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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Ecleralimab (CSJ117)

Trial Indication(s)

Severe uncontrolled asthma

Protocol Number

CCSJ117A12201C

Protocol Title

A 12-week, multicenter, randomized, double-blind, parallel-arm, placebo-controlled study to assess the efficacy and safety of CSJ117, when added to existing asthma therapy in patients ≥ 18 years of age with severe uncontrolled asthma

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2

Study Start/End Dates

Study Start Date: September 09, 2020 (Actual)
Primary Completion Date: July 12, 2022 (Actual)
Study Completion Date: September 06, 2022 (Actual)

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Reason for Termination (If applicable)

Due to deprioritization of the program, the study was terminated early and the study centers were notified by letter on date 14 Jun 2022. There were no safety findings that contributed to this decision.

Study Design/Methodology

This was a randomized, multicenter, multi-national, double-blind, placebo-controlled, parallel-arm study evaluating the effect of 5 dose levels of CSJ117 in adult subjects with inadequately controlled asthma despite medium to high dose inhaled corticosteroid (ICS) plus long-acting beta agonist (LABA).

Subjects were assigned to one of the following six treatment arms/groups in a ratio of 2:1:1:1:2:2:

- Placebo inhaled once daily
- CSJ117 0.5 mg inhaled once daily
- CSJ117 1.0 mg inhaled once daily
- CSJ117 2.0 mg inhaled once daily
- CSJ117 4.0 mg inhaled once daily
- CSJ117 8.0 mg inhaled once daily

The study included:

- A screening period of approximately 2 weeks
- A single blinded placebo run-in period of 4 weeks (extended to 8 weeks for subjects experiencing an asthma exacerbation or respiratory tract infection during the run-in period)
- A double blinded treatment period of 12 weeks.
- A follow-up period of up to 12 weeks, study drug free, following the last dose of study treatment.

Patients who successfully completed 12 weeks of treatment in this study could be offered participation in the Safety Extension Study CCSJ117A12201E1 (NCT04946318).

Centers

116 centers in 15 countries: Japan(12), United States(21), Guatemala(4), Canada(6), Hungary(5), Poland(6), Germany(17), Czech Republic(4), Latvia(5), Belgium(2), Argentina(19), Bulgaria(2), Philippines(5), Russia(6), Slovakia (Slovak Republic)(2)

Objectives:

The primary objective was:

- To characterize the dose-response relationship of five doses of CSJ117 inhaled daily on lung function, compared with placebo, at the end of the 12-week active-treatment period

The secondary objectives were:

- To characterize the dose-response relationship of five doses of CSJ117 inhaled daily on Fractional exhaled Nitric Oxide (FeNO) compared with placebo, during the 12-week active-treatment period
- To assess immunogenicity of five doses of CSJ117 during the study
- To characterize the systemic pharmacokinetic (PK) profile of multiple inhaled daily doses of CSJ117 during the 12-week active-treatment period and the 12-week follow-up period
- To characterize the efficacy of five doses of CSJ117 once daily, compared with placebo, on peak expiratory flow (PEF) (AM and PM), as assessed by mean morning and mean evening PEF over the 12-week active-treatment period
- To characterize the efficacy of five doses of CSJ117 once daily, compared with placebo, on Asthma Control Questionnaire-5 (ACQ-5) over the 12-week active-treatment period

- To characterize the efficacy of five doses of CSJ117 once daily, compared with placebo, on change from baseline in Asthma Quality of Life Questionnaire (AQLQ) score at the end of the 12-week active-treatment period
- To characterize the efficacy of five doses of CSJ117 once daily, compared with placebo, on daytime and nighttime asthma symptoms over the 12-week active-treatment period
- To characterize the efficacy of five doses of CSJ117 once daily, compared with placebo, on daily short-acting β-agonist (SABA) use over the 12-week active-treatment period
- To assess the safety of five doses of CSJ117 once daily, compared with placebo, with respect to AEs, electrocardiograms (ECGs), vital signs and laboratory tests

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

During the single blinded placebo run-in period, patients received placebo inhaled once daily (in the morning) for 4 weeks. Placebo dosing could be extended to 8 weeks in case of asthma exacerbation or respiratory tract infection during this period.

During the double blinded treatment period, patients were randomized to one of the following six treatment arms/groups in a ratio of 2:1:1:1:2:2: placebo, CSJ117 0.5 mg, CSJ117 1.0 mg, CSJ117 2.0 mg, CSJ117 4.0 mg and CSJ117 8.0 mg. CSJ117 and matching placebo were inhaled once daily (in the morning) for 12 weeks.

CSJ117 and matching placebo were provided as powder filled capsules with a Concept1 inhalation device.

All CSJ117 doses and matching placebo were prepared for a single inhalation.

Statistical Methods

The analysis of all efficacy variables was based on the full analysis set (FAS) and the analysis of all safety variables was based on the Safety Set.

The full analysis set (FAS) comprised of subjects to whom double-blind treatment had been assigned and who received at least one dose of double-blind treatment. Subjects were analyzed according to the treatment they had been assigned to during the randomization procedure.

The Safety Set included all subjects who received at least one dose of double-blind treatment. Subjects were analyzed according to the treatment they received, where treatment received was defined as the randomized/assigned treatment if the participant took at least one dose of that treatment or the first treatment received if the randomized/assigned treatment was never received.

Primary efficacy endpoint analysis:

The Multiple comparison procedures modelling (MCP-Mod) methodology was used on the primary endpoint of the average change from baseline in pre-dose forced expiratory volume in 1 second (FEV1) at Week 8 and Week 12 to address the primary objective.

The adjusted mean responses at each individual dose were estimated by modeling the primary endpoint using a mixed effects model for repeated measures (MMRM). The null hypothesis of flat dose response (DR) relationship was tested at a two-sided significance level of 5% against the alternative hypothesis of a non-constant DR curve using a multiple contrast test, taking model uncertainty into account by considering a wide range of possible DR relationships. Once the DR signal was declared, the final DR curve was estimated by model averaging. Corresponding 95% confidence intervals were obtained using bootstrapping.

Secondary efficacy endpoints analyses:

The following secondary efficacy endpoints were analyzed using MMRM: average change from baseline in FeNO, ACQ-5, and AQLQ+12 at Week 8 and Week 12. No multiplicity adjustment was carried out for analyses of secondary endpoint. In addition, the treatment effect of CSJ117 compared to placebo that would have been observed had all subjects remained on their assigned treatment were estimated. Only on-treatment data were used.

The change from baseline in Asthma Daytime Symptom Diary (ADSD) and Asthma Nighttime Symptom Diary (ANSD) score at Week 8 and Week 12, change from baseline in morning and evening PEF at Week 12 and change from baseline in number of puffs of SABA taken per day at Week 12 were summarized with descriptive statistics.

Safety analyses:

Treatment-emergent adverse events were summarized.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Diagnosed asthma
- Male and female patients aged ≥18 and ≤75 years
- Patients who have been treated with medium or high dose ICS plus LABA with up to 2 additional controllers
- Morning pre-BD FEV1 value of ≥ 40% and ≤ 85% of the predicted normal
- A positive reversibility test
- ACQ-5 score of ≥ 1.5 at screening and end of run-in visits.

Exclusion Criteria:

- Patients who have a cigarette smoking history of greater than 10 pack years or current smokers
- Pregnant or nursing (lactating) women
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using specified methods of contraception during dosing of study drug and until 12 weeks after last study drug treatment
- Patients with a history of immunodeficiency disease or hepatitis B, untreated and not cured hepatitis C or HIV.

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Participant Flow Table

Overall Study

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo	Total
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily	
Started	36	37	37	76	74	75	335
Completed	32	32	35	69	71	65	304
Not Completed	4	5	2	7	3	10	31
Study terminated by sponsor	1	3	2	6	3	4	19
Adverse Event	1	0	0	0	0	2	3
Lost to Follow-up	0	1	0	0	0	0	1
Physician Decision	0	1	0	0	0	0	1
Pregnancy	0	0	0	0	0	1	1
Protocol deviation	0	0	0	0	0	2	2
Subject decision	2	0	0	1	0	1	4

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Baseline Characteristics

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo	Total
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily	
Number of Participants [units: participants]	36	37	37	76	74	75	335
Baseline Analysis Population Description							
Age, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)							
18 - <40 years	9	6	8	16	10	19	68
40 - <65 years	23	26	23	50	50	41	213
≥65 years	4	5	6	10	14	15	54
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation							
	49.8±12.89	51.2±12.09	51.4±13.31	50.3±12.80	52.7±12.22	51.5±13.46	51.3±12.76
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)							
Female	27	25	21	43	48	45	209
Male	9	12	16	33	26	30	126
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)							

Asian	8	8	7	17	16	17	73
American Indian or Alaska Native	1	3	0	1	1	3	9
Black or African American	1	0	0	2	5	2	10
White	26	26	30	56	52	53	243

Primary Outcome Result(s)

Average change from baseline in pre-dose FEV1 at Week 8 and Week 12

Description	FEV1 (forced expiratory volume in one second) is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing. Pre-dose FEV1 is defined as average of the two FEV1 measurements taken at approximately 45 minutes and 15 minutes prior to dosing. The baseline pre-dose FEV1 value is defined as the average of the values taken approximately 2 hours 45 minutes and 2 hours 15 minutes prior to the first dose of double-blind treatment at Day 1. The least-squares means for change from baseline in pre-dose FEV1 averaged between Week 8 and Week 12 visits for each individual dose group were obtained from a linear mixed effects model for repeated measures (MMRM). A positive average change from baseline in pre-dose FEV1 is considered a favorable outcome.
Time Frame	Baseline, Weeks 8-12
Analysis Population Description	Full Analysis Set (FAS). The FAS included all participants to whom double-blind treatment had been assigned and who received at least one dose of double-blind treatment.

	CSJ117 0.5mg	**CSJ117 1mg**	**CSJ117 2mg**	**CSJ117 4mg**	**CSJ117 8mg**	**Placebo**
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	36	37	37	76	74	75
Average change from baseline in pre-dose FEV1 at Week 8 and Week 12 (units: liters (L))	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**

Average of Week 8 and Week 12	0.173 ± 0.0445	0.109 ± 0.0446	0.116 ± 0.0419	0.060 ± 0.0299	0.043 ± 0.0305	0.051 ± 0.0309

Statistical Analysis

Groups	CSJ117 0.5mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.025	
Method	Other MMRM	
Other Least Squares mean	0.122	Treatment difference (CSJ117-placebo)
Standard Error of the mean	0.0541	
95 % Confidence Interval 2-Sided	0.016 to 0.229	

Statistical Analysis

Groups	CSJ117 1mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.286	
Method	Other MMRM	
Other Least Squares mean	0.058	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.0542	
95 % Confidence Interval 2-Sided	-0.049 to 0.165	

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Statistical Analysis

Groups	CSJ117 2mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.212	
Method	Other MMRM	
Other Least Squares mean	0.065	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.0521	
95 % Confidence Interval 2-Sided	-0.037 to 0.168	

Statistical Analysis

Groups	CSJ117 4mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.831	
Method	Other MMRM	
Other Least Squares mean	0.009	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.0430	
95 % Confidence Interval 2-Sided	-0.076 to 0.094	

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Statistical Analysis

Groups	CSJ117 8mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.852	
Method	Other MMRM	
Other Least Squares mean	-0.008	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.0434	
95 % Confidence Interval 2-Sided	-0.094 to 0.077	

Secondary Outcome Result(s)

Average change from baseline in FeNO at Week 8 and Week 12

Description	Fractional exhaled Nitric Oxide (FeNO) pre-dose measurements were done at the investigational sites prior to spirometry assessments. FeNO is defined as the mean of two serial measurements. The measurement of exhaled nitric oxide is widely accepted as a non-invasive marker of airway inflammation (inflammation leads to elevation of FeNO). The baseline FeNO pre-dose measurements were taken at the end of the run-in period. The least-squares means for change from baseline in FeNO averaged between Week 8 and Week 12 visits for each individual dose group were obtained from a linear mixed effects model for repeated measures (MMRM). A negative average change from baseline in FeNO is considered a favorable outcome.
Time Frame	Baseline, Weeks 8-12
Analysis Population Description	Full Analysis Set

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	36	37	37	76	74	75
Average change from baseline in FeNO at Week 8 and Week 12 (units: parts per billion (ppb))	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Average of Week 8 and Week 12	-2.869 ± 1.9670	-5.299 ± 1.9872	-4.190 ± 1.8760	-1.587 ± 1.3312	-0.208 ± 1.3248	-1.301 ± 1.3142

Statistical Analysis

Groups	CSJ117 0.5mg, Placebo
Type of Statistical Test	Superiority
P Value	0.508
Method	Other MMRM
Other Least Squares mean	-1.568
Standard Error of the mean	2.3630
95 % Confidence Interval 2-Sided	-6.219 to 3.083

Treatment difference (CSJ117-placebo)

Statistical Analysis

Groups	CSJ117 1mg, Placebo
Type of Statistical Test	Superiority

P Value	0.095	
Method	Other MMRM	
Other Least Squares mean	-3.998	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	2.3840	
95 % Confidence Interval 2-Sided	-8.691 to 0.695	

Statistical Analysis

Groups	CSJ117 2mg, Placebo
Type of Statistical Test	Superiority
P Value	0.209
Method	Other MMRM
Other Least Squares mean	-2.889
Standard Error of the mean	2.2943
95 % Confidence Interval 2-Sided	-7.405 to 1.627

Statistical Analysis

Groups	CSJ117 4mg, Placebo
Type of Statistical Test	Superiority
P Value	0.878

Method	Other MMRM	
Other Least Squares mean	-0.287	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	1.8718	
95 % Confidence Interval 2-Sided	-3.971 to 3.398	

Statistical Analysis

Groups	CSJ117 8mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.558	
Method	Other MMRM	
Other Least Squares mean	1.093	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	1.8652	
95 % Confidence Interval 2-Sided	-2.578 to 4.765	

Change from baseline in morning PEF at Week 12

Description	PEF (Peak Expiratory Flow) is a person's maximum speed of expiration. All participants were instructed to record PEF twice daily before taking any medication using an electronic peak expiratory flow device (eDiary/ePEF), once in the morning and once approximately 12 hours later in the evening at home. At each timepoint, the participant was instructed to perform 3 consecutive manoeuvres within 10 minutes. These PEF values were captured in the eDiary/ePEF. Mean morning and evening PEF values were calculated by weekly intervals. The baseline values of PEF were the mean values in the run-in period. A positive change from baseline in PEF is considered a favorable outcome.
Time Frame	Baseline, Week 12

Analysis Population Description	Participants in the Full Analysis Set with a valid measurement for the outcome measure

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	31	33	32	65	66	61
Change from baseline in morning PEF at Week 12 (units: liters/minute)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	-0.9785 ± 22.73169	-1.7035 ± 28.83957	18.9496 ± 50.09045	-0.0319 ± 33.56218	3.5702 ± 37.05293	-2.2060 ± 24.56187

Change from baseline in evening PEF at Week 12

Description	PEF (Peak Expiratory Flow) is a person's maximum speed of expiration. All participants were instructed to record PEF twice daily before taking any medication using an electronic peak expiratory flow device (eDiary/ePEF), once in the morning and once approximately 12 hours later in the evening at home. At each timepoint, the participant was instructed to perform 3 consecutive manoeuvres within 10 minutes. These PEF values were captured in the eDiary/ePEF. Mean morning and evening PEF values were calculated by weekly intervals. The baseline values of PEF were the mean values in the run-in period. A positive change from baseline in PEF is considered a favorable outcome.
Time Frame	Baseline, Week 12
Analysis Population Description	Participants in the Full Analysis Set with a valid measurement for the outcome measure

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily

Number of Participants Analyzed [units: participants]	29	30	31	59	62	58
Change from baseline in evening PEF at Week 12 (units: liters/minute)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	-5.3894 ± 29.13968	-7.8709 ± 29.06055	14.0265 ± 44.90062	0.3893 ± 30.47064	2.6905 ± 32.27860	-3.2785 ± 22.93816

Average change from baseline in ACQ-5 score at Week 8 and Week 12

Description	The Asthma Control Questionnaire-5 (ACQ-5) is a five-item, self-completed questionnaire, which is used as a measure of asthma symptom control. Patients were asked to recall how their asthma had been during the previous week and to respond to the symptom questions on a 7-point scale (0=no impairment, 6=maximum impairment). The questions are equally weighted and the overall ACQ-5 score is the mean of all 5 questions, therefore between 0 (totally controlled) and 6 (severely uncontrolled). The baseline values of ACQ-5 were collected at the end of the run-in period. The least-squares means for change from baseline in ACQ-5 score averaged between Week 8 and Week 12 visits for each individual dose group were obtained from a linear mixed effects model for repeated measures (MMRM). A negative change from baseline in ACQ-5 is considered a favorable outcome.
Time Frame	Baseline, Weeks 8-12
Analysis Population Description	Full Analysis Set

	CSJ117 0.5mg	**CSJ117 1mg**	**CSJ117 2mg**	**CSJ117 4mg**	**CSJ117 8mg**	**Placebo**
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	36	37	37	76	74	75
Average change from baseline in ACQ-5 score at Week 8 and Week 12 (units: score on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Average of Week 8 and Week 12	-0.764 ± 0.1230	-1.142 ± 0.1225	-1.011 ± 0.1171	-0.739 ± 0.0824	-0.837 ± 0.0829	-0.722 ± 0.0846

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Statistical Analysis

Groups	CSJ117 0.5mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.780	
Method	Other MMRM	
Other Least Squares mean	-0.042	Treatment difference (CSJ117-placebo)
Standard Error of the mean	0.1493	
95 % Confidence Interval 2-Sided	-0.336 to 0.252	

Statistical Analysis

Groups	CSJ117 1mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.005	
Method	Other MMRM	
Other Least Squares mean	-0.420	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.1489	
95 % Confidence Interval 2-Sided	-0.713 to -0.127	

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Statistical Analysis

Groups	CSJ117 2mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.047	
Method	Other MMRM	
Other Least Squares mean	-0.289	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.1446	
95 % Confidence Interval 2-Sided	-0.573 to 0.004	

Statistical Analysis

Groups	CSJ117 4mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.887	
Method	Other MMRM	
Other Least Squares mean	-0.017	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.1182	
95 % Confidence Interval 2-Sided	-0.249 to 0.216	

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Statistical Analysis

Groups	CSJ117 8mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.333	
Method	Other MMRM	
Other Least Squares mean	-0.115	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.1184	
95 % Confidence Interval 2-Sided	-0.348 to 0.118	

Average change from baseline in AQLQ+12 score at Week 8 and Week 12

Description	The Asthma Quality of Life Questionnaire+12 (AQLQ+12) is a disease specific questionnaire, which is used as a measure of health-related quality of life. The AQLQ+12 comprises a total of 32 individual questions that span a total of 4 domains: symptoms, activity limitation, emotional function, and environmental stimuli. Patients are asked to recall their experiences during the previous 2 weeks and to score each item on a 7-point scale (7 = not at all impaired to 1 = severely impaired). The overall AQLQ+12 score is the mean of all 32 individual responses, therefore between 7 and 1 with higher scores indicating less impairment in health-related quality of life. The baseline values of AQLQ+12 were collected at the end of the run-in period. The least-squares means for change from baseline in AQLQ+12 score averaged between Week 8 and Week 12 visits were obtained from a linear mixed effects model for repeated measures (MMRM). A positive change from baseline is considered a favorable outcome.
Time Frame	Baseline, Weeks 8-12
Analysis Population Description	Full Analysis Set

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily

Number of Participants Analyzed [units: participants]	36	37	37	76	74	75
Average change from baseline in AQLQ+12 score at Week 8 and Week 12 (units: score on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Average of Week 8 and Week 12	0.467 ± 0.1223	0.781 ± 0.1220	0.642 ± 0.1177	0.597 ± 0.0828	0.636 ± 0.0826	0.564 ± 0.0842

Statistical Analysis

Groups	CSJ117 0.5mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.515	
Method	Other MMRM	
Other Least Squares mean	-0.097	Treatment difference (CSJ117-placebo)
Standard Error of the mean	0.1485	
95 % Confidence Interval 2-Sided	-0.389 to 0.195	

Statistical Analysis

Groups	CSJ117 1mg, Placebo
Type of Statistical Test	Superiority
P Value	0.143
Method	Other MMRM

Other Least Squares mean	0.218	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.1484	
95 % Confidence Interval 2-Sided	-0.074 to 0.510	

Statistical Analysis

Groups	CSJ117 2mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.590	
Method	Other MMRM	
Other Least Squares mean	0.078	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.1450	
95 % Confidence Interval 2-Sided	-0.207 to 0.364	

Statistical Analysis

Groups	CSJ117 4mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.778	
Method	Other MMRM	
Other Least Squares mean	0.033	Treatment difference (CCSJ117-placebo)

Standard Error of the mean	0.1180	
95 % Confidence Interval 2-Sided	-0.199 to 0.265	

Statistical Analysis

Groups	CSJ117 8mg, Placebo	
Type of Statistical Test	Superiority	
P Value	0.539	
Method	Other MMRM	
Other Least Squares mean	0.073	Treatment difference (CCSJ117-placebo)
Standard Error of the mean	0.1180	
95 % Confidence Interval 2-Sided	-0.160 to 0.305	

Change from baseline in ADSD score at Week 8 and Week 12

Description	Asthma Daytime Symptom Diary (ADSD) and Asthma Nighttime Symptom Diary (ANSD) are patient reported outcome measures of asthma symptom severity. Patients recorded asthma symptoms twice daily in the eDiary. Severity of daytime asthma symptoms were assessed before going to bed and severity of nighttime symptoms upon waking. Both diaries comprised of 6 items assessing breathing symptoms (difficulty breathing, wheezing, and shortness of breath), chest symptoms (chest tightness and chest pain), and cough symptoms (cough). All items were assessed using an 11-point numeric rating scale ranging from 0 ('None') to 10 ('As bad as you can imagine'). The overall score is the mean of all 6 individual responses, therefore between 0 and 10 with higher scores indicating more severe symptoms. Mean daily scores of both diaries were calculated by weekly intervals. The baseline values were defined as the average score during the run-in period. A negative change from baseline is a favorable outcome.
Time Frame	Baseline, Week 8 and Week 12
Analysis Population Description	Participants in the Full Analysis Set with a valid measurement for the outcome measure at each timepoint

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	33	33	37	73	72	67
Change from baseline in ADSD score at Week 8 and Week 12 (units: score on a scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 8 (n=33,33,37,73,72,67)	-0.24 ± 0.678	-0.42 ± 0.622	-0.35 ± 0.773	-0.32 ± 0.555	-0.33 ± 0.787	-0.25 ± 0.580
Week 12 (n=32,32,32,68,65,64)	-0.29 ± 0.752	-0.59 ± 0.938	-0.38 ± 0.687	-0.33 ± 0.581	-0.35 ± 0.820	-0.37 ± 0.754

Change from baseline in ANSD score at Week 8 and Week 12

Description	Asthma Daytime Symptom Diary (ADSD) and Asthma Nighttime Symptom Diary (ANSD) are patient reported outcome measures of asthma symptom severity. Patients recorded asthma symptoms twice daily in the eDiary. Severity of daytime asthma symptoms were assessed before going to bed and severity of nighttime symptoms upon waking. Both diaries comprised of 6 items assessing breathing symptoms (difficulty breathing, wheezing, and shortness of breath), chest symptoms (chest tightness and chest pain), and cough symptoms (cough). All items were assessed using an 11-point numeric rating scale ranging from 0 ('None') to 10 ('As bad as you can imagine'). The overall score is the mean of all 6 individual responses, therefore between 0 and 10 with higher scores indicating more severe symptoms. Mean daily scores of both diaries were calculated by weekly intervals. The baseline values were defined as the average score during the run-in period. A negative change from baseline is a favorable outcome.
Time Frame	Baseline, Week 8 and Week 12
Analysis Population Description	Participants in the Full Analysis Set with a valid measurement for the outcome measure at each timepoint

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	34	34	37	74	72	69

Change from baseline in ANSD score at Week 8 and Week 12 (units: score on a scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 8 (n=33,34,37,74,72,69)	-0.15 ± 0.637	-0.35 ± 0.629	-0.30 ± 0.760	-0.27 ± 0.547	-0.26 ± 0.753	-0.25 ± 0.634
Week 12 (n=34,33,35,70,69,66)	-0.19 ± 0.480	-0.46 ± 0.868	-0.29 ± 0.695	-0.26 ± 0.590	-0.23 ± 0.769	-0.33 ± 0.729

Change from baseline in number of puffs of SABA taken per day at Week 12

Description	Participants were given a short acting β2-agonist (SABA) such as salbutamol (100 µg) or albuterol (90 µg) to use as rescue medication throughout the study. Participants recorded in the eDiary, once in the morning and once in the evening, the use of rescue medication (number of puffs of SABA taken in the previous 12 hours). The total number of puffs of SABA taken per day was calculated and the mean daily use of puffs of SABA was derived by weekly intervals. The baseline value of number of puffs of SABA taken per day is the average of total daily SABA use during the run-in period. A negative change from baseline is considered a favorable outcome.
Time Frame	Baseline, Week 12
Analysis Population Description	Participants in the Full Analysis Set with a valid measurement for the outcome measure

	CSJ117 0.5mg	**CSJ117 1mg**	**CSJ117 2mg**	**CSJ117 4mg**	**CSJ117 8mg**	**Placebo**
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	34	33	35	70	70	68
Change from baseline in number of puffs of SABA taken per day at Week 12 (units: puffs of SABA per day)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	-0.2189 ± 0.72340	-0.4548 ± 0.88125	-0.3420 ± 0.68267	-0.4310 ± 0.80279	-0.3766 ± 0.98070	-0.3543 ± 0.78420

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Number of participants with on-treatment adverse events (AEs) and serious adverse events (SAEs) during the on-treatment period

Description	Number of participants with AEs and SAEs, including asthma exacerbations, changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs during the on-treatment period. The on-treatment period is between the date of first dose of double-blind study treatment and date of the last dose of randomized study treatment. Grades to characterize the severity of the adverse events were based on the Common Terminology Criteria for Adverse Events (CTCAE). For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE. The number of participants in each category is reported in the table.
Time Frame	From first dose of double-blind study treatment up to last dose (Week 12)
Analysis Population Description	Safety Analysis Set defined as participants who received at least one dose of double-blind treatment.

	CSJ117 0.5mg	CSJ117 1mg	CSJ117 2mg	CSJ117 4mg	CSJ117 8mg	Placebo
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	36	37	37	76	74	75
Number of participants with on-treatment adverse events (AEs) and serious adverse events (SAEs) (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
At least one AE	12 (33.33%)	10 (27.03%)	13 (35.14%)	22 (28.95%)	25 (33.78%)	23 (30.67%)
Mild AEs	5 (13.89%)	8 (21.62%)	6 (16.22%)	9 (11.84%)	13 (17.57%)	13 (17.33%)
Moderate AEs	6 (16.67%)	2 (5.41%)	7 (18.92%)	12 (15.79%)	12 (16.22%)	10 (13.33%)
Severe AEs	1 (2.78%)	0 (%)	0 (%)	1 (1.32%)	0 (%)	0 (%)

Study treatment-related AEs	0 (%)	1 (2.7%)	1 (2.7%)	2 (2.63%)	4 (5.41%)	2 (2.67%)
SAEs	1 (2.78%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (1.33%)
AEs leading to discontinuation	1 (2.78%)	0 (%)	0 (%)	0 (%)	0 (%)	2 (2.67%)

Number of participants with anti-CSJ117 antibodies

Description	Immunogenicity (antibody formation against CSJ117) was evaluated in serum by a validated bridging electrochemiluminescence immunoassay (ECLIA).
Time Frame	Day 1 and Weeks 2, 4, 8, 12, 14, 16, 20 and 24
Analysis Population Description	Participants in the Safety Analysis Set with a valid measurement for the outcome measure. Safety Analysis Set is defined as participants who received at least one dose of double-blind treatment. The number analyzed per row represents participants with data at the corresponding time point.

	CSJ117 0.5mg	**CSJ117 1mg**	**CSJ117 2mg**	**CSJ117 4mg**	**CSJ117 8mg**	**Placebo**
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily	Placebo inhaled once daily
Number of Participants Analyzed [units: participants]	36	36	37	76	74	75
Number of participants with anti-CSJ117 antibodies (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Day 1 : Negative (n=36,36,37,76,74,75)	30 (83.33%)	33 (91.67%)	31 (83.78%)	66 (86.84%)	63 (85.14%)	63 (84%)
Day 1 : Positive (n=36,36,37,76,74,75)	6 (16.67%)	3 (8.33%)	6 (16.22%)	10 (13.16%)	11 (14.86%)	12 (16%)
Week 2 : Negative (n=35,35,37,75,74,69)	27 (77.14%)	31 (88.57%)	31 (83.78%)	65 (86.67%)	64 (86.49%)	56 (81.16%)

Week 2 : Positive (n=35,35,37,75,74,69)	8 (22.86%)	4 (11.43%)	6 (16.22%)	10 (13.33%)	10 (13.51%)	13 (18.84%)
Week 4 : Negative (n=33,35,37,74,71,71)	26 (78.79%)	29 (82.86%)	26 (70.27%)	49 (66.22%)	47 (66.2%)	57 (80.28%)
Week 4 : Positive (n=33,35,37,74,71,71)	7 (21.21%)	6 (17.14%)	11 (29.73%)	25 (33.78%)	24 (33.8%)	14 (19.72%)
Week 8 : Negative (n=34,33,37,72,72,67)	17 (50%)	16 (48.48%)	10 (27.03%)	22 (30.56%)	18 (25%)	58 (86.57%)
Week 8 : Positive (n=34,33,37,72,72,67)	17 (50%)	17 (51.52%)	27 (72.97%)	50 (69.44%)	54 (75%)	9 (13.43%)
Week 12 : Negative (n=33,33,35,71,71,66)	9 (27.27%)	11 (33.33%)	5 (14.29%)	19 (26.76%)	11 (15.49%)	53 (80.3%)
Week 12 : Positive (n=33,33,35,71,71,66)	24 (72.73%)	22 (66.67%)	30 (85.71%)	52 (73.24%)	60 (84.51%)	13 (19.7%)
Week 14 : Negative (n=26,25,29,59,52,56)	7 (26.92%)	6 (24%)	3 (10.34%)	13 (22.03%)	6 (11.54%)	49 (87.5%)
Week 14 : Positive (n=26,25,29,59,52,56)	19 (73.08%)	19 (76%)	26 (89.66%)	46 (77.97%)	46 (88.46%)	7 (12.5%)
Week 16 : Negative (n=26,25,29,58,53,56)	7 (26.92%)	8 (32%)	3 (10.34%)	12 (20.69%)	7 (13.21%)	49 (87.5%)
Week 16 : Positive (n=26,25,29,58,53,56)	19 (73.08%)	17 (68%)	26 (89.66%)	46 (79.31%)	46 (86.79%)	7 (12.5%)
Week 20 : Negative (n=26,25,29,58,53,55)	9 (34.62%)	9 (36%)	6 (20.69%)	13 (22.41%)	6 (11.32%)	47 (85.45%)
Week 20 : Positive (n=26,25,29,58,53,55)	17 (65.38%)	16 (64%)	23 (79.31%)	45 (77.59%)	47 (88.68%)	8 (14.55%)
Week 24 : Negative (n=26,25,28,56,53,56)	11 (42.31%)	10 (40%)	5 (17.86%)	13 (23.21%)	8 (15.09%)	49 (87.5%)
Week 24 : Positive (n=26,25,28,56,53,56)	15 (57.69%)	15 (60%)	23 (82.14%)	43 (76.79%)	45 (84.91%)	7 (12.5%)

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CSJ117 serum concentration

Description	CSJ117 concentration was determined in serum by a validated immunoassay method. Concentrations below the lower limit of quantification (LLOQ) were treated as “zero”.
Time Frame	Day 1 and Week 12: pre-dose, 2 and 4 hours post-dose; Weeks 2, 4 and 8: pre-dose and 4 hours post-dose; Weeks 14, 16, 20 and 24: pre-dose
Analysis Population Description	Participants in the PK set with a valid measurement for the outcome measure. PK set is defined as participants with at least one evaluable drug concentration data sample. The number analyzed per row represents participants with data at the corresponding time point.

	CSJ117 0.5mg	**CSJ117 1mg**	**CSJ117 2mg**	**CSJ117 4mg**	**CSJ117 8mg**
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 8 mg inhaled once daily
Number of Participants Analyzed [units: participants]	36	37	37	75	74
CSJ117 serum concentration (units: ng/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Day 1, pre-dose (n=36,37,36,74,73)	0.00 ± 0.00	0.00 ± 0.00	1.34 ± 8.02	0.00 ± 0.00	0.00 ± 0.00
Day 1, 2 hours post-dose (n=36,37,37,74,74)	0.00 ± 0.00	0.00 ± 0.00	1.86 ± 7.36	0.00 ± 0.00	0.157 ± 0.947
Day 1, 4 hours post-dose (n=36,37,37,74,73)	0.00 ± 0.00	0.00 ± 0.00	1.97 ± 7.90	0.214 ± 1.33	0.924 ± 2.58
Week 2, pre-dose (n=35,35,37,75,74)	0.320 ± 1.89	0.00 ± 0.00	2.32 ± 8.57	2.00 ± 4.74	6.58 ± 7.61
Week 2, 2 hours post-dose (n=36,34,37,73,74)	0.389 ± 2.30	0.00 ± 0.00	2.20 ± 8.05	1.66 ± 3.51	7.66 ± 7.83
Week 4, pre-dose (n=33,35,36,74,70)	0.336 ± 1.93	0.00 ± 0.00	2.89 ± 9.03	2.86 ± 5.11	12.0 ± 19.5
Week 4, 2 hours post-dose (n=33,34,37,74,69)	0.467 ± 2.68	0.00 ± 0.00	3.19 ± 9.01	3.59 ± 5.69	13.8 ± 22.2
Week 8, pre-dose (n=33,33,37,72,71)	1.69 ± 4.34	3.15 ± 6.50	6.79 ± 12.0	11.5 ± 15.8	39.3 ± 51.0

Week 8, 2 hours post-dose (n=33,33,36,71,68)	1.84 ± 4.69	3.29 ± 6.85	6.94 ± 12.2	11.1 ± 14.7	39.8 ± 49.9
Week 12, pre-dose (n=32,33,31,69,70)	1.83 ± 4.69	2.20 ± 4.61	10.3 ± 16.8	14.6 ± 20.3	49.5 ± 62.1
Week 12, 2 hours post-dose (n=32,32,31,68,68)	2.02 ± 4.68	2.49 ± 4.81	10.2 ± 16.4	14.3 ± 20.3	45.7 ± 49.7
Week 12, 4 hours post-dose (n=32,32,31,68,68)	2.11 ± 4.84	2.51 ± 4.79	10.1 ± 16.3	15.2 ± 20.7	46.7 ± 52.2
Week 14, pre-dose (n=25,25,27,58,52)	0.239 ± 1.19	0.00 ± 0.00	2.97 ± 10.1	1.59 ± 4.43	7.26 ± 15.7
Week 16, pre-dose (n=25,25,27,57,53)	0.00 ± 0.00	0.00 ± 0.00	2.16 ± 10.0	0.424 ± 1.92	2.53 ± 8.10
Week 20, pre-dose (n=25,25,27,58,53)	0.00 ± 0.00	0.00 ± 0.00	1.94 ± 8.99	0.00 ± 0.00	0.163 ± 1.19
Week 24, pre-dose (n=25,25,26,55,53)	0.00 ± 0.00	0.00 ± 0.00	1.86 ± 6.81	0.00 ± 0.00	0.00 ± 0.00

Safety Results

Time Frame	From first dose of double-blind study treatment up to 12 weeks after last dose (Week 24)
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	CSJ117 0.5mg N = 36	**CSJ117 1mg N = 37**	**CSJ117 2mg N = 37**	**CSJ117 4mg N = 76**	**CSJ117 8mg N = 74**	**Placebo N = 75**
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 1 mg inhaled once daily	Placebo inhaled once daily

Total Number Affected	0	0	0	0	0	0
Total Number At Risk	36	37	37	76	74	75

Serious Adverse Events

	CSJ117 0.5mg N = 36	**CSJ117 1mg N = 37**	**CSJ117 2mg N = 37**	**CSJ117 4mg N = 76**	**CSJ117 8mg N = 74**	**Placebo N = 75**
Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 1 mg inhaled once daily	Placebo inhaled once daily
Total # Affected by any Serious Adverse Event	1	0	0	1	0	1
Total # at Risk by any Serious Adverse Event	36	37	37	76	74	75
Infections and infestations						
COVID-19	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia viral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.33%)
Respiratory, thoracic and mediastinal disorders						
Asthma	1 (2.78%)	0 (0.00%)	0 (0.00%)	1 (1.32%)	0 (0.00%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold 2%

	CSJ117 0.5mg N = 36	**CSJ117 1mg N = 37**	**CSJ117 2mg N = 37**	**CSJ117 4mg N = 76**	**CSJ117 8mg N = 74**	**Placebo N = 75**

Arm/Group Description	CSJ117 0.5 mg inhaled once daily	CSJ117 1 mg inhaled once daily	CSJ117 2 mg inhaled once daily	CSJ117 4 mg inhaled once daily	CSJ117 1 mg inhaled once daily	Placebo inhaled once daily
Total # Affected by any Other Adverse Event	12	14	20	31	23	27
Total # at Risk by any Other Adverse Event	36	37	37	76	74	75
Blood and lymphatic system disorders						
Anaemia	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutropenia	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Splenomegaly	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytopenia	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders						
Diarrhoea	0 (0.00%)	0 (0.00%)	2 (5.41%)	1 (1.32%)	0 (0.00%)	0 (0.00%)
Dry mouth	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.70%)	0 (0.00%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.70%)	0 (0.00%)
General disorders and administration site conditions						
Non-cardiac chest pain	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.33%)
Vaccination site swelling	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatobiliary disorders						
Cholelithiasis	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic steatosis	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations						
Acarodermatitis	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Acute sinusitis	1 (2.78%)	0 (0.00%)	2 (5.41%)	0 (0.00%)	0 (0.00%)	1 (1.33%)

Bronchitis	0 (0.00%)	1 (2.70%)	1 (2.70%)	1 (1.32%)	1 (1.35%)	0 (0.00%)
Candida infection	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Conjunctivitis	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	4 (11.11%)	2 (5.41%)	0 (0.00%)	3 (3.95%)	1 (1.35%)	7 (9.33%)
Cystitis	0 (0.00%)	0 (0.00%)	3 (8.11%)	3 (3.95%)	0 (0.00%)	0 (0.00%)
Gastroenteritis	0 (0.00%)	0 (0.00%)	1 (2.70%)	1 (1.32%)	1 (1.35%)	0 (0.00%)
Laryngitis	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	1 (1.33%)
Nasopharyngitis	2 (5.56%)	2 (5.41%)	1 (2.70%)	4 (5.26%)	2 (2.70%)	4 (5.33%)
Oral fungal infection	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	1 (1.35%)	0 (0.00%)
Oral herpes	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	1 (1.35%)	0 (0.00%)
Otitis media	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Otitis media acute	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Papilloma viral infection	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pharyngitis	0 (0.00%)	1 (2.70%)	0 (0.00%)	2 (2.63%)	2 (2.70%)	2 (2.67%)
Pharyngitis bacterial	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sinusitis	1 (2.78%)	0 (0.00%)	2 (5.41%)	1 (1.32%)	3 (4.05%)	2 (2.67%)
Tracheitis	0 (0.00%)	1 (2.70%)	0 (0.00%)	1 (1.32%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection	1 (2.78%)	0 (0.00%)	0 (0.00%)	1 (1.32%)	1 (1.35%)	0 (0.00%)
Urinary tract infection	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vaginal infection	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Viral upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.63%)	2 (2.70%)	1 (1.33%)
Injury, poisoning and procedural complications						
Vaccination complication	0 (0.00%)	2 (5.41%)	0 (0.00%)	1 (1.32%)	0 (0.00%)	1 (1.33%)

Investigations						
Blood glucose increased	1 (2.78%)	0 (0.00%)	0 (0.00%)	1 (1.32%)	0 (0.00%)	1 (1.33%)
Electrocardiogram QT prolonged	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.33%)
Gamma-glutamyltransferase increased	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders						
Hypercholesterolaemia	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders						
Arthralgia	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.33%)
Back pain	0 (0.00%)	1 (2.70%)	1 (2.70%)	2 (2.63%)	1 (1.35%)	0 (0.00%)
Muscle tightness	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Spinal osteoarthritis	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders						
Cervicobrachial syndrome	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysgeusia	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Headache	1 (2.78%)	0 (0.00%)	0 (0.00%)	1 (1.32%)	1 (1.35%)	2 (2.67%)
Migraine	1 (2.78%)	0 (0.00%)	0 (0.00%)	1 (1.32%)	0 (0.00%)	0 (0.00%)
Spinal cord herniation	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders						
Chronic kidney disease	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pollakiuria	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders						

Intermenstrual bleeding	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders						
Asthma	2 (5.56%)	4 (10.81%)	6 (16.22%)	12 (15.79%)	7 (9.46%)	10 (13.33%)
Bronchial hyperreactivity	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chronic rhinosinusitis with nasal polyps	0 (0.00%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.32%)	3 (4.05%)	0 (0.00%)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.67%)
Dyspnoea	1 (2.78%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasal polyps	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinitis allergic	0 (0.00%)	0 (0.00%)	1 (2.70%)	1 (1.32%)	0 (0.00%)	0 (0.00%)
Rhinorrhoea	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	1 (1.35%)	0 (0.00%)
Skin and subcutaneous tissue disorders						
Eczema	1 (2.78%)	0 (0.00%)	0 (0.00%)	1 (1.32%)	0 (0.00%)	0 (0.00%)
Rash	1 (2.78%)	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urticaria	0 (0.00%)	1 (2.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders						
Hypertension	0 (0.00%)	2 (5.41%)	0 (0.00%)	0 (0.00%)	1 (1.35%)	0 (0.00%)
Hypertensive crisis	0 (0.00%)	1 (2.70%)	0 (0.00%)	1 (1.32%)	0 (0.00%)	0 (0.00%)

Conclusion:

- Clinical efficacy of CSJ117 was not demonstrated. Observed data does not support following up with a Phase III study.
- CSJ117 at doses up to 8 mg was generally safe and well tolerated in uncontrolled asthma patients previously treated with a medium or high dose of an ICS in combination with a LABA.

Date of Clinical Trial Report

2-Mar-2023