INSTITUT DE RECHERCHE PIERRE FABRE

Ref.: V00114 CP 305 2A study cancellation

The aim of the clinical trial 2008-008734-36 "*Efficacy and safety study of the antihistamine V0114CP 2.5 mg in the treatment of seasonal allergic rhinitis. Randomised, double-blind, three arm parallel group study including placebo and active control arm (levocetirizine 5 mg)*", protocol number V00114 CP 305 2A" was to demonstrate the efficacy in adult patients of a 2-week treatment by the antihistamine V0114CP 2.5 mg versus placebo in reducing symptoms during seasonal allergic rhinitis.

V0114 is mainly metabolized by the cytochrome CYP450 2D6. Previous Pharmacokinetic studies showed that V0114 systemic exposure was increased in poor CYP2D6 metabolizers.

As part of the development of the compound, the V0114 cardiac safety has been investigated in that particular population, in order to analyze the safety parameters when there is a high exposure to the drug. More precisely, a thorough QT/QTc study has recently been performed in compliance with the corresponding guidance (ICH E14), i.e. under condition of maximal exposure (repeatedly supra-therapeutic dose of V0114 and CYP2D6 activity limited by a potent inhibitor, paroxetine). In these specific conditions, no QTc value was above the upper limit of 450ms for men and 470ms for women, but we observed an unexpected mean increasing in QTc value concomitant to an increase in heart rate.

From a safety point of view, the risk for patients in normal conditions of use is very limited. But subjects 2D6 poor metabolizers (5-8% in Caucasian population) receiving V0114 by oral route in repeated dose (more than 2 weeks) could be concerned by this issue.

Considering this data, the sponsor of the Study has taken the strategic decision to stop the development of V0114 by oral route in the therapeutic indication "Allergic rhinitis", and therefore not to perform the Study. The early termination of the study took place on May 19, 2009.

INSTITUT DE RECHERCHE PIERRE FABRE
Centre de Recherche & Développement : 3, Avenue Hubert Curien, F 31035 Toulouse Cedex 1 – France
Tél (33).5.34.50.60.00 – Fax : (33) 5.34.50.30.00
Société par actions simplifiée au Capital de 1 763 200 Euros - Siren 334 924 362 RCS Nanterre
Siège Social : 45, place Abel Gance, F 92654 Boulogne Cedex - France
Tél : (33).1.49.10.80.00 - Fax : (33).1.49.10.97.12