



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study, with an Active-Treatment Dose-Blinded Period, to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of BIIB054 in Subjects with Parkinson's Disease

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-004610-95 |
| Trial protocol | GB AT DE FR ES IT |
| Global end of trial date | 29 April 2021 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 02 April 2022 |
| First version publication date | 02 April 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 228PD201 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03318523 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Biogen |
| Sponsor organisation address | 250 Binney Street, Cambridge, United States, 02142 |
| Public contact | Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com |
| Scientific contact | Biogen Study Medical Director, Biogen, clinicaltrials@biogen.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 | 29 April 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 April 2021 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the clinical efficacy of BIIB054 via dose response using the change from baseline in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score.

The secondary objectives of the study are to evaluate the dose-related safety of BIIB054, to evaluate the clinical efficacy of BIIB054 via MDS-UPDRS total score, to assess the pharmacokinetic (PK) profile of BIIB054, to evaluate the clinical efficacy of BIIB054 based on MDS-UPDRS subparts, to evaluate the pharmacodynamic effects of BIIB054 on the integrity of nigrostriatal dopaminergic nerve terminals and to evaluate the immunogenicity of BIIB054.

Protection of trial subjects:

Written informed consent was obtained from each subject or subject's legally authorised representative (e.g., parent or legal guardian), as applicable, prior to evaluations performed for eligibility. Subjects or the subject's legally authorised representative were given adequate time to review the information in the informed consent/assent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 10 January 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 167 |
| Country: Number of subjects enrolled | Italy: 70 |
| Country: Number of subjects enrolled | Spain: 48 |
| Country: Number of subjects enrolled | Germany: 18 |
| Country: Number of subjects enrolled | France: 19 |
| Country: Number of subjects enrolled | Israel: 12 |
| Country: Number of subjects enrolled | United Kingdom: 12 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | Austria: 3 |
| Worldwide total number of subjects | 357 |
| EEA total number of subjects | 158 |

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) | 232 |
| From 65 to 84 years | 125 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 75 investigational sites from 10 January 2018 to 29 April 2021.

Pre-assignment

Screening details:

Subjects with Parkinson's Disease(PD) were randomised to receive placebo or BIIB054 250/1250/3500 milligrams(mg) for Year 1 in Placebo-Controlled(PC) Period. After Year 1, those on placebo [delayed start (DS)] received BIIB054 250/1250/3500 mg, and others on BIIB054 in Year 1 continued to receive same dose until Week 96 visit.

Period 1

| | |
|------------------------------|---|
| Period 1 title | PC Period: Up to Year 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | PC Period: Placebo |

Arm description:

Subjects received BIIB054-matching placebo, intravenous (IV) infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

| | |
|--|---------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | BIIB054-matching placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054-matching placebo administered via IV infusion, on Day 1 and then every 4 weeks for Year 1.

| | |
|------------------|---|
| Arm title | PC Period: BIIB054 250 mg (Early Start) |
|------------------|---|

Arm description:

Subjects received BIIB054, 250 milligrams (mg), IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 250 mg administered via IV infusion, on Day 1 and then every 4 weeks for Year 1.

| | |
|------------------|--|
| Arm title | PC Period: BIIB054 1250 mg (Early Start) |
|------------------|--|

Arm description:

Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

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

| | |
|---|--|
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| BIIB054 1250 mg administered via IV infusion, on Day 1 and then every 4 weeks for Year 1. | |
| Arm title | PC Period: BIIB054 3500 mg (Early Start) |

Arm description:

Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 3500 mg administered via IV infusion, on Day 1 and then every 4 weeks for Year 1.

| Number of subjects in period 1 | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) |
|---------------------------------------|--------------------|---|--|
| Started | 100 | 55 | 102 |
| Completed | 96 | 53 | 100 |
| Not completed | 4 | 2 | 2 |
| Adverse Event | 1 | - | 2 |
| Consent Withdrawn | 3 | 2 | - |

| Number of subjects in period 1 | PC Period: BIIB054 3500 mg (Early Start) |
|---------------------------------------|--|
| Started | 100 |
| Completed | 96 |
| Not completed | 4 |
| Adverse Event | - |
| Consent Withdrawn | 4 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | DBE Period:Year 2 to EOS (Up to 3 Years) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|--|
| Arm title | DBE Period: Placebo to BIIB054 250 mg (DS) |
|------------------|--|

Arm description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to end of study (EOS) (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

| | |
|------------------|---|
| Arm title | DBE Period: Placebo to BIIB054 1250 mg (DS) |
|------------------|---|

Arm description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 1250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

| | |
|------------------|---|
| Arm title | DBE Period: Placebo to BIIB054 3500 mg (DS) |
|------------------|---|

Arm description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 3500 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

| | |
|------------------|--|
| Arm title | DBE Period: BIIB054 250 mg (Early Start) |
|------------------|--|

Arm description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 250 mg in the PC period were included in this arm.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

| | |
|------------------|---|
| Arm title | DBE Period: BIIB054 1250 mg (Early Start) |
|------------------|---|

Arm description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 1250 mg in the PC period were included in this arm.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 1250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

| | |
|------------------|---|
| Arm title | DBE Period: BIIB054 3500 mg (Early Start) |
|------------------|---|

Arm description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 3500 mg in the PC period were included in this arm.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BIIB054 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BIIB054 3500 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

| Number of subjects in period 2^[1] | DBE Period: Placebo to BIIB054 250 mg (DS) | DBE Period: Placebo to BIIB054 1250 mg (DS) | DBE Period: Placebo to BIIB054 3500 mg (DS) |
|---|--|---|---|
| Started | 20 | 37 | 39 |
| Number of Subjects Dosed | 20 | 37 | 39 |
| Completed | 0 | 0 | 0 |
| Not completed | 20 | 37 | 39 |
| Adverse Event | 1 | - | - |
| Death | - | - | - |
| Not Specified | 1 | - | - |
| Investigator Decision | - | 1 | - |
| Study Terminated by Sponsor | 17 | 36 | 39 |
| Consent Withdrawn | 1 | - | - |

| Number of subjects in period 2 | DBE Period: BIIB054 250 mg (Early Start) | DBE Period: BIIB054 1250 mg (Early | DBE Period: BIIB054 3500 mg (Early |
|---------------------------------------|--|------------------------------------|------------------------------------|
|---------------------------------------|--|------------------------------------|------------------------------------|

| [1] | | Start) | Start) |
|-----------------------------|----|--------|--------|
| Started | 52 | 100 | 96 |
| Number of Subjects Dosed | 52 | 100 | 94 |
| Completed | 0 | 0 | 0 |
| Not completed | 52 | 100 | 96 |
| Adverse Event | 1 | - | 2 |
| Death | - | - | 1 |
| Not Specified | 2 | 3 | - |
| Investigator Decision | - | - | - |
| Study Terminated by Sponsor | 48 | 94 | 91 |
| Consent Withdrawn | 1 | 3 | 2 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 345 subjects completed the PC Period, out of which only 344 subjects entered in DBE Period. 1 subject from PC Period did not enter DBE Period.

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | PC Period: Placebo |
| Reporting group description: Subjects received BIIB054-matching placebo, intravenous (IV) infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Reporting group title | PC Period: BIIB054 250 mg (Early Start) |
| Reporting group description: Subjects received BIIB054, 250 milligrams (mg), IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Reporting group title | PC Period: BIIB054 1250 mg (Early Start) |
| Reporting group description: Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Reporting group title | PC Period: BIIB054 3500 mg (Early Start) |
| Reporting group description: Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |

| Reporting group values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) |
|------------------------------------|--------------------|---|--|
| Number of subjects | 100 | 55 | 102 |
| Age Categorical Units: Subjects | | | |

| | | | |
|--|----------------|----------------|----------------|
| Age Continuous Units: years arithmetic mean standard deviation | 61.0 ± 8.39 | 61.3 ± 9.24 | 59.2 ± 8.48 |
| Gender Categorical Units: subjects | | | |
| Female | 28 | 16 | 29 |
| Male | 72 | 39 | 73 |
| Race Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 3 |
| Black or African American | 0 | 0 | 1 |
| White | 96 | 53 | 92 |
| Unknown or Not Reported | 4 | 2 | 6 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 3 | 1 | 1 |
| Not Hispanic or Latino | 96 | 54 | 101 |
| Unknown or Not Reported | 1 | 0 | 0 |
| Baseline Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale Total Score | | | |
| Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale (MDS-UPDRS) is multimodal scale assessing impairment and disability consisting of 4 parts. Part I: non-motor | | | |

| | | | |
|---|----------|----------|----------|
| experiences of daily living and has 2 components (13 questions[Q], Range[R] 0-52). Part II: motor experiences of daily living (13 Q, R 0-52). Part III: motor signs of PD and was administered by rater (33 Q, R 0-132). Numeric score for each question is between 0-4; 0=Normal,1=Slight,2=Mild,3=Moderate,4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=more severe symptoms of PD. | | | |
| Units: score on a scale | | | |
| arithmetic mean | 31.9 | 31.9 | 32.9 |
| standard deviation | ± 12.41 | ± 12.25 | ± 12.58 |
| Baseline MDS-UPDRS Subpart I Score | | | |
| MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. It is separated into 4 subscales: Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. | | | |
| Units: score on a scale | | | |
| arithmetic mean | 4.3 | 3.3 | 4.8 |
| standard deviation | ± 3.50 | ± 2.74 | ± 3.99 |
| Baseline MDS-UPDRS Subpart II Score | | | |
| MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. | | | |
| Units: score on a scale | | | |
| arithmetic mean | 5.4 | 5.0 | 5.3 |
| standard deviation | ± 3.87 | ± 3.30 | ± 3.66 |
| Baseline MDS-UPDRS Subpart III Score | | | |
| MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of Parkinson's Disease (PD) and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. | | | |
| Units: score on a scale | | | |
| arithmetic mean | 22.2 | 23.5 | 22.8 |
| standard deviation | ± 9.31 | ± 9.38 | ± 8.69 |
| Baseline Total Striatum Striatal Binding Ratio (SBR) | | | |
| Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99). | | | |
| Units: striatal binding ratio | | | |
| arithmetic mean | 1.295 | 1.409 | 1.342 |
| standard deviation | ± 0.3177 | ± 0.3875 | ± 0.3197 |
| Baseline Total Putamen SBR | | | |
| Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99). | | | |
| Units: striatal binding ratio | | | |
| arithmetic mean | 1.255 | 1.388 | 1.291 |
| standard deviation | ± 0.3429 | ± 0.4294 | ± 0.3269 |
| Baseline Total Caudate SBR | | | |
| Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99). | | | |
| Units: striatal binding ratio | | | |
| arithmetic mean | 1.336 | 1.433 | 1.397 |
| standard deviation | ± 0.3279 | ± 0.3751 | ± 0.3417 |

| | | | |
|------------------------------------|---|-------|--|
| Reporting group values | PC Period: BIIB054 3500 mg (Early Start) | Total | |
| Number of subjects | 100 | 357 | |
| Age Categorical Units: Subjects | | | |

| | | | |
|--|-----------------|-----|--|
| Age Continuous Units: years arithmetic mean standard deviation | 59.3 ± 9.92 | - | |
| Gender Categorical Units: subjects | | | |
| Female | 34 | 107 | |
| Male | 66 | 250 | |
| Race Units: Subjects | | | |
| American Indian or Alaska Native | 2 | 2 | |
| Asian | 3 | 6 | |
| Black or African American | 0 | 1 | |
| White | 84 | 325 | |
| Unknown or Not Reported | 11 | 23 | |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 6 | 11 | |
| Not Hispanic or Latino | 94 | 345 | |
| Unknown or Not Reported | 0 | 1 | |
| Baseline Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale Total Score | | | |
| <p>Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale (MDS-UPDRS) is multimodal scale assessing impairment and disability consisting of 4 parts. Part I: non-motor experiences of daily living and has 2 components (13 questions[Q], Range[R] 0-52). Part II: motor experiences of daily living (13 Q, R 0-52). Part III: motor signs of PD and was administered by rater (33 Q, R 0-132). Numeric score for each question is between 0-4; 0=Normal,1=Slight,2=Mild,3=Moderate,4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=more severe symptoms of PD.</p> | | | |
| Units: score on a scale arithmetic mean standard deviation | 32.6 ± 13.46 | - | |
| Baseline MDS-UPDRS Subpart I Score | | | |
| <p>MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. It is separated into 4 subscales: Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.</p> | | | |
| Units: score on a scale arithmetic mean standard deviation | 4.3 ± 3.60 | - | |
| Baseline MDS-UPDRS Subpart II Score | | | |
| <p>MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.</p> | | | |
| Units: score on a scale | | | |

| | | | |
|--|----------|---|--|
| arithmetic mean | 5.5 | | |
| standard deviation | ± 4.30 | - | |
| Baseline MDS-UPDRS Subpart III Score | | | |
| MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of Parkinson's Disease (PD) and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. | | | |
| Units: score on a scale | | | |
| arithmetic mean | 22.9 | | |
| standard deviation | ± 8.86 | - | |
| Baseline Total Striatum Striatal Binding Ratio (SBR) | | | |
| Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99). | | | |
| Units: striatal binding ratio | | | |
| arithmetic mean | 1.351 | | |
| standard deviation | ± 0.3495 | - | |
| Baseline Total Putamen SBR | | | |
| Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99). | | | |
| Units: striatal binding ratio | | | |
| arithmetic mean | 1.286 | | |
| standard deviation | ± 0.3627 | - | |
| Baseline Total Caudate SBR | | | |
| Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99). | | | |
| Units: striatal binding ratio | | | |
| arithmetic mean | 1.416 | | |
| standard deviation | ± 0.3643 | - | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | PC Period: Placebo |
| Reporting group description: Subjects received BIIB054-matching placebo, intravenous (IV) infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Reporting group title | PC Period: BIIB054 250 mg (Early Start) |
| Reporting group description: Subjects received BIIB054, 250 milligrams (mg), IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Reporting group title | PC Period: BIIB054 1250 mg (Early Start) |
| Reporting group description: Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Reporting group title | PC Period: BIIB054 3500 mg (Early Start) |
| Reporting group description: Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Reporting group title | DBE Period: Placebo to BIIB054 250 mg (DS) |
| Reporting group description: Subjects received BIIB054 250 mg, IV infusion from Year 2 up to end of study (EOS) (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm. | |
| Reporting group title | DBE Period: Placebo to BIIB054 1250 mg (DS) |
| Reporting group description: Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm. | |
| Reporting group title | DBE Period: Placebo to BIIB054 3500 mg (DS) |
| Reporting group description: Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm. | |
| Reporting group title | DBE Period: BIIB054 250 mg (Early Start) |
| Reporting group description: Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 250 mg in the PC period were included in this arm. | |
| Reporting group title | DBE Period: BIIB054 1250 mg (Early Start) |
| Reporting group description: Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 1250 mg in the PC period were included in this arm. | |
| Reporting group title | DBE Period: BIIB054 3500 mg (Early Start) |
| Reporting group description: Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 3500 mg in the PC period were included in this arm. | |
| Subject analysis set title | PC Period: Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects who received BIIB054-matching placebo in Year 1 followed by BIIB054 250 mg or 1250 mg or 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) were pooled in this arm. | |
| Subject analysis set title | PC Period: Early Start BIIB054 250 mg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Subject analysis set title | PC Period: Early Start BIIB054 1250 mg |

| | |
|--|--|
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period. | |
| Subject analysis set title | PC Period: Early Start BIIB054 3500 mg |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period. | |
| Subject analysis set title | BIIB054 250 mg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subjects received BIIB054, 250 mg, IV infusion, from Day 1 up to EOS (approximately 3 years). | |
| Subject analysis set title | BIIB054 1250 mg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subjects received BIIB054, 1250 mg, IV infusion, from Day 1 up to EOS (approximately 3 years). | |
| Subject analysis set title | BIIB054 3500 mg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subjects received BIIB054, 3500 mg, IV infusion, from Day 1 up to EOS (approximately 3 years). | |
| Subject analysis set title | PC Period: Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects who received BIIB054-matching placebo in Year 1 followed by BIIB054 250 mg or 1250 mg or 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) were pooled in this arm. | |
| Subject analysis set title | PC Period: Early Start BIIB054 250 mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Subject analysis set title | PC Period: Early Start BIIB054 1250 mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period. | |
| Subject analysis set title | PC Period: Early Start BIIB054 3500 mg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period. | |
| Subject analysis set title | PC Period: Placebo |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects received BIIB054-matching placebo, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Subject analysis set title | PC Period: BIIB054 250 mg (Early Start) |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period. | |
| Subject analysis set title | PC Period: BIIB054 1250 mg (Early Start) |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.

| | |
|----------------------------|--|
| Subject analysis set title | PC Period: BIIB054 3500 mg (Early Start) |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.

Primary: Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 52

| | |
|-----------------|---|
| End point title | Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 52 |
|-----------------|---|

End point description:

MDS-UPDRS is multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range [R] 0-52). Part IA: 6 questions (Qs) assessed by examiner (R 0-24). Part IB: 7 Qs completed by subject (R 0-28). Part II assessed motor experiences of daily living (R 0-52). It contained 13 Qs completed by subject. Part III assessed motor signs of PD and was administered by rater (R 0-132). Part III contained 33 scores based on 18 items. Numeric score for each question is between 0-4, where 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). A higher score indicated more severe symptoms of PD. ITT Population. The mean values reported are the adjusted mean values.

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

End point timeframe:

Baseline, Week 52

| End point values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) | PC Period: BIIB054 3500 mg (Early Start) |
|----------------------------------|----------------------|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 53 ^[1] | 29 ^[2] | 57 ^[3] | 51 ^[4] |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 10.78 (± 1.490) | 10.48 (± 1.951) | 11.29 (± 1.446) | 10.86 (± 1.518) |

Notes:

[1] - Number of subjects analysed were subjects analysed for this endpoint.

[2] - Number of subjects analysed were subjects analysed for this endpoint.

[3] - Number of subjects analysed were subjects analysed for this endpoint.

[4] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 250 mg |
|----------------------------|------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% confidence interval (CI), and p-value were based on a mixed model for repeated measures (MMRM) model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|--|
| Comparison groups | PC Period: BIIB054 250 mg (Early Start) v PC Period: Placebo |
|-------------------|--|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8976 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.888 |
| upper limit | 4.287 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 1250 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.796 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.31 |
| upper limit | 4.312 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 3500 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start) |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9695 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.08 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.805 |
| upper limit | 3.956 |

Primary: Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 72

| | |
|-----------------|---|
| End point title | Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 72 |
|-----------------|---|

End point description:

MDS-UPDRS is multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range [R] 0-52). Part IA: 6 questions (Qs) assessed by examiner (R 0-24). Part IB: 7 Qs completed by subject (R 0-28). Part II assessed motor experiences of daily living (R 0-52). It contained 13 Qs completed by subject. Part III assessed motor signs of PD and was administered by rater (R 0-132). Part III contained 33 scores based on 18 items. Numeric score for each question is between 0-4, where 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=severe symptoms of PD. ITT Population. As prespecified in protocol, data for delayed start BIIB054 were pooled from Placebo/BII054 250/1250/3500 mg for analysis of this endpoint. The mean values reported=adjusted mean values.

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

End point timeframe:

Baseline, Week 72

| End point values | PC Period: Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) | PC Period: Early Start BIIB054 250 mg | PC Period: Early Start BIIB054 1250 mg | PC Period: Early Start BIIB054 3500 mg |
|----------------------------------|--|---------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 68 ^[5] | 32 ^[6] | 62 ^[7] | 64 ^[8] |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 7.11 (± 1.476) | 6.83 (± 2.032) | 8.66 (± 1.496) | 6.94 (± 1.508) |

Notes:

[5] - Number of subjects analysed were subjects analysed for this endpoint.

[6] - Number of subjects analysed were subjects analysed for this endpoint.

[7] - Number of subjects analysed were subjects analysed for this endpoint.

[8] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 250 mg |
|----------------------------|---|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9093 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.035 |
| upper limit | 4.483 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 1250 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |
| Number of subjects included in analysis | 130 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4327 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 1.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.336 |
| upper limit | 5.44 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 3500 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
|-------------------|---|

| | |
|---|------------------------------------|
| Number of subjects included in analysis | 132 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.933 |
| Method | Mixed Model with repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.051 |
| upper limit | 3.719 |

Secondary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose, results in death; in the view of the investigator places the subject at immediate risk of death; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; is a medically important event. The safety population was defined as all subjects who received at least one dose of study treatment (BIIB054).

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

End point timeframe:

Up to 3 years

| End point values | PC Period:Placebo to BIIB054 250/1250/350 0 mg (DS- Pooled) | PC Period: Early Start BIIB054 250 mg | PC Period: Early Start BIIB054 1250 mg | PC Period: Early Start BIIB054 3500 mg |
|-------------------------------|--|--|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 96 | 55 | 102 | 100 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| AEs | 77.1 | 85.5 | 89.2 | 93.0 |
| SAEs | 8.3 | 10.9 | 8.8 | 12.0 |

Statistical analyses

Secondary: Change From Baseline in MDS-UPDRS Total Score (Sum of Parts I, II, and III) at Week 96

| | |
|--|--|
| End point title | Change From Baseline in MDS-UPDRS Total Score (Sum of Parts I, II, and III) at Week 96 |
| End point description: | |
| MDS-UPDRS is multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range [R] 0-52). Part IA: 6 questions (Qs) assessed by examiner (R 0-24). Part IB: 7 Qs completed by subject (R 0-28). Part II assessed motor experiences of daily living (R 0-52). It contained 13 Qs completed by subject. Part III assessed motor signs of PD and was administered by rater (R 0-132). Part III contained 33 scores based on 18 items. Numeric score for each question is between 0-4, where 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=Severe symptoms of PD. ITT population. As prespecified in protocol, data for delayed start BIIB054 were pooled from Placebo/BIIIB054 250/1250/3500 mg for analysis of this endpoint. The mean values reported are the adjusted mean values. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 96 | |

| End point values | PC Period: Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) | PC Period: Early Start BIIB054 250 mg | PC Period: Early Start BIIB054 1250 mg | PC Period: Early Start BIIB054 3500 mg |
|----------------------------------|--|---------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 67 ^[9] | 28 ^[10] | 62 ^[11] | 59 ^[12] |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 7.88 (± 1.616) | 8.28 (± 2.317) | 8.71 (± 1.628) | 8.87 (± 1.659) |

Notes:

[9] - Number of subjects analysed were subjects analysed for this endpoint.

[10] - Number of subjects analysed were subjects analysed for this endpoint.

[11] - Number of subjects analysed were subjects analysed for this endpoint.

[12] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 250 mg |
| Statistical analysis description: | |
| Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period: Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8828 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.41 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.013 |
| upper limit | 5.825 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 1250 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |
| Number of subjects included in analysis | 129 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7019 |
| Method | Mixed Model for Repeated Measure |
| Parameter estimate | Difference |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.458 |
| upper limit | 5.128 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 3500 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
| Number of subjects included in analysis | 126 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6519 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.323 |
| upper limit | 5.301 |

Secondary: Serum Concentration of BIIB054

| | |
|---|--------------------------------|
| End point title | Serum Concentration of BIIB054 |
| End point description: | |
| The pharmacokinetic (PK) population was defined as all subjects in the ITT population who had at least one measurable BIIB054 concentration in serum or cerebrospinal fluid (CSF). The 'n' signifies the number of subjects analysed at the specified time point. '99999' signifies that mean and SD were non-determinable. | |
| End point type | Secondary |
| End point timeframe: | |
| Pre-dose and 1 hour post-dose of Baseline, Weeks 4, 8, 12, 16, 24, 32, 36, 44, 52, 60, 68, 84, 96, 120 and 144 | |

| End point values | BIIB054 250 mg | BIIB054 1250 mg | BIIB054 3500 mg | |
|--|----------------------|----------------------|----------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 75 | 139 | 139 | |
| Units: micrograms per millilitre (ug/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Pre-dose) (n=48,95,92) | 0 (± 0) | 7.47 (± 51.281) | 0.01 (± 0.065) | |
| Baseline (1 Hour Post-dose) (n=62,121,114) | 75.02 (± 15.829) | 374.79 (± 86.004) | 1137.28 (± 335.336) | |
| Week 4 (Pre-dose) (n=46,95,91) | 20.37 (± 5.004) | 95.36 (± 27.882) | 306.20 (± 95.257) | |
| Week 4 (1 Hour Post-dose) (n=47,94,91) | 97.09 (± 19.711) | 468.56 (± 190.589) | 1354.19 (± 364.468) | |
| Week 8 (Pre-dose) (n=63,125,122) | 29.73 (± 8.371) | 169.79 (± 68.025) | 495.79 (± 153.357) | |
| Week 8 (1 Hour Post-dose) (n=64,127,122) | 103.69 (± 26.964) | 543.91 (± 143.212) | 1591.57 (± 465.798) | |
| Week 12 (Pre-dose) (n=50,97,96) | 36.76 (± 11.830) | 195.16 (± 51.020) | 580.43 (± 185.761) | |
| Week 12 (1 Hour Post-dose) (n=54,99,97) | 112.61 (± 27.378) | 569.41 (± 141.250) | 1632.29 (± 459.839) | |
| Week 16 (Pre-dose) (n=51,99,98) | 40.82 (± 11.421) | 201.33 (± 73.451) | 642.06 (± 194.288) | |
| Week 16 (1 Hour Post-dose) (n=50,99,98) | 117.08 (± 27.401) | 614.85 (± 186.892) | 1739.98 (± 506.346) | |
| Week 24 (Pre-dose) (n=54,98,94) | 43.31 (± 12.906) | 235.69 (± 84.454) | 724.60 (± 228.295) | |
| Week 24 (1 Hour Post-dose) (n=46,90,87) | 125.79 (± 36.695) | 664.26 (± 209.251) | 1867.92 (± 470.283) | |
| Week 32 (Pre-dose) (n=11,19,24) | 42.69 (± 13.486) | 260.35 (± 104.397) | 772.75 (± 299.703) | |
| Week 32 (1 Hour Post-dose) (n=15,25,28) | 139.00 (± 34.758) | 626.16 (± 164.497) | 1985.71 (± 497.545) | |
| Week 36 (Pre-dose) (n=51,100,96) | 45.77 (± 11.867) | 262.80 (± 85.052) | 819.83 (± 328.774) | |
| Week 36 (1 Hour Post-dose) (n=51,100,95) | 123.67 (± 29.536) | 665.60 (± 145.235) | 1916.84 (± 543.373) | |
| Week 44 (Pre-dose) (n=3,5,7) | 58.17 (± 22.774) | 280.40 (± 116.590) | 858.43 (± 349.573) | |

| | | | | |
|---|--------------------|--------------------|----------------------|--|
| Week 44 (1 Hour Post-dose) (n=3,5,8) | 143.33 (± 41.004) | 582.40 (± 194.431) | 2066.25 (± 579.555) | |
| Week 52 (Pre-dose) (n=49,98,82) | 46.70 (± 19.343) | 232.08 (± 87.529) | 787.35 (± 341.229) | |
| Week 52 (1 Hour Post-dose) (n=35,74,64) | 114.59 (± 25.913) | 645.36 (± 264.270) | 1920.78 (± 479.511) | |
| Week 60 (Pre-dose) (n=42,86,84) | 43.41 (± 15.973) | 254.52 (± 88.446) | 724.77 (± 314.854) | |
| Week 60 (1 Hour Post-dose) (n=41,83,80) | 122.55 (± 29.374) | 657.94 (± 149.654) | 1905.43 (± 494.136) | |
| Week 68 (Pre-dose) (n=2,3,2) | 706.25 (± 966.969) | 202.33 (± 34.210) | 1362.50 (± 533.866) | |
| Week 68 (1 Hour Post-dose) (n=2,3,2) | 171.50 (± 44.548) | 576.33 (± 85.290) | 2305.00 (± 1025.305) | |
| Week 84 (Pre-dose) (n=28,50,42) | 47.00 (± 15.535) | 255.54 (± 81.407) | 746.43 (± 249.770) | |
| Week 84 (1 Hour Post-dose) (n=38,60,52) | 134.91 (± 33.035) | 648.62 (± 120.163) | 1942.02 (± 501.095) | |
| Week 96 (Pre-dose) (n=11,18,16) | 41.25 (± 15.345) | 274.56 (± 71.718) | 654.70 (± 262.926) | |
| Week 96 (1 Hour Post-dose) (n=10,20,16) | 122.00 (± 29.527) | 682.30 (± 123.653) | 1822.50 (± 475.682) | |
| Week 120 (Pre-dose) (n=6,6,7) | 34.98 (± 12.042) | 279.00 (± 99.499) | 727.29 (± 116.793) | |
| Week 120 (1 Hour Post-dose) (n=6,6,7) | 119.67 (± 15.629) | 769.83 (± 279.182) | 1717.14 (± 320.037) | |
| Week 144 (Pre-dose) (n=0,1,0) | 99999 (± 99999) | 365.00 (± 99999) | 99999 (± 99999) | |
| Week 144 (1 Hour Post-dose) (n=0,1,0) | 99999 (± 99999) | 721.00 (± 99999) | 99999 (± 99999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MDS-UPDRS Subpart I Score at Week 52

| | |
|-----------------|--|
| End point title | Change From Baseline in MDS-UPDRS Subpart I Score at Week 52 |
|-----------------|--|

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). The mean values reported are the adjusted mean values.

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

End point timeframe:

Baseline, Week 52

| End point values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) | PC Period: BIIB054 3500 mg (Early Start) |
|----------------------------------|-----------------------|--|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 53 ^[13] | 29 ^[14] | 57 ^[15] | 51 ^[16] |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 1.43 (± 0.436) | 0.90 (± 0.570) | 1.56 (± 0.423) | 1.65 (± 0.446) |

Notes:

[13] - Number of subjects analysed were subjects analysed for this endpoint.

[14] - Number of subjects analysed were subjects analysed for this endpoint.

[15] - Number of subjects analysed were subjects analysed for this endpoint.

[16] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

| Statistical analysis title | Week 52: Placebo vs BIIB054 250 mg |
|---|--|
| Statistical analysis description: | |
| Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start) |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4327 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.851 |
| upper limit | 0.794 |

| Statistical analysis title | Week 52: Placebo vs BIIB054 1250 mg |
|---|---|
| Statistical analysis description: | |
| Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8155 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.13 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.965 |
| upper limit | 1.225 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 3500 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start) |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7015 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.899 |
| upper limit | 1.334 |

Secondary: Change From Baseline in MDS-UPDRS Subpart I Score at Weeks 72 and 96

| | |
|-----------------|--|
| End point title | Change From Baseline in MDS-UPDRS Subpart I Score at Weeks 72 and 96 |
|-----------------|--|

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from Placebo/BII054 250/1250/3500 mg for the analysis of this endpoint. The 'n' signifies number of subjects analysed at the specified time point. The mean values reported are the adjusted mean values.

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

End point timeframe:

Baseline, Weeks 72 and 96

| End point values | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) | PC Period: Early Start BIIB054 250 mg | PC Period: Early Start BIIB054 1250 mg | PC Period: Early Start BIIB054 3500 mg |
|---|---|---------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 100 | 55 | 102 | 100 |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | | | | |
| Change from Baseline at Week 72 (n=68,32,62,64) | 1.65 (± 0.395) | 0.61 (± 0.538) | 1.73 (± 0.402) | 1.63 (± 0.405) |
| Change from Baseline at Week 96 (n=67,28,62,59) | 1.95 (± 0.398) | 1.69 (± 0.568) | 1.93 (± 0.403) | 1.72 (± 0.414) |

Statistical analyses

| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 250 mg |
|---|---|
| Statistical analysis description: | |
| Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
| Number of subjects included in analysis | 155 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1038 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -1.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.276 |
| upper limit | 0.213 |

| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 1250 mg |
|---|--|
| Statistical analysis description: | |
| Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 202 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8689 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.933 |
| upper limit | 1.103 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 3500 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.982 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.026 |
| upper limit | 1.003 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 250 mg |
|-----------------------------------|---|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
|-------------------|--|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 155 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.693 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.563 |
| upper limit | 1.04 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 1250 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |
| Number of subjects included in analysis | 202 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9606 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.053 |
| upper limit | 1.001 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 3500 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
|-------------------|---|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6512 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.269 |
| upper limit | 0.794 |

Secondary: Change From Baseline in MDS-UPDRS Subpart II Score at Week 52

| | |
|-----------------|---|
| End point title | Change From Baseline in MDS-UPDRS Subpart II Score at Week 52 |
|-----------------|---|

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). The mean values reported are the adjusted mean values.

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

End point timeframe:

Baseline, Week 52

| End point values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) | PC Period: BIIB054 3500 mg (Early Start) |
|----------------------------------|-----------------------|--|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 54 ^[17] | 29 ^[18] | 58 ^[19] | 51 ^[20] |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 3.17 (± 0.473) | 2.72 (± 0.621) | 3.16 (± 0.460) | 3.01 (± 0.486) |

Notes:

[17] - Number of subjects analysed were subjects analysed for this endpoint.

[18] - Number of subjects analysed were subjects analysed for this endpoint.

[19] - Number of subjects analysed were subjects analysed for this endpoint.

[20] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 250 mg |
|----------------------------|------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|--|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start) |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5497 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.889 |
| upper limit | 1.007 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 1250 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start) |
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.998 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.2 |
| upper limit | 1.197 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 3500 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start) |
|-------------------|---|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8069 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.374 |
| upper limit | 1.07 |

Secondary: Change From Baseline in MDS-UPDRS Subpart II Score at Weeks 72 and 96

| | |
|-----------------|---|
| End point title | Change From Baseline in MDS-UPDRS Subpart II Score at Weeks 72 and 96 |
|-----------------|---|

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from (Placebo/BII054 250/1250/3500 mg) for the analysis of this endpoint. The 'n' signifies number of subjects analysed at the specified time point. The mean values reported are the adjusted mean values.

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

End point timeframe:

Baseline, Weeks 72 and 96

| End point values | PC Period: Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) | PC Period: Early Start BIIB054 250 mg | PC Period: Early Start BIIB054 1250 mg | PC Period: Early Start BIIB054 3500 mg |
|---|--|---------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 100 | 55 | 102 | 100 |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | | | | |
| Change from Baseline at Week 72 (n=69,33,62,64) | 1.83 (± 0.491) | 1.62 (± 0.672) | 2.36 (± 0.497) | 1.68 (± 0.503) |
| Change from Baseline at Week 96 (n=67,28,62,60) | 1.87 (± 0.529) | 1.33 (± 0.762) | 2.39 (± 0.533) | 2.22 (± 0.541) |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 250 mg |
| Statistical analysis description: | |
| Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
| Number of subjects included in analysis | 155 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7968 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.786 |
| upper limit | 1.372 |

| | |
|---|--|
| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 1250 mg |
| Statistical analysis description: | |
| Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |
| Number of subjects included in analysis | 202 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4211 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.766 |
| upper limit | 1.827 |

| | |
|--|--|
| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 3500 mg |
| Statistical analysis description: | |
| Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time | |

interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8166 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.448 |
| upper limit | 1.143 |

Statistical analysis title

Week 96: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
| Number of subjects included in analysis | 155 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5535 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.31 |
| upper limit | 1.24 |

Statistical analysis title

Week 96: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |
|-------------------|---|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 202 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4654 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.881 |
| upper limit | 1.922 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 3500 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6184 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.051 |
| upper limit | 1.763 |

Secondary: Change From Baseline in MDS-UPDRS Subpart III Score at Week 52

| | |
|-----------------|--|
| End point title | Change From Baseline in MDS-UPDRS Subpart III Score at Week 52 |
|-----------------|--|

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of PD and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). The mean values reported are the adjusted mean values.

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

End point timeframe:

Baseline, Week 52

| End point values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) | PC Period: BIIB054 3500 mg (Early Start) |
|----------------------------------|-----------------------|--|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 53 ^[21] | 29 ^[22] | 58 ^[23] | 51 ^[24] |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 6.10 (± 1.083) | 6.69 (± 1.419) | 6.76 (± 1.046) | 6.20 (± 1.104) |

Notes:

[21] - Number of subjects analysed were subjects analysed for this endpoint.

[22] - Number of subjects analysed were subjects analysed for this endpoint.

[23] - Number of subjects analysed were subjects analysed for this endpoint.

[24] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

| Statistical analysis title | Week 52: Placebo vs BIIB054 250 mg |
|---|--|
| Statistical analysis description: | |
| Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start) |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7274 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.742 |
| upper limit | 3.925 |

| Statistical analysis title | Week 52: Placebo vs BIIB054 1250 mg |
|---|---|
| Statistical analysis description: | |
| Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction. | |
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start) |

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6385 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.094 |
| upper limit | 3.411 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 3500 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start) |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9467 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.718 |
| upper limit | 2.91 |

Secondary: Change From Baseline in MDS-UPDRS Subpart III Score at Weeks 72 ad 96

| | |
|-----------------|---|
| End point title | Change From Baseline in MDS-UPDRS Subpart III Score at Weeks 72 ad 96 |
|-----------------|---|

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of PD and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from (Placebo/BII054 250/1250/3500 mg) for the analysis of this endpoint. The 'n' signifies number of subjects analysed at the specified time point. The mean values reported are the adjusted mean values.

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

End point timeframe:

Baseline, Weeks 72 and 96

| End point values | PC Period:Placebo to BIIB054 250/1250/350 0 mg (DS- Pooled) | PC Period: Early Start BIIB054 250 mg | PC Period: Early Start BIIB054 1250 mg | PC Period: Early Start BIIB054 3500 mg |
|--|--|--|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 100 | 55 | 102 | 100 |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | | | | |
| Change from Baseline at Week 72 (n=68,32,62,64) | 3.64 (± 1.027) | 4.48 (± 1.404) | 4.49 (± 1.038) | 3.69 (± 1.048) |
| Change from Baseline at Week 96 (n=67,28,62,60) | 4.49 (± 1.174) | 5.14 (± 1.679) | 4.39 (± 1.180) | 5.17 (± 1.201) |

Statistical analyses

| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 250 mg |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
| Number of subjects included in analysis | 155 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6112 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.423 |
| upper limit | 4.114 |

| Statistical analysis title | Week 72: Pooled Placebo vs BIIB054 3500 mg |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time

interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9673 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.608 |
| upper limit | 2.719 |

Statistical analysis title

Week 72: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |
| Number of subjects included in analysis | 202 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.527 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.806 |
| upper limit | 3.52 |

Statistical analysis title

Week 96: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|--|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg |
|-------------------|--|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 155 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7455 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.274 |
| upper limit | 4.569 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 1250 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|---|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg |
| Number of subjects included in analysis | 202 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9506 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.192 |
| upper limit | 2.997 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Week 96: Pooled Placebo vs BIIB054 3500 mg |
|-----------------------------------|--|

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

| | |
|-------------------|---|
| Comparison groups | PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg |
|-------------------|---|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6643 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.422 |
| upper limit | 3.794 |

Secondary: Change From Baseline in Striatal Binding Ratio (SBR) in the Putamen as Measured by Single-Photon Emission Computed Tomography (SPECT) Imaging of the Dopamine Transporter (DaT) at Week 52

| | |
|--|--|
| End point title | Change From Baseline in Striatal Binding Ratio (SBR) in the Putamen as Measured by Single-Photon Emission Computed Tomography (SPECT) Imaging of the Dopamine Transporter (DaT) at Week 52 |
| End point description: SBR in the putamen as measured by SPECT imaging of the dopamine transporter (DaT) with ¹²³ I-ioflupane (DaTscan™). The pharmacodynamic population was defined as a subset of the ITT population with at least 1 post-baseline pharmacodynamic measurement. The mean values reported are the adjusted mean values. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 52 | |

| End point values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) | PC Period: BIIB054 3500 mg (Early Start) |
|----------------------------------|----------------------|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 52 | 97 | 84 |
| Units: SBR | | | | |
| arithmetic mean (standard error) | -0.093 (± 0.0151) | -0.098 (± 0.0199) | -0.102 (± 0.0146) | -0.125 (± 0.0155) |

Statistical analyses

| | |
|--|------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 250 mg |
| Statistical analysis description: Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction. | |

| | |
|---|--|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start) |
| Number of subjects included in analysis | 143 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8274 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.005 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0548 |
| upper limit | 0.0438 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 1250 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start) |
| Number of subjects included in analysis | 188 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6671 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.009 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0504 |
| upper limit | 0.0323 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 3500 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

| | |
|-------------------|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start) |
|-------------------|---|

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1313 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.033 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0751 |
| upper limit | 0.0098 |

Secondary: Change From Baseline in SBR in the Striatum as Measured by SPECT Imaging of the DaT at Week 52

| | |
|------------------------|--|
| End point title | Change From Baseline in SBR in the Striatum as Measured by SPECT Imaging of the DaT at Week 52 |
| End point description: | SBR in the striatum as measured by SPECT imaging of the DaT with ¹²³ I-ioflupane (DaTscan™). The pharmacodynamic population was defined as a subset of the ITT population with at least 1 post-baseline pharmacodynamic measurement. The mean values reported are the adjusted mean values. |
| End point type | Secondary |
| End point timeframe: | Baseline, Week 52 |

| End point values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) | PC Period: BIIB054 3500 mg (Early Start) |
|----------------------------------|----------------------|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 52 | 97 | 84 |
| Units: SBR | | | | |
| arithmetic mean (standard error) | -0.081 (± 0.0145) | -0.090 (± 0.0191) | -0.081 (± 0.0140) | -0.108 (± 0.0148) |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Week 52: Placebo vs BIIB054 250 mg |
| Statistical analysis description: | Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction. |
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start) |

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 143 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7079 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.009 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0562 |
| upper limit | 0.0382 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 1250 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start) |
| Number of subjects included in analysis | 188 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9835 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.04 |
| upper limit | 0.0392 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 3500 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start) |
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1869 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.027 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0682 |
| upper limit | 0.0134 |

Secondary: Change From Baseline in SBR in the Caudate as Measured by SPECT Imaging of the DaT at Week 52

| | |
|---|---|
| End point title | Change From Baseline in SBR in the Caudate as Measured by SPECT Imaging of the DaT at Week 52 |
| End point description: | |
| SBR in the caudate as measured by SPECT imaging of the DaT with ¹²³ I-ioflupane (DaTscan™). The pharmacodynamic population was defined as a subset of the ITT population with at least 1 post-baseline pharmacodynamic measurement. The mean values reported are the adjusted mean values. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) | PC Period: BIIB054 3500 mg (Early Start) |
|----------------------------------|----------------------|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 | 52 | 97 | 84 |
| Units: SBR | | | | |
| arithmetic mean (standard error) | -0.067 (± 0.0166) | -0.075 (± 0.0219) | -0.060 (± 0.0161) | -0.089 (± 0.0171) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Week 52: Placebo vs BIIB054 250 mg |
| Statistical analysis description: | |
| Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction. | |
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start) |
| Number of subjects included in analysis | 143 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7585 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.008 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0625 |
| upper limit | 0.0456 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 1250 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start) |
| Number of subjects included in analysis | 188 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7808 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | 0.006 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0391 |
| upper limit | 0.052 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Week 52: Placebo vs BIIB054 3500 mg |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

| | |
|---|---|
| Comparison groups | PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start) |
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3532 |
| Method | Mixed Model for Repeated Measures |
| Parameter estimate | Difference |
| Point estimate | -0.022 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.0691 |
| upper limit | 0.0248 |

Secondary: Percentage of Subjects With Anti-BIIB054 Antibodies in the Serum

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Anti-BIIB054 Antibodies in the Serum |
|-----------------|--|

End point description:

The analysis population for immunogenicity was defined as all subjects in the safety population. As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from Placebo/BII054 250/1250/3500 mg for the analysis of this endpoint.

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

End point timeframe:

Up to Week 144

| End point values | PC Period:Placebo to BIIB054 250/1250/350 0 mg (DS- Pooled) | PC Period: Early Start BIIB054 250 mg | PC Period: Early Start BIIB054 1250 mg | PC Period: Early Start BIIB054 3500 mg |
|-------------------------------|--|--|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 96 | 55 | 100 | 99 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 0 | 1.8 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3 years

Adverse event reporting additional description:

Safety Population included all subjects who received at least one dose of the study treatment (BIIB054 250 mg, 1250 mg, 3500 mg).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | PC Period: Placebo |
|-----------------------|--------------------|

Reporting group description:

Subjects received BIIB054-matching placebo, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

| | |
|-----------------------|---|
| Reporting group title | PC Period: BIIB054 250 mg (Early Start) |
|-----------------------|---|

Reporting group description:

Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

| | |
|-----------------------|--|
| Reporting group title | PC Period: BIIB054 1250 mg (Early Start) |
|-----------------------|--|

Reporting group description:

Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

| | |
|-----------------------|--|
| Reporting group title | PC Period: BIIB054 3500 mg (Early Start) |
|-----------------------|--|

Reporting group description:

Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

| | |
|-----------------------|---|
| Reporting group title | DBE Period: Placebo to BIIB054 250 mg (Delayed Start) |
|-----------------------|---|

Reporting group description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

| | |
|-----------------------|--|
| Reporting group title | DBE Period: BIIB054 250 mg (Early Start) |
|-----------------------|--|

Reporting group description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 250 mg in the PC period were included in this arm.

| | |
|-----------------------|--|
| Reporting group title | DBE Period: Placebo to BIIB054 1250 mg (Delayed Start) |
|-----------------------|--|

Reporting group description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

| | |
|-----------------------|--|
| Reporting group title | DBE Period: Placebo to BIIB054 3500 mg (Delayed Start) |
|-----------------------|--|

Reporting group description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

| | |
|-----------------------|---|
| Reporting group title | DBE Period: BIIB054 1250 mg (Early Start) |
|-----------------------|---|

Reporting group description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 1250 mg in the PC period were included in this arm.

| | |
|-----------------------|---|
| Reporting group title | DBE Period: BIIB054 3500 mg (Early Start) |
|-----------------------|---|

Reporting group description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 3500 mg in the PC period were included in this arm.

| Serious adverse events | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) |
|---|--------------------|--|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 100 (7.00%) | 4 / 55 (7.27%) | 4 / 102 (3.92%) |
| 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) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Glioblastoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Invasive lobular breast carcinoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 55 (1.82%) | 0 / 102 (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 |
| General disorders and administration site conditions | | | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Arthropod sting | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Fall | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Femur fracture | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Jaw fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Ulna fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 disorders | | | |
| Palpitations | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 55 (1.82%) | 0 / 102 (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 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 | | | |
| Intracranial mass | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| Monoclonal B-cell lymphocytosis subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatitis toxic subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Back pain subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Lumbar spinal stenosis subjects affected / exposed | 0 / 100 (0.00%) | 1 / 55 (1.82%) | 0 / 102 (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 |
| Musculoskeletal chest pain | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal stenosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 55 (1.82%) | 0 / 102 (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 |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Infections and infestations | | | |
| Perirectal abscess | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| COVID-19 pneumonia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | PC Period: BIIB054 3500 mg (Early Start) | DBE Period: Placebo to BIIB054 250 mg (Delayed Start) | DBE Period: BIIB054 250 mg (Early Start) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 100 (6.00%) | 2 / 20 (10.00%) | 3 / 52 (5.77%) |
| 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) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Glioblastoma | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive lobular breast carcinoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Prostate cancer | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Impaired healing | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| Arthropod sting | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Fall | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaw fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Spinal compression fracture | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Ulna fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 | | | |
| Intracranial mass | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 20 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sciatica | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 20 (5.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Monoclonal B-cell lymphocytosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Hepatobiliary disorders | | | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 | | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Back pain | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 chest pain | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal stenosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Infections and infestations | | | |
| Perirectal abscess | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Viral infection | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 0 / 52 (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 |

| Serious adverse events | DBE Period: Placebo to BIIB054 1250 mg (Delayed Start) | DBE Period: Placebo to BIIB054 3500 mg (Delayed Start) | DBE Period: BIIB054 1250 mg (Early Start) |
|---|--|--|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 37 (8.11%) | 3 / 39 (7.69%) | 5 / 100 (5.00%) |
| 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) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glioblastoma | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Invasive lobular breast carcinoma | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| General disorders and administration site conditions | | | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Psychiatric disorders | | | |
| Depression | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 39 (2.56%) | 0 / 100 (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 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 | | | |
| Arthropod sting | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Jaw fracture | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Post lumbar puncture syndrome | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Ulna fracture | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Myocardial infarction | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 | | | |
| Intracranial mass | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 1 / 100 (1.00%) |
| 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 | | | |
| Monoclonal B-cell lymphocytosis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Hepatobiliary disorders | | | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 | | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Back pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 chest pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 39 (2.56%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Spinal stenosis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Spondylolisthesis | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 37 (0.00%) | 1 / 39 (2.56%) | 0 / 100 (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 |
| Infections and infestations | | | |
| Perirectal abscess | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 1 / 37 (2.70%) | 0 / 39 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 1 / 100 (1.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (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 |

| | | | |
|---|--|--|--|
| Serious adverse events | DBE Period: BIIB054 3500 mg (Early Start) | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 94 (7.45%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from | 1 | | |

| | | | |
|---|----------------|--|--|
| adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Glioblastoma | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Invasive lobular breast carcinoma | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------|--|--|
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Arthropod sting | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Jaw fracture | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Pelvic fracture | | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post lumbar puncture syndrome | | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Road traffic accident | | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal compression fracture | | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ulna fracture | | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| Palpitations | | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pericarditis | | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinus bradycardia | | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bradycardia | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Nervous system disorders | | | |
| Intracranial mass | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Monoclonal B-cell lymphocytosis | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Hepatitis toxic | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Spinal stenosis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Perirectal abscess | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | PC Period: Placebo | PC Period: BIIB054 250 mg (Early Start) | PC Period: BIIB054 1250 mg (Early Start) |
|---|--------------------|--|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 58 / 100 (58.00%) | 32 / 55 (58.18%) | 61 / 102 (59.80%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign neoplasm of skin | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 2 / 55 (3.64%) | 3 / 102 (2.94%) |
| occurrences (all) | 5 | 3 | 4 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diaphragmatic paralysis | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Hypoxia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 4 / 100 (4.00%) 4 | 0 / 55 (0.00%) 0 | 9 / 102 (8.82%) 9 |
| Depression subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 3 / 55 (5.45%) 3 | 3 / 102 (2.94%) 3 |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Investigations | | | |
| Blood cholesterol increased subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Blood glucose increased subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Transaminases increased subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 5 / 100 (5.00%) 7 | 5 / 55 (9.09%) 13 | 6 / 102 (5.88%) 6 |
| Skin laceration subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Ligament rupture | | | |

| | | | |
|---|-------------------------|----------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Cardiac disorders Ventricular extrasystoles subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 3 / 100 (3.00%) 3 | 4 / 55 (7.27%) 4 | 9 / 102 (8.82%) 10 |
| Headache subjects affected / exposed occurrences (all) | 18 / 100 (18.00%) 37 | 6 / 55 (10.91%) 8 | 19 / 102 (18.63%) 43 |
| Parkinson's disease subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 4 / 55 (7.27%) 4 | 9 / 102 (8.82%) 9 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Restless legs syndrome subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Somnolence subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Transient ischaemic attack subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Coagulopathy | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Paraesthesia ear | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 3 / 55 (5.45%) | 5 / 102 (4.90%) |
| occurrences (all) | 5 | 3 | 5 |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 100 (4.00%) | 5 / 55 (9.09%) | 5 / 102 (4.90%) |
| occurrences (all) | 4 | 7 | 6 |
| Nausea | | | |
| subjects affected / exposed | 6 / 100 (6.00%) | 1 / 55 (1.82%) | 6 / 102 (5.88%) |
| occurrences (all) | 10 | 1 | 9 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 55 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 1 / 55 (1.82%) | 0 / 102 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Skin irritation | | | |

| | | | |
|---|-------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Skin ulcer subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 7 / 100 (7.00%) 10 | 5 / 55 (9.09%) 8 | 9 / 102 (8.82%) 12 |
| Back pain subjects affected / exposed occurrences (all) | 8 / 100 (8.00%) 11 | 3 / 55 (5.45%) 4 | 8 / 102 (7.84%) 15 |
| Musculoskeletal stiffness subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 100 (2.00%) 2 | 4 / 55 (7.27%) 4 | 5 / 102 (4.90%) 6 |
| Infections and infestations | | | |
| Covid-19 subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 3 / 100 (3.00%) 3 | 1 / 55 (1.82%) 1 | 7 / 102 (6.86%) 9 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 12 / 100 (12.00%) 13 | 10 / 55 (18.18%) 13 | 10 / 102 (9.80%) 12 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 3 / 100 (3.00%) 5 | 2 / 55 (3.64%) 2 | 6 / 102 (5.88%) 7 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Bronchitis | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Tooth infection subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Metabolism and nutrition disorders Calcium deficiency subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 55 (0.00%) 0 | 0 / 102 (0.00%) 0 |

| Non-serious adverse events | PC Period: BIIB054 3500 mg (Early Start) | DBE Period: Placebo to BIIB054 250 mg (Delayed Start) | DBE Period: BIIB054 250 mg (Early Start) |
|---|--|---|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 63 / 100 (63.00%) | 16 / 20 (80.00%) | 25 / 52 (48.08%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Benign neoplasm of skin subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 1 / 52 (1.92%) 1 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 9 / 100 (9.00%) 25 | 1 / 20 (5.00%) 1 | 1 / 52 (1.92%) 1 |
| Asthenia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 2 | 0 / 52 (0.00%) 0 |
| Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diaphragmatic paralysis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 1 / 20 (5.00%) | 1 / 52 (1.92%) |
| occurrences (all) | 6 | 1 | 1 |
| Depression | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 20 (0.00%) | 3 / 52 (5.77%) |
| occurrences (all) | 0 | 0 | 3 |
| Investigations | | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 20 (5.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Weight decreased | | | |

| | | | |
|--|-------------------------|----------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed occurrences (all) | 14 / 100 (14.00%) 16 | 2 / 20 (10.00%) 3 | 10 / 52 (19.23%) 12 |
| Skin laceration | | | |
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 3 / 52 (5.77%) 5 |
| Ligament rupture | | | |
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Procedural pain | | | |
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 2 / 20 (10.00%) 2 | 0 / 52 (0.00%) 0 |
| Cardiac disorders | | | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed occurrences (all) | 6 / 100 (6.00%) 7 | 0 / 20 (0.00%) 0 | 1 / 52 (1.92%) 1 |
| Headache | | | |
| subjects affected / exposed occurrences (all) | 21 / 100 (21.00%) 25 | 3 / 20 (15.00%) 3 | 1 / 52 (1.92%) 2 |
| Parkinson's disease | | | |
| subjects affected / exposed occurrences (all) | 8 / 100 (8.00%) 9 | 1 / 20 (5.00%) 1 | 1 / 52 (1.92%) 2 |
| Paraesthesia | | | |
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Restless legs syndrome | | | |
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Somnolence | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Transient ischaemic attack subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 2 | 0 / 52 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Coagulopathy subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Paraesthesia ear subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 2 | 0 / 52 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Constipation subjects affected / exposed occurrences (all) | 6 / 100 (6.00%) 6 | 1 / 20 (5.00%) 2 | 1 / 52 (1.92%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 6 / 100 (6.00%) 9 | 1 / 20 (5.00%) 1 | 1 / 52 (1.92%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 6 / 100 (6.00%) 7 | 1 / 20 (5.00%) 1 | 2 / 52 (3.85%) 4 |
| Dysphagia subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Haemorrhoids | | | |

| | | | |
|---|-------------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 20 (0.00%) 0 | 1 / 52 (1.92%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Rash subjects affected / exposed occurrences (all) | 5 / 100 (5.00%) 5 | 0 / 20 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| Skin irritation subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Skin ulcer subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 11 / 100 (11.00%) 11 | 1 / 20 (5.00%) 1 | 3 / 52 (5.77%) 3 |
| Back pain subjects affected / exposed occurrences (all) | 13 / 100 (13.00%) 15 | 0 / 20 (0.00%) 0 | 5 / 52 (9.62%) 5 |
| Musculoskeletal stiffness subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 20 (0.00%) 0 | 2 / 52 (3.85%) 2 |
| Infections and infestations | | | |
| Covid-19 subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 1 / 100 (1.00%) 1 | 0 / 20 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| Nasopharyngitis | | | |

| | | | |
|--|-------------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 13 / 100 (13.00%) 14 | 2 / 20 (10.00%) 2 | 2 / 52 (3.85%) 2 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 7 / 100 (7.00%) 11 | 0 / 20 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 2 / 20 (10.00%) 2 | 3 / 52 (5.77%) 3 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| Tooth infection subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 1 / 52 (1.92%) 1 |
| Metabolism and nutrition disorders Calcium deficiency subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 100 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 52 (0.00%) 0 |

| Non-serious adverse events | DBE Period: Placebo to BIIB054 1250 mg (Delayed Start) | DBE Period: Placebo to BIIB054 3500 mg (Delayed Start) | DBE Period: BIIB054 1250 mg (Early Start) |
|---|--|--|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 22 / 37 (59.46%) | 22 / 39 (56.41%) | 51 / 100 (51.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Benign neoplasm of skin subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 2 / 39 (5.13%) 2 | 5 / 100 (5.00%) 6 |
| General disorders and administration site conditions | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| Fatigue subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 4 / 100 (4.00%) 4 |
| Asthenia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 39 (5.13%) 2 | 1 / 100 (1.00%) 1 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 1 / 39 (2.56%) 1 | 1 / 100 (1.00%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 1 / 39 (2.56%) 2 | 2 / 100 (2.00%) 2 |
| Atelectasis subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Diaphragmatic paralysis subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Hypoxia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 39 (5.13%) 2 | 1 / 100 (1.00%) 1 |
| Depression subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 39 (0.00%) 0 | 2 / 100 (2.00%) 2 |
| Insomnia subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 4 | 2 / 39 (5.13%) 2 | 2 / 100 (2.00%) 2 |

| | | | |
|--|----------------|----------------|-------------------|
| Investigations | | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 1 / 100 (1.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 3 / 39 (7.69%) | 16 / 100 (16.00%) |
| occurrences (all) | 4 | 4 | 21 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 1 / 100 (1.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 39 (0.00%) | 0 / 100 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 37 (5.41%) | 2 / 39 (5.13%) | 4 / 100 (4.00%) |
| occurrences (all) | 2 | 2 | 4 |
| Headache | | | |

| | | | |
|---|----------------------|-----------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 5 / 37 (13.51%) 9 | 5 / 39 (12.82%) 15 | 7 / 100 (7.00%) 14 |
| Parkinson's disease subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 1 / 100 (1.00%) 1 |
| Restless legs syndrome subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Somnolence subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 1 / 39 (2.56%) 1 | 1 / 100 (1.00%) 1 |
| Transient ischaemic attack subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 2 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Coagulopathy subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Ear and labyrinth disorders Paraesthesia ear subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 1 / 100 (1.00%) 1 |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 1 / 39 (2.56%) 1 | 4 / 100 (4.00%) 4 |
| Diarrhoea | | | |

| | | | |
|---|----------------------|----------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 2 / 100 (2.00%) 3 |
| Nausea subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 4 | 4 / 39 (10.26%) 5 | 4 / 100 (4.00%) 5 |
| Dysphagia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 1 / 39 (2.56%) 1 | 0 / 100 (0.00%) 0 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 1 / 39 (2.56%) 1 | 2 / 100 (2.00%) 2 |
| Haemorrhoids subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 39 (5.13%) 2 | 0 / 100 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 3 / 39 (7.69%) 3 | 0 / 100 (0.00%) 0 |
| Skin irritation subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Skin ulcer subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 5 | 3 / 39 (7.69%) 4 | 7 / 100 (7.00%) 8 |
| Back pain subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 4 | 6 / 39 (15.38%) 6 | 5 / 100 (5.00%) 12 |
| Musculoskeletal stiffness | | | |

| | | | |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 39 (5.13%) 2 | 2 / 100 (2.00%) 3 |
| Infections and infestations | | | |
| Covid-19 subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 2 / 39 (5.13%) 2 | 6 / 100 (6.00%) 6 |
| Influenza subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 4 / 100 (4.00%) 4 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 3 | 1 / 39 (2.56%) 1 | 2 / 100 (2.00%) 2 |
| Bronchitis subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Tooth infection subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 1 / 100 (1.00%) 1 |
| Metabolism and nutrition disorders | | | |
| Calcium deficiency subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 39 (0.00%) 0 | 0 / 100 (0.00%) 0 |

| | | | |
|-----------------------------------|---|--|--|
| Non-serious adverse events | DBE Period: BIIB054 3500 mg (Early Start) | | |
|-----------------------------------|---|--|--|

| | | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 56 / 94 (59.57%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Benign neoplasm of skin subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 3 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 2 / 94 (2.13%) 2 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) | 5 / 94 (5.32%) 14 1 / 94 (1.06%) 1 | | |
| Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Atelectasis subjects affected / exposed occurrences (all) Diaphragmatic paralysis subjects affected / exposed occurrences (all) Hypoxia | 2 / 94 (2.13%) 2 1 / 94 (1.06%) 1 0 / 94 (0.00%) 0 0 / 94 (0.00%) 0 | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 4 / 94 (4.26%) | | |
| occurrences (all) | 5 | | |
| Depression | | | |
| subjects affected / exposed | 4 / 94 (4.26%) | | |
| occurrences (all) | 5 | | |
| Insomnia | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | | |
| occurrences (all) | 2 | | |
| Investigations | | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 16 / 94 (17.02%) | | |
| occurrences (all) | 19 | | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences (all) | 1 | | |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Procedural pain | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 | | |
| Cardiac disorders Ventricular extrasystoles subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Parkinson's disease subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Restless legs syndrome subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) Transient ischaemic attack subjects affected / exposed occurrences (all) | 4 / 94 (4.26%) 4 12 / 94 (12.77%) 13 0 / 94 (0.00%) 0 2 / 94 (2.13%) 2 0 / 94 (0.00%) 0 1 / 94 (1.06%) 1 0 / 94 (0.00%) 0 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Coagulopathy subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 0 / 94 (0.00%) 0 | | |
| Ear and labyrinth disorders | | | |

| | | | |
|--|----------------------|--|--|
| Paraesthesia ear subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | | |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | | |
| Gastrointestinal disorders | | | |
| Constipation subjects affected / exposed occurrences (all) | 7 / 94 (7.45%) 7 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 94 (3.19%) 3 | | |
| Nausea subjects affected / exposed occurrences (all) | 7 / 94 (7.45%) 11 | | |
| Dysphagia subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 | | |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | | |
| Haemorrhoids subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 | | |
| Toothache subjects affected / exposed occurrences (all) | 3 / 94 (3.19%) 4 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash subjects affected / exposed occurrences (all) | 2 / 94 (2.13%) 2 | | |
| Skin irritation subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | | |
| Skin ulcer | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | | |
| occurrences (all) | 2 | | |
| Back pain | | | |
| subjects affected / exposed | 8 / 94 (8.51%) | | |
| occurrences (all) | 10 | | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |
| Covid-19 | | | |
| subjects affected / exposed | 3 / 94 (3.19%) | | |
| occurrences (all) | 3 | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 94 (5.32%) | | |
| occurrences (all) | 5 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | | |
| occurrences (all) | 4 | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | | |
| occurrences (all) | 1 | | |
| Tooth infection | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 | | |
| Metabolism and nutrition disorders | | | |
| Calcium deficiency | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 09 August 2017 | <ul style="list-style-type: none"> - Reduced the length of the treatment period and total duration of subject participation in the study. - Increased the number of subjects in the study and updated the sample size considerations supporting that change. - Modified inclusion criteria to reduce the time from past diagnosis with PD, to clarify clinical presentation details, and to indicate that subjects with Lewy body dementia would not be included in the study. - Modified inclusion criteria to lengthen the washout duration for levodopa treatment before entry into the study from 4 weeks to 12 weeks, to describe PD medications excluded, and to shorten the maximum duration of allowed prior PD treatment regimens from 3 months to 30 days. - Changed the dose levels from 3 mg/kg, 15 mg/kg, and 45 mg/kg (dosing based on body weight) to 250 mg, 1250 mg, and 3500 mg (fixed dosing) for both cohorts. |
| 22 October 2017 | Added a 1-year active-treatment dose-blinded period, extending the total study treatment period to 2 years. |
| 15 August 2018 | Added retesting and rescreening flexibility for subjects with nonclinically significant out-of-range laboratory results as well as those who cannot complete the Day 1 visit within the designated screening period. |
| 12 February 2019 | Extended the screening period by 1 week (7 days). |
| 11 July 2019 | Extended the active treatment dose-blinded period from Year 2 into Years 3 and 4. Dosing would end when the last subject has received the last dose in Year 2 (at Week 96), and the study would end when the last subject has had the Final Visit in Year 2 (12 weeks after the last dose [Week 108 visit]). |
| 03 February 2020 | Specified the timing of DaT/SPECT scans for certain subjects, as requested by the German Radiology Authority. |
| 11 August 2020 | <p>This amendment was for 2 primary reasons: the addition of remote visits to ease the conduct of the study during any public health emergency and changes to the study objectives and endpoints to increase the scientific value of the study as detailed below.</p> <ol style="list-style-type: none"> 1. Added the use of remote visits 2. Modified the study objectives and endpoints as follows: <ul style="list-style-type: none"> - Primary objective and endpoints: <ul style="list-style-type: none"> - Upgraded the evaluation of clinical efficacy of BIIB054 via MDS-UPDRS Total Score from an exploratory to primary objective along with its associated endpoints - Updated the objective to clearly state that the clinical efficacy of BIIB054 will be assessed via dose response using the change from baseline in MDS-UPDRS Total Score - Added the change from baseline to Week 72 evaluation to the primary endpoint - Moved the current primary objective and endpoint related to safety from primary to secondary objective and endpoint. - Added the following objects and/or endpoints and/or evaluation timepoints: <ul style="list-style-type: none"> - Added the secondary objective and endpoint: To evaluate the clinical efficacy of BIIB054 via MDS-UPDRS Total Score as measured by the change from baseline in MDS-UPDRS Total Score (Sum of Parts I, II, and III) at end of study - Added the secondary endpoint: Change from baseline to Week 52, Week 72, and end of study in MDS-UPDRS of Subparts I, II, and III (each part separately) - Removed the delineation between Year 1 (Placebo-Controlled Portion of the Study) |

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.

| |
|--|
| The study did not meet its primary endpoint for year 1 and failed to meet secondary endpoints resulting in the development of BIIB054 for Parkinson's disease to be discontinued and SPARK study was closed. |
|--|

Notes: