Clinical trial results:
A randomized, placebo-controlled, double-blind, parallel group, multicenter study to investigate the efficacy and safety of 5 fixed doses of BAY 85- 3934 administered orally in the correction of anemia in pre-dialysis subjects with chronic kidney disease not currently treated with erythropoiesis-stimulating agent in Europe and Asia Pacific

Summary

EudraCT number	2013-001193-14
Trial protocol	DE IT HU BG ES PL
Global end of trial date	23 September 2015

Results information

Result version number	v1 (current)
This version publication date	30 September 2016
First version publication date	30 September 2016

Trial information

Trial identification

Sponsor protocol code	BAY85-3934/15141

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02021370
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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	23 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy for up to 16 weeks of fixed dose treatment with BAY85-3934 versus placebo as measured by haemoglobin (Hb) levels.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 February 2014
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	Bulgaria: 12
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 18
Country: Number of subjects enrolled	Japan: 23
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 20
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 5
Worldwide total number of subjects	121
EEA total number of subjects	75

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)	38
From 65 to 84 years	77
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 53 active centers, enrolled subjects in 13 countries: Australia, Bulgaria, France, Germany, Hungary, Israel, Italy, Japan, Korea, Poland, Romania, Spain, and UK between 10 February 2014 (first subject first visit) and 23 September 2015 (last subject last visit).

Pre-assignment

Screening details:

Of 210 subjects who were screened, 121 were randomised and treated and 89 subjects were not randomised. Of the treated subjects, 30 entered follow-up period and 87 subjects entered an extension study. Though all arms in follow-up period were mutually exclusive, in the respective section it is ticked "No" due to database validation rule constraints.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Molidustat (BAY85-3934) 25 mg Once Daily

Arm description:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 milligram (mg) along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg in the morning daily for 16 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Arm title	Molidustat (BAY85-3934) 50 mg Once Daily

Arm description:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Arm type	Experimental

Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) in the morning daily for 16 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Arm title	Molidustat (BAY85-3934) 75 mg Once Daily

Arm description:

Subjects received orally 3 tablets of Molidustat (BAY85-3934) (3 * 25 mg) in the morning and with approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 3 tablets of Molidustat (BAY85-3934) (3 * 25 mg) in the morning daily for 16 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 3 tablets of matching placebo in the evening daily for 16 weeks.

Arm title	Molidustat (BAY85-3934) 25 mg Twice Daily

Arm description:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Arm title	Molidustat (BAY85-3934) 50 mg Twice Daily

Arm description:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Arm title	Placebo Twice Daily

Arm description:

Subjects received orally 3 tablets of matching placebo to Molidustat (BAY85-3934) tablets orally in the morning and approximately 12 hours apart in the evening daily for 16 weeks.

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

Dosage and administration details:

Subjects received orally 3 tablets of matching placebo to Molidustat (BAY85-3934) tablets in the morning and approximately 12 hours apart in the evening daily for 16 weeks.

Number of subjects in period 1	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily
Started	19	21	22
Completed	10	11	4
Not completed	9	10	18
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	3	-	3
Other	1	-	1

Protocol Violation	1	1	1
Protocol-driven decision point	4	8	13
Lost to follow-up	-	-	-

Number of subjects in period 1	Molidustat (BAY85-3934) 25 mg Twice Daily	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily
Started	19	20	20
Completed	11	5	18
Not completed	8	15	2
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	2	1	-
Other	-	-	1
Protocol Violation	-	-	-
Protocol-driven decision point	5	14	1
Lost to follow-up	1	-	-

Period 2

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

Arms

Are arms mutually exclusive?	No
Arm title	Molidustat (BAY85-3934) 25 mg Once Daily

Arm description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg in the morning daily for 16 weeks during treatment period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks during treatment period.

Arm title	Molidustat (BAY85-3934) 50 mg Once Daily

Arm description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) in the morning daily for 16 weeks during treatment period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks during treatment period.

Arm title	Molidustat (BAY85-3934) 75 mg Once Daily

Arm description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 3 tablets of Molidustat (BAY85-3934) (3 * 25 mg) in the morning daily for 16 weeks during treatment period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 3 tablets of matching placebo in the evening daily for 16 weeks during treatment period.

Arm title	Molidustat (BAY85-3934) 25 mg Twice Daily

Arm description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg in the morning, and approximately 12 hours apart in the evening daily for 16 weeks during treatment period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks during treatment period.

Arm title	Molidustat (BAY85-3934) 50 mg Twice Daily

Arm description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Arm type	Experimental
Investigational medicinal product name	Molidustat
Investigational medicinal product code	BAY85-3934
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) in the morning, and approximately 12 hours apart in the evening daily for 16 weeks during treatment period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received orally 1 tablet of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks during treatment period.

Arm title	Placebo Twice Daily

Arm description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

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

Dosage and administration details:

Subjects received orally 3 tablets of matching placebo to Molidustat (BAY85-3934) tablets in the morning and approximately 12 hours apart in the evening daily for 16 weeks during treatment period.

Number of subjects in period 2	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily
Started	5	5	7
Completed	4	3	7
Not completed	1	2	0
Consent withdrawn by subject	-	1	-

Adverse event, non-fatal	-	-	-
Other	-	-	-
Protocol Violation	-	1	-
Lost to follow-up	1	-	-

Number of subjects in period 2	Molidustat (BAY85-3934) 25 mg Twice Daily	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily
Started	8	3	2
Completed	5	3	1
Not completed	3	0	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	1	-	-
Other	1	-	1
Protocol Violation	-	-	-
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Molidustat (BAY85-3934) 25 mg Once Daily
Reporting group description:	
Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 milligram (mg) along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.	
Reporting group title	Molidustat (BAY85-3934) 50 mg Once Daily
Reporting group description:	
Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.	
Reporting group title	Molidustat (BAY85-3934) 75 mg Once Daily
Reporting group description:	
Subjects received orally 3 tablets of Molidustat (BAY85-3934) (3 * 25 mg) in the morning and with approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.	
Reporting group title	Molidustat (BAY85-3934) 25 mg Twice Daily
Reporting group description:	
Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.	
Reporting group title	Molidustat (BAY85-3934) 50 mg Twice Daily
Reporting group description:	
Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.	
Reporting group title	Placebo Twice Daily
Reporting group description:	
Subjects received orally 3 tablets of matching placebo to Molidustat (BAY85-3934) tablets orally in the morning and approximately 12 hours apart in the evening daily for 16 weeks.	

Reporting group values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily
Number of subjects	19	21	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	69.2	68.2	70.7
standard deviation	± 12.09	± 13.3	± 9.7
Gender categorical Units: Subjects			
Female	5	12	9
Male	14	9	13
Number of Japanese and Non-Japanese Subjects Units: Subjects			
Japanese Subjects	2	8	5
Non-Japanese Subjects	17	13	17

Estimated Glomerular Filtration Rate (eGFR)			
eGFR is calculated using Modification of Diet in Renal Disease (MDRD) formula.			
Units: milliliter/minute/1.73 square meter			
arithmetic mean	25.206	22.858	23.477
standard deviation	± 14.0846	± 11.5707	± 10.0174
Local Laboratory Hemoglobin Levels			
Units: gram/deciliter (g/dL)			
arithmetic mean	9.373	9.548	9.643
standard deviation	± 0.6965	± 0.6604	± 0.6496
Erythropoietin			
The number of subjects evaluated for Erythropoietin for the arms BAY85-3934 25 mg once daily, 50 mg once daily, 75 mg once daily, 25 mg twice daily, 50 mg twice daily, were n = 19,20,22,17,19,18 respectively.			
Units: international units/liter			
arithmetic mean	20.327	12.476	12.194
standard deviation	± 23.3699	± 6.9364	± 10.66
Reticulocyte Count			
The number of subjects evaluated for Reticulocyte Count for the arms BAY85-3934 25 mg once daily, 50 mg once daily, 75 mg once daily, 25 mg twice daily, 50 mg twice daily, were n = 9,7,13,9,13,8 respectively.			
Units: giga/liter			
arithmetic mean	77.8	48.7	65.1
standard deviation	± 21.93	± 19.41	± 30.56

Reporting group values	Molidustat (BAY85-3934) 25 mg Twice Daily	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily
Number of subjects	19	20	20
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	69.8	65.3	67.1
standard deviation	± 12.22	± 12.84	± 15.92
Gender categorical			
Units: Subjects			
Female	9	10	11
Male	10	10	9
Number of Japanese and Non-Japanese Subjects			
Units: Subjects			
Japanese Subjects	1	6	1
Non-Japanese Subjects	18	14	19
Estimated Glomerular Filtration Rate (eGFR)			
eGFR is calculated using Modification of Diet in Renal Disease (MDRD) formula.			
Units: milliliter/minute/1.73 square meter			
arithmetic mean	25.157	20.573	22.994
standard deviation	± 11.8923	± 14.2655	± 11.5534
Local Laboratory Hemoglobin Levels			
Units: gram/deciliter (g/dL)			

arithmetic mean	9.347	9.46	9.535
standard deviation	± 0.4982	± 1.0751	± 0.6473
Erythropoietin			
The number of subjects evaluated for Erythropoietin for the arms BAY85-3934 25 mg once daily, 50 mg once daily, 75 mg once daily, 25 mg twice daily, 50 mg twice daily, were n = 19,20,22,17,19,18 respectively.			
Units: international units/liter			
arithmetic mean	15.458	10.111	10.097
standard deviation	± 15.5526	± 4.6627	± 5.8497
Reticulocyte Count			
The number of subjects evaluated for Reticulocyte Count for the arms BAY85-3934 25 mg once daily, 50 mg once daily, 75 mg once daily, 25 mg twice daily, 50 mg twice daily, were n = 9,7,13,9,13,8 respectively.			
Units: giga/liter			
arithmetic mean	57.9	60.2	72.8
standard deviation	± 19.68	± 19.45	± 22.35

Reporting group values	Total		
Number of subjects	121		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	56		
Male	65		
Number of Japanese and Non-Japanese Subjects			
Units: Subjects			
Japanese Subjects	23		
Non-Japanese Subjects	98		
Estimated Glomerular Filtration Rate (eGFR)			
eGFR is calculated using Modification of Diet in Renal Disease (MDRD) formula.			
Units: milliliter/minute/1.73 square meter			
arithmetic mean			
standard deviation	-		
Local Laboratory Hemoglobin Levels			
Units: gram/deciliter (g/dL)			
arithmetic mean			
standard deviation	-		
Erythropoietin			
The number of subjects evaluated for Erythropoietin for the arms BAY85-3934 25 mg once daily, 50 mg once daily, 75 mg once daily, 25 mg twice daily, 50 mg twice daily, were n = 19,20,22,17,19,18 respectively.			
Units: international units/liter			
arithmetic mean			
standard deviation	-		
Reticulocyte Count			

The number of subjects evaluated for Reticulocyte Count for the arms BAY85-3934 25 mg once daily, 50 mg once daily, 75 mg once daily, 25 mg twice daily, 50 mg twice daily, were n = 9,7,13,9,13,8 respectively.			
Units: giga/liter			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Molidustat (BAY85-3934) 25 mg Once Daily

Reporting group description:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 milligram (mg) along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 50 mg Once Daily

Reporting group description:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 75 mg Once Daily

Reporting group description:

Subjects received orally 3 tablets of Molidustat (BAY85-3934) (3 * 25 mg) in the morning and with approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 25 mg Twice Daily

Reporting group description:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 50 mg Twice Daily

Reporting group description:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Reporting group title	Placebo Twice Daily

Reporting group description:

Subjects received orally 3 tablets of matching placebo to Molidustat (BAY85-3934) tablets orally in the morning and approximately 12 hours apart in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 25 mg Once Daily

Reporting group description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Reporting group title	Molidustat (BAY85-3934) 50 mg Once Daily

Reporting group description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Reporting group title	Molidustat (BAY85-3934) 75 mg Once Daily

Reporting group description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Reporting group title	Molidustat (BAY85-3934) 25 mg Twice Daily

Reporting group description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Reporting group title	Molidustat (BAY85-3934) 50 mg Twice Daily

Reporting group description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Reporting group title	Placebo Twice Daily

Reporting group description:

Subjects entered a follow-up period for a duration of 8 weeks after completing treatment.

Subject analysis set title	Modified Intent-To-Treat set (mITT)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

mITT (N= 121) included all subjects randomized to study treatment, who received at least 1 dose of study treatment, and who had at least 1 post-baseline efficacy value available.

Subject analysis set title	Safety Analysis set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

SAF (N= 121) included all randomized subjects who received at least 1 dose of study treatment.

Subject analysis set title	Pharmacodynamic set (PDS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PDS (N= 121) included all subjects randomized with at least 1 available valid PD measurement.

Primary: Change in Local Laboratory Hemoglobin Level From Baseline to the Study Evaluation Period (Last 4 Weeks of Treatment Period)

End point title	Change in Local Laboratory Hemoglobin Level From Baseline to the Study Evaluation Period (Last 4 Weeks of Treatment Period)

End point description:

Study Evaluation Period (SEP) was defined as the last 4 planned weeks of the study treatment period. The values represented here are the average of all measurements taken during the last 4 weeks of the study treatment period.

End point type	Primary

End point timeframe:

Baseline, Weeks 13 to 16

End point values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily	Molidustat (BAY85-3934) 25 mg Twice Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12[1]	11[2]	5[3]	13[4]
Units: gram/deciliter (g/dL)				
arithmetic mean (standard deviation)				
Change at SEP	1.43 (± 1.115)	1.42 (± 1.053)	1.82 (± 0.701)	1.66 (± 1.132)

Notes:

[1] - mITT with number of subjects evaluable for this end point.

[2] - mITT with number of subjects evaluable for this end point.

[3] - mITT with number of subjects evaluable for this end point.

[4] - mITT with number of subjects evaluable for this end point.

End point values	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[5]	19[6]		
Units: gram/deciliter (g/dL)				
arithmetic mean (standard deviation)				
Change at SEP	1.84 (± 1.192)	0.17 (± 0.864)		

Notes:

[5] - mITT with number of subjects evaluable for this end point.

[6] - mITT with number of subjects evaluable for this end point.

Statistical analyses

Statistical analysis title	SEP: Analysis for Molidustat 25 mg Once Daily

Statistical analysis description:

Results are reported including Least square mean (LS-mean) difference and 95 percent (%) confidence intervals (CI). LS mean difference was based on constrained longitudinal data analysis (cLDA) model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	LS Mean Difference
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	2.08
Variability estimate	Standard error of the mean
Dispersion value	0.418

Notes:

[7] - Analysis type involved here is exploratory.

Statistical analysis title	SEP: Analysis for Molidustat 50 mg Once Daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	LS Mean Difference
Point estimate	1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.63
Variability estimate	Standard error of the mean
Dispersion value	0.397

Notes:

[8] - Analysis type involved here is exploratory.

Statistical analysis title	SEP: Analysis for Molidustat 75 mg Once Daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit),

the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 75 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	LS Mean Difference
Point estimate	2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	3.16
Variability estimate	Standard error of the mean
Dispersion value	0.447

Notes:

[9] - Analysis type involved here is exploratory.

Statistical analysis title	SEP: Analysis for Molidustat 25 mg Twice Daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	LS Mean Difference
Point estimate	1.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.47
Variability estimate	Standard error of the mean
Dispersion value	0.366

Notes:

[10] - Analysis type involved here is exploratory.

Statistical analysis title	SEP: Analysis for Molidustat 50 mg Twice Daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Twice Daily v Placebo Twice Daily

Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	LS Mean Difference
Point estimate	2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	3.37
Variability estimate	Standard error of the mean
Dispersion value	0.503

Notes:

[11] - Analysis type involved here is exploratory.

Secondary: Change in Local Laboratory Hemoglobin Level From Baseline to Multiple Time Points in First 12 Weeks of Treatment Period

End point title	Change in Local Laboratory Hemoglobin Level From Baseline to Multiple Time Points in First 12 Weeks of Treatment Period

End point description:

Here 'n' signifies those subjects who were evaluable for this measure at given time points for each group.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 3, 5, 7, 9, 11

End point values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily	Molidustat (BAY85-3934) 25 mg Twice Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[12]	21[13]	22[14]	19[15]
Units: g/dL				
arithmetic mean (standard deviation)				
Change at Week 2 (n= 19,21,22,19,20,20)	0.35 (± 0.536)	0.11 (± 0.454)	0.28 (± 0.395)	0.12 (± 0.547)
Change at Week 3 (n= 19,20,22,18,20,19)	0.41 (± 0.619)	0.44 (± 0.531)	0.58 (± 0.553)	0.53 (± 0.565)
Change at Week 5 (n= 19,19,20,16,19,20)	0.49 (± 0.758)	0.82 (± 0.809)	1.26 (± 0.793)	1.01 (± 0.588)
Change at Week 7 (n= 16,13,16,16,15,20)	0.7 (± 0.676)	0.95 (± 0.981)	1.58 (± 0.938)	1.24 (± 1.022)
Change at Week 9 (n= 16,13,13,14,12,19)	1.15 (± 0.938)	1.1 (± 1.026)	1.44 (± 1.056)	1.3 (± 0.937)
Change at Week 11 (n= 15,10,10,13,10,19)	1.28 (± 1.274)	1.14 (± 0.864)	1.67 (± 0.958)	1.36 (± 0.788)

Notes:

[12] - mITT

[13] - mITT

[14] - mITT

[15] - mITT

End point values	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[16]	20[17]		
Units: g/dL				
arithmetic mean (standard deviation)				
Change at Week 2 (n= 19,21,22,19,20,20)	0.47 (± 0.812)	0.06 (± 0.491)		
Change at Week 3 (n= 19,20,22,18,20,19)	0.56 (± 0.716)	0.08 (± 0.577)		
Change at Week 5 (n= 19,19,20,16,19,20)	1.26 (± 1.064)	0.08 (± 0.568)		
Change at Week 7 (n= 16,13,16,16,15,20)	1.32 (± 0.873)	-0.09 (± 0.71)		
Change at Week 9 (n= 16,13,13,14,12,19)	1.81 (± 1.054)	0.05 (± 0.709)		
Change at Week 11 (n= 15,10,10,13,10,19)	1.96 (± 1.248)	-0.03 (± 0.883)		

Notes:

[16] - mITT

[17] - mITT

Statistical analyses

Statistical analysis title	Week 2: Analysis for Molidustat 25 mg once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[18]
Parameter estimate	LS Mean Difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.66
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[18] - Analysis type involved here is exploratory.

Statistical analysis title	Week 2: Analysis for Molidustat 50 mg once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Once Daily v Placebo Twice Daily

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	LS Mean Difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.34
Variability estimate	Standard error of the mean
Dispersion value	0.146

Notes:

[19] - Analysis type involved here is exploratory.

Statistical analysis title	Week 2: Analysis for Molidustat 75 mg once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 75 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[20]
Parameter estimate	LS Mean Difference
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	0.21

Notes:

[20] - Analysis type involved here is exploratory.

Statistical analysis title	Week 2: Analysis for Molidustat 25 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[21]
Parameter estimate	LS Mean Difference
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.44
Variability estimate	Standard error of the mean
Dispersion value	0.167

Notes:

[21] - Analysis type involved here is exploratory.

Statistical analysis title	Week 2: Analysis for Molidustat 50 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[22]
Parameter estimate	LS Mean Difference
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.214

Notes:

[22] - Analysis type involved here is exploratory.

Statistical analysis title	Week 3: Analysis for Molidustat 25 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[23]
Parameter estimate	LS Mean Difference
Point estimate	0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.79
Variability estimate	Standard error of the mean
Dispersion value	0.191

Notes:

[23] - Analysis type involved here is exploratory. Number of subjects in this analysis were 38. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 3: Analysis for Molidustat 50 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[24]
Parameter estimate	LS Mean Difference
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.176

Notes:

[24] - Analysis type involved here is exploratory. Number of subjects in this analysis were 39. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 3: Analysis for Molidustat 75 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 75 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[25]
Parameter estimate	LS Mean Difference
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	0.97
Variability estimate	Standard error of the mean
Dispersion value	0.212

Notes:

[25] - Analysis type involved here is exploratory. Number of subjects in this analysis were 41. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 3: Analysis for Molidustat 25 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA

model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[26]
Parameter estimate	LS Mean Difference
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.91
Variability estimate	Standard error of the mean
Dispersion value	0.197

Notes:

[26] - Analysis type involved here is exploratory. Number of subjects in this analysis were 37. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 3: Analysis for Molidustat 50 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[27]
Parameter estimate	LS Mean Difference
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.95
Variability estimate	Standard error of the mean
Dispersion value	0.204

Notes:

[27] - Analysis type involved here is exploratory. Number of subjects in this analysis were 39. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 5: Analysis for Molidustat 25 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Once Daily v Placebo Twice Daily

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[28]
Parameter estimate	LS Mean Difference
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.89
Variability estimate	Standard error of the mean
Dispersion value	0.216

Notes:

[28] - Analysis type involved here is exploratory. Number of subjects in this analysis were 39. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 5: Analysis for Molidustat 50 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[29]
Parameter estimate	LS Mean Difference
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.25
Variability estimate	Standard error of the mean
Dispersion value	0.233

Notes:

[29] - Analysis type involved here is exploratory. Number of subjects in this analysis were 39. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 5: Analysis for Molidustat 75 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 75 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[30]
Parameter estimate	LS Mean Difference
Point estimate	1.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.64
Variability estimate	Standard error of the mean
Dispersion value	0.214

Notes:

[30] - Analysis type involved here is exploratory. Number of subjects in this analysis were 40. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 5: Analysis for Molidustat 25 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[31]
Parameter estimate	LS Mean Difference
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.38
Variability estimate	Standard error of the mean
Dispersion value	0.195

Notes:

[31] - Analysis type involved here is exploratory. Number of subjects in this analysis were 36. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 5: Analysis for Molidustat 50 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[32]
Parameter estimate	LS Mean Difference
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.77
Variability estimate	Standard error of the mean
Dispersion value	0.271

Notes:

[32] - Analysis type involved here is exploratory. Number of subjects in this analysis were 39. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 7: Analysis for Molidustat 25 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[33]
Parameter estimate	LS Mean Difference
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.251

Notes:

[33] - Analysis type involved here is exploratory. Number of subjects in this analysis were 36. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 7: Analysis for Molidustat 50 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[34]
Parameter estimate	LS Mean Difference
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.75
Variability estimate	Standard error of the mean
Dispersion value	0.296

Notes:

[34] - Analysis type involved here is exploratory. Number of subjects in this analysis were 33. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 7: Analysis for Molidustat 75 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA

model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 75 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[35]
Parameter estimate	LS Mean Difference
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	2.21
Variability estimate	Standard error of the mean
Dispersion value	0.223

Notes:

[35] - Analysis type involved here is exploratory. Number of subjects in this analysis were 36. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 7: Analysis for Molidustat 25 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[36]
Parameter estimate	LS Mean Difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.89
Variability estimate	Standard error of the mean
Dispersion value	0.291

Notes:

[36] - Analysis type involved here is exploratory. Number of subjects in this analysis were 36. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 7: Analysis for Molidustat 50 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Twice Daily v Placebo Twice Daily

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[37]
Parameter estimate	LS Mean Difference
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	2.25
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[37] - Analysis type involved here is exploratory. Number of subjects in this analysis were 35. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 9: Analysis for Molidustat 25 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[38]
Parameter estimate	LS Mean Difference
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.69
Variability estimate	Standard error of the mean
Dispersion value	0.302

Notes:

[38] - Analysis type involved here is exploratory. Number of subjects in this analysis were 35. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 9: Analysis for Molidustat 50 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[39]
Parameter estimate	LS Mean Difference
Point estimate	1.29

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.93
Variability estimate	Standard error of the mean
Dispersion value	0.315

Notes:

[39] - Analysis type involved here is exploratory. Number of subjects in this analysis were 32. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 9: Analysis for Molidustat 75 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 75 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[40]
Parameter estimate	LS Mean Difference
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.13
Variability estimate	Standard error of the mean
Dispersion value	0.235

Notes:

[40] - Analysis type involved here is exploratory. Number of subjects in this analysis were 32. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 9: Analysis for Molidustat 25 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[41]
Parameter estimate	LS Mean Difference
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	2.05
Variability estimate	Standard error of the mean
Dispersion value	0.299

Notes:

[41] - Analysis type involved here is exploratory. Number of subjects in this analysis were 33. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 9: Analysis for Molidustat 50 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[42]
Parameter estimate	LS Mean Difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	2.64
Variability estimate	Standard error of the mean
Dispersion value	0.356

Notes:

[42] - Analysis type involved here is exploratory. Number of subjects in this analysis were 31. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 11: Analysis for Molidustat 25 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[43]
Parameter estimate	LS Mean Difference
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.11
Variability estimate	Standard error of the mean
Dispersion value	0.381

Notes:

[43] - Analysis type involved here is exploratory. Number of subjects in this analysis were 34. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 11: Analysis for Molidustat 50 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA

model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other[44]
Parameter estimate	LS Mean Difference
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	2.34
Variability estimate	Standard error of the mean
Dispersion value	0.353

Notes:

[44] - Analysis type involved here is exploratory. Number of subjects in this analysis were 29. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 11: Analysis for Molidustat 75 mg Once daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 75 mg Once Daily v Placebo Twice Daily
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[45]
Parameter estimate	LS Mean Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.51
upper limit	2.5
Variability estimate	Standard error of the mean
Dispersion value	0.25

Notes:

[45] - Analysis type involved here is exploratory. Number of subjects in this analysis were 29. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 11: Analysis for Molidustat 25 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 25 mg Twice Daily v Placebo Twice Daily

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[46]
Parameter estimate	LS Mean Difference
Point estimate	1.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	2.29
Variability estimate	Standard error of the mean
Dispersion value	0.306

Notes:

[46] - Analysis type involved here is exploratory. Number of subjects in this analysis were 32. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Statistical analysis title	Week 11: Analysis for Molidustat 50 mg Twice daily

Statistical analysis description:

Results are reported including LS-mean difference and 95 % CI. LS mean difference was based on cLDA model including the response vector consisting of baseline and values at each post-baseline time point, and the repeated measures model including treatment, randomization stratification factors, time (visit), the interaction of time by treatment, and the interaction of time by randomization factors.

Comparison groups	Molidustat (BAY85-3934) 50 mg Twice Daily v Placebo Twice Daily
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[47]
Parameter estimate	LS Mean Difference
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.51
upper limit	3.45
Variability estimate	Standard error of the mean
Dispersion value	0.468

Notes:

[47] - Analysis type involved here is exploratory. Number of subjects in this analysis were 29. The number of subjects mentioned in the above table is auto-generated which cannot be edited.

Secondary: Rate of Change in Hemoglobin Level Over Time

End point title	Rate of Change in Hemoglobin Level Over Time

End point description:

Rate of change is defined as change in Hb values divided by duration between two Hb values (involved in the calculation of the change). Here, n indicates the number of subjects evaluable for this measure at specified time points for each arm group respectively. Data for rate of change in local Hb per 4-week interval is represented here.

End point type	Secondary

End point timeframe:

From Baseline up to 16 weeks

End point values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily	Molidustat (BAY85-3934) 25 mg Twice Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[48]	19[49]	20[50]	16[51]
Units: g/dL/day				
arithmetic mean (standard deviation)				
Week 5 (n= 19,19,20,16,19,20)	0.017 (± 0.0258)	0.03 (± 0.0311)	0.043 (± 0.0271)	0.035 (± 0.02)
Week 9 (n= 16,13,13,14,12,19)	0.018 (± 0.0254)	0.016 (± 0.0343)	0.023 (± 0.0287)	0.011 (± 0.0218)
Week 13 (n= 13,11,9,13,9,19)	0.012 (± 0.0234)	0.023 (± 0.0162)	0.017 (± 0.0206)	0.015 (± 0.0194)
Week 17 (n= 10,11,4,12,6,18)	0.004 (± 0.0217)	0.003 (± 0.0168)	-0.013 (± 0.0126)	0.002 (± 0.0301)

Notes:

[48] - mITT

[49] - mITT with number of subjects evaluable for this end point.

[50] - mITT with number of subjects evaluable for this end point.

[51] - mITT with number of subjects evaluable for this end point.

End point values	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[52]	20[53]		
Units: g/dL/day				
arithmetic mean (standard deviation)				
Week 5 (n= 19,19,20,16,19,20)	0.043 (± 0.0392)	0.003 (± 0.0187)		
Week 9 (n= 16,13,13,14,12,19)	0.03 (± 0.0333)	-0.002 (± 0.0219)		
Week 13 (n= 13,11,9,13,9,19)	0.021 (± 0.0362)	0.006 (± 0.0189)		
Week 17 (n= 10,11,4,12,6,18)	-0.003 (± 0.0288)	0.001 (± 0.0237)		

Notes:

[52] - mITT with number of subjects evaluable for this end point.

[53] - mITT

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment Exposure

End point title	Duration of Treatment Exposure

End point description:

Study treatment exposure measured as duration of exposure, defined as duration in days between the first dose date and last dose date.

End point type	Secondary

End point timeframe:

From Baseline up to 16 Weeks

End point values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily	Molidustat (BAY85-3934) 25 mg Twice Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[54]	21[55]	22[56]	19[57]
Units: days				
arithmetic mean (standard deviation)	88.7 (± 33.56)	73.8 (± 43.17)	60.5 (± 36.33)	84.9 (± 42.33)

Notes:

[54] - mITT

[55] - mITT

[56] - mITT

[57] - mITT

End point values	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[58]	20[59]		
Units: days				
arithmetic mean (standard deviation)	68.5 (± 38.9)	108.9 (± 16.07)		

Notes:

[58] - mITT

[59] - mITT

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Adjudicated Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adjudicated Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. A Serious Adverse Event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent SAEs that required adjudication (cardiac and vascular events) were reviewed by an independent Central Adjudication Committee (CAC) comprising of individual clinical experts.

End point type	Other pre-specified

End point timeframe:

From the start of study drug administration up to the end of the treatment plus 3 days (Up to 119 days)

End point values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily	Molidustat (BAY85-3934) 25 mg Twice Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19[60]	21[61]	22[62]	19[63]
Units: Subjects	0	0	1	2

Notes:

[60] - SAF

[61] - SAF

[62] - SAF

[63] - SAF

End point values	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[64]	20[65]		
Units: Subjects	1	2		

Notes:

[64] - SAF

[65] - SAF

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Erythropoietin at Specified Time Point

End point title	Change From Baseline in Erythropoietin at Specified Time Point

End point description:

Erythropoietin was determined at different timepoints using sparse sampling approach. Here, EOT = End of the Treatment, AT = At Trough, 8TO12 = 8 to 12 hours post morning dose time window during which maximum erythropoietin is expected. Here 'n' signifies those subjects who were evaluable for this measure at given time points for each group, and '99999' here indicates that data was not calculated. Arithmetic mean and Standard deviation was not estimated if evaluable subjects were less than 3, as 2 or less collected values were not sufficient to calculate a reliable estimation.

End point type	Other pre-specified

End point timeframe:

Baseline, Weeks 3, 5, 7, 9, 11, 13, 17 and EOT (last day of Week 16)

End point values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily	Molidustat (BAY85-3934) 25 mg Twice Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17[66]	19[67]	22[68]	16[69]
Units: international units/liter				
arithmetic mean (standard deviation)				
Change at Baseline-8TO12 (n= 16,19,22,16,16,17)	9.883 (± 17.8128)	14.446 (± 10.8185)	25.204 (± 20.9353)	8.263 (± 7.5428)

Change at Week 3 - AT (n= 17,18,18,16,18,17)	5.446 (± 18.5299)	4.103 (± 7.0193)	10.011 (± 17.537)	4.986 (± 9.1742)
Change at Week 5 - AT (n= 15,13,16,12,14,16)	-3.649 (± 14.0522)	-0.115 (± 2.5551)	12.883 (± 17.9653)	-0.183 (± 8.8559)
Change at Week 7-8TO12 (n= 16,11,13,11,12,17)	5.417 (± 16.5243)	13.982 (± 10.9644)	38.453 (± 29.0531)	7.102 (± 9.2733)
Change at Week 9 - AT (n= 16,10,10,10,9,17)	-3.316 (± 12.9551)	-0.67 (± 2.1217)	12.852 (± 20.9382)	-1.027 (± 4.0031)
Change at Week 11-8TO12 (n= 2,1,2,2,2,5)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Week 13 - AT (n= 12,10,5,11,8,17)	3.614 (± 21.4524)	0.724 (± 2.4879)	3.288 (± 7.5673)	0.634 (± 6.4031)
Change at Week 17 - AT (n= 10,10,3,9,4,16)	14.753 (± 50.8998)	0.38 (± 4.9197)	21.01 (± 33.6173)	2.977 (± 4.2593)
Change at Week 17-8TO12 (n= 7,5,1,9,2,15)	17.361 (± 25.8176)	12.536 (± 17.3382)	99999 (± 99999)	10.846 (± 10.8155)
Change at EOT - AT (n= 17,16,18,14,16,18)	5.142 (± 40.6265)	2.689 (± 6.8917)	6.821 (± 18.863)	2.31 (± 6.8794)
Change at EOT-8TO12 (n= 10,6,5,10,3,15)	11.976 (± 23.678)	11.15 (± 15.8751)	38.834 (± 25.8589)	9.71 (± 10.8108)

Notes:

[66] - PDS with number of subjects evaluable for this end point.

[67] - PDS with number of subjects evaluable for this end point.

[68] - PDS

[69] - PDS with number of subjects evaluable for this end point.

End point values	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[70]	18[71]		
Units: international units/liter				
arithmetic mean (standard deviation)				
Change at Baseline-8TO12 (n= 16,19,22,16,16,17)	11.397 (± 11.798)	1.136 (± 3.3001)		
Change at Week 3 - AT (n= 17,18,18,16,18,17)	23.852 (± 24.4867)	-0.509 (± 2.2008)		
Change at Week 5 - AT (n= 15,13,16,12,14,16)	23.361 (± 34.4752)	0.184 (± 4.0278)		
Change at Week 7-8TO12 (n= 16,11,13,11,12,17)	27.283 (± 32.9348)	-0.345 (± 3.8187)		
Change at Week 9 - AT (n= 16,10,10,10,9,17)	20.349 (± 41.3935)	-0.49 (± 4.3537)		
Change at Week 11-8TO12 (n= 2,1,2,2,2,5)	99999 (± 99999)	0.344 (± 2.7867)		
Change at Week 13 - AT (n= 12,10,5,11,8,17)	34.348 (± 62.4966)	-0.373 (± 4.4162)		
Change at Week 17 - AT (n= 10,10,3,9,4,16)	65.613 (± 74.0708)	-0.484 (± 5.3113)		
Change at Week 17-8TO12 (n= 7,5,1,9,2,15)	99999 (± 99999)	1.659 (± 8.3329)		
Change at EOT - AT (n= 17,16,18,14,16,18)	22.034 (± 45.2669)	-0.622 (± 5.2914)		
Change at EOT-8TO12 (n= 10,6,5,10,3,15)	21.48 (± 21.0086)	1.659 (± 8.3329)		

Notes:

[70] - PDS with number of subjects evaluable for this end point.

[71] - PDS with number of subjects evaluable for this end point.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Reticulocyte Count at Specified Time Point

End point title	Change From Baseline in Reticulocyte Count at Specified Time Point

End point description:

Reticulocytes are slightly immature red blood cells in the blood. Here 'n' signifies those subjects who were evaluable for this measure at given time points for each group, and '99999' here indicates that data was not calculated. Arithmetic mean and Standard deviation was not estimated if evaluable subjects were less than 3, as 2 or less collected values were not sufficient to calculate a reliable estimation.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 3, 5, 9, 13, 17, EOT (last day of Week 16)

End point values	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily	Molidustat (BAY85-3934) 25 mg Twice Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[72]	7[73]	12[74]	9[75]
Units: giga/liter				
arithmetic mean (standard deviation)				
Change at Week 3 (n= 8,7,8,9,10,7)	9.6 (± 16.39)	27 (± 20.49)	21.8 (± 31.25)	31.8 (± 25.81)
Change at Week 5 (n= 6,3,7,8,7,7)	1 (± 26.26)	12.7 (± 11.72)	11.3 (± 22.51)	28.4 (± 25.22)
Change at Week 9 (n= 8,5,5,6,5,7)	-4.6 (± 10)	7.6 (± 10.11)	5.4 (± 4.72)	23.3 (± 27.43)
Change at Week 13 (n= 6,5,3,7,5,7)	-9.2 (± 9.37)	11.2 (± 8.04)	-4.3 (± 13.28)	17.4 (± 30.24)
Change at Week 17 (n= 4,4,2,5,2,6)	-8.5 (± 6.45)	7.5 (± 5.57)	99999 (± 99999)	25.4 (± 28.82)
Change at EOT (n= 8,6,12,8,11,8)	-13.3 (± 16.02)	23.8 (± 26.1)	11.9 (± 32.66)	20.3 (± 23.18)

Notes:

[72] - PDS with number of subjects evaluable for this end point.

[73] - PDS with number of subjects evaluable for this end point.

[74] - PDS with number of subjects evaluable for this end point.

[75] - PDS with number of subjects evaluable for this end point.

End point values	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[76]	8[77]		
Units: giga/liter				
arithmetic mean (standard deviation)				
Change at Week 3 (n= 8,7,8,9,10,7)	35.5 (± 21.79)	-2 (± 13.44)		
Change at Week 5 (n= 6,3,7,8,7,7)	18.4 (± 11.4)	-8 (± 9.92)		
Change at Week 9 (n= 8,5,5,6,5,7)	3.6 (± 24.74)	2 (± 15.35)		
Change at Week 13 (n= 6,5,3,7,5,7)	13.6 (± 9.69)	4.4 (± 12.87)		

Change at Week 17 (n= 4,4,2,5,2,6)	99999 (± 99999)	-7.5 (± 15.41)		
Change at EOT (n= 8,6,12,8,11,8)	18.6 (± 36.92)	-11.6 (± 18.81)		

Notes:

[76] - PDS with number of subjects evaluable for this end point.

[77] - PDS with number of subjects evaluable for this end point.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of study drug administration up to the end of the treatment plus 3 days (Up to 119 days)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Molidustat (BAY85-3934) 25 mg Once Daily

Reporting group description:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 50 mg Once Daily

Reporting group description:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 75 mg Once Daily

Reporting group description:

Subjects received orally 3 tablets of Molidustat (BAY85-3934) (3 * 25 mg) in the morning and with approximately 12 hours apart received 3 tablets of matching placebo in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 25 mg Twice Daily

Reporting group description:

Subjects received orally 1 tablet of Molidustat (BAY85-3934) 25 mg along with 2 tablets of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Reporting group title	Molidustat (BAY85-3934) 50 mg Twice Daily

Reporting group description:

Subjects received orally 2 tablets of Molidustat (BAY85-3934) (2 * 25 mg) along with 1 tablet of matching placebo in the morning, and approximately 12 hours apart in the evening daily for 16 weeks.

Reporting group title	Placebo Twice Daily

Reporting group description:

Subjects received orally 3 placebo tablets matched to Molidustat (BAY85-3934) tablets in the morning and approximately 12 hours apart in the evening daily for 16 weeks.

Serious adverse events	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 19 (26.32%)	1 / 21 (4.76%)	2 / 22 (9.09%)
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)			
Bladder transitional cell carcinoma			

subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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
Angina unstable			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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
Coronary artery disease			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (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
Myocardial infarction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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

Surgical and medical procedures			
Arteriovenous fistula operation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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			
Anaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (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
Gastrointestinal disorders			
Gastric polyps			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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			
Cholecystitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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			
Chronic kidney disease			

subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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			
Flank pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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			
Pyelonephritis acute			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (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
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urachal abscess			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (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
Decreased appetite			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (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	Molidustat (BAY85-3934) 25 mg Twice Daily	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 19 (26.32%)	1 / 20 (5.00%)	5 / 20 (25.00%)
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)			
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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			
Femur fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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			
Acute myocardial infarction			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (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
Angina unstable			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (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
Cardiac failure acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Arteriovenous fistula operation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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			
Gastric polyps			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (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
Mallory-Weiss syndrome			

subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (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
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis acute			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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
Urachal abscess			

subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (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

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

Non-serious adverse events	Molidustat (BAY85-3934) 25 mg Once Daily	Molidustat (BAY85-3934) 50 mg Once Daily	Molidustat (BAY85-3934) 75 mg Once Daily
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 19 (68.42%)	12 / 21 (57.14%)	15 / 22 (68.18%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 19 (15.79%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	5	1	2
Hypotension			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Arterial occlusive disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Peripheral artery thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Peripheral venous disease			

subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Generalised oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Nipple pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Bronchospasm			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	1 / 19 (5.26%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Carotid bruit			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Foreign body in eye			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Atrioventricular block first degree			

subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Cardiac failure chronic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Coronary artery disease			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Extrasystoles			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Headache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0

Myoclonus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	2 / 19 (10.53%)	1 / 21 (4.76%)	2 / 22 (9.09%)
occurrences (all)	2	1	2
Diarrhoea			

subjects affected / exposed	2 / 19 (10.53%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	2	3	0
Dyspepsia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastric polyps			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pancreatitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 19 (10.53%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			

Biliary colic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Rash			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Asteatosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hyperparathyroidism secondary			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			

subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Periarthritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Chest wall mass			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Cystitis			

subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infected skin ulcer			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	3
Onychomycosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 19 (5.26%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Post procedural infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Hyperkalaemia			
subjects affected / exposed	1 / 19 (5.26%)	2 / 21 (9.52%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Hyperuricaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Vitamin D deficiency			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Molidustat (BAY85-3934) 25 mg Twice Daily	Molidustat (BAY85-3934) 50 mg Twice Daily	Placebo Twice Daily
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	13 / 19 (68.42%)	13 / 20 (65.00%)	16 / 20 (80.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 19 (10.53%)	2 / 20 (10.00%)	5 / 20 (25.00%)
occurrences (all)	5	3	6
Hypotension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Arterial occlusive disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Peripheral artery thrombosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Peripheral venous disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oedema			

subjects affected / exposed	1 / 19 (5.26%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	2	2	0
Oedema peripheral			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Nipple pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Carotid bruit			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Foot fracture			

subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Foreign body in eye			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac failure chronic			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Coronary artery disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Tachycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
Headache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Cognitive disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Carotid arteriosclerosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Thrombocytopenia			

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Gastric polyps			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Inguinal hernia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Pancreatitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Epigastric discomfort			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Faeces soft			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			

subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Onychoclasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Asteatosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hyperparathyroidism secondary			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	3 / 20 (15.00%)
occurrences (all)	0	1	3
Hypothyroidism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Osteoarthritis			

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Periarthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest wall mass			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Infected skin ulcer			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	3 / 20 (15.00%)	2 / 20 (10.00%)
occurrences (all)	1	3	4
Onychomycosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Periodontitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	3 / 20 (15.00%)
occurrences (all)	0	1	3
Escherichia urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Post procedural infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	3 / 20 (15.00%)
occurrences (all)	0	1	3
Hyperuricaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Hypokalaemia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Metabolic acidosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Vitamin D deficiency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2014	This protocol amendment included the following modifications: mean screening Hb value was changed from less than 10 to less than or equal to 10.5 g/dL, heart failure was added to the list of SAEs to be adjudicated, End of the treatment (EoT) text was corrected, status of the BAY85-3934 phase I data was updated, concomitant medications in the exclusion criterion was clarified for the study population, timing of Hb assessment was adjusted from within 2 days to 3 days prior to visit to improve logistical planning of visits at sites, to increase study feasibility for subjects, some PK / PD assessments were removed, coagulation tests at baseline and month 1 and TSH at month 1 were added to calculate the change from baseline, modifications were made to improve the general clarity of the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

'99999' in the posting indicates that data was not calculated as evaluable subjects were less than 3, collected values were not sufficient to calculate a reliable estimation. Decimal places were automatically truncated if last decimal equals zero.

Notes: