NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

CSJ117

Trial Indication(s)

Asthma

Protocol Number

CCSJ117X2201

Protocol Title

A randomized, subject and investigator-blinded, placebo-controlled, parallel-design, broncho-provocation study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of multiple doses of inhaled CSJ117 in adult subjects with mild atopic asthma

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase I

Study Start/End Dates

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

Reason for Termination (If applicable)

The study was terminated because the study met its stated objectives. The decision for early termination was not based on any safety concerns regarding CSJ117.

Study Design/Methodology

The study was a randomized, subject and investigator-blinded, placebo-controlled, parallel-design, broncho-provocation study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of multiple doses of inhaled CSJ117 in adult subjects with mild atopic asthma

Adult participants with stable mild atopic asthma who exhibited an Early Asthmatic Response (EAR) and Late Asthmatic Response (LAR) to a common inhaled allergen were randomized to receive 4 mg QD (once a day) of inhaled CSJ117 or placebo over 12 weeks of treatment and the following key parameters were assessed:

- The safety and tolerability of CSJ117 by evaluation of Adverse Events (AEs), Severe Adverse Events (SAEs) and other safety parameters.
- The pharmacokinetic (PK) profile of CSJ117 by measurement of total serum concentrations.
- The pharmacodynamics (PD) response to CSJ117 by analysis of the LAR following Allergen Inhalation challenge (AIC) after a 12-week treatment period.

Participants were exposed to an allergen (Allergen Inhalation Challenge (AIC) procedure) at screening, Day 42 and Day 84. Spirometry (FEV1) assessments to evaluate Pharmacodynamics effects were performed before and at: 10min, 20min, 30min, 45min, 60min, 90min, 2h, 3h, 4h, 5h, 6h, 7h post AIC. Two sequential dose cohorts were enrolled for this study:

- Cohort 1: 24 participants (12 active and 12 placebo)
- Cohort 2a: 4 participants (3 active and 1 placebo)

There was only one active dose used in the study, i.e. CSJ117 4 mg used for both Cohort 1 & 2a. The study was terminated after four participants enrolled in Cohort 2a and a total 27 participants completed the study. Participants from both cohorts were pooled for analyses.

For all cohorts, the study consisted of a 35-day screening period, a baseline evaluation; a 12- week treatment period (consisting of a single dose on Day 1, safety evaluation Days 1-3 and commencement of QD dosing on Day 3) and a 30-day follow up period.

Centers

9 centers in 2 countries: Canada(6), Germany(3)

Objectives:

Primary objectives:

- To evaluate the safety and tolerability of multiple dose administration of CSJ117 over 12 weeks in subjects with mild atopic asthma.
- To evaluate the late asthmatic response (LAR) after an allergen inhalation challenge (AIC) on Day 84 in subjects with mild atopic asthma receiving multiple doses of CSJ117 over 12 weeks.
-

Secondary objectives:

- To evaluate the early asthmatic response (EAR) and additional measures of the LAR after an AIC on Day 42 and Day 84 in subjects with mild atopic asthma receiving multiple doses of CSJ117 over 12 weeks.
- To characterize the systemic PK profile of CSJ117 in subjects with mild atopic asthma after administration of multiple inhaled doses.
- To evaluate additional measures of the safety and tolerability of multiple dose administration of CSJ117 over 12 weeks in subjects with mild atopic asthma.
- To evaluate the immunogenicity of multiple dose administration of CSJ117 over 12 weeks in subjects with mild atopic asthma.

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

The investigational drug, CSJ117, was formulated as a PulmoSol powder in hard capsules for inhalation. 4 mg CSJ117 was administered as once daily inhaled dose over 12 weeks. Similarly, Placebo comparator was administered as once daily dose over 12 weeks.

Statistical Methods

The safety analysis set included all subjects that received any study drug.

The PK analysis set included all subjects with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data.

The PD analysis set included all subjects with any available PD data, who received any study drug and experienced no protocol deviations with relevant impact on PD data.

Data for background and demographic variables (age, gender, race and ethnicity) were summarized by treatment.

Primary endpoints analysis:
Two primary endpoints were to evaluate the LAR after an AIC on Day 84.

- LAR Time-adjusted AUC3-7h of percentage fall from pre-AIC FEV1, defined as the area under the curve (AUC) for the time-adjusted percentage fall from pre-AIC FEV1 between 3 and 7 hours after the administration of the AIC at the respective study day the endpoint was derived using the linear trapezoidal rule for the time points 3 to 7 hours (3h, 4h, 5h, 6h & 7h). The resulting AUC3-7h was then time adjusted prior to analysis by dividing by the length of time over which the AUC was calculated.

- LAR Maximum percentage fall from pre-AIC FEV1 between 3 and 7 hours after the administration of the AIC at the respective study day the endpoint was derived as the largest percentage fall (or smallest percentage increase) from pre-AIC FEV1 between 3 and 7 hours after the administration of the AIC.

Secondary Endpoints analysis

- EAR Time-adjusted AUC0-2h of percentage fall from pre-AIC FEV1, defined as the AUC for the time-adjusted percentage fall from pre-AIC FEV1 between 0 and 2 hours after the administration of the AIC at the respective study day the endpoint was derived using the linear trapezoidal rule for the time points 0 to 2 hours (0h, 0.16h, 0.33h, 0.5h, 0.75h, 1h, 1.5h & 2h). The resulting AUC0-2h was then time adjusted prior to analysis by dividing by the length of time over which the AUC was calculated.

- EAR Maximum percentage fall from pre-AIC FEV1 between 0 and 2 hours after the administration of the AIC at the respective study day the endpoint was derived as the largest percentage fall (or smallest percentage increase) from pre-AIC FEV1 between 0 and 2 hours after the administration of the AIC.

- EAR Minimum of the absolute FEV1 (L) between 0 and 2 hours after the administration of the AIC at the respective study day the endpoint was derived as the smallest value of FEV1 between 0 and 2 hours after the administration of the AIC.

- LAR Time-adjusted AUC3-7h of percentage fall from pre-AIC FEV1, defined as the AUC for the time-adjusted percentage fall from pre-AIC FEV1 between 3 and 7 hours after the administration of the AIC at the respective study day the endpoint was derived.

- LAR Maximum percentage fall from pre-AIC FEV1 between 3 and 7 hours after the administration of the AIC at the respective study day the endpoint was derived.

- LAR Minimum of the absolute FEV1 (L) between 3 and 7 hours after the administration of the AIC at the respective study day the endpoint was derived as the smallest value of FEV1 between 3 and 7 hours after the administration of the AIC.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Diagnosis of stable mild atopic asthma, as defined by the American Thoracic Society/ European Respiratory Society statement, who exhibit an early and late asthmatic response to a common inhaled allergen during the screening allergen inhalation challenge.
- Throughout the screening period and at baseline, only infrequent use of inhaled short-acting beta2-agonists (less than or equal to twice weekly) to treat asthma and/or prophylactic use prior to exercise. Inhaled short-acting beta2-agonist must be withheld for 8

hours before spirometry.

Exclusion Criteria:
- Hospitalization or emergency room treatment for acute asthma in the 6 months prior to screening or during the screening period.
- Any worsening or exacerbation of asthma (e.g., an event requiring a change in treatment) in the six weeks before screening or during the screening period.
- A history of any clinically significant chronic pulmonary disease other than mild atopic asthma, including but not limited to COPD, interstitial lung disease or bronchiectasis
- Use of immunosuppressive medications or allergen-specific immunotherapy within 6 months prior to screening.

Participant Flow Table

Overall Study

	CSJ117 4 mg	Placebo	Total
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks	
Started	15	13	28
Safety analysis set	15	13	28
Pharmacokinetics (PK) analysis set	15	0[1]	15
Pharmacodynamics (PD) analysis set	15	13	28
Completed	14	13	27
Not Completed	1	0	1
Physician Decision	1	0	1

[1] PK samples were evaluated only in the participants treated with CSJ117

Baseline Characteristics

	CSJ117 4 mg	Placebo	Total
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks	
Number of Participants [units: participants]	15	13	28
Age Continuous (units: Years) Mean ± Standard Deviation			
	34.1±10.92	34.1±12.59	34.1±11.50
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)			
Female	8	9	17
Male	7	4	11
Race/Ethnicity, Customized (units: Participants)			
Race : American Indian Or Alaska Native	1	0	1
Race : Asian	1	0	1
Race : Other	1	0	1
Race : Unknown	1	0	1
Race : White	11	13	24
Race/Ethnicity, Customized (units: Participants)			
Ethnicity : Hispanic or Latino	3	0	3

Ethnicity : Not Hispanic or Latino	12	13	25

Summary of Efficacy

Primary Outcome Result(s)

Number of adverse events (AEs) and serious adverse events (SAEs)

(Time Frame: 12 weeks treatment + 4 weeks follow up)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	15	13
Number of adverse events (AEs) and serious adverse events (SAEs) (units: Number of Adverse Events)		
Total AEs	51	42
Serious AEs	0	0

Late Asthmatic Response (LAR) as measured by the AUC3-7h for time adjusted percent decrease in Forced Expiratory Volume (FEV1)

(Time Frame: Day 84 at pre-AIC and 3 hours, 4 hours, 5 hours, 6 hours and 7 hours post-AIC)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	13	13
Late Asthmatic Response (LAR) as measured by the AUC3-7h for time adjusted percent decrease in Forced Expiratory Volume (FEV1) (units: Percent) Mean (90% Confidence Interval)		
Day 84	4.20 (0.84 to 7.56)	11.38 (8.04 to 14.73)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo
P Value	0.008
Method	ANCOVA
Mean Difference (Net)	-7.18

90 % Confidence Interval 2-Sided	-11.92 to -2.44

Late Asthmatic Response (LAR) as measured by the maximum percentage decrease in FEV1

(Time Frame: Day 84 at pre-AIC and 3 hours, 4 hours, 5 hours, 6 hours and 7 hours post-AIC)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	13	13
Late Asthmatic Response (LAR) as measured by the maximum percentage decrease in FEV1 (units: Percent) Mean (90% Confidence Interval)		
	9.28 (4.16 to 14.39)	17.70 (12.59 to 22.81)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo
P Value	0.029
Method	ANCOVA

Mean Difference (Net)	-8.42
90 % Confidence Interval 2-Sided	-15.66 to -1.18

Secondary Outcome Result(s)

Early Asthmatic Response (EAR) as measured by the time adjusted AUC0-2h percent decrease in FEV1

(Time Frame: Day 42 and Day 84 at 0 hours, 0.16 hours, 0.33 hours, 0.5 hours, 0.75 hours, 1 hours, 1.5 hours & 2 hours)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	15	13
Early Asthmatic Response (EAR) as measured by the time adjusted AUC0-2h percent decrease in FEV1 (units: Percent) Mean (90% Confidence Interval)		
Day 42 (n=12,11)	15.11 (11.61 to 18.61)	16.14 (12.57 to 19.70)
Day 84 (n=13,13)	12.83 (9.01 to 16.64)	17.09 (13.25 to 20.92)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 42
P Value	0.364	
Method	ANCOVA	
Mean Difference (Net)	-1.02	
90 % Confidence Interval 2-Sided	-6.06 to 4.01	

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 84
P Value	0.097	
Method	ANCOVA	
Mean Difference (Net)	-4.26	
90 % Confidence Interval 2-Sided	-9.72 to 1.21	

Early Asthmatic Response (EAR) as measured by the maximum percentage decrease in FEV1

(Time Frame: Day 42 and Day 84 at 0 hours, 0.16 hours, 0.33 hours, 0.5 hours, 0.75 hours, 1 hours, 1.5 hours & 2 hours)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks

Number of Participants Analyzed [units: participants]	15	13
Early Asthmatic Response (EAR) as measured by the maximum percentage decrease in FEV1 (units: Percent) Mean (90% Confidence Interval)		
Day 42 (n=12,11)	27.85 (21.97 to 33.73)	32.56 (26.57 to 38.54)
Day 84 (n=13,13)	25.48 (20.39 to 30.58)	30.90 (25.80 to 36.00)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 42
P Value	0.172	
Method	ANCOVA	
Mean Difference (Net)	-4.70	
90 % Confidence Interval 2-Sided	-13.10 to 3.69	

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 84
P Value	0.105	
Method	ANCOVA	

Mean Difference (Net)	-5.41
90 % Confidence Interval 2-Sided	-12.62 to 1.79

Early Asthmatic Response (EAR) as measured by the minimum of the absolute in FEV1

(Time Frame: Day 42 and Day 84 at 0 hours, 0.16 hours, 0.33 hours, 0.5 hours, 0.75 hours, 1 hours, 1.5 hours & 2 hours)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	15	13
Early Asthmatic Response (EAR) as measured by the minimum of the absolute in FEV1 (units: Litres) Mean (90% Confidence Interval)		
Day 42 (n=12,11)	2.35 (2.14 to 2.55)	2.20 (1.99 to 2.40)
Day 84 (n=13,13)	2.42 (2.24 to 2.59)	2.25 (2.07 to 2.42)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 42
P Value	0.186	
Method	ANCOVA	

Mean Difference (Net)	0.15
90 % Confidence Interval 2-Sided	-0.14 to 0.45

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 84
P Value	0.130	
Method	ANCOVA	
Mean Difference (Net)	0.17	
90 % Confidence Interval 2-Sided	-0.08 to 0.42	

Late Asthmatic Response (LAR) as measured by the time adjusted AUC3-7h in FEV1

(Time Frame: Day 42 at pre-AIC and 3 hours, 4 hours, 5 hours, 6 hours and 7 hours post-AIC)

	CSJ117 4 mg	**Placebo**
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	12	11
Late Asthmatic Response (LAR) as measured by the time adjusted AUC3-7h in FEV1		

(units: Percent) Mean (90% Confidence Interval)		
	6.46 (3.29 to 9.63)	9.36 (6.14 to 12.58)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo
P Value	0.141
Method	ANCOVA
Mean Difference (Net)	-2.90
90 % Confidence Interval 2-Sided	-7.43 to 1.62

Late Asthmatic Response (LAR) as measured by the maximum percentage decrease in FEV1

(Time Frame: Day 42 at pre-AIC and 3 hours, 4 hours, 5 hours, 6 hours and 7 hours post-AIC)

	CSJ117 4 mg	**Placebo**
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	12	11
Late Asthmatic Response (LAR) as measured by the		

maximum percentage decrease in FEV1 (units: Percent) Mean (90% Confidence Interval)		
	13.11 (8.64 to 17.58)	15.75 (11.20 to 20.29)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo
P Value	0.243
Method	ANCOVA
Mean Difference (Net)	-2.64
90 % Confidence Interval 2-Sided	-9.02 to 3.74

Late Asthmatic Response (LAR) as measured by the minimum absolute FEV1

(Time Frame: Day 42 and Day 84 at pre-AIC and 3 hours, 4 hours, 5 hours, 6 hours and 7 hours post-AIC)

	CSJ117 4 mg	**Placebo**
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	15	13

Late Asthmatic Response (LAR) as measured by the minimum absolute FEV1 (units: Litres) Mean (90% Confidence Interval)		
Day 42 (n=12,11)	2.84 (2.65 to 3.04)	2.75 (2.55 to 2.95)
Day 84 (n=13,13)	2.96 (2.77 to 3.16)	2.69 (2.49 to 2.88)

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 42
P Value	0.293	
Method	ANCOVA	
Mean Difference (Net)	0.09	
90 % Confidence Interval 2-Sided	-0.19 to 0.37	

Statistical Analysis

Groups	CSJ117 4 mg, Placebo	Day 84
P Value	0.050	
Method	ANCOVA	
Mean Difference (Net)	0.27	
90 % Confidence Interval 2-Sided	-0.00 to 0.55	

Measurement of CSJ117 serum concentration and calculation of Tmax at Day 84

(Time Frame: Day 84)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	14	0
Measurement of CSJ117 serum concentration and calculation of Tmax at Day 84 (units: hours) Median (Full Range)		
	4.03 (0.00 to 25.8)	

Measurement of CSJ117 serum concentration and calculation of Cmax at Day 84

(Time Frame: Day 84)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	14	0

Measurement of CSJ117 serum concentration and calculation of Cmax at Day 84 (units: ng/mL) Mean ± Standard Deviation	53.8 ± 40.7

Measurement of CSJ117 serum concentration and calculation of AUCtau at Day 84

(Time Frame: Day 84)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	14	0
Measurement of CSJ117 serum concentration and calculation of AUCtau at Day 84 (units: hr*ng/mL) Mean ± Standard Deviation	1180 ± 906	

Measurement of CSJ117 serum concentration and calculation of Ctrough at Day 84

(Time Frame: Day 84)

	CSJ117 4 mg	Placebo

Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	14	0
Measurement of CSJ117 serum concentration and calculation of Ctrough at Day 84 (units: ng/mL) Mean ± Standard Deviation	49.9 ± 41.0	

Measurement of CSJ117 serum concentration and calculation of Raccmin at Day 84

(Time Frame: Day 84)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	14	0
Measurement of CSJ117 serum concentration and calculation of Raccmin at Day 84 (units: Ratio)		

Mean ± Standard Deviation
19.2 ± 15.0

Measurement of CSJ117 serum concentration and calculation of Lambda_z at Day 84

(Time Frame: Day 84)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	9	0
Measurement of CSJ117 serum concentration and calculation of Lambda_z at Day 84 (units: 1/hr) Mean ± Standard Deviation	0.00652 ± 0.00985	

Measurement of CSJ117 serum concentration and calculation of T1/2 at Day 84

(Time Frame: Day 84)

	CSJ117 4 mg	Placebo
Arm/Group Description	4 mg CSJ117 administered as once daily	placebo comparator administered as once daily

	inhaled dose over 12 weeks	inhaled dose over 12 weeks
Number of Participants Analyzed [units: participants]	9	0
Measurement of CSJ117 serum concentration and calculation of T1/2 at Day 84 (units: days) Mean ± Standard Deviation		
	11.0 ± 7.99	

Summary of Safety

Safety Results

All-Cause Mortality

	CSJ117 4mg N = 15	**Placebo N = 13**
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Total participants affected	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Other Adverse Events by System Organ Class

Time Frame	Adverse events were collected throughout the study which includes the treatment period of 12 weeks and the follow-up period of 4 weeks.
Source Vocabulary for Table Default	MedDRA (22.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	CSJ117 4mg N = 15	**Placebo N = 13**
Arm/Group Description	4 mg CSJ117 administered as once daily inhaled dose over 12 weeks	placebo comparator administered as once daily inhaled dose over 12 weeks
Total participants affected	10 (66.67%)	12 (92.31%)
Blood and lymphatic system disorders		
Lymph node pain	0 (0.00%)	1 (7.69%)
Cardiac disorders		
Tachycardia	0 (0.00%)	1 (7.69%)
Ear and labyrinth disorders		
Ear discomfort	1 (6.67%)	0 (0.00%)

Vertigo	1 (6.67%)	1 (7.69%)
Endocrine disorders		
Thyroid mass	0 (0.00%)	1 (7.69%)
Eye disorders		
Eye swelling	0 (0.00%)	1 (7.69%)
Gastrointestinal disorders		
Abdominal pain	1 (6.67%)	0 (0.00%)
Abdominal pain lower	0 (0.00%)	1 (7.69%)
Abdominal pain upper	2 (13.33%)	0 (0.00%)
Aphthous ulcer	1 (6.67%)	0 (0.00%)
Constipation	0 (0.00%)	1 (7.69%)
Diarrhoea	2 (13.33%)	0 (0.00%)
Nausea	2 (13.33%)	0 (0.00%)
Vomiting	3 (20.00%)	0 (0.00%)
General disorders and administration site conditions		
Chest discomfort	1 (6.67%)	0 (0.00%)
Fatigue	1 (6.67%)	0 (0.00%)
Malaise	1 (6.67%)	0 (0.00%)
Non-cardiac chest pain	1 (6.67%)	0 (0.00%)
Vessel puncture site pain	0 (0.00%)	1 (7.69%)
Immune system disorders		
Allergy to arthropod bite	1 (6.67%)	0 (0.00%)

Infections and infestations		
Bacterial vaginosis	0 (0.00%)	1 (7.69%)
Conjunctivitis	0 (0.00%)	1 (7.69%)
Infected bite	0 (0.00%)	1 (7.69%)
Influenza	0 (0.00%)	1 (7.69%)
Nasopharyngitis	2 (13.33%)	3 (23.08%)
Paronychia	0 (0.00%)	1 (7.69%)
Rhinitis	2 (13.33%)	1 (7.69%)
Tonsillitis	1 (6.67%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	2 (15.38%)
Urinary tract infection	1 (6.67%)	0 (0.00%)
Investigations		
Blood creatine phosphokinase increased	1 (6.67%)	0 (0.00%)
Musculoskeletal and connective tissue disorders		
Back pain	1 (6.67%)	2 (15.38%)
Bone pain	1 (6.67%)	0 (0.00%)
Muscular weakness	1 (6.67%)	0 (0.00%)
Myalgia	1 (6.67%)	0 (0.00%)
Nervous system disorders		
Headache	4 (26.67%)	3 (23.08%)
Migraine	1 (6.67%)	1 (7.69%)

Psychiatric disorders		
Depression	1 (6.67%)	0 (0.00%)
Insomnia	0 (0.00%)	1 (7.69%)
Reproductive system and breast disorders		
Dysmenorrhoea	0 (0.00%)	1 (7.69%)
Respiratory, thoracic and mediastinal disorders		
Cough	2 (13.33%)	2 (15.38%)
Dyspnoea	1 (6.67%)	0 (0.00%)
Oropharyngeal pain	2 (13.33%)	3 (23.08%)
Respiratory tract congestion	1 (6.67%)	0 (0.00%)
Rhinitis allergic	1 (6.67%)	0 (0.00%)
Sneezing	1 (6.67%)	0 (0.00%)
Throat tightness	0 (0.00%)	1 (7.69%)
Skin and subcutaneous tissue disorders		
Pruritus	1 (6.67%)	0 (0.00%)
Rash	0 (0.00%)	1 (7.69%)

Other Relevant Findings

None

Conclusion:

In this study, CSJ117 demonstrated a statistically significant attenuation in the late asthmatic response after an allergen induced challenge (AIC) on Day 84, as measured by the (1) time-adjusted AUC percent fall from pre-AIC in the FEV1 and (2) maximum percent fall from pre-AIC in the FEV1 between 3 and 7 hours after the administration of the AIC. On Day 84, a statistically significant attenuation in the early asthmatic response was observed when measured by maximum % fall, but not when measured by the time adjusted AUC % fall On Day 42, such attenuation was not noted in the late or early asthmatic responses.

CSJ117 at a dose of 4 mg was generally safe and well tolerated by the mild asthmatic subjects enrolled in this study. The number, incidence, and severity of treatment-emergent adverse events were comparable between the treatment groups, although more subjects receiving placebo (92.3%) developed at least one adverse event compared with those receiving in CSJ117 (66.7%). The most frequent treatment-emergent adverse events were headache, nasopharyngitis, and oropharyngeal pain. All events were mild or moderate in severity. No deaths, serious, or severe adverse events occurred. Study drug related four subjects experienced adverse events, out of which three were of mild severity. No clinically relevant changes in the hematology, chemistry, urinalysis, ECG, and spirometry results occurred.

Pharmacokinetics of total CSJ117 appear to be driven by PK-sustaining nature of anti-CSJ117 antibodies. An accumulation ratio (Ctrough Day 84/Day 1) of 19.2 was observed for total CSJ117. Although majority of subjects (13/15) treated with CSJ117 developed CSJ117 anti-drug antibodies, no impact on pharmacodynamics or safety was noted.

CSJ117, the first inhaled anti-TSLP (thymic stromal lymphopoietin), was safe and well tolerated in adult mild asthmatics. It reduced allergen-induced bronchoconstriction. These findings support TSLP's role in allergen-induced airway responses and airway inflammation, and suggest that anti-TSLP may be a promising, new therapeutic class for asthma treatment.

Date of Clinical Trial Report

01 June 2020