



Clinical trial results:

Phase I/II study with oral panobinostat maintenance therapy following allogeneic stem cell transplantation in patients with high risk MDS or AML (PANOBEST)

Summary

EudraCT number	2010-018699-26
Trial protocol	DE
Global end of trial date	19 June 2020

Results information

Result version number	v1 (current)
This version publication date	24 October 2021
First version publication date	24 October 2021

Trial information

Trial identification

Sponsor protocol code	CLBH589BDE05T
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01451268
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Goethe University
Sponsor organisation address	Theodor-Stern-Kai 7, Frankfurt am Main, Germany, 60590
Public contact	PD Dr. Gesine Bug, Coordinating , Universitätsklinikum Frankfurt, 0049 6963017760, g.bug@em.uni-frankfurt.de
Scientific contact	PD Dr. Gesine Bug, Coordinating , Universitätsklinikum Frankfurt, 0049 6963017760, g.bug@em.uni-frankfurt.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	31 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2018
Global end of trial reached?	Yes
Global end of trial date	19 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of Panobinostat when administered within 150 days after HSCT and given in conjunction with standard immunosuppressive therapy after HSCT for patients with high-risk MDS or AML

Protection of trial subjects:

Adverse events of panobinostat reported in other clinical trials are generally mild or moderate and rapidly reversible upon discontinuation. Possible drug-drug interactions are known and can be avoided by alternative medication and drug level testing. The panobinostat dose will be escalated in successive cohorts of 3 patients in order to carefully monitor adverse reactions.

Background therapy:

Standard immunosuppressive therapy and supportive care on individual demand and the investigators' discretion

Evidence for comparator:

No comparator used

Actual start date of recruitment	21 January 2011
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: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	57
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited by treating physician/investigator upon relevant diagnosis/medical condition at the hospital

Pre-assignment

Screening details:

Additional screening procedures compared to standard diagnostics: informed consent, electrocardiogram, echocardiogram, thyroid profile

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

None

Arms

Are arms mutually exclusive?	Yes
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Arm title	Schedule A
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Arm description:

Panobinostat TIW, every week

Arm type	Experimental
Investigational medicinal product name	Panobinostat
Investigational medicinal product code	LBH589
Other name	ATC code: L01XH03
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

T10mg, 20mg, or 30mg once a day three times a week on Monday-Wednesday-Friday every week, assignment to dose at inclusion, no intra-patient dose escalation

Arm title	Schedule B
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Arm description:

Panobinostat TIW, every second week

Arm type	Experimental
Investigational medicinal product name	Panobinostat
Investigational medicinal product code	LBH589
Other name	ATC code: L01XH03
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Maximum tolerated dose of Schedule A (i.e. 20mg), 30mg or 40mg once a day three times a week on Monday-Wednesday-Friday every second week, assignment to dose at inclusion, no intra-patient dose escalation

Number of subjects in period 1	Schedule A	Schedule B
Started	31	31
Completed	12	17
Not completed	19	14
Adverse event, not serious	4	6
Consent withdrawn by subject	2	1
Deterioration of general condition	-	1
Adverse event, serious non-fatal	6	2
concomittant medication	1	-
Lack of efficacy	5	4
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Schedule A
Reporting group description: Panobinostat TIW, every week	
Reporting group title	Schedule B
Reporting group description: Panobinostat TIW, every second week	

Reporting group values	Schedule A	Schedule B	Total
Number of subjects	31	31	62
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	29	57
From 65-84 years	3	2	5
85 years and over	0	0	0
Age continuous			
Units: years			
median	54	55	
full range (min-max)	21 to 71	30 to 71	-
Gender categorical			
Units: Subjects			
Female	16	10	26
Male	15	21	36

End points

End points reporting groups

Reporting group title	Schedule A
Reporting group description:	
Panobinostat TIW, every week	
Reporting group title	Schedule B
Reporting group description:	
Panobinostat TIW, every second week	
Subject analysis set title	Schedule A, schedule B (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Schedule A: Panobinostat TIW, every week	
Schedule B: Panobinostat TIW, every second week	
Subject analysis set title	Three months of panobinostat treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients of schedule A and schedule B who have completed at least three months of panobinostat treatment	

Primary: Maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of panobinostat after 28 days of administration.

End point title	Maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of panobinostat after 28 days of administration. ^[1]
End point description:	
Maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of panobinostat after 28 days of administration.	
Patients of schedule A and schedule B that have been treated with LBH589 for ≥ 9 doses in arm 1 and for ≥ 4 doses for arm 2 within the first 28 days. In the patients must have been observed for ≥ 28 days following the first dose, and must have completed all required safety evaluations or the patient experiences DLT during the first 28 days	
End point type	Primary
End point timeframe:	
after 28 days of administration	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: Only descriptive statistics provided	

End point values	Schedule A	Schedule B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mg				
number (not applicable)				
MTD	20	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative incidence of hematologic relapse and death at one year after HSCT

End point title	Cumulative incidence of hematologic relapse and death at one year after HSCT
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End point description:

All patients of schedule A and schedule B who have completed at least three months of panobinostat treatment

End point type	Secondary
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End point timeframe:

One year after HSCT

End point values	Three months of panobinostat treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: Patients				
Relapse	5			
Death	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of panobinostat until end of treatment (AE) or until 28 days after last intake (SAE)

Adverse event reporting additional description:

n.a.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	v3.0
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Reporting groups

Reporting group title	Schedule A (N=31)
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Reporting group description:

Panobinostat TIW, every week

Reporting group title	Schedule B (N=31)
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Reporting group description:

Panobinostat TIW, every second week

Serious adverse events	Schedule A (N=31)	Schedule B (N=31)	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 31 (45.16%)	9 / 31 (29.03%)	
number of deaths (all causes)	10	8	
number of deaths resulting from adverse events	1	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Aura of migraine sans migraine subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	2 / 31 (6.45%)	2 / 31 (6.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reduced general condition			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
GvHD of the gut			
subjects affected / exposed	5 / 31 (16.13%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
GvHD liver			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Sore throat	Additional description: Fever, sore throat, viral infection		

subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Relapse of NSCLC			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroid function high			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Herpes stomatitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Aspergillosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infection - Fever and Diarrhea subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection - Portinfection subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection - Infection of unknown origin subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection - Herpes Zoster infection subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia subjects affected / exposed	3 / 31 (9.68%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fever subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Schedule A (N=31)	Schedule B (N=31)	
Total subjects affected by non-serious adverse events subjects affected / exposed	31 / 31 (100.00%)	31 / 31 (100.00%)	
Vascular disorders Deep vein thrombosis subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences (all)	1	0	

General disorders and administration site conditions			
Constitutional symptoms - other: Reduced general condition			
subjects affected / exposed	1 / 31 (3.23%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
Fatigue			
subjects affected / exposed	6 / 31 (19.35%)	3 / 31 (9.68%)	
occurrences (all)	6	3	
Fever			
subjects affected / exposed	0 / 31 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Weight loss			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Pain NOS			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Pain headache			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Pain: abdomen NOS			
subjects affected / exposed	2 / 31 (6.45%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	2	
Pulmonary fibrosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Relapse of NSCLC			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Cardiac disorders			
Prolonged QTc interval			

subjects affected / exposed	1 / 31 (3.23%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Cardiac arrhythmia - other: T-deviation			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Cardiac arrhythmia - other: ST-deviation			
subjects affected / exposed	1 / 31 (3.23%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
Cardiac arrhythmia - other: QRS-prolongation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Supraventricular and nodal arrhythmia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Cardiac arrhythmia other: Negative T in II, III			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Cardiac Troponin T			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Cardiac ischemia/infarction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Syncope (fainting)			
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Neuropathy: sensory			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
Aphasia			

subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Seizure subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Confusion subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Memory impairment subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Blood and lymphatic system disorders			
Hemoglobin subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	1 / 31 (3.23%) 1	
Iron overload subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 31 (3.23%) 1	
Leukocytes subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4	4 / 31 (12.90%) 4	
Neutrophils /Granulocytes subjects affected / exposed occurrences (all)	9 / 31 (29.03%) 9	5 / 31 (16.13%) 5	
Platelets subjects affected / exposed occurrences (all)	14 / 31 (45.16%) 14	8 / 31 (25.81%) 8	
Gastrointestinal disorders			
Anorexia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Colitis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Diarrhea			

subjects affected / exposed occurrences (all)	8 / 31 (25.81%) 6	4 / 31 (12.90%) 4	
Enterocolitis infection subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 31 (3.23%) 1	
Fistula, GI-Anus subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 31 (3.23%) 1	
Mucositis, oral cavity subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 31 (3.23%) 1	
Nausea subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 6	2 / 31 (6.45%) 2	
Vomiting subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4	0 / 31 (0.00%) 0	
Hepatobiliary disorders Hepatobiliary/ pancreas, other: cGvHD liver subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 31 (3.23%) 1	
Skin and subcutaneous tissue disorders Dermatology/Skin, other: Keratosis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Dermatology/Skin, other: Basalioma subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 31 (3.23%) 1	
Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 31 (3.23%) 1	
Endocrine disorders			

Thyroid function high subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	5 / 31 (16.13%) 5	
Infections and infestations			
Infection NOS subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	4 / 31 (12.90%) 4	
Infection, other: catheter related subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 31 (3.23%) 1	
Infection, other: gastrointestinal subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Infection, other: Lung, pneumonia subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4	1 / 31 (3.23%) 1	
Infection, other: oral cavity, HSV subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Infection, other: sepsis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Infection, other: skin (herpes zoster) subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 31 (6.45%) 2	
Infection. Other: upper airway NOS, cold subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	2 / 31 (6.45%) 2	
Infection general: Blood subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Viral hepatitis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 31 (0.00%) 0	
Metabolism and nutrition disorders			

Alkaline phosphatase		
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Amylase		
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Creatinine		
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Diabetes		
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	0
GGT		
subjects affected / exposed	1 / 31 (3.23%)	4 / 31 (12.90%)
occurrences (all)	1	4
Hemoglobin		
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	0
Hyperkalemia		
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	0
Hypertriglyceridemia		
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	1
Hyperuricemia		
subjects affected / exposed	2 / 31 (6.45%)	0 / 31 (0.00%)
occurrences (all)	2	0
Hypocalcemia		
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	0
Hypokalemia		
subjects affected / exposed	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	2
Leucocytes		
subjects affected / exposed	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	0

Lipase			
subjects affected / exposed	2 / 31 (6.45%)	2 / 31 (6.45%)	
occurrences (all)	2	2	
Platelets			
subjects affected / exposed	1 / 31 (3.23%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
SGPT			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	
SGOT			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2012	(Amendment 1) The aim of this amendment was to clarify specific protocol sections, to correct typing errors and to facilitate the study management in the participating centers. With the amendment, FACS analysis II is established as an additional tool to investigate the impact of panobinostat on the immune system.
30 June 2014	Protocol V04 (Amendment 2) was released on 30 June 2014 In the scheduled protocol amendment, the expansion cohort will encompass additional 20 patients (ten in each treatment arm) in order to collect more data on the safety and tolerability of a one year treatment at the respective MTD. In particular, we aim to determine (1) the number of patients experiencing a dose reduction, dose delay or treatment discontinuation as a consequence of panobinostat associated toxicities (2) the duration of treatment until a dose reduction, dose delay or treatment discontinuation as a consequence of panobinostat associated toxicities is required (cumulative dose) (3) the cumulative incidence of chronic graft-versus-host disease (cGvHD) requiring treatment Aside from the assessments performed to date, additional analyses, evaluations and changes will be implemented: (1) Assessment of patient reported health related quality of life (HRQL) in all additional patients (2) Evaluation of regulatory T cells function in all additional patients: Results of T cell analyses in the PANOBEST trial show an influence of panobinostat on the population of regulatory T cells. More detailed research will help to better understand the immunoregulatory effects of panobinostat. (3) Analysis of B cell reconstitution in all additional patients: The analysis of B cell development will add to the understanding of immunoregulatory effects of panobinostat and its effect on the incidence of cGvHD under panobinostat therapy. (4) Further changes e.g. in the number of examinations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported