# Anhang 4-G: Ergänzende Daten zur Studie OASIS-4

## Inhaltsverzeichnis

**Anhang 4-G1: Ergänzende Analysen zu den Subgruppen (Wirksamkeit)**

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean daily frequency of moderate to severe VMS: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 7.96 (4.39) | 2 | | 2 | 8.18 (2.37) | 2 | | | | | |
| | | Rest of the World | 314 | 11.44 (6.91) | 312 | | 155 | 11.56 (6.46) | 154 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.1794 |
| | | Tamoxifen | 175 | 11.64 (7.81) | 173 | -6.72 (0.26) | 89 | 10.77 (5.16) | 89 | -3.15 (0.37) | -3.57 (-4.46, -2.68) | <.0001 | -1.03 (-1.30, -0.76) | |
| | | Aromatase Inhibitors | 141 | 11.14 (5.56) | 141 | -6.76 (0.22) | 68 | 12.49 (7.72) | 67 | -4.00 (0.33) | -2.76 (-3.54, -1.98) | <.0001 | -1.03 (-1.34, -0.73) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean daily frequency of mild, moderate and severe VMS: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 10.79 (3.23) | 2 | | 2 | 9.43 (4.14) | 2 | | | | | |
| | | Rest of the World | 314 | 14.02 (8.47) | 312 | | 155 | 14.24 (7.58) | 154 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.1767 |
| | | Tamoxifen | 175 | 14.33 (9.56) | 173 | -7.32 (0.30) | 89 | 13.20 (5.91) | 89 | -3.36 (0.42) | -3.96 (-4.98, -2.95) | <.0001 | -1.00 (-1.27, -0.73) | |
| | | Aromatase Inhibitors | 141 | 13.59 (6.83) | 141 | -7.61 (0.26) | 68 | 15.45 (9.17) | 67 | -4.58 (0.38) | -3.03 (-3.94, -2.13) | <.0001 | -0.98 (-1.29, -0.68) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean daily severity of moderate to severe VMS (incl. mild VMS post-baseline): MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Elinzanetant 120mg (N=316) Baseline Mean (SD) | Elinzanetant 120mg (N=316) Change from BL N* | Elinzanetant 120mg (N=316) Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Placebo (N=158) Baseline Mean (SD) | Placebo (N=158) Change from BL N* | Placebo (N=158) Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 2.27 (0.29) | 2 | | 2 | 2.02 (0.12) | 2 | | | | | |
| | | Rest of the World | 314 | 2.49 (0.24) | 312 | | 155 | 2.50 (0.22) | 154 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.7826 |
| | | Tamoxifen | 175 | 2.48 (0.26) | 173 | -0.80 (0.03) | 89 | 2.48 (0.19) | 89 | -0.46 (0.05) | -0.34 (-0.46, -0.23) | <.0001 | -0.77 (-1.04, -0.51) | |
| | | Aromatase Inhibitors | 141 | 2.50 (0.22) | 141 | -0.77 (0.04) | 68 | 2.51 (0.26) | 67 | -0.45 (0.06) | -0.32 (-0.47, -0.17) | <.0001 | -0.61 (-0.90, -0.31) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Improvement of mean daily frequency of moderate to severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|
| Improvement >=50% | Week 12 | Region | | | | | |
| | | North America | 2/ 2 (100.0) | 0/ 2 ( 0.0) | | | |
| | | Rest of the World | 215/ 314 ( 68.5) | 53/ 156 ( 34.0) | | | |
| | | Type of treatment for the pre-existing condition | | | | | 0.9620 |
| | | Tamoxifen | 120/ 175 ( 68.6) | 30/ 90 ( 33.3) | 2.06 (1.51, 2.80) | <.0001 | |
| | | Aromatase Inhibitors | 97/ 141 ( 68.8) | 23/ 68 ( 33.8) | 2.03 (1.43, 2.89) | <.0001 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Improvement of mean daily frequency of moderate to severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|
| Improvement >=80% | Week 12 | Region | | | | | |
| | | North America | 1/ 2 ( 50.0) | 0/ 2 ( 0.0) | | | |
| | | Rest of the World | 147/ 314 ( 46.8) | 22/ 156 ( 14.1) | | | |
| | | Type of treatment for the pre-existing condition | | | | | 0.4056 |
| | | Tamoxifen | 86/ 175 ( 49.1) | 15/ 90 ( 16.7) | 2.95 (1.81, 4.79) | <.0001 | |
| | | Aromatase Inhibitors | 62/ 141 ( 44.0) | 7/ 68 ( 10.3) | 4.27 (2.07, 8.83) | <.0001 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Improvement of mean daily frequency of mild, moderate and severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|
| Improvement >=50% | Week 12 | Region | | | | | |
| | | North America | 1/ 2 ( 50.0) | 0/ 2 ( 0.0) | | | |
| | | Rest of the World | 191/ 314 ( 60.8) | 44/ 156 ( 28.2) | | | |
| | | Type of treatment for the pre-existing condition | | | | | 0.7380 |
| | | Tamoxifen | 106/ 175 ( 60.6) | 24/ 90 ( 26.7) | 2.27 (1.58, 3.27) | <.0001 | |
| | | Aromatase Inhibitors | 86/ 141 ( 61.0) | 20/ 68 ( 29.4) | 2.07 (1.40, 3.07) | 0.0003 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Improvement of mean daily frequency of mild, moderate and severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|
| Improvement >=80% | Week 12 | Region | | | | | |
| | | North America | 1/ 2 ( 50.0) | 0/ 2 ( 0.0) | | | |
| | | Rest of the World | 94/ 314 ( 29.9) | 13/ 156 ( 8.3) | | | |
| | | Type of treatment for the pre-existing condition | | | | | 0.7320 |
| | | Tamoxifen | 60/ 175 ( 34.3) | 9/ 90 ( 10.0) | 3.43 (1.78, 6.59) | 0.0002 | |
| | | Aromatase Inhibitors | 35/ 141 ( 24.8) | 4/ 68 ( 5.9) | 4.22 (1.56, 11.39) | 0.0045 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of mild VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=50% | Until Week 12 | Region | | | | | | | |
| | | North America | 2/ 2 (100.0) | | 0/ 2 ( 0.0) | | | | |
| | | Rest of the World | 194/ 314 ( 61.8) | | 92/ 156 ( 59.0) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.1210 |
| | | Tamoxifen | 106/ 175 ( 60.6) | 6.0 ( 3.0, 9.0) | 46/ 90 ( 51.1) | 12.0 ( 8.0, NE ) | 1.38 (0.98, 1.95) | 0.0680 | |
| | | Aromatase Inhibitors | 90/ 141 ( 63.8) | 4.0 ( 3.0, 5.0) | 46/ 68 ( 67.6) | 5.0 ( 2.0, 9.0) | 0.92 (0.65, 1.32) | 0.6594 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of mild VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=80% | Until Week 12 | Region | | | | | | | |
| | | North America | 1/ 2 ( 50.0) | | 0/ 2 ( 0.0) | | | | |
| | | Rest of the World | 142/ 314 ( 45.2) | | 59/ 156 ( 37.8) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.0187 |
| | | Tamoxifen | 78/ 175 ( 44.6) | NE (10.0, NE ) | 25/ 90 ( 27.8) | NE ( NE , NE ) | 1.85 (1.18, 2.90) | 0.0078 | |
| | | Aromatase Inhibitors | 65/ 141 ( 46.1) | NE ( 7.0, NE ) | 34/ 68 ( 50.0) | 12.0 ( 6.0, NE ) | 0.87 (0.58, 1.32) | 0.5269 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of moderate VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=50% | Until Week 12 | Region | | | | | | | |
| | | North America | 2/ 2 (100.0) | | 1/ 2 ( 50.0) | | | | |
| | | Rest of the World | 247/ 314 ( 78.7) | | 79/ 156 ( 50.6) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.5055 |
| | | Tamoxifen | 137/ 175 ( 78.3) | 3.0 ( 2.0, 4.0) | 43/ 90 ( 47.8) | NE ( 6.0, NE ) | 2.24 (1.59, 3.16) | <.0001 | |
| | | Aromatase Inhibitors | 112/ 141 ( 79.4) | 3.0 ( 3.0, 4.0) | 37/ 68 ( 54.4) | 8.0 ( 5.0, NE ) | 1.92 (1.32, 2.79) | 0.0006 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of moderate VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=80% | Until Week 12 | Region | | | | | | | |
| | | North America | 1/ 2 ( 50.0) | | 1/ 2 ( 50.0) | | | | |
| | | Rest of the World | 171/ 314 ( 54.5) | | 51/ 156 ( 32.7) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.1310 |
| | | Tamoxifen | 101/ 175 ( 57.7) | 9.0 ( 6.0, 12.0) | 28/ 90 ( 31.1) | NE ( NE , NE ) | 2.48 (1.63, 3.77) | <.0001 | |
| | | Aromatase Inhibitors | 71/ 141 ( 50.4) | 12.0 ( 9.0, NE ) | 24/ 68 ( 35.3) | NE ( NE , NE ) | 1.52 (0.96, 2.42) | 0.0746 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=50% | Until Week 12 | Region | | | | | | | |
| | | North America | 2/ 2 (100.0) | | 1/ 2 ( 50.0) | | | | |
| | | Rest of the World | 286/ 314 ( 91.1) | | 110/ 156 ( 70.5) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.5171 |
| | | Tamoxifen | 156/ 175 ( 89.1) | 1.1 ( 1.1, 2.0) | 59/ 90 ( 65.6) | 4.0 ( 2.0, 8.0) | 1.96 (1.45, 2.67) | <.0001 | |
| | | Aromatase Inhibitors | 132/ 141 ( 93.6) | 2.0 ( 1.1, 2.0) | 52/ 68 ( 76.5) | 3.0 ( 2.0, 5.0) | 1.78 (1.28, 2.47) | 0.0006 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
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Study population
Time to Improvement of mean daily frequency of severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=80% | Until Week 12 | Region | | | | | | | |
| | | North America | 2/ 2 (100.0) | | 1/ 2 ( 50.0) | | | | |
| | | Rest of the World | 245/ 314 ( 78.0) | | 71/ 156 ( 45.5) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.8303 |
| | | Tamoxifen | 132/ 175 ( 75.4) | 4.0 ( 3.0, 5.0) | 40/ 90 ( 44.4) | NE ( 9.0, NE ) | 2.46 (1.73, 3.52) | <.0001 | |
| | | Aromatase Inhibitors | 115/ 141 ( 81.6) | 3.0 ( 3.0, 4.0) | 32/ 68 ( 47.1) | NE ( 7.0, NE ) | 2.41 (1.62, 3.57) | <.0001 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

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Study population
Time to Improvement of mean daily frequency of mild, moderate and severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=50% | Until Week 12 | Region | | | | | | | |
| | | North America | 2/ 2 (100.0) | | 1/ 2 ( 50.0) | | | | |
| | | Rest of the World | 247/ 314 ( 78.7) | | 66/ 156 ( 42.3) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.8638 |
| | | Tamoxifen | 134/ 175 ( 76.6) | 3.0 ( 3.0, 4.0) | 38/ 90 ( 42.2) | NE (10.0, NE ) | 2.73 (1.90, 3.92) | <.0001 | |
| | | Aromatase Inhibitors | 115/ 141 ( 81.6) | 3.0 ( 3.0, 5.0) | 29/ 68 ( 42.6) | NE (10.0, NE ) | 3.03 (2.00, 4.57) | <.0001 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

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Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of mild, moderate and severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=80% | Until Week 12 | Region | | | | | | | |
| | | North America | 1/ 2 ( 50.0) | | 0/ 2 ( 0.0) | | | | |
| | | Rest of the World | 134/ 314 ( 42.7) | | 20/ 156 ( 12.8) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.7253 |
| | | Tamoxifen | 76/ 175 ( 43.4) | NE (11.0, NE ) | 13/ 90 ( 14.4) | NE ( NE , NE ) | 3.90 (2.16, 7.02) | <.0001 | |
| | | Aromatase Inhibitors | 59/ 141 ( 41.8) | NE (12.0, NE ) | 7/ 68 ( 10.3) | NE ( NE , NE ) | 4.68 (2.14, 10.26) | 0.0001 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of moderate to severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=50% | Until Week 12 | Region | | | | | | | |
| | | North America | 2/ 2 (100.0) | | 1/ 2 ( 50.0) | | | | |
| | | Rest of the World | 274/ 314 ( 87.3) | | 81/ 156 ( 51.9) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.8795 |
| | | Tamoxifen | 151/ 175 ( 86.3) | 2.0 ( 2.0, 3.0) | 46/ 90 ( 51.1) | 11.0 ( 7.0, NE ) | 2.84 (2.03, 3.98) | <.0001 | |
| | | Aromatase Inhibitors | 125/ 141 ( 88.7) | 2.0 ( 2.0, 3.0) | 36/ 68 ( 52.9) | 11.0 ( 6.0, NE ) | 2.78 (1.91, 4.07) | <.0001 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Time to Improvement of mean daily frequency of moderate to severe VMS - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) n/ N (%) | Elinzanetant 120mg (N=316) Median (95%-CI) | Placebo (N=158) n/ N (%) | Placebo (N=158) Median (95%-CI) | Elinzanetant 120mg vs. Placebo Hazard Ratio (95% CI) | Elinzanetant 120mg vs. Placebo p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|
| Time to Improvement >=80% | Until Week 12 | Region | | | | | | | |
| | | North America | 2/ 2 (100.0) | | 0/ 2 ( 0.0) | | | | |
| | | Rest of the World | 181/ 314 ( 57.6) | | 39/ 156 ( 25.0) | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | 0.9605 |
| | | Tamoxifen | 103/ 175 ( 58.9) | 8.0 ( 5.0, 11.0) | 24/ 90 ( 26.7) | NE ( NE , NE ) | 3.05 (1.96, 4.77) | <.0001 | |
| | | Aromatase Inhibitors | 80/ 141 ( 56.7) | 10.0 ( 7.0, 12.0) | 15/ 68 ( 22.1) | NE ( NE , NE ) | 3.15 (1.81, 5.48) | <.0001 | |

Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Kaplan-Meier estimates for Median based on the Brookmeyer and Crowley method.
Hazard Ratio, connfidence intervall and p-value estimated using Cox Proportional Hazard Model.
p-Value for interaction is calculated from Cox Proportional Hazard Model with additional factors for subgroup and treatment-by-subgroup interaction.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; HR=Hazard Ratio; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean daily frequency of mild, moderate and severe VMS: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 10.79 (3.23) | 2 | | 2 | 9.43 (4.14) | 2 | | | | | |
| | | Rest of the World | 314 | 14.02 (8.47) | 312 | | 155 | 14.24 (7.58) | 154 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.1767 |
| | | Tamoxifen | 175 | 14.33 (9.56) | 173 | -7.32 (0.30) | 89 | 13.20 (5.91) | 89 | -3.36 (0.42) | -3.96 (-4.98, -2.95) | <.0001 | -1.00 (-1.27, -0.73) | |
| | | Aromatase Inhibitors | 141 | 13.59 (6.83) | 141 | -7.61 (0.26) | 68 | 15.45 (9.17) | 67 | -4.58 (0.38) | -3.03 (-3.94, -2.13) | <.0001 | -0.98 (-1.29, -0.68) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean daily severity of moderate to severe VMS (incl. mild VMS post-baseline): MMRM analysis - Subgroup analysis
Full Analysis Set

| | | | Elinzanetant 120mg (N=316) | | | | Placebo (N=158) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline | | Change from BL | | Baseline | | Change from BL | | | | | |
| Analysis | Timepoint | Subgroup Level | N | Mean (SD) | N* | LSMean (SE) | N | Mean (SD) | N* | LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 2.27 (0.29) | 2 | | 2 | 2.02 (0.12) | 2 | | | | | |
| | | Rest of the World | 314 | 2.49 (0.24) | 312 | | 155 | 2.50 (0.22) | 154 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.7826 |
| | | Tamoxifen | 175 | 2.48 (0.26) | 173 | -0.80 (0.03) | 89 | 2.48 (0.19) | 89 | -0.46 (0.05) | -0.34 (-0.46, -0.23) | <.0001 | -0.77 (-1.04, -0.51) | |
| | | Aromatase Inhibitors | 141 | 2.50 (0.22) | 141 | -0.77 (0.04) | 68 | 2.51 (0.26) | 67 | -0.45 (0.06) | -0.32 (-0.47, -0.17) | <.0001 | -0.61 (-0.90, -0.31) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean severity of moderate and severe hot flushes: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 2.36 (0.18) | 2 | | 2 | 2.10 (0.02) | 2 | | | | | |
| | | Rest of the World | 314 | 2.50 (0.22) | 312 | | 155 | 2.51 (0.21) | 154 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.7874 |
| | | Tamoxifen | 175 | 2.50 (0.23) | 173 | -0.33 (0.03) | 89 | 2.49 (0.19) | 89 | -0.11 (0.04) | -0.22 (-0.32, -0.12) | <.0001 | -0.55 (-0.81, -0.29) | |
| | | Aromatase Inhibitors | 141 | 2.50 (0.21) | 141 | -0.36 (0.04) | 68 | 2.53 (0.25) | 67 | -0.16 (0.06) | -0.20 (-0.33, -0.06) | 0.0049 | -0.42 (-0.72, -0.13) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean severity of all hot flushes: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 1.98 (0.39) | 2 | | 2 | 1.99 (0.14) | 2 | | | | | |
| | | Rest of the World | 314 | 2.26 (0.33) | 312 | | 155 | 2.24 (0.33) | 154 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.9250 |
| | | Tamoxifen | 175 | 2.26 (0.35) | 173 | -0.41 (0.03) | 89 | 2.22 (0.29) | 89 | -0.16 (0.04) | -0.25 (-0.34, -0.16) | <.0001 | -0.70 (-0.96, -0.44) | |
| | | Aromatase Inhibitors | 141 | 2.26 (0.31) | 141 | -0.41 (0.04) | 68 | 2.26 (0.38) | 67 | -0.15 (0.05) | -0.26 (-0.39, -0.13) | <.0001 | -0.60 (-0.90, -0.30) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in mean frequency of nighttime awakening: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Elinzanetant 120mg (N=316) Baseline Mean (SD) | Elinzanetant 120mg (N=316) Change from BL N* | Elinzanetant 120mg (N=316) Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Placebo (N=158) Baseline Mean (SD) | Placebo (N=158) Change from BL N* | Placebo (N=158) Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 2.61 (1.36) | 2 | | 2 | 2.68 (0.76) | 2 | | | | | |
| | | Rest of the World | 310 | 3.72 (2.27) | 309 | | 155 | 3.56 (1.97) | 153 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.9861 |
| | | Tamoxifen | 173 | 3.96 (2.50) | 172 | -1.77 (0.08) | 89 | 3.50 (1.82) | 88 | -0.98 (0.11) | -0.80 (-1.06, -0.53) | <.0001 | -0.78 (-1.04, -0.51) | |
| | | Aromatase Inhibitors | 139 | 3.42 (1.91) | 139 | -1.61 (0.07) | 68 | 3.61 (2.14) | 67 | -0.82 (0.10) | -0.79 (-1.04, -0.55) | <.0001 | -0.94 (-1.24, -0.63) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in proportion of days with quite a bit or very much sleep disturbance: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Elinzanetant 120mg (N=316) Baseline Mean (SD) | Elinzanetant 120mg (N=316) Change from BL N* | Elinzanetant 120mg (N=316) Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Placebo (N=158) Baseline Mean (SD) | Placebo (N=158) Change from BL N* | Placebo (N=158) Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 0.29 (0.20) | 2 | | 2 | 0.07 (0.10) | 2 | | | | | |
| | | Rest of the World | 310 | 0.51 (0.36) | 309 | | 155 | 0.50 (0.37) | 153 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.8157 |
| | | Tamoxifen | 173 | 0.51 (0.36) | 172 | -0.37 (0.01) | 89 | 0.54 (0.35) | 88 | -0.26 (0.02) | -0.11 (-0.16, -0.06) | <.0001 | -0.61 (-0.87, -0.35) | |
| | | Aromatase Inhibitors | 139 | 0.49 (0.36) | 139 | -0.37 (0.01) | 68 | 0.43 (0.38) | 67 | -0.27 (0.02) | -0.10 (-0.15, -0.06) | <.0001 | -0.64 (-0.93, -0.34) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in MENQOL Total score: MMRM analysis - Subgroup analysis
Full Analysis Set

| | | | Elinzanetant 120mg (N=316) | | | | Placebo (N=158) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline | | Change from BL | | Baseline | | Change from BL | | | | | |
| Analysis | Timepoint | Subgroup Level | N | Mean (SD) | N* | LSMean (SE) | N | Mean (SD) | N* | LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 4.26 (1.70) | 2 | | 2 | 5.48 (0.87) | 2 | | | | | |
| | | Rest of the World | 309 | 4.83 (1.16) | 302 | | 153 | 4.76 (1.25) | 149 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.8716 |
| | | Tamoxifen | 172 | 4.69 (1.16) | 168 | -1.16 (0.06) | 90 | 4.46 (1.21) | 89 | -0.45 (0.08) | -0.70 (-0.91, -0.50) | <.0001 | -0.89 (-1.16, -0.63) | |
| | | Aromatase Inhibitors | 139 | 4.99 (1.16) | 136 | -1.17 (0.07) | 65 | 5.20 (1.18) | 62 | -0.44 (0.10) | -0.73 (-0.98, -0.48) | <.0001 | -0.90 (-1.21, -0.58) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in MENQOL domain score - Physical: MMRM analysis - Subgroup analysis
Full Analysis Set

| | | | Elinzanetant 120mg (N=316) | | | | Placebo (N=158) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline | | Change from BL | | Baseline | | Change from BL | | | | | |
| Analysis | Timepoint | Subgroup Level | N | Mean (SD) | N* | LSMean (SE) | N | Mean (SD) | N* | LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 3.63 (1.33) | 2 | | 2 | 4.13 (2.21) | 2 | | | | | |
| | | Rest of the World | 309 | 4.24 (1.27) | 302 | | 153 | 4.33 (1.32) | 149 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.9315 |
| | | Tamoxifen | 172 | 4.18 (1.28) | 168 | -0.75 (0.06) | 90 | 4.13 (1.32) | 89 | -0.30 (0.08) | -0.46 (-0.66, -0.25) | <.0001 | -0.57 (-0.83, -0.31) | |
| | | Aromatase Inhibitors | 139 | 4.31 (1.27) | 136 | -0.70 (0.07) | 65 | 4.60 (1.30) | 62 | -0.23 (0.10) | -0.47 (-0.71, -0.23) | 0.0002 | -0.59 (-0.89, -0.28) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in MENQOL domain score - Psychosocial: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 4.57 (3.84) | 2 | | 2 | 4.64 (1.52) | 2 | | | | | |
| | | Rest of the World | 309 | 3.97 (1.77) | 302 | | 153 | 3.60 (1.76) | 149 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.3300 |
| | | Tamoxifen | 172 | 3.82 (1.81) | 168 | -0.77 (0.07) | 90 | 3.32 (1.76) | 89 | -0.47 (0.10) | -0.30 (-0.53, -0.06) | 0.0136 | -0.33 (-0.59, -0.07) | |
| | | Aromatase Inhibitors | 139 | 4.17 (1.74) | 136 | -0.86 (0.08) | 65 | 4.02 (1.68) | 62 | -0.38 (0.13) | -0.48 (-0.78, -0.19) | 0.0016 | -0.49 (-0.79, -0.19) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in MENQOL domain score - Sexual: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 3.17 (0.71) | 2 | | 2 | 7.50 (0.71) | 2 | | | | | |
| | | Rest of the World | 307 | 4.46 (2.25) | 299 | | 153 | 4.41 (2.41) | 149 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.7683 |
| | | Tamoxifen | 171 | 4.09 (2.17) | 166 | -0.62 (0.10) | 90 | 3.67 (2.35) | 89 | -0.04 (0.13) | -0.58 (-0.91, -0.25) | 0.0006 | -0.46 (-0.72, -0.20) | |
| | | Aromatase Inhibitors | 138 | 4.90 (2.28) | 135 | -0.52 (0.11) | 65 | 5.52 (2.10) | 62 | -0.02 (0.17) | -0.50 (-0.91, -0.10) | 0.0153 | -0.38 (-0.68, -0.07) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in MENQOL domain score - Vasomotor: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 5.67 (0.94) | 2 | | 2 | 5.67 (0.94) | 2 | | | | | |
| | | Rest of the World | 309 | 6.63 (1.29) | 302 | | 153 | 6.72 (1.20) | 149 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.9487 |
| | | Tamoxifen | 172 | 6.66 (1.30) | 168 | -2.51 (0.11) | 90 | 6.73 (1.20) | 89 | -1.08 (0.15) | -1.43 (-1.79, -1.06) | <.0001 | -1.01 (-1.28, -0.73) | |
| | | Aromatase Inhibitors | 139 | 6.58 (1.28) | 136 | -2.59 (0.12) | 65 | 6.68 (1.21) | 62 | -1.18 (0.19) | -1.41 (-1.85, -0.97) | <.0001 | -0.97 (-1.28, -0.65) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in PROMIS Total T-score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Elinzanetant 120mg (N=316) Baseline Mean (SD) | Elinzanetant 120mg (N=316) Change from BL N* | Elinzanetant 120mg (N=316) Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Placebo (N=158) Baseline Mean (SD) | Placebo (N=158) Change from BL N* | Placebo (N=158) Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 56.30 (1.41) | 2 | | 2 | 56.35 (4.31) | 2 | | | | | |
| | | Rest of the World | 311 | 60.63 (6.34) | 309 | | 153 | 60.80 (6.81) | 151 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.3296 |
| | | Tamoxifen | 174 | 61.01 (6.26) | 172 | -9.55 (0.33) | 90 | 60.51 (7.08) | 89 | -4.79 (0.46) | -4.76 (-5.88, -3.65) | <.0001 | -1.10 (-1.37, -0.82) | |
| | | Aromatase Inhibitors | 139 | 60.09 (6.41) | 139 | -9.11 (0.34) | 65 | 61.06 (6.42) | 64 | -3.54 (0.49) | -5.57 (-6.75, -4.39) | <.0001 | -1.40 (-1.73, -1.07) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in BDI-II Total score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 15.50 (19.09) | 2 | | 2 | 12.50 (6.36) | 2 | | | | | |
| | | Rest of the World | 314 | 10.35 (7.96) | 305 | | 156 | 10.68 (9.37) | 152 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.8843 |
| | | Tamoxifen | 175 | 10.03 (7.90) | 169 | 1.20 (0.45) | 90 | 8.92 (8.32) | 89 | 1.67 (0.62) | -0.47 (-1.98, 1.03) | 0.5357 | -0.08 (-0.34, 0.18) | |
| | | Aromatase Inhibitors | 141 | 10.82 (8.16) | 138 | 1.71 (0.52) | 68 | 13.06 (10.10) | 65 | 2.36 (0.76) | -0.65 (-2.47, 1.18) | 0.4845 | -0.11 (-0.40, 0.19) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in EQ-5D VAS score: MMRM analysis - Subgroup analysis
Full Analysis Set

| | | | Elinzanetant 120mg (N=316) | | | | Placebo (N=158) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline | | Change from BL | | Baseline | | Change from BL | | | | | |
| Analysis | Timepoint | Subgroup Level | N | Mean (SD) | N* | LSMean (SE) | N | Mean (SD) | N* | LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 76.50 (12.02) | 2 | | 2 | 72.00 (2.83) | 2 | | | | | |
| | | Rest of the World | 309 | 69.81 (17.72) | 306 | | 153 | 69.19 (18.28) | 151 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.0611 |
| | | Tamoxifen | 172 | 70.15 (17.91) | 170 | 3.97 (0.59) | 90 | 72.11 (18.77) | 89 | 3.99 (0.82) | -0.02 (-2.01, 1.97) | 0.9841 | -0.00 (-0.26, 0.25) | |
| | | Aromatase Inhibitors | 139 | 69.48 (17.45) | 138 | 4.80 (0.76) | 65 | 65.23 (16.63) | 64 | 1.66 (1.12) | 3.14 (0.48, 5.80) | 0.0210 | 0.35 (0.05, 0.65) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in Insomnia Severity Index (ISI) total score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 12.50 (3.54) | 2 | | 2 | 10.50 (2.12) | 2 | | | | | |
| | | Rest of the World | 311 | 16.29 (5.17) | 304 | | 153 | 16.27 (5.33) | 150 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.3413 |
| | | Tamoxifen | 174 | 16.59 (5.08) | 170 | -6.97 (0.31) | 90 | 16.24 (5.51) | 89 | -3.96 (0.43) | -3.01 (-4.05, -1.97) | <.0001 | -0.74 (-1.01, -0.48) | |
| | | Aromatase Inhibitors | 139 | 15.85 (5.27) | 136 | -6.75 (0.34) | 65 | 16.12 (5.12) | 63 | -2.97 (0.50) | -3.77 (-4.96, -2.59) | <.0001 | -0.95 (-1.27, -0.64) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Mental Component Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 45.00 (19.80) | 2 | | 2 | 36.50 (0.71) | 1 | | | | | |
| | | Rest of the World | 307 | 45.56 (10.54) | 280 | | 151 | 46.80 (10.94) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.8039 |
| | | Tamoxifen | 171 | 45.73 (10.62) | 156 | 2.74 (0.58) | 89 | 47.43 (11.68) | 84 | 2.64 (0.81) | 0.10 (-1.86, 2.07) | 0.9168 | 0.01 (-0.25, 0.28) | |
| | | Aromatase Inhibitors | 138 | 45.35 (10.54) | 126 | 1.30 (0.72) | 64 | 45.61 (9.79) | 56 | 0.79 (1.08) | 0.51 (-2.04, 3.07) | 0.6939 | 0.06 (-0.25, 0.38) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Physical Component Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 46.50 (4.95) | 2 | | 2 | 54.00 (2.83) | 1 | | | | | |
| | | Rest of the World | 307 | 45.78 (8.66) | 280 | | 151 | 44.49 (7.98) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.3812 |
| | | Tamoxifen | 171 | 46.22 (8.42) | 156 | 2.42 (0.45) | 89 | 46.28 (7.70) | 84 | 0.89 (0.62) | 1.53 (0.02, 3.05) | 0.0476 | 0.27 (0.00, 0.54) | |
| | | Aromatase Inhibitors | 138 | 45.23 (8.91) | 126 | 0.71 (0.56) | 64 | 42.30 (7.90) | 56 | -1.93 (0.84) | 2.64 (0.65, 4.64) | 0.0097 | 0.42 (0.10, 0.74) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Bodily Pain Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 52.50 (3.54) | 2 | | 2 | 50.50 (6.36) | 1 | | | | | |
| | | Rest of the World | 307 | 44.03 (9.81) | 280 | | 151 | 44.12 (9.12) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.9954 |
| | | Tamoxifen | 171 | 44.53 (9.96) | 156 | 1.94 (0.62) | 89 | 46.63 (8.73) | 84 | -0.64 (0.86) | 2.58 (0.50, 4.67) | 0.0155 | 0.33 (0.06, 0.60) | |
| | | Aromatase Inhibitors | 138 | 43.54 (9.61) | 126 | 1.21 (0.64) | 64 | 40.83 (8.58) | 56 | -1.36 (0.97) | 2.57 (0.27, 4.87) | 0.0285 | 0.36 (0.04, 0.67) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 General Health Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 45.00 (14.14) | 2 | | 2 | 50.00 (1.41) | 1 | | | | | |
| | | Rest of the World | 307 | 46.90 (8.74) | 280 | | 151 | 46.40 (9.37) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.5772 |
| | | Tamoxifen | 171 | 47.23 (8.79) | 156 | 1.13 (0.49) | 89 | 48.13 (9.18) | 84 | 0.31 (0.69) | 0.83 (-0.85, 2.51) | 0.3332 | 0.13 (-0.13, 0.40) | |
| | | Aromatase Inhibitors | 138 | 46.47 (8.73) | 126 | -0.05 (0.60) | 64 | 44.09 (9.07) | 56 | -1.65 (0.91) | 1.60 (-0.56, 3.76) | 0.1448 | 0.24 (-0.08, 0.55) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Mental Health Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 44.00 (15.56) | 2 | | 2 | 46.50 (2.12) | 1 | | | | | |
| | | Rest of the World | 307 | 46.17 (9.49) | 280 | | 151 | 47.26 (9.71) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.4067 |
| | | Tamoxifen | 171 | 46.57 (9.51) | 156 | 2.13 (0.55) | 89 | 48.33 (9.86) | 84 | 1.87 (0.00) | 0.25 (-0.56, 1.07) | 0.5406 | 0.05 (-0.22, 0.31) | |
| | | Aromatase Inhibitors | 138 | 45.64 (9.51) | 126 | 0.51 (0.70) | 64 | 45.77 (9.22) | 56 | -0.84 (1.04) | 1.35 (-1.13, 3.83) | 0.2831 | 0.17 (-0.14, 0.49) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Physical Function Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 41.00 (7.07) | 2 | | 2 | 52.00 (5.66) | 1 | | | | | |
| | | Rest of the World | 307 | 47.54 (8.66) | 280 | | 151 | 46.52 (8.37) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.0084 |
| | | Tamoxifen | 171 | 48.43 (8.33) | 156 | 2.24 (0.38) | 89 | 48.28 (7.63) | 84 | 1.89 (0.53) | 0.34 (-0.95, 1.63) | 0.6011 | 0.07 (-0.19, 0.34) | |
| | | Aromatase Inhibitors | 138 | 46.33 (8.94) | 126 | 1.08 (0.56) | 64 | 44.25 (8.79) | 56 | -2.44 (0.84) | 3.53 (1.52, 5.53) | 0.0006 | 0.56 (0.24, 0.88) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Role Physical Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 47.50 (7.78) | 2 | | 2 | 49.50 (2.12) | 1 | | | | | |
| | | Rest of the World | 307 | 44.21 (8.98) | 280 | | 151 | 43.62 (7.71) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.8614 |
| | | Tamoxifen | 171 | 44.37 (9.16) | 156 | 4.16 (0.52) | 89 | 44.12 (8.37) | 84 | 2.88 (0.73) | 1.28 (-0.48, 3.05) | 0.1525 | 0.19 (-0.07, 0.46) | |
| | | Aromatase Inhibitors | 138 | 44.05 (8.75) | 126 | 1.17 (0.59) | 64 | 43.09 (6.64) | 56 | -0.36 (0.89) | 1.53 (-0.59, 3.64) | 0.1555 | 0.23 (-0.09, 0.54) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Role of Emotional Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 48.00 (11.31) | 2 | | 2 | 35.00 (2.83) | 1 | | | | | |
| | | Rest of the World | 307 | 45.31 (10.73) | 280 | | 151 | 46.72 (11.10) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | NE |
| | | Tamoxifen | 171 | 46.02 (10.71) | 156 | NE | 89 | 47.42 (11.37) | 84 | NE | NE | | NE | |
| | | Aromatase Inhibitors | 138 | 44.46 (10.70) | 126 | 2.32 (0.72) | 64 | 45.39 (10.71) | 56 | 0.74 (1.08) | 1.58 (-0.98, 4.14) | 0.2247 | 0.20 (-0.12, 0.51) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Social Functioning Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| | | | Elinzanetant 120mg (N=316) | | | | Placebo (N=158) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline | | Change from BL | | Baseline | | Change from BL | | | | | |
| Analysis | Timepoint | Subgroup Level | N | Mean (SD) | N* | LSMean (SE) | N | Mean (SD) | N* | LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 39.50 (24.75) | 2 | | 2 | 37.00 (0.00) | 1 | | | | | |
| | | Rest of the World | 307 | 45.06 (9.99) | 280 | | 151 | 45.31 (10.01) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.6030 |
| | | Tamoxifen | 171 | 45.07 (10.25) | 156 | 3.64 (0.60) | 89 | 46.21 (10.63) | 84 | 3.18 (0.83) | 0.46 (-1.56, 2.48) | 0.6549 | 0.06 (-0.20, 0.33) | |
| | | Aromatase Inhibitors | 138 | 44.97 (9.86) | 126 | 1.33 (0.75) | 64 | 43.80 (8.93) | 56 | -0.01 (1.12) | 1.34 (-1.32, 4.00) | 0.3221 | 0.16 (-0.16, 0.47) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Change from baseline in SF36 Vitality Standardized Score: MMRM analysis - Subgroup analysis
Full Analysis Set

| Analysis | Timepoint | Subgroup Level | Elinzanetant 120mg (N=316) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Placebo (N=158) Baseline N | Baseline Mean (SD) | Change from BL N* | Change from BL LSMean (SE) | Difference of LSMeans (95% CI) | p-Value | Hedges'g (95% CI) | Interaction p-Value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MMRM until week 12 | OVERALL | Region | | | | | | | | | | | | |
| | | North America | 2 | 48.50 (17.68) | 2 | | 2 | 44.50 (3.54) | 1 | | | | | |
| | | Rest of the World | 307 | 45.35 (9.10) | 280 | | 151 | 44.14 (8.78) | 139 | | | | | |
| | | Type of treatment for the pre-existing condition | | | | | | | | | | | | 0.9533 |
| | | Tamoxifen | 171 | 45.16 (9.07) | 156 | 3.32 (0.58) | 89 | 45.49 (9.18) | 84 | 2.68 (0.80) | 0.64 (-1.30, 2.58) | 0.5159 | 0.09 (-0.18, 0.35) | |
| | | Aromatase Inhibitors | 138 | 45.63 (9.23) | 126 | 0.98 (0.61) | 64 | 42.27 (7.74) | 56 | 0.43 (0.93) | 0.55 (-1.65, 2.76) | 0.6205 | 0.08 (-0.23, 0.40) | |

Effect measures are calculated if each subgroup level comprises at least 10 patients.
Mixed model for repeated measures (MMRM) for change from baseline includes factors for baseline, time as a continuous variable, treatment, treatment-by-time interaction and baseline-by-time interaction. An unstructured covariance structure is used.
N* describes number of patients included in the MMRM, e.g. all patients with non-missing values at baseline and at least one post-baseline visit up to visit cutpoint.
p-Value for interaction from test for heterogeneity of the mean differences in the subgroups using Cochrane`s Q statistic.
BL: Baseline, N: Number of subjects included in the analysis, SD: Standard Deviation; LSMean: Least Square Mean, SE: Standard Error; CI=Confidence Interval

## Anhang 4-G2: Ergänzende Analysen zu den Subgruppen (Sicherheit)

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 1/ 2 ( 50.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 219/ 313 ( 70.0) | 98/ 156 ( 62.8) | | | |
| | Type of treatment for the pre-existing condition | | | | | 0.1019 |
| | Tamoxifen | 119/ 174 ( 68.4) | 49/ 90 ( 54.4) | 1.26 (1.01, 1.56) | 0.0370 | |
| | Aromatase Inhibitors | 101/ 141 ( 71.6) | 49/ 68 ( 72.1) | 0.99 (0.83, 1.19) | 0.9486 | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Serious Adverse Events - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 8/ 313 ( 2.6) | 1/ 156 ( 0.6) | | | |
| | Type of treatment for the pre-existing condition | | | | | |
| | Tamoxifen | 5/ 174 ( 2.9) | 0/ 90 ( 0.0) | | | |
| | Aromatase Inhibitors | 3/ 141 ( 2.1) | 1/ 68 ( 1.5) | | | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Severe Adverse Events - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 13/ 313 ( 4.2) | 4/ 156 ( 2.6) | | | |
| | Type of treatment for the pre-existing condition | | | | | |
| | Tamoxifen | 6/ 174 ( 3.4) | 2/ 90 ( 2.2) | | | |
| | Aromatase Inhibitors | 7/ 141 ( 5.0) | 2/ 68 ( 2.9) | | | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events leading to discontinuation of study drug - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 23/ 313 ( 7.3) | 4/ 156 ( 2.6) | | | |
| | Type of treatment for the pre-existing condition | | | | | 0.6322 |
| | Tamoxifen | 14/ 174 ( 8.0) | 2/ 90 ( 2.2) | 3.62 (0.84, 15.58) | 0.0840 | |
| | Aromatase Inhibitors | 9/ 141 ( 6.4) | 2/ 68 ( 2.9) | 2.17 (0.48, 9.77) | 0.3128 | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events leading to death - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 0/ 313 ( 0.0) | 0/ 156 ( 0.0) | | | |
| | Type of treatment for the pre-existing condition | | | | | |
| | Tamoxifen | 0/ 174 ( 0.0) | 0/ 90 ( 0.0) | | | |
| | Aromatase Inhibitors | 0/ 141 ( 0.0) | 0/ 68 ( 0.0) | | | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events excluding disease-related events - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 1/ 2 ( 50.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 219/ 313 ( 70.0) | 98/ 156 ( 62.8) | | | |
| | Type of treatment for the pre-existing condition | | | | | 0.1019 |
| | Tamoxifen | 119/ 174 ( 68.4) | 49/ 90 ( 54.4) | 1.26 (1.01, 1.56) | 0.0370 | |
| | Aromatase Inhibitors | 101/ 141 ( 71.6) | 49/ 68 ( 72.1) | 0.99 (0.83, 1.19) | 0.9486 | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Serious Adverse Events excluding disease-related events - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 8/ 313 ( 2.6) | 1/ 156 ( 0.6) | | | |
| | Type of treatment for the pre-existing condition | | | | | |
| | Tamoxifen | 5/ 174 ( 2.9) | 0/ 90 ( 0.0) | | | |
| | Aromatase Inhibitors | 3/ 141 ( 2.1) | 1/ 68 ( 1.5) | | | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Severe Adverse Events excluding disease-related events - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 13/ 313 ( 4.2) | 4/ 156 ( 2.6) | | | |
| | Type of treatment for the pre-existing condition | | | | | |
| | Tamoxifen | 6/ 174 ( 3.4) | 2/ 90 ( 2.2) | | | |
| | Aromatase Inhibitors | 7/ 141 ( 5.0) | 2/ 68 ( 2.9) | | | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events leading to discontinuation of study drug excluding disease-related events - Subgroup analysis
Safety Analysis Set

| Timepoint | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|
| Week 1-12 | Region | | | | | |
| | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | Rest of the World | 23/ 313 ( 7.3) | 4/ 156 ( 2.6) | | | |
| | Type of treatment for the pre-existing condition | | | | | 0.6322 |
| | Tamoxifen | 14/ 174 ( 8.0) | 2/ 90 ( 2.2) | 3.62 (0.84, 15.58) | 0.0840 | |
| | Aromatase Inhibitors | 9/ 141 ( 6.4) | 2/ 68 ( 2.9) | 2.17 (0.48, 9.77) | 0.3128 | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

| Timepoint | SOC/PT | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|
| Week 1-12 | SOC: General disorders and administration site conditions | Region | | | | | |
| | | North America | 1/ 2 ( 50.0) | 0/ 2 ( 0.0) | | | |
| | | Rest of the World | 59/ 313 ( 18.8) | 12/ 156 ( 7.7) | | | |
| | | Type of treatment for the pre-existing condition | | | | | 0.5061 |
| | | Tamoxifen | 33/ 174 ( 19.0) | 8/ 90 ( 8.9) | 2.13 (1.03, 4.42) | 0.0417 | |
| | | Aromatase Inhibitors | 27/ 141 ( 19.1) | 4/ 68 ( 5.9) | 3.26 (1.19, 8.93) | 0.0219 | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with frequent Adverse Event by SOC and PT (incidence in either arm >= 10% or both incidence >=1% and >=10 patients affected in either arm) - Subgroup analysis
Safety Analysis Set

| Timepoint | SOC/PT | Subgroup Level | Elinzanetant 120mg (N=315) n/ N (%) | Placebo (N=158) n/ N (%) | Elinzanetant 120mg vs. Placebo Relative Risk (95% CI) | p-Value | Interaction p-Value |
|---|---|---|---|---|---|---|---|
| Week 1-12 | SOC: Nervous system disorders, PT: Somnolence | Region | | | | | |
| | | North America | 0/ 2 ( 0.0) | 0/ 2 ( 0.0) | | | |
| | | Rest of the World | 34/ 313 ( 10.9) | 6/ 156 ( 3.8) | | | |
| | | Type of treatment for the pre-existing condition | | | | | 0.3550 |
| | | Tamoxifen | 23/ 174 ( 13.2) | 3/ 90 ( 3.3) | 3.97 (1.22, 12.85) | 0.0217 | |
| | | Aromatase Inhibitors | 11/ 141 ( 7.8) | 3/ 68 ( 4.4) | 1.77 (0.51, 6.13) | 0.3689 | |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.
Subgroup analysis only for SOC / PT with significant overall treatment effect based on relative risk (alpha=0.05).
RR estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test). Analysis includes factor for study.
p-Value for interaction is calculated from test for heterogeneity of the Relative Risks in the subgroups using Cochrane`s Q statistic.
n=Number of subjects with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; NE=Not estimable

## Anhang 4-G3: Langzeitdaten (Sicherheit)

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 267/315 ( 84.8) | 126/158 ( 79.7) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Serious Adverse Events
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 20/315 ( 6.3) | 13/158 ( 8.2) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Severe Adverse Events
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 23/315 ( 7.3) | 13/158 ( 8.2) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events leading to discontinuation of study drug
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 29/315 ( 9.2) | 12/158 ( 7.6) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events leading to death
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 0/315 ( 0.0) | 0/158 ( 0.0) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events excluding disease-related events
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 266/315 ( 84.4) | 125/158 ( 79.1) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Serious Adverse Events excluding disease-related events
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 20/315 ( 6.3) | 13/158 ( 8.2) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Severe Adverse Events excluding disease-related events
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 23/315 ( 7.3) | 13/158 ( 8.2) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.

Bayer Vital GmbH
Elinzanetant - Study 21656 (OASIS-4) - Last patient last visit: 14 Nov 2024
Study population
Analysis of number of subjects with Adverse Events leading to discontinuation of study drug excluding disease-related events
Safety Analysis Set

| Timepoint | | Elinzanetant 120mg | Placebo |
|---|---|---|---|
| During study | Number of subjects with event, n/N (%) | 29/315 ( 9.2) | 12/158 ( 7.6) |

Analysis based on Treatment-Emergent Adverse Events (TEAEs).
RR, OR, RD estimated using Mantel-Haenszel method or logit method in case of zero events. 95% confidence intervals and p-values constructed using normal approximation (Wald test).
n=Number of patients with event; N=Number of patients included in the analysis; CI=Confidence Interval; RR=Relative Risk; OR=Odds Ratio; RD=Risk Difference; NE=Not estimable.