Clinical trial results:
Phase II multicenter clinical trial to evaluate the efficacy and safety of ibrutinib in combination with rituximab, gemcitabine, oxaliplatin, and dexamethasone followed by ibrutinib as maintenance treatment in patients with refractory or relapsed non-treatment-resistant diffuse large B-cell lymphoma no candidates to receive a ASCT

Summary

EudraCT number	2015-005390-21
Trial protocol	ES
Global end of trial date	19 January 2021

Results information

Result version number	v1 (current)
This version publication date	13 February 2022
First version publication date	13 February 2022

Trial information

Trial identification

Sponsor protocol code	IBDCL-GELTAMO-2015

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02692248
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GELTAMO
Sponsor organisation address	C. de Fortuny, 51, Madrid, Spain, 28010
Public contact	Angel Cedillo, SecretarIa Cientifica GELTAMO, +34 913195780, sc@geltamo.com
Scientific contact	Angel Cedillo, SecretarIa Cientifica GELTAMO, +34 913195780, sc@geltamo.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 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of the combination (IR-GEMOX-dexa) as salvage treatment in patients with relapsing or refractory non-GCB-type DLBCL, in terms of overall response rate (ORR).

Protection of trial subjects:

Study drug administration should be permanently discontinued in the event of toxicity lasting longer than 21 days, unless the center investigators consider that the benefit of continuing ibrutinib treatment outweighs the risk.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2016
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: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	64
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Initially 72 patients from 15 different hospitals were registered, 8 patients could not be considered analyzable since they were screening failures.
Finally the analyzed population has 64 patients

Pre-assignment

Screening details:

Initially 72 patients from 15 different hospitals were registered, 8 patients could not be considered analyzable since they were screening failures.
Finally the analyzed population has 64 patients

Period 1

Period 1 title	Full data analysis (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Full data analysis

Arm description:

Subjects will receive Ibrutinib (Ib) with R-GEMOX-Dexa followed by Ib maintenance according to:

Induction phase:
Rituximab (R) 375 mg/m2 IV day 1 during 4 cycles; Gemcitabine (Gem) 1000 mg/m2 IV (30-minute infusion) on day 1 or 2, 4 cycles every 14 days; Oxaliplatine (Ox)100 mg/m2 on day 1 or 2 (after Gem adm.) 4 cycles every 14 days; Dex: 20 mg orally or IV on day 1 and orally on days 2-3, 4 cycles every 14 days; Ib 560 mg daily for 14 days.
Responding patients will receive 2 (if CR) or 4 (if PR) additional cycles every 14 days. Patients with SD and ABC profile will receive 4 additional cycles.

Maintenance phase: Responding patients will receive Ib 560 mg daily - Continuous cycles until a maximum of 2 years, disease progression or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Responsable person designated by the sponsor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Subjects will receive Ibrutinib (Ib) with R-GEMOX-Dexa followed by Ib maintenance according to:

Induction phase:
Rituximab (R) 375 mg/m2 IV day 1 during 4 cycles; Gemcitabine (Gem) 1000 mg/m2 IV (30-minute infusion) on day 1 or 2, 4 cycles every 14 days; Oxaliplatine (Ox)100 mg/m2 on day 1 or 2 (after Gem adm.) 4 cycles every 14 days; Dex: 20 mg orally or IV on day 1 and orally on days 2-3, 4 cycles every 14 days; Ib 560 mg daily for 14 days.
Responding patients will receive 2 (if CR) or 4 (if PR) additional cycles every 14 days. Patients with SD and ABC profile will receive 4 additional cycles.

Maintenance phase: Responding patients will receive Ib 560 mg daily - Continuous cycles until a maximum of 2 years, disease progression or unacceptable toxicity.

Number of subjects in period 1	Full data analysis
Started	64
Completed	64

Baseline characteristics

Reporting groups	
Reporting group title	Full data analysis

Reporting group description: -

Reporting group values	Full data analysis	Total	
Number of subjects	64	64	
Age categorical Units: Subjects			
>18	64	64	
Age continuous Units: years			
median	62.57		
standard deviation	± 14.56	-	
Gender categorical Units: Subjects			
Female	26	26	
Male	38	38	
ECOG-PS Units: Subjects			
ECOG 0	23	23	
ECOG 1	31	31	
ECOG 2	10	10	
Diagnosis Units: Subjects			
DLBCL without specification	60	60	
DLBCL rich in T lymphocytes	3	3	
Follicular lymphoma	1	1	
International prognostic index (IPI) Units: Subjects			
0-1	6	6	
2-3	43	43	
4-5	13	13	
Unk	2	2	
Disease stage at diagnosis Units: Subjects			
Stage I	1	1	
Stage II	9	9	
Stage III	5	5	
Stage IV	46	46	
Unk	3	3	
LDH levels Units: Subjects			
Normal	20	20	
Elevated	42	42	
Unk	2	2	

Previous lines of treatment			
Units: Previous lines of treatment			
median	2		
full range (min-max)	1 to 5	-	

Subject analysis sets

Subject analysis set title	Full data analysis
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects will receive Ibrutinib (Ib) with R-GEMOX-Dexa followed by Ib maintenance according to:
Induction phase:
Rituximab (R) 375 mg/m2 IV day 1 during 4 cycles; Gemcitabine (Gem) 1000 mg/m2 IV (30-minute infusion) on day 1 or 2, 4 cycles every 14 days; Oxaliplatine (Ox)100 mg/m2 on day 1 or 2 (after Gem adm.) 4 cycles every 14 days; Dex: 20 mg orally or IV on day 1 and orally on days 2-3, 4 cycles every 14 days; Ib 560 mg daily for 14 days.
Responding patients will receive 2 (if CR) or 4 (if PR) additional cycles every 14 days. Patients with SD and ABC profile will receive 4 additional cycles.
Maintenance phase: Responding patients will receive Ib 560 mg daily - Continuous cycles until a maximum of 2 years, disease progression or unacceptable toxicity.

Reporting group values	Full data analysis		
Number of subjects	64		
Age categorical			
Units: Subjects			
>18	64		
Age continuous			
Units: years			
median	62.57		
standard deviation	± 14.56		
Gender categorical			
Units: Subjects			
Female	26		
Male	38		
ECOG-PS			
Units: Subjects			
ECOG 0	23		
ECOG 1	31		
ECOG 2	10		
Diagnosis			
Units: Subjects			
DLBCL without specification	60		
DLBCL rich in T lymphocytes	3		
Follicular lymphoma	1		
International prognostic index (IPI)			
Units: Subjects			
0-1	6		
2-3	43		
4-5	13		
Unk	2		
Disease stage at diagnosis			
Units: Subjects			
Stage I	1		

Stage II	9		
Stage III	5		
Stage IV	46		
Unk	3		
LDH levels Units: Subjects			
Normal	20		
Elevated	42		
Unk	2		
Previous lines of treatment Units: Previous lines of treatment			
median	2		
full range (min-max)	1 to 5		

End points

End points reporting groups

Reporting group title	Full data analysis

Reporting group description:

Subjects will receive Ibrutinib (Ib) with R-GEMOX-Dexa followed by Ib maintenance according to:

Induction phase:
Rituximab (R) 375 mg/m2 IV day 1 during 4 cycles; Gemcitabine (Gem) 1000 mg/m2 IV (30-minute infusion) on day 1 or 2, 4 cycles every 14 days; Oxaliplatine (Ox)100 mg/m2 on day 1 or 2 (after Gem adm.) 4 cycles every 14 days; Dex: 20 mg orally or IV on day 1 and orally on days 2-3, 4 cycles every 14 days; Ib 560 mg daily for 14 days.
Responding patients will receive 2 (if CR) or 4 (if PR) additional cycles every 14 days. Patients with SD and ABC profile will receive 4 additional cycles.

Maintenance phase: Responding patients will receive Ib 560 mg daily - Continuous cycles until a maximum of 2 years, disease progression or unacceptable toxicity.

Subject analysis set title	Full data analysis
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects will receive Ibrutinib (Ib) with R-GEMOX-Dexa followed by Ib maintenance according to:
Induction phase:
Rituximab (R) 375 mg/m2 IV day 1 during 4 cycles; Gemcitabine (Gem) 1000 mg/m2 IV (30-minute infusion) on day 1 or 2, 4 cycles every 14 days; Oxaliplatine (Ox)100 mg/m2 on day 1 or 2 (after Gem adm.) 4 cycles every 14 days; Dex: 20 mg orally or IV on day 1 and orally on days 2-3, 4 cycles every 14 days; Ib 560 mg daily for 14 days.
Responding patients will receive 2 (if CR) or 4 (if PR) additional cycles every 14 days. Patients with SD and ABC profile will receive 4 additional cycles.
Maintenance phase: Responding patients will receive Ib 560 mg daily - Continuous cycles until a maximum of 2 years, disease progression or unacceptable toxicity.

Primary: Overall Response (OR) Rate (Complete Remission + Partial Response)

End point title	Overall Response (OR) Rate (Complete Remission + Partial Response)[1]

End point description:

End point type	Primary

End point timeframe:

Treatment responses will be evaluated 30 days after end of study treatment wich can be ocurred after 2 years and 4 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: this is a single arm trial

End point values	Full data analysis			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: Percentage of patients presented CR+PR	36			

Statistical analyses

No statistical analyses for this end point

Secondary: CR Rate During Induction and Maintenance Phases.

End point title	CR Rate During Induction and Maintenance Phases.

End point description:

Complete treatment responses evaluation during 21-35 days after initiation of 6 or 8 cycle of study treatment (depend of treatment responses obtained from cycle 4) and 30 days after end of study treatment which can be occurred after 2 years and 4 months

End point type	Secondary

End point timeframe:

2 years

End point values	Full data analysis			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: percentage of the patients presented CR	25			

Statistical analyses

No statistical analyses for this end point

Secondary: Response duration

End point title	Response duration

End point description:

Response duration defined as the time from the documentation of tumor response to disease progression or death, in the event of no documented recurrence, or start of a new anti - lymphoma treatment because of refractory or persistent disease.

End point type	Secondary

End point timeframe:

Response duration will be evaluated at any time during the study when tumor response is documented or after end of study treatment which can be occurred after 2 years and 4 months.

End point values	Full data analysis			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: months				
median (full range (min-max))	6.5 (0.0 to 38.3)			

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 defined as the time between start of treatment and the first documentation of recurrence, progression, or death in the event of no documented recurrence, or start of a new anti - lymphoma treatment, due a refractory or persistent disease

End point type	Secondary

End point timeframe:

Progression free survival will be evaluated at any time during the study when first documentation of recurrence, progression, or death or after end of study treatment which can be occurred after 2 years and 4 months

End point values	Full data analysis			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: months				
median (confidence interval 95%)	4.1 (2.2 to 6.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival

End point title	Event-free Survival

End point description:

Event-free survival defined as the time between start of treatment and the first documentation of adverse events and serious adverse events graded according to NCI CTCAE v4.0

End point type	Secondary

End point timeframe:

2 years

End point values	Full data analysis			
Subject group type	Reporting group			
Number of subjects analysed	63[2]			
Units: months				
median (confidence interval 95%)	4.03 (2.5 to 5.6)			

Notes:

[2] - pts with new neoplasia, not required new therapeutic strategy and was not considered as an EFS event

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival is defined as the time between the start of treatment and death from any cause. Patients that are withdrawn from the trial or lost of follow-up, will be censored with the date of last contact. Patients who are still alive at the end of the study will be censored at that time.

End point type	Secondary

End point timeframe:

2 years

End point values	Full data analysis			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: months				
median (confidence interval 95%)	11.67 (7 to 16.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability of Ibrutinib in Combination Rituximab, Gemcitabine, Oxaliplatin and Dexamethasone

End point title	Safety and Tolerability of Ibrutinib in Combination Rituximab, Gemcitabine, Oxaliplatin and Dexamethasone

End point description:

Safety and tolerability will be assessed during any phase of study treatment and 30 days after end of study treatment which can be occurred after 2 years and 4 months and will be classified according to the Common Toxicity CNC.

Unist: Percentage of patients that present AE related to the treatment

End point type	Secondary

End point timeframe:

2 years

End point values	Full data analysis			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: Percentage of patients that present AE	55			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Deberán registrarse en el CRD todos los acontecimientos adversos ocurridos durante la realización del ensayo clínico (en el caso de AAG desde la firma del consentimiento informado) y hasta 30 días después de la última dosis de la medicación del estudio.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI-CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 64 (51.56%)		
number of deaths (all causes)	46		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal tumor grade 4			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumor lysis syndrome - Grade 4			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
fracture grade 3			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture grade 3			

subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Patient took expired medication grade Unknown				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Subarachnoid hemorrhage - Grade 2				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Heart failure - Grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial tamponade - Grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis - Grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Akathisia Grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Confusion grade 3			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischemic attacks - Grade 2			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia - Grade 3			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia - Grade 2			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia - Grade 3			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hematoma - Grade 2			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Back pain grade 3			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
fatigue grade 3			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

fever grade 1				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
fever grade 2				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
fever grade 3				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flu like symptoms grade 2				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clinical deterioration Grade 5				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise Grade 5				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea grade 2				

subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea grade 3				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia grade 2				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting grade 2				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pleural effusion grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure grade 3				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure grade 5				

subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Partial Respiratory failure grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Herpes zoster grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
candidiasis grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection grade 5				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis grade 3				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock grade 5				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
upper respiratory infection grade 3				

subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infection grade 5			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection grade 3			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection grade 4			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 64 (98.44%)		
Nervous system disorders			
Paresthesia			
subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	14 / 64 (21.88%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	22 / 64 (34.38%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	39 / 64 (60.94%)		
occurrences (all)	0		

Lymphocyte count decreased			
subjects affected / exposed	10 / 64 (15.63%)		
occurrences (all)	0		
Hypomagnesemia			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	0		
General disorders and administration site conditions			
Nausea			
subjects affected / exposed	14 / 64 (21.88%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 64 (31.25%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2016	Modification of the title of the trial due to a typographical error.
31 January 2017	Modifications corresponding to the Patient Information and Informed Consent, as a result of the update of the safety aspects reflected in the new edition of the IB of IBRUTINIB and the IBRUTINIB data sheet.
19 September 2020	Change of the principal investigator of the study at a Hospital and safety changes included in the new IB of Ibrutinib that apply to HIP-CI.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported