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**Clinical Study Report Synopsis**

Drug Substance	NA
Study Code	NIS-RGR-DUM-2008/1
Edition Number	1.0
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**TITLE:**  
**OPINION OF PATIENTS UNDER TREATMENT THAT MEETS THE CRITERIA  
OF NEW TREATMENT STRATEGY ACCORDING TO GINA 2006 (EPAGGELIA)**

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**Study dates:**

First patient enrolled: 1 April 2008  
Last patient completed: 12 June 2008

**Phase of development:**

Not Applicable (Epidemiological survey)

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents

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## **LIST OF ABBREVIATIONS AND DEFINITION OF TERMS**

The following abbreviations and special terms are used in this study protocol.

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<b>Abbreviation or special term</b>	<b>Explanation</b>
GINA	Global Initiative for Asthma
ACQ-5	Asthma Control Questionnaire-5
MiniAQLQ	Asthma Quality of Life Questionnaire – short version
SATQ	Satisfaction with Asthma Treatment Questionnaire
SD	Standard Deviation
NA	Not Available

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### **Study centers**

104 office-based physicians.

### **Publications**

Not applicable

### **Objectives**

Primary objective

- To evaluate patients' satisfaction and asthma control.

Secondary objectives

- To record treatment compliance.
- To evaluate quality of life
- To evaluate the use of health care resources.

### **Study design**

Epidemiological, descriptive, cross-sectional study. Study data were collected during a single visit.

### **Target patient population and sample size**

The study sample consisted of the first 8 consecutive patients visiting an office-based primary care physician (internist or pneumonologist) with moderate or severe persistent asthma for at least 6 months, who were under treatment according to the new strategies for asthma management (GINA 2006) for at least 3 months. A total of 801 patients were eventually enrolled in the study.

### **Duration of treatment**

Not applicable

**Investigational product and comparator(s): dosage, mode of administration and batch numbers**

Not applicable

**Criteria for evaluation (main variables)**

*Primary variables*

- Asthma treatment satisfaction
- Asthma disease control

*Secondary variables*

- Quality of life
- Compliance
- Use of health care resources due to asthma.

**Patient-reported outcomes (PROs)**

All study subjects completed the ACQ-5, the MiniAQLQ and the SATQ questionnaires during the study's single visit.

**Criteria for evaluation - safety**

Not applicable

**Statistical methods**

Descriptive statistical methodology was applied, with frequencies and percentages presented in tables in case of categorical variables, and basic summary statistics for the continuous ones.

## Summary of results

### Baseline characteristics

In total, 801 patients were enrolled and analyzed in the present study. Demographic and baseline characteristics are summarized on Table 1.

**Table 1: Demographic and Baseline Characteristics**

<b>Sex</b>	
Male (n, %)	353, 44.3
Female (n, %)	443, 55.7
<b>Age</b> (mean ± sd) [years]	49.3 ± 15.5 (n=796)
<b>BMI</b> (mean ± sd) [kgr/m <sup>2</sup> ]	26.5 ± 4.2 (n=797)
<b>Smoking</b>	
Yes (n, %)	520, 65.7
No (n, %)	270, 34.1
<b>Pack-years</b> (mean ± sd)	19.0 ± 4.6 (n=239)
<b>Quit smoking</b>	
Yes (n, %)	117, 30.3
No (n, %)	267, 69.2
<b>Years diagnosed with asthma</b> (mean ± sd)	11.2 ± 8.9 (n=791)

### Asthma treatment

Study subjects were treated according to the 2006 GINA guidelines. Information on treatment strategy (number of daily inhalations and additional inhalations used) is depicted in table 2.

**Table 2: Asthma Treatment**

	<b>N</b>	<b>%</b>
<b>Treatment of Asthma before the current one</b>		
Yes	552	69.0
No	248	31.0
<b>Daily inhalations</b>		
1 inhalation twice daily	410	52.6
2 inhalations twice daily	370	47.4
<b>Additional daily relieving inhalations</b>		
No inhalations	347	45.5
1 inhalation	150	19.7
2 inhalations	180	23.6
>2 inhalations	86	11.3

### Patient satisfaction

Patient satisfaction with their current treatment was assessed by means of the SATQ self-administered questionnaire as well as with a 7-point evaluation scale. The relevant results of the latter are depicted in table 3.

**Table 3: Patient satisfaction according to a 7-point scale evaluation**

Satisfaction	N	%
Very high	315	40.2
High	250	31.9
Adequate	125	15.9
Moderate	48	6.1
Low	21	2.7
Very low	14	1.8
None	11	1.4
Total	784	
NA	17	

The mean ( $\pm$  SD) SATQ score for the study population is shown in table 4.

**Table 4: SATQ score**

Questionnaire	N	Mean $\pm$ SD
SATQ	766	5.43 $\pm$ 0.9

### Asthma control

Asthma control was assessed by means of the ACQ-5 questionnaire as well as with a direct question to the study subjects of whether they believe that their asthma was controlled during the study period. The relevant percentages are shown in table 5.

**Table 5: Asthma Control (ACQ-5 & self perception)**

	N	%
<b>Asthma Control (ACQ-5)</b>		
Adequately controlled (ACQ $\leq$ 1.0)	416	52.6
Not well controlled (ACQ $>$ 1)	375	47.4
<b>Patients' perception of asthma control</b>		
Controlled	607	76.4
Not controlled	187	23.6

The mean ( $\pm$  SD) total ACQ-5 score is shown below (table 6).

**Table 6: ACQ-5 score**

Questionnaire	N	Mean $\pm$ SD
ACQ-5	791	1.3 $\pm$ 1.1

### Quality of life

Quality of life was assessed with the MiniAQLQ self-administered questionnaire. The mean ( $\pm$  SD) total MiniAQLQ score is presented in table 7.

**Table 7: MiniAQLQ score**

Questionnaire	N	Mean $\pm$ SD
MiniAQLQ	645	5.3 $\pm$ 1.1

### Treatment compliance

For the evaluation of compliance, study subjects were asked whether they had interrupted their asthma treatment within the last 6 months. The results are shown below (table 8).

**Table 8: Treatment compliance**

	N	%
Treatment interruption within the previous 6 months		
Yes	428	53.9
No	366	46.1

Furthermore, information on duration and reason of the potential interruptions was collected (table 9).

**Table 9: Duration and reason for treatment interruptions**

	N	%
<b>Duration of interruption</b>		
1 day	30	7.1
1 week	133	31.4
1 month	146	34.5
Other	114	27.0
<b>Reason for interruption</b>		
Disease improvement	294	71.9
Other	115	28.1

Use of health care resources

Use of health care resources was evaluated by means of reporting patients' visits to hospital emergency units (EU), hospitalizations due to asthma and visits to physicians (tables 10 & 11).

**Table 10: Visits to hospital EU and physicians**

		0	1	2	3	≥ 4	Total	NA
EU visits during last year	N	587	88	75	18	16	784	17
	%	74.9	11.2	9.6	2.3	2		
EU visits during last month	N	729	37	11	3	1	781	20
	%	93.3	4.7	1.4	0.4	0.1		
Physician visit during last month	N	75	397	233	62	28	795	6
	%	9.4	49.9	29.3	7.8	3.5		

**Table 11: Hospitalizations due to asthma**

		0	1-2	3	> 3	Total	NA
Last year	N	737	49	6	2	794	7
	%	92.8	6.2	0.8	0.3		
Last month	N	777	15	-	-	792	9
	%	98.1	1.9	-	-		

Other variables

Study subjects expressed their views on factors, which can potentially worsen their asthma. The results are shown in table 12.

**Table 12: Factors, which could potentially worsen asthma symptoms (patients' perception)**

Factor	N	%
Respiratory infection	596	74.4
High Humidity	562	70.3
Pollen	441	55.1
Poor compliance to treatment	357	44.6
Psychological factors	282	35.3
Physical activity	276	34.5
Very cold weather	240	30.0
Presence of animals	123	15.4
Total	800	
NA	1	



Patients were also asked how many times their asthma symptoms became troublesome, worsened or restrictive for their daily activities, during the previous year and last month (table 13).

**Table 13: Symptom worsening incidence during the last year and last month**

Time period	N	Mean ± SD	Median	Range
During the last 12 months	571	3.3 ± 3.3	2	0 - 37
During the last month	197	2.2 ± 1.9	2	0 - 10
None	133			

Additionally, study subjects who did not answer “None” in the previous question were asked about the time interval between the initiation of symptom worsening and the time their symptoms became restrictive for their daily activities (table 14).

**Table 14: Time interval from symptom worsening to restriction of activities**

	N	Mean ± SD	Median	Range
Time (hrs)	646	41.7 ± 46.1	28	0 - 360

Finally, patients were asked whether there were any “indications/signs” before asthma worsening and which were their symptoms when their asthma was in the worst condition (tables 15 & 16).

**Table 15: Presence of indication/sign of asthma worsening**

	No	Yes	Total	NA
N	130	646	776	25
%	16.8	83.2		

**Table 16: Symptoms during worst asthma condition**

Symptoms	N	%
Chest tightness	404	50.9
Cough	520	65.6
Productive cough	279	35.2
Fatigue	278	35.1
Exhaustion	147	18.5
Neck itching	200	25.2
Neck tightness	120	15.1
Whistling or wheezing	558	70.4
None	4	0.5
NA	8	

### Subgroup analyses

Results of patients' perceived satisfaction with current treatment as evaluated by a 7-point scale and the actual satisfaction according to SATQ scores are depicted in table 17.

**Table 17: Satisfaction with current treatment and corresponding SATQ scores**

Satisfaction with treatment	SATQ score	
	N	Mean ± SD
Very high	306	5.9 ± 0.6
High	239	5.5 ± 0.7
Adequate	116	4.7 ± 0.8
Modest	45	4.6 ± 0.9
Low	20	4.3 ± 1.0
Very low	12	5.3 ± 1.1
Not at all	11	4.9 ± 1.7

The percentage of patients with actually controlled asthma as assessed by ACQ-5 from the subpopulation of patients who perceived their asthma as controlled is shown in table 18, whereas the mean (± SD) ACQ-5 scores for those whose perceived their asthma as controlled or not controlled are presented in table 19.

**Table 18: Actual Asthma control in patients who perceived their asthma as controlled**

Actual Asthma Control (ACQ-5) in patients who perceived their asthma as controlled	N	%
Adequately controlled	397	65.7
Not well controlled	207	34.3

**Table 19: Asthma control perception and ACQ-5 score**

Asthma control as perceived by patients	ACQ-5 Score	
	N	Mean ± SD
Controlled	604	0.9 ± 0.9
Non-controlled	180	2.6 ± 1.0

The percentages of patients within specific ACQ-5 score ranges are shown in table 20.

**Table 20: Percentage of patients within ACQ-5 ranges**

ACQ-5 score	N	%
< 0.75	302	38.2
0.75-0.99	53	6.7
1-1.5	151	19.1
>1.5	285	36.0
Total	791	

The respective MiniAQLQ and SATQ mean ( $\pm$  SD) scores for the above ACQ-5 score categories are illustrated in table 21.

**Table 21: ACQ-5 range and respective MiniAQLQ and SATQ scores**

ACQ-5 Score Category	Questionnaire	N	Mean $\pm$ SD
<0.75	MiniAQLQ	260	6.1 $\pm$ 0.6
	SATQ	294	5.8 $\pm$ 0.7
0.75-0.99	MiniAQLQ	39	5.4 $\pm$ 0.7
	SATQ	52	5.4 $\pm$ 0.7
1-1.5	MiniAQLQ	118	5.2 $\pm$ 0.9
	SATQ	142	5.4 $\pm$ 0.7
>1.5	MiniAQLQ	220	4.5 $\pm$ 1.1
	SATQ	270	5.05 $\pm$ 1.0

The mean ( $\pm$  SD) ACQ-5, MiniAQLQ and SATQ scores according to treatment compliance are shown in table 22, while the percentages of patients with actual and perceived asthma control in the subgroup of patients with any treatment interruption are presented in table 23.

**Table 22: Treatment compliance and ACQ-5, MiniAQLQ and SATQ scores**

Compliance	Questionnaire	N	Mean $\pm$ SD
No treatment interruption within the previous 6 months	ACQ-5	424	1.2 $\pm$ 1.2
	MiniAQLQ	352	5.4 $\pm$ 0.2
	SATQ	409	5.5 $\pm$ 0.9
Any treatment interruption within the previous 6 months	ACQ-5	361	1.5 $\pm$ 1.1
	MiniAQLQ	286	5.2 $\pm$ 1.0
	SATQ	351	5.3 $\pm$ 0.9

**Table 23: Treatment interruption and asthma control (perceived and actual)**

	N	%
Asthma control perception in patients with any interruption		
Controlled	338	80.1
Not controlled	84	19.9
Actual asthma control (ACQ-5) in patients with any interruption		
Adequately controlled	252	59.4
Not well controlled	172	40.6

The results of the patients' mean ( $\pm$  SD) ACQ-5, MiniAQLQ and SATQ scores according to their maintenance treatment strategy are shown in table 24.

**Table 24: Maintenance treatment and ACQ-5, AQLQ and SATQ scores**

Maintenance Dose	Questionnaire	N	Mean $\pm$ SD
Low (1x2)	ACQ-5	404	1.1 $\pm$ 1.0
	MiniAQLQ	338	5.5 $\pm$ 1.0
	SATQ	396	5.5 $\pm$ 0.8
High (2x2)	ACQ-5	367	1.6 $\pm$ 1.2
	MiniAQLQ	290	5.1 $\pm$ 1.2
	SATQ	350	5.3 $\pm$ 0.9

Finally, the patients' mean ( $\pm$  SD) ACQ-5, MiniAQLQ and SATQ scores according to the specialty of their treating physician are depicted in table 25.

**Table 25: ACQ-5, MiniAQLQ and SATQ scores according to physician's specialty**

Investigator's specialty	ACQ-5		MiniAQLQ		SATQ	
	N	Mean $\pm$ SD	N	Mean $\pm$ SD	N	Mean $\pm$ SD
Internist	332	1.4 $\pm$ 1.1	286	5.2 $\pm$ 1.1	325	5.4 $\pm$ 0.9
Pneumonologist	381	1.2 $\pm$ 1.1	303	5.4 $\pm$ 1.0	371	5.4 $\pm$ 0.8

#### Summary of pharmacokinetic results

Not applicable

#### Summary of pharmacodynamic results

Not applicable

#### Summary of pharmacokinetic/pharmacodynamic relationships

Not applicable

#### Summary of pharmacogenetic results

Not applicable

#### Summary of safety results

Not applicable