ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 11/15/2011

ClinicalTrials.gov ID: NCT00400764

Study Identification

Unique Protocol ID:	APO3585g
Brief Title:	A Study of Dulanermin in Combination With Rituximab in Subjects With Follicular and Other Low Grade, CD20+, Non-Hodgkin's Lymphomas
Official Title:	A Phase Ib/II, Open-Label, Multicenter Study of the Safety, Pharmacokinetics, and Efficacy of Dulanermin Administered Intravenously in Combination With Rituximab to Subjects With Follicular and Other Low-Grade, CD20+, B-Cell Non-Hodgkin's Lymphomas That Have Progressed Following Previous Rituximab Therapy
Secondary IDs:	

Study Status

Record Verification:	November 2011
Overall Status:	Terminated
Study Start:	June 2006
Primary Completion:	May 2010 [Actual]
Study Completion:	

Sponsor/Collaborators

Sponsor:	Genentech, Inc.
Responsible Party:	Sponsor
Collaborators:	Amgen

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 11583 Serial Number: 030 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This Phase Ib/II, open-label, multicenter trial is designed to evaluate the safety, pharmacokinetics, and efficacy of dulanermin when combined with rituximab in subjects with follicular, CD20+, B-cell Non-Hodgkin's Lymphoma (NHL) that has progressed following a response of ≥ 6 months duration to a prior rituximab-containing therapy. The multicenter, international, randomized Phase II part of this study will commence only after the safety and available pharmacokinetic data from the Phase Ib part of the study have been evaluated by the Sponsor and have been provided to participating investigators and the FDA.
Detailed Description:	

Conditions

Conditions:	Non-Hodgkin's Lymphoma
Keywords:	NHL Follicular NHL Rituxan Apo2L/TRAIL APO2L/TRAIL

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 1/Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	5
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	
Enrollment:	72 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Phase Ib: Dulanermin 4 mg/kg Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.	Drug: Dulanermin Dulanermin was administered by intravenous (IV) infusion over 1 hour on days 1-5 of each 21-day cycle. Drug: Rituximab Rituximab was administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Experimental: Phase Ib: Dulanermin 8 mg/kg Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.	Drug: Dulanermin Dulanermin was administered by intravenous (IV) infusion over 1 hour on days 1-5 of each 21-day cycle. Drug: Rituximab Rituximab was administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Active Comparator: Phase II: Rituximab Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.	Drug: Rituximab Rituximab was administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Experimental: Phase II: Combination Therapy Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.	Drug: Dulanermin Dulanermin was administered by intravenous (IV) infusion over 1 hour on days 1-5 of each 21-day cycle. Drug: Rituximab Rituximab was administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Experimental: Phase II: Dulanermin	Drug: Dulanermin Dulanermin was administered by intravenous (IV) infusion over 1 hour on days 1-5 of each 21-day cycle.

Arms	Assigned Interventions
Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.	

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Signed Informed Consent Form
- Age ≥ 18 years
- History of histologically confirmed CD20+ follicular NHL Grade 1, 2, or 3a
- Progression of disease following the most recent treatment with rituximab-containing therapy that resulted in stable disease or a partial or complete response lasting ≥ 6 months
- Measurable disease
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- For subjects of reproductive potential (males and females), use of a reliable means of contraception (e.g., contraceptive pill, intrauterine device [IUD], physical barrier throughout the trial and for 1 year following their final exposure to study treatment).
- Life expectancy of > 3 months

Exclusion Criteria:

- Prior radiotherapy to a measurable, metastatic lesion(s) to be used to measure response unless that lesion shows unequivocal progression at baseline
- Radiation therapy to a peripheral lesion within 14 days prior to Day 1; Radiation therapy to a thoracic, abdominal, or pelvic field within 28 days prior to Day 1
- Chemotherapy, hormonal therapy, radiotherapy, or immunotherapy within 4 weeks prior to Day 1
- Patients who have received radioimmunotherapy for relapsed or refractory, follicular NHL are eligible for the study if they received this therapy at least 1 year prior to Day 1, they have adequate bone marrow function, and they have no evidence of myelodysplastic syndrome on bone marrow aspirate/biopsy
- Prior treatment with dulanermin or an agonist antibody to DR4 or DR5
- Concurrent systemic corticosteroid therapy
- Evidence of clinically detectable ascites on Day 1
- Other invasive malignancies within 5 years prior to Day 1

- History or evidence upon physical examination of central nervous system (CNS) disease within 1 year prior to study entry
- Active infection requiring parenteral antibiotics on Day 1
- Major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to Day 1 or anticipation of need for major surgical procedure during the course of the study and fine needle aspirations within 7 days prior to Day 1
- Pregnancy or lactation
- Serious nonhealing wound, ulcer, or bone fracture
- Current or recent participation in another experimental drug study
- Clinically significant cardiovascular disease
- Known positive test result for HIV, hepatitis B surface antigen (sAg), hepatitis B IgG or IgM core antibody, or hepatitis C antibody
- Known sensitivity to murine or human antibodies
- History of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates use of an investigational drug or that might affect interpretation of the results of the study or render the subject at high risk from treatment complications

Contacts/Locations

Study Officials: Chia Portera, PhD., M.D
Study Director
Genentech, Inc.

Locations:

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	The Phase Ib part of this study was completed prior to the start of Phase II. Phase Ib participants were not eligible for participation in Phase II.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Phase Ib

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Started	6	6	0	0	0
Treated	6	6	0	0	0
Completed	0 [1]	2	0	0	0
Not Completed	6	4	0	0	0
Adverse Event	1	0	0	0	0
Death	1	0	0	0	0
Disease Progression	4	4	0	0	0

[1] One patient reported as discontinued due to an AE should have been reported as death.

Phase II

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Started	0	0	23	26	11

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Treated	0	0	22 [1]	26	11
Completed	0	0	0	0	0
Not Completed	0	0	23	26	11
Death	0	0	1	2	0
Lost to Follow-up	0	0	1	0	0
Physician Decision	0	0	1	1	0
Sponsor's decision to terminate	0	0	18	22	11
Patient began new, non-protocol, therapy	0	0	1	0	0
Withdrawal by Subject	0	0	1	1	0

[1] One patient in the Rituximab arm withdrew prior to treatment

Baseline Characteristics

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Baseline Measures

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin	Total
Number of Participants	6	6	22	26	11	71
Age, Continuous [1] [units: years] Mean (Standard Deviation)	56.3 (15.9)	63.7 (9.0)	NA (NA) [1]	NA (NA) [1]	NA (NA) [1]	60.0 (12.9)
Age, Customized [2] [units: years] Mean (Standard Deviation)	NA (NA) [2]	NA (NA) [2]	58.0 (8.5)	58.4 (9.8)	61.4 (13.3)	58.8 (10.0)
Gender, Male/Female [units: participants]						
Female	1	1	9	7	2	20
Male	5	5	13	19	9	51

[1] Age demographic data for the Phase Ib population.

[2] Age demographic data for the Phase II population.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Phase Ib: Number of Participants With a Dose-limiting Toxicity
Measure Description	A dose-limiting toxicity (DLT) was defined as a National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v3.0 Grade ≥ 3 hematologic or major organ toxicity that was related to study drug (i.e., dulanermin). Although a patient may have experienced a DLT at any time during the study, only events that occurred within the DLT assessment window were considered for dose-escalation decisions and determination of the maximum tolerated dose (MTD).
Time Frame	The DLT assessment window was defined as the duration required to complete two full cycles of treatment with dulanermin (2 * 21 days) and four doses of rituximab (usually through Day 28).
Safety Issue?	No

Analysis Population Description

The DLT-evaluable population consisted of all patients enrolled in the Phase Ib who received at least two complete cycles of dulanermin and four doses of rituximab and complete study assessments through the DLT Assessment Window without a DLT (usually through Day 28) or experienced a DLT and withdrew from the study within the DLT Assessment Window.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.

Measured Values

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg
Number of Participants Analyzed	6	6
Phase Ib: Number of Participants With a Dose-limiting Toxicity [units: participants]	0	0

2. Primary Outcome Measure:

Measure Title	Number of Participants With Treatment-Emergent Adverse Events by Severity Grade
Measure Description	Safety was assessed through summaries of treatment-emergent adverse events (AEs); AEs were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 3.0, according to the following guidelines: Grade 1 (Mild); Grade 2 (Moderate); Grade 3 (Severe); Grade 4 (Life-threatening or disabling) and Grade 5 (Death related to AE).
Time Frame	From Baseline through Study Termination (up to a maximum of approximately 13 months for phase Ib and up to approximately 33 months for phase II)
Safety Issue?	No

Analysis Population Description

Safety Evaluable population, consisting of all randomized patients who received at least one dose of treatment.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.

	Description
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Number of Participants Analyzed	6	6	22	26	11
Number of Participants With Treatment-Emergent Adverse Events by Severity Grade [units: participants]					
Grade 5 AE	0	0	1	0	0
Grade 4 AE	1	0	0	0	0
Grade 3 AE	1	3	1	6	0
Grade 2 AE	4	1	8	10	4
Grade 1 AE	0	2	6	7	4
Any Grade AEs	6	6	16	23	8

3. Primary Outcome Measure:

Measure Title	Phase II: Objective Response as Assessed by the Independent Review Facility (IRF)

Measure Description	Objective response was defined as a confirmed or unconfirmed complete response (CR, CRu) or partial response (PR) assessed on the basis of clinical, radiographic (computed tomography (CT) scans of the neck, chest, abdomen, pelvis and inguinal region), and pathologic (i.e., bone marrow) criteria and according to the modified International Working Group (IWG) criteria. All radiographic and clinical data for the evaluation of objective response were submitted to an IRF for blinded and impartial assessment. Patients without a post-baseline tumor assessment were considered non-responders.
Time Frame	From Baseline through Study Termination (up to approximately 33 months)
Safety Issue?	No

Analysis Population Description

The phase II Efficacy-Evaluable population consisted of all randomized patients who received at least one dose of study treatment and had measurable disease at baseline, as assessed by the IRF.

Reporting Groups

	Description
Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Rituximab	Combination Therapy	Dulanermin
Number of Participants Analyzed	22	25	11
Phase II: Objective Response as Assessed by the Independent Review Facility (IRF) [units: participants]			
Total Objective Response	14	16	1
Complete Response	5	3	0
Complete Response unconfirmed	0	2	0
Partial Response	9	11	1

4. Primary Outcome Measure:

Measure Title	Vital Signs: Change From Baseline in Diastolic and Systolic Blood Pressure at Treatment Termination Visit
Measure Description	Blood pressure was measured at baseline and throughout the study. Change from baseline was calculated using the patient's last recorded measurement at the completion of treatment visit - baseline measurement.
Time Frame	Baseline and Treatment Termination visit (8 weeks for Rituximab arm and 12 weeks for combination and Dulanermin arms)
Safety Issue?	No

Analysis Population Description

Safety Evaluable population, consisting of all randomized patients who received at least one dose of treatment.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Number of Participants Analyzed	6	6	22	26	11
Vital Signs: Change From Baseline in Diastolic and Systolic Blood Pressure at Treatment Termination Visit [units: mmHg] Mean (Standard Deviation)					

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Diastolic Blood Pressure	-8.7 (10.9)	-5.2 (7.9)	2.3 (9.9)	1.6 (9.2)	-0.8 (5.6)
Systolic Blood Pressure	-3.2 (16.8)	-4.7 (10.9)	-3.4 (14.8)	-2.2 (19.6)	-4.2 (9.5)

5. Primary Outcome Measure:

Measure Title	Vital Signs: Change From Baseline in Heart Rate at Treatment Termination Visit
Measure Description	Heart rate was measured at baseline and throughout the study. Change from baseline was calculated using the patient's last recorded measurement at the completion of treatment visit - baseline measurement.
Time Frame	Baseline and Treatment Termination visit (8 weeks for Rituximab arm and 12 weeks for combination and Dulanermin arms)
Safety Issue?	No

Analysis Population Description

Safety Evaluable population, consisting of all randomized patients who received at least one dose of treatment.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Number of Participants Analyzed	6	6	22	26	11
Vital Signs: Change From Baseline in Heart Rate at Treatment Termination Visit [units: beats/minute] Mean (Standard Deviation)	7.0 (21.4)	-1.5 (6.7)	0.5 (9.6)	3.3 (10.6)	5.0 (13.2)

6. Primary Outcome Measure:

Measure Title	Vital Signs: Change From Baseline in Body Temperature at Treatment Termination Visit
Measure Description	Body temperature was measured at baseline and throughout the study. Change from baseline was calculated using the patients last recorded measurement at the completion of treatment visit - baseline measurement.
Time Frame	Baseline and Treatment Termination visit (8 weeks for Rituximab arm and 12 weeks for combination and Dulanermin arms)
Safety Issue?	No

Analysis Population Description

Safety Evaluable population, consisting of all randomized patients who received at least one dose of treatment.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.

	Description
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Number of Participants Analyzed	6	6	22	26	11
Vital Signs: Change From Baseline in Body Temperature at Treatment Termination Visit [units: degrees Celsius] Mean (Standard Deviation)	-0.0 (0.6)	-0.3 (0.7)	2.8 (13.1)	-0.1 (0.4)	0.0 (0.4)

7. Primary Outcome Measure:

Measure Title	Number of Participants With a Clinically Significant Laboratory Abnormality
Measure Description	Laboratory Parameters were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE). A clinically significant abnormality was defined as a Grade 3 (severe) or Grade 4 (very severe, life threatening, or disabling) laboratory toxicity according to the NCI CTCAE v3.0.
Time Frame	Baseline and Treatment Termination visit (8 weeks for Rituximab arm and 12 weeks for combination and Dulanermin arms).
Safety Issue?	No

Analysis Population Description

Safety Evaluable population consisting of all randomized patients who received at least one dose of study drug.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.

	Description
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
Number of Participants Analyzed	6	6	22	26	11
Number of Participants With a Clinically Significant Laboratory Abnormality [units: participants]	3	4	5	11	5

8. Primary Outcome Measure:

Measure Title	Mean Serum Concentration of Dulanermin
Measure Description	The dulanermin serum concentration was measured using enzyme linked immunosorbent assay (ELISA).
Time Frame	Blood samples were taken 0.5, 1.5, 2, 3, 5, 7 and 24 hours after the start of the infusion on Day 1 of Cycle 1.
Safety Issue?	No

Analysis Population Description

Safety-evaluable population

Reporting Groups

	Description
Phase Ib Dulanermin	Participants received 4.0 mg/kg/day or 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.

	Description
Phase II Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants may also have received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.

Measured Values

	Phase Ib Dulanermin	Phase II Dulanermin
Number of Participants Analyzed	12	43
Mean Serum Concentration of Dulanermin [units: µg/ml] Mean (Standard Deviation)		
30 minutes after the start of infusion	0.109 (0.37)	0.001 (0.00)
1.5 hours after the start of infusion	40.4 (19.03)	51.5 (14.00)
2 hours after the start of infusion	49.9 (32.04)	79.8 (22.54)
3 hours after the start of infusion	29.5 (20.75)	28.7 (10.13)
5 hours after the start of infusion	2.21 (1.87)	9.89 (21.86)
7 hours after the start of infusion	4.89 (15.69)	0.445 (0.26)
24 hours after the start of infusion	0.324 (0.66)	0.002 (0.00)

9. Secondary Outcome Measure:

Measure Title	Phase II: Progression Free Survival
Measure Description	Progression free survival (PFS) was defined as the time from randomization to documented disease progression or death, whichever occurred first and was based on the investigator's assessment using the modified IWG criteria. Kaplan−Meier methods were used to estimate median time to PFS. Data for patients without disease progression or death on study were censored at the time of the last tumor assessment.
Time Frame	From Baseline through Study Termination (up to approximately 33 months)
Safety Issue?	No

Analysis Population Description

Safety-Evaluable population consisting of all randomized patients who received at least one dose of study treatment

Reporting Groups

	Description
Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Rituximab	Combination Therapy	Dulanermin
Number of Participants Analyzed	22	26	11
Phase II: Progression Free Survival [units: months] Median (95% Confidence Interval)	29.9 (9.2 to 29.9)	17.9 (9.9 to 18.4)	6.9 (2.9 to NA) [1]

[1] The upper limit of the confidence interval was not estimable due to low numbers of events.

10. Secondary Outcome Measure:

Measure Title	Phase II: Overall Survival
Measure Description	Median overall survival could not be estimated because of the low number of deaths at the time of study termination.
Time Frame	From Baseline through Study Termination (up to approximately 33 months)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.

	Description
Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Rituximab	Combination Therapy	Dulanermin
Number of Participants Analyzed	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

11. Secondary Outcome Measure:

Measure Title	Phase II: Objective Response as Assessed by the Investigator
Measure Description	Objective response was defined as a confirmed or unconfirmed complete response(CR, CRu) or partial response (PR) assessed on the basis of clinical, radiographic (computed tomography (CT) scans of the neck, chest, abdomen, pelvis and inguinal region), and pathologic (i.e., bone marrow) criteria and according to the modified International Working Group (IWG) criteria. Patients without a post-baseline tumor assessment were considered non-responders.
Time Frame	From Baseline through Study Termination (up to approximately 33 months)
Safety Issue?	No

Analysis Population Description

Safety Evaluable population, consisting of all randomized patients who received at least one dose of treatment.

Reporting Groups

	Description
Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Rituximab	Combination Therapy	Dulanermin
Number of Participants Analyzed	22	26	11

	Rituximab	Combination Therapy	Dulanermin
Phase II: Objective Response as Assessed by the Investigator [units: participants]			
Total Objective Response	15	17	1
Complete Response	7	7	1
Complete Response unconfirmed	0	1	0
Partial Response	8	9	0

12. Secondary Outcome Measure:

Measure Title	Phase II: Duration of Response as Assessed by the Investigator
Measure Description	An event was defined as documented disease progression or death on study, whichever occurred first. Duration of objective response was defined only for patients with an objective response as determined by the investigator and was the time from the initial response to disease progression or death on study. Kaplan−Meier methods were used to estimate median, percentiles, and range of duration of response.
Time Frame	From Baseline through Study Termination (up to approximately 33 months)
Safety Issue?	No

Analysis Population Description

Safety-evaluable patients with an objective response determined by the Investigator.

Reporting Groups

	Description
Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Measured Values

	Rituximab	Combination Therapy	Dulanermin
Number of Participants Analyzed	15	17	1
Phase II: Duration of Response as Assessed by the Investigator [units: months] Median (95% Confidence Interval)	21.4 (7.7 to 21.4)	11.3 (8.0 to NA) [1]	NA (NA to NA) [2]

[1] Could not be calculated due to low number of patients with events.

[2] Median duration of objective response could not be estimated for the dulanermin only arm because only 1 patient had an objective response based on investigator assessment

Reported Adverse Events

Time Frame	Adverse events occurring on or after the first treatment through Study Termination (up to approximately 13 months for phase Ib and up to approximately 33 months for phase II) are summarized.
Additional Description	Evaluation is on all Treated Patients.

Reporting Groups

	Description
Phase Ib - Dulanermin 4 mg/kg	Participants received 4.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase Ib - Dulanermin 8 mg/kg	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Rituximab	Participants received rituximab administered by intravenous (IV) infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Combination Therapy	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles. Participants also received rituximab administered by IV infusion at 375 mg/m^2 weekly for up to eight doses.
Phase II - Dulanermin	Participants received 8.0 mg/kg/day dose of dulanermin, administered by intravenous (IV) infusion for 5 consecutive days at the start of each 21-day treatment cycle for up to four cycles.

Serious Adverse Events

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/6 (16.67%)	1/6 (16.67%)	1/22 (4.55%)	4/26 (15.38%)	0/11 (0%)
Gastrointestinal disorders					
ABDOMINAL PAIN [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	1/26 (3.85%)	0/11 (0%)
CONSTIPATION [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	1/26 (3.85%)	0/11 (0%)
ILEUS PARALYTIC [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
General disorders					
INFUSION RELATED REACTION [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	1/26 (3.85%)	0/11 (0%)
Infections and infestations					
PNEUMONIA [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	1/26 (3.85%)	0/11 (0%)
SEPSIS [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
MYELODYSPLASTIC SYNDROME [A] †	0/6 (0%)	0/6 (0%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (Unspecified)

Other Adverse Events

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

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/6 (100%)	6/6 (100%)	16/22 (72.73%)	22/26 (84.62%)	8/11 (72.73%)
Blood and lymphatic system disorders					
ANAEMIA [A] †	1/6 (16.67%)	0/6 (0%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)
COAGULOPATHY [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
DISSEMINATED INTRAVASCULAR COAGULATION [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
NEUTROPENIA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
THROMBOCYTOPENIA [A] †	1/6 (16.67%)	0/6 (0%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)
Cardiac disorders					
LEFT VENTRICULAR DYSFUNCTION [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
RIGHT VENTRICULAR DYSFUNCTION [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Ear and labyrinth disorders					
DEAFNESS UNILATERAL [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Endocrine disorders					
ADRENAL INSUFFICIENCY [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Eye disorders					
DRY EYE [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
VISION BLURRED [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	1/26 (3.85%)	1/11 (9.09%)
Gastrointestinal disorders					
ABDOMINAL DISCOMFORT [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
ABDOMINAL PAIN [A] †	0/6 (0%)	0/6 (0%)	2/22 (9.09%)	2/26 (7.69%)	0/11 (0%)
ABDOMINAL PAIN UPPER [A] †	2/6 (33.33%)	0/6 (0%)	0/22 (0%)	1/26 (3.85%)	0/11 (0%)
CONSTIPATION [A] †	0/6 (0%)	2/6 (33.33%)	1/22 (4.55%)	4/26 (15.38%)	0/11 (0%)
DIARRHOEA [A] †	2/6 (33.33%)	2/6 (33.33%)	2/22 (9.09%)	2/26 (7.69%)	0/11 (0%)
DYSPHAGIA [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
HAEMORRHOIDS [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	1/11 (9.09%)

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
NAUSEA [A] †	2/6 (33.33%)	2/6 (33.33%)	4/22 (18.18%)	4/26 (15.38%)	0/11 (0%)
ORAL PAIN [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
SENSITIVITY OF TEETH [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
STOMATITIS [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
TOOTHACHE [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
VOMITING [A] †	2/6 (33.33%)	1/6 (16.67%)	3/22 (13.64%)	3/26 (11.54%)	0/11 (0%)
General disorders					
ASTHENIA [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	4/26 (15.38%)	2/11 (18.18%)
CATHETER SITE ERYTHEMA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
CATHETER SITE PAIN [A] †	2/6 (33.33%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
CATHETER SITE PRURITUS [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
CHEST PAIN [A] †	2/6 (33.33%)	0/6 (0%)	1/22 (4.55%)	1/26 (3.85%)	0/11 (0%)
CHILLS [A] †	1/6 (16.67%)	3/6 (50%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
FATIGUE [A] †	6/6 (100%)	3/6 (50%)	2/22 (9.09%)	3/26 (11.54%)	3/11 (27.27%)
FEELING COLD [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
GAIT DISTURBANCE [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
HERNIA [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	1/11 (9.09%)
MUCOSAL INFLAMMATION [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
OEDEMA PERIPHERAL [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	1/26 (3.85%)	0/11 (0%)
PAIN [A] †	0/6 (0%)	1/6 (16.67%)	1/22 (4.55%)	1/26 (3.85%)	0/11 (0%)
PYREXIA [A] †	2/6 (33.33%)	1/6 (16.67%)	0/22 (0%)	5/26 (19.23%)	0/11 (0%)

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
SWELLING [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Hepatobiliary disorders					
HEPATIC FAILURE [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Immune system disorders					
DRUG HYPERSENSITIVITY [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	2/26 (7.69%)	0/11 (0%)
Infections and infestations					
GROIN INFECTION [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
HERPES ZOSTER [A] †	1/6 (16.67%)	0/6 (0%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)
ORAL HERPES [A] †	0/6 (0%)	0/6 (0%)	1/22 (4.55%)	4/26 (15.38%)	0/11 (0%)
PNEUMONIA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
RHINITIS [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	1/11 (9.09%)
UPPER RESPIRATORY TRACT INFECTION [A] †	2/6 (33.33%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
VIRAL INFECTION [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	2/11 (18.18%)
Injury, poisoning and procedural complications					
CONTUSION [A] †	0/6 (0%)	1/6 (16.67%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)
INCISION SITE PAIN [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Investigations					
BACTERIAL TEST POSITIVE [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
BLOOD AMYLASE INCREASED [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
LIPASE INCREASED [A] †	1/6 (16.67%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Metabolism and nutrition disorders					

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
DECREASED APPETITE [A] †	3/6 (50%)	1/6 (16.67%)	2/22 (9.09%)	0/26 (0%)	0/11 (0%)
FLUID RETENTION [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	1/11 (9.09%)
HYPERKALAEMIA [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
HYPOMAGNESAEMIA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
METABOLIC ACIDOSIS [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Musculoskeletal and connective tissue disorders					
ARTHRALGIA [A] †	3/6 (50%)	0/6 (0%)	4/22 (18.18%)	0/26 (0%)	0/11 (0%)
MUSCULOSKELETAL PAIN [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	1/26 (3.85%)	0/11 (0%)
PAIN IN EXTREMITY [A] †	1/6 (16.67%)	1/6 (16.67%)	0/22 (0%)	2/26 (7.69%)	0/11 (0%)
Nervous system disorders					
DIZZINESS [A] †	0/6 (0%)	1/6 (16.67%)	1/22 (4.55%)	0/26 (0%)	1/11 (9.09%)
DYSGEUSIA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
HEADACHE [A] †	1/6 (16.67%)	1/6 (16.67%)	1/22 (4.55%)	4/26 (15.38%)	0/11 (0%)
HYPOGEUSIA [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
NEUROPATHY PERIPHERAL [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	2/26 (7.69%)	0/11 (0%)
PARAESTHESIA [A] †	0/6 (0%)	2/6 (33.33%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
SINUS HEADACHE [A] †	0/6 (0%)	2/6 (33.33%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
TREMOR [A] †	1/6 (16.67%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Psychiatric disorders					
ANXIETY [A] †	0/6 (0%)	1/6 (16.67%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)
INSOMNIA [A] †	1/6 (16.67%)	0/6 (0%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
NERVOUSNESS [A] †	0/6 (0%)	1/6 (16.67%)	1/22 (4.55%)	0/26 (0%)	0/11 (0%)
Renal and urinary disorders					
NOCTURIA [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
RENAL FAILURE ACUTE [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Respiratory, thoracic and mediastinal disorders					
COUGH [A] †	1/6 (16.67%)	1/6 (16.67%)	3/22 (13.64%)	2/26 (7.69%)	0/11 (0%)
DYSPNOEA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	2/26 (7.69%)	1/11 (9.09%)
HYPOXIA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
LUNG CONSOLIDATION [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
NASAL CONGESTION [A] †	0/6 (0%)	0/6 (0%)	2/22 (9.09%)	0/26 (0%)	0/11 (0%)
OROPHARYNGEAL PAIN [A] †	1/6 (16.67%)	2/6 (33.33%)	3/22 (13.64%)	1/26 (3.85%)	0/11 (0%)
PRODUCTIVE COUGH [A] †	1/6 (16.67%)	0/6 (0%)	1/22 (4.55%)	1/26 (3.85%)	0/11 (0%)
RESPIRATORY DISTRESS [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
RESPIRATORY TRACT CONGESTION [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
RHINORRHOEA [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
SINUS CONGESTION [A] †	1/6 (16.67%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Skin and subcutaneous tissue disorders					
DRY SKIN [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
EXFOLIATIVE RASH [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
HYPERHIDROSIS [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
NIGHT SWEATS [A] †	0/6 (0%)	2/6 (33.33%)	0/22 (0%)	0/26 (0%)	0/11 (0%)

	Phase Ib - Dulanermin 4 mg/kg	Phase Ib - Dulanermin 8 mg/kg	Phase II - Rituximab	Phase II - Combination Therapy	Phase II - Dulanermin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
PRURITUS [A] †	1/6 (16.67%)	1/6 (16.67%)	2/22 (9.09%)	0/26 (0%)	0/11 (0%)
RASH [A] †	2/6 (33.33%)	3/6 (50%)	2/22 (9.09%)	0/26 (0%)	0/11 (0%)
SKIN INDURATION [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
Vascular disorders					
DEEP VEIN THROMBOSIS [A] †	0/6 (0%)	1/6 (16.67%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
HYPERTENSION [A] †	0/6 (0%)	0/6 (0%)	1/22 (4.55%)	1/26 (3.85%)	1/11 (9.09%)
HYPOTENSION [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)
PHLEBITIS [A] †	0/6 (0%)	0/6 (0%)	0/22 (0%)	2/26 (7.69%)	0/11 (0%)
PHLEBITIS SUPERFICIAL [A] †	1/6 (16.67%)	0/6 (0%)	0/22 (0%)	0/26 (0%)	0/11 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (Unspecified)

Limitations and Caveats

The Sponsor terminated the study on 5 May 2010, prior to the completion of the 36-month follow-up (FU) period, based on the primary analysis results. All patients were off-study or in survival FU (the treatment period was completed).

More Information

Certain Agreements:

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

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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