NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

CCJM112X2204

Trial Indication(s)

Inadequately controlled moderate to severe asthma

Protocol Number

CCJM112X2204

Protocol Title

A randomized, subject- and investigator-blinded, placebo controlled, multi-center, multiple dose study to assess the efficacy and safety of CJM112 in patients with inadequately controlled moderate to severe asthma

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II

Study Start/End Dates

Study Start Date: November 2017 (Actual)
Primary Completion Date: April 2019 (Actual)
Study Completion Date: July 2019 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a non-confirmatory, randomized, subject- and investigator-blinded, placebo-controlled, multi-center, parallel-arm study evaluating the efficacy of CJM112 on top of standard of care in subjects with inadequately controlled moderate to severe asthma.

After an initial screening visit, run-in period and baseline assessments, the eligible subjects entered the treatment period and were randomized in a 3:2 ratio to one of the two treatment groups:

- 300 mg CJM112 s.c. injection received once per week for the first 4 weeks, followed by once every two weeks up to Week 12 (Day 85) + standard of care treatment.
- Matching placebo + standard of care treatment

After completion of the last dose on Day 85 of treatment period, subjects returned for the final efficacy assessment on Day 92.

Following the treatment period, all subjects entered a 13-week safety follow-up period, including the End of Study visit on Day 176.

Centers

33 centers in 8 countries: United States(8), Belgium(3), Germany(5), France(3), Denmark(4), Israel(3), Argentina(5), Slovakia (Slovak Republic)(2)

Objectives:

Primary objective:

To determine whether treatment with CJM112 in subjects with inadequately controlled moderate to severe asthma leads to an improvement in airflow obstruction, assessed by change from baseline in trough (pre-bronchodilator) FEV1.

Secondary objectives:

- To determine whether treatment with CJM112 in subjects with inadequately controlled moderate to severe asthma leads to an improvement in forced expiratory volume in one second percentage (FEV1%) of predicted
- To determine whether treatment with CJM112 in subjects with inadequately controlled moderate to severe asthma leads to an improvement in asthma control (ACQ)
- To assess the safety and tolerability of CJM112 in subjects with inadequately controlled moderate to severe asthma

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

300 mg CJM112 subcutaneous injection

Placebo to match CJM112 subcutaneous injection

Statistical Methods

The change from baseline in trough (pre-bronchodilator) FEV1 was analyzed using a Bayesian linear repeated measures model. Contrasts for treatment differences and time points were provided together with 80% two-sided credible intervals under Bayesian framework and the posterior probability that the treatment effect better than placebo was derived. Posterior probabilities ≥ 90% were considered as a statistically significant signal of efficacy. Change from baseline in secondary variables (ACQ6 and ACQ7 score and FEV1% of predicted) was analyzed using a repeated measure mixed effects model (MMRM).

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
1. Patients with a physician-diagnosed history of moderate to severe asthma for a period of at least one year prior to screening.
2. Patients on a stable therapy regimen of asthma for at least 3 months prior to screening with at least medium dose inhaled glucocorticoid and at least one additional asthma controller medication (such as inhaled long-acting bronchodilator, leukotriene antagonist, theophylline, stable low dose glucocorticoid, etc).
3. Acceptable and reproducible spirometry with FEV1 ≥ 40 and ≤ 90% of predicted at screening and baseline (re-testing is allowed once).
4. ACQ score ≥ 1.5 at screening and baseline (re-testing is allowed once).
5. Total serum IgE < 150 IU/mL
6. Peripheral blood eosinophils <300/µL

Exclusion Criteria:
1. Previous use of biologics or other concomitant medications within the time periods specified in the SOM/protocol.
2. History of ongoing, chronic, or recurrent moderate or severe infectious disease.
3. Patients who have smoked or inhaled nicotine or tobacco products within the 6 month period prior to Visit 1 or who have a smoking history of greater than 10 pack years.
4. Patients who have had an asthma attack/exacerbation requiring systemic corticosteroids for at least 3 continuous days within 4 weeks prior to screening.
5. Patients who have had a respiratory tract infection or asthma worsening within 4 weeks prior to Visit 1 or during the screening period.
6. Women of child-bearing potential unless they use highly effective methods of contraception during dosing and for 13 weeks after stopping of investigational drug.

Participant Flow Table

Treatment Epoch

	CJM112 300 mg	Placebo	Total
Arm/Group Description	Study treatment	Placebo to CJM112	
Started	70	48	118

Completed	59	44	103
Not Completed	11	4	15
Subject/Guardian Decision	2	0	2
Physician Decision	1	0	1
Adverse Event	8	4	12

Follow-up Epoch

	CJM112 300 mg	Placebo	Total
Arm/Group Description	Study treatment	Placebo to CJM112	
Started	59	44	103
Completed	59	43	102
Not Completed	0	1	1
Subject/Guardian Decision	0	1	1

Baseline Characteristics

	CJM112 300 mg	Placebo	Total
Arm/Group Description	Study treatment	Placebo to CJM112	
Number of Participants [units: participants]	70	48	118

Age Continuous (units: Years) Mean ± Standard Deviation			
	57.1±12.79	55.9±11.62	56.6±12.29
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)			
Female	39	32	71
Male	31	16	47
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)			
Asian	2	0	2
Black or African American	6	1	7
Other	1	0	1
White	61	47	108

Summary of Efficacy

Primary Outcome Result(s)

Change from baseline in Forced Expiratory Volume in one second (FEV1)

(Time Frame: Baseline, Day 92)

	CJM112 300 mg	Placebo
Arm/Group Description	Study treatment	Placebo to CJM112
Number of Participants Analyzed [units: participants]	53	36
Change from baseline in Forced Expiratory Volume in one second (FEV1) (units: Liters) Mean ± Standard Deviation		
	0.043 ± 0.031	0.016 ± 0.030

Statistical Analysis

Groups	CJM112 300 mg, Placebo
Probability	0.7374
Method	Other Bayesian linear repeated measures model
Mean Difference (Net)	0.027
Standard Deviation	0.043
80 % Credible Interval 2-Sided	-0.029 to 0.082

Secondary Outcome Result(s)

Change from baseline in Forced Expiratory Volume 1 (FEV1) % of predicted

(Time Frame: Baseline, Day 92)

	CJM112 300 mg	Placebo
Arm/Group Description	Study treatment	Placebo to CJM112
Number of Participants Analyzed [units: participants]	53	36
Change from baseline in Forced Expiratory Volume 1 (FEV1) % of predicted (units: Percent) Least Squares Mean ± Standard Error		
	1.064 ± 0.914	0.151 ± 1.105

Statistical Analysis

Groups	CJM112 300 mg, Placebo	
P Value	0.263	1-sided p-value; p-value smaller than 0.1 is considered as statistically significant
Method	Mixed Models Analysis	

Mean Difference (Net)	0.913
Standard Error of the mean	1.434
80 % Confidence Interval 2-Sided	-0.939 to 2.766

Change from baseline in Asthma Control Questionnaire 6 (ACQ6) score

(Time Frame: Baseline, Day 92)

	CJM112 300 mg	Placebo
Arm/Group Description	Study treatment	Placebo to CJM112
Number of Participants Analyzed [units: participants]	56	41
Change from baseline in Asthma Control Questionnaire 6 (ACQ6) score (units: units on scale) Least Squares Mean ± Standard Error		
	-0.93 ± 0.09	-0.71 ± 0.11

Statistical Analysis

Groups	CJM112 300 mg, Placebo	
P Value	0.061	1-sided p-value; p-value smaller than 0.1 is considered as statistically significant
Method	Mixed Models Analysis	

Mean Difference (Net)	-0.22
Standard Error of the mean	0.14
80 % Confidence Interval 2-Sided	-0.41 to -0.04

Change from baseline in Asthma Control Questionnaire 7 (ACQ7) score

(Time Frame: Baseline, Day 92)

	CJM112 300 mg	Placebo
Arm/Group Description	Study treatment	Placebo to CJM112
Number of Participants Analyzed [units: participants]	53	36
Change from baseline in Asthma Control Questionnaire 7 (ACQ7) score (units: units on scale) Least Squares Mean ± Standard Error		
	-0.83 ± 0.08	-0.60 ± 0.10

Statistical Analysis

Groups	CJM112 300 mg, Placebo	
P Value	0.040	1-sided p-value; p-value smaller than 0.1 is considered as statistically significant

Method	Mixed Models Analysis
Mean Difference (Net)	-0.23
Standard Error of the mean	0.13
80 % Confidence Interval 2-Sided	-0.40 to -0.06

Percentage of patients with at least 0.5 decrease in ACQ7 score

(Time Frame: Baseline, Day 92)

	CJM112 300 mg	Placebo
Arm/Group Description	Study treatment	Placebo to CJM112
Number of Participants Analyzed [units: participants]	53	36
Percentage of patients with at least 0.5 decrease in ACQ7 score (units: participants) Count of Participants (Not Applicable)		
	38 (71.7%)	19 (52.78%)

Percentage of patients with Adverse Events (AEs) leading to discontinuation of study treatment

(Time Frame: 85 days)

	CJM112 300 mg	Placebo
Arm/Group Description	Study treatment	Placebo to CJM112

Number of Participants Analyzed [units: participants]	70	48
Percentage of patients with Adverse Events (AEs) leading to discontinuation of study treatment (units: Participants) Count of Participants (Not Applicable)		
	8 (11.43%)	4 (8.33%)

Summary of Safety

Safety Results

All-Cause Mortality

	CJM112 300 mg N = 70	**Placebo N = 48**
Arm/Group Description	CJM112 300 mg	Placebo
Total participants affected	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were collected from first dose of study treatment until end of study treatment plus 91 days post treatment, up to maximum duration of 6 months
Additional Description	Any sign or symptom that occurs during the study treatment plus the 91 days post treatment
Source Vocabulary for Table Default	MedDRA (22.0)
Assessment Type for Table Default	Systematic Assessment

	CJM112 300 mg N = 70	**Placebo N = 48**
Arm/Group Description	CJM112 300 mg	Placebo
Total participants affected	3 (4.29%)	2 (4.17%)
Cardiac disorders		
Stress cardiomyopathy	0 (0.00%)	1 (2.08%)
General disorders and administration site conditions		
Asthenia	1 (1.43%)	0 (0.00%)
Infections and infestations		
Pneumonia	0 (0.00%)	1 (2.08%)
Urinary tract infection	1 (1.43%)	0 (0.00%)

Psychiatric disorders		
Depression	1 (1.43%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Asthmatic crisis	1 (1.43%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Adverse events were collected from first dose of study treatment until end of study treatment plus 91 days post treatment, up to maximum duration of 6 months
Additional Description	Any sign or symptom that occurs during the study treatment plus the 91 days post treatment
Source Vocabulary for Table Default	MedDRA (22.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	2%

	CJM112 300 mg N = 70	**Placebo N = 48**
Arm/Group Description	CJM112 300 mg	Placebo
Total participants affected	55 (78.57%)	38 (79.17%)

Cardiac disorders		
Arrhythmia supraventricular	0 (0.00%)	1 (2.08%)
Endocrine disorders		
Hypothyroidism	0 (0.00%)	1 (2.08%)
Gastrointestinal disorders		
Abdominal pain	0 (0.00%)	1 (2.08%)
Constipation	0 (0.00%)	1 (2.08%)
Diarrhoea	3 (4.29%)	3 (6.25%)
Gastrooesophageal reflux disease	2 (2.86%)	1 (2.08%)
Nausea	3 (4.29%)	2 (4.17%)
Proctalgia	0 (0.00%)	1 (2.08%)
Toothache	1 (1.43%)	1 (2.08%)
Vomiting	0 (0.00%)	2 (4.17%)
General disorders and administration site conditions		
Asthenia	0 (0.00%)	1 (2.08%)
Fatigue	4 (5.71%)	3 (6.25%)
Injection site haematoma	1 (1.43%)	1 (2.08%)
Oedema peripheral	1 (1.43%)	1 (2.08%)
Pyrexia	1 (1.43%)	1 (2.08%)
Infections and infestations		
Bronchitis	5 (7.14%)	3 (6.25%)

Conjunctivitis	0 (0.00%)	1 (2.08%)
Cystitis	2 (2.86%)	1 (2.08%)
Gastroenteritis	2 (2.86%)	1 (2.08%)
Gastroenteritis viral	0 (0.00%)	1 (2.08%)
Lower respiratory tract infection	2 (2.86%)	0 (0.00%)
Nasopharyngitis	16 (22.86%)	6 (12.50%)
Oral candidiasis	4 (5.71%)	0 (0.00%)
Oral herpes	0 (0.00%)	1 (2.08%)
Pharyngitis	1 (1.43%)	2 (4.17%)
Respiratory tract infection	2 (2.86%)	1 (2.08%)
Respiratory tract infection viral	2 (2.86%)	1 (2.08%)
Rhinitis	0 (0.00%)	1 (2.08%)
Sinusitis	3 (4.29%)	0 (0.00%)
Tooth abscess	0 (0.00%)	1 (2.08%)
Upper respiratory tract infection	4 (5.71%)	2 (4.17%)
Urinary tract infection	1 (1.43%)	2 (4.17%)
Viral upper respiratory tract infection	2 (2.86%)	1 (2.08%)
Injury, poisoning and procedural complications		
Arthropod sting	0 (0.00%)	1 (2.08%)
Fall	0 (0.00%)	1 (2.08%)
Ligament sprain	0 (0.00%)	1 (2.08%)
Rib fracture	0 (0.00%)	1 (2.08%)

Spinal compression fracture	0 (0.00%)	1 (2.08%)
Subcutaneous haematoma	0 (0.00%)	1 (2.08%)
Investigations		
Alanine aminotransferase increased	0 (0.00%)	2 (4.17%)
Amylase increased	0 (0.00%)	1 (2.08%)
Aspartate aminotransferase increased	0 (0.00%)	1 (2.08%)
Blood alkaline phosphatase increased	0 (0.00%)	1 (2.08%)
Blood bicarbonate decreased	0 (0.00%)	1 (2.08%)
Blood cholesterol increased	1 (1.43%)	1 (2.08%)
Blood creatine phosphokinase increased	1 (1.43%)	1 (2.08%)
Blood creatinine increased	1 (1.43%)	1 (2.08%)
Blood lactate dehydrogenase increased	1 (1.43%)	1 (2.08%)
Blood potassium increased	0 (0.00%)	1 (2.08%)
Blood triglycerides increased	0 (0.00%)	1 (2.08%)

Gamma-glutamyltransferase increased	0 (0.00%)	1 (2.08%)
Lipase increased	0 (0.00%)	1 (2.08%)
Protein urine present	0 (0.00%)	1 (2.08%)
Red blood cell sedimentation rate increased	0 (0.00%)	1 (2.08%)
Metabolism and nutrition disorders		
Gout	0 (0.00%)	1 (2.08%)
Type 2 diabetes mellitus	0 (0.00%)	1 (2.08%)
Musculoskeletal and connective tissue disorders		
Arthralgia	3 (4.29%)	1 (2.08%)
Back pain	3 (4.29%)	5 (10.42%)
Intervertebral disc protrusion	0 (0.00%)	1 (2.08%)
Limb discomfort	2 (2.86%)	0 (0.00%)
Musculoskeletal pain	0 (0.00%)	1 (2.08%)
Musculoskeletal stiffness	0 (0.00%)	1 (2.08%)
Osteoarthritis	0 (0.00%)	2 (4.17%)
Pain in extremity	2 (2.86%)	0 (0.00%)
Nervous system disorders		
Dizziness	4 (5.71%)	0 (0.00%)
Headache	8 (11.43%)	6 (12.50%)
Intercostal neuralgia	0 (0.00%)	1 (2.08%)

Migraine	2 (2.86%)	0 (0.00%)
Sciatica	0 (0.00%)	1 (2.08%)
Psychiatric disorders		
Insomnia	0 (0.00%)	1 (2.08%)
Reproductive system and breast disorders		
Prostatitis	0 (0.00%)	1 (2.08%)
Respiratory, thoracic and mediastinal disorders		
Asthma	16 (22.86%)	13 (27.08%)
Cough	4 (5.71%)	4 (8.33%)
Dysphonia	2 (2.86%)	0 (0.00%)
Dyspnoea	2 (2.86%)	0 (0.00%)
Epistaxis	0 (0.00%)	1 (2.08%)
Haemoptysis	0 (0.00%)	1 (2.08%)
Nasal congestion	0 (0.00%)	1 (2.08%)
Oropharyngeal pain	3 (4.29%)	3 (6.25%)
Skin and subcutaneous tissue disorders		
Rash	1 (1.43%)	3 (6.25%)

Other Relevant Findings

None

Conclusion:

This study was conducted to determine if CJM112, an anti-IL-17A antibody, when added to existing therapy, displays the clinical efficacy and safety profile to support further development in subjects with inadequately controlled moderate to severe asthma with low IgE and low circulating eosinophil levels.
Clinically significant improvement in FEV1 (analyzed by protocol-specified methods) was not observed, which was the primary endpoint of the study. While a statistically significant improvement from baseline of 0.2 units in ACQ6 and ACQ7 was observed between the CJM112 and placebo-treated groups, the difference was small compared to the improvement observed in the placebo arm during the course of treatment.
The safety profile of CJM112 was acceptable for the target population. Incidences of AEs were comparable across both treatment groups. No deaths were reported during the study.
Five subjects (4.2%) had at least one SAE post-screening: 3 subjects (4.3%) from the CJM112 group and 2 subjects (4.2%) from the placebo group. None of the SAEs were considered related to the study treatment.
In conclusion, CJM112 was well-tolerated in the target population. Small changes were observed in FEV1, ACQ6 and ACQ7 after treatment with CJM112.

Date of Clinical Trial Report

03-July-2020