ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: February 8, 2021

ClinicalTrials.gov ID: NCT00495079

Study Identification

Unique Protocol ID:	HBS407
Brief Title:	Safety and Efficacy of Marqibo in Relapsed Acute Lymphoblastic Leukemia
Official Title:	A Phase 2 Study to Evaluate the Safety and Efficacy of Weekly Doses of Marqibo® (Vincristine Sulfate Liposomes Injection) in Adult Patients With Philadelphia Chromosome-negative Acute Lymphoblastic Leukemia (ALL) in Second Relapse or Adult Patients With Philadelphia Chromosome-negative ALL Who Failed Two Treatment Lines of Anti-leukemia Chemotherapy
Secondary IDs:	

Study Status

Record Verification:	February 2021
Overall Status:	Completed
Study Start:	May 2007 []
Primary Completion:	August 8, 2010 [Actual]
Study Completion:	August 8, 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Spectrum Pharmaceuticals, Inc
Responsible Party:	Sponsor
Collaborators:	Parexel

Oversight

U.S. FDA-regulated Drug:	

U.S. FDA-regulated Device:	
Unapproved/Uncleared Device:	No
U.S. FDA IND/IDE:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 59,056 Serial Number: 202 Has Expanded Access: No
Human Subjects Review:	Board Status:
Data Monitoring:	
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary: This was a Phase 2, international, multicenter, open-label, single-arm trial evaluating Marqibo (VSLI) in adult subjects with: 1) Ph- ALL or lymphoblastic lymphoma in second or greater relapse; or 2) Ph- ALL or lymphoblastic lymphoma who failed 2 or greater treatment lines of anti-leukemia chemotherapy. The original enrollment target for this study was approximately 56 subjects. Per a protocol amendment, enrollment was increased from 56 to 65.

The primary objective of this study was to evaluate:

- The efficacy of the study treatment as determined by the rate of CR plus CR with incomplete blood count recovery (CRi) in adult subjects with Philadelphia chromosome-negative (Ph-) ALL in second relapse or adult subjects with (Ph-) ALL who failed 2 treatment lines of anti-leukemia chemotherapy. Subjects must have achieved a CR to at least 1 prior anti-leukemia therapy as defined by a leukemia-free interval of ≥ 90 days.

Detailed Description: The secondary objectives of this study were to evaluate:

- Duration of CR plus CRi
- Overall survival
- Safety and tolerability

Conditions

Conditions:	Acute Lymphoblastic Leukemia (ALL)
Keywords:	acute lymphoblastic lymphocytic leukemia

leukaemia
lukemia
leukimia
ALL
Marqibo
Hana Biosciences
vincristine
liposomal
liposome
optisome
hematology
malignancy
hematological
relapsed
anti-leukemia
adult
chemotherapy

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Interventional Study Model:	Single Group Assignment
Number of Arms:	1
Masking:	None (Open Label)
Allocation:	N/A
Enrollment:	65 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Marqibo Eligible subjects received study drug at 2.25 mg/m^2 intravenously via peripheral or central venous access over 60 minutes (± 10 minutes).	Drug: Marqibo® (vincristine sulfate liposomes injection) Dosing was done every 7 days (± 3 days) on Days 1, 8, 15, and 22 with no less than 4 days between dosing days. Dose calculations were based on body surface area using the subject's height (from Screening) and actual weight for each course. Other Names:

Arms	Assigned Interventions
	• VSLI, Vincristine Sulfate Liposomes Injection

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Sex: All

Gender Based:

Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria:

- Age ≥18 years.
- Had Ph- ALL or lymphoblastic lymphoma and was in second relapse, or had failed 2 treatment lines of anti-leukemia chemotherapy.
- Had histologically or cytologically proven ALL and ≥ 10% bone marrow blasts. If < 10% bone marrow blasts, subject must have had histologically or cytologically proven ALL and evaluable extramedullary disease. Sponsor approval was obtained prior to enrolling subjects who had < 10% bone marrow blasts with evaluable extramedullary disease.
- Had achieved a CR to at least 1 prior anti-leukemia therapy as defined by a leukemia-free interval of ≥ 90 days.
- For subjects with a prior history of stem cell transplantation, had ≤ Grade 1 active skin graft-versus-host disease (GVHD). No active gastrointestinal or liver graft-versus-host disease.
- Had an Eastern Cooperative Oncology Group (ECOG) performance status 0 to 3.
- Had normal renal and liver function as defined below within 14 days, inclusive, prior to first dose of VSLI, unless the abnormality was considered attributable to leukemia:
    - Total bilirubin ≤ 2.0 × institutional upper limit of normal, unless the subject had a known diagnosis of Gilbert's disease. If a subject had Gilbert's disease, he/she could have participated in this study, however must have been monitored closely during the study.
    - Aspartate transaminase (AST) or alanine transaminase (ALT) ≤ 3 × institutional upper limit of normal.
    - Serum creatinine ≤ 2.0 g/dL or calculated estimated creatinine clearance ≥ 50 mL/minute/1.73 m2 based on Cockcroft and Gault formula, unless renal dysfunction was considered due to hematologic malignancy.
- Had never received prior VSLI treatment.
- For women of childbearing potential, had a negative serum or urine pregnancy test within 14 days prior to enrollment.
- If female, the subject was postmenopausal, surgically sterilized, or willing to use acceptable methods of birth control (e.g., hormonal contraceptive, intra-uterine device, diaphragm with spermicide, and condom with spermicide or abstinence) from the Screening visit through 30 days after the last dose of VSLI.
- If male, the subject agreed to use an acceptable barrier method for contraception from the Screening visit through 30 days after the last dose of VSLI.

- Before enrollment, the subject was capable of understanding and complying with parameters as outlined in the protocol and able to sign a written informed consent according to ICH/GCP and national/local regulations.

Exclusion Criteria:

- Had Burkitt's lymphoma or Burkitt's leukemia.
- Had a history of Philadelphia chromosome-positive (Ph+) ALL and/or BCR/ABL rearrangements documented by fluorescent in situ hybridization or polymerase chain reaction.
- Had a history of Philadelphia chromosome-positive (Ph+) ALL and/or BCR/ABL rearrangements documented by fluorescent in situ hybridization or polymerase chain reaction.
- Had active CNS disease. History of treated CNS disease was allowable. The CNS disease must have resolved in order for the subject to be eligible.
- Was eligible for stem cell transplantation. This implied that a suitable donor was readily available, the subject was willing to undergo stem cell transplantation, and the Investigator believed this was a better treatment option than VSLI. This was at the Investigator's discretion.
- Was treated with any investigational agents or chemotherapy agents in the last 21 days before the first dose of VSLI, unless full recovery from side effects had occurred or the subject had rapidly progressing disease judged to be life threatening by the Investigator.
- Was receiving any other standard or investigational treatment for the subject's leukemia.
    - Intrathecal chemotherapy for CNS prophylaxis was allowable.
    - The use of hydroxyurea (Hydrea®) to control leukocytosis was allowable but must have been tapered off by Day 14 of Course 1. From Day 15 of Course 1 on through the end of study participation, hydroxyurea (Hydrea®) was not allowed.
    - Systemic corticosteroids must have been tapered off, preferably before the start of study treatment, but no later than by Day 5 of Course 1. From Day 6 of Course 1 on through the end of study participation, systemic corticosteroids were not allowed.
- Had persistent chronic clinically significant toxicities from prior chemotherapy ≥ Grade 2 (National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] version 3.0).
- Had persistent ≥ Grade 2 active neuropathy (NCI CTCAE v3.0).
- Had a history of persistent ≥ Grade 2 active neurologic disorders unrelated to chemotherapy (including demyelinating form of Charcot-Marie-Tooth syndrome, acquired demyelinating disorders, or other demyelinating condition).
- Had a history of allergic reactions or sensitivity attributed to compounds of similar chemical or biologic composition to vincristine or components of study drug.
- Was female who was pregnant or breast-feeding.
- Had active serious infection not controlled by oral or intravenous antibiotics or antifungals.
- Had human immunodeficiency virus positive status.
- Had any medical condition which in the opinion of the investigator placed the subject at an unacceptably high risk for toxicities.
- Had any condition or circumstance which in the opinion of the investigator would significantly interfere with the subject's protocol compliance and put the subject at increased risk.

Contacts/Locations

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IPDSharing

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References

Citations:

Links:

Available IPD/Information:

Study Results

Participant Flow

Recruitment Details	Subjects were enrolled and treated at 22 sites in United States, Canada, Germany, Israel and United Kingdom. The first subject was infused on August 2, 2007. The last subject completed study on August 8, 2010.
Pre-assignment Details	2.25 mg/m^2 Marqibo administered intravenously via peripheral or central venous access over 60 minutes (+-10 minutes)

Reporting Groups

	Description
Marqibo	Eligible subjects received study drug at 2.25 mg/m2 intravenously via peripheral or central venous access over 60 minutes (± 10 minutes).

Overall Study

	Marqibo
Started	65
Completed	65
Not Completed	0

Baseline Characteristics

Reporting Groups

	Description
Marqibo	Eligible subjects received study drug at 2.25 mg/m2 intravenously via peripheral or central venous access over 60 minutes (± 10 minutes).

Baseline Measures

		Marqibo
Overall Number of Participants		65
Age, Categorical Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	65 participants
	<=18 years	0 0%
	Between 18 and 65 years	59 90.77%

		Marqibo
	>=65 years	6 9.23%
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	65 participants
		36.3 (16.37)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	65 participants
	Female	32 49.23%
	Male	33 50.77%
Region of Enrollment Measure Type: Number Unit of measure: participants	Number Analyzed	65 participants
United States		53
Canada		2
Israel		6
Germany		4

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Complete Remission Plus Complete Remission Without Full Platelet Recovery (CR + CRi)
Measure Description	CR is defined as no evidence of ALL: ANC>or=1x10^9/L or platelet count>100x10^9/L, absence of leukemia blast cells in blood and marrow (<5% blasts), resolution of all sites of extramedullary disease (EMD). CR with incomplete blood count recovery (CRi): As per CR but platelet count< 100x10^9/L or ANC< 1x10^9/L. Partial remission(PR):CR with>5-25% abnormal cells in the marrow or 50% decrease in bone marrow blasts. Reduction in EMD by at least 50%. Hematologic Improvement. Bone marrow blast(BMB) response: BMB<5% in the absence of HI. Stable disease(SD):No significant hematological and extramedullary change from baseline.
Time Frame	Response assessment performed at the end of each 28 day course.

Analysis Population Description

Subjects who had CR plus CRi by the PI and the IRRC assessments using the International Working Group Criteria. The Intent-to-Treat Analysis, n=65, minimum 1 dose. The IRRC, n=53, 1 dose, assess response as determined by the IRRC. Analyses, a Simon's 2-stage minimax design where the type I error alpha was set at 0.10 and the power was 80%.

Reporting Groups

	Description
Marqibo	Eligible subjects received study drug at 2.25 mg/m2 intravenously via peripheral or central venous access over 60 minutes (± 10 minutes).

Measured Values

	Marqibo
Overall Number of Participants Analyzed	65
Complete Remission Plus Complete Remission Without Full Platelet Recovery (CR + CRi) Measure Type: Number Unit of measure: participants	13

2. Primary Outcome Measure:

Measure Title	Clinical Response Assessment Per Independent Response Review Committee (IRRC) Evaluation
Measure Description	Number of subjects who achieved Complete Remission (CR)as assessed by the IRRC. CR is defined as no evidence of ALL. ANC>=1X10^9/L or Platelet count>=100x10^9/L, absence of blasts in blood and morrow (<5%), resolution of all sites of extramedullary disease (EMD). CR with incomplete blood count recovery(CRi)is defined as per CR but platelet count <100x10^9/L or ANC<1x10^9/L.
Time Frame	Response assessment at the end of each 28 days course

Analysis Population Description

The IRRC evaluable population included all subjects who received at least 1 dose of study drug and who has reviewable data to assess and determine response or lack of response as determined by the IRRC.

Reporting Groups

	Description
Marqibo	Proportion if subjects who achieved CR+CRi as determined by the IRRC using the International Working Group (IWG)Criteria. The IRRC Evaluable analysis set(n=53) included subjects who received at least 1 dose of study drug and reviewable data. Eligible subjects received Marqibo at 2.25mg^m2 intravenously via peripheral or central venous access over 60 minutes (+/-10 minutes) every 7 days (+/-3days)

Measured Values

	Marqibo
Overall Number of Participants Analyzed	53
Clinical Response Assessment Per Independent Response Review Committee (IRRC) Evaluation Measure Type: Number Unit of measure: participants	11

3. Secondary Outcome Measure:

Measure Title	Duration of CR + CRi
Measure Description	Duration of response for those subjects who achieved CR or CRi
Time Frame	CR + CRi duration was calculated from the date the subject first met the definition of CR or CRi until the date of relapse

Analysis Population Description

Based on the first date of CR or CRi to the date of the last available histologic assessment of the same response (n=8)

Reporting Groups

	Description
Marqibo	Duration of response derived using the IRRC determined response dates for subjects who achieved CR or CRi (n=8). The K-M product limit method was used to estimate the median event time. Eligible subjects received Marqibo at 2.25mg^m2 intravenously via peripheral or central venous access over 60 minutes (+- 10 minutes)every 7 days (+/- 3 days)

Measured Values

	Marqibo
Overall Number of Participants Analyzed	8

	Marqibo
Duration of CR + CRi Median (95% Confidence Interval) Unit of measure: days	28 (7 to 36)

4. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	Time, in days, from informed consent date until the date of death or date of last contact
Time Frame	unlimited

Analysis Population Description

Based on the first date of CR or CRi to date of documented relapse, death, or subsequent chemotherapies including hematopoietic stem cell transplant (HSCT)(n=10)

Reporting Groups

	Description
Marqibo	The population analyzed included all subjects who received at least one dose of Marqibo. Subjects who did not die had their survival times censored on the date of last contact. The K-M method was used to estimate the distribution of overall survival. Eligible subjects received study drug at 2.25 mg/m2 intravenously via peripheral or central venous access over 60 minutes (± 10 minutes)every 7 days (+/- 3 days)

Measured Values

	Marqibo
Overall Number of Participants Analyzed	10
Overall Survival Median (95% Confidence Interval) Unit of measure: days	56 (9 to 65)

Reported Adverse Events

Time Frame	From date of first dose of study drug until 30 days after last Marqibo dose (+ 5 days)
Adverse Event Reporting Description	[Not specified]

Reporting Groups

	Description
Marqibo	Eligible subjects received study drug at 2.25 mg/m2 intravenously via peripheral or central venous access over 60 minutes (± 10 minutes).

All-Cause Mortality

	Marqibo	
	Affected/At Risk (%)	# Events
Total All-Cause Mortality	/	

Serious Adverse Events

	Marqibo	
	Affected/At Risk (%)	# Events
Total	21/65 (32.31%)	
Blood and lymphatic system disorders		
Anaemia [A] *	1/65 (1.54%)	1
Febrile neutropenia [A] *	12/65 (18.46%)	12
Neutropenia [A] *	1/65 (1.54%)	1
Pancytopenia [A] *	1/65 (1.54%)	1
Thrombocytopenia [A] *	2/65 (3.08%)	2
Cardiac disorders		
Cardiac Arrest [A] *	3/65 (4.62%)	3
Cardiac arrest [A] *	1/65 (1.54%)	1
Cardio-Respiratory Arrest [A] *	2/65 (3.08%)	2
Cardiogenic Shock [A] *	1/65 (1.54%)	1

	Marqibo	
	Affected/At Risk (%)	# Events
Cardiomyopathy [A] *	1/65 (1.54%)	1
Endocrine disorders		
Inappropriate Antidiuretic Hormone Secretion [A] *	1/65 (1.54%)	1
Inappropriate antidiuretic hormone secretion [A] *	1/65 (1.54%)	1
Gastrointestinal disorders		
Abdominal pain [A] *	1/65 (1.54%)	1
Constipation [A] *	2/65 (3.08%)	2
Diarrhoea [A] *	3/65 (4.62%)	3
Gastrointestinal haemorrhage [A] *	1/65 (1.54%)	1
Ileus [A] *	1/65 (1.54%)	1
Nausea [A] *	1/65 (1.54%)	1
Subileus [A] *	1/65 (1.54%)	1
Vomiting [A] *	1/65 (1.54%)	1
General disorders		
Gait Disturbance [A] *	1/65 (1.54%)	1
Multi-Organ Failure [A] *	1/65 (1.54%)	1
Pain [A] *	1/65 (1.54%)	1
Pyrexia [A] *	1/65 (1.54%)	1
Hepatobiliary disorders		
Cholecystitis, chronic [A] *	1/65 (1.54%)	1
Immune system disorders		
Graft Versus Host Disease [A] *	1/65 (1.54%)	1

	Marqibo	
	Affected/At Risk (%)	# Events
Graft versus host disease [A] *	1/65 (1.54%)	1
Infections and infestations		
Acute Sinusitis [A] *	1/65 (1.54%)	1
Bacteraemia [A] *	1/65 (1.54%)	1
Bronchiectasis [A] *	1/65 (1.54%)	1
Bronchopulmonary Aspergillosis [A] *	1/65 (1.54%)	1
Cellulitis [A] *	1/65 (1.54%)	1
Entrococcocal Bacteraemia [A] *	1/65 (1.54%)	1
Escherichia Sepsis [A] *	1/65 (1.54%)	1
Klebsiella Sepsis [A] *	1/65 (1.54%)	1
Neutropenic Sepsis [A] *	1/65 (1.54%)	1
Parainfluenzae Virus Infection [A] *	1/65 (1.54%)	1
Pneumonia [A [1]] *	1/65 (1.54%)	1
Pneumonia Bacterial [A] *	1/65 (1.54%)	1
Rhinitis [A] *	1/65 (1.54%)	1
Sepsis [A] *	2/65 (3.08%)	2
Septic Shock [A] *	2/65 (3.08%)	2
Sinusitis [A] *	1/65 (1.54%)	1
Staphylococcal bacteraemia [A] *	1/65 (1.54%)	1
Injury, poisoning and procedural complications		
Subdural Haematoma [A] *	1/65 (1.54%)	1
Investigations		
Csf Bacteria Identified [A] *	1/65 (1.54%)	1

	Marqibo	
	Affected/At Risk (%)	# Events
Metabolism and nutrition disorders		
Decreased appetite [A] *	1/65 (1.54%)	1
Dehydration [A] *	1/65 (1.54%)	1
Hyponatraemia [A] *	1/65 (1.54%)	1
Tumor lysis syndrome [A] *	3/65 (4.62%)	3
Musculoskeletal and connective tissue disorders		
Musculoskeletal Pain [A] *	1/65 (1.54%)	1
Musculoskeletal pain [A] *	1/65 (1.54%)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Acute Lymphocytic Leukaemia Recurrent [A] *	1/65 (1.54%)	1
Acute Lymphocytic Leukemia [A] *	9/65 (13.85%)	9
Leukaemia [A] *	1/65 (1.54%)	1
Leukaemia Infiltration Brain [A] *	1/65 (1.54%)	1
Lymphocytic Leukaemia [A] *	1/65 (1.54%)	1
Lymphocytic leukaemia [A] *	1/65 (1.54%)	1
Nervous system disorders		
Cerebral Infarction [A] *	1/65 (1.54%)	1
Convulsion [A] *	1/65 (1.54%)	1
Facial palsy [A] *	1/65 (1.54%)	1
Heamorrhage Intracranial [A] *	1/65 (1.54%)	1
Neuropathy, peripheral [A] *	4/65 (6.15%)	4
Peripheral Motor Neuropathy [A] *	1/65 (1.54%)	1
Peripheral sensory neuropath [A] *	1/65 (1.54%)	1

	Marqibo	
	Affected/At Risk (%)	# Events
Psychiatric disorders		
Mental Status Changes [A] *	2/65 (3.08%)	2
Renal and urinary disorders		
Cystitis Haemorrhagic [A] *	1/65 (1.54%)	1
Renal Failure [A] *	1/65 (1.54%)	1
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [A] *	1/65 (1.54%)	1
Hypoxia [A] *	1/65 (1.54%)	1
Organising pneumonia [A] *	1/65 (1.54%)	1
Pulmonary Haemorrhage [A] *	1/65 (1.54%)	1
Respiratory Failure [A] *	3/65 (4.62%)	3
Respiratory distress [A] *	3/65 (4.62%)	3
Vascular disorders		
Hypotension [A] *	2/65 (3.08%)	2
Venoocclusive Disease [A] *	1/65 (1.54%)	1
Venoocclusive disease [A] *	1/65 (1.54%)	1

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA12.1

[1] 1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Marqibo	
	Affected/At Risk (%)	# Events
Total	65/65 (100%)	
Blood and lymphatic system disorders		

	Marqibo	
	Affected/At Risk (%)	# Events
Anaemia [A] *	17/65 (26.15%)	17
Febrile neutropenia [A] *	24/65 (36.92%)	24
Leukopenia [A] *	5/65 (7.69%)	5
Neutropenia [A] *	15/65 (23.08%)	15
Thrombocytopenia [A] *	15/65 (23.08%)	15
Cardiac disorders		
Tachycardia [A] *	11/65 (16.92%)	11
Gastrointestinal disorders		
Abdominal distension [A] *	7/65 (10.77%)	7
Abdominal pain [A] *	13/65 (20%)	13
Constipation [A] *	34/65 (52.31%)	34
Diarrhoea [A] *	22/65 (33.85%)	22
Dry mouth [A] *	4/65 (6.15%)	4
Dysphagia [A] *	4/65 (6.15%)	4
Flatulence [A] *	4/65 (6.15%)	4
Gingival bleeding [A] *	6/65 (9.23%)	6
Nausea [A] *	35/65 (53.85%)	35
Stomatitis [A] *	9/65 (13.85%)	9
Vomiting [A] *	17/65 (26.15%)	17
General disorders		
Asthenia [A] *	15/65 (23.08%)	15
Chest pain [A] *	7/65 (10.77%)	7
Chills [A] *	8/65 (12.31%)	8

	Marqibo	
	Affected/At Risk (%)	# Events
Fatigue [A] *	19/65 (29.23%)	19
Oedema, peripheral [A] *	10/65 (15.38%)	10
Pain [A] *	15/65 (23.08%)	15
Pyrexia [A] *	25/65 (38.46%)	25
Infections and infestations		
Oral candidiasis [A] *	4/65 (6.15%)	4
Pneumonia [A] *	9/65 (13.85%)	9
Septic shock [A] *	4/65 (6.15%)	4
Urinary tract infection [A] *	4/65 (6.15%)	4
Investigations		
Alanine aminotransferase increased [A] *	7/65 (10.77%)	7
Aspartate aminotransferase increased [A] *	7/65 (10.77%)	7
Blood alkaline phosphatase increased [A] *	4/65 (6.15%)	4
Blood lactate dehydrogenase increased [A] *	7/65 (10.77%)	7
Weight decreased [A] *	10/65 (15.38%)	10
Metabolism and nutrition disorders		
Cachexia [A] *	4/65 (6.15%)	4
Decreased appetite [A] *	24/65 (36.92%)	24
Dehydration [A] *	5/65 (7.69%)	5
Hyperglycaemia [A] *	6/65 (9.23%)	6
Hypocalcaemia [A] *	7/65 (10.77%)	7
Hypokalaemia [A] *	17/65 (26.15%)	17
Hypomagnesaemia [A] *	9/65 (13.85%)	9

	Marqibo	
	Affected/At Risk (%)	# Events
Hyponatraemia [A] *	5/65 (7.69%)	5
Hypophosphataemia [A] *	7/65 (10.77%)	7
Tumor lysis syndrome [A] *	5/65 (7.69%)	5
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	12/65 (18.46%)	12
Back pain [A] *	13/65 (20%)	13
Bone pain [A] *	9/65 (13.85%)	9
Muscular weakness [A] *	6/65 (9.23%)	6
Myalgia [A] *	5/65 (7.69%)	5
Pain in extremity [A] *	8/65 (12.31%)	8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Acute lymphocytic leukemia [A] *	9/65 (13.85%)	9
Nervous system disorders		
Areflexia [A] *	6/65 (9.23%)	6
Cranial neuropathy [A] *	4/65 (6.15%)	4
Dizziness [A] *	10/65 (15.38%)	10
Facial neuralgia [A] *	4/65 (6.15%)	4
Headache [A] *	17/65 (26.15%)	17
Hypoaesthesia [A] *	16/65 (24.62%)	16
Hyporeflexia [A] *	5/65 (7.69%)	5
Neuralgia [A] *	4/65 (6.15%)	4
Neuropathy, peripheral [A] *	20/65 (30.77%)	20
Paraesthesia [A] *	14/65 (21.54%)	14

	Marqibo	
	Affected/At Risk (%)	# Events
Psychiatric disorders		
Agitation [A] *	4/65 (6.15%)	4
Anxiety [A] *	6/65 (9.23%)	6
Confusional state [A] *	10/65 (15.38%)	10
Depression [A] *	5/65 (7.69%)	5
Insomnia [A] *	16/65 (24.62%)	16
Renal and urinary disorders		
Urinary incontinence [A] *	4/65 (6.15%)	4
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	7/65 (10.77%)	7
Dyspnoea [A] *	16/65 (24.62%)	16
Epistaxis [A] *	10/65 (15.38%)	10
Hypoxia [A] *	4/65 (6.15%)	4
Oropharyngeal pain [A] *	10/65 (15.38%)	10
Skin and subcutaneous tissue disorders		
Petechiae [A] *	4/65 (6.15%)	4
Pruritis [A] *	4/65 (6.15%)	4
Rash [A] *	8/65 (12.31%)	8
Vascular disorders		
Hypertension [A] *	11/65 (16.92%)	11
Hypotension [A] *	10/65 (15.38%)	10
Orthostatic hypotension [A] *	4/65 (6.15%)	4

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA12.1

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

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