---|---|--|---|--|--|------------------------|---|
| | Participants with Event N ^b n (%) | Median Time ^c in Weeks [95 %-CI] | Participants with Event N ^b n (%) | Median Time ^c in Weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} | |
| Severe Adverse Events | | | | | | | |
| subgroup categories necessary); PAH: Pulmonary Arterial Hypertension; REVEAL: Registry to Evaluate Early and Long-Term PAH Disease Management; WHO: World Health Organization | | | | | | | |

Therapieabbruch wegen unerwünschter Ereignisse

Es trat lediglich ein Therapieabbruch unter Placebo auf. Details siehe Modul 4.

Anhang 4-G8: Ergebnisse des Datenschnitts zum Studienende

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1 die Ergebnisse der Studie ZENITH des finalen Database Cut-off vom 18.02.2025 dargestellt. Dies ist kein relevanter Datenschnitt für das Dossier, da die formalen Anforderungen für eine Darstellung im Dossier nicht erfüllt sind.

Aufgrund der vorzeitigen Beendigung der Studie durch die sehr guten Ergebnisse der Interimanalyse wurde die formal geplante finale Analyse nicht durchgeführt. Nachdem alle Patient:innen in die LTFU Studie SOTERIA überführt wurden oder die Studie verlassen hatten, wurde die Studie ZENITH beendet. Für diesen Datenschnitt wurden bei der FDA Sicherheitsdaten eingereicht, er wurde jedoch nicht explizit angefordert.

Da die Ergebnisse für die vorliegende Nutzenbewertung nicht zur Ableitung des Zusatznutzens herangezogen werden, werden ausschließlich die Hauptanalysen dargestellt.

Da dieser Analysezeitpunkt nicht präspezifiziert war, wurden keine Sensitivitätsanalysen durchgeführt. Damit liegt für das Gesamtüberleben lediglich die primäre Auswertung der Studie (Sensitivitätsanalyse im Dossier) vor, siehe hierzu auch Abschnitt 4.2.5.4 des Dossiers.

Tabelle 4G-18: Charakterisierung der Studienpopulation (Therapieabbrecher, Studienabbrecher) – RCT mit dem zu bewertenden Arzneimittel (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

| Study: ZENITH (MK-7962-006)^a | Sotatercept n (%) | Placebo n (%) |
|--|------------------------------|--------------------------|
| Participants in Population ^b | 20 | 24 |
| Status For Trial | | |
| Completed | 15 (75.0) | 19 (79.2) |
| Discontinued | 5 (25.0) | 5 (20.8) |
| Death | 1 (5.0) | 2 (8.3) |
| Qtcf Above 500 Ms | 0 (0.0) | 1 (4.2) |
| Unwillingness Or Inability To Comply With Protocol | 1 (5.0) | 0 (0.0) |
| Withdrawal By Subject | 1 (5.0) | 0 (0.0) |
| Other | 2 (10.0) | 2 (8.3) |
| Status For Study Medication in Trial | | |
| Started ^c | 20 | 24 |
| Completed | 2 (10.0) | 11 (45.8) |
| Discontinued | 18 (90.0) | 13 (54.2) |
| Death | 1 (5.0) | 2 (8.3) |
| Qtcf > 500 Ms During The Treatment Period | 0 (0.0) | 1 (4.2) |
| Study Terminated By Sponsor | 13 (65.0) | 8 (33.3) |
| Unwillingness Or Inability To Comply With Protocol | 1 (5.0) | 0 (0.0) |
| Withdrawal By Subject | 1 (5.0) | 0 (0.0) |
| Other | 2 (10.0) | 2 (8.3) |
| a: Database Cutoff Date: 06JUN2025 | | |
| b: Number of participants: full analysis set, participants with WHO FC IV at baseline | | |
| c: Number of participants: all participants as treated population, participants with WHO FC IV at baseline | | |

| Study: ZENITH (MK-7962-006) ^a | Sotatercept n (%) | Placebo n (%) |
|--|----------------------|------------------|
| Each participant is counted once for Trial Disposition based on the latest corresponding disposition record. | | |
| Participants are considered to have completed the study if they experienced an event of PAH worsening-related hospitalization of ≥ 24 hours or lung transplantation, or they discontinued the study treatment due to 'study terminated by sponsor'. | | |
| Other reasons include starting commercial drug and PI discretion. | | |
| FC: Functional Class; Ms: Milliseconds; PAH: Pulmonary Arterial Hypertension; PI: Principal Investigator; QTcF: Fridericia's corrected QT interval; WHO: World Health Organization | | |

Tabelle 4G-19: Behandlungs- und Beobachtungszeiten (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

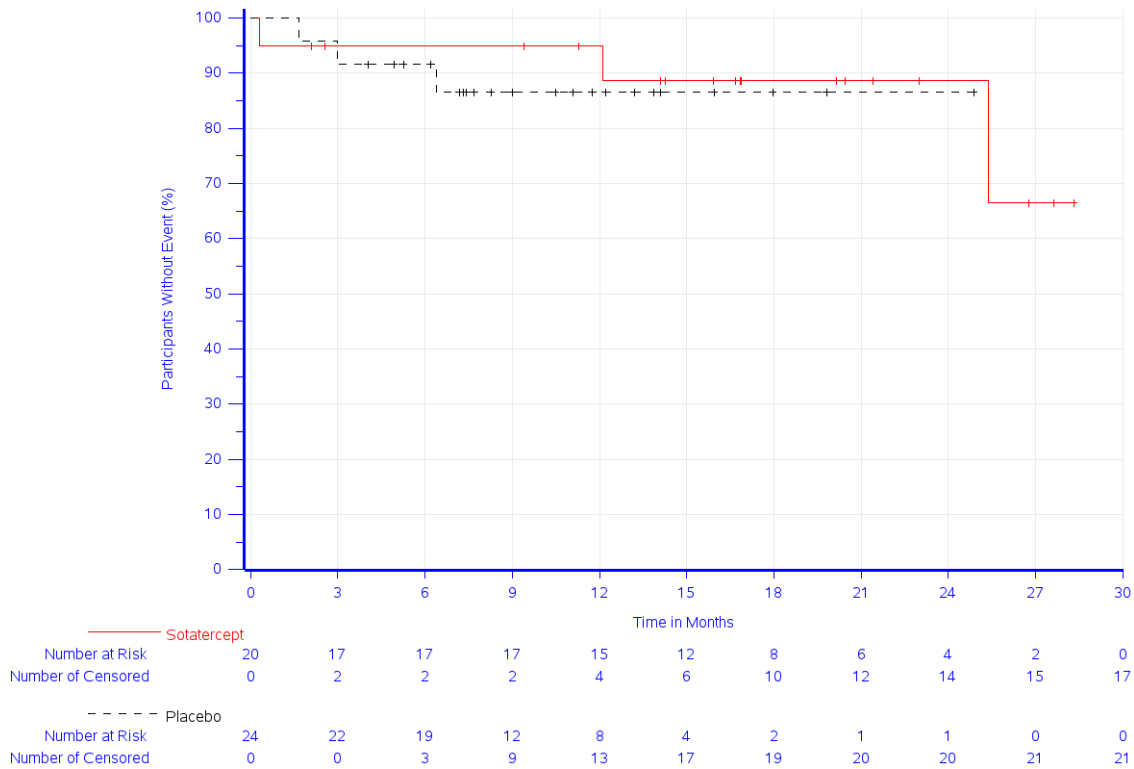
| Study: ZENITH (MK-7962-006) ^a | Sotatercept | Placebo |
|--|-------------------|-------------------|
| Duration of Treatment (Weeks)^b | | |
| N ^c | 20 | 24 |
| Mean (SD) | 64.7 (35.3) | 43.8 (24.2) |
| Median (Q1; Q3) | 64.5 (44.4; 90.2) | 37.4 (28.5; 57.2) |
| Min; Max | 3.0; 123.0 | 3.0; 108.0 |
| Observation Period | | |
| Overall Survival - Primary Analysis / Time to First Morbidity or Death (Weeks)^d | | |
| N ^c | 20 | 24 |
| Mean (SD) | 70.8 (36.2) | 44.2 (24.5) |
| Median (Q1; Q3) | 72.9 (50.9; 96.6) | 37.6 (27.4; 58.9) |
| Min; Max | 1.3; 123.1 | 7.3; 108.1 |
| Adverse Event / Serious Adverse Event (Weeks)^f | | |
| N ^c | 20 | 24 |
| Mean (SD) | 65.8 (35.7) | 44.0 (24.7) |
| Median (Q1; Q3) | 68.3 (44.9; 90.4) | 37.6 (27.4; 58.9) |
| Min; Max | 1.3; 123.1 | 3.1; 108.1 |
| 6-Minute Walk Distance (Weeks)^e | | |
| N ^c | 20 | 24 |
| Mean (SD) | 60.0 (39.0) | 42.1 (26.0) |
| Median (Q1; Q3) | 64.7 (24.1; 88.6) | 36.1 (24.1; 58.9) |
| Min; Max | 0.1; 120.1 | 0.1; 108.1 |
| Dyspnea Score (Pre-Vital Signs 6-Min Walk) Assessed by Borg CR10 (Weeks)^e | | |
| N ^c | 20 | 24 |
| Mean (SD) | 60.0 (39.0) | 42.1 (26.0) |
| Median (Q1; Q3) | 64.7 (24.1; 88.6) | 36.1 (24.1; 58.9) |
| Min; Max | 0.1; 120.1 | 0.1; 108.1 |
| EQ-5D-VAS (Weeks)^e | | |
| N ^c | 19 | 21 |
| Mean (SD) | 62.3 (30.4) | 41.3 (27.8) |
| Median (Q1; Q3) | 67.4 (37.9; 73.3) | 37.0 (24.4; 48.1) |
| Min; Max | 0.1; 116.4 | 0.1; 108.1 |
| a: Database Cutoff Date: 06JUN2025 | | |
| b: Calculated from date of first dose until date of last dose + 3 weeks (dosing period) | | |
| c: Number of participants: all participants as treated population, participants with WHO FC IV at baseline | | |
| d: Calculated from date of randomization until date of death, date of last contact, or the database cutoff date if the participant is still alive | | |
| e: Number of participants: full analysis set, participants with WHO FC IV at baseline | | |
| f: Calculated from the date of first dose to the earliest of the date of last dose + planned safety follow-up time (up to 8 weeks after the date of last dose of treatment), date of death, date of last contact or the database cutoff date if the participant is still alive | | |
| g: Calculated from date of randomization until date of last assessment | | |
| CR10: 10 Point Category Ratio scale; EQ-5D: European Quality of Life 5 Dimensions; FC: Functional Class; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation; VAS: Visual Analog Scale; WHO: World Health Organization | | |

Mortalität***Gesamtüberleben***

Tabelle 4G-20: Ergebnisse für den Endpunkt Gesamtüberleben (primäre Analysedefinition der Studie) aus RCT mit dem zu bewertenden Arzneimittel (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|--|----------------|----------------------------------|---|----------------|----------------------------------|---|--|------------------------|
| | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| Overall Survival | 20 | 3 (15.0) | Not reached [25.4; -] | 24 | 3 (12.5) | Not reached [-; -] | 0.68 [0.11; 4.19] | 0.679 |

^a Database Cutoff Date: 06JUN2025
^b Number of participants: full analysis set, participants with WHO FC IV at baseline
^c From product-limit (Kaplan-Meier) method for censored data
^d Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
^e Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
This table includes all-cause deaths up to the study completion date, except for those occurring after lung transplantation or enrollment in SOTERIA
CI: Confidence Interval; FC: Functional Class; WHO: World Health Organization



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 06JUN2025)
 Overall Survival
 This figure includes all-cause deaths up to the study completion, except for those occurring after lung transplantation or enrollment in SOTERIA

Abbildung 4G-10: Kaplan-Meier-Kurve für den Endpunkt Gesamtüberleben (primäre Analysedefinition der Studie) der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

Morbidität

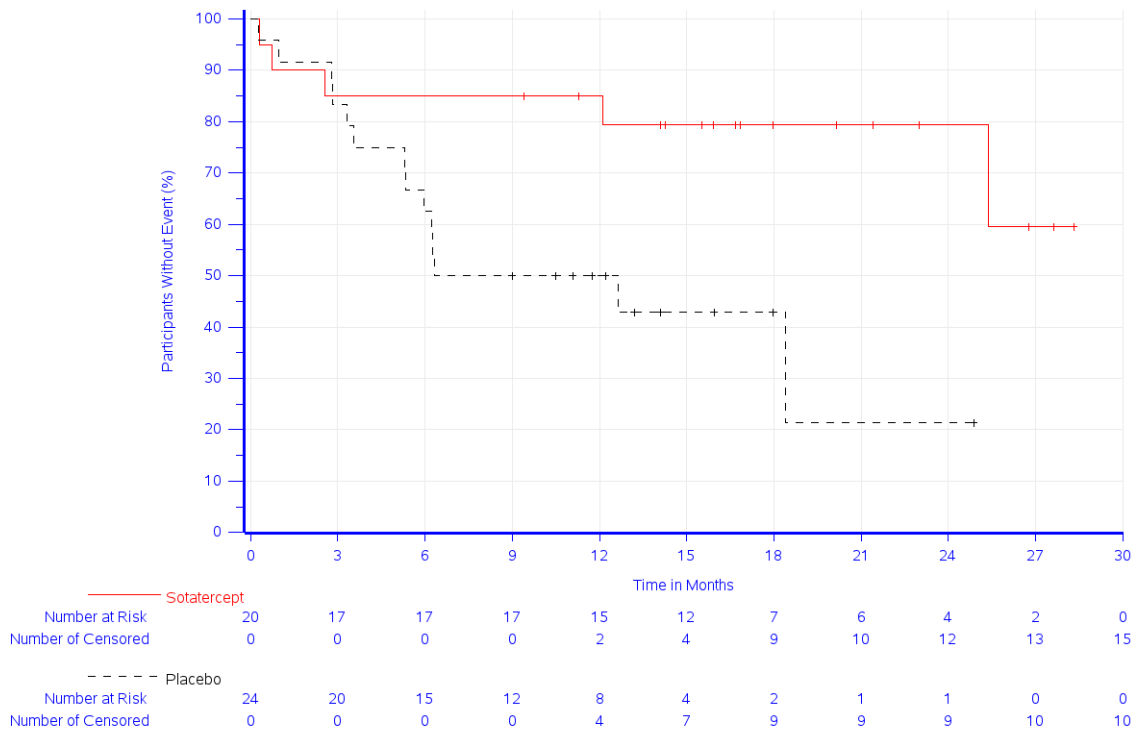
Tabelle 4G-21: Ergebnisse für den Endpunkt Zeit bis Tod jeglicher Ursache, Lungentransplantation oder Hospitalisierung von ≥ 24 Stunden aufgrund von PAH-Verschlechterung aus RCT mit dem zu bewertenden Arzneimittel (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|--|----------------|-------------------------------|--|----------------|-------------------------------|--|-------------------------------------|------------------------|
| | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| All-cause Death, Lung Transplantation, or PAH Worsening-related Hospitalization of ≥ 24 Hours | 20 | 5 (25.0) | Not reached [25.4; -] | 24 | 14 (58.3) | 9.5 [5.3; -] | 0.25 [0.08; 0.78] | 0.017 |

^a Database Cutoff Date: 06JUN2025
^b Number of participants: full analysis set, participants with WHO FC IV at baseline
^c From product-limit (Kaplan-Meier) method for censored data
^d Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method
^e Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

This table includes only the first adjudication-confirmed event of PAH worsening-related hospitalization ≥ 24 hours, lung transplantation, or all-cause death that occurred prior to the study completion date, excluding events that occurred in SOTERIA. For hospitalization and lung transplantation, events were only collected up to the individual participant's study completion date. Deaths are included regardless of adjudication

CI: Confidence Interval; FC: Functional Class; PAH: Pulmonary Arterial Hypertension; WHO: World Health Organization

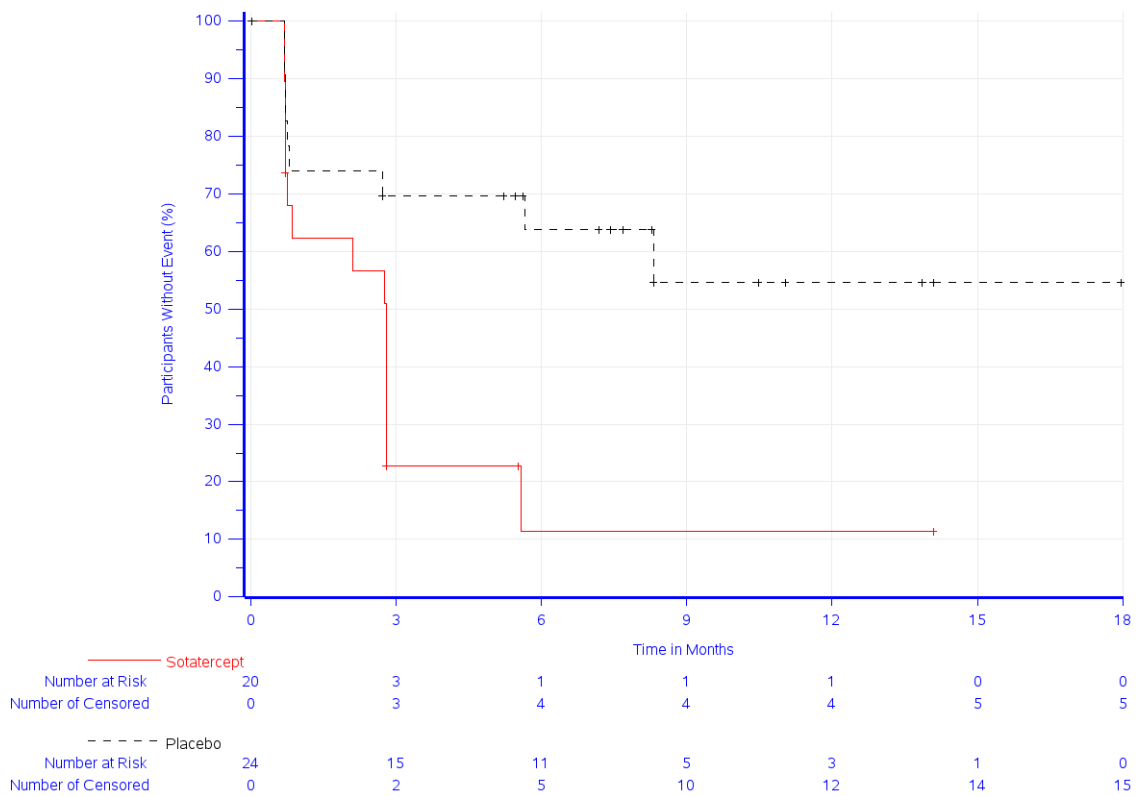


Study: ZENITH (MK-7962-006) (Database Cutoff Date: 06JUN2025)
 All-cause Death, Lung Transplantation, or PAH Worsening-related Hospitalization of ≥ 24 Hours
 This figure includes only the first adjudication-confirmed event of PAH worsening-related hospitalization ≥ 24 hours, lung transplantation, or all-cause death that occurred prior to the study completion date, excluding events that occurred in SOTERIA. For hospitalization and lung transplantation, events were only collected up to the individual participant's study completion date. Deaths are included regardless of adjudication

Abbildung 4G-11: Kaplan-Meier-Kurve für den Endpunkt Zeit bis Tod jeglicher Ursache, Lungentransplantation oder Hospitalisierung von ≥ 24 Stunden aufgrund von PAH-Verschlechterung der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

Tabelle 4G-22: Ergebnisse für den Endpunkt Zeit bis zur Verbesserung der 6MWD aus RCT mit dem zu bewertenden Arzneimittel (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|--|----------------|-------------------------------|--|----------------|-------------------------------|--|-------------------------------------|------------------------|
| | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in Months [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| Time to First 6-Minute Walk Distance Improvement (Increase From Baseline ≥ 40 Meters) | 20 | 15 (75.0) | 2.8 [0.7; 2.8] | 24 | 9 (37.5) | Not reached [2.7; -] | 3.18 [1.34; 7.53] | 0.009 |
| ^a Database Cutoff Date: 06JUN2025 ^b Number of participants: full analysis set, participants with WHO FC IV at baseline ^c From product-limit (Kaplan-Meier) method for censored data ^d Based on Cox regression model with treatment as a covariate. Ties are handled using Efron's method ^e Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) CI: Confidence Interval; FC: Functional Class; WHO: World Health Organization | | | | | | | | |



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 06JUN2025)
 Time to First 6-Minute Walk Distance Improvement (Increase From Baseline >= 40 Meters)

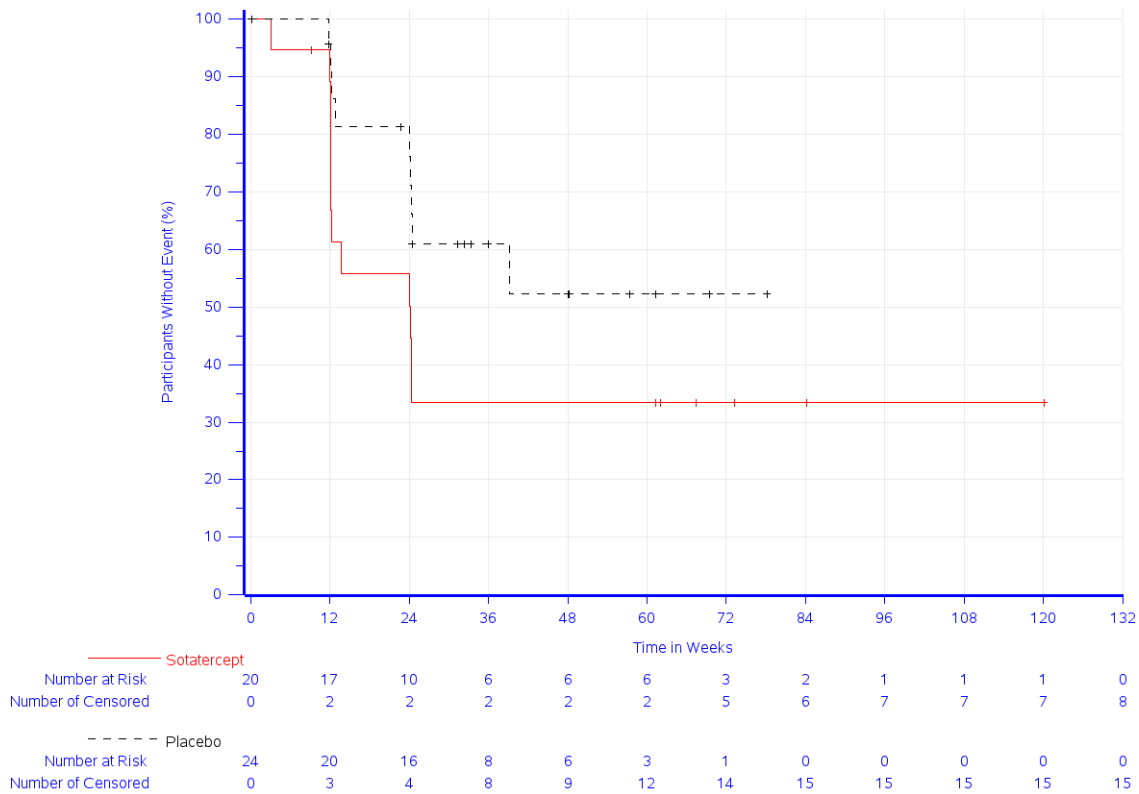
Abbildung 4G-12: Kaplan-Meier-Kurve für den Endpunkt Zeit bis zur Verbesserung der 6MWD der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Tabelle 4G-23: Ergebnisse für den Endpunkt Zeit bis zur ersten Verbesserung $\geq 15\%$ der Skalenspannweite des Pre-6MWD Dyspnoe Wertes gemäß Borg-Skala aus RCT mit dem zu bewertenden Arzneimittel (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|--|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|
| | N ^b | Participants with Event n (%) | Median Time ^c in weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| Time to First Improvement $\geq 15\%$ of Scale Range in Pre-6MWD Dyspnea Score (Assessed by Borg CR10 Scale) | 20 | 12 (60.0) | 24.14 [12.14; -] | 24 | 9 (37.5) | Not reached [24.14; -] | 2.04 [0.86; 4.85] | 0.107 |

a: Database Cutoff Date: 06JUN2025
b: Number of participants: full analysis set population, participants with WHO FC IV at baseline and without missing assessment at baseline and have at least one post-baseline assessment
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
6MWD: Six-Minute Walk Distance; CI: Confidence Interval; CR10: 10 Point Category Ratio scale; FC: Functional Class; WHO: World Health Organization



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 06JUN2025)
 Time to First Improvement >= 15% of Scale Range in Pre-6MWD Dyspnea Score (Assessed by Borg CR10 Scale)

Abbildung 4G-13: Kaplan-Meier-Kurve für den Endpunkt Zeit bis zur Verbesserung der Dyspnoe gemäß Borg-Skala der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Tabelle 4G-24: Ergebnisse für den Endpunkt die Zeit bis zur ersten Verbesserung $\geq 15\%$ der Skalenspannweite in der EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|---|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|
| | N ^b | Participants with Event n (%) | Median Time ^c in weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| Time to First Improvement $\geq 15\%$ of Scale Range in EQ-5D VAS | 18 | 13 (72.2) | 24.21 [12.14; 49.14] | 22 | 7 (31.8) | Not reached [12.29; -] | 2.04 [0.81; 5.16] | 0.130 |

a: Database Cutoff Date: 06JUN2025
b: Number of participants: full analysis set population, participants with WHO FC IV at baseline and without missing assessment at baseline and have at least one post-baseline assessment
c: From product-limit (Kaplan-Meier) method for censored data
d: Based on Cox regression model with treatment as a covariate
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
CI: Confidence Interval; EQ-5D: European Quality of Life 5 Dimensions; FC: Functional Class; VAS: Visual Analog Scale; WHO: World Health Organization

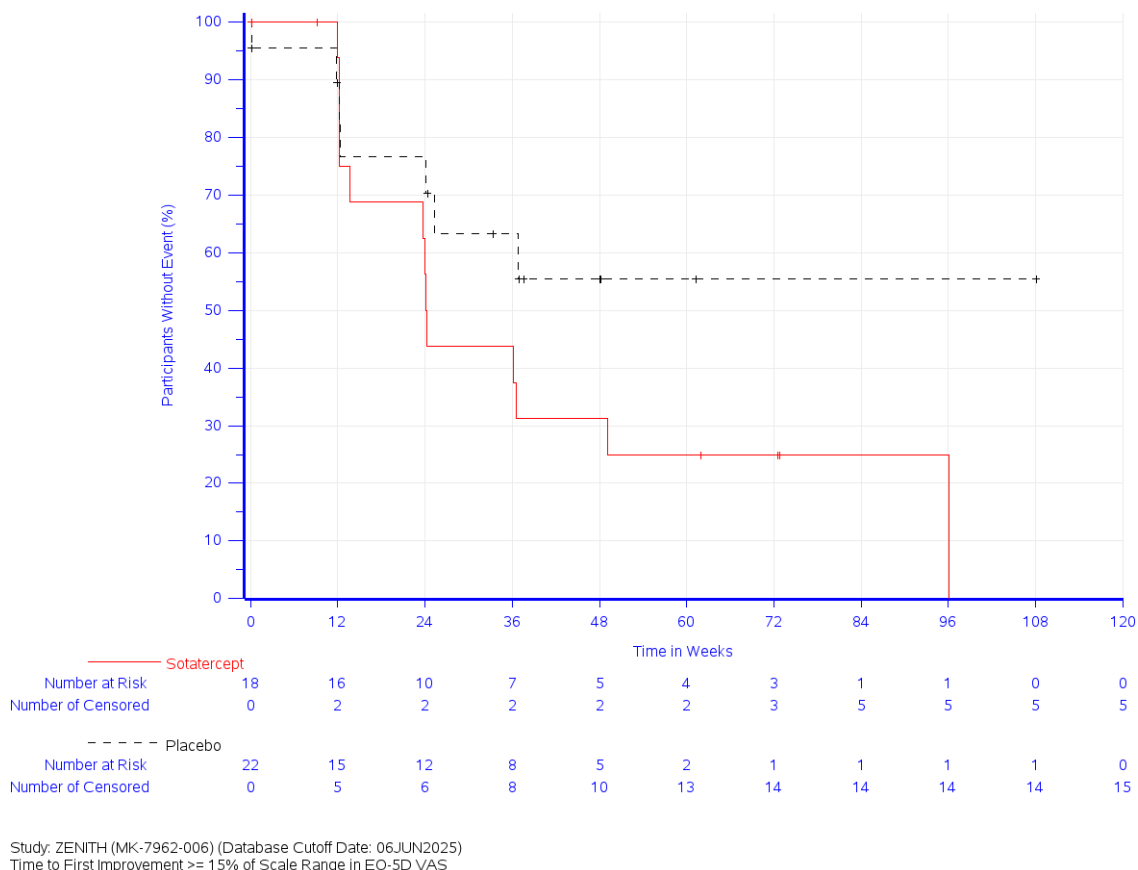


Abbildung 4G-14: Kaplan-Meier-Kurve für den Endpunkt Zeit bis zur Verbesserung der EQ-5D VAS der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

Nebenwirkungen

Tabelle 4G-25: Ergebnisse für den Endpunkt Unerwünschte Ereignisse Gesamtraten aus RCT mit dem zu bewertenden Arzneimittel (Finaler Datenschnitt mit Database Cut-off 18.02.2025)

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|---|----------------|-------------------------------|---|----------------|-------------------------------|---|-------------------------------------|------------------------|
| | N ^b | Participants with Event n (%) | Median Time ^c in weeks [95 %-CI] | N ^b | Participants with Event n (%) | Median Time ^c in weeks [95 %-CI] | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| | | | | | | | | |
| Adverse Events | 20 | 19 (95.0) | 0.93 [0.14; 3.14] | 24 | 23 (95.8) | 5.21 [2.29; 9.14] | 2.39 [1.23; 4.63] | 0.010 |
| Serious Adverse Events | 20 | 12 (60.0) | 46.43 [10.29; -] | 24 | 17 (70.8) | 23.07 [11.86; 55.00] | 0.71 [0.34; 1.49] | 0.365 |
| Severe Adverse Events | 20 | 8 (40.0) | Not reached [35.29; -] | 24 | 15 (62.5) | 34.86 [9.29; -] | 0.45 [0.19; 1.08] | 0.074 |
| Adverse Events Leading to Treatment Discontinuation | 20 | 0 (0.0) | Not reached [-; -] | 24 | 1 (4.2) | Not reached [-; -] | n.a. [n.a.; n.a.] | 0.374 |

a: Database Cutoff Date: 06JUN2025
b: Number of participants: all participants as treated population, participants with WHO FC IV at baseline
c: From product-limit (Kaplan-Meier) method for censored data

| Study: ZENITH (MK-7962-006) ^a | Sotatercept | | | Placebo | | | Sotatercept vs. Placebo | |
|---|-------------------------|---|----------------------|-------------------------|---|----------------------|-------------------------------------|------------------------|
| | Participants with Event | Median Time ^c in weeks [95 %-CI] | N ^b n (%) | Participants with Event | Median Time ^c in weeks [95 %-CI] | N ^b n (%) | Hazard Ratio [95 %-CI] ^d | p-Value ^{d,e} |
| | | | | | | | | |
| d: Based on Cox regression model with treatment as a covariate e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) CI: Confidence Intervals; FC: Functional Class; n.a.: not applicable (when estimation not possible); WHO: World Health Organization | | | | | | | | |

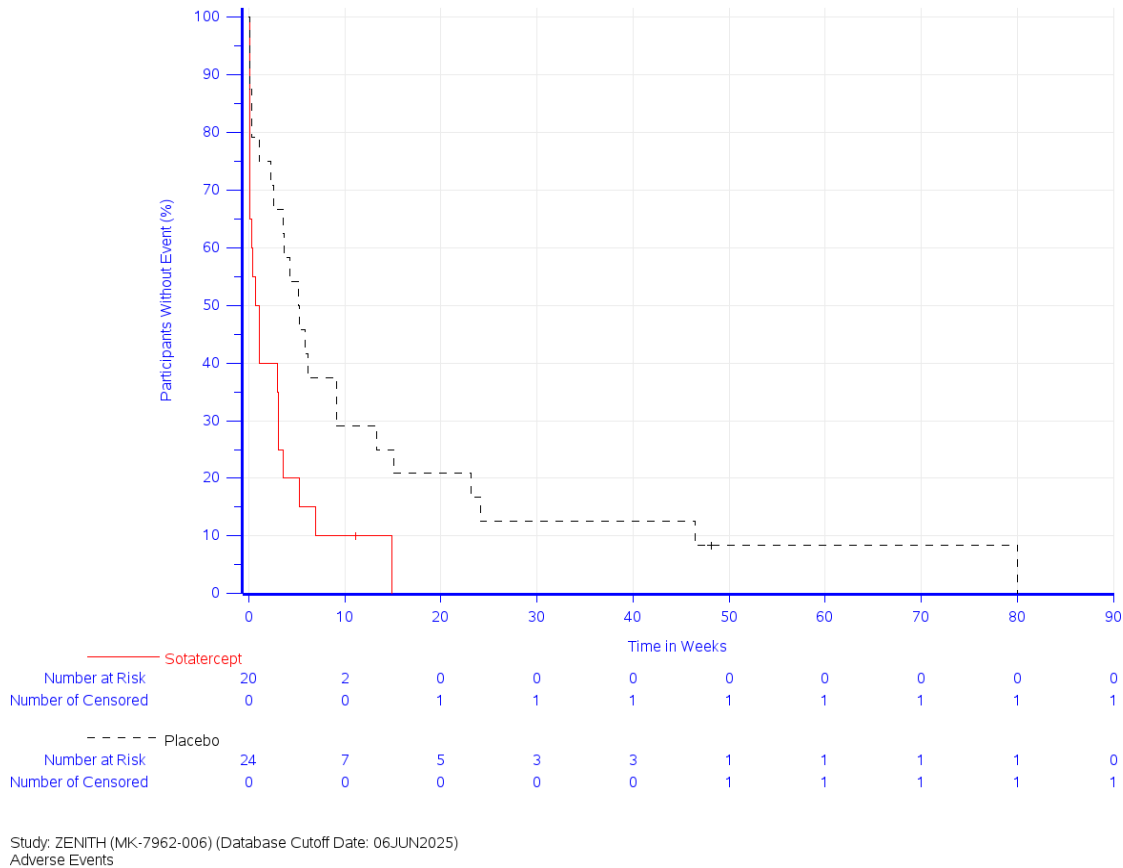
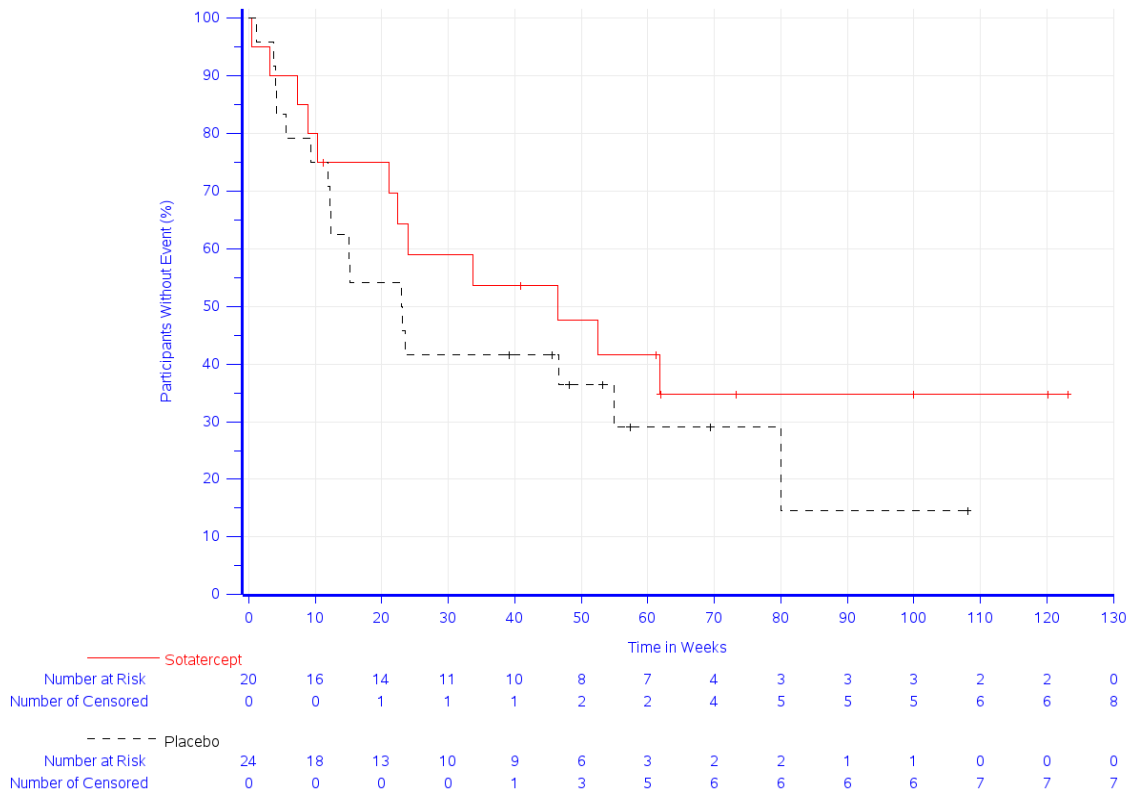
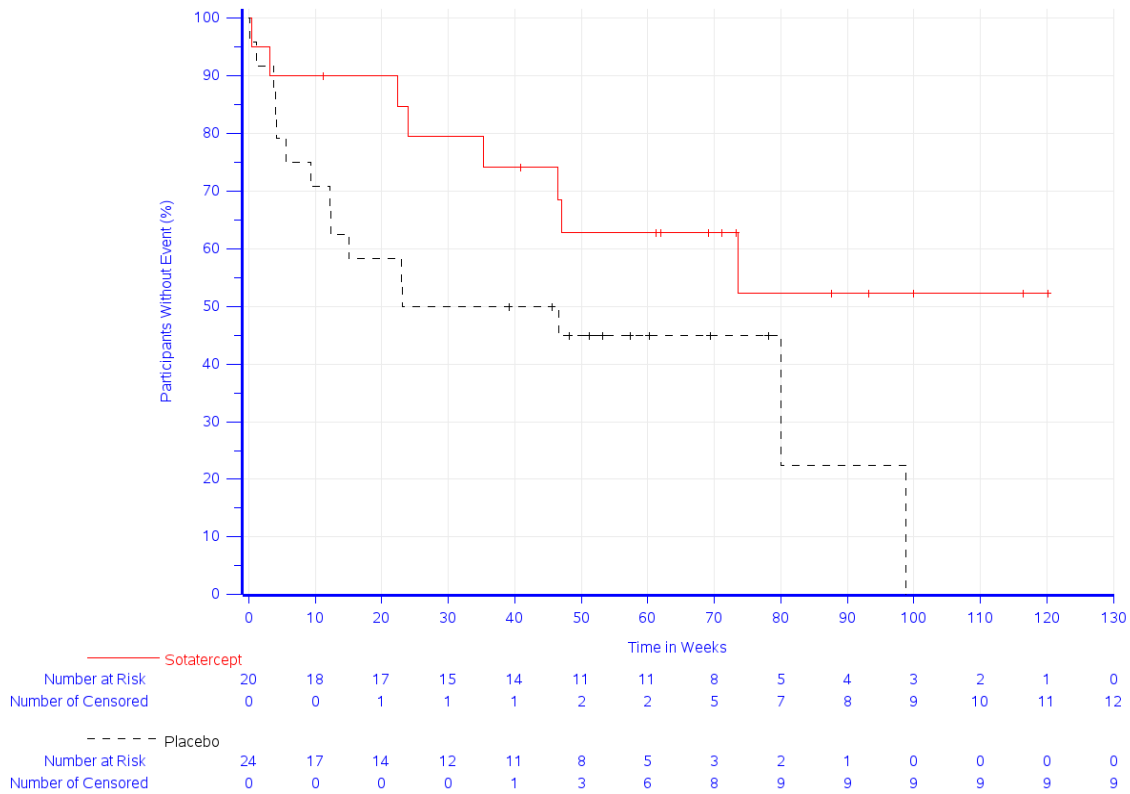


Abbildung 4G-15: Kaplan-Meier-Kurve für den Endpunkt Unerwünschte Ereignisse Gesamtraten der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)



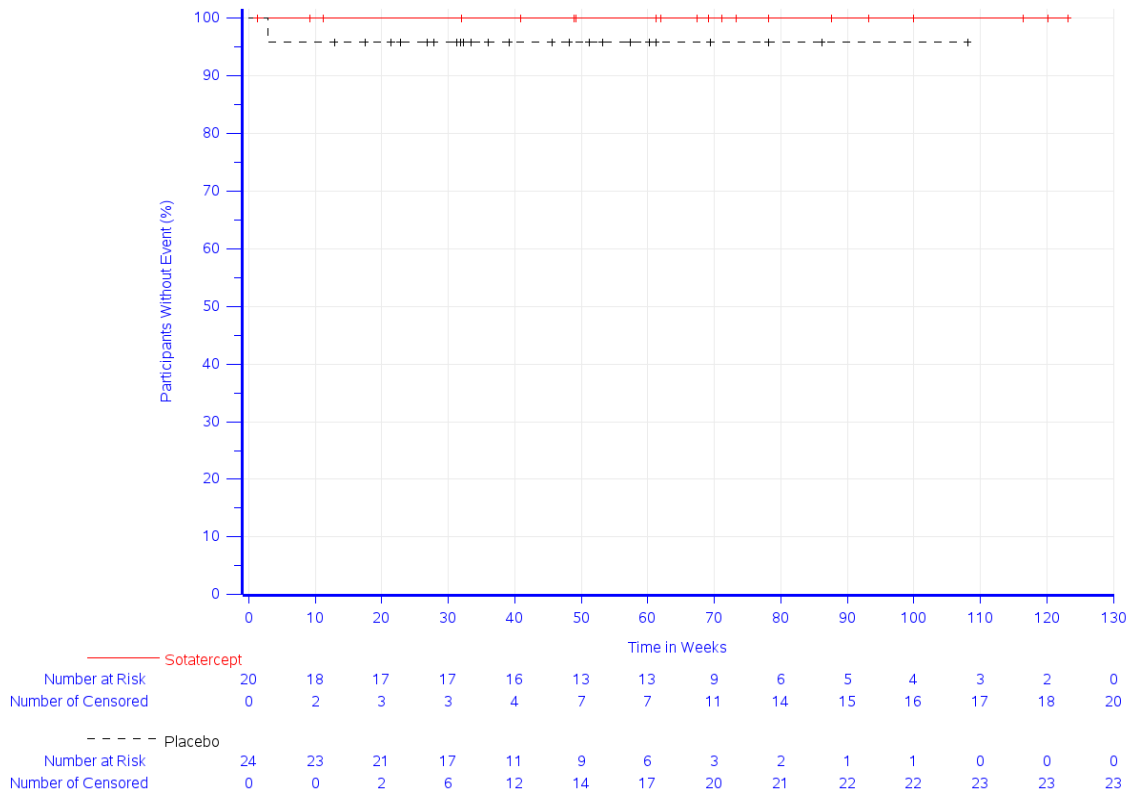
Study: ZENITH (MK-7962-006) (Database Cutoff Date: 06JUN2025)
 Serious Adverse Events

Abbildung 4G-16: Kaplan-Meier-Kurve für den Endpunkt Schwerwiegende Unerwünschte Ereignisse Gesamtraten der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 06JUN2025)
Severe Adverse Events

Abbildung 4G-17: Kaplan-Meier-Kurve für den Endpunkt Schwere unerwünschte Ereignisse Gesamtraten der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)



Study: ZENITH (MK-7962-006) (Database Cutoff Date: 06JUN2025)
 Adverse Events Leading to Treatment Discontinuation

Abbildung 4G-18: Kaplan-Meier-Kurve für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse der Studie ZENITH (Finaler Datenschnitt mit Database Cut-off 18.02.2025)