Clinical trial results:
Multi-Center Phase II Study with Pomalidomide in Patients with Myeloproliferative Neoplasms in Fibrotic Stage

Summary

EudraCT number	2009-010738-23
Trial protocol	DE
Global end of trial date	14 September 2016

Results information

Result version number	v1 (current)
This version publication date	04 March 2021
First version publication date	04 March 2021

Trial information

Trial identification

Sponsor protocol code	MPN-SG 01-09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00949364
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Ulm
Sponsor organisation address	Albert-Einstein-Allee 23, Ulm, Germany, 89081
Public contact	Innere Medizin III, Studienzentrale, Universitätsklinikum Ulm, +49 731500 45901, frank.stegelmann@uniklinik-ulm.de
Scientific contact	Innere Medizin III, Studienzentrale, Universitätsklinikum Ulm, +49 731500 45901, frank.stegelmann@uniklinik-ulm.de

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	13 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 September 2016
Global end of trial reached?	Yes
Global end of trial date	14 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate clinical efficacy (disease response) of pomalidomide in MF patients based on the consensus criteria of the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT), extended by the criterion RBC-transfusion independence (TI)

Protection of trial subjects:

In this study, safety was assessed by evaluating the following: reported adverse events, clinical laboratory test results, vital signs measurements, ECG findings, chest X-ray, sonographic assessment of the Spleen, physical examination findings, monitoring of concomitant therapy. For each safety parameter, all findings
(whether normal or abnormal) were recorded in the CRF.

Background therapy:

-

Evidence for comparator:

-

Actual start date of recruitment	03 December 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 103
Worldwide total number of subjects	103
EEA total number of subjects	103

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)	16

From 65 to 84 years	86
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

First Patient in: 03.12.2009
Last Patient in: 23.04.2013
Last Patient out: 14.09.2016
After the enrolment and Treatment of 38 patients recruitment was interrupted in September 2010 until approval of teh amended protocol Version 2.0 (26.06.2011). Recruitment was restarted in October 2011.

Pre-assignment

Screening details:

Diagnosis of myeloproliferative neoplasms (de novo, secondary, or unclassifiable) with biopsy proven MF; Anemia with hemoglobin <10g/dl or Transfusion-dependent anemia or thrombocytopenia <50 G/l or Transfusion-dependent thrombocytopenia

Pre-assignment period milestones

Number of subjects started	103
Number of subjects completed	96

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 6
Reason: Number of subjects	Consent withdrawn by subject: 1

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Treatment started with a Phase of pomalidomide with 2 mg per day. Individual dose reduction as outlined in the safety section was allowed. If no Response was achieved after 3 months, prednisolone was added in a starting dose of 30 mg per day. In the Absence of progressive disease, at least 6 months of Treatment with pomalidomide was intended. In patietns without disease Progression after 6 months and those with Response to Treatment were intended to receive pomalidomide for at least 12 months.

Arm type	Experimental
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1 Capsule of 2 mg per day for 12 months

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

Dosage and administration details:

If no complete Response, partial Response or clinical improvement occurred after 3 cycles, prednisolone is added to pomalidomide in a starting dose of 30 mg/day for 28 days followed by 15 mg/day and 10 mg/day for 28 days, respectively, consequently thereafter. In case of progressive disease Treatment ist stopped. Otherwise, continous Treatment at least until end of cycle 12 is intended. For patients responding to the combination Treatment a concomitant Treatment after cycle 6 with prednisolone in doses equal or below 7.5 mg/day are allowed.

Arm title	Cohort 2: 3-month prednisolone

Arm description:

Treatment for all patients starts with pomalidomide as single Agent at a dose of 0.5 mg/day. The Addition of prednisolone will be initiated as randomized at start of cycle 4 (starting dose 30 mg/day). In the Absence of progressive disease, at least 12 cycles of Treatment with pomalidomide are intended.

Arm type	Experimental
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1 Capsule of 0.5 mg per day for 12 months

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

Dosage and administration details:

Treatment starts with pomalidomide as a single agent therapy with 0.5 mg/day. Prednisolone will be started in the absence of progressive disease as randomized as start of cycle 4 in a starting dose of 30 mg/day for 28 days followed by 15 mg/day and 10 mg/day for 28 days, respectively, consequently thereafter, if no response was achieved. In case of progressive disease Treatment ist stopped. Otherwise, continuous Treatment at least until end of cycle 12 is intended. For patients responding to the combination Treatment a concomitant Treatment after cycle 6 with prednisolone in doses equal or below 7.5 mg/day are allowed.

Arm title	Cohort 2: 6-month prednisolone

Arm description:

Treatment for all patients starts with pomalidomide as single Agent at a dose of 0.5 mg/day. The Addition of prednisolone will be initiated as randomized at start of cycle 7 (starting dose 30 mg/day). In the Absence of progressive disease, at least 12 cycles of Treatment with pomalidomide are intended

Arm type	Experimental
Investigational medicinal product name	Pomalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1 Capsule of 0.5 mg per day for 12 months

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

Dosage and administration details:

Treatment starts with pomalidomide as a single agent therapy with 0.5 mg/day. Prednisolone will be started in the absence of progressive disease as randomized at start of cycle 7 in a starting dose of 30 mg/day for 28 days followed by 15 mg/day and 10 mg/day for 28 days, respectively, consequently thereafter, if no response was achieved. In case of progressive disease Treatment ist stopped.

Otherwise, continuous Treatment at least until end of cycle 12 is intended. For patients responding to the combination Treatment a concomitant Treatment after cycle 9 with prednisolone in doses equal or below 7.5 mg/day are allowed.

Number of subjects in period 1[1]	Cohort 1	Cohort 2: 3-month prednisolone	Cohort 2: 6-month prednisolone
Started	38	27	31
Completed	19	7	7
Not completed	19	20	24
Adverse event, serious fatal	-	4	3
allo-HSCT	-	-	2
Consent withdrawn by subject	1	8	5
Adverse event, non-fatal	14	1	9
Non-compliance	1	-	-
Lack of efficacy	3	7	5

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 103 patients were registered into the study.
Cohort1: 3 patients were not eligible and did not enter the Treatment Phase.
Cohort2: 3 Patient were not eligible and 1 patient withdrew his consent and did not enter the Treatment Phase. This was before the randomization to "Cohort2: 3-month prednisolone" and "Cohort2: 6-month prednisolone" happened.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Treatment started with a Phase of pomalidomide with 2 mg per day. Individual dose reduction as outlined in the safety section was allowed. If no Response was achieved after 3 months, prednisolone was added in a starting dose of 30 mg per day. In the Absence of progressive disease, at least 6 months of Treatment with pomalidomide was intended. In patietns without disease Progression after 6 months and those with Response to Treatment were intended to receive pomalidomide for at least 12 months.	
Reporting group title	Cohort 2: 3-month prednisolone
Reporting group description:	
Treatment for all patients starts with pomalidomide as single Agent at a dose of 0.5 mg/day. The Addition of prednisolone will be initiated as randomized at start of cycle 4 (starting dose 30 mg/day). In the Absence of progressive disease, at least 12 cycles of Treatment with pomalidomide are intended.	
Reporting group title	Cohort 2: 6-month prednisolone
Reporting group description:	
Treatment for all patients starts with pomalidomide as single Agent at a dose of 0.5 mg/day. The Addition of prednisolone will be initiated as randomized at start of cycle 7 (starting dose 30 mg/day). In the Absence of progressive disease, at least 12 cycles of Treatment with pomalidomide are intended	

Reporting group values	Cohort 1	Cohort 2: 3-month prednisolone	Cohort 2: 6-month prednisolone
Number of subjects	38	27	31
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	70.6	73	71.4
full range (min-max)	50 to 82	49 to 85	58 to 80
Gender categorical Units: Subjects			
Female	13	10	10
Male	25	17	21
Type of Myelofibrosis Units: Subjects			
PMF	26	21	23
post ET-MF	3	2	2
post PV-MF	8	2	5
unclassified MF	1	2	1
DIPPS			

Units: Subjects			
High	10	4	9
Intermediate-2	23	19	20
Intermediate-1	5	4	2
Constitutional symptoms			
defined as fever, sweating or weight loss			
Units: Subjects			
present	8	8	10
not present	30	19	21
ECOG Units: Subjects			
ECOG 0	17	12	7
ECOG 1	20	13	22
ECOG 2	1	2	2
RBC transfusion dependent Units: Subjects			
yes	28	22	23
no	10	5	8
Platelet transfusion dependent Units: Subjects			
yes	7	5	6
no	31	22	25
Cytogenetics Units: Subjects			
Low-Risk	24	12	19
High-Risk	9	4	4
Missing	5	11	8
JAK2V617F Mutation			
Is a Jak2V617F Mutation available?			
Units: Subjects			
Yes	1	14	19
No	37	13	12
CALR mutations			
Is a CALR Mutation available?			
Units: Subjects			
Yes	5	6	7
No	33	21	24
MPLW515L Mutation			
Is a MPLW515L Mutation available?			
Units: Subjects			
Yes	5	1	0
No	33	26	31
ASXL1 mutation			
Is a ASXL1 Mutation available?			
Units: Subjects			
Yes	13	6	10
No	25	21	21
DNMT2A mutation			
Is a DNMT2A Mutation available?			
Units: Subjects			
Yes	2	3	6

No	36	24	25
TET2 mutation			
Is a TET2 Mutation available?			
Units: Subjects			
Yes	4	2	4
No	34	25	27
EZH2 mutation			
Is a EZH2 Mutation available?			
Units: Subjects			
Yes	3	1	1
No	35	26	30
IDH 1/2 mutation			
Is a IDH 1/2 Mutation available?			
Units: Subjects			
Yes	1	0	0
No	37	27	31
SRSF2 mutation			
IS a SRSF2 Mutation available?			
Units: Subjects			
Yes	5	2	3
No	33	25	28
TP53 mutation			
Is a TP53 Mutation available?			
Units: Subjects			
Yes	1	0	0
No	37	27	31
Splenomegaly			
Units: cm			
median	19.6	19	17.5
full range (min-max)	10 to 32	10 to 32	12 to 43
LDH			
Units: U/l			
median	490	612	544
full range (min-max)	200 to 2376	156 to 1599	153 to 1136
Hemoglobin			
Units: g/dl			
median	9.4	8.5	9.0
full range (min-max)	4.8 to 10.9	5.8 to 13.7	5.5 to 12.8
Platelets			
Units: G/l			
median	122.5	139	91
full range (min-max)	11 to 1400	3 to 716	12 to 394

Reporting group values	Total		
Number of subjects	96		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	33		
Male	63		
Type of Myelofibrosis			
Units: Subjects			
PMF	70		
post ET-MF	7		
post PV-MF	15		
unclassified MF	4		
DIPPS			
Units: Subjects			
High	23		
Intermediate-2	62		
Intermediate-1	11		
Constitutional symptoms			
defined as fever, sweating or weight loss			
Units: Subjects			
present	26		
not present	70		
ECOG			
Units: Subjects			
ECOG 0	36		
ECOG 1	55		
ECOG 2	5		
RBC transfusion dependent			
Units: Subjects			
yes	73		
no	23		
Platelet transfusion dependent			
Units: Subjects			
yes	18		
no	78		
Cytogenetics			
Units: Subjects			
Low-Risk	55		
High-Risk	17		
Missing	24		
JAK2V617F Mutation			
Is a Jak2V617F Mutation available?			

Units: Subjects			
Yes	34		
No	62		
CALR mutations			
Is a CALR Mutation available?			
Units: Subjects			
Yes	18		
No	78		
MPLW515L Mutation			
Is a MPLW515L Mutation available?			
Units: Subjects			
Yes	6		
No	90		
ASXL1 mutation			
Is a ASXL1 Mutation available?			
Units: Subjects			
Yes	29		
No	67		
DNMT2A mutation			
Is a DNMT2A Mutation available?			
Units: Subjects			
Yes	11		
No	85		
TET2 mutation			
Is a TET2 Mutation available?			
Units: Subjects			
Yes	10		
No	86		
EZH2 mutation			
Is a EZH2 Mutation available?			
Units: Subjects			
Yes	5		
No	91		
IDH 1/2 mutation			
Is a IDH 1/2 Mutation available?			
Units: Subjects			
Yes	1		
No	95		
SRSF2 mutation			
IS a SRSF2 Mutation available?			
Units: Subjects			
Yes	10		
No	86		
TP53 mutation			
Is a TP53 Mutation available?			
Units: Subjects			
Yes	1		
No	95		
Splenomegaly Units: cm median			

full range (min-max)	-		
LDH Units: U/l median full range (min-max)	-		
Hemoglobin Units: g/dl median full range (min-max)	-		
Platelets Units: G/l median full range (min-max)	-		

Subject analysis sets

Subject analysis set title	Full analysis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes all patients who received the study medication at least once

Reporting group values	Full analysis		
Number of subjects	96		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median full range (min-max)	71.5 49 to 85		
Gender categorical Units: Subjects			
Female Male	33 63		
Type of Myelofibrosis Units: Subjects			
PMF post ET-MF post PV-MF unclassified MF	70 7 15 4		
DIPPS Units: Subjects			

High	23		
Intermediate-2	62		
Intermediate-1	11		
Constitutional symptoms			
defined as fever, sweating or weight loss			
Units: Subjects			
present	26		
not present	70		
ECOG Units: Subjects			
ECOG 0	36		
ECOG 1	55		
ECOG 2	5		
RBC transfusion dependent Units: Subjects			
yes	73		
no	23		
Platelet transfusion dependent Units: Subjects			
yes	18		
no	78		
Cytogenetics Units: Subjects			
Low-Risk	55		
High-Risk	17		
Missing	24		
JAK2V617F Mutation			
Is a Jak2V617F Mutation available?			
Units: Subjects			
Yes	34		
No	62		
CALR mutations			
Is a CALR Mutation available?			
Units: Subjects			
Yes	18		
No	78		
MPLW515L Mutation			
Is a MPLW515L Mutation available?			
Units: Subjects			
Yes	6		
No	90		
ASXL1 mutation			
Is a ASXL1 Mutation available?			
Units: Subjects			
Yes	29		
No	67		
DNMT2A mutation			
Is a DNMT2A Mutation available?			
Units: Subjects			
Yes	11		
No	85		

TET2 mutation			
Is a TET2 Mutation available?			
Units: Subjects			
Yes	10		
No	86		
EZH2 mutation			
Is a EZH2 Mutation available?			
Units: Subjects			
Yes	5		
No	91		
IDH 1/2 mutation			
Is a IDH 1/2 Mutation available?			
Units: Subjects			
Yes	1		
No	95		
SRSF2 mutation			
IS a SRSF2 Mutation available?			
Units: Subjects			
Yes	10		
No	86		
TP53 mutation			
Is a TP53 Mutation available?			
Units: Subjects			
Yes	1		
No	95		
Splenomegaly Units: cm median full range (min-max)	 18.6 10 to 43		
LDH Units: U/l median full range (min-max)	 542 153 to 2376		
Hemoglobin Units: g/dl median full range (min-max)	 9.05 4.8 to 13.7		
Platelets Units: G/l median full range (min-max)	 103.5 3 to 1400		

End points

End points reporting groups

Reporting group title	Cohort 1

Reporting group description:

Treatment started with a Phase of pomalidomide with 2 mg per day. Individual dose reduction as outlined in the safety section was allowed. If no Response was achieved after 3 months, prednisolone was added in a starting dose of 30 mg per day. In the Absence of progressive disease, at least 6 months of Treatment with pomalidomide was intended. In patietns without disease Progression after 6 months and those with Response to Treatment were intended to receive pomalidomide for at least 12 months.

Reporting group title	Cohort 2: 3-month prednisolone

Reporting group description:

Treatment for all patients starts with pomalidomide as single Agent at a dose of 0.5 mg/day. The Addition of prednisolone will be initiated as randomized at start of cycle 4 (starting dose 30 mg/day). In the Absence of progressive disease, at least 12 cycles of Treatment with pomalidomide are intended.

Reporting group title	Cohort 2: 6-month prednisolone

Reporting group description:

Treatment for all patients starts with pomalidomide as single Agent at a dose of 0.5 mg/day. The Addition of prednisolone will be initiated as randomized at start of cycle 7 (starting dose 30 mg/day). In the Absence of progressive disease, at least 12 cycles of Treatment with pomalidomide are intended

Subject analysis set title	Full analysis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes all patients who received the study medication at least once

Primary: Disease response

End point title	Disease response

End point description:

Objective disease response as defined by the IWG-MRT for response in MF patients, extended by the criterion RBC-Transfusion dependence (TI).

End point type	Primary

End point timeframe:

The end point disease response was examined at the end of each cycle until at least cycle 12.

End point values	Cohort 1	Cohort 2: 3-month prednisolone	Cohort 2: 6-month prednisolone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	38	26	30	
Units: Number of subjects				
Complete remission	0	0	0	
Partial remission	1	1	2	
Clinical improvement	11	2	2	
RBC Transfusion dependence	3	4	3	
No change	23	19	23	

Statistical analyses

Statistical analysis title	Logistic regression model
Comparison groups	Cohort 1 v Cohort 2: 3-month prednisolone v Cohort 2: 6-month prednisolone
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.05
Method	Regression, Cox
Parameter estimate	Odds ratio (OR)
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	6.87
Variability estimate	Standard deviation

Notes:

[1] - The superiority was supported by the results of a logistic regression model, which revealed that a higher dose of pomaldomide of 2.0 mg/day instead of 0.5 mg/day as significantly associated with a higher Response rate (OR, 2.62; 95% CI, 1.00 - 6.87).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for reporting adverse events: Adverse Events were reported from Informed Consent signature up to 28 days after last study drug administration or until all drug-related toxicities had been resolved, whichever was later.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	Study population

Reporting group description:

Includes cohort 1 and cohort 2

Serious adverse events	Study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	75 / 96 (78.13%)		
number of deaths (all causes)	19		
number of deaths resulting from adverse events	19		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	12 / 96 (12.50%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 3		
Bladder cancer			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchial carcinoma			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer female			

subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Chloroma				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal cell carcinoma				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Langerhans' cell histiocytosis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Syncope				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				

subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
arterial stenosis limb			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Transurethral prostatectomy			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatic operation			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arterial bypass operation			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toe amputation			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Asthenia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	3 / 96 (3.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Condition aggravated				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Drug hypersensitivity				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Lung infiltration				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood glucose increased				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Wound hemorrhage				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac failure				
subjects affected / exposed	4 / 96 (4.17%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	5 / 96 (5.21%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				

subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bradyarrhythmia			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left ventricular dysfunction			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachyarrhythmia			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	3 / 96 (3.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Blood and lymphatic system disorders			

Acute myeloid leukaemia				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Anaemia				
subjects affected / exposed	4 / 96 (4.17%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Haemolysis				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Polycythaemia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	3 / 96 (3.13%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Transfusion reaction				

subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Ascites				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis haemorrhagic				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastritis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal pain				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal perforation				

subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Erysipelas				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
rash				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal disorder				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema due to renal disease				
subjects affected / exposed	3 / 96 (3.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	3 / 96 (3.13%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Renal colic				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue				

disorders				
Back pain				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bacterial prostatitis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Chronic sinusitis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium colitis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Cystitis				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastroenteritis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media acute				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural Infection				

subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paronychia				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	10 / 96 (10.42%)			
occurrences causally related to treatment / all	1 / 12			
deaths causally related to treatment / all	0 / 3			
Sinusitis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Septic shock				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Urosepsis				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Metabolism and nutrition disorders				
Hepatic steatosis				

subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

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

Non-serious adverse events	Study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 96 (97.92%)		
Investigations			
Bilirubin			
subjects affected / exposed	5 / 96 (5.21%)		
occurrences (all)	5		
Hyperuricemia			
subjects affected / exposed	7 / 96 (7.29%)		
occurrences (all)	7		
Vascular disorders			
Hematoma			
subjects affected / exposed	9 / 96 (9.38%)		
occurrences (all)	9		
Hemorrhage pulmonary - Select			
subjects affected / exposed	13 / 96 (13.54%)		
occurrences (all)	13		
Petechiae			
subjects affected / exposed	7 / 96 (7.29%)		
occurrences (all)	8		
Edema: limb			
subjects affected / exposed	12 / 96 (12.50%)		
occurrences (all)	13		
Cardiac disorders			

Palpitations			
subjects affected / exposed	6 / 96 (6.25%)		
occurrences (all)	6		
Hypertension			
subjects affected / exposed	11 / 96 (11.46%)		
occurrences (all)	11		
Nervous system disorders			
Dizziness			
subjects affected / exposed	18 / 96 (18.75%)		
occurrences (all)	20		
Neurology - Other			
subjects affected / exposed	9 / 96 (9.38%)		
occurrences (all)	9		
Neuropathy - sensory			
subjects affected / exposed	5 / 96 (5.21%)		
occurrences (all)	5		
Blood and lymphatic system disorders			
Blood - Other			
subjects affected / exposed	8 / 96 (8.33%)		
occurrences (all)	9		
Hemoglobin			
subjects affected / exposed	25 / 96 (26.04%)		
occurrences (all)	25		
Leukocytes			
subjects affected / exposed	8 / 96 (8.33%)		
occurrences (all)	8		
Neutrophils			
subjects affected / exposed	13 / 96 (13.54%)		
occurrences (all)	13		
Platelets			
subjects affected / exposed	26 / 96 (27.08%)		
occurrences (all)	27		
General disorders and administration site conditions			
Constitutional symptoms - Other			
subjects affected / exposed	15 / 96 (15.63%)		
occurrences (all)	15		

Fatigue			
subjects affected / exposed	40 / 96 (41.67%)		
occurrences (all)	44		
Fever			
subjects affected / exposed	10 / 96 (10.42%)		
occurrences (all)	10		
Insomnia			
subjects affected / exposed	8 / 96 (8.33%)		
occurrences (all)	8		
Sweating			
subjects affected / exposed	15 / 96 (15.63%)		
occurrences (all)	15		
Weight loss			
subjects affected / exposed	7 / 96 (7.29%)		
occurrences (all)	7		
Pain Gastrointestinal: Abdomen NOS			
subjects affected / exposed	18 / 96 (18.75%)		
occurrences (all)	23		
Pain Musculoskeletal: Bone			
subjects affected / exposed	5 / 96 (5.21%)		
occurrences (all)	5		
Pain Musculoskeletal: Extremity-limb			
subjects affected / exposed	6 / 96 (6.25%)		
occurrences (all)	6		
Pain Musculoskeletal: Joint			
subjects affected / exposed	7 / 96 (7.29%)		
occurrences (all)	7		
Pain Musculoskeletal: Muscle			
subjects affected / exposed	12 / 96 (12.50%)		
occurrences (all)	15		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	13 / 96 (13.54%)		
occurrences (all)	15		
Diarrhea			

subjects affected / exposed	19 / 96 (19.79%)		
occurrences (all)	22		
Nausea			
subjects affected / exposed	10 / 96 (10.42%)		
occurrences (all)	10		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 96 (15.63%)		
occurrences (all)	18		
Dyspnea			
subjects affected / exposed	30 / 96 (31.25%)		
occurrences (all)	32		
Pulmonary - Other			
subjects affected / exposed	6 / 96 (6.25%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Dermatology - Other			
subjects affected / exposed	19 / 96 (19.79%)		
occurrences (all)	23		
Pruritus			
subjects affected / exposed	11 / 96 (11.46%)		
occurrences (all)	11		
Rash			
subjects affected / exposed	7 / 96 (7.29%)		
occurrences (all)	7		
Renal and urinary disorders			
Renal - Other			
subjects affected / exposed	26 / 96 (27.08%)		
occurrences (all)	27		
Infections and infestations			
Infection - Other			
subjects affected / exposed	17 / 96 (17.71%)		
occurrences (all)	20		
Infection with unknown ANC			
subjects affected / exposed	5 / 96 (5.21%)		
occurrences (all)	5		

Infection Pulmonary/Upper respiratory: Upper airway NOS subjects affected / exposed occurrences (all)	 10 / 96 (10.42%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2011	Amendment 1 (dated 02 August 2011) was issued after enrolment of n = 38 patients. The following Major procedural changes were made to the protocol: - Dose reduction of Pomalidomide to 0,5 mg once daily. - Additionally, randomisation into either additional prednisolone after 3 months or 6 months when patients have a stable disease. - Change of sample size to 95 patients

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.

None reported

Notes: