



## Clinical trial results:

**An open-label multi-center single agent panobinostat roll-over protocol for patients who have completed a previous Novartis-sponsored panobinostat study and are judged by the investigator to benefit from continued single agent panobinostat treatment**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2012-005252-41   |
| Trial protocol           | ES NL            |
| Global end of trial date | 19 November 2018 |

### Results information

|                                |                                                                                                                                                                                                           |
|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number          | v2 (current)                                                                                                                                                                                              |
| This version publication date  | 26 July 2020                                                                                                                                                                                              |
| First version publication date | 18 December 2019                                                                                                                                                                                          |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Update to data to align with title of "Percentage..". Number of participants in data changed to percentage of participants. |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CLBH589B2402B |
|-----------------------|---------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01802879 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                  |
|------------------------------|----------------------------------------------------------------------------------|
| Sponsor organisation name    | Novartis Pharma AG                                                               |
| Sponsor organisation address | CH-4002, Basel, Switzerland,                                                     |
| Public contact               | Study Director, Novartis Pharma AG, 41 613241111,<br>Novartis.email@novartis.com |
| Scientific contact           | Study Director, Novartis Pharma AG, 41 613241111,<br>Novartis.email@novartis.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                       | 19 November 2018 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 19 November 2018 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 19 November 2018 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate long term safety data (serious adverse events and adverse events)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 24 June 2013 |
| 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 | Spain: 2         |
| Country: Number of subjects enrolled | United States: 4 |
| Country: Number of subjects enrolled | Israel: 1        |
| Country: Number of subjects enrolled | Netherlands: 1   |
| Worldwide total number of subjects   | 8                |
| EEA total number of subjects         | 3                |

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)                      | 5 |
| From 65 to 84 years                       | 3 |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

There was no screening period. Patients enrolled into trial directly from the parent protocol.

### Period 1

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

### Arms

|                  |                                        |
|------------------|----------------------------------------|
| <b>Arm title</b> | Panobinostat - 10 to 40 mg/day TIW QoW |
|------------------|----------------------------------------|

Arm description:

10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design

|                                        |               |
|----------------------------------------|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Panobinostat  |
| Investigational medicinal product code | LBH589        |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

10 - 40 mg/day TIW QoW (three times a week every other week)

|                                       |                                        |
|---------------------------------------|----------------------------------------|
| <b>Number of subjects in period 1</b> | Panobinostat - 10 to 40 mg/day TIW QoW |
| Started                               | 8                                      |
| Completed                             | 0                                      |
| Not completed                         | 8                                      |
| Disease progression                   | 6                                      |
| Administrative problems               | 2                                      |

## Baseline characteristics

### Reporting groups

|                                                                                                                      |                                        |
|----------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Reporting group title                                                                                                | Panobinostat - 10 to 40 mg/day TIW QoW |
| Reporting group description:<br>10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design |                                        |

| Reporting group values                                                  | Panobinostat - 10 to 40 mg/day TIW QoW | Total |  |
|-------------------------------------------------------------------------|----------------------------------------|-------|--|
| Number of subjects                                                      | 8                                      | 8     |  |
| Age categorical<br>Units: Subjects                                      |                                        |       |  |
| Adults (18-64 years)                                                    | 5                                      | 5     |  |
| From 65-84 years                                                        | 3                                      | 3     |  |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 54<br>± 14.5                           | -     |  |
| Sex: Female, Male<br>Units: Subjects                                    |                                        |       |  |
| Female                                                                  | 4                                      | 4     |  |
| Male                                                                    | 4                                      | 4     |  |
| Parent protocol participants<br>Units: Subjects                         |                                        |       |  |
| CLBH589B2201                                                            | 2                                      | 2     |  |
| CLBH589B2207                                                            | 3                                      | 3     |  |
| CLBH589E2214                                                            | 1                                      | 1     |  |
| CLBH589X2105                                                            | 2                                      | 2     |  |

## End points

### End points reporting groups

|                                                                                                                      |                                        |
|----------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Reporting group title                                                                                                | Panobinostat - 10 to 40 mg/day TIW QoW |
| Reporting group description:<br>10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design |                                        |

### Primary: Overview of adverse events (Safety Set)

|                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                        |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                        | Overview of adverse events (Safety Set) <sup>[1]</sup> |
| End point description:<br>Adverse events were collected from baseline up to 30 days post treatment at scheduled visits. Severity of adverse events was assessed according to the current version of Common Terminology Criteria for Adverse Events (CTCAE). If CTCAE grading did not exist for an adverse event, the severity of mild, moderate, severe, and life-threatening, corresponding to Grades 1 - 4, was used |                                                        |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                         | Primary                                                |
| End point timeframe:<br>Baseline up to approximately 60 months                                                                                                                                                                                                                                                                                                                                                         |                                                        |

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: No analysis done

|                                                    |                                        |  |  |  |
|----------------------------------------------------|----------------------------------------|--|--|--|
| <b>End point values</b>                            | Panobinostat - 10 to 40 mg/day TIW QoW |  |  |  |
| Subject group type                                 | Reporting group                        |  |  |  |
| Number of subjects analysed                        | 8                                      |  |  |  |
| Units: participants                                |                                        |  |  |  |
| Any adverse event (AE)                             | 6                                      |  |  |  |
| Any treatment related AE                           | 2                                      |  |  |  |
| Any serious adverse event (SAE)                    | 2                                      |  |  |  |
| Grade 3 or 4 AE                                    | 3                                      |  |  |  |
| Grade 3 or 4 AE - suspected to be related          | 1                                      |  |  |  |
| AEs leading discontinuation                        | 0                                      |  |  |  |
| AEs leading to dose adjust/ temp dose interruption | 2                                      |  |  |  |
| On-treatment death                                 | 0                                      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of patients with clinical benefit as assessed by the investigator.

|                 |                                                                               |
|-----------------|-------------------------------------------------------------------------------|
| End point title | Percentage of patients with clinical benefit as assessed by the investigator. |
|-----------------|-------------------------------------------------------------------------------|

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End point description:

Patients were assessed by investigators at scheduled visits to determine if patient continued to benefit from panobinostat therapy.

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

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End point timeframe:

baseline up to approximately 5 years

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| End point values                          | Panobinostat -<br>10 to 40<br>mg/day TIW<br>QoW |  |  |  |
|-------------------------------------------|-------------------------------------------------|--|--|--|
| Subject group type                        | Reporting group                                 |  |  |  |
| Number of subjects analysed               | 8                                               |  |  |  |
| Units: Percentage of patients             |                                                 |  |  |  |
| number (not applicable)                   |                                                 |  |  |  |
| Percent of patients with clinical benefit | 87.5                                            |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 60 months

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |                                        |
|-----------------------|----------------------------------------|
| Reporting group title | Panobinostat - 10 to 40 mg/day TIW QoW |
|-----------------------|----------------------------------------|

Reporting group description:

10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design

| <b>Serious adverse events</b>                        | Panobinostat - 10 to 40 mg/day TIW QoW |  |  |
|------------------------------------------------------|----------------------------------------|--|--|
| Total subjects affected by serious adverse events    |                                        |  |  |
| subjects affected / exposed                          | 2 / 8 (25.00%)                         |  |  |
| number of deaths (all causes)                        | 0                                      |  |  |
| number of deaths resulting from adverse events       |                                        |  |  |
| Nervous system disorders                             |                                        |  |  |
| Cerebrovascular accident                             |                                        |  |  |
| subjects affected / exposed                          | 1 / 8 (12.50%)                         |  |  |
| occurrences causally related to treatment / all      | 0 / 1                                  |  |  |
| deaths causally related to treatment / all           | 0 / 0                                  |  |  |
| General disorders and administration site conditions |                                        |  |  |
| Non-cardiac chest pain                               |                                        |  |  |
| subjects affected / exposed                          | 1 / 8 (12.50%)                         |  |  |
| occurrences causally related to treatment / all      | 0 / 1                                  |  |  |
| deaths causally related to treatment / all           | 0 / 0                                  |  |  |

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

| <b>Non-serious adverse events</b>                     | Panobinostat - 10 to 40 mg/day TIW QoW |  |  |
|-------------------------------------------------------|----------------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                                        |  |  |
| subjects affected / exposed                           | 4 / 8 (50.00%)                         |  |  |

|                                                                                                                                                   |                     |  |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| Investigations                                                                                                                                    |                     |  |  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                                                                    | 1 / 8 (12.50%)<br>1 |  |  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)                                                                      | 1 / 8 (12.50%)<br>1 |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Benign muscle neoplasm<br>subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1 |  |  |
| Nervous system disorders<br>Neuropathy peripheral<br>subjects affected / exposed<br>occurrences (all)                                             | 2 / 8 (25.00%)<br>1 |  |  |
| Blood and lymphatic system disorders<br>Neutropenia<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 8 (12.50%)<br>1 |  |  |
| General disorders and administration site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 8 (12.50%)<br>1 |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                                       | 1 / 8 (12.50%)<br>1 |  |  |
| Gastric disorder<br>subjects affected / exposed<br>occurrences (all)                                                                              | 1 / 8 (12.50%)<br>1 |  |  |
| Skin and subcutaneous tissue disorders<br>Pruritus<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 8 (12.50%)<br>1 |  |  |
| Psychiatric disorders<br>Insomnia                                                                                                                 |                     |  |  |

|                                                                                                                                                                                            |                                                |  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                           | 1 / 8 (12.50%)<br>1                            |  |  |
| Musculoskeletal and connective tissue disorders<br>Bone pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Osteoarthritis<br>subjects affected / exposed<br>occurrences (all) | 1 / 8 (12.50%)<br>1<br><br>1 / 8 (12.50%)<br>1 |  |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                                                                                         | 1 / 8 (12.50%)<br>1                            |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                                                                                                                                                                                                                 |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 11 March 2016 | The main purpose of the amendment is to change the primary endpoint to safety to better characterize the long-term safety of the compound. In addition, the protocol has been amended to include the collection of all AEs (including nonserious AEs) and an investigator descriptive attestation of continued clinical benefit (Yes/No). |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported