



Clinical trial results:

A MULTICENTER, PHASE 2B, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP, DOSE-RANGING STUDY TO EVALUATE THE EFFICACY AND SAFETY OF BIMEKIZUMAB IN SUBJECTS WITH ACTIVE ANKYLOSING SPONDYLITIS

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-001102-42 |
| Trial protocol | HU ES CZ DE BG GB |
| Global end of trial date | 30 August 2018 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 02 December 2020 |
| First version publication date | 21 September 2019 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review. |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | AS0008 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02963506 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UCB Biopharma SPRL |
| Sponsor organisation address | Allée de la Recherche 60, Brussels, Belgium, 1070 |
| Public contact | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |
| Scientific contact | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 12 February 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 August 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Assess the dose-response based on the efficacy of bimekizumab

Protection of trial subjects:

During the conduct of the study all subjects were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not Applicable

| | |
|---|-----------------|
| Actual start date of recruitment | 27 October 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 4 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Bulgaria: 9 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Czech Republic: 96 |
| Country: Number of subjects enrolled | Germany: 13 |
| Country: Number of subjects enrolled | Hungary: 7 |
| Country: Number of subjects enrolled | Poland: 100 |
| Country: Number of subjects enrolled | Russian Federation: 34 |
| Country: Number of subjects enrolled | Spain: 9 |
| Country: Number of subjects enrolled | Ukraine: 21 |
| Country: Number of subjects enrolled | United States: 12 |
| Worldwide total number of subjects | 303 |
| EEA total number of subjects | 234 |

Notes:

Subjects enrolled per age group

| | |
|----------|---|
| In utero | 0 |
|----------|---|

| | |
|---|-----|
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 291 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in October 2016 and concluded in August 2018.

Pre-assignment

Screening details:

The study included a 28-Day Screening Period, followed by a Double-Blind Period from Day 1 to Week 12, prior to treatment re-randomization, a Dose-blind Period, from Week 12 after the treatment re-randomization and up to Week 48 and a Safety Follow-Up (SFU) Period, post Week 48.

The Participant Flow refers to the Randomized Set and Dose-Blind Set.

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Double-Blind Period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

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

Arm description:

Participants received placebo during the 12 weeks Double-Blind Period.

| | |
|--|------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | PBO |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered placebo, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|-----------|
| Arm title | BKZ 16 mg |
|------------------|-----------|

Arm description:

Participants received bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|-----------|
| Arm title | BKZ 64 mg |
|------------------|-----------|

Arm description:

Participants received bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|------------|
| Arm title | BKZ 160 mg |
|------------------|------------|

Arm description:

Participants received bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|------------|
| Arm title | BKZ 320 mg |
|------------------|------------|

Arm description:

Participants received bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| Number of subjects in period 1 | Placebo | BKZ 16 mg | BKZ 64 mg |
|--|---------|-----------|-----------|
| Started | 60 | 61 | 61 |
| Completed Double-Blind Period | 60 | 59 | 59 |
| Completed Week 12 - started Dose-Blind | 60 | 58 | 59 |
| Completed | 60 | 58 | 59 |
| Not completed | 0 | 3 | 2 |
| Adverse event, serious fatal | - | - | - |
| Consent withdrawn by subject | - | - | 1 |
| Adverse event, non-fatal | - | - | 1 |
| Adverse event, non fatal after Wk12 | - | 1 | - |
| Lost to follow-up | - | 1 | - |

| | | | |
|---------------|---|---|---|
| No compliance | - | 1 | - |
|---------------|---|---|---|

| Number of subjects in period 1 | BKZ 160 mg | BKZ 320 mg |
|--|------------|------------|
| Started | 60 | 61 |
| Completed Double-Blind Period | 58 | 61 |
| Completed Week 12 - started Dose-Blind | 58 | 61 |
| Completed | 58 | 61 |
| Not completed | 2 | 0 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 1 | - |
| Adverse event, non-fatal | - | - |
| Adverse event, non fatal after Wk12 | - | - |
| Lost to follow-up | - | - |
| No compliance | - | - |

Period 2

| | |
|------------------------------|---------------------------------|
| Period 2 title | Dose-Blind Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

| | |
|------------------------------|----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo - BKZ 160 mg |

Arm description:

After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|----------------------|
| Arm title | Placebo - BKZ 320 mg |
|------------------|----------------------|

Arm description:

After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|------------------------|
| Arm title | BKZ 16 mg - BKZ 160 mg |
|------------------|------------------------|

Arm description:

After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|------------------------|
| Arm title | BKZ 16 mg - BKZ 320 mg |
|------------------|------------------------|

Arm description:

After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|------------------------|
| Arm title | BKZ 64 mg - BKZ 160 mg |
|------------------|------------------------|

Arm description:

After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|------------------------|
| Arm title | BKZ 64 mg - BKZ 320 mg |
|------------------|------------------------|

Arm description:

After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|-------------------------|
| Arm title | BKZ 160 mg - BKZ 160 mg |
|------------------|-------------------------|

Arm description:

Participants randomized to bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 160 mg Q4W in the 36 weeks Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| | |
|------------------|-------------------------|
| Arm title | BKZ 320 mg - BKZ 320 mg |
|------------------|-------------------------|

Arm description:

Participants randomized to bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 320 mg Q4W in the 36 weeks Dose-Blind Period.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bimekizumab |
| Investigational medicinal product code | BKZ |
| Other name | UCB4940 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants were administered different BKZ dose regimens, as 2 subcutaneous injections, in the lateral abdominal wall, or upper outer thigh.

| Number of subjects in period 2 | Placebo - BKZ 160 mg | Placebo - BKZ 320 mg | BKZ 16 mg - BKZ 160 mg |
|---------------------------------------|----------------------|----------------------|------------------------|
| Started | 24 | 36 | 31 |
| Completed | 20 | 31 | 26 |
| Not completed | 4 | 5 | 5 |
| Consent withdrawn by subject | 1 | 2 | 2 |
| Adverse event, non-fatal | 1 | 3 | 2 |
| Lost to follow-up | 1 | - | - |
| Sponsor decision | 1 | - | - |
| Meeting exclusion criteria 9 | - | - | - |
| Lack of efficacy | - | - | 1 |

| Number of subjects in period 2 | BKZ 16 mg - BKZ 320 mg | BKZ 64 mg - BKZ 160 mg | BKZ 64 mg - BKZ 320 mg |
|---------------------------------------|------------------------|------------------------|------------------------|
| Started | 27 | 34 | 25 |
| Completed | 24 | 30 | 24 |
| Not completed | 3 | 4 | 1 |
| Consent withdrawn by subject | - | 1 | - |
| Adverse event, non-fatal | 2 | 2 | 1 |
| Lost to follow-up | 1 | - | - |
| Sponsor decision | - | - | - |
| Meeting exclusion criteria 9 | - | - | - |
| Lack of efficacy | - | 1 | - |

| Number of subjects in period 2 | BKZ 160 mg - BKZ 160 mg | BKZ 320 mg - BKZ 320 mg |
|---------------------------------------|-------------------------|-------------------------|
| Started | 58 | 61 |
| Completed | 56 | 54 |
| Not completed | 2 | 7 |
| Consent withdrawn by subject | - | - |
| Adverse event, non-fatal | 1 | 6 |
| Lost to follow-up | 1 | - |
| Sponsor decision | - | - |
| Meeting exclusion criteria 9 | - | 1 |
| Lack of efficacy | - | - |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo during the 12 weeks Double-Blind Period. | |
| Reporting group title | BKZ 16 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period. | |
| Reporting group title | BKZ 64 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period. | |
| Reporting group title | BKZ 160 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period. | |
| Reporting group title | BKZ 320 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period. | |

| Reporting group values | Placebo | BKZ 16 mg | BKZ 64 mg |
|---------------------------------------|---------|-----------|-----------|
| Number of subjects | 60 | 61 | 61 |
| Age categorical Units: Subjects | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 60 | 56 | 59 |
| >=65 years | 0 | 5 | 2 |
| Age continuous Units: years | | | |
| arithmetic mean | 39.65 | 43.31 | 40.41 |
| standard deviation | ± 10.30 | ± 12.59 | ± 10.93 |
| Gender categorical Units: Subjects | | | |
| Male | 49 | 53 | 52 |
| Female | 11 | 8 | 9 |

| Reporting group values | BKZ 160 mg | BKZ 320 mg | Total |
|------------------------------------|------------|------------|-------|
| Number of subjects | 60 | 61 | 303 |
| Age categorical Units: Subjects | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 56 | 60 | 291 |
| >=65 years | 4 | 1 | 12 |
| Age continuous Units: years | | | |
| arithmetic mean | 42.38 | 45.02 | - |
| standard deviation | ± 13.11 | ± 11.39 | - |

| | | | |
|--------------------|----|----|-----|
| Gender categorical | | | |
| Units: Subjects | | | |
| Male | 52 | 50 | 256 |
| Female | 8 | 11 | 47 |

End points

End points reporting groups

| | |
|---|-------------------------|
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo during the 12 weeks Double-Blind Period. | |
| Reporting group title | BKZ 16 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period. | |
| Reporting group title | BKZ 64 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period. | |
| Reporting group title | BKZ 160 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period. | |
| Reporting group title | BKZ 320 mg |
| Reporting group description: Participants received bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period. | |
| Reporting group title | Placebo - BKZ 160 mg |
| Reporting group description: After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period. | |
| Reporting group title | Placebo - BKZ 320 mg |
| Reporting group description: After the 12 weeks Double-Blind Period participants randomized to placebo were re-randomized to receive bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) for 36 weeks in the Dose-Blind Period | |
| Reporting group title | BKZ 16 mg - BKZ 160 mg |
| Reporting group description: After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period. | |
| Reporting group title | BKZ 16 mg - BKZ 320 mg |
| Reporting group description: After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 16 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period. | |
| Reporting group title | BKZ 64 mg - BKZ 160 mg |
| Reporting group description: After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 160 mg Q4W for 36 weeks in the Dose-Blind Period. | |
| Reporting group title | BKZ 64 mg - BKZ 320 mg |
| Reporting group description: After the 12 weeks Double-Blind Period participants randomized to bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) were re-randomized to receive BKZ 320 mg Q4W for 36 weeks in the Dose-Blind Period. | |
| Reporting group title | BKZ 160 mg - BKZ 160 mg |
| Reporting group description: Participants randomized to bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 160 mg Q4W in the 36 weeks Dose-Blind Period. | |
| Reporting group title | BKZ 320 mg - BKZ 320 mg |
| Reporting group description: Participants randomized to bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) in the 12 weeks Double-Blind Period, continued to receive BKZ 320 mg Q4W in the 36 weeks Dose-Blind Period. | |

| | |
|---|-------------------------------|
| Subject analysis set title | Placebo (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants received placebo during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS). | |
| Subject analysis set title | BKZ 16 mg (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants received bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS). | |
| Subject analysis set title | BKZ 64 mg (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants received bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period, forming the Full Analysis Set (FAS). | |
| Subject analysis set title | BKZ 160 mg (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants received bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period, forming the Full Analysis Set (FAS). | |
| Subject analysis set title | BKZ 320 mg (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants received bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) during the 12 weeks Double-Blind Period followed by the same dose during the 36 weeks Dose-Blind Period, forming the Full Analysis Set (FAS). | |
| Subject analysis set title | Placebo (SS) - up to Wk 12 |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: This arm consisted of all participants who received placebo at any time in the study (up to Week 12). Participants formed the Safety Set (SS). | |
| Subject analysis set title | BKZ 16 mg (SS) - up to Wk 12 |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: This arm consisted of all participants who received bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) at any time in the study (up to Week 12). Participants formed the SS. | |
| Subject analysis set title | BKZ 64 mg (SS) - up to Wk 12 |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: This arm consisted of all participants who received bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) at any time in the study (up to Week 12). Participants formed the SS. | |
| Subject analysis set title | BKZ 160 mg (SS) - up to Wk 73 |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: This arm consisted of all participants who received bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) at any time in the study (up to Week 73). Participants formed the SS. | |
| Subject analysis set title | BKZ 320 mg (SS) - up to Wk 73 |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: This arm consisted of all participants who received bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) at any time in the study (up to Week 73). Participants formed the SS. | |

Primary: Percentage of participants with Axial Spondyloarthritis International Society 40% response criteria (ASAS40) at Week 12

| | |
|-----------------|---|
| End point title | Percentage of participants with Axial Spondyloarthritis International Society 40% response criteria (ASAS40) at Week 12 |
|-----------------|---|

End point description:

The ASAS40 response was defined as relative improvements of at least 40% and absolute improvement of at least 2 units on a 0 to 10 Numeric Rating Scale (NRS), where 0 is "not active" and 10 is "very active" in at least 3 of the 4 domains: Patient's Global Assessment of Disease Activity (PGADA), Pain assessment (total spinal pain NRS score), Function (Bath Ankylosing Spondylitis Functional Index (BASFI)), Inflammation (mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 concerning morning stiffness intensity and duration) and no worsening at all in the remaining domain.

Note: Participants with missing data or who discontinue study treatment prior to Week 12 were counted as non-responders.

The FAS consisted of all randomized participants who received at least 1 dose of investigational medicinal product (IMP) and had a valid measurement of the primary efficacy variable at Baseline.

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

End point timeframe:

Week 12

| End point values | Placebo (FAS) | BKZ 16 mg (FAS) | BKZ 64 mg (FAS) | BKZ 160 mg (FAS) |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 61 | 60 |
| Units: percentage of participants | | | | |
| number (not applicable) | 13.3 | 29.5 | 42.6 | 46.7 |

| End point values | BKZ 320 mg (FAS) | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 61 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 45.9 | | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Statistic and p-value were calculated using a Cochran-Mantel-Haenszel test (test for non-zero correlation statistic) based on modified ridit scores and including geographic region and prior Tumor Necrosis Factor (TNF) inhibitor exposure as stratification factors.

Note: 999 and 0% CI are used as placeholders. Using this methodology no point estimator will be calculated. The respective correlation statistic was 17.9.

| | |
|-------------------|---|
| Comparison groups | Placebo (FAS) v BKZ 16 mg (FAS) v BKZ 64 mg (FAS) v BKZ 160 mg (FAS) v BKZ 320 mg (FAS) |
|-------------------|---|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 303 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Correlation statistic |
| Point estimate | 999 |
| Confidence interval | |
| level | Other: 0 % |
| sides | 2-sided |
| lower limit | 999 |
| upper limit | 999 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior tumor necrosis factor (TNF) inhibitor exposure.

| | |
|---|---------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 16 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | = 0.04 ^[2] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.04 |
| upper limit | 6.48 |

Notes:

[1] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of alpha=0.05, then the pairwise testing continued and the comparison was seen as non-significant.

[2] - The p-values were displayed as nominal p-values.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|---------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 64 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[3] |
| P-value | = 0.001 ^[4] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 4.5 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.83 |
| upper limit | 10.86 |

Notes:

[3] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of $\alpha=0.05$, then the pairwise testing continued and the comparison was seen as non-significant.

[4] - The p-values were displayed as nominal p-values.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 160 mg (FAS) |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| P-value | < 0.001 ^[6] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.27 |
| upper limit | 13.48 |

Notes:

[5] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of $\alpha=0.05$, then the pairwise testing continued and the comparison was seen as non-significant.

[6] - The p-values were displayed as nominal p-values.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 320 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[7] |
| P-value | < 0.001 ^[8] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.3 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.19 |
| upper limit | 12.92 |

Notes:

[7] - The pairwise testing of each bimekizumab dose versus placebo accounted for multiplicity by using a fixed sequence testing procedure with each bimekizumab dose being tested sequentially from the highest dose to the lowest dose. If the sequential testing failed to reach significance at a significance level of $\alpha=0.05$, then the pairwise testing continued and the comparison was seen as non-significant.

[8] - The p-values were displayed as nominal p-values.

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score - C-Reactive Protein (ASDAS [CRP]) at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in Ankylosing Spondylitis Disease Activity Score - C-Reactive Protein (ASDAS [CRP]) at Week 12 |
|-----------------|---|

End point description:

The ASDAS was the sum of the following:

0.121xBack pain (BASDAI Q2 result)

0.058xDuration of morning stiffness (BASDAI Q6 result)

0.110xPGADA

0.073xPeripheral pain/swelling (BASDAI Q3 result)

0.579x(ln(hs-CRP [mg/L]+1))

Back pain, PGADA, duration of morning stiffness, peripheral pain/swelling and fatigue are assessed on a numerical scale (0-10 units).

The change from Baseline is calculated, a '-' value indicating improvement and a '+' one worsening.

There is a minimum score of 0.636 for the total ASDAS score, but no defined upper score as CRP does not have an upper limit.

If a component for the ASDAS-CRP was missing at a given visit that component was imputed by carrying the last observation forward and the ASDAS-CRP was calculated accordingly. If the hs-CRP value was <2 mg/L, then it was imputed as the constant value of 2 mg/L.

The FAS consisted of all randomized participants who received at least 1 dose of IMP and had a valid measurement of the primary efficacy variable at Baseline.

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

End point timeframe:

From Baseline to Week 12

| End point values | Placebo (FAS) | BKZ 16 mg (FAS) | BKZ 64 mg (FAS) | BKZ 160 mg (FAS) |
|-------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 61 | 60 |
| Units: scores on a scale | | | | |
| least squares mean (standard error) | -0.3 (± 0.17) | -0.8 (± 0.17) | -1.4 (± 0.17) | -1.3 (± 0.17) |

| End point values | BKZ 320 mg (FAS) | | | |
|-------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 61 | | | |
| Units: scores on a scale | | | | |
| least squares mean (standard error) | -1.4 (± 0.17) | | | |

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|--|---------------------------------|
| Statistical analysis description: | |
| Least squares (LS) Mean, standard error, confidence interval and p-value were derived using the analysis of covariance (ANCOVA) model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 16 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.86 |
| upper limit | -0.24 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.16 |

| Statistical analysis title | Statistical analysis 2 |
|---|---------------------------------|
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 64 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.47 |
| upper limit | -0.83 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.16 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 160 mg (FAS) |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.35 |
| upper limit | -0.72 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.16 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis 4 |
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 320 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.45 |
| upper limit | -0.82 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.16 |

Secondary: Percentage of participants with Axial Spondyloarthritis International Society 20% response criteria (ASAS20) at Week 12

| | |
|---|---|
| End point title | Percentage of participants with Axial Spondyloarthritis International Society 20% response criteria (ASAS20) at Week 12 |
| End point description: | |
| The ASAS20 response was defined as an improvement of at least 20% and absolute improvement of at least 1 unit on a 0 to 10 NRS, where 0 is "not active" and 10 is "very active" in at least 3 of the 4 domains: PGADA, Pain assessment (total spinal pain NRS scores), Function (BASFI), Inflammation (mean of BASDAI questions 5 and 6 concerning morning stiffness intensity and duration) and absence of deterioration in the potential remaining domain [deterioration was defined as a relative worsening of at least 20% and an absolute worsening of at least 1 unit]. | |
| Note: Participants with missing data or who discontinue study treatment prior to Week 12 were counted as non-responders. | |
| The FAS consisted of all randomized participants who received at least 1 dose of IMP and had a valid measurement of the primary efficacy variable at Baseline. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| End point values | Placebo (FAS) | BKZ 16 mg (FAS) | BKZ 64 mg (FAS) | BKZ 160 mg (FAS) |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 61 | 60 |
| Units: percentage of participants | | | | |
| number (not applicable) | 28.3 | 41.0 | 62.3 | 58.3 |

| End point values | BKZ 320 mg (FAS) | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 61 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 72.1 | | | |

Statistical analyses

| | |
|--|---------------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: | |
| For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure. | |
| Comparison groups | Placebo (FAS) v BKZ 16 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.163 ^[9] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 3.67 |

Notes:

[9] - The p-values were displayed as nominal p-values.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|---------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 64 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[10] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.84 |
| upper limit | 8.48 |

Notes:

[10] - The p-values were displayed as nominal p-values.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 160 mg (FAS) |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.001 ^[11] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.66 |
| upper limit | 7.61 |

Notes:

[11] - The p-values were displayed as nominal p-values.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 320 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[12] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 6.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.92 |
| upper limit | 14.28 |

Notes:

[12] - The p-values were displayed as nominal p-values.

Secondary: Percentage of participants with Axial Spondyloarthritis International Society (ASAS) 5/6 response at Week 12

| | |
|-----------------|--|
| End point title | Percentage of participants with Axial Spondyloarthritis International Society (ASAS) 5/6 response at Week 12 |
|-----------------|--|

End point description:

The ASAS 5/6 response was defined as at least 20% improvement in at least 5 of the 6 domains: PGADA, Pain assessment (total spinal pain NRS scores), Function (BASFI), Inflammation (mean of BASDAI questions 5 and 6 concerning morning stiffness intensity and duration), spinal mobility (lateral spinal flexion) and high sensitivity C-reactive protein (hs-CRP).

Note: Participants with missing data or who discontinue study treatment prior to Week 12 were counted as non-responders.

The FAS consisted of all randomized participants who received at least 1 dose of IMP and had a valid measurement of the primary efficacy variable at Baseline.

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

End point timeframe:

Week 12

| End point values | Placebo (FAS) | BKZ 16 mg (FAS) | BKZ 64 mg (FAS) | BKZ 160 mg (FAS) |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 61 | 60 |
| Units: percentage of participants | | | | |
| number (not applicable) | 6.7 | 29.5 | 49.2 | 53.3 |

| End point values | BKZ 320 mg (FAS) | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 61 | | | |
| Units: percentage of participants | | | | |

| | | | | |
|-------------------------|------|--|--|--|
| number (not applicable) | 54.1 | | | |
|-------------------------|------|--|--|--|

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|---------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 16 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.003 ^[13] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.74 |
| upper limit | 15.96 |

Notes:

[13] - The p-values were displayed as nominal p-values.

| Statistical analysis title | Statistical analysis 2 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|---------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 64 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[14] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 11.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.03 |
| upper limit | 35.38 |

Notes:

[14] - The p-values were displayed as nominal p-values.

| Statistical analysis title | Statistical analysis 3 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 160 mg (FAS) |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[15] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 14.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.81 |
| upper limit | 42.46 |

Notes:

[15] - The p-values were displayed as nominal p-values.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

For differences in relation to placebo: Odds Ratio, confidence interval and p-value were derived from a logistic regression model including fixed effects for treatment, geographic region and prior TNF inhibitor exposure.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 320 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[16] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 14.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.02 |
| upper limit | 44.27 |

Notes:

[16] - The p-values were displayed as nominal p-values.

Secondary: Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

| | |
|-----------------|--|
| End point title | Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) |
|-----------------|--|

End point description:

The BASDAI is a validated self-reported instrument, which consists of six 10-unit horizontal Numeric Rating Scales (NRS) to measure severity of fatigue, spinal and peripheral joint pain and swelling, enthesitis, and morning stiffness (both severity and duration, respectively) over the last week. The final BASDAI score ranges from 0 to 10, with lower scores indicating lower disease activity. The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.

Note: Missing data was imputed using multiple imputation based on the Markov-Chain Monte Carlo

method for the intermittent missing data, followed by monotone regression for the monotone missing data assuming missing at random.

The FAS consisted of all randomized participants who received at least 1 dose of IMP and had a valid measurement of the primary efficacy variable at Baseline.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to Week 12 | |

| End point values | Placebo (FAS) | BKZ 16 mg (FAS) | BKZ 64 mg (FAS) | BKZ 160 mg (FAS) |
|-------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 61 | 60 |
| Units: scores on a scale | | | | |
| least squares mean (standard error) | -1.0 (\pm 0.38) | -1.6 (\pm 0.38) | -2.6 (\pm 0.38) | -2.6 (\pm 0.38) |

| End point values | BKZ 320 mg (FAS) | | | |
|-------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 61 | | | |
| Units: scores on a scale | | | | |
| least squares mean (standard error) | -2.9 (\pm 0.38) | | | |

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 16 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.094 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.31 |
| upper limit | 0.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.36 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 64 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.34 |
| upper limit | -0.91 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.37 |

| | |
|---|----------------------------------|
| Statistical analysis title | Statistical analysis 3 |
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 160 mg (FAS) |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.35 |
| upper limit | -0.91 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.37 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 320 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.6 |
| upper limit | -1.18 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.36 |

Secondary: Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Functional Index (BASFI)

| | |
|-----------------|---|
| End point title | Change from Baseline to Week 12 in the Bath Ankylosing Spondylitis Functional Index (BASFI) |
|-----------------|---|

End point description:

The BASFI is a validated disease-specific instrument for assessing physical function. The BASFI comprises 10 items relating to the past week. The BASFI is the mean of the 10 scores such that the total score ranges from 0 (Easy) to 10 (Impossible), with lower scores indicating better physical function. The change from Baseline is calculated, a negative value indicating improvement and a positive value worsening.

Note: Missing data was imputed using multiple imputation based on the Markov-Chain Monte Carlo method for the intermittent missing data, followed by monotone regression for the monotone missing data assuming missing at random.

The FAS consisted of all randomized participants who received at least 1 dose of IMP and had a valid measurement of the primary efficacy variable at Baseline.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to Week 12 | |

| End point values | Placebo (FAS) | BKZ 16 mg (FAS) | BKZ 64 mg (FAS) | BKZ 160 mg (FAS) |
|-------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 61 | 60 |
| Units: scores on a scale | | | | |
| least squares mean (standard error) | -0.7 (± 0.39) | -1.4 (± 0.38) | -1.8 (± 0.38) | -1.9 (± 0.38) |

| | | | | |
|-------------------------------------|----------------------|--|--|--|
| End point values | BKZ 320 mg (FAS) | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 61 | | | |
| Units: scores on a scale | | | | |
| least squares mean (standard error) | -2.2 (\pm 0.38) | | | |

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 16 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.075 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.35 |
| upper limit | 0.07 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.36 |

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical analysis 2 |
| Statistical analysis description: | |
| LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate. | |
| Comparison groups | Placebo (FAS) v BKZ 64 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.003 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.79 |
| upper limit | -0.37 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.36 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 160 mg (FAS) |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.002 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.84 |
| upper limit | -0.42 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.36 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

LS Mean, standard error, confidence interval and p-value were derived using the ANCOVA model with treatment, geographic region and prior TNF inhibitor exposure as fixed effects and the Baseline value as covariate.

| | |
|---|----------------------------------|
| Comparison groups | Placebo (FAS) v BKZ 320 mg (FAS) |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference vs placebo |
| Point estimate | -1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.22 |
| upper limit | -0.81 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.36 |

Secondary: Percentage of participants with at least one adverse event (AE) during the study

| | |
|-----------------|--|
| End point title | Percentage of participants with at least one adverse event (AE) during the study |
|-----------------|--|

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

The SS consisted of all randomized participants who received at least 1 dose of IMP.

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

End point timeframe:

From Screening until Safety Follow-Up Visit (up to Week 77)

| End point values | Placebo (SS) - up to Wk 12 | BKZ 16 mg (SS) - up to Wk 12 | BKZ 64 mg (SS) - up to Wk 12 | BKZ 160 mg (SS) - up to Wk 73 |
|-----------------------------------|----------------------------|------------------------------|------------------------------|-------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 58 | 149 |
| Units: percentage of participants | | | | |
| number (not applicable) | 45.0 | 44.3 | 34.5 | 69.8 |

| End point values | BKZ 320 mg (SS) - up to Wk 73 | | | |
|-----------------------------------|-------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 150 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 82.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with at least one serious adverse event (SAE) during the study

| | |
|-----------------|---|
| End point title | Percentage of participants with at least one serious adverse event (SAE) during the study |
|-----------------|---|

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that at any dose:

- Results in death
- Is life-threatening
- Requires in patient hospitalisation or prolongation of existing hospitalisation
- Is a congenital anomaly or birth defect
- Is an infection that requires treatment parenteral antibiotics
- Other important medical events which based on medical or scientific judgement may jeopardise the patients, or may require medical or surgical intervention to prevent any of the above.

The SS consisted of all randomized participants who received at least 1 dose of IMP.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Screening until Safety Follow-Up Visit (up to Week 77) | |

| End point values | Placebo (SS) - up to Wk 12 | BKZ 16 mg (SS) - up to Wk 12 | BKZ 64 mg (SS) - up to Wk 12 | BKZ 160 mg (SS) - up to Wk 73 |
|-----------------------------------|----------------------------|------------------------------|------------------------------|-------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 58 | 149 |
| Units: percentage of participants | | | | |
| number (not applicable) | 3.3 | 0 | 3.4 | 3.4 |

| End point values | BKZ 320 mg (SS) - up to Wk 73 | | | |
|-----------------------------------|-------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 150 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 4.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who withdrew due to an adverse event (AE) during the study

| | |
|-----------------|---|
| End point title | Percentage of participants who withdrew due to an adverse event (AE) during the study |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a participant or trial subject that is administered a drug or biologic (medicinal product) or that is using a medical device.

The event does not necessarily have a causal relationship with that treatment or usage. The results of this Secondary Outcome Measure were summarized from the adverse event pages of the Case Report Forms.

The SS consisted of all randomized participants who received at least 1 dose of IMP.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Screening until Safety Follow-Up Visit (up to Week 77) | |

| End point values | Placebo (SS) - up to Wk 12 | BKZ 16 mg (SS) - up to Wk 12 | BKZ 64 mg (SS) - up to Wk 12 | BKZ 160 mg (SS) - up to Wk 73 |
|-----------------------------------|----------------------------|------------------------------|------------------------------|-------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 60 | 61 | 58 | 149 |
| Units: percentage of participants | | | | |
| number (not applicable) | 1.7 | 3.3 | 1.7 | 4.7 |

| End point values | BKZ 320 mg (SS) - up to Wk 73 | | | |
|-----------------------------------|-------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 150 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 6.7 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) were collected from Baseline until the Safety Follow-Up Visit (up to Week 73)

Adverse event reporting additional description:

At Week 12, placebo, BKZ 16 mg and BKZ 64 mg subjects were re-randomized to either BKZ 160 mg or BKZ 320 mg. Subjects randomized to BKZ 160 mg group or BKZ 320 mg at Baseline were not re-randomized at Week 12 and remained on their original treatment. The Safety Set is based on actual treatment, other populations are based on planned treatment.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------------------|
| Reporting group title | BKZ 16 mg (SS) - up to Wk 12 |
|-----------------------|------------------------------|

Reporting group description:

This arm consisted of all participants who received bimekizumab (BKZ) 16 milligrams (mg) every 4 weeks (Q4W) at any time in the study (up to Week 12). Participants formed the SS.

| | |
|-----------------------|----------------------------|
| Reporting group title | Placebo (SS) - up to Wk 12 |
|-----------------------|----------------------------|

Reporting group description:

This arm consisted of all participants who received placebo at any time in the study (up to Week 12). Participants formed the Safety Set (SS).

| | |
|-----------------------|-------------------------------|
| Reporting group title | BKZ 320 mg (SS) - up to Wk 73 |
|-----------------------|-------------------------------|

Reporting group description:

This arm consisted of all participants who received bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) at any time in the study (up to Week 73). Participants formed the SS.

| | |
|-----------------------|-------------------------------|
| Reporting group title | BKZ 160 mg (SS) - up to Wk 73 |
|-----------------------|-------------------------------|

Reporting group description:

This arm consisted of all participants who received bimekizumab (BKZ) 160 mg every 4 weeks (Q4W) at any time in the study (up to Week 73). Participants formed the SS.

| | |
|-----------------------|------------------------------|
| Reporting group title | BKZ 64 mg (SS) - up to Wk 12 |
|-----------------------|------------------------------|

Reporting group description:

This arm consisted of all participants who received bimekizumab (BKZ) 64 mg every 4 weeks (Q4W) at any time in the study (up to Week 12). Participants formed the SS.

| Serious adverse events | BKZ 16 mg (SS) - up to Wk 12 | Placebo (SS) - up to Wk 12 | BKZ 320 mg (SS) - up to Wk 73 |
|---|------------------------------|----------------------------|-------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 2 / 60 (3.33%) | 6 / 150 (4.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon adenoma | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Inner ear disorder | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 60 (1.67%) | 0 / 150 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bursitis infective | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 60 (1.67%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | BKZ 160 mg (SS) - up to Wk 73 | BKZ 64 mg (SS) - up to Wk 12 | |
|---|-------------------------------|------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 2 / 58 (3.45%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

| | | | |
|---|-----------------|----------------|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon adenoma | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 58 (1.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 58 (1.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laceration | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 58 (1.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |

| | | | |
|---|-----------------|----------------|--|
| Inner ear disorder | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 58 (1.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 58 (1.72%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bursitis infective | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pilonidal cyst | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 58 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | BKZ 16 mg (SS) - up to Wk 12 | Placebo (SS) - up to Wk 12 | BKZ 320 mg (SS) - up to Wk 73 |
|--|---------------------------------|-------------------------------|----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 61 (3.28%) | 2 / 60 (3.33%) | 56 / 150 (37.33%) |
| Infections and infestations | | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 8 / 150 (5.33%) |
| occurrences (all) | 0 | 0 | 11 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 6 / 150 (4.00%) |
| occurrences (all) | 0 | 0 | 8 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 60 (1.67%) | 12 / 150 (8.00%) |
| occurrences (all) | 0 | 1 | 12 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 61 (3.28%) | 0 / 60 (0.00%) | 19 / 150 (12.67%) |
| occurrences (all) | 2 | 0 | 22 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 0 / 60 (0.00%) | 7 / 150 (4.67%) |
| occurrences (all) | 0 | 0 | 7 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 60 (1.67%) | 11 / 150 (7.33%) |
| occurrences (all) | 0 | 1 | 11 |

| Non-serious adverse events | BKZ 160 mg (SS) - up to Wk 73 | BKZ 64 mg (SS) - up to Wk 12 | |
|--|----------------------------------|---------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 149 (28.19%) | 4 / 58 (6.90%) | |
| Infections and infestations | | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 8 / 149 (5.37%) | 0 / 58 (0.00%) | |
| occurrences (all) | 10 | 0 | |
| Oral fungal infection | | | |
| subjects affected / exposed | 8 / 149 (5.37%) | 0 / 58 (0.00%) | |
| occurrences (all) | 8 | 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 2 / 58 (3.45%) | |
| occurrences (all) | 4 | 2 | |
| Nasopharyngitis | | | |

| | | | |
|-----------------------------------|------------------|----------------|--|
| subjects affected / exposed | 13 / 149 (8.72%) | 1 / 58 (1.72%) | |
| occurrences (all) | 19 | 1 | |
| Pharyngitis | | | |
| subjects affected / exposed | 11 / 149 (7.38%) | 0 / 58 (0.00%) | |
| occurrences (all) | 11 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 1 / 58 (1.72%) | |
| occurrences (all) | 7 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 09 March 2018 | <p>The purpose of this substantial protocol amendment was the following:</p> <ul style="list-style-type: none">- To update the study contact details for the sponsor study physician and clinical trial biostatistician.- To revise the withdrawal criteria section to provide instructions for the management of participants with newly diagnosed inflammatory bowel disease (IBD) or with IBD flares during the study.- Amend the time window between doses during the Double-Blind Period of the study.- To revise and clarify the SAE criteria for pregnancy for consistency.- Amend the table for identification/exclusion of alternative etiology to include alanine aminotransferase (ALT) and aspartate aminotransferase (AST). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported