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Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

CJM112, and spartalizumab (PDR001) in combination with LCL161 or CJM112

Trial Indication(s)

Relapsed and/or refractory multiple myeloma

Protocol Number

CPDR001X2106

Protocol Title

Phase I/Ib, multi-center, open-label, study of single agent CJM112, and PDR001 in combination with LCL161 or CJM112 in patients with relapsed and/or refractory multiple myeloma

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase I/Ib

Study Start/End Dates

Study Start Date: December 2017 (Actual)
Primary Completion Date: March 2020 (Actual)
Study Completion Date: March 2020 (Actual)

Reason for Termination (If applicable)

The study was terminated early due to challenges in recruitment. Patients were recruited over a period of about 18 months, until the decision was made to halt further enrollment.

Study Design/Methodology

This was a phase I/Ib, multi-center, open-label study to identify the Maximum tolerated dose (MTD) and/or Recommended dose (RD) of single agent CJM112, and CJM112 or LCL161 in combination with spartalizumab in patients with relapsed or refractory multiple myeloma who had failed 2 or more lines of prior therapy, including an Immunomodulatory drugs (IMiD) and a proteasome inhibitor.

The study comprised of 6 treatment arms which opened in parallel:

1. CJM112 50mg Q4W
2. CJM112 100mg Q4W
3. CJM112 50mg Q4W + PDR001 400mg Q4W
4. CJM112 100mg Q4W + PDR001 400mg Q4W
5. LCL161 300mg QW + PDR001 400mg Q4W
6. LCL161 600mg QW + PDR001 400mg Q4W

The assignment of a patient to a particular arm or dose level was coordinated by Novartis and based on the dose levels available at the time the patient consented to participation in the study, and taking into account whether patients had toxicity leading to discontinuation of prior Programmed cell death receptor 1 (PD-1), Programmed death-ligand 1 (PDL-1) or mmunoglobulin-17 (IL-17) directed therapy. Each study treatment was planned to be administered in 28-day dosing cycles. Patients were to continue to receive the assigned treatment until disease progression as defined by International Multiple Myeloma Working Group (IMWG) criteria, unacceptable toxicity, start of a new anti-neoplastic therapy, discontinuation at the discretion of the patient or investigator, loss to follow-up, death or study termination by Novartis. A patient was allowed to switch from treatment of CJM112 50mg once every 4 weeks (Q4W) or CJM112 100mg Q4W to the to the corresponding CJM112 dose level on CJM112 50mg Q4W + PDR001 400mg Q4W or CJM112 100mg Q4W +

PDR001 400mg Q4W at the time of disease progression if that dose level had been declared safe and if the patient had not experienced any Dose limiting toxicities (DLTs) on single-agent CJM112.

Dose escalation within each arm was guided by an adaptive Bayesian logistic regression model (BLRM) following the Escalation with overdose control (EWOC) principle. Dose levels were planned to be explored until the Maximum tolerated dose (MTD) and/or Recommended dose (RD) was established; however, the study was terminated early due to challenges in recruitment after only two dose levels within each treatment arm were tested.

Centers

8 centers in 4 countries: United States(2), Italy(1), Germany(3), Spain(2)

Objectives:

The primary objective was to characterize the safety, tolerability, and Maximum tolerated dose (MTD)(s)/ Recommended dose (RD)(s) of single agent CJM112, and CJM112 or LCL161 in combination with spartalizumab.

The secondary objectives were to evaluate the anti-tumor activity of single agent CJM112, and of spartalizumab in combination with CJM112 and LCL161; To determine the Pharmacokinetics (PK) of single agent CJM112, and of spartalizumab in combination with CJM112 or LCL161; and To assess the immunogenicity of spartalizumab and CJM112.

Test Product (s), Dose(s), and Mode(s) of Administration

Spartalizumab 100 mg powder for solution for Infusion, CJM112 150 mg liquid in vial for infusion, and LCL161 300 mg tablet were prepared and supplied by Novartis.

Statistical Methods

Three adaptive Bayesian logistic regression model (BLRMs) guided by Escalation with overdose control (EWOC) principle were used to make dose recommendations and identify the Maximum tolerated dose (MTD)(s)/ Recommended dose (RD)(s) for CJM112 single agent and spartalizumab in combination with CJM112 orv LCL161. The Dose limiting toxicity (DLT) relationship of CJM112 single agent was described by a 2-parameter BLRM; and spartalizumab in combination with CJM112 or LCL161 was described by separate 5-parameter BLRMs.

The BLRMs were fitted on the dose-limiting toxicity data (i.e. absence or presence of DLT) during the 28 day DLT window (CJM112 single agent) or 56 day DLT window (spartalizumab in combination with CJM112 or LCL161) accumulated throughout the dose escalations to model the dose-toxicity relationship.

Available spartalizumab, CJM112 and LCL161 single agent data were used to derive meta-analytic-predictive priors for the corresponding single agent component of the models.

A new BLRM was set up to incorporate a change in dosing schedule from once weekly (QW) schedule to once in 2 weeks schedule. This new BLRM incorporated down-weighted existing LCL161 QW schedule data in the prior distribution.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Must have been able to provide written informed consent before any screening procedures.
- Male or female patients ≥18 years of age.
- Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2.
- Patients with a confirmed diagnosis of multiple myeloma who have received two or more lines of therapy including an IMiD and PI, and are relapsed and/or refractory to their most recent line of therapy. Patients who have received a prior autologous bone marrow transplant and otherwise meet the inclusion criteria are eligible for this study.
-Must have had measurable disease defined by at least 1 of the following 3 measurements:
-Serum M-protein ≥ 0.5 g/dL
OR
-Urine M-protein ≥ 200 mg/24 hours
OR
-Serum free light chain (FLC) > 100 mg/L of involved FLC
- All patients must have been willing to undergo a mandatory serial bone marrow aspirate and/or biopsy at screening and

subsequently following treatment for the assessment of biomarker/pharmacodynamics and disease status. Exceptions may be considered after documented discussion with Novartis.

Exclusion Criteria:
- Use of systemic chronic steroid therapy (≥10mg /day of prednisone or equivalent), or any immunosuppressive therapy within 7 days of first dose of study treatment. Topical, inhaled, nasal, or ophthalmic steroids are allowed.
- Malignant disease, other than that being treated in this study. Exceptions to this exclusion include the following: malignancies that were treated curatively and have not recurred within 2 years prior to study treatment; completely resected basal cell and squamous cell skin cancers, and completely resected carcinoma in situ of any type.
- Active, known or suspected autoimmune disease other than patients with vitiligo, residual hypothyroidism only requiring hormone replacement, psoriasis not requiring systemic treatment or conditions not expected to recur.
- Patients with prior known toxicity attributed to PD-1 or PDL-1 directed therapy, which led to discontinuation of these agents, will be excluded from the PDR001 containing arms of the study.
- Patients with prior known toxicity from IL-17A directed therapy, which led to discontinuation of the study treatment, will be excluded from CJM112 containing arms of the study.
- Any of the following clinical laboratory results during screening (i.e., within 28 days before the first dose of study treatment):
• Absolute neutrophil count (ANC) < 1,000/mm3 without growth factor support within 7 days prior to testing
• Platelet count < 75,000 mm3 without transfusion support within 7 days prior to testing
• Bilirubin > 1.5 times the upper limit of the normal range (ULN)
• Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 times the ULN
• Calculated creatinine clearance < 30 ml/min according to Cockcroft-Gault equation

Participant Flow Table

Overall Study

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W	Total
Arm/Group Description	CJM112 50mg Q4W - Dose	CJM112 100mg Q4W - Dose	CJM112 50mg Q4W + PDR001	CJM112 100mg Q4W +PDR001	LCL161 300mg QW + PDR001	LCL161 600mg QW + PDR001	

	escalation of CJM112	escalation of CJM112	400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	
Started	4	2	6	5	4	5	26
Completed	0	0	0	0	0	0	0
Not Completed	4	2	6	5	4	5	26
Death	1	1	0	0	0	0	2
Adverse Event	0	0	0	1	0	1	2
Progressive disease	3	1	6	4	4	4	22

Baseline Characteristics

	CJM112 50mg Q4W	**CJM112 100mg Q4W**	**CJM112 50mg Q4W + PDR001 400mg Q4W**	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**	**Total**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed	

			dose of PDR001	dose of PDR001	dose of PDR001	dose of PDR001	
Number of Participants [units: participants]	4	2	6	5	4	5	26
Age Continuous (units: years) Mean ± Standard Deviation							
	72.3±4.79	64.0±1.41	67.5±3.78	73.0±8.43	62.8±6.85	65.8±5.76	NA±NA[]
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)							
Female	1	1	4	3	1	0	10
Male	3	1	2	2	3	5	16
Race (NIH/OMB) (units: Participants) Count of Participants (Not Applicable)							
American Indian or Alaska Native	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0
White	4	2	5	5	3	5	24
More than one race	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	1	0	1	0	2

Primary Outcome Result(s)

Number of patients reporting dose limiting toxicities

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	4	5	2	3
Number of patients reporting dose limiting toxicities (units: Participants)						
	1	0	0	1	0	1

The number of patients who experience a treatment-related adverse event after being treated with a single dose of single agent CJM112, or two doses of PDR001 in combination with CJM112 or LCL161

(Time Frame: 24 months)

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W

Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	1	6	5	3	5
The number of patients who experience a treatment-related adverse event after being treated with a single dose of single agent CJM112, or two doses of PDR001 in combination with CJM112 or LCL161 (units: Participants)						
Adverse events - all grades	4	1	6	5	3	5
Adverse events - Treatment-related - all grades	2	1	3	4	2	3
SAEs - all grades	2	1	4	1	3	1
SAEs - Treatment-related - all grades	1	0	0	1	0	0
Fatal SAEs - all grades	1	1	0	0	0	1
AEs requiring additional therapy - all grades	3	1	4	4	3	4
AEs leading to discontinuation - all grades	0	0	0	1	1	1
AEs leading to discontinuation - Treatment-related - all grades	0	0	0	1	0	1

AEs leading to dose adjustment/interruption - all grades	0	0	0	1	1	0

The number of patients requiring no interruptions after a single dose of CJM112

(Time Frame: 24 months)

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	6	5
The number of patients requiring no interruptions after a single dose of CJM112 (units: Participants)				
CJM112 Dose interruption - Number of subjects -n - With no dose interruption	4	2	6	5

The number of patients who discontinued treatment of CJM112

(Time Frame: 24 months)

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	6	5
The number of patients who discontinued treatment of CJM112 (units: Participants)				
CJM112 - Permanent discontinuation - n - Number of subjects	4	2	6	5
CJM112 - Reason for permanent discontinuation - n - Death	1	1	0	0
CJM112 - Reason for permanent discontinuation - n - Progressive Disease	3	1	6	4
CJM112 - Reason for permanent discontinuation - n - Adverse Event	0	0	0	1

The number of patients requiring a dose reduction of CJM112

(Time Frame: 24 months)

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	6	5
The number of patients requiring a dose reduction of CJM112 (units: Participants)				
CJM112 - Dose reduction - Number of subjects -n - With no dose reduction	4	2	6	3
CJM112 - Dose reduction - Number of subjects -n - With at least one dose reduction	0	0	0	2
CJM112 - Dose reduction - Number of subjects -n - Only one dose reduction	0	0	0	1
CJM112 - Dose reduction - Number of subjects -n -	0	0	0	1

More than two dose reduction				
Number of subjects with at least one dose reduction by reason -n - Adverse Event	0	0	0	1
Number of subjects with at least one dose reduction by reason -n - As Per Protocol	0	0	0	1
Number of subjects with at least one dose reduction by reason -n - Physician Decision	0	0	0	1

The number of patients requiring no interruptions of PDR001 in combination with CJM112 or LCL161

(Time Frame: 24 months)

	CJM112 50mg Q4W + PDR001 400mg Q4W	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	6	5	4	5

The number of patients requiring no interruptions of PDR001 in combination with CJM112 or LCL161 (units: Participants)				
PDR001 Dose interruption - Number of subjects -n - With no dose interruption	6	5	4	5

The number of patients who discontinued treatment of PDR001 in combination with CJM112 or LCL161

(Time Frame: 24 months)

	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	6	5	4	5

The number of patients who discontinued treatment of PDR001 in combination with CJM112 or LCL161 (units: Participants)

PDR001 - Permanent discontinuation -n - Number of subjects	6	5	4	5
PDR001 - Reason for permanent discontinuation -n - Adverse Event	0	1	1	1
PDR001 - Reason for permanent discontinuation -n - Progressive Disease	6	4	3	4

The number of patients requiring no dose reduction of PDR001 in combination with CJM112 or LCL161

(Time Frame: 24 months)

	CJM112 50mg Q4W + PDR001 400mg Q4W	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	6	5	4	5
The number of patients requiring no dose reduction of PDR001 in combination with CJM112 or LCL161				

(units: Participants)

PDR001 Dose reductions - Number of subjects - n - With no dose reduction	6	5	4	5

The number of patients requiring interruptions of LCL161

(Time Frame: 24 months)

	LCL161 300mg QW + PDR001 400mg Q4W	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	5

The number of patients requiring interruptions of LCL161

(units: Participants)

LCL161 Dose interruption - Number of subjects - n - With no dose interruption	3	5
LCL161 - Number of subjects - n - With at least one dose interruption	1	0

LCL161 - Number of subjects - n - Only one dose interruption	1	0

The number of patients who discontinued treatment of LCL161

(Time Frame: 24 months)

	LCL161 300mg QW + PDR001 400mg Q4W	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	5
The number of patients who discontinued treatment of LCL161 (units: Participants)		
LCL161- Permanent discontinuation -n	4	5
LCL161- Reason for permanent discontinuation - n - Adverse Event	0	1

LCL161- Reason for permanent discontinuation - n - Progressive Disease	4	4

The number of patients requiring no dose reduction of LCL161

(Time Frame: 24 months)

	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	5
The number of patients requiring no dose reduction of LCL161 (units: Participants)		
LCL161 Number of subjects - n - With no dose reduction	4	5

Secondary Outcome Result(s)

Immunogenicity of CJM112 - prevalence

(Time Frame: Day 1 (cycle 1))

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	5	4
Immunogenicity of CJM112 - prevalence (units: Percentage of Participants)				
Percentage of participants with positive Anti-drug antibodies (ADA) at Day 1 (Cycle 1)	0	50	0	25

Immunogenicity of PDR001 - prevalence

(Time Frame: Day 1 (cycle 1))

	CJM112 50mg Q4W +	CJM112 100mg Q4W	LCL161 300mg QW +	LCL161 600mg QW +

	PDR001 400mg Q4W	+PDR001 400mg Q4W	PDR001 400mg Q4W	PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	5	3	0	0
Immunogenicity of PDR001 - prevalence (units: Percentage of Participants)				
Percentage of participants with positive Anti-drug antibodies (ADA) at Day 1 (Cycle 1)	40	33.3		

Immunogenicity of CJM112 - incidence

(Time Frame: Day 1 (cycle 1))

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose	CJM112 100mg Q4W - Dose	CJM112 50mg Q4W + PDR001 400mg Q4W -	CJM112 100mg Q4W +PDR001 400mg Q4W -

	escalation of CJM112	escalation of CJM112	Dose escalation of CJM112 in combination with a fixed dose of PDR001	Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	1	4	2
Immunogenicity of CJM112 - incidence (units: Percentage of Participants)				
Percentage of participants with positive Anti-drug antibodies (ADA) at Day 1 (Cycle 1)	0	0	0	0

Immunogenicity of PDR001 - incidence

(Time Frame: Day 1 (cycle 1))

	CJM112 50mg Q4W + PDR001 400mg Q4W	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001

Number of Participants Analyzed [units: participants]	5	2	2	2
Immunogenicity of PDR001 - incidence (units: Percentage of Participants)				
Percentage of participants with positive Anti-drug antibodies (ADA) at Day 1 (Cycle 1)	20	50	0	0

Overall Response Rate (ORR)

(Time Frame: 24 Months)

	CJM112 50mg Q4W	**CJM112 100mg Q4W**	**CJM112 50mg Q4W + PDR001 400mg Q4W**	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	6	5	4	5
Overall Response Rate (ORR) (units: Percentage)						

Number (95% Confidence Interval)						
Overall response rate (ORR) (PR, VGPR, CR, sCR)	0 (0.0 to 60.2)	0 (0.0 to 84.2)	0 (0.0 to 45.9)	0 (0.0 to 52.2)	0 (0.0 to 60.2)	0 (0.0 to 52.2)

Best Overall Response (BOR)

(Time Frame: 24 Months)

	CJM112 50mg Q4W	**CJM112 100mg Q4W**	**CJM112 50mg Q4W + PDR001 400mg Q4W**	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	6	5	4	5
Best Overall Response (BOR) (units: Percentage)						
Best overall response % - Stable Disease	25	0	16.7	100	50	20
Best overall response % - Progressive Disease (PD)	25	0	83.3	0	25	20
Best overall response % - Unknown (UNK)	50	100	0	0	25	60

Progression Free Survival (PFS)

(Time Frame: 24 Months)

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0
Progression Free Survival (PFS) (units: Percentage of Participant)						

Disease Control Rate (DCR)

(Time Frame: 24 Months)

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W

Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	6	5	4	5
Disease Control Rate (DCR) (units: Percentage) Number (95% Confidence Interval)						
Disease control rate (DCR) (Stable disease, MR, PR, VGPR, CR, sCR)	25.0 (0.6 to 80.6)	0 (0.0 to 84.2)	16.7 (0.4 to 64.1)	100 (47.8 to 100)	50.0 (6.8 to 93.2)	20.0 (0.5 to 71.6)

Half-life of PDR001, CJM112 and LCL161

(Time Frame: 24 months)

	CJM112 50mg Q4W	**CJM112 100mg Q4W**	**CJM112 50mg Q4W + PDR001 400mg Q4W**	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination

			with a fixed dose of PDR001	with a fixed dose of PDR001	with a fixed dose of PDR001	with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0
Half-life of PDR001, CJM112 and LCL161 (units: days)						

AUClast of serum CJM112

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W	**CJM112 100mg Q4W**	**CJM112 50mg Q4W + PDR001 400mg Q4W**	**CJM112 100mg Q4W +PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	2	0	5	4
AUClast of serum CJM112 (units: h*ng/mL)				

Mean ± Standard Deviation				
	3290000 ± 1750000		2080000 ± 864000.0	6000000 ± 2600000

AUClast of serum PDR001

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W + PDR001 400mg Q4W	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	4	1	0
AUClast of serum PDR001 (units: h*ng/mL) Mean ± Standard Deviation				
	13400000 ± NA[12]	33300000 ± 12000000	19000000 ± NA[12]	

[1] not evaluable
[2] not evaluable

AUClast of plasma LCL161

(Time Frame: day 1 to day 28 (cycle 1))

	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	1
AUClast of plasma LCL161 (units: h*ng/mL) Mean ± Standard Deviation		
	3550.0 ± NA[12]	3390.0 ± NA[12]

[1] not evaluable
[2] not evaluable

Cmax of serum CJM112

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W

Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	2	0	5	4
Cmax of serum CJM112 (units: ng/mL) Mean ± Standard Deviation				
	15400.0 ± 1840.0		10800.0 ± 2170.0	26700.0 ± 11000.0

Cmax of serum PDR001

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W + PDR001 400mg Q4W	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed

	dose of PDR001	dose of PDR001	dose of PDR001	dose of PDR001
Number of Participants Analyzed [units: participants]	1	4	1	0
Cmax of serum PDR001 (units: ng/mL) Mean ± Standard Deviation				
	67300.0 ± NA[12]	92000.0 ± 21800.0	41100.0 ± NA[12]	

[1] not evaluable
[2] not evaluable

Cmax of plasma LCL161

(Time Frame: day 1 to day 28 (cycle 1))

	LCL161 300mg QW + PDR001 400mg Q4W	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	1
Cmax of plasma LCL161 (units: ng/mL)		

Mean ± Standard Deviation		
	960.0 ± NA[12]	904.0 ± NA[12]

[1] not evaluable
[2] not evaluable

Tmax of serum CJM112

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	2	0	5	4
Tmax of serum CJM112 (units: hours (h)) Median (Full Range)				
	3.0 (2.6 to 3.4)		2.2 (2.1 to 3.5)	2.1 (1.9 to 2.7)

Tmax of serum PDR001

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	4	1	0
Tmax of serum PDR001 (units: hours (h)) Median (Full Range)				
	1.4 (1.4 to 1.4)	1.5 (1.0 to 1.5)	1.5 (1.5 to 1.5)	

Tmax of plasma LCL161

(Time Frame: day 1 to day 28 (cycle 1))

	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of

	LCL161 in combination with a fixed dose of PDR001	LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	1
Tmax of plasma LCL161 (units: hours (h)) Median (Full Range)		
	3.0 (3.0 to 3.0)	2.9 (2.9 to 2.9)

Cmin of serum CJM112

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W	**CJM112 100mg Q4W**	**CJM112 50mg Q4W + PDR001 400mg Q4W**	**CJM112 100mg Q4W +PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112	CJM112 100mg Q4W - Dose escalation of CJM112	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	2	0	5	4
Cmin of serum CJM112 (units: ng/mL)				

Mean ± Standard Deviation				
	1750.0 ± 2080.0		873.0 ± 861.0	3490.0 ± 2210.0

Cmin of serum PDR001

(Time Frame: day 1 to day 28 (cycle 1))

	CJM112 50mg Q4W + PDR001 400mg Q4W	**CJM112 100mg Q4W +PDR001 400mg Q4W**	**LCL161 300mg QW + PDR001 400mg Q4W**	**LCL161 600mg QW + PDR001 400mg Q4W**
Arm/Group Description	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	CJM112 100mg Q4W +PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	4	1	0
Cmin of serum PDR001 (units: ng/mL) Mean ± Standard Deviation				
	8690.0 ± NA[12]	25200.0 ± 12300.0	9980.0 ± NA[12]	

[1] not evaluable
[2] not evaluable

Cmin of plasma LCL161

(Time Frame: day 1 to day 28 (cycle 1))

	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	1	1
Cmin of plasma LCL161 (units: ng/mL) Mean ± Standard Deviation		
	503.0 ± NA[12]	785.0 ± NA[12]

[1] not evaluable
[2] not evaluable

Post-Hoc: All Collected Deaths

(Time Frame: up to 50 weeks)

	CJM112 50mg Q4W	CJM112 100mg Q4W	CJM112 50mg Q4W + PDR001 400mg Q4W	CJM112 100mg Q4W +PDR001 400mg Q4W	LCL161 300mg QW + PDR001 400mg Q4W	LCL161 600mg QW + PDR001 400mg Q4W
Arm/Group Description	CJM112 50mg Q4W - Dose	CJM112 100mg Q4W - Dose	CJM112 50mg Q4W + PDR001 400mg Q4W -	CJM112 100mg Q4W +PDR001 400mg Q4W -	LCL161 300mg QW + PDR001 400mg Q4W -	LCL161 600mg QW + PDR001 400mg Q4W -

	escalation of CJM112	escalation of CJM112	Dose escalation of CJM112 in combination with a fixed dose of PDR001	Dose escalation of CJM112 in combination with a fixed dose of PDR001	Dose escalation of LCL161 in combination with a fixed dose of PDR001	Dose escalation of LCL161 in combination with a fixed dose of PDR001
Number of Participants Analyzed [units: participants]	4	2	6	5	4	5
All Collected Deaths (units: Participants)						
On-treatment deaths	2	1	1	0	1	1
All deaths	3	1	3	0	2	2

Safety Results

All-Cause Mortality

	CJM112 50mg Q4W N = 4	**CJM112 100mg Q4W N = 2**	**CJM112 50mg Q4W + PDR001 400mg Q4W N = 6**	**CJM112 100mg Q4W + PDR001 400mg Q4W N = 5**	**LCL161 300mg QW + PDR001 400mg Q4W N = 4**	**LCL161 600mg QW + PDR001 400mg Q4W N = 5**	**All subjects N = 26**
Arm/Group Description	CJM112 50mg Q4W -	CJM112 100mg Q4W -	CJM112 50mg Q4W +	CJM112 100mg Q4W	LCL161 300mg QW +	LCL161 600mg QW +	All subjects

	Dose escalation of CJM112 n	Dose escalation of CJM112 n	PDR001 400mg Q4W - Dose escalation of CJM112 in combination with PDR001 fixed dose n	+ PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001 n	PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001 n	PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001 n	
Total participants affected	2 (50.00%)	1 (50.00%)	1 (16.67%)	0 (0.00%)	1 (25.00%)	1 (20.00%)	6 (23.08%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment (for single agent CJM112); plus 150 days post treatment (for PDR001 in combination with CJM112); and 150 days post treatment (for PDR001 in combination with LCL161), up to a maximum duration of 50 weeks.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment

	CJM112 50mg Q4W N = 4	**CJM112 100mg Q4W N = 2**	**CJM112 50mg Q4W + PDR001 400mg Q4W N = 6**	**CJM112 100mg Q4W + PDR001 400mg Q4W N = 5**	**LCL161 300mg QW + PDR001 400mg Q4W N = 4**	**LCL161 600mg QW + PDR001 400mg Q4W N = 5**	**All subjects N = 26**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112 n	CJM112 100mg Q4W - Dose escalation of CJM112 n	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination	CJM112 100mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination	All subjects

			with PDR001 fixed dose n	with a fixed dose of PDR001 n	with a fixed dose of PDR001 n	with a fixed dose of PDR001 n	
Total participants affected	2 (50.00%)	1 (50.00%)	4 (66.67%)	1 (20.00%)	3 (75.00%)	1 (20.00%)	12 (46.15%)
General disorders and administration site conditions							
Condition aggravated	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Disease progression	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Infections and infestations							
Respiratory tract infection	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Sepsis	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Upper respiratory tract infection	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Metabolism and nutrition disorders							
Tumour lysis syndrome	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Tumour pain	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Renal and urinary disorders							
Acute kidney injury	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	2 (50.00%)	1 (20.00%)	4 (15.38%)
Renal failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (3.85%)
Renal impairment	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)

Respiratory, thoracic and mediastinal disorders							
Pneumonitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)

Other Adverse Events by System Organ Class

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment (for single agent CJM112); plus 150 days post treatment (for PDR001 in combination with CJM112); and 150 days post treatment (for PDR001 in combination with LCL161), up to a maximum duration of 50 weeks.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	CJM112 50mg Q4W N = 4	**CJM112 100mg Q4W N = 2**	**CJM112 50mg Q4W + PDR001 400mg Q4W N = 6**	**CJM112 100mg Q4W + PDR001 400mg Q4W N = 5**	**LCL161 300mg QW + PDR001 400mg Q4W N = 4**	**LCL161 600mg QW + PDR001 400mg Q4W N = 5**	**All subjects N = 26**
Arm/Group Description	CJM112 50mg Q4W - Dose escalation of CJM112 n	CJM112 100mg Q4W - Dose escalation of CJM112 n	CJM112 50mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with PDR001 fixed dose n	CJM112 100mg Q4W + PDR001 400mg Q4W - Dose escalation of CJM112 in combination with a fixed dose of PDR001 n	LCL161 300mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001 n	LCL161 600mg QW + PDR001 400mg Q4W - Dose escalation of LCL161 in combination with a fixed dose of PDR001 n	All subjects
Total participants affected	4 (100.00%)	1 (50.00%)	6 (100.00%)	5 (100.00%)	2 (50.00%)	5 (100.00%)	23 (88.46%)

Blood and lymphatic system disorders							
Anaemia	1 (25.00%)	1 (50.00%)	2 (33.33%)	0 (0.00%)	1 (25.00%)	2 (40.00%)	7 (26.92%)
Leukopenia	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
Lymphopenia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Neutropenia	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
Pancytopenia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Thrombocytopenia	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	2 (7.69%)
Cardiac disorders							
Cardiac failure	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Eye disorders							
Vision blurred	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Gastrointestinal disorders							
Diarrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	1 (20.00%)	3 (11.54%)
Flatulence	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Nausea	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	1 (25.00%)	1 (20.00%)	4 (15.38%)
Odynophagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Vomiting	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
General disorders and administration site conditions							
Asthenia	1 (25.00%)	1 (50.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	4 (15.38%)
Chills	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Fatigue	0 (0.00%)	0 (0.00%)	2 (33.33%)	1 (20.00%)	0 (0.00%)	1 (20.00%)	4 (15.38%)
Generalised oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)

Oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Infections and infestations							
Clostridium difficile infection	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Cystitis	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Oral herpes	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Pulpitis dental	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Upper respiratory tract infection	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (20.00%)	3 (11.54%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
Injury, poisoning and procedural complications							
Arthropod bite	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Radiation associated pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Investigations							
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (20.00%)	2 (7.69%)
Amylase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (20.00%)	2 (7.69%)

Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (40.00%)	3 (11.54%)
Blood lactate dehydrogenase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Blood triglycerides increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Blood uric acid increased	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Gamma-glutamyltransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Lipase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
White blood cell count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Metabolism and nutrition disorders							
Decreased appetite	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	2 (7.69%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	2 (7.69%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Hyperphosphataemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	2 (7.69%)

Hypokalaemia	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)
Musculoskeletal and connective tissue disorders							
Back pain	1 (25.00%)	0 (0.00%)	2 (33.33%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	5 (19.23%)
Muscle spasms	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (3.85%)
Nervous system disorders							
Ataxia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Memory impairment	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Psychiatric disorders							
Confusional state	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Renal and urinary disorders							
Bladder pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (3.85%)
Reproductive system and breast disorders							
Pelvic pain	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Respiratory, thoracic and mediastinal disorders							
Bronchial obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (20.00%)	2 (7.69%)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Dyspnoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Epistaxis	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)

Oropharyngeal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)
Skin and subcutaneous tissue disorders							
Dry skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (3.85%)
Night sweats	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	2 (7.69%)
Pruritus	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)

Conclusion:

In this study, single agent CJM112 and CJM112 or LCL161 in combination with spartalizumab, was generally well tolerated with no significant safety findings observed at the dose levels that were explored during dose escalation and before study termination. Amongst the patients treated during dose escalation who were evaluable for response, only minimal evidence of clinically meaningful, durable, efficacy was observed in any treatment arm. However as recruitment to the study was halted after only two dose levels were tested in each treatment arm and before determination of the Maximum tolerated dose (MTD)(s)/ Recommended dose (RD)(s), only limited conclusions can be drawn on Overall response rate (ORR) or durability of response. Enrolment was challenging due to the difficulty in identifying patients with relapsed or refractory Multiple myeloma (MM) who had progressive disease stable enough to benefit from Immunomodulatory drugs (IMiD)- and Proteasome inhibitor-free I-O based therapies and taking into consideration the data generated on the study thus far, the decision was taken to terminate the study early.

Date of Clinical Trial Report

27 Oct 2020