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, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, 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.

Number of subjects in period 1	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 Units: Subjects			
Adults (18-64 years)	1	1	
From 65-84 years	1	1	
Gender categorical Units: Subjects			
Female	2	2	
Male	0	0	

End points

End points 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.

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[1]

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[2]			
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[3]			
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 (± 7 days) post-vaccination

End point values	Idelalisib/Influenza Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
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

End point timeframe:

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

End point values	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 Pyrexia subjects affected / exposed occurrences (all)	 1 / 2 (50.00%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 1 / 2 (50.00%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 1 / 2 (50.00%) 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: