Sponsor Protocol Code	ModAll-Der/07
EUDRACT Number	2007-003058-26
Name of the Sponsor	Lofarma S.p.A.
Sponsor Organization Address	Viale Cassala, 40 20143 Milano Italia
Coordinating Investigator, study Centre	Dipartimento di Allergologia ed Immunologia Clinica ASO Maggiore della Carità Novara
Date First Subject Entered	24 Ottobre 2007
Date Last Subject Completed	14 Maggio 2008
Study phase:	II
Studied period (years):	8 months
CRO	CRONOS Ricerche Cliniche. Via Tonale, 22 20124 Milano
Name of Sperimental product:	Dermatophagoides injective allergoid
Name of active ingredients:	mixture containing allergenic extracts of mite (Dermatophagoides pteronyssinus 50% e Dermatophagoides farinae 50%) absorbed on Calcium Phosphate titrated in Carbamylated Units (UC / mL)
Route of administration and dose:	Suspension for injection - Subcutaneous use IMP dose Increase Administration: Induction phase: 100 UC/mL: 0,10 - 0,30 - 0,50 - 0,80 ml 1000 UC/mL: 0,10 - 0,30 - 0,50 - 0,80 ml 10000 UC/mL: 0,10-0,30-0,50-0,80 ml Induction phase 10000 UC/mL: 0,80-0,80-0,80-0,80 ml
Title of study:	Pilot study on tolerability of specific immunotherapy with injective allergoid adsorbed on calcium phosphate in patients with respiratory allergy to house dust mite.
Objective:	Safety and Tolerability
Endpoints:	Adverse events: Evaluation based on the appearance of local and, or systemic reactions. Other adverse events reported in a systemic or spontaneous way, whom relation to the IMP is considered by investigators as possible related, probable related or related. Global Evaluation: Investigators evaluated the global tolerability on the base of the following scale: *Excellent* No adverse event possible related, probable related or related to the IMP. *Good* Adverse events of mild or moderate intensity, appeared once and of short duration, spontaneously resolved and judged by investigator as possible related, probable related or related to the IMP. *Discrete:*

	Adverse events of moderate intensity, judged by investigator as possible related, probable related or related to the IMP and appeared more then once for long period of time, nevertheless not requiring IMP suspension. *Not satisfying:* Adverse events judged by investigator as possible related, probable related or related to the IMP and of intensity, frequency or duration to require IMP suspension and the need of rescue medication.
Population of trial subjects	Planned population of 50 subjects. 47 enrolled. Male or female adults (18-50)
Study Design	Pilot study, phase II, multicentric, open label on patients affected by respiratory allergy to house dust mite. Treated with three dilution of IMP increasing dosage. During the clinical trial, the use of the following concomitant therapies was allowed: • cetirizine or loratadine 1 tablet of 10 mg / day; • salbutamol 2 puffs of 100 μg in case of asthmatic attack; • fluticasone nasal spray 1 puff of 50 μg per nostril / day for cycles of 10 days in case of severe rhinitis; • prednisone or equivalent 2 tablets of 25 mg / day for 3 days in case of symptoms not responsive to other treatments.
Duration of treatment:	Each patient was treated for 16 weeks.
Statistical methods:	Semple size population has been calculated on an empiric base. The statistical evaluation considered the correlations between incidence of adverse events and the different concentrations of IMP administered. Correlations between the incidence of each single adverse event on the total number of adverse events.
Efficacy results:	No efficacy evaluation planned
Safety results:	Forty-seven subjects were enrolled and 2 were screening failures. Forty-five subjects were analyzed (35.6% males, 64.4% females). Mean age was 33.62 (18-49 range). Subjects with at least an adverse event were 20 (44.4%). 23 (79.3%) single event, 2 (6.9%) recurrent events, 4 (13.8%) continuous events. The intensity of adverse events was mild in 11 (37.9%), moderate in 16 (55.2%) and severe in 2 (6.9%) of cases. In twenty-six of the cases (89.7%) the subject recovered. A relationship of adverse events with the treatment was attributed in 12 cases (41.4%). Other causes were attributed to the disease object of the treatment (3.4%), to concomitant diseases (37.9%) or unknow (17.2%). Adverse events frequency (cases) reported according to SOC: 10021881 - Infections and infestations and infestations: 7 (15.6%) 10028395 - Musculoskeletal and connective tissue disorders: 1 (2.2%) 10029205 - Nervous system disorders: 1 (2.2%) 10013993 - Ear and labyrinth disorders: 4 (8.9%) 10019805 - Hepatobiliary disorders: 1 (2.2%) 10038738 - Respiratory, thoracic and mediastinal disorders: 3 (6.7%) 10018065 - General disorders and administration site conditions: 5 (11.1%) 10042613 - Surgical and medical procedures: 1 (2.2%) 10022117 - Injury, poisoning and procedural complications: 2 (4.4%)

	During the trial two serious adverse events (SAEs) occurred, both judged by investigators as unrelated to the investigational drug: • A patient hospitalized 7 weeks after the first dose of ITS, following a right peritonsillar abscess: The one-week event was judged by the investigators to be unrelated to either the investigational drug or the patient's underlying disease. Such event led to discontinuation of study treatment for only one week, and resolved with an intervention of tonsillectomy scheduled about 2 months after admission. • A patient had biliary colic, with consequent hospitalization, approximately 4 weeks after the first administration of the experimental drug; the event resolved completely after two days, did not lead to any interruption of the study treatment and was judged by the investigators to be unrelated to the investigational drug or to the patient's underlying disease. The tolerability of the investigational drug was defined by the investigators as excellent for 41 (93.2%) patients, good for 1 (2.3%) patient, fair for 1 (2.3%) patient and insufficient in only 1 (2.3%) patient.
Conclusion:	Trial results confirms the excellent safety profile of the therapy with the monomeric allergoid, as evidenced by the reduced incidence of adverse reactions and the absence of unexpected adverse events related to the administration of ITS. The tolerability judgment expressed by the investigators of the three participating centers clearly demonstrates that the majority of patients tolerated the study treatment optimally. Considering the logistical and personal problems related to the need to receive injections weekly by going to the experimental center (which led to some deviations from the weekly schedule of injections) it is possible to state that the "compliance" to the treatment was overall satisfactory for the great part of the participating patients.