



## Clinical trial results: Immune Response to Influenza Vaccine in Subjects with B-cell Malignancies Treated with Idelalisib

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2017-003055-30  |
| Trial protocol           | FR GB CZ PL ES  |
| Global end of trial date | 09 October 2019 |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 07 August 2020 |
| First version publication date | 07 August 2020 |

### Trial information

#### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-313-4100 |
|-----------------------|----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03701438 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                               |
|------------------------------|-----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Gilead Sciences                                                                               |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404                                     |
| Public contact               | Gilead Clinical Study Information Center, Gilead Sciences,<br>GileadClinicalTrials@gilead.com |
| Scientific contact           | Gilead Clinical Study Information Center, Gilead Sciences,<br>GileadClinicalTrials@gilead.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                       | 09 October 2019 |
| Is this the analysis of the primary completion data? | No              |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 09 October 2019 |
| Was the trial ended prematurely? | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the immune response to an influenza vaccine in adults with B-cell malignancies who were receiving treatment with idelalisib in a Gilead-sponsored study (parent study: GS-US-313-1580 [NCT02536300]).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 23 October 2018 |
| 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: 1          |
| Country: Number of subjects enrolled | Czech Republic: 1 |
| Worldwide total number of subjects   | 2                 |
| EEA total number of subjects         | 2                 |

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)      | 1 |
| From 65 to 84 years       | 1 |
| 85 years and over         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe. The first participant was screened on 23 October 2018.

### Pre-assignment

Screening details:

2 participants were screened.

### Period 1

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

### Arms

|           |                              |
|-----------|------------------------------|
| Arm title | Idelalisib/Influenza Vaccine |
|-----------|------------------------------|

Arm description:

Participants who were receiving treatment with idelalisib (100 mg or 150 mg tablets orally twice daily) for at least 7 consecutive days prior to receiving an influenza vaccine in a Gilead-sponsored parent study (GS-US-313-1580 [NCT02536300]), continued to receive idelalisib (per dose and schedule of parent study) along with the influenza vaccine within 7 days of baseline (Day 1) blood sample collection, administered per standard of care using a vaccine licensed and recommended in the site's country.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Influenza Vaccine      |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Administered per standard of care using a vaccine licensed and recommended in the site's country.

|                                        |            |
|----------------------------------------|------------|
| Investigational medicinal product name | Idelalisib |
| Investigational medicinal product code |            |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Administered per dose and schedule of parent study.

|                                       |                              |
|---------------------------------------|------------------------------|
| <b>Number of subjects in period 1</b> | Idelalisib/Influenza Vaccine |
| Started                               | 2                            |
| Completed                             | 2                            |



## Baseline characteristics

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Idelalisib/Influenza Vaccine |
|-----------------------|------------------------------|

Reporting group description:

Participants who were receiving treatment with idelalisib (100 mg or 150 mg tablets orally twice daily) for at least 7 consecutive days prior to receiving an influenza vaccine in a Gilead-sponsored parent study (GS-US-313-1580 [NCT02536300]), continued to receive idelalisib (per dose and schedule of parent study) along with the influenza vaccine within 7 days of baseline (Day 1) blood sample collection, administered per standard of care using a vaccine licensed and recommended in the site's country.

| Reporting group values                | Idelalisib/Influenza Vaccine | Total |  |
|---------------------------------------|------------------------------|-------|--|
| Number of subjects                    | 2                            | 2     |  |
| Age categorical<br>Units: Subjects    |                              |       |  |
| Adults (18-64 years)                  | 1                            | 1     |  |
| From 65-84 years                      | 1                            | 1     |  |
| Gender categorical<br>Units: Subjects |                              |       |  |
| Female                                | 2                            | 2     |  |
| Male                                  | 0                            | 0     |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Idelalisib/Influenza Vaccine |
| Reporting group description:<br>Participants who were receiving treatment with idelalisib (100 mg or 150 mg tablets orally twice daily) for at least 7 consecutive days prior to receiving an influenza vaccine in a Gilead-sponsored parent study (GS-US-313-1580 [NCT02536300]), continued to receive idelalisib (per dose and schedule of parent study) along with the influenza vaccine within 7 days of baseline (Day 1) blood sample collection, administered per standard of care using a vaccine licensed and recommended in the site's country. |                              |

### Primary: Seroconversion Rate: Percentage of Participants with Either a Pre-Vaccination Hemagglutination Inhibition (HI) Titer < 1:10 and a Post-Vaccination HI titer ≥ 1:40, or a Pre-Vaccination HI titer ≥ 1:10 and a ≥ 4-fold Increase in Post-Vaccination HI Titer

|                 |                                                                                                                                                                                                                                                                              |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Seroconversion Rate: Percentage of Participants with Either a Pre-Vaccination Hemagglutination Inhibition (HI) Titer < 1:10 and a Post-Vaccination HI titer ≥ 1:40, or a Pre-Vaccination HI titer ≥ 1:10 and a ≥ 4-fold Increase in Post-Vaccination HI Titer <sup>[1]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

28 days (± 7 days) post-vaccination

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: Due to early termination of study, no efficacy analyses were performed.

| End point values                  | Idelalisib/Influenza Vaccine |  |  |  |
|-----------------------------------|------------------------------|--|--|--|
| Subject group type                | Reporting group              |  |  |  |
| Number of subjects analysed       | 0 <sup>[2]</sup>             |  |  |  |
| Units: percentage of participants |                              |  |  |  |
| number (not applicable)           |                              |  |  |  |

Notes:

[2] - Due to early termination of study, no efficacy analyses were performed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Seroprotection Rate: Percentage of Participants with HI titer ≥ 1:40 Post-Vaccination

|                 |                                                                                       |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Seroprotection Rate: Percentage of Participants with HI titer ≥ 1:40 Post-Vaccination |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

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

End point timeframe:

28 days (± 7 days) post-vaccination

| End point values                  | Idelalisib/Influenza Vaccine |  |  |  |
|-----------------------------------|------------------------------|--|--|--|
| Subject group type                | Reporting group              |  |  |  |
| Number of subjects analysed       | 0 <sup>[3]</sup>             |  |  |  |
| Units: percentage of participants |                              |  |  |  |
| number (not applicable)           |                              |  |  |  |

Notes:

[3] - Due to early termination of study, no efficacy analyses were performed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titers (GMTs) of Antibodies: Pre- and Post-Vaccination GMTs of HI Antibodies

|                                                              |                                                                                             |
|--------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| End point title                                              | Geometric Mean Titers (GMTs) of Antibodies: Pre- and Post-Vaccination GMTs of HI Antibodies |
| End point description:                                       |                                                                                             |
| End point type                                               | Secondary                                                                                   |
| End point timeframe:                                         |                                                                                             |
| Pre-vaccination and 28 days ( $\pm$ 7 days) post-vaccination |                                                                                             |

| End point values                         | Idelalisib/Influenza Vaccine |  |  |  |
|------------------------------------------|------------------------------|--|--|--|
| Subject group type                       | Reporting group              |  |  |  |
| Number of subjects analysed              | 0 <sup>[4]</sup>             |  |  |  |
| Units: titers (1/dilutions)              |                              |  |  |  |
| geometric mean (confidence interval 95%) | ( to )                       |  |  |  |

Notes:

[4] - Due to early termination of study, no efficacy analyses were performed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with Adverse Events or Serious Adverse Events

|                                                                                                                                          |                                                                          |
|------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| End point title                                                                                                                          | Percentage of Participants with Adverse Events or Serious Adverse Events |
| End point description:                                                                                                                   |                                                                          |
| All Enrolled Analysis Set included all participants who enrolled into the study after screening and had a subject identification number. |                                                                          |
| End point type                                                                                                                           | Secondary                                                                |



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End point timeframe:

Date of Informed consent up to Day 28 (post-vaccination visit)

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|                                   |                              |  |  |  |
|-----------------------------------|------------------------------|--|--|--|
| <b>End point values</b>           | Idelalisib/Influenza Vaccine |  |  |  |
| Subject group type                | Reporting group              |  |  |  |
| Number of subjects analysed       | 2                            |  |  |  |
| Units: percentage of participants |                              |  |  |  |
| number (not applicable)           |                              |  |  |  |
| Adverse Events                    | 100                          |  |  |  |
| Serious Adverse Events            | 0                            |  |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Date of Informed consent up to Day 28 (post-vaccination visit)

Adverse event reporting additional description:

All Enrolled Analysis Set included all participants who enrolled into the study after screening and had a subject identification number.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Idelalisib/Influenza Vaccine |
|-----------------------|------------------------------|

Reporting group description:

Participants who were receiving treatment with idelalisib (100 mg or 150 mg tablets orally twice daily) for at least 7 consecutive days prior to receiving an influenza vaccine in a Gilead-sponsored parent study (GS-US-313-1580 [NCT02536300]), continued to receive idelalisib (per dose and schedule of parent study) along with the influenza vaccine within 7 days of baseline (Day 1) blood sample collection, administered per standard of care using a vaccine licensed and recommended in the site's country.

| Serious adverse events                            | Idelalisib/Influenza Vaccine |  |  |
|---------------------------------------------------|------------------------------|--|--|
| Total subjects affected by serious adverse events |                              |  |  |
| subjects affected / exposed                       | 0 / 2 (0.00%)                |  |  |
| number of deaths (all causes)                     | 0                            |  |  |
| number of deaths resulting from adverse events    | 0                            |  |  |

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

| Non-serious adverse events                            | Idelalisib/Influenza Vaccine |  |  |
|-------------------------------------------------------|------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                              |  |  |
| subjects affected / exposed                           | 2 / 2 (100.00%)              |  |  |
| Blood and lymphatic system disorders                  |                              |  |  |
| Neutropenia                                           |                              |  |  |
| subjects affected / exposed                           | 1 / 2 (50.00%)               |  |  |
| occurrences (all)                                     | 1                            |  |  |
| Thrombocytopenia                                      |                              |  |  |
| subjects affected / exposed                           | 1 / 2 (50.00%)               |  |  |
| occurrences (all)                                     | 1                            |  |  |
| General disorders and administration                  |                              |  |  |

|                                                                                                              |                     |  |  |
|--------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 2 (50.00%)<br>1 |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 2 (50.00%)<br>1 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 31 January 2018 | Based on responses from site selection and feasibility discussions, the protocol was revised to allow participants to receive an influenza vaccination per Standard of Care (SoC) in an inpatient or outpatient medical setting, including but not necessarily limited to hospitals, clinics, health departments, and general practitioner offices. In addition, revisions were made to improve the operational feasibility of the study. |
| 12 April 2018   | Following submission of the clinical trial application via the Voluntary Harmonization Procedure (VHP), Gilead received requests to amend the study from the participating member states in VHP. This protocol amendment addressed the VHP's requests.                                                                                                                                                                                    |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date            | Interruption                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Restart date |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| 09 October 2019 | Study GS-US-313-4100 was initially planned and conducted to fulfill a post-marketing clinical stipulation from Swissmedic to collect data on the investigation of the impact of idelalisib on the immune system and to submit the study report by no later than 31 October 2020. On 01 October 2019, Swissmedic agreed with Gilead's request to be released from this stipulation as not enough participants were able to be recruited for this study. As a result, Gilead terminated Study GS-US-313-4100 early. A letter to investigators was issued globally on 09 October 2019 providing notification regarding study termination. | -            |

Notes:

### Limitations and caveats

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

The study was terminated early and only 2 participants were enrolled so no efficacy analyses and no summary analyses were conducted.

Notes: