

UPDATE ON THE ORALAIR CLINICAL DEVELOPMENT PROGRAM (SUBLINGUAL DESENSITISATION TABLETS)

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STALLERGENES updates the clinical development of its ORALAIR program of desensitisation tablets for grass pollen, mites and birch pollen (rBet v 1).

Grass pollen ORALAIR Program

V034 study

The **V034** Phase IIB / III trial, involving more than 600 adult patients from 44 centres in 10 countries and completed in 2005, has demonstrated the efficacy and safety of the grass pollen sublingual desensitisation tablets in rhino-conjunctivitis in the first season of treatment.

The study compared three doses (100 IR, 300 IR, and 500 IR versus placebo) in a once daily uptake protocol started four months before the grass pollen season and continued until the end of the season:

- The study showed a dose response, with the 100 IR dose arm demonstrating no difference versus the placebo one, the 300 IR and 500 IR arms highly significant differences versus placebo but none between them.
- The 300 IR dose has been validated by an independent panel of experts as the therapeutic dose for registration.
- It showed a highly significant difference versus placebo, 37% improvement on the median for the RTSS¹ and 63% on the median for the rescue medication score.

The V034 is the pivotal study of the registration dossier currently under evaluation at the Paul Ehrlich Institute (Germany).

V052 study

The **V052** Phase III trial, involving 278 randomized patients aged between 5 and 17 years old suffering from grass pollen related rhino-conjunctivitis, carried out in 5 European countries, has successfully met its primary and secondary endpoints. The treatment was given four months before and during the season (pre-co-seasonal protocol).

Major results of this trial are:

- Reduction in Rhino-conjunctivitis Total Symptom Score (RTSS): 40% ⁽²⁾
- Reduction in Rescue Medication Score (RMS): 50% ⁽²⁾

The good safety profile of the tablet has been confirmed.

The V052 results are quite consistent with those of the V034. With this pivotal study, STALLERGENES intends to file a labelling variation in paediatrics through a Mutual Recognition Procedure (MRP), Germany remaining the reference member state.

¹ Rhino conjunctivitis Total Symptom Score, sum of the six individual symptom scores: sneezing, runny nose, itchy nose, nasal congestion, watery eyes, itchy eyes

² These reductions are based on median scores calculations

Other studies

- STALLERGENES has obtained the result of the **VO23** clinical trial, which demonstrated for the first time a long term effect in a fourth observational year following a three year sublingual desensitisation in an exclusively seasonal treatment.
This trial is a double blind placebo controlled Proof of Concept study, carried out in Germany from 2000 to 2005, in 213 patients with STALORAL[®] grass pollen.
- The **VO53** phase III trial, aiming at assessing the long term efficacy and carry-over effect, is currently underway in 47 centres in 10 countries with 634 patients enrolled. The RTSS is the primary endpoint. Three arms are compared: a 4 month pre-co-seasonal, a 2 month pre-co-seasonal and a placebo.
Based on an interim analysis of year 1, an independent Data Safety Monitoring Board (DSMB) of experts has recently recommended the continuation of this trial for a second year with the same design.
- An exploratory trial (**VO56**) is currently underway in an allergen exposure chamber to assess the tablet onset of action and select potential biomarkers. The analysis report will be available by Q3 2008.

Mites ORALAIR program

VO57 study

- The **VO57** Phase II/III trial aims at assessing the efficacy and safety of sublingual desensitisation tablets in adult patients suffering from house dust mite allergic rhinitis. Conducted in 8 countries, over a one year treatment ending Q1 2009, it includes 486 patients randomized in three arms (a 500 IR daily dose one, a 300 IR daily dose and a placebo). The Average Rhinitis Total Symptom Score (ARTSS) of the four rhinitis symptoms is the primary endpoint.
The enrolment of this trial (VO57) is in line with the initial plan.

VO55 study

- The **VO55** is a two arms phase III study (STALORAL[®] 300 mites vs placebo) currently conducted in China, with 540 asthmatic patients enrolled in 13 centres. Well-Controlled Asthma is the primary endpoint.
This trial is probably the largest desensitization one ever conducted in patients suffering from allergic asthma.

Birch ORALAIR program

- STALLERGENES is carrying out a Phase I study (**VO58**) to investigate the tolerability and pharmacodynamic effects of sublingual recombinant Bet v 1 desensitisation tablets. The trial report will be available in Q2 2008.
- A Phase IIb / III is planned in H2 2008.

Wrap up

The ORALAIR clinical development program is progressing according to plan.