



Clinical trial results:

A Multicenter, Double-Blind, Randomized, Parallel, Placebo Controlled Trial Assessing the Analgesic Efficacy of a Single, Oral Dose of a Fast Release Aspirin 650 mg in Postsurgical Dental Pain

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-005278-12 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 06 August 2010 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 12 July 2016 |
| First version publication date | 16 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY1019036/15082 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01122602 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bayer HealthCare AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, D-51368, Leverkusen, Germany, |
| Public contact | Clinical Trials Contact, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com |
| Scientific contact | Clinical Trials Contact, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.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? | Yes |

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 06 August 2010 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 August 2010 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the analgesic efficacy of a single oral dose of fast release aspirin tablets, 650 milligram (mg) (2 × 325 mg) compared to regular aspirin tablets, 650 mg (2 × 325 mg) and placebo in subjects with post-surgical dental pain.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. This study was conducted according to the principles of the International Conference on Harmonisation harmonised tripartite guideline E6(R1): Good Clinical Practice, the World Medical Association Declaration of Helsinki and its most recent amendments, and United States Title 21 of the Code of Federal Regulations Parts 50 and 56 concerning informed consent and Institutional Review Board regulations. Before entering the study, the informed consent form was read by and explained to all subjects and/or their legally authorized representative. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 29 April 2010 |
| 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 | United States: 500 |
| Worldwide total number of subjects | 500 |
| EEA total number of subjects | 0 |

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) | 123 |
| Adults (18-64 years) | 377 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at two study centers in the United States between 29 Apr 2010 (first subject first visit) and 06 August 2010 (last subject last visit).

Pre-assignment

Screening details:

A total of 500 subjects entered the study and were randomly assigned to 1 of 3 treatment groups; 497 subjects completed the study.

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 | Investigator, Data analyst, Subject |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

Arm description:

Single oral dose of fast release aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 milliliter [mL]) between 1-4 hours post dental surgery.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Acetylsalicyclic acid (Fast release Aspirin) |
| Investigational medicinal product code | BAY1019036 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single oral dose of fast release aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 mL) between 1-4 hours post dental surgery.

| | |
|------------------|---|
| Arm title | Acetylsalicyclic acid (Aspirin, BAYE4465) |
|------------------|---|

Arm description:

Single oral dose of regular aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 mL) between 1-4 hours post dental surgery.

| | |
|--|-----------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Acetylsalicyclic acid |
| Investigational medicinal product code | BAYE4465 |
| Other name | Aspirin |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Single oral dose of regular aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 mL) between 1-4 hours post dental surgery.

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

Arm description:

Single oral dose of 2 placebo tablets with a full glass of water (240 mL) between 1-4 hours post dental surgery.

| | |
|----------|---------|
| 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:

Single oral dose of 2 placebo tablets with a full glass of water (240 mL) between 1-4 hours post dental surgery.

| Number of subjects in period 1 | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo |
|--------------------------------|---|--|---------|
| | | | |
| Started | 200 | 200 | 100 |
| Completed | 200 | 199 | 98 |
| Not completed | 0 | 1 | 2 |
| Consent withdrawn by subject | - | - | 1 |
| Adverse event | - | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Reporting group description: Single oral dose of fast release aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 milliliter [mL]) between 1-4 hours post dental surgery. | |
| Reporting group title | Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Reporting group description: Single oral dose of regular aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 mL) between 1-4 hours post dental surgery. | |
| Reporting group title | Placebo |
| Reporting group description: Single oral dose of 2 placebo tablets with a full glass of water (240 mL) between 1-4 hours post dental surgery. | |

| Reporting group values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo |
|------------------------------------|--|---|---------|
| Number of subjects | 200 | 200 | 100 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------|--------|--------|
| Age continuous | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 20.3 | 20.8 | 20.7 |
| standard deviation | ± 3.33 | ± 4.05 | ± 3.57 |
| Gender categorical | | | |
| Gender categorical | | | |
| Units: subjects | | | |
| Female | 137 | 117 | 66 |
| Male | 63 | 83 | 34 |
| Baseline Pain Intensity by Categorical Scale | | | |
| Pain Intensity (PI) was rated by subjects on a 4-point categorical Pain Intensity Scale (0 = no pain, 1 = mild pain, 2 = moderate pain, and 3 = severe pain). | | | |
| Units: Subjects | | | |
| Moderate pain | 114 | 111 | 56 |
| Severe pain | 86 | 89 | 44 |
| Baseline Pain by 11-Point Pain Intensity | | | |
| When subjects indicated at least moderate pain, they were asked to score their pain on the 11-Point Numerical Pain Intensity Rating Scale (0 = no pain, 10 = very painful). | | | |
| Units: scores on a scale | | | |
| arithmetic mean | 7.3 | 7.4 | 7.5 |
| standard deviation | ± 1.3 | ± 1.35 | ± 1.4 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 500 | | |

| | | | |
|---|-----|--|--|
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Gender categorical | | | |
| Units: subjects | | | |
| Female | 320 | | |
| Male | 180 | | |
| Baseline Pain Intensity by Categorical Scale | | | |
| Pain Intensity (PI) was rated by subjects on a 4-point categorical Pain Intensity Scale (0 = no pain, 1 = mild pain, 2 = moderate pain, and 3 = severe pain). | | | |
| Units: Subjects | | | |
| Moderate pain | 281 | | |
| Severe pain | 219 | | |
| Baseline Pain by 11-Point Pain Intensity | | | |
| When subjects indicated at least moderate pain, they were asked to score their pain on the 11-Point Numerical Pain Intensity Rating Scale (0 = no pain, 10 = very painful). | | | |
| Units: scores on a scale | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Reporting group description: Single oral dose of fast release aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 milliliter [mL]) between 1-4 hours post dental surgery. | |
| Reporting group title | Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Reporting group description: Single oral dose of regular aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 mL) between 1-4 hours post dental surgery. | |
| Reporting group title | Placebo |
| Reporting group description: Single oral dose of 2 placebo tablets with a full glass of water (240 mL) between 1-4 hours post dental surgery. | |
| Subject analysis set title | Safety analysis set (SAF) population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: SAF population included all randomized subjects who took at least 1 dose of the study drug. | |
| Subject analysis set title | Intent-to-treat (ITT) population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: ITT population included all randomized subjects who took at least 1 dose of the study drug and who had at least 1 post-dose assessment on an efficacy parameter. | |

Primary: Time to First Perceptible Pain Relief (PR)

| | |
|---|--|
| End point title | Time to First Perceptible Pain Relief (PR) |
| End point description: The double-stopwatch method was used to record time to first perceptible PR. Time to first perceptible PR was defined as the duration from the subject taking the study drug until the subject first began to feel any pain-relieving effect from the study drug. | |
| End point type | Primary |
| End point timeframe: 0 to 6 hours | |

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|----------------------------------|--|---|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[1] | 200 ^[2] | 100 ^[3] | |
| Units: minutes | | | | |
| median (confidence interval 95%) | 19.8 (18.23 to 20) | 23.7 (19.2 to 30) | 41.4 (30.68 to 103.9) | |

Notes:

[1] - ITT population.

[2] - ITT population.

[3] - ITT population.

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

Primary: Time to First Perceptible Pain Relief Confirmed

| | |
|--|---|
| End point title | Time to First Perceptible Pain Relief Confirmed |
| End point description: The double-stopwatch method was used to record time to first perceptible PR confirmed. Time to first perceptible PR confirmed was defined as the duration from the subject taking the study drug until the first stopwatch was stopped as long as the subject stopped the second stopwatch at some later time or recorded either a PR score of at least 1 or a Pain Intensity Difference (PID) score of at least 1 at the next time point assessment. '99999' in the below table indicates data was not analysed as upper limit of 95 percent (%) confidence interval was not reached. | |
| End point type | Primary |
| End point timeframe: 0 to 6 hours | |

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|----------------------------------|--|---|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[4] | 200 ^[5] | 100 ^[6] | |
| Units: minutes | | | | |
| median (confidence interval 95%) | 19.8 (18.25 to 20.58) | 27.1 (19.77 to 30.37) | 57.6 (32.98 to 99999) | |

Notes:

[4] - ITT population

[5] - ITT population

[6] - ITT population

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|--|
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| Statistical analysis title | Statistical analysis 2 |
|---|--|
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| Statistical analysis title | Statistical analysis 3 |
|---|---|
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

Secondary: Time to Meaningful Pain Relief

| | |
|-----------------|--------------------------------|
| End point title | Time to Meaningful Pain Relief |
|-----------------|--------------------------------|

End point description:

Meaningful pain relief was defined as when the subject felt the degree of pain relief was meaningful to

them. Time to meaningful pain relief was determined by a double-stopwatch measurement using Kaplan-Meier estimate, provided that the subject experienced both "perceptible" and "meaningful" pain relief. Those subjects who do not achieve meaningful pain relief after 6 hours after dosing or those who took rescue medication before experiencing meaningful pain relief was censored in the analysis. '99999' in the below table indicates, the median time to meaningful PR could not be calculated for the placebo group due to timing and number of censored observations.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 0 to 6 hours | |

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|----------------------------------|--|---|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[7] | 200 ^[8] | 100 ^[9] | |
| Units: minutes | | | | |
| median (confidence interval 95%) | 48.9 (41.85 to 54.52) | 119.2 (93.55 to 192.27) | 99999 (99999 to 99999) | |

Notes:

[7] - ITT population

[8] - ITT population

[9] - ITT population

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|--|
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| Statistical analysis title | Statistical analysis 2 |
|---|--|
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| Statistical analysis title | Statistical analysis 3 |
|----------------------------|---|
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|---------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

Secondary: Pain Intensity at 10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours After Dosing

| | |
|-----------------|--|
| End point title | Pain Intensity at 10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours After Dosing |
|-----------------|--|

End point description:

Pain intensity was evaluated using a 4-point Categorical Pain Intensity Rating Scale (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain) for all pain intensity assessments post-dose.

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

End point timeframe:

10, 20, 30, 40, and 50 minutes and at 1, 2, 3, 4, 5, and 6 hours post-dose

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|-----------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[10] | 200 ^[11] | 100 ^[12] | |
| Units: subjects | | | | |
| 10 minutes: No pain | 0 | 0 | 0 | |
| 10 minutes: Mild pain | 20 | 15 | 7 | |
| 10 minutes: Moderate pain | 93 | 100 | 44 | |
| 10 minutes: Severe pain | 87 | 85 | 49 | |
| 20 minutes: No pain | 3 | 2 | 0 | |
| 20 minutes: Mild pain | 32 | 30 | 10 | |
| 20 minutes: Moderate pain | 107 | 89 | 41 | |
| 20 minutes: Severe pain | 58 | 79 | 49 | |
| 30 minutes: No pain | 11 | 2 | 0 | |
| 30 minutes: Mild pain | 75 | 39 | 12 | |
| 30 minutes: Moderate pain | 86 | 90 | 37 | |
| 30 minutes: Severe pain | 28 | 69 | 51 | |
| 40 minutes: No pain | 23 | 5 | 1 | |
| 40 minutes: Mild pain | 101 | 55 | 16 | |
| 40 minutes: Moderate pain | 60 | 80 | 36 | |
| 40 minutes: Severe pain | 16 | 60 | 47 | |
| 50 minutes: No pain | 38 | 7 | 1 | |
| 50 minutes: Mild pain | 107 | 74 | 12 | |
| 50 minutes: Moderate pain | 43 | 71 | 38 | |
| 50 minutes: Severe pain | 12 | 48 | 49 | |
| 1 hour: No Pain | 54 | 13 | 1 | |
| 1 hour: Mild Pain | 100 | 76 | 10 | |
| 1 hour: Moderate Pain | 35 | 63 | 35 | |
| 1 hour: Severe Pain | 11 | 48 | 54 | |

| | | | | |
|------------------------|----|----|----|--|
| 2 hours: No Pain | 33 | 24 | 0 | |
| 2 hours: Mild Pain | 70 | 76 | 14 | |
| 2 hours: Moderate Pain | 46 | 45 | 25 | |
| 2 hours: Severe Pain | 51 | 55 | 61 | |
| 3 hours: No Pain | 21 | 31 | 1 | |
| 3 hours: Mild Pain | 62 | 64 | 18 | |
| 3 hours: Moderate Pain | 44 | 40 | 21 | |
| 3 hours: Severe Pain | 73 | 65 | 60 | |
| 4 hours: No Pain | 24 | 30 | 3 | |
| 4 hours: Mild Pain | 45 | 57 | 20 | |
| 4 hours: Moderate Pain | 48 | 44 | 18 | |
| 4 hours: Severe Pain | 83 | 69 | 59 | |
| 5 hours: No Pain | 21 | 22 | 5 | |
| 5 hours: Mild Pain | 39 | 56 | 19 | |
| 5 hours: Moderate Pain | 48 | 48 | 17 | |
| 5 hours: Severe Pain | 92 | 74 | 59 | |
| 6 hours: No Pain | 20 | 21 | 5 | |
| 6 hours: Mild Pain | 37 | 48 | 19 | |
| 6 hours: Moderate Pain | 44 | 52 | 17 | |
| 6 hours: Severe Pain | 99 | 79 | 59 | |

Notes:

[10] - ITT population

[11] - ITT population

[12] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1: 10 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.921 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 2: 10 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) v Placebo |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.297 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 3: 10 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.32 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 4: 20 minutes postdose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.064 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 5: 20 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 6: 20 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.071 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 7: 30 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 8: 30 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 9: 30 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 10: 40 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 11: 40 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) v Placebo |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 12: 40 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 13: 50 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 14: 50 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 15: 50 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 16: 1 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 17: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 18: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 19: 2 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.453 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 20: 2 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 21: 2 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 22: 3 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.17 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 23: 3 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 24: 3 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 25: 4 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.076 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 26: 4 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 27: 4 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 28: 5 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.059 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 29: 5 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.041 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 30: 5 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 31: 6 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.074 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 32: 6 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.122 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 33: 6 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Pain Intensity Difference (PID) at 10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours After Dosing

| | |
|-----------------|---|
| End point title | Pain Intensity Difference (PID) at 10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours After Dosing |
|-----------------|---|

End point description:

Pain intensity was evaluated using a 4-point Categorical Pain Intensity Rating Scale (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain) for all pain intensity assessments post-dose. For each post-dose time point, PID was derived by subtracting the pain intensity at the post-dose time point from the baseline intensity score (baseline score – post-baseline score). A positive difference was indicative of improvement.

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

End point timeframe:

10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours post-dose

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|--------------------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[13] | 200 ^[14] | 100 ^[15] | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| 10 Minutes post-dose | 0.1 (± 0.43) | 0.1 (± 0.45) | 0 (± 0.45) | |
| 20 Minutes post-dose | 0.3 (± 0.61) | 0.2 (± 0.62) | 0.1 (± 0.54) | |
| 30 Minutes post-dose | 0.8 (± 0.79) | 0.3 (± 0.7) | 0.1 (± 0.61) | |
| 40 Minutes post-dose | 1.1 (± 0.81) | 0.5 (± 0.8) | 0.2 (± 0.75) | |
| 50 Minutes post-dose | 1.3 (± 0.86) | 0.7 (± 0.84) | 0.1 (± 0.76) | |
| 1 Hour post-dose | 1.4 (± 0.91) | 0.7 (± 0.9) | 0 (± 0.75) | |
| 2 Hours post-dose | 0.9 (± 1.11) | 0.8 (± 1.01) | 0 (± 0.77) | |
| 3 Hours post-dose | 0.6 (± 1.08) | 0.8 (± 1.07) | 0.1 (± 0.8) | |
| 4 Hours post-dose | 0.5 (± 1.09) | 0.7 (± 1.09) | 0.1 (± 0.87) | |
| 5 Hours post-dose | 0.4 (± 1.06) | 0.6 (± 1.03) | 0.2 (± 0.91) | |
| 6 Hours post-dose | 0.3 (± 1.05) | 0.5 (± 1.03) | 0.2 (± 0.92) | |

Notes:

[13] - ITT population

[14] - ITT population

[15] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1: 10 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.875 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 2: 10 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.275 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 3: 10 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.222 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 4: 20 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.073 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 5: 20 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 6: 20 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.026 |
| Method | ANCOVA |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 7: 30 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

| | |
|---|---------------|
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 8: 30 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 9: 30 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 10: 30 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 11: 40 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 12: 40 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 13: 50 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 14: 50 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 15: 50 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 16: 1 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

| | |
|---|---------------|
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 17: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 18: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 19: 2 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.456 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 20: 2 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 21: 2 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 22: 3 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.106 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 23: 3 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 24: 3 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 25: 4 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

| | |
|---|---------------|
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.049 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 26: 4 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 27: 4 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 28: 5 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.048 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 29: 5 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.057 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 30: 5 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 31: 6 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.073 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 32: 6 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.144 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 33: 6 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | ANCOVA |

Secondary: Pain Relief at 10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours After Dosing

| | |
|-----------------|---|
| End point title | Pain Relief at 10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours After Dosing |
|-----------------|---|

End point description:

Subjects rated pain relief on a 5-point categorical Pain Relief Rating Scale (0 = no relief, 1 = a little relief, 2 = some relief, 3 = a lot of relief, 4 = complete relief).

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

End point timeframe:

10, 20, 30, 40, 50, and 60 minutes and at 2, 3, 4, 5, and 6 hours post-dose

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|-----------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[16] | 200 ^[17] | 100 ^[18] | |
| Units: subjects | | | | |
| 10 minutes: No relief | 145 | 143 | 80 | |
| 10 minutes: Little relief | 43 | 46 | 15 | |
| 10 minutes: Some relief | 10 | 11 | 5 | |
| 10 minutes: Lot of relief | 2 | 0 | 0 | |
| 10 minutes: Complete relief | 0 | 0 | 0 | |
| 20 minutes: No relief | 81 | 110 | 68 | |
| 20 minutes: Little relief | 81 | 67 | 22 | |
| 20 minutes: Some relief | 26 | 16 | 9 | |
| 20 minutes: Lot of relief | 9 | 6 | 1 | |
| 20 minutes: Complete relief | 3 | 1 | 0 | |
| 30 minutes: No relief | 34 | 90 | 66 | |
| 30 minutes: Little relief | 74 | 64 | 20 | |
| 30 minutes: Some relief | 44 | 34 | 11 | |
| 30 minutes: Lot of relief | 37 | 10 | 3 | |
| 30 minutes: Complete relief | 11 | 2 | 0 | |
| 40 minutes: No relief | 19 | 67 | 59 | |
| 40 minutes: Little relief | 55 | 69 | 20 | |
| 40 minutes: Some relief | 47 | 34 | 16 | |
| 40 minutes: Lot of relief | 56 | 25 | 4 | |
| 40 minutes: Complete relief | 23 | 5 | 1 | |
| 50 minutes: No relief | 13 | 57 | 59 | |
| 50 minutes: Little relief | 37 | 61 | 22 | |
| 50 minutes: Some relief | 39 | 37 | 14 | |
| 50 minutes: Lot of relief | 73 | 38 | 4 | |
| 50 minutes: Complete relief | 38 | 7 | 1 | |
| 1 hour: No relief | 13 | 53 | 57 | |
| 1 hour: Little relief | 32 | 47 | 28 | |
| 1 hour: Some relief | 30 | 44 | 10 | |
| 1 hour: Lot of relief | 71 | 43 | 4 | |
| 1 hour: Complete relief | 54 | 13 | 1 | |
| 2 hours: No relief | 57 | 64 | 71 | |
| 2 hours: Little relief | 29 | 22 | 12 | |
| 2 hours: Some relief | 26 | 44 | 12 | |
| 2 hours: Lot of relief | 55 | 46 | 5 | |
| 2 hours: Complete relief | 33 | 24 | 0 | |
| 3 hours: No relief | 83 | 75 | 71 | |

| | | | | |
|--------------------------|-----|-----|----|--|
| 3 hours: Little relief | 28 | 18 | 10 | |
| 3 hours: Some relief | 20 | 35 | 8 | |
| 3 hours: Lot of relief | 48 | 41 | 10 | |
| 3 hours: Complete relief | 21 | 31 | 1 | |
| 4 hours: No relief | 108 | 85 | 72 | |
| 4 hours: Little relief | 14 | 19 | 5 | |
| 4 hours: Some relief | 17 | 25 | 9 | |
| 4 hours: Lot of relief | 37 | 41 | 11 | |
| 4 hours: Complete relief | 24 | 30 | 3 | |
| 5 hours: No relief | 117 | 96 | 73 | |
| 5 hours: Little relief | 13 | 21 | 5 | |
| 5 hours: Some relief | 14 | 20 | 9 | |
| 5 hours: Lot of relief | 35 | 41 | 9 | |
| 5 hours: Complete relief | 21 | 22 | 4 | |
| 6 hours: No relief | 127 | 106 | 74 | |
| 6 hours: Little relief | 8 | 15 | 5 | |
| 6 hours: Some relief | 17 | 19 | 6 | |
| 6 hours: Lot of relief | 28 | 39 | 11 | |
| 6 hours: Complete relief | 20 | 21 | 4 | |

Notes:

[16] - ITT population

[17] - ITT population

[18] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1: 10 minutes post-dose |
| Comparison groups | Acetylsalicylic acid (Aspirin, BAYE4465) v Acetylsalicylic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.869 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 2: 10 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicylic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.168 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 3: 10 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicylic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 4: 20 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 5: 20 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 6: 20 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.045 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 7: 30 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 8: 30 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 9: 30 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 10: 40 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 11: 40 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 12: 40 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 13: 50 minutes post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 14: 50 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 15: 50 minutes post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 16: 1 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 17: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 18: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 19: 2 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.205 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 20: 2 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 21: 2 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 22: 3 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.233 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 23: 3 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 24: 3 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 25: 4 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.049 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 26: 4 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 27: 4 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 28: 5 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.101 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 29: 5 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.006 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 30: 5 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 31: 6 hours post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.067 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 32: 6 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.042 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 33: 6 hours post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Summed Pain Intensity Differences (SPID) from Hour 0 through Hour 2, Hour 4 and Hour 6

| | |
|-----------------|---|
| End point title | Summed Pain Intensity Differences (SPID) from Hour 0 through Hour 2, Hour 4 and Hour 6 |
|-----------------|---|

End point description:

Pain intensity was evaluated using a 4-point categorical Pain Intensity Rating Scale (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain) for all pain intensity assessments post-dose. Time-weighted SPID was calculated by multiplying the PID score at each post-dose time point by the duration (in hours) since the preceding time point and then summing these values for 0-2, 0-4, 0-6 hour intervals, respectively. The possible total score ranges of SPIDs are: SPID0-2: 0 to 6, SPID0-4: 0 to 12, SPID0-6: 0 to 18. The higher the SPID value, the more improvement of pain relief.

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

End point timeframe:

0 - 6 hours post-dose

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|--------------------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[19] | 200 ^[20] | 100 ^[21] | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| SPID 0 - 2 | 1.7 (± 1.6) | 1.2 (± 1.51) | 0.1 (± 1.19) | |
| SPID 0 - 4 | 2.8 (± 3.53) | 2.7 (± 3.42) | 0.3 (± 2.72) | |
| SPID 0 - 6 | 3.5 (± 5.4) | 3.8 (± 5.29) | 0.6 (± 4.45) | |

Notes:

[19] - ITT population

[20] - ITT population

[21] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1: SPID 0-2 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 2: SPID 0-2 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 3: SPID 0-2 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|---------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 4: SPID 0-4 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.668 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 5: SPID 0-4 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 6: SPID 0-4 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 7: SPID 0-6 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.631 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 8: SPID 0-6 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 9: SPID 0-6 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

Secondary: Summed Total Pain Relief (TOTPAR) from Hour 0 through Hour 2, Hour 4 and Hour 6

| | |
|-----------------|--|
| End point title | Summed Total Pain Relief (TOTPAR) from Hour 0 through Hour 2, Hour 4 and Hour 6 |
|-----------------|--|

End point description:

Subjects rated pain relief on a 5-point categorical Pain Relief Rating Scale (0 = no relief, 1 = a little relief, 2 = some relief, 3 = a lot of relief, 4 = complete relief).

TOTPAR was calculated by multiplying the pain relief score at each post-dose time point by the duration (in hours) since the preceding time point and then summing these values. The possible total score ranges of TOTPARs are: TOTPAR0-2: 0 to 6, TOTPAR0-4: 0 to 12, TOTPAR0-6: 0 to 18. The higher the LS Means scores, the more pain relief was obtained.

| | |
|----------------------|---------------------|
| End point type | Secondary |
| End point timeframe: | 0-6 hours post-dose |

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|--------------------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[22] | 200 ^[23] | 100 ^[24] | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| TOTPAR 0 - 2 | 3.6 (± 2.15) | 2.7 (± 2.09) | 1.1 (± 1.38) | |
| TOTPAR 0 - 4 | 6.3 (± 4.79) | 6 (± 4.76) | 2.3 (± 3.37) | |
| TOTPAR 0 - 6 | 8.5 (± 7.43) | 8.6 (± 7.43) | 3.7 (± 5.66) | |

Notes:

[22] - ITT population

[23] - ITT population

[24] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1: TOTPAR 0-2 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 2: TOTPAR 0-2 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 3: TOTPAR 0-2 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 4: TOTPAR 0-4 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.437 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 5: TOTPAR 0-4 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 6: TOTPAR 0-4 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 7: TOTPAR 0-6 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.875 |
| Method | ANCOVA |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 8: TOTPAR 0-6 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical analysis 9: TOTPAR 0-6 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |

| | |
|---|---------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

Secondary: Time to First use of Rescue Medication

| | |
|---|--|
| End point title | Time to First use of Rescue Medication |
| End point description: | |
| Time to first use of rescue medication was estimated using the Kaplan-Meier method and analyzed by a log rank test stratified by trial site and baseline pain intensity (PI). The criteria were if adequate pain relief was not achieved, then subjects were permitted to take rescue medication. '99999' in the below table indicates data was not analysed as upper limit of 95% confidence interval was not reached. | |
| End point type | Secondary |
| End point timeframe: | |
| 0 to 6 hours | |

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|----------------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[25] | 200 ^[26] | 100 ^[27] | |
| Units: hours | | | | |
| median (confidence interval 95%) | 267.5 (227 to 307) | 322 (252 to 99999) | 104.5 (78 to 126) | |

Notes:

[25] - ITT population

[26] - ITT population

[27] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.378 |
| Method | Logrank |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

| | |
|---|---------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Logrank |

| | |
|---|--|
| Secondary: Cumulative Percentage of Subjects Taking Rescue Medication | |
| End point title | Cumulative Percentage of Subjects Taking Rescue Medication |
| End point description: The cumulative percentage taking rescue medication by time point was analyzed using Chi-square tests. | |
| End point type | Secondary |
| End point timeframe: 1, 2, 3, 4, 5, and 6 hours post-dose | |

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|-------------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[28] | 200 ^[29] | 100 ^[30] | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| 1 hour post-dose | 0.5 | 2 | 6 | |
| 2 hour post-dose | 13 | 20.5 | 57 | |
| 3 hour post-dose | 31.5 | 31 | 68 | |
| 4 hour post-dose | 43.5 | 38.5 | 72 | |
| 5 hour post-dose | 52.5 | 45.5 | 72 | |
| 6 hour post-dose | 59 | 51 | 72 | |

Notes:

[28] - ITT population

[29] - ITT population

[30] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1: 1 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.372 |
| Method | Fisher exact |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 2: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.006 |
| Method | Chi-squared |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 3: 1 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.089 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 4: 2 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.045 |
| Method | Chi-squared |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 5: 2 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

| | |
|---|---------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 6: 2 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 7: 3 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.914 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 8: 3 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 9: 3 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 10: 4 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.309 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 11: 4 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 12: 4 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 13: 5 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.161 |
| Method | Chi-squared |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 14: 5 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

| | |
|---|---------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Chi-squared |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 15: 5 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 16: 6 hour post-dose |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.108 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | Statistical analysis 17: 6 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.028 |
| Method | Chi-squared |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 18: 6 hour post-dose |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Chi-squared |

Secondary: Global Assessment of the Investigational Product as a Pain Reliever at 6 hours After Dosing or Immediately Before the First Intake of Rescue Medication

| | |
|-----------------|---|
| End point title | Global Assessment of the Investigational Product as a Pain Reliever at 6 hours After Dosing or Immediately Before the First Intake of Rescue Medication |
|-----------------|---|

End point description:

Global assessment of the study drug as a pain reliever was analyzed using the Cochran-Mantel-Haenszel (CMH) test with modified ridit scores.

Categorical Scale: Poor (0), Fair (1), Good (2), Very Good (3), Excellent (4).

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

End point timeframe:

At 6 hours postdose or immediately before first use of rescue medication

| End point values | Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) | Acetylsalicyclic acid (Aspirin, BAYE4465) | Placebo | |
|-----------------------------|--|---|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 200 ^[31] | 200 ^[32] | 100 ^[33] | |
| Units: subjects | | | | |
| Poor | 39 | 58 | 60 | |
| Fair | 33 | 37 | 17 | |
| Good | 58 | 48 | 16 | |
| Very good | 44 | 39 | 5 | |
| Excellent | 25 | 16 | 0 | |

Notes:

[31] - ITT population

[32] - ITT population

[33] - ITT population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups | Acetylsalicyclic acid (Aspirin, BAYE4465) v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |
| Number of subjects included in analysis | 400 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.013 |
| Method | Cochran-Mantel-Haenszel |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis 2 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Fast release Aspirin, BAY1019036) |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical analysis 3 |
| Comparison groups | Placebo v Acetylsalicyclic acid (Aspirin, BAYE4465) |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded throughout the treatment period through 5 days after investigational product administration. All serious adverse events were collected through about 30 days after the last dose of investigational product or placebo.

Adverse event reporting additional description:

A treatment-emergent adverse event was defined as any adverse event that began after study drug administration, or any ongoing event that worsened in severity after study drug administration.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 12.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Single oral dose of 2 placebo tablets with a full glass of water (240 mL) between 1-4 hours post dentalsurgery.

| | |
|-----------------------|-----------------|
| Reporting group title | Regular Aspirin |
|-----------------------|-----------------|

Reporting group description:

Single oral dose of regular aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 mL) between 1-4 hours post dental surgery.

| | |
|-----------------------|----------------------|
| Reporting group title | Fast Release Aspirin |
|-----------------------|----------------------|

Reporting group description:

Single oral dose of fast release aspirin tablet 650 mg (2 x 325 mg) with a full glass of water (240 mL) between 1-4 hours post dental surgery.

| Serious adverse events | Placebo | Regular Aspirin | Fast Release Aspirin |
|---|-----------------|-----------------|----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | 0 / 200 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | 0 / 200 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Placebo | Regular Aspirin | Fast Release Aspirin |
|---|-------------------|-------------------|----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 100 (18.00%) | 29 / 200 (14.50%) | 29 / 200 (14.50%) |
| Injury, poisoning and procedural complications | | | |
| Operative haemorrhage | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | 1 / 200 (0.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | 1 / 200 (0.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural site reaction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | 1 / 200 (0.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | 1 / 200 (0.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 3 / 200 (1.50%) | 4 / 200 (2.00%) |
| occurrences (all) | 3 | 3 | 5 |
| Headache | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 8 / 200 (4.00%) | 1 / 200 (0.50%) |
| occurrences (all) | 1 | 9 | 1 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 200 (0.00%) | 0 / 200 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | 0 / 200 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | 0 / 200 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | 1 / 200 (0.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| Ear pain subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |
| Eye disorders Eye pruritus subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 200 (0.50%) 1 | 0 / 200 (0.00%) 0 |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 2 / 200 (1.00%) 2 | 0 / 200 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 200 (0.00%) 0 | 0 / 200 (0.00%) 0 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |
| Dysphagia subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 200 (0.00%) 0 | 0 / 200 (0.00%) 0 |
| Hypoaesthesia oral subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 6 / 100 (6.00%) 6 | 5 / 200 (2.50%) 5 | 9 / 200 (4.50%) 9 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 2 / 200 (1.00%) 2 | 3 / 200 (1.50%) 3 |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 1 / 200 (0.50%) 1 | 1 / 200 (0.50%) 1 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 200 (0.00%) 0 | 0 / 200 (0.00%) 0 |
| Pleuritic pain subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Hypoaesthesia facial subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 200 (0.50%) 1 | 1 / 200 (0.50%) 1 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 200 (0.00%) 0 | 0 / 200 (0.00%) 0 |
| Pruritus generalised subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 200 (0.00%) 0 | 0 / 200 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 200 (0.00%) 0 | 0 / 200 (0.00%) 0 |
| Pain in jaw subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 200 (0.50%) 1 | 0 / 200 (0.00%) 0 |
| Infections and infestations | | | |
| Abscess jaw subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 200 (0.50%) 1 | 0 / 200 (0.00%) 0 |
| Alveolar osteitis subjects affected / exposed occurrences (all) | 3 / 100 (3.00%) 3 | 6 / 200 (3.00%) 6 | 6 / 200 (3.00%) 6 |

| | | | |
|---|----------------------|----------------------|----------------------|
| Postoperative abscess subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |
| Postoperative wound infection subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 200 (0.50%) 1 | 1 / 200 (0.50%) 1 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 200 (0.00%) 0 | 1 / 200 (0.50%) 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 19 April 2010 | This amendment added physical examination and urine drug screen assessments. |
| 14 June 2010 | This amendment clarified inclusion criterion for removal of 2 versus 4 teeth. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

'99999' in the posting indicates that data was not available. Decimal places were automatically truncated if last decimal equals zero.

Notes: