CURETALL™

PROTOCOL NUMBER PH123012

A MULTICENTER DOUBLE-BLIND RANDOMIZED STUDY TO EVALUATE THE SAFETY AND EFFICACY OF CURETALL IN PATIENTS WITH ALLERGIES SUFFERING FROM CHRONIC ASTHMA

PRELIMINARY RESULTS

Final results to follow

PROCEDURES IN CASE OF EMERGENCY

Table 1: Emergency Contact Information

Role in Study	Name	Address and Telephone number
Clinical Study Leader	Jocelyn M. Taget, RN	2976 S. Market Street West Chester, PA 88765 215-787-5668 215-455-2323 (Cell)
Responsible Physician	Franklin L. Researcher, M.D.	2976 S. Market Street West Chester, PA 88765 215-787-5467
Drug Safety Physician	Rebecca L. Tanaka, M.D.	2743 N. Covington St. Allentown, PA 18897 610-446-5566
24-Hour emergency contact	Jocelyn M. Taget, RN	2976 S. Market Street West Chester, PA 88765 215-787-5668 215-455-2323 (Cell)

2. SYNOPSIS

CuretALL is a registered trademark.

Name of Sponsor/Company:
Pharma Corporation

Name of Investigational Product:
CuretALL

Name of Active Ingredient:
Sugar

Title of Study:
A Multicenter Double-Blind Randomized Study to Evaluate the Safety and Efficacy of CuretALL in Patients with allergies suffering from chronic asthma

Study center(s):
American Medical Research, Inc.
1234 S. Lakeshore Blvd.
Chicago, IL 99876

Principal Investigator: Harry L. Tanaka, M.D.
Investigators: Janet Jones, M.D., Lionel N. Winter, M.D., John Jones, R.N.

Studied period (years):	**Phase of development:**
Estimated date first patient enrolled: 01-September-2007 Estimated date last patient completed: 30-April-2008	III

Objectives:

Primary:

- To evaluate the efficacy of oral CuretALL across a range of doses for the treatment of allergies in patients suffering from chronic asthma
- To evaluate the safety of the long-term use of oral 5.0 mg CuretALL for the treatment of allergies in patients suffering from chronic asthma

Secondary:

- Evaluation of tolerability and evaluation of long-term

Methodology:
The detailed methodology is attached as Appendix 1.1

Number of patients (planned):
It it anticipated that a total of 800 patients will be randomized from approximately 40 centers in the United States.

Diagnosis and main criteria for inclusion: Patients suffering from allergies that require on-going medical monitoring with a minimum of 4 asthma attacks per year and a maximum of 18 asthma attacks per year.
Investigational product, dosage and mode of administration: CuretALL 5mg tablet daily compared to placebo
Duration of treatment: 12 months
Reference therapy, dosage and mode of administration: Placebo tablet
Criteria for evaluation: **Efficacy:** Primary variable: 2-point scale allergy response at 1 hour Secondary variables: Secondary variables included measurement of 2-point scale allergy response at 30 minutes. 4-point scale allergy relief; change from baseline in allergy intensity symptoms at 30 minutes, 1 hour and 2 hours. **Safety:** Data will be collected and recorded for all adverse events, specified clinical laboratory tests, electrocardiogram (ECG) and vital signs, and medical history and physical examination findings.
Statistical methods: Binary response data will be analyzed using logistic regression for the primary and selected secondary efficacy variables; including terms for treatment, region, and baseline (either baseline severity 2-point scale or continuous baseline as appropriate) will be fitted irrespective of significance because intensity is known to influence efficacy. Analyses will be done primarily on the intent-to-treat (ITT) population with some analyses being done on the per-protocol (PP) population. All formal statistical tests for treatment difference will be performed using a 2-sided hypothesis test with a significance level of 0.030.

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4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

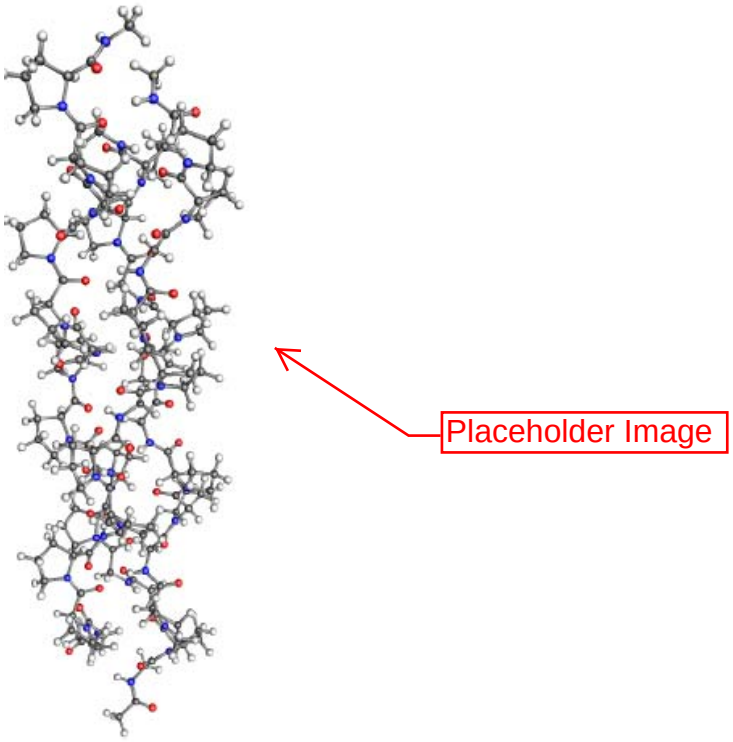
Table 2: Abbreviations and specialist terms

Abbreviation or specialist term	Explanation
AE	Adverse event
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IRB	Institutional Review Board
OAE	Other significant adverse event
PI	Principal Investigator The investigator who leads the study conduct at an individual study center. Every study center has a principal investigator.
SAE	Serious adverse event

5. INTRODUCTION

Background Information

The investigational product is CuretALL which is a compound created by Pharma Corporation for the purpose of relieving severe allergic symptoms and can be used by patients suffering from chronic asthma. The chemical structure for the compound is as follows:



Chemical Structure of CuretAll

Nonclinical Summary

The findings from 12 nonclinical studies (Appendices 2.1 through 2.12) indicate acceptable results for development of CuretALL for the indications stated.

Potential Risks and Benefits

There are no known potential risks to humans based on studies to date. There is a potential benefit to patients suffering from chronic asthma who are also suffering from allergies.

Route of Administration, Dosage, Dosage Regimen and Treatment Periods

We believe the study will support the premise that a 5mg tablet taken orally upon rising will deliver the most efficacious dosage to study subjects.

GCP Requirements

The study will be conducted in compliance with the details of this Protocol and in accordance with current GCP requirements.

Population Studied

It it anticipated that a total of 800 patients will be randomized from approximately 40 centers in the United States providing a population of 750 patients who will actually complete the study.

Literature

A listing of relevant literature is attached as Appendix 3.1.

6. TRIAL OBJECTIVES AND PURPOSE

6.1. Primary objective: To evaluate the efficacy of oral CuretALL across a range of doses for the treatment of allergies in patients suffering from chronic asthma.

6.2. To evaluate the safety of the long-term use of oral 5.0 mg CuretALL for the treatment of allergies in patients suffering from chronic asthma.

6.3. Secondary objectives: Evaluation of tolerability and evaluation of long-term

7. INVESTIGATIONAL PLAN

7.1. Overall Study Design and Plan: Description

The following is a full description of the study design and plan. This document would include specific details if this were a real Protocol.

Figure 1: Study design and schedule of assessments

TREATMENT PERIOD	A		B		C	
	B1	B2	C1	C2		

Run-in

TEST DRUG/ INVESTIGATIONAL PRODUCT A: 5 mg, 10 mg

TEST DRUG/ INVESTIGATIONAL PRODUCT A: 5 mg, 10 mg

TEST DRUG/ INVESTIGATIONAL PRODUCT B: 5 mg, 10 mg

TEST DRUG/ INVESTIGATIONAL PRODUCT B: 5 mg, 10 mg

Weeks	-2(-3)		0	3	6	9	12
Visit	1		2	3	4	5	6
Exercise test 24 h		X[1]	X[2]	X	X	X	X
Medical history	X						
Physical examination	X						x
ECG	X						X
Lab. Invest.	x						X
Adverse events			X	X	X	X	X

1 = 14-20 days after visit 1
2 = 1-7 days after the first exercise test

Table 3: Study design and schedule of assessments

Assessment	**Screening**	**Run-in**	**Baseline**	**Treatment**				**Follow-up**		
Study Week	**-2**	**-1**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**8**
Informed Consent	X									
Inclusion/ Exclusion	X									
Medical History	X									
Physical Exam.	X									X
Effectiveness										
Primary variable	X	X	X	X	X	X	X	X	X	X
Secondary variable	X	X	X	X		X			X	X
Safety										
Adverse events	X	X	X	X	X	X	X	X	X	X
Lab. Tests	X		X	X			X		X	X
Body weight	X		X						X	X

8. SELECTION AND WITHDRAWAL OF SUBJECTS

8.1. Subject Inclusion Criteria

Patients suffering from allergies that require on-going medical monitoring with a minimum of 4 asthma attacks per year and a maximum of 18 asthma attacks per year.

8.2. Subject Exclusion Criteria

Patients that do not require on-going medical monitoring or patients that have <4 or >18 asthma attacks per year.

8.3. Subject Withdrawal Criteria

Patients that do not report for study procedures, or voluntarily withdraw from the study. Subjects that withdraw from the study will not be followed.

9. TREATMENT OF SUBJECTS

9.1. Description of Study Drug

9.2. Concomitant Medications

9.3. Treatment Compliance

9.4. Randomization and Blinding

10. STUDY DRUG MATERIALS AND MANAGEMENT

10.1. Study Drug

10.2. Study Drug Packaging and Labeling

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14.1. Study Monitoring

14.2. Audits and Inspections

14.3. Institutional Review Board (IRB)

15. QUALITY CONTROL AND QUALITY ASSURANCE

16. ETHICS

16.1. Ethics Review

16.2. Ethical Conduct of the Study

16.3. Written Informed Consent

Each subject will be required to agree in writing to an Informed Consent which is attached as Appendix 4.1.

17. DATA HANDLING AND RECORDKEEPING

17.1. Inspection of Records

17.2. Retention of Records

18. REFERENCES

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1. Methodolgy

1.1 Detailed Methodology

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2.5. Name, date and title of Non-Clinical Study #5

2.6. Name, date and title of Non-Clinical Study #6

2.7. Name, date and title of Non-Clinical Study #7

2.8. Name, date and title of Non-Clinical Study #8

2.9. Name, date and title of Non-Clinical Study #9

2.10. Name, date and title of Non-Clinical Study #10

2.11. Name, date and title of Non-Clinical Study #11

2.12. Name, date and title of Non-Clinical Study #12

3. Relevant Literature

3.1 List of Relevant Literature

4. Study Documents

4.1 Informed Consent

4.2 Sample Case Report Forms

Appendix 1.1 – Detailed Methodology

This document will provide details concerning the Methodology that will be used to conduct the following study:

CURETALL™
PROTOCOL NUMBER PH123012
A MULTICENTER DOUBLE-BLIND RANDOMIZED STUDY TO EVALUATE THE SAFETY AND EFFICACY OF CURETALL IN PATIENTS WITH ALLERGIES SUFFERING FROM CHRONIC ASTHMA

The number of subjects to be included in the study is: 800

Criteria for Inclusion: Patients suffering from allergies that require on-going medical monitoring with a minimum of 4 asthma attacks per year and a maximum of 18 asthma attacks per year.

The Investigational product is CuretALL 5mg tablet daily compared to placebo

The duration of treatment for all subjects is12 months

The criteria for evaluation will be:
Efficacy:
Primary variable: 2-point scale allergy response at 1 hour
Secondary variables: Secondary variables included measurement of 2-point scale allergy response at 30 minutes. 4-point scale allergy relief; change from baseline in allergy intensity symptoms at 30 minutes, 1 hour and 2 hours.
Safety:
Data will be collected and recorded for all adverse events, specified clinical laboratory tests, electrocardiogram (ECG) and vital signs, and medical history and physical examination findings. Statistical methods: Binary response data will be analyzed using logistic regression for the primary and selected secondary efficacy variables; including terms for treatment, region, and baseline (either baseline severity 2-point scale or continuous baseline as appropriate) will be fitted irrespective of significance because intensity is known to influence efficacy. Analyses will be done primarily on the intent-to-treat (ITT) population with some analyses being done on the per-protocol (PP) population. All formal statistical tests for treatment difference will be performed using a 2-sided hypothesis test with a significance level of 0.030

Appendix 2.1 – Non-Clinical Study #1

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.10 – Non-Clinical Study #10

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.2 – Non-Clinical Study #2

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.3 – Non-Clinical Study #3

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.4 – Non-Clinical Study #4

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.5 – Non-Clinical Study #5

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.6 – Non-Clinical Study #6

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.7 – Non-Clinical Study #7

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.8 – Non-Clinical Study #8

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 2.9 – Non-Clinical Study #9

This document would list all of the relevant information about the Non-Clinical Study, including title, synopsis, methodology, findings, results, summary and appendices.

Appendix 3.1 – List of Relevant Literature

3.1.1 Article 1 (include title, author, date, synopsis)

3.1.2 Article 2 (include title, author, date, synopsis)

3.1.3 Article 3 (include title, author, date, synopsis)

3.1.4 Article 4 (include title, author, date, synopsis)

3.1.5 Article 5 (include title, author, date, synopsis)

3.1.6 Article 6 (include title, author, date, synopsis)

3.1.7 Article 7 (include title, author, date, synopsis)

3.1.8 Article 8(include title, author, date, synopsis)

3.1.9 Article 9 (include title, author, date, synopsis)

3.1.10 Article 10 (include title, author, date, synopsis)

Investigational Study for Curetall – Protocol # ____ (Harry use the same Protocol Number that we are using for other documents)

Subject ID _____

INFORMED CONSENT

To be completed and signed by the subject
and signed by the Investigator

Read each item below and sign in the space provided if you understand each item and agree to follow the instructions as outlined in the Protocol and presented to you by the study investigator or designate.

Do not sign this Informed Consent and do not participate in this study if there is anything that you do not understand or about the information you have received about participating in this study.

I understand that the therapies distributed in this study are medicines used to treat severe asthma and allergies.

The nature and purpose of this Clinical Study including its benefits and risks, have been fully explained to me by the Study Investigator. I have been given the opportunity to ask any questions regarding my participation in this study. All of my questions have been answered to my satisfaction.

I have been fully informed about the treatments provided in the study.

I understand that there are side effects that may happen while I am participating in the study. These have been explained to me.

I understand that I may receive the therapy being investigated, a comparable therapy or a placebo while participating in this study. Neither my physician nor the investigator conducting the study will have knowledge of the therapy that I am receiving.

All costs associated with physical examinations, treatment therapies, diagnostic tests, office visits, laboratory tests and any other medical treatment required by virtue of my participation in this study will be covered by Health Corporation.

I agree to comply with all restrictions as outlined in the Protocol and agree not to take any medications not expressly permitted under the Protocol as explained to me by the investigator.

I agree to be available for all scheduled visits and to strictly comply with the dosing routine as outlined in the Protocol.

I acknowledge that I have received all relevant information and copies of documents (including a copy of this Informed Consent), as outlined in the GCP's.

Subject signature _____ Date _____

Witness signature: _____ Date _____