



Clinical trial results:

A Phase 2a, Proof of Concept, Randomized, Double-blind, Placebo-controlled Clinical Trial, to Evaluate the Efficacy and Safety of MK-7264 in Women with Moderate to Severe Endometriosis-related Pain

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-001098-26 |
| Trial protocol | ES PL |
| Global end of trial date | 30 June 2020 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 01 July 2021 |
| First version publication date | 01 July 2021 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | MK-7264-034 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03654326 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 30 June 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 June 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 June 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy, safety, and tolerability of gefapixant (MK-7264) in premenopausal female participants with moderate to severe endometriosis-related pain. The primary hypothesis: gefapixant is superior to placebo in reducing the average daily pelvic pain score (cyclic and non-cyclic, combined) during Treatment Cycle 2.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 11 September 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 4 |
| Country: Number of subjects enrolled | Chile: 6 |
| Country: Number of subjects enrolled | New Zealand: 6 |
| Country: Number of subjects enrolled | Poland: 29 |
| Country: Number of subjects enrolled | Puerto Rico: 20 |
| Country: Number of subjects enrolled | Russian Federation: 53 |
| Country: Number of subjects enrolled | Ukraine: 21 |
| Country: Number of subjects enrolled | United States: 48 |
| Worldwide total number of subjects | 187 |
| EEA total number of subjects | 29 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |

| | |
|--|-----|
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 187 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a baseline menstrual cycle (approximately 4 weeks) prior to randomization to either gefapixant or placebo.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Gefapixant |

Arm description:

Participants received a gefapixant 45 mg tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Gefapixant |
| Investigational medicinal product code | |
| Other name | MK-7264 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Gefapixant 45 mg tablet twice a day for approximately 8 weeks (2 menstrual cycles).

| | |
|--|----------|
| Investigational medicinal product name | Naproxen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Naproxen sodium 275 mg tablets taken orally as rescue medication for endometriosis-related pain, at dose prescribed by sites' principal investigator

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Participants received a placebo matching gefapixant tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo-matching gefapixant tablet twice a day for approximately 8 weeks (2 menstrual cycles).

| | |
|--|----------|
| Investigational medicinal product name | Naproxen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Naproxen sodium 275 mg tablets taken orally as rescue medication for endometriosis-related pain, at dose prescribed by sites' principal investigator

| Number of subjects in period 1 | Gefapixant | Placebo |
|---------------------------------------|------------|---------|
| Started | 94 | 93 |
| Completed | 88 | 87 |
| Not completed | 6 | 6 |
| Consent withdrawn by subject | 5 | 3 |
| Physician decision | - | 1 |
| Unable to adhere to study schedule | - | 1 |
| Lost to follow-up | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|------------|
| Reporting group title | Gefapixant |
| Reporting group description: | |
| Participants received a gefapixant 45 mg tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received a placebo matching gefapixant tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain. | |

| Reporting group values | Gefapixant | Placebo | Total |
|---|------------|---------|-------|
| Number of subjects | 94 | 93 | 187 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 94 | 93 | 187 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 34.5 | 34.8 | |
| standard deviation | ± 6.6 | ± 7.3 | - |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 94 | 93 | 187 |
| Male | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 35 | 31 | 66 |
| Not Hispanic or Latino | 59 | 62 | 121 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 1 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 4 | 3 | 7 |
| White | 88 | 86 | 174 |
| More than one race | 1 | 4 | 5 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Average Daily Pelvic Pain Score | | | |
| Pelvic pain severity was measured using a 0-10 numeric rating scale (NRS), with 0 representing no pain and 10 representing extremely severe pain. The average of the daily pelvic pain scores entered in participants' electronic diaries (eDiaries) was calculated for the baseline cycle (approximately 28 days). | | | |
| Units: Scores on a Scale | | | |
| arithmetic mean | 6.5 | 6.5 | |
| standard deviation | ± 1.0 | ± 1.0 | - |

End points

End points reporting groups

| | |
|--|------------|
| Reporting group title | Gefapixant |
| Reporting group description: Participants received a gefapixant 45 mg tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received a placebo matching gefapixant tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain. | |

Primary: Change From Baseline in Average Daily Pelvic Pain Score During Treatment Cycle 2

| | |
|---|--|
| End point title | Change From Baseline in Average Daily Pelvic Pain Score During Treatment Cycle 2 |
| End point description: Pelvic pain (cyclic pain associated with menses, and non-cyclic pain not associated with menses) severity score was measured using a 0-10 numeric rating scale (NRS), with 0 representing no pain and 10 representing extremely severe pain. The averages of the daily pelvic pain scores (cyclic and non-cyclic, combined) entered in participants' electronic diaries (eDiaries) were calculated for Baseline and Treatment Cycle 2 (approximately Week 4 to Week 8). A negative change indicates a decrease in pain severity from baseline. The population analyzed included all randomized participants who received at least one dose of double-blind study intervention and had at least one day of eDiary entries during the post-randomization treatment cycle. | |
| End point type | Primary |
| End point timeframe: Baseline and Treatment Cycle 2 (Week 4 to Week 8; each cycle is approximately 28 days) | |

| End point values | Gefapixant | Placebo | | |
|--|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 94 | 93 | | |
| Units: Scores on a Scale | | | | |
| least squares mean (confidence interval 95%) | -2.2 (-2.79 to -1.62) | -1.7 (-2.30 to -1.13) | | |

Statistical analyses

| | |
|----------------------------|----------------------------------|
| Statistical analysis title | Difference in Least Squares Mean |
| Comparison groups | Gefapixant v Placebo |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 187 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.066 ^[1] |
| Method | ANCOVA |
| Parameter estimate | Difference in Least Squares Mean |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.01 |
| upper limit | 0.03 |

Notes:

[1] - Based on the longitudinal analysis of covariance (ANCOVA) model including factors for average pelvic pain scores at baseline cycle, stratum, treatment, cycle, interaction of stratum-by-cycle, and the interaction of treatment-by-cycle as covariates

Primary: Percentage of Participants Who Experienced an Adverse Event

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Experienced an Adverse Event |
|-----------------|---|

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. Per protocol, this analysis included AEs reported up to 14 days after end of study intervention (up to approximately 10 weeks). The population analyzed included all randomized participants who received at least one dose of study intervention.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to approximately 10 weeks

| End point values | Gefapixant | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 94 | 93 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 53.2 | 35.5 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference in Percentage of Participants |
| Comparison groups | Gefapixant v Placebo |
| Number of subjects included in analysis | 187 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| Parameter estimate | Difference in % vs Placebo |
| Point estimate | 17.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.4 |
| upper limit | 31.3 |

Notes:

[2] - Based on Miettinen & Nurminen method

Primary: Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The population analyzed included all randomized participants who received at least one dose of study intervention.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to approximately 8 weeks

| End point values | Gefapixant | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 94 | 93 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 3.2 | 0 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference in Percentage of Participants |
| Comparison groups | Gefapixant v Placebo |
| Number of subjects included in analysis | 187 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[3] |
| Parameter estimate | Difference in % vs Placebo |
| Point estimate | 3.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 9 |

Notes:

[3] - Based on Miettinen & Nurminen method.

Secondary: Change From Baseline in Average Daily Cyclic Pelvic Pain Score During

Treatment Cycle 2

| | |
|-----------------|---|
| End point title | Change From Baseline in Average Daily Cyclic Pelvic Pain Score During Treatment Cycle 2 |
|-----------------|---|

End point description:

Cyclic pelvic pain (associated with menses) severity score was measured using a 0-10 NRS, with 0 representing no pain and 10 representing extremely severe pain. The average of the daily cyclic pelvic pain scores entered in participants' eDiaries was calculated for Baseline and Treatment Cycle 2 (Week 4 to Week 8). A negative change indicates a decrease in pain severity from baseline. The population analyzed included all randomized participants who received at least one dose of double-blind study intervention, had at least one day of eDiary entry during the post-randomization treatment cycle, and had available cyclic pelvic pain score data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Treatment Cycle 2 (Week 4 to Week 8; each cycle is approximately 28 days)

| End point values | Gefapixant | Placebo | | |
|--|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 89 | 90 | | |
| Units: Scores on a Scale | | | | |
| least squares mean (confidence interval 95%) | -2.0 (-2.55 to -1.35) | -1.3 (-1.94 to -0.73) | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Difference in Least Squares Mean |
| Comparison groups | Gefapixant v Placebo |
| Number of subjects included in analysis | 179 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[4] |
| Parameter estimate | Difference in Least Squares Mean |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.18 |
| upper limit | -0.06 |

Notes:

[4] - The difference in least squares mean was based on the longitudinal analysis of covariance (ANCOVA) model including factors for average pelvic pain scores at baseline cycle, stratum, treatment, cycle, interaction of stratum-by-cycle, and the interaction of treatment-by-cycle as covariates

Secondary: Change From Baseline in Average Daily Non-Cyclic Pelvic Pain Score During Treatment Cycle 2

| | |
|-----------------|---|
| End point title | Change From Baseline in Average Daily Non-Cyclic Pelvic Pain Score During Treatment Cycle 2 |
|-----------------|---|

End point description:

Non-cyclic pelvic pain (not associated with menses) severity score was measured using a 0-10 NRS, with 0 representing no pain and 10 representing extremely severe pain. The average of the non-cyclic daily pelvic pain scores entered in participants' eDiaries was calculated for the Baseline and Treatment Cycle 2 (Week 4 to Week 8). A negative change indicates decrease in pain severity from baseline. The population analyzed included all randomized participants who received at least one dose of double-blind

study intervention, had at least one day of eDiary entry during the post-randomization treatment cycle, and had available non-cyclic pelvic pain score data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Treatment Cycle 2 (Week 4 to Week 8; each cycle is approximately 28 days)

| End point values | Gefapixant | Placebo | | |
|--|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 90 | | |
| Units: Scores on a Scale | | | | |
| least squares mean (confidence interval 95%) | -2.3 (-2.90 to -1.69) | -1.8 (-2.40 to -1.18) | | |

Statistical analyses

| Statistical analysis title | Difference in Least Squares Mean |
|---|----------------------------------|
| Comparison groups | Gefapixant v Placebo |
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| Parameter estimate | Difference in Least Squares Mean |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.04 |
| upper limit | 0.03 |

Notes:

[5] - The difference in least squares mean was based on the longitudinal analysis of covariance (ANCOVA) model including factors for average pelvic pain scores at baseline cycle, stratum, treatment, cycle, interaction of stratum-by-cycle, and the interaction of treatment-by-cycle as covariates

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: Up to approximately 24 weeks

Serious adverse events and non-serious adverse events: Up to approximately 12 weeks

Adverse event reporting additional description:

All randomized participants who received at least one dose of study intervention.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Gefapixant |
|-----------------------|------------|

Reporting group description:

Participants received a gefapixant 45 mg tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received a placebo matching gefapixant tablet twice a day for approximately 8 weeks (2 menstrual cycles). Naproxen sodium 275 mg tablets were also provided to participants, as needed, for endometriosis-related pain.

| Serious adverse events | Gefapixant | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 93 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Gefapixant | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 36 / 94 (38.30%) | 12 / 93 (12.90%) | |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 9 / 94 (9.57%) | 1 / 93 (1.08%) | |
| occurrences (all) | 9 | 1 | |
| Dysgeusia | | | |

| | | | |
|--|------------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 15 / 94 (15.96%) 16 | 2 / 93 (2.15%) 2 | |
| Headache subjects affected / exposed occurrences (all) | 4 / 94 (4.26%) 4 | 7 / 93 (7.53%) 7 | |
| Hypogeusia subjects affected / exposed occurrences (all) | 5 / 94 (5.32%) 5 | 0 / 93 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 6 / 94 (6.38%) 6 | 0 / 93 (0.00%) 0 | |
| Dry mouth subjects affected / exposed occurrences (all) | 6 / 94 (6.38%) 6 | 2 / 93 (2.15%) 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported