Clinical trial results:
A Phase 2, Single Arm Study Evaluating the Efficacy and Safety of Idelalisib in Combination with Rituximab in Patients with Previously Untreated Chronic Lymphocytic Leukemia with 17p Deletion

Summary

EudraCT number	2013-003314-41
Trial protocol	AT GB PT HU IT BE CZ DK ES PL
Global end of trial date	17 May 2016

Results information

Result version number	v1 (current)
This version publication date	15 April 2017
First version publication date	15 April 2017

Trial information

Trial identification

Sponsor protocol code	GS-US-312-0133

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02044822
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	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@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	17 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2016
Global end of trial reached?	Yes
Global end of trial date	17 May 2016
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 evaluate overall response rate (ORR) following treatment with idelalisib plus rituximab in participants with previously untreated chronic lymphocytic leukemia (CLL) with 17p deletion.

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	06 August 2014
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	Poland: 15
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czech Republic: 9
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Australia: 6

Worldwide total number of subjects	102
EEA total number of subjects	77

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)	41
From 65 to 84 years	58
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Europe, and the United States. The first participant was screened on 06 August 2014. The last study visit occurred on 17 May 2016.

Pre-assignment

Screening details:

130 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 + Rituximab

Arm description:

Idelalisib continuously throughout the study (up to 10 years) + rituximab for 8 weeks

Arm type	Experimental
Investigational medicinal product name	Idelalisib
Investigational medicinal product code	
Other name	Zydelig®, GS-1101, CAL-101
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg administered twice daily

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	Rituxan, Mabthera
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m^2 once weekly

Number of subjects in period 1	Idelalisib + Rituximab
Started	102
Completed	9
Not completed	93
Withdrew Consent	3
Initiation of Anti-Neoplastic Therapy	2
Investigator's Discretion	10
Study Terminated by Sponsor	77
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Idelalisib + Rituximab
Reporting group description:	
Idelalisib continuously throughout the study (up to 10 years) + rituximab for 8 weeks	

Reporting group values	Idelalisib + Rituximab	Total	
Number of subjects	102	102	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	66		
standard deviation	± 9.9	-	
Gender categorical Units: Subjects			
Female	44	44	
Male	58	58	
Race Units: Subjects			
Asian	2	2	
Black or African American	2	2	
White	94	94	
Not Permitted	4	4	
Ethnicity Units: Subjects			
Hispanic or Latino	6	6	
Not Hispanic or Latino	91	91	
Not Permitted	5	5	

End points

End points reporting groups

Reporting group title	Idelalisib + Rituximab

Reporting group description:

Idelalisib continuously throughout the study (up to 10 years) + rituximab for 8 weeks

Primary: Overall Response Rate

End point title	Overall Response Rate[1]

End point description:

Overall response rate (ORR) was defined as the proportion of participants who achieve a confirmed complete or partial response. ORR was to be assessed by an independent review committee (IRC). Due to the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

End point type	Primary

End point timeframe:

Not applicable

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 the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

End point values	Idelalisib + Rituximab			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Not applicable				

Notes:

[2] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Duration of response (DOR) was defined as the interval from the first documentation of confirmed complete response or partial response (by IRC) to the first documentation of definitive disease progression or death from any cause. Definitive disease progression is CLL progression based on standard criteria, excluding lymphocytosis alone. Due to the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

End point type	Secondary

End point timeframe:

Not applicable

End point values	Idelalisib + Rituximab			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Not applicable				

Notes:

[3] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Nodal Response Rate

End point title	Nodal Response Rate

End point description:

Nodal response rate was defined as the proportion of participants who achieve a 50% decrease from baseline in the sum of the products of the greatest perpendicular diameters of index lesions. Nodal response rate was to be assessed by an IRC. Due to the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

End point type	Secondary

End point timeframe:

Not applicable

End point values	Idelalisib + Rituximab			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Not applicable				

Notes:

[4] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate

End point title	Complete Response Rate

End point description:

Complete response rate was defined as the proportion of participants who achieve a confirmed complete response. Complete response rate was to be assessed by an IRC. Due to the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

End point type	Secondary

End point timeframe:

Not applicable

End point values	Idelalisib + Rituximab			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Not applicable				

Notes:

[5] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

End point title	Progression-Free Survival

End point description:

Progression-free survival (PFS) was defined as the interval from first dose of study drug to the first documentation of definitive disease progression or death from any cause. Definitive disease progression is CLL progression based on standard criteria, excluding lymphocytosis alone. PFS was to be assessed by an IRC. Due to the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

End point type	Secondary

End point timeframe:

Not applicable

End point values	Idelalisib + Rituximab			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Not applicable				

Notes:

[6] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the interval from the start of study treatment to death from any cause. Due to the early termination of the study, efficacy data were not mature for all participants, and therefore the prespecified analyses were not conducted.

End point type	Secondary

End point timeframe:

Not applicable

End point values	Idelalisib + Rituximab			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Not applicable				

Notes:

[7] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal Residual Disease Negativity Rate at Week 36

End point title	Minimal Residual Disease Negativity Rate at Week 36

End point description:

Minimal residual disease (MRD) negativity rate was defined as the proportion of participants with MRD < 10^-4 assessed by flow cytometry in bone marrow at Week 36 after therapy initiation. For participants receiving the final dose of rituximab after the original scheduled date, the MRD assessment will be performed no fewer than 12 weeks after the last dose of rituximab. Due to the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

End point type	Secondary

End point timeframe:

Not applicable

End point values	Idelalisib + Rituximab			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Not applicable				

Notes:

[8] - Analysis was not performed due to early study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 17 months plus 30 days	
Adverse event reporting additional description:	
ITT Analysis Set; NOTE: Serious adverse events and deaths causally related to "treatment" refers to events deemed related to idelalisib treatment per investigator assessment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Idelalisib + Rituximab
Reporting group description:	
Idelalisib continuously throughout the study (up to 10 years) + rituximab for 8 weeks	

Serious adverse events	Idelalisib + Rituximab		
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 102 (45.10%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Malaise				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	11 / 102 (10.78%)			
occurrences causally related to treatment / all	8 / 15			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hiccups				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Laryngeal pain				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Pleuritic pain				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Body temperature increased				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Transaminases increased			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Coronary artery disease			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Facial nerve disorder			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			

subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	3 / 102 (2.94%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Colitis				
subjects affected / exposed	6 / 102 (5.88%)			
occurrences causally related to treatment / all	6 / 6			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	6 / 102 (5.88%)			
occurrences causally related to treatment / all	5 / 6			
deaths causally related to treatment / all	0 / 0			
Diarrhoea haemorrhagic				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Glossitis				

subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mouth ulceration				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Oral mucosal eruption				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis exfoliative				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eczema				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psoriasis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Rash maculo-papular				

subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Polymyalgia rheumatica			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Conjunctivitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cytomegalovirus infection			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal sepsis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection fungal			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumocystis jirovecii infection			

subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	5 / 102 (4.90%)			
occurrences causally related to treatment / all	3 / 6			
deaths causally related to treatment / all	0 / 1			
Pneumonia bacterial				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia influenzal				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pseudomonal				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pseudomonal bacteraemia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Septic shock				
subjects affected / exposed	2 / 102 (1.96%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dyslipidaemia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolic acidosis				

subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Idelalisib + Rituximab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	98 / 102 (96.08%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	7		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	15 / 102 (14.71%)		
occurrences (all)	18		
Chills			
subjects affected / exposed	13 / 102 (12.75%)		
occurrences (all)	13		
Fatigue			
subjects affected / exposed	16 / 102 (15.69%)		
occurrences (all)	20		
Oedema peripheral			
subjects affected / exposed	11 / 102 (10.78%)		
occurrences (all)	12		
Pyrexia			
subjects affected / exposed	24 / 102 (23.53%)		
occurrences (all)	34		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	19 / 102 (18.63%)		
occurrences (all)	25		
Dyspnoea			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	9		
Epistaxis			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	7		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	7		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	39 / 102 (38.24%)		
occurrences (all)	58		
Aspartate aminotransferase increased			
subjects affected / exposed	22 / 102 (21.57%)		
occurrences (all)	33		
Transaminases increased			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	11		
Weight decreased			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	9		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	9		
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	9		
Headache			

subjects affected / exposed	10 / 102 (9.80%)		
occurrences (all)	12		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 102 (13.73%)		
occurrences (all)	21		
Neutropenia			
subjects affected / exposed	24 / 102 (23.53%)		
occurrences (all)	33		
Thrombocytopenia			
subjects affected / exposed	10 / 102 (9.80%)		
occurrences (all)	13		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	10		
Constipation			
subjects affected / exposed	15 / 102 (14.71%)		
occurrences (all)	18		
Diarrhoea			
subjects affected / exposed	36 / 102 (35.29%)		
occurrences (all)	67		
Dyspepsia			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	8		
Mouth ulceration			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	19 / 102 (18.63%)		
occurrences (all)	23		
Vomiting			
subjects affected / exposed	17 / 102 (16.67%)		
occurrences (all)	21		
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	10		
Rash			
subjects affected / exposed	28 / 102 (27.45%)		
occurrences (all)	35		
Rash maculo-papular			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	9		
Back pain			
subjects affected / exposed	10 / 102 (9.80%)		
occurrences (all)	10		
Myalgia			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	8		
Pain in extremity			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	8		
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	6		
Nasopharyngitis			
subjects affected / exposed	10 / 102 (9.80%)		
occurrences (all)	12		
Oral candidiasis			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	6		
Respiratory tract infection			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	6		
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 8		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all)	 9 / 102 (8.82%) 10 10 / 102 (9.80%) 12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 May 2014	Revisions made to address VHP concerns with the GS-US-312-0123 protocol and to align with global changes made to all protocols in the idelalisib (IDELA) frontline CLL program.
07 November 2014	The protocol was revised primarily to align with IDELA Investigator's Brochure (IB) Edition 11 and to align with global changes made to all protocols in the idelalisib (IDELA) frontline CLL program.
25 November 2014	The protocol was revised primarily to update the creatinine clearance value required prior to entry into the study. This change is being made to correct an error in Amendment 2, where the value was incorrectly changed. The criteria of ≥ 30 mL/min should not have changed from Amendment 1.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
11 March 2016	An increased rate of deaths and serious adverse events (SAEs) among participants with front-line CLL and early-line iNHL treated with idelalisib in combination with standard therapies was observed by the independent data monitoring committee (DMC) during regular review of 3 Gilead Phase 3 studies. Gilead reviewed the unblinded data and terminated those studies in agreement with the DMC recommendation and in consultation with the US Food and Drug Administration (FDA). All front-line studies of idelalisib, including this study, were also terminated.	-

Notes:

Limitations and caveats

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

Due to the early termination of the study, efficacy data were not available for all participants, and therefore the prespecified analyses were not conducted.

Notes: