Sponsor

Novartis

Generic Drug Name

Panobinostat

Therapeutic Area of Trial

Hodgkin's lymphoma

Approved Indication

Investigational

Protocol Number

CLBH589E2301

Title

A Phase III randomized, double blind, placebo controlled multi-center study of panobinostat for maintenance of response in patients with Hodgkin's lymphoma who are at risk for relapse after high dose chemotherapy and autologous stem cell transplant.

Study Phase

Phase III

Study Start/End Dates

10-Jun-2010 (first patient first visit) to 14-May-2012 (last patient last visit)

Due to poor patient recruitment, this study was prematurely closed to enrollment on 03-May-2011 after 41 patients were enrolled.

Study Design/Methodology

This was a multi-center, multinational, two arm, randomized, double-blind, placebo-controlled phase III study. All patients were to be treated with panobinostat 45 mg or placebo administered three times in a week (TIW), every other week (QOW). The treatment duration for each patient was planned to be 13 cycles, where one cycle consists of four weeks (28 days), or until occurrence of intolerable toxicity, progression of disease or withdrawal of consent, whichever occurred first.

Due to early termination of enrollment to the trial and thus, the limited number of patients recruited, the protocol was amended to reflect significant changes in the purpose and objectives of this trial, most notably related to analyses of efficacy. After approval of Amendment 2, active patients still receiving study treatment were un-blinded. Patients who received panobinostat were allowed to continue receiving study drug in an open-label phase, while patients who received placebo were discontinued from further study treatment.

Outcome Measures

Primary endpoint:

As per protocol amendment 2, the primary objective was to provide drug to ongoing patients who were receiving panobinostat and to characterize the safety and tolerability of panobinostat in patients with Hodgkin's Lymphoma (HL) after achieving a complete response following and autologous hematopoietic stem cell transplant (AHSCT) with high-dose chemotherapy (HDT).

Safety assessments consisted of collecting all adverse events (AEs), serious adverse events (SAEs), with their severity and relationship to study drug, and pregnancies. They included the regular monitoring of hematology, blood chemistry and regular assessment of physical conditions and ECG. Additional safety assessments of thyroid function, urine values, coagulation, regular vital signs and ECOG performance status were performed as per standard of care or as clinically indicated.

Secondary variables:

No secondary objectives were included for this trial as per protocol amendment 2.

Centers

28 participating centers in 13 countries enrolled patients into the study (Australia 1; Belgium 1: Brazil 2; France 2; Germany 3; Israel 2: Italy 1; Netherlands 1; New Zealand 1; Poland 2; Russia 2; Singapore 1; United States 9).

Test Product , Dose, and Mode of Administration

Oral capsule dosing of panobinostat (also known as LBH589), 45 mg three-times in a week (TIW), every other week (QOW).

Statistical Methods

The Reporting and Analysis Plan was amended to incorporate changes resulting from stoppage of enrollment to the study. Data from all centers that participated in this trial was used in the final analysis. Data collected from randomization phase and open-label phase were summarized or listed separately or together as necessary.

After implementation of Amendment 2 to the protocol, the primary objective was safety and tolerability of PAN in patients with HL after achieving a CR following AHSCT with HDT.

All AEs recorded during the study were listed and summarized. The incidence of treatment-emergent AEs (new or worsening from baseline) was summarized by system organ class (SOC), severity (based on maximum Common Terminology Criteria (CTC) Adverse event (AE) grades), AE type and relation to the study drug by treatment group. The treatment emergent AEs were defined as on or after the day of the first intake of study treatment and no later than 28 days after study treatment discontinuation. Laboratory data collected from both central and local laboratories were combined. All values were converted into SI units and severity grade calculated using CTCAE (version 3.0). The values were listed by laboratory parameter, patient, and treatment group.

After implementation of Amendment 2, efficacy evaluations were to be completed as per standard of care.

DFS was defined as the time from the date of randomization to the date of the first documented relapse or death due to any cause. DFS was listed by treatment group.

OS was defined as the time from date of randomization to date of death due to any cause. If a patient was not known to have died, survival was censored at the date of last contact. OS was listed by treatment group.

PK concentration data, both for trough and C_{max}, was listed using the full analysis set (FAS). Concentrations out of predefined time windows and concentrations for patients who vomited within 2 hours of dosing were flagged.

Study Population: Inclusion/Exclusion Criteria and Demographics

Adult patients with HL, who are at risk for relapse after HDT and AHSCT.

Key inclusion criteria:

- Patients aged ≥ 18 years
- Patients with history of histologically confirmed classical HL (i.e. NSHL, MCHL, LRHL, and LDHL)
- Patient had achieved a CR by CT/MRI scan between 6 and 12 weeks from the day of their first autologous peripheral blood/bone marrow stem cell transfusion (AHSCT) following HDT.

- Patient with at least one of the following factors that placed them at risk for relapse:
- Primary refractory disease (including relapse in ≤ 3 months of completion of 1st line treatment)
- First relapse >3 but <12 months from last dose of 1st line treatment
- Multiple relapses (at relapse, prior to transplant)
- Stage III/IV disease (at relapse, prior to transplant)
- Hemoglobin <10.5 gm/dL (at relapse, prior to transplant)
- Patient with an ECOG performance status of ≤ 2
- Patient with the following laboratory values within 3 weeks of starting study drug (if required labs was to be repeated to obtain acceptable values before concluding screening failure)
- Absolute neutrophil count ≥ 1.5 x 10^9/L
- Platelet count ≥ 100 x 10^9/L
- AST/SGOT and ALT/SGPT ≤ 2.5 x Upper Limit of Normal (ULN)
- Serum total bilirubin ≤ 1.5 x ULN
- Serum creatinine ≤ 1.5 x ULN
- Serum potassium, magnesium, sodium, total calcium (corrected for serum albumin) or ionized calcium within normal limit

Key exclusion criteria:

- Patient had been treated with allogeneic transplant
- Patient had received any anti-lymphoma therapy after AHSCT including but not limited to chemotherapy prior to start of study, biologic immunotherapy including monoclonal antibodies or experimental therapy prior to start of study, radiation therapy
- Patient had not recovered from reversible toxicity due to any prior therapies (e.g. returned to baseline or grade ≤ 1) except for hematological laboratory parameters
- Patient had received prior treatment with DAC inhibitors including PAN
- Patient had received investigational agent of any kind, within 28 days of randomization
- Patient was taking any anti-cancer therapy concomitantly
- Patient needed valproic acid within 5 days prior to first administration of PAN/ study treatment
- Patient had evidence of another malignancy not in remission or history of such a malignancy within the last 3 years (except for treated basal or squamous cell carcinoma, or in situ cancer of the cervix).
- Patient had undergone major surgery ≤ 2 weeks prior to starting study drug or had not recovered from side effects of such procedure to < grade 1 common terminology criteria for adverse events (CTCAE) or baseline
- Patient had impaired cardiac function
- Patient was taking medications with relative risk of prolonging the QT interval or inducing torsade de pointes, if such treatment was not discontinued or switched to a different medication prior to starting study drug

- Patient had impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of PAN
- Patient had any other concurrent severe and/or uncontrolled medical conditions that could cause unacceptable safety risks or compromise compliance with the protocol such as uncontrolled diabetes, active or uncontrolled infection, chronic obstructive or chronic restrictive pulmonary disease, uncontrolled thyroid dysfunction, and recent, acute or active bleeding.

Participant Flow

Patient disposition by treatment group (FAS)

Disposition Reason	PAN N=27 n (%)	PBO N=14 n (%)	All patients N=41 n (%)
Patients randomized	27 (100)	14 (100)	41 (100)
Untreated[1]	1 (3.7)	2 (14.3)	3 (7.3)
Treated[2]	26 (96.3)	12 (85.7)	38 (92.7)
Patients entered open-phase	5 (18.5)	0	5 (12.2)
Patients did not enter open-phase	21 (77.8)	12 (85.7)	33 (80.5)
Primary reason for end of treatment			
Abnormal laboratory value(s)	1 (3.7)	0	1 (2.4)
Administrative problems	0	1 (7.1)	1 (2.4)
Adverse Event(s)	6 (22.2)	0	6 (14.6)
Disease progression	3 (11.1)	4 (28.6)	7 (17.1)
Protocol deviation	1 (3.7)	0	1 (2.4)
Subject withdrew consent	8 (29.6)	2 (14.3)	10 (24.4)
Treatment duration completed as per protocol	8 (29.6)	7 (50.0)	15 (36.6)

PAN, panobinostat; PBO, placebo

[1] Patient randomized and did not receive any dose of treatment.

[2] Patients treated with at least one dose of PAN or PBO.

Baseline Characteristics

Demographic summary by treatment group (FAS)

	PAN N=27	PBO N=14	All patients N=41
Age (years)			
n	27	14	41
Mean (SD)	34.0 (10.72)	30.6 (10.56)	32.9 (10.66)
Median	31.0	25.0	30.0
Min - Max	19.0 - 53.0	21.0 - 52.0	19.0 - 53.0
Age category (years) - n (%)			
< 35	14 (51.9)	10 (71.4)	24 (58.5)
≥ 35 and < 65	13 (48.1)	4 (28.6)	17 (41.5)
Sex - n (%)			
Female	8 (29.6)	7 (50.0)	15 (36.6)
Male	19 (70.4)	7 (50.0)	26 (63.4)
Race - n (%)			
Caucasian	27 (100)	11 (78.6)	38 (92.7)
Black	0	1 (7.1)	1 (2.4)
Oriental	0	2 (14.3)	2 (4.9)
ECOG - n (%)			
0	20 (74.1)	8 (57.1)	28 (68.3)
1	7 (25.9)	5 (35.7)	12 (29.3)
Weight (kg)			
n	27	13	40
Mean (SD)	77.5 (13.76)	67.7 (16.15)	74.4 (15.1)
Median	74.3	60.0	73.8
Min - Max	47.0 - 106.6	48.0 - 101.4	47.0 - 106.6
Height (cm)			
n	27	13	40
Mean (SD)	175.0 (8.42)	172.2 (7.83)	174.1 (8.24)
Median	175.0	171.0	175.0
Min - Max	157.5 - 193.0	159.0 - 185.0	157.5 - 193.0
Body surface area (m^2)			
n	27	13	40
Mean (SD)	2.0 (0.20)	1.8 (0.24)	1.9 (0.22)
Median	1.9	1.7	1.9
Min - Max	1.5 - 2.4	1.5 – 2.3	1.5 – 2.4

PAN, panobinostat; PBO, placebo

Disease history by treatment group (FAS)

	PAN N=27	PBO N=14	All patients N=41
Hodgkin's lymphoma classification at time of diagnosis -n (%)			
Nodular sclerosing	23 (85.2)	11 (78.6)	34 (82.9)
Mixed cellularity	3 (11.1)	3 (21.4)	6 (14.6)
Lymphocyte-rich	1 (3.7)	0	1 (2.4)
Stage at initial diagnosis – n (%)			
Stage Ib	1 (3.7)	0	1 (2.4)
Stage IIa	1 (3.7)	3 (21.4)	4 (9.8)
Stage IIb	8 (29.6)	0	8 (19.5)
Stage IIIa	2 (7.4)	1 (7.1)	3 (7.3)
Stage IIIb	5 (18.5)	2 (14.3)	7 (17.1)
Stage IVa	2 (7.4)	3 (21.4)	5 (12.2)
Stage IVb	8 (29.6)	5 (35.7)	13 (31.7)
Time since initial diagnosis of HL to start of study treatment (months)			
n	27	14	41
Mean (SD)	29.1 (26.67)	24.6 (8.63)	27.6 (22.16)
Median	17.4	23.3	20.5
Min - Max	9.8 - 130.9	13.5 - 42.3	9.8 - 130.9
Time since first recurrence/relapse to start of study treatment (months)			
n	26	13	39
Mean (SD)	9.2 (9.17)	9.4 (6.19)	9.3 (8.21)
Median	7.0	7.5	7.4
Min - Max	4.5 - 50.9	2.0 - 27.5	2.0 - 50.9
Time since most recent stem cell transfusion to start of study treatment (months)			
n	27	14	41
Mean (SD)	2.5 (0.37)	2.7 (0.93)	2.6 (0.61)
Median	2.6	2.5	2.5
Min - Max	1.6 - 3.1	1.8 - 5.7	1.6 - 5.7
Total number of relapses prior to transplant - n (%)			
1	22 (81.5)	10 (71.4)	32 (78.0)
2	1 (3.7)	2 (14.3)	3 (7.3)
≥ 3	1 (3.7)	1 (7.1)	2 (4.9)
Total number of relapses prior to transplant			
n	27	14	41
Mean (SD)	1.0 (0.55)	1.2 (0.70)	1.1 (0.61)
Median	1.0	1.0	1.0
Min - Max	0.0 - 3.0	0.0 - 3.0	0.0 - 3.0
Extra nodal disease at most recent relapse prior to transplant- n (%)			
Yes	10 (37.0)	7 (50.0)	17 (41.5)
No	15 (55.6)	6 (42.9)	21 (51.2)
Number of stem cells collected (10^6/kg)			
n	26	12	38

Mean (SD)	10.1 (9.86)	14.2 (17.65)	11.4 (12.73)
Median	6.9	7.7	7.3
Min - Max	2.3 - 49.0	0.6 - 64.5	0.6 - 64.5
Number of stem cells transfused (10^6/kg)			
n	26	13	39
Mean (SD)	5.8 (4.69)	6.7 (5.01)	6.1 (4.75)
Median	3.7	6.6	4.2
Min – Max	2.4 - 22.9	0.3 - 19.5	0.3 - 22.9
Stage at most recent relapse – n (%)			
Stage IIa	2 (7.4)	2 (14.3)	4 (9.8)
Stage IIb	7 (25.9)	2 (14.3)	9 (22.0)
Stage IIIa	4 (14.8)	3 (21.4)	7 (17.1)
Stage IIIb	3 (11.1)	3 (21.4)	6 (14.6)
Stage IVa	4 (14.8)	1 (7.1)	5 (12.2)
Stage IVb	5 (18.5)	2 (14.3)	7 (17.1)
Best response to last therapy prior to transplant regimen – n (%)			
Complete Response	23 (85.2)	13 (92.9)	36 (87.8)
Partial Response	2 (7.4)	1 (7.1)	3 (7.3)
Complete Response/Unconfirmed	1 (3.7)	0	1 (2.4)
Unknown	1 (3.7)	0	1 (2.4)

PAN, panobinostat; PBO, placebo

Duration of Exposure to Study Treatment

Overall duration of exposure to study treatment by treatment group (Safety set)

	PAN			PBO N=12
	Randomization phase N=26	Open-Label phase N=5	All phases N=26	
Exposure categories – n (%)				
< 4 weeks	3 (11.5)	1 (20.0)	3 (11.5)	0
≥ 4 weeks and < 8 weeks	5 (19.2)	0	5 (19.2)	1 (8.3)
≥ 8 weeks and < 16 weeks	2 (7.7)	4 (80.0)	2 (7.7)	2 (16.7)
≥ 16 weeks and < 24 weeks	2 (7.7)	0	2 (7.7)	0
≥ 24 weeks and < 48 weeks	9 (34.6)	0	6 (23.1)	5 (41.7)
≥ 48 weeks	5 (19.2)	0	8 (30.8)	4 (33.3)
Duration of study treatment exposure (days)				
n	26	5	26	12
Mean (SD)	177.8 (132.13)	65.8 (30.65)	190.5 (141.82)	228.3 (120.44)
Median	176.0	75.0	198.5	217.0
Min - Max	1.0 - 390.0	19.0 - 101.0	1.0 - 390.0	54.0 - 363.0

PAN, Panobinostat; PBO, placebo

- Duration of study treatment exposure (days) = [date of last administration of study treatment] - [date of first administration of study treatment] + 1

- All patients have a randomization phase, while some also have an open-label phase

- For all patients, data from the randomization phase is summarized under the column titled 'Randomization phase, data from the open-label phase (if there is one) is summarized under the column titled 'Open-Label phase', and the pooled data from both phases is summarized under the column titled 'All phases'

Safety Results

Adverse Events by System Organ Class

Adverse events regardless of study drug relationship by primary system organ class, maximum grade, and treatment group (Safety set)

	PAN						PBO N=12	
	Randomization phase N=26		Open-label phase N=5		All phases N=26			
Primary System organ class	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)
Any primary system organ class	26 (100.0)	17 (65.4)	2 (40.0)	0	26 (100.0)	17 (65.4)	11 (91.7)	5 (41.7)
Gastrointestinal disorders	24 (92.3)	5 (19.2)	1 (20.0)	0	24 (92.3)	5 (19.2)	6 (50.0)	0
General disorders and administration site conditions	16 (61.5)	4 (15.4)	2 (40.0)	0	16 (61.5)	4 (15.4)	6 (50.0)	0
Infections and infestations	15 (57.7)	2 (7.7)	0	0	15 (57.7)	2 (7.7)	8 (66.7)	2 (16.7)
Nervous system disorders	15 (57.7)	4 (15.4)	0	0	15 (57.7)	4 (15.4)	2 (16.7)	0
Blood and lymphatic system disorders	11 (42.3)	9 (34.6)	1 (20.0)	0	11 (42.3)	9 (34.6)	5 (41.7)	4 (33.3)
Metabolism and nutrition disorders	9 (34.6)	3 (11.5)	1 (20.0)	0	10 (38.5)	3 (11.5)	4 (33.3)	0
Respiratory, thoracic and mediastinal disorders	10 (38.5)	0	0	0	10 (38.5)	0	1 (8.3)	0
Musculoskeletal and connective tissue disorders	9 (34.6)	1 (3.8)	0	0	9 (34.6)	1 (3.8)	3 (25.0)	0
Skin and subcutaneous tissue disorders	7 (26.9)	0	0	0	7 (26.9)	0	3 (25.0)	0
Injury, poisoning and procedural complications	4 (15.4)	0	0	0	4 (15.4)	0	0	0
Psychiatric disorders	3 (11.5)	0	0	0	3 (11.5)	0	1 (8.3)	0
Renal and urinary	3 (11.5)	0	0	0	3 (11.5)	0	0	0

disorders								
Investigations	2 (7.7)	2 (7.7)	0	0	2 (7.7)	2 (7.7)	2 (16.7)	0
Vascular disorders	2 (7.7)	0	0	0	2 (7.7)	0	1 (8.3)	0
Cardiac disorders	1 (3.8)	0	0	0	1 (3.8)	0	0	0
Immune system disorders	1 (3.8)	0	0	0	1 (3.8)	0	0	0

PAN, Panobinostat; PBO, placebo

- Primary system organ classes are presented by descending frequency in total row of Any grade of All phases column

- A patient with multiple adverse events within a system organ class is counted only once

- All patients have a randomization phase, while some also have an open-label phase

- For all patients, data from the randomization phase is summarized under the column titled 'Randomization phase, data from the open-label phase (if there is one) is summarized under the column titled 'Open-Label phase', and the pooled data from both phases is summarized under the column titled 'All phases'

Most Frequently Reported AEs Overall by Preferred Term n (%)

Adverse events regardless of study drug relationship by preferred term and treatment group (reported in at least 10% of patients in either treatment group) (Safety set)

	PAN						PBO N=12	
	Randomization phase N=26		Open-label phase N=5		All phases N=26			
Preferred Term	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)
Any AE	26 (100)	17 (65.4)	2 (40.0)	0	26 (100)	17 (65.4)	11 (91.7)	5 (41.7)
Diarrhea	23 (88.5)	3 (11.5)	1 (20.0)	0	23 (88.5)	3 (11.5)	3 (25.0)	0
Nausea	15 (57.7)	2 (7.7)	0	0	15 (57.7)	2 (7.7)	1 (8.3)	0
Vomiting	12 (46.2)	3 (11.5)	0	0	12 (46.2)	3 (11.5)	3 (25.0)	0
Fatigue	9 (34.6)	3 (11.5)	0	0	9 (34.6)	3 (11.5)	3 (25.0)	0
Neutropenia	7 (26.9)	7 (26.9)	0	0	7 (26.9)	7 (26.9)	4 (33.3)	4 (33.3)
Oropharyngeal pain	7 (26.9)	0	0	0	7 (26.9)	0	0	0
Thrombocytopenia	7 (26.9)	4 (15.4)	1 (20.0)	0	7 (26.9)	4 (15.4)	1 (8.3)	0
Headache	6 (23.1)	1 (3.8)	0	0	6 (23.1)	1 (3.8)	0	0
Decreased appetite	4 (15.4)	1 (3.8)	1 (20.0)	0	5 (19.2)	1 (3.8)	2 (16.7)	0
Nasopharyngitis	5 (19.2)	0	0	0	5 (19.2)	0	0	0
Pyrexia	4 (15.4)	0	1 (20.0)	0	5 (19.2)	0	1 (8.3)	0
Upper respiratory tract infection	5 (19.2)	0	0	0	5 (19.2)	0	1 (8.3)	0
Influenza like illness	4 (15.4)	0	1 (20.0)	0	4 (15.4)	0	0	0
Sinusitis	4 (15.4)	0	0	0	4 (15.4)	0	1 (8.3)	0
Arthralgia	3 (11.5)	0	0	0	3 (11.5)	0	0	0
Asthenia	3 (11.5)	1 (3.8)	0	0	3 (11.5)	1 (3.8)	1 (8.3)	0
Cough	3 (11.5)	0	0	0	3 (11.5)	0	1 (8.3)	0

Depression	3 (11.5)	0	0	0	3 (11.5)	0	0	0
Dysgeusia	3 (11.5)	0	0	0	3 (11.5)	0	0	0
Gastroesophageal reflux disease	3 (11.5)	0	0	0	3 (11.5)	0	0	0
Leukopenia	3 (11.5)	2 (7.7)	0	0	3 (11.5)	2 (7.7)	2 (16.7)	2 (16.7)
Muscle spasms	3 (11.5)	0	0	0	3 (11.5)	0	1 (8.3)	0
Abdominal pain	1 (3.8)	0	0	0	1 (3.8)	0	2 (16.7)	0
Herpes zoster	0	0	0	0	0	0	2 (16.7)	2 (16.7)

PAN, Panobinostat; PBO, placebo

- Preferred terms are presented by descending frequency in the Any grade of All phases column
- A patient with multiple occurrences of an AE is counted only once in that AE category
- All patients have a randomization phase, while some also have an open-label phase
- For all patients, data from the randomization phase is summarized under the column titled 'Randomization phase, data from the open-label phase (if there is one) is summarized under the column titled 'Open-Label phase', and the pooled data from both phases is summarized under the column titled 'All phases'

Serious Adverse Events and Deaths

Summary of adverse event categories (deaths, other serious or clinically significant adverse events or related discontinuations) by treatment group (Safety set)

	PAN			PBO
	Randomization phase N=26 n (%)	Open-label phase N=5 n (%)	All phases N=26 n (%)	N=12 n (%)
All Deaths	0	0	0	0
Adverse events (AEs)[1]				
Adverse events of grade 3-4	17 (65.4)	0	17 (65.4)	5 (41.7)
Adverse events of grade 3-4 suspected to be related to study drug	13 (50.0)	0	13 (50.0)	4 (33.3)
Serious adverse events	2 (7.7)	0	2 (7.7)	1 (8.3)
Adverse events leading to any study treatment discontinuation*	6 (23.1)	0	6 (23.1)	0 (0.0)
Adverse events leading to any study treatment discontinuation suspected to be related to study drug	5 (19.2)	0	5 (19.2)	0 (0.0)

PAN, Panobinostat; PBO, placebo

-[1] Adverse events occurring more than 28 days after the discontinuation of study treatment are not summarized.

- All patients have a randomization phase, while some also have an open-label phase
- For all patients, data from the randomization phase is summarized under the column titled 'Randomization phase, data from the open-label phase (if there is one) is summarized under the column titled 'Open-Label phase', and the pooled data from both phases is summarized under the column titled 'All phases'

Serious adverse events regardless of study drug relationship by preferred term and treatment group (Safety set)

	PAN						PBO N=12	
	Randomization phase N=26		Open-label phase N=5		All phases N=26			
Preferred Term	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)	Any grade n (%)	Grade 3/4 n (%)
Any SAE	2 (7.7)	2 (7.7)	0	0	2 (7.7)	2 (7.7)	1 (8.3)	1 (8.3)
Cellulitis	1 (3.8)	1 (3.8)	0	0	1 (3.8)	1 (3.8)	0	0
Gastroenteritis salmonella	1 (3.8)	1 (3.8)	0	0	1 (3.8)	1 (3.8)	0	0
Pyrexia	1 (3.8)	0	0	0	1 (3.8)	0	0	0
Sinusitis bacterial	1 (3.8)	1 (3.8)	0	0	1 (3.8)	1 (3.8)	0	0
Herpes zoster	0	0	0	0	0	0	1 (8.3)	1 (8.3)

PAN, Panobinostat; PBO, placebo

- Preferred terms are presented by descending frequency in the Any grade of All phases column
- A patient with multiple occurrences of an AE is counted only once in that AE category
- All patients have a randomization phase, while some also have an open-label phase
- For all patients, data from the randomization phase is summarized under the column titled 'Randomization phase, data from the open-label phase (if there is one) is summarized under the column titled 'Open-Label phase', and the pooled data from both phases is summarized under the column titled 'All phases'

Other Relevant Findings

There were no patients in either of the treatment arms who had new QTcF >450ms or increase from baseline >30ms.

As there were no deaths reported in the study, all patients were censored for OS. For disease progression events, there were 4 (14.8%) events reported in the PAN arm and 4 (28.6%) events in the placebo arm as of the data cut-off date of 13-Aug-2012. The DFS time ranged from 1 day to 393 days in the PAN arm and from 1 day to 372 days in the placebo arm.

Date of Clinical Trial Report

27-Mar-2013

Date Inclusion on Novartis Clinical Trial Results Database

7-May-2013

Date of Latest Update