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## 2.6 Methods of assessment

### 2.6.1 Efficacy

Allergic symptoms collected by means of the symptom score cards and the global efficacy assessments provided by the patients were used to evaluate the efficacy of the trial medication.

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#### (a) Symptomatology and global evaluation

While the patients were in the park on Days 1 and 2, they were seen hourly by a member of the University of Iowa Allergy and Immunology Clinic, and each patient’s allergic symptoms and general health were assessed. Periodically during the allergy-symptom screening and double-blind treatment periods, patients were asked to describe any protocol-specified allergy symptoms that they had on symptom score cards. Each patient was instructed to document the type and severity of allergy symptoms that occurred. The allergy symptoms listed on the symptom score card included sneezing, stuffy nose, rhinorrhea, itchy nose or throat, and allergic eye symptoms. The severity of each allergy symptom was scored using the following symptom scale:

<u>Score</u>	<u>Severity</u>
0	None
1	Slight (detectable but not bothersome)
2	Mild (noticeable with mild discomfort)
3	Moderate (clearly noticeable and uncomfortable)
4	Severe (definitely present and causing interference in daily activities)

Before leaving the park on Day 2, each patient was asked to evaluate the global efficacy of the trial medication and to record this evaluation on the symptom score card for Day 2 according to the following scale:

<u>Score</u>	<u>Efficacy evaluation</u>
1	Good or substantial control of allergy symptoms
2	Fair or moderate control of allergy symptoms
3	Doubtful or minor control of allergy symptoms
4	No control of allergy symptoms
5	Allergy symptoms aggravated

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TABLE T2.1.5 SYMPTOM SCORE CARD: MEAN ALLERGIC EYE SYMPTOMS

VISIT	TIME	TREATMENT														
		PLACEBO			ICI 204219 10MG			ICI 204219 20MG			ICI 204219 40MG			ICI 204219 100MG		
		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD
DAY 1	08:30	33	2.1	1.4	33	2.2	1.2	33	1.9	1.2	33	2.2	1.2	32	2.1	1.1
	09:30	33	2.5	1.3	33	2.3	1.1	33	1.8	1.1	33	2.5	1.1	32	2.1	1.2
	10:30	33	2.5	1.3	33	2.5	1.2	33	2.1	0.9	33	2.5	1.1	32	2.3	1.1
	11:30	33	1.8	1.2	33	2.2	1.3	33	1.8	1.0	33	1.9	1.1	32	1.8	1.2
	12:30	33	1.3	1.2	33	1.6	1.2	33	1.2	1.0	33	1.5	1.0	32	1.3	0.9
	13:30	33	1.4	1.2	33	1.6	1.2	32	1.2	1.1	33	1.2	1.1	32	1.3	1.1
	14:30	33	1.4	1.2	33	1.4	1.2	33	1.1	1.1	33	1.1	1.0	32	1.3	1.1
	15:30	33	1.6	1.4	33	1.4	1.0	33	1.1	1.0	33	1.3	1.1	32	1.4	1.2
	16:30	33	1.8	1.3	33	1.7	1.1	33	1.2	1.1	33	1.4	1.2	32	1.4	1.1
	18:30	32	2.0	1.3	33	1.9	1.2	33	1.3	1.0	33	1.6	1.1	32	1.8	1.4
	20:30	32	2.1	1.6	33	2.1	1.1	33	1.4	1.0	33	1.8	1.1	32	1.9	1.4
22:30	32	2.2	1.6	33	2.2	1.3	33	1.5	1.1	32	2.0	1.3	32	2.0	1.2	
DAY 2	08:30	31	2.0	1.3	32	1.9	1.2	33	1.8	1.0	33	2.0	1.2	31	1.9	1.1
	09:30	30	1.8	1.4	31	1.9	1.0	33	1.5	1.1	33	1.7	1.1	31	1.5	0.9
	10:30	31	1.6	1.3	32	1.9	1.2	33	1.4	0.9	33	1.6	1.1	31	1.5	0.9
	11:30	31	1.7	1.3	32	1.8	1.3	33	1.4	1.1	33	1.6	1.0	31	1.5	1.2

(CONTINUED)

## SYMPTOM SCALE

0 = NONE

1 = SLIGHT (DETECTABLE BUT NOT BOTHERSOME)

2 = MILD (NOTICEABLE BUT NO DISCOMFORT)

3 = MODERATE (CLEARLY NOTICEABLE AND UNCOMFORTABLE)

4 = SEVERE (DEFINITELY PRESENT, INTERFERING IN ACTIVITIES)

TABLE T2.1.5 SYMPTOM SCORE CARD: MEAN ALLERGIC EYE SYMPTOMS

VISIT	TIME	TREATMENT														
		PLACEBO			ICI 204219 10MG			ICI 204219 20MG			ICI 204219 40MG			ICI 204219 100MG		
		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD
DAY 2	12:30	31	1.8	1.4	32	2.0	1.3	33	1.3	1.1	33	1.9	1.2	31	1.8	1.2
	13:30	31	1.8	1.5	32	1.7	1.3	33	1.4	1.1	33	1.6	1.1	31	1.5	1.2
	14:30	31	1.8	1.4	32	1.6	1.3	33	1.2	1.1	33	1.5	1.1	31	1.3	1.1
	15:30	31	1.8	1.3	32	1.6	1.2	33	1.2	1.0	33	1.4	1.2	31	1.3	1.0
	16:30	31	2.0	1.3	30	1.7	1.2	33	1.5	1.2	33	1.4	1.2	31	1.3	0.9
	18:30	31	2.1	1.2	32	1.9	1.2	33	1.3	1.1	32	1.8	1.0	31	1.7	1.2
	20:30	31	2.0	1.3	32	1.8	1.2	33	1.4	1.1	32	1.9	1.1	31	1.7	1.3
	22:30	31	1.9	1.3	31	2.0	1.4	31	1.3	1.1	32	2.1	1.4	31	1.7	1.4

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TABLE T2.2.5 BASELINE ADJUSTED COMPARISONS OF MEAN EYE SYMPTOMS  
BETWEEN ICI 204,219 DOSE AND PLACEBO AT EACH ENDPOINT

## SYMPTOM SCORE

-TIMEPOINT	TREATMENT (MG)	SUMMARY STATISTICS					ANALYSIS OF COVARIANCE							
		N	BEFORE DOSE 1		AFTER DOSE		AFTER DOSE		DIFFERENCE BETWEEN TREATMENTS					
			MEAN	SD	MEAN	SD	LSMEAN	SE	DIFF	SE	LCL	UCL	P-VALUE	
DAY 1 - ENDPOINT 1	PLACEBO	33	2.34	1.26	1.53	1.05	1.46	0.12						
	ICI 204219 10	33	2.32	1.07	1.65	1.00	1.60	0.12						
	ICI 204219 20	33	1.93	0.95	1.26	0.95	1.45	0.13						
	ICI 204219 40	33	2.40	1.01	1.42	0.91	1.31	0.12						
	ICI 204219 100	32	2.18	1.05	1.44	0.96	1.48	0.13						
	PLACEBO - 10								-0.14	0.18	-0.49	0.21	0.4323	
	PLACEBO - 20								0.01	0.18	-0.34	0.36	0.9627	
PLACEBO - 40								0.14	0.18	-0.20	0.49	0.4163		
PLACEBO - 100								-0.02	0.18	-0.37	0.33	0.907		
DAY 1 - ENDPOINT2	PLACEBO	32	2.32	1.27	2.08	1.42	2.03	0.18						
	ICI 204219 10	33	2.32	1.07	2.07	1.06	2.02	0.17						
	ICI 204219 20	33	1.93	0.95	1.40	0.95	1.58	0.17						
	ICI 204219 40	33	2.40	1.01	1.77	1.10	1.67	0.17						
	ICI 204219 100	32	2.18	1.05	1.90	1.27	1.93	0.18						
	PLACEBO - 10								0.01	0.25	-0.47	0.50	0.9586	
	PLACEBO - 20								0.45	0.25	-0.04	0.94	0.0715	
PLACEBO - 40								0.36	0.25	-0.12	0.85	0.1426		
PLACEBO - 100								0.10	0.25	-0.39	0.59	0.6803		
DAY 1 - ENDPOINT 3	PLACEBO	33	2.34	1.26	1.72	1.07	1.65	0.12						
	ICI 204219 10	33	2.32	1.07	1.79	0.97	1.74	0.12						
	ICI 204219 20	33	1.93	0.95	1.31	0.86	1.50	0.12						
	ICI 204219 40	33	2.40	1.01	1.54	0.88	1.43	0.12						
	ICI 204219 100	32	2.18	1.05	1.59	0.99	1.63	0.12						
	PLACEBO - 10								-0.09	0.17	-0.43	0.25	0.6111	
	PLACEBO - 20								0.15	0.17	-0.19	0.50	0.384	
PLACEBO - 40								0.22	0.17	-0.12	0.56	0.2112		
PLACEBO - 100								0.02	0.17	-0.32	0.37	0.9058		
DAY 2 - ENDPOINT 1	PLACEBO	31	2.27	1.26	1.82	1.15	1.79	0.13						
	ICI 204219 10	32	2.30	1.08	1.79	1.02	1.74	0.13						

(CONTINUED)

SD = STANDARD DEVIATION  
LSMEAN = LEAST-SQUARES MEAN  
SE = STANDARD ERROR FOR LEAST-SQUARES MEAN  
LCL = LOWER 95% CONFIDENCE LIMIT  
UCL = UPPER 95% CONFIDENCE LIMIT

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BETWEEN ICI 204,219 DOSE AND PLACEBO AT EACH ENDPOINT

## SYMPTOM SCORE

-TIMEPOINT	TREATMENT (MG)	SUMMARY STATISTICS					ANALYSIS OF COVARIANCE							
		N	BEFORE DOSE 1		AFTER DOSE		AFTER DOSE		DIFFERENCE BETWEEN TREATMENTS					
			MEAN	SD	MEAN	SD	LSMEAN	SE	DIFF	SE	LCL	UCL	P-VALUE	
DAY 2 - ENDPOINT 1	ICI 204219 20	33	1.93	0.95	1.40	0.88	1.57	0.13						
	ICI 204219 40	33	2.40	1.01	1.65	0.95	1.54	0.13						
	ICI 204219 100	31	2.20	1.05	1.50	0.81	1.51	0.13						
	PLACEBO - 10								0.05	0.19	-0.32	0.42	0.7904	
	PLACEBO - 20								0.23	0.19	-0.15	0.60	0.2343	
DAY 2 - ENDPOINT2	PLACEBO - 40								0.25	0.19	-0.12	0.62	0.1821	
	PLACEBO - 100								0.28	0.19	-0.09	0.66	0.1413	
	PLACEBO	31	2.27	1.26	1.97	1.21	1.94	0.17						
	ICI 204219 10	32	2.30	1.08	1.89	1.19	1.84	0.17						
	ICI 204219 20	33	1.93	0.95	1.32	0.98	1.49	0.17						
DAY 2 - ENDPOINT 3	ICI 204219 40	32	2.38	1.01	1.95	1.03	1.85	0.17						
	ICI 204219 100	31	2.20	1.05	1.73	1.25	1.74	0.17						
	PLACEBO - 10								0.10	0.24	-0.38	0.57	0.6866	
	PLACEBO - 20								0.45	0.24	-0.03	0.92	0.0634	
	PLACEBO - 40								0.08	0.24	-0.39	0.55	0.7321	
DAY 2 - ENDPOINT 3	PLACEBO - 100								0.20	0.24	-0.28	0.67	0.4104	
	PLACEBO	31	2.27	1.26	1.86	1.08	1.83	0.13						
	ICI 204219 10	32	2.30	1.08	1.81	1.00	1.76	0.13						
	ICI 204219 20	33	1.93	0.95	1.38	0.87	1.55	0.13						
	ICI 204219 40	33	2.40	1.01	1.72	0.92	1.61	0.13						
DAY 2 - ENDPOINT 3	ICI 204219 100	31	2.20	1.05	1.56	0.88	1.57	0.13						
	PLACEBO - 10								0.07	0.18	-0.30	0.43	0.7199	
	PLACEBO - 20								0.28	0.18	-0.08	0.64	0.1295	
	PLACEBO - 40								0.22	0.18	-0.14	0.58	0.2314	
	PLACEBO - 100								0.26	0.18	-0.10	0.63	0.1586	

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