Clinical trial results:
A Study of IPI-145 and Ofatumumab in Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Previously Enrolled in Study IPI-145-07 Duvelisib (IPI-145)

Summary

EudraCT number	2013-003639-31
Trial protocol	IT HU ES GB BE AT DE FR LV GR
Global end of trial date	12 June 2020

Results information

Result version number	v1
This version publication date	08 June 2023
First version publication date	08 June 2023

Trial information

Trial identification

Sponsor protocol code	IPI-145-12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02049515
WHO universal trial number (UTN)	U1111-1138-8603

Notes:

Sponsors

Sponsor organisation name	Secura Bio
Sponsor organisation address	1995 Village Center Circle, Suite 128, Las Vegas, NV, United States, 89134
Public contact	Darlene Noci, Infinity Pharmaceuticals, Inc, 001 6174531391, Darlene.noci@infi.com
Scientific contact	Darlene Noci, Infinity Pharmaceuticals, Inc, 001 6174531391, Darlene.noci@infi.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	12 June 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A Phase 3 (extension) clinical trial to examine the efficacy of IPI-145 (duvelisib) monotherapy or ofatumumab monotherapy in participants with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma who experienced disease progression after treatment with IPI-145 or ofatumumab in study IPI-145-07 (2013-002405-61).

Protection of trial subjects:

This study was conducted in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 December 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	Australia: 7
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Italy: 13
Worldwide total number of subjects	99
EEA total number of subjects	69

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)	38
From 65 to 84 years	59
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participants previously enrolled in study IPI-145-07 (2013-002405-61) who experienced radiologically confirmed disease progression while on treatment in that study were eligible to participate in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	IPI-145

Arm description:

IPI-145 was administered orally and supplied as 5 milligram (mg) and 25 mg formulated capsules.

Arm type	Experimental
Investigational medicinal product name	IPI-145
Investigational medicinal product code	
Other name	Duvelisib, Copiktra, PI3K Inhibitor
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Doses of 5, 10, 15, and 25 mg were administered orally.

Arm title	Ofatumumab

Arm description:

Ofatumumab was administered as an intravenous (IV) infusion and was supplied in single-use vials at two strengths, 100 mg/5 millilitres (mL) and 1000 mg/50 mL.

Arm type	Active comparator
Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	Arzerra
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Doses of 300 and 2000 mg were administered IV.

Number of subjects in period 1	IPI-145	Ofatumumab
Started	90	9
Received at Least 1 Dose of Study Drug	90	9
Completed	0	3
Not completed	90	6

Treatment Interruption >42 Days	1	-
Physician decision	5	1
Consent withdrawn by subject	3	-
Clinical Deterioration	1	-
Adverse event, non-fatal	46	2
Death	6	-
Need Treatment for Metastatic Melanoma	1	-
Suspected and Unconfirmed Disease Progression	1	-
Protocol-specified Disease Progression	23	2
Termination of the Study by Sponsor	2	-
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	IPI-145
Reporting group description:	
IPI-145 was administered orally and supplied as 5 milligram (mg) and 25 mg formulated capsules.	
Reporting group title	Ofatumumab
Reporting group description:	
Ofatumumab was administered as an intravenous (IV) infusion and was supplied in single-use vials at two strengths, 100 mg/5 millilitres (mL) and 1000 mg/50 mL.	

Reporting group values	IPI-145	Ofatumumab	Total
Number of subjects	90	9	99
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	35	3	38
From 65-84 years	53	6	59
85 years and over	2	0	2
Gender categorical Units: Subjects			
Female	33	4	37
Male	57	5	62
Race (National Institutes of Health/Office of Management and Budget) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	82	9	91
More than one race	0	0	0
Unknown or Not Reported	8	0	8

End points

End points reporting groups

Reporting group title	IPI-145
Reporting group description:	
IPI-145 was administered orally and supplied as 5 milligram (mg) and 25 mg formulated capsules.	
Reporting group title	Ofatumumab
Reporting group description:	
Ofatumumab was administered as an intravenous (IV) infusion and was supplied in single-use vials at two strengths, 100 mg/5 millilitres (mL) and 1000 mg/50 mL.	
Subject analysis set title	All-treated Analysis Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All participants who received any amount of study drug (IPI-145 or ofatumumab).	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[1]
End point description:	
ORR was defined as the percentage of participants with a best response (per investigator assessment) of complete response (CR), CR with incomplete marrow recovery (CRi), partial response (PR), or PR with lymphocytosis (PRwL), according to the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) or revised International Working Group Response (IWG) Criteria, with modification for treatment-related lymphocytosis. The 95% confidence interval was calculated using exact binomial method. Select IWCLL criteria for tumour load assessed by computed tomography (CT): CR/CRi (CLL only), lymphadenopathy (none >1.5 centimetres [cm]), hepatomegaly/splenomegaly (none); PR, lymphadenopathy/hepatomegaly/splenomegaly (decrease ≥50%); PRwL, lymphadenopathy only (decrease ≥50%). Select IWG criteria for tumour load assessed by CT: CR, lymphadenopathy/hepatomegaly/splenomegaly (normal size); PR, lymphadenopathy/hepatomegaly/splenomegaly (decrease ≥50%); PRwL, lymphadenopathy only (decrease ≥50%).	
End point type	Primary
End point timeframe:	
Until progressive disease (PD), death, or other anticancer therapy is initiated (up to 4.5 years)	

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: Only descriptive statistics (percentage plus confidence interval) are reported for ORR.

End point values	IPI-145	Ofatumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90[2]	9[3]		
Units: percentage of participants				
number (confidence interval 95%)	76.7 (66.6 to 84.9)	0 (0 to 0)		

Notes:

[2] - All-treated Analysis Set

[3] - All-treated Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was defined as the time from the first documentation of response per investigator assessment to either PD or death due to any cause. DOR was evaluated using the Kaplan-Meier method based on all treated participants with a documentation of response (that is, CR, CRi, PR, or PRwL) as determined by investigator assessment. Select IWCLL criteria for tumour load assessed by CT: CR/CRi (CLL only), lymphadenopathy (none >1.5 cm), hepatomegaly/splenomegaly (none); PR, lymphadenopathy/hepatomegaly/splenomegaly (decrease ≥50%); PRwL, lymphadenopathy only (decrease ≥50%). Select IWG criteria for tumour load assessed by CT: CR, lymphadenopathy/hepatomegaly/splenomegaly (normal size); PR, lymphadenopathy/hepatomegaly/splenomegaly (decrease ≥50%); PRwL, lymphadenopathy only (decrease ≥50%).

End point type	Secondary

End point timeframe:

From the first documentation of response to the first documentation of PD or death due to any cause (up to 4.5 years)

End point values	IPI-145	Ofatumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90[4]	0[5]		
Units: months				
median (confidence interval 95%)	14.9 (8.55 to 18.6)	(to)		

Notes:

[4] - All-treated Analysis Set

[5] - DOR was determined only for treated participants with documentation of response.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)

End point description:

PFS was defined as the time from the first dose of study treatment to the first documentation of either investigator-assessed PD or death resulting from any cause. PFS was determined using the Kaplan-Meier method based on all treated participants with a documentation of response (that is, CR, CRi, PR, or PRwL) as determined by investigator assessment.

End point type	Secondary

End point timeframe:

From the first dose of study treatment to the first documentation of PD or death from any cause (up to 4.5 years)

End point values	IPI-145	Ofatumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90[6]	0[7]		
Units: month				
median (confidence interval 95%)	15.3 (12.2 to 20.6)	(to)		

Notes:

[6] - All-treated Analysis Set

[7] - PFS was determined only for treated participants with documentation of response.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
4.5 years	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	IPI-145
Reporting group description:	
IPI-145 was administered orally and supplied as 5 mg and 25 mg formulated capsules.	
Reporting group title	Ofatumumab
Reporting group description:	
Ofatumumab was administered as an IV infusion and was supplied in single-use vials at two strengths, 100 mg/5 mL and 1000 mg/50 mL.	

Serious adverse events	IPI-145	Ofatumumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 90 (75.56%)	4 / 9 (44.44%)	
number of deaths (all causes)	20	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basosquamous carcinoma			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			

subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arterial rupture			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 90 (3.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Drug intolerance			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Multi-organ failure			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oedema			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutrophil count decreased			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental impairment			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle contractions involuntary			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 90 (3.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancytopenia			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	16 / 90 (17.78%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 17	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	8 / 90 (8.89%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			

subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal ulcer			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth ulceration			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Actinic keratosis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			

subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pityriasis lichenoides et varioliformis acuta			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pityriasis rubra pilaris			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	4 / 90 (4.44%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			

subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pollakiuria			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	13 / 90 (14.44%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 14	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Sepsis			
subjects affected / exposed	4 / 90 (4.44%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	3 / 90 (3.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	3 / 90 (3.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 90 (2.22%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter infection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal bacteraemia			

subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal infection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia haemophilus			

subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonas aeruginosa			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal skin infection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	IPI-145	Ofatumumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 90 (88.89%)	8 / 9 (88.89%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 90 (2.22%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	21 / 90 (23.33%)	0 / 9 (0.00%)	
occurrences (all)	33	0	
Asthenia			
subjects affected / exposed	11 / 90 (12.22%)	0 / 9 (0.00%)	
occurrences (all)	14	0	
Oedema peripheral			
subjects affected / exposed	6 / 90 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	8	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 90 (1.11%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed[1]	0 / 33 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Vulvovaginal pruritus			
subjects affected / exposed[2]	0 / 33 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	15 / 90 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	20	0	
Dyspnoea			
subjects affected / exposed	3 / 90 (3.33%)	1 / 9 (11.11%)	
occurrences (all)	3	3	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 90 (1.11%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Investigations			
Lipase increased			
subjects affected / exposed	9 / 90 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	13	0	
Weight decreased			
subjects affected / exposed	7 / 90 (7.78%)	0 / 9 (0.00%)	
occurrences (all)	7	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 90 (0.00%)	3 / 9 (33.33%)	
occurrences (all)	0	3	
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 90 (7.78%)	0 / 9 (0.00%)	
occurrences (all)	7	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	23 / 90 (25.56%)	1 / 9 (11.11%)	
occurrences (all)	41	2	
Anaemia			

subjects affected / exposed	8 / 90 (8.89%)	2 / 9 (22.22%)	
occurrences (all)	13	7	
Thrombocytopenia			
subjects affected / exposed	9 / 90 (10.00%)	1 / 9 (11.11%)	
occurrences (all)	11	2	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 90 (2.22%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	43 / 90 (47.78%)	0 / 9 (0.00%)	
occurrences (all)	92	0	
Abdominal pain			
subjects affected / exposed	9 / 90 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	10	0	
Nausea			
subjects affected / exposed	10 / 90 (11.11%)	1 / 9 (11.11%)	
occurrences (all)	10	1	
Vomiting			
subjects affected / exposed	10 / 90 (11.11%)	0 / 9 (0.00%)	
occurrences (all)	10	0	
Abdominal pain upper			
subjects affected / exposed	7 / 90 (7.78%)	0 / 9 (0.00%)	
occurrences (all)	8	0	
Colitis			
subjects affected / exposed	6 / 90 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	7	0	
Dyspepsia			
subjects affected / exposed	5 / 90 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	6	0	
Constipation			
subjects affected / exposed	5 / 90 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	5	0	
Gastrooesophageal reflux disease			

subjects affected / exposed	3 / 90 (3.33%)	1 / 9 (11.11%)	
occurrences (all)	3	1	
Oesophagitis			
subjects affected / exposed	1 / 90 (1.11%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Stomatitis			
subjects affected / exposed	1 / 90 (1.11%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	21 / 90 (23.33%)	0 / 9 (0.00%)	
occurrences (all)	24	0	
Skin lesion			
subjects affected / exposed	3 / 90 (3.33%)	1 / 9 (11.11%)	
occurrences (all)	3	1	
Urticaria			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 90 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	10	0	
Pain in extremity			
subjects affected / exposed	5 / 90 (5.56%)	1 / 9 (11.11%)	
occurrences (all)	5	1	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	7 / 90 (7.78%)	0 / 9 (0.00%)	
occurrences (all)	9	0	
Bronchitis			
subjects affected / exposed	8 / 90 (8.89%)	0 / 9 (0.00%)	
occurrences (all)	8	0	
Respiratory tract infection			
subjects affected / exposed	5 / 90 (5.56%)	0 / 9 (0.00%)	
occurrences (all)	6	0	
Urinary tract infection			

subjects affected / exposed	6 / 90 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	6	1	
Fungal infection			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 90 (12.22%)	0 / 9 (0.00%)	
occurrences (all)	13	0	
Hypokalaemia			
subjects affected / exposed	7 / 90 (7.78%)	1 / 9 (11.11%)	
occurrences (all)	8	1	
Hyperuricaemia			
subjects affected / exposed	2 / 90 (2.22%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Metabolic acidosis			
subjects affected / exposed	0 / 90 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This adverse event only affected female participants.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This adverse event only affected female participants.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2014	• Increased complete blood count frequency to every 2 months from Baseline through Cycle 24. • Treatment modification guidelines updated with clinical data from Study IPI-145-02, including safety, efficacy, pharmacokinetic (PK), and pharmacodynamic data as of 28 October 2014; in response to PK/pharmacodynamic findings from that study, dose reduction levels changed to 15 mg twice daily (BID) for Level -1, 10 mg BID for Level -2, and 5 mg BID for Level -3 (new level), and text added to clarify that participants with a history of cytomegalovirus or Epstein-Barr virus infection and/or who enter the study while receiving antiviral prophylaxis should be monitored for reactivation via serology or viral load detection per institutional guidelines while on study treatment. • Detail added for Grade 3 or higher nonhematologic toxicity (infections, hepatic events, gastrointestinal events, skin rash, cardiac events). • In response to safety findings from Study IPI-145-07 (2013-002405-61): Detail added for Grade 2 or higher nonhematologic toxicity (new pulmonary symptoms). • Changed criteria for discontinuation of participants due to treatment-related toxicities from <25 mg once-daily dose to <15 mg BID. • In response to regulatory agency feedback, added guidance to withhold ofatumumab until return to ≤Grade 1 or Baseline level for Grade 3 thrombocytopenia associated with ≥Grade 2 hemorrhage to align with duvelisib treatment modifications. • Added new Photosafety section.
02 March 2015	• Revised treatment interruption/hold/modification guidelines to recommend treatment interruption for all events of QT interval corrected with Fridericia's method prolongation ≥Grade 3 (≥500 milliseconds). • Added clarifying text to response criteria definitions for both chronic lymphocytic leukemia and small lymphocytic lymphoma, specifically, language defining progressive disease.
24 March 2016	• To permit continued access to duvelisib beyond 24 months for participants demonstrating evidence of clinical benefit after 1 year of treatment, added text indicating that these participants were permitted to receive duvelisib monotherapy until PD, unacceptable toxicity, participant withdrawal, or start of alternate therapy (amended from the last version of the protocol, in which participants could receive treatment for only up to 2 years). • Clarified that ofatumumab was to be given for a maximum of 7 cycles and that there would be no follow-up after 2 years (Cycle 24). • Changed the frequency of clinic visits after Cycle 18 to once every 3 cycles (previously every 2 cycles).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported