

Vaccine to treat allergic diseases shows significant long-term efficacy in house dust mite allergy patients

Median allergen tolerance remains increased by a factor of 100 at 8 months follow-up visit ($p < 0.0001$). Significant therapeutic benefit conferred in management of allergic rhinitis and asthma.

Schlieren (Zurich), Switzerland, April 25, 2006 – Cytos Biotechnology AG (SWX:CYTN) announced today positive follow-up results from its phase IIa study with CYT005-AllQbG10 to treat allergic diseases. The phase IIa trial in 20 patients with allergic rhinoconjunctivitis and asthma due to house dust mite allergy evaluated the safety, tolerability and exploratory efficacy of a 10 week treatment with 300 µg CYT005-AllQbG10 in conjunction with house dust mite allergen. First positive results of the study were announced end of last year (see Press Release, December 14, 2005).

The follow-up results obtained 8 months after start of treatment (i.e. 24 weeks after the last injection) show that the powerful efficacy achieved with CYT005-AllQbG10 treatment offers significant therapeutic benefit for an extended period of time. At the follow-up visit, the allergen tolerance of the patients was recorded by the conjunctival provocation test, which served as the primary efficacy measure. In this test, the median allergen tolerance after 8 months remained increased by a factor of 100 ($p < 0.0001$). The primary efficacy endpoint of the study was defined as a median ten-fold increase in allergen tolerance upon conjunctival provocation with house dust mite allergen 3 months after start of treatment. Allergic rhinitis and asthma in daily life also remained significantly improved at 8 months. The table below shows the median symptom scores of allergic rhinitis and asthma in daily life before treatment, and at 3 months and 8 months after start of treatment. Also shown are the median scores for the consequences of allergic rhinitis and asthma, which describe restrictions due to the disease during work, leisure time, or sleep.

(Median scores are shown)	Before treatment	3 months	8 months
Allergic rhinitis symptom score (p-value)	10.5	1.5 $p < 0.0001$	3 $p < 0.0001$
Consequences of allergic rhinitis (p-value)	3	0 $p < 0.0001$	1 $p < 0.0001$
Asthma symptom score (p-value)	2	0 $p < 0.0001$	0 $p = 0.0007$
Consequences of asthma (p-value)	3	0 $p < 0.0001$	0 $p = 0.0001$

Wolfgang Renner, CEO of Cytos Biotechnology, commented: “Today’s allergic rhinitis and asthma medications target only symptoms and offer just short-term amelioration of the disease. For patients this means chronic use of corticosteroids and antihistamines – often with multiple daily doses. With CYT005-AllQbG10 we are developing a novel disease-modifying treatment for allergic diseases, which has now shown to confer significant long-term benefit in allergic rhinitis and asthma management. Patients experienced a significant and lasting improvement suggesting that the treatment effectively modified the underlying cause of the disease.”

About allergic diseases

Allergy as a whole is a widespread disease that ranges from hay fever to seriously life threatening forms of asthma and anaphylaxis. According to the World Health Organization, more than 20% of the world population suffers from allergic diseases (WHO, 2002). An allergic reaction in general is caused by hypersensitivity of the immune system to a normally harmless substance, the so called allergen, causing a misdirected, so called Th2 type immune response. Today, three general approaches are being pursued to relieve the symptoms of allergic diseases: the avoidance of the allergen, the application of medications that target the symptoms of the disease, and a specific immunotherapy, also known as desensitization, which is the only disease-modifying treatment available today and which reduces the allergy symptoms over a longer period of time. A typical desensitization therapy, however, can consist of up to 80 allergen injections over three to five years and is thus time-consuming, costly, and inconvenient for the patient.

About CYT005-AllQbG10

CYT005-AllQbG10 is a therapeutic vaccine in development for treatment of allergic diseases. The vaccine is currently being tested for treatment of house dust mite allergy and grass pollen allergy (hay fever). CYT005-AllQbG10 is comprised of the Immunodrug™ carrier QbG10 mixed with the natural allergen extract of choice – house dust mite allergen for this study. QbG10 itself consists of the virus-like particle Qb filled with an immunostimulatory DNA sequence called G10. QbG10 is believed to enhance the establishment of a Th1 type immune response. Th1 type immune responses have been shown to suppress “allergic” Th2 type immune responses. CYT005-AllQbG10 thus aims at induction of such a Th1 type immune response to balance an existing Th2 type immune response. As such, CYT005-AllQbG10 is thought to act as a causal and disease-modifying treatment for allergic diseases.

About the phase IIa study

The phase IIa study was an open-label, single arm study in 20 patients with mild to moderate allergic rhinoconjunctivitis and mild asthma due to house dust mite allergy. This type of allergy afflicts about 50% of all allergic patients (Clin Exp Allergy, 2004; 34:597). The study was designed to evaluate the safety, tolerability and exploratory efficacy of the vaccine and was conducted at the University Hospital in Zurich, Switzerland. Male and female otherwise healthy subjects, aged 18-56 years were included in the study. Upon entry into the study, the allergic status was recorded by allergen provocation tests (conjunctival provocation test, skin prick test). Allergy symptoms and impact of disease on daily life during the past two weeks were also recorded. Then, at the first two weekly visits, the allergen was injected subcutaneously and up-titrated. Thereafter, at the next 4 weekly visits, allergen was further up-titrated, but now co-administered subcutaneously with 300 µg CYT005-AllQbG10. Finally, at an additional two biweekly visits, 300 µg CYT005-AllQbG10 were co-administered with the highest targeted allergen dose. 24 weeks (follow-up) after the last dose, the allergic status of the patients was again assessed by the conjunctival provocation test and allergy symptoms and impact of disease on daily life were recorded for the last two weeks.

About the analysis

All patients were included into the follow-up analysis who received at least one injection of the study medication CYT005-AllQbG10 and who were available for the follow-up visit (n=19). The conjunctival provocation test is a commonly used test to monitor the allergic status of an individual. Standardized aqueous allergen solutions are applied in the form of eye-drops to the conjunctiva in increasing concentrations (no allergen; dilutions 1/1,000; 1/100; 1/10; 1/1) and the following allergy symptoms are recorded: conjunctival hyperemia, tearing, itching, burning, and swelling of eyelids. Each symptom can be absent (0 points), mild (1 point), moderate (2 points), or severe (3 points). The predefined minimal threshold level (when symptoms are considered to be above background) is reached at 3 of 15 points.

For assessment of allergic rhinitis symptoms during daily life, the following symptoms were recorded: runny nose, clogged nose, periods of sneezing, itchy nose, itchy throat, itchy eyes, and red eyes. Each symptom can be absent (0 points), mild (1 point), moderate (2 points), or severe (3 points). The scale ranges from 0-21 points. For assessment of asthma symptoms during daily life, the following symptoms were recorded: dry cough and asthma bronchiale. Each symptom can be absent (0 points), mild (1 point), moderate (2 points), or severe (3 points). The scale ranges from 0-6 points. For assessment of the consequences of allergic rhinitis and asthma on daily life, patients were asked i) whether there were annoying symptoms in daily life, ii) whether there were sleeping disorders, iii) whether activities during work or school were restricted and iv) whether activities during leisure time were restricted. Patients could answer each of the four questions with yes (1 point) or no (0 points), the scales ranging from 0-4 points.

Glossary

Allergen: a normally harmless substance that elicits a misdirected immune response.

Allergen tolerance: non-reactivity to a certain allergen or reactivity only up to the level of a predefined minimal symptoms score.

Allergic rhinitis: a condition due to allergy that mimics a chronic cold. Rhinitis means "irritation of the nose".

Anaphylaxis: is an acute and life-threatening reaction of the immune system to specific stimuli. If untreated, it can result in shock, respiratory and cardiac failure, and death.

Asthma: is a chronic inflammatory disorder of the airways leading to recurrent episodes of wheezing, breathlessness, chest tightness and cough in susceptible individuals.

Conjunctival hyperaemia: reddening of the eyes.

Conjunctival provocation test: a commonly used test to monitor the allergic status of an individual.

Desensitization: a certain form of immune therapy applied to treat allergy.

Disease-modifying: in contrast to symptomatic treatment, a disease-modifying treatment aims at addressing the cause of disease and to modify the disease progression.

Efficacy: strength, effectiveness; the ability of a drug to control or cure an illness.

Endpoint: an outcome measure in a clinical trial.

Hypersensitivity: an excessive reaction.

Open-label: a set-up used in clinical trials where the doctor and the patient know what is administered, in contrast to e.g. double-blind, placebo-controlled studies, where neither the doctor nor the patient have this knowledge.

Phase IIa: a clinical trial that examines a new drug candidate's safety and exploratory efficacy in the targeted population and involves 10-100 people.

Rhinoconjunctivitis: a combination of rhinitis (inflammation of the nose) and conjunctivitis (inflammation of the eye).

Single-arm: all patients in the study receive the same drug regimen (CYT005-AllQbG10 plus allergen in this study).

Subcutaneously: under the skin.

Th1 and Th2 type responses: describe a subset of T helper cell responses. T helper cells are a subset of T cells that secrete a variety of mediators (cytokines) playing a role in activation of other immune cells. A Th1 type immune response is usually

induced by viral infection, or also by potent vaccination. A Th2 type immune response usually manifests an allergic reaction.

Therapeutic vaccine: a preparation of disease-related molecules (antigens) that is capable of inducing an immune response to such antigens with the goal to modulate the disease process.

Up-titration of allergen: the allergen is applied in raising concentrations up to the highest targeted allergen dose pre-defined in the protocol.

About Cytos Biotechnology AG

Cytos Biotechnology AG is a public Swiss biotechnology company that specializes in the discovery, development and commercialization of a new class of biopharmaceutical products – the Immunodrugs™. Immunodrugs™ are intended for use in the treatment and prevention of common chronic diseases, which afflict millions of people worldwide. Immunodrugs™ are designed to instruct the patient's immune system to produce desired therapeutic antibody or cytotoxic T-cell responses that modulate chronic disease processes. Taking advantage of the high flexibility of its Immunodrug™ platform, Cytos Biotechnology has built a pipeline of 26 different Immunodrug™ candidates in various disease areas, of which 7 are currently in clinical development. The Immunodrug™ candidates are developed both in-house (23) and together with Novartis (1) and Pfizer Animal Health (2). Founded in 1995 as a spin-off from the Swiss Federal Institute of Technology (ETH) in Zurich, the company is located in Schlieren (Zurich). Currently, the company has 125 employees. Cytos Biotechnology AG has been listed on the SWX Swiss Exchange (SWX:CYTN) since October 2002.

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