SYNOPSIS CLINICAL STUDY RESULTS

Name of Sponsor

Poxel, 259/261, avenue Jean Jaurès, 69007 Lyon, France

Name of Finished Test Product

Imeglimin (developmental product)

Name of Active Ingredient

Imeglimin

Title of Study (Study ID: PXL008-017 and Eudra CT No: 2016-003215-35)

A phase 2a, randomised, double-blind, placebo-controlled, cross-over, single and multiple dose study to assess the effects of imeglimin on nicotine-induced endothelial dysfunction in young non-smoker healthy male subjects

Study Period (First Subject First Visit – Last Subject Last Visit)

11 Jan 2017 – 09 May 2017

Date of decision of temporary hold of study by sponsor

27 Dec 2017

Date of decision of (premature) final termination of study (end of study)

11 Sep 2018

Phase of Development

2a

RESULTS – SUMMARY

Limitations

Due to inconsistent and limited effects of inducing endothelial stress by oral intake of nicotine tablets observed during a preliminary blinded data review, the decision to end the study prematurely was made. Safety data only were analysed.

Subject Disposition, Demographic and Baseline Characteristics

Twenty (20) subjects were screened for enrolment of which 2 fulfilled an exclusion criterion (insufficient ultrasound imaging quality of subject's brachial artery for FMD analysis) and 1 subject did not further participate due to a wrist fracture. Seventeen (17) subjects were randomised to one of the treatment sequences of imeglimin and placebo of which 2 subjects discontinued study participation prematurely on own initiative after Visit 2 (dosing with imeglimin). Thus, 15 subjects completed the trial. The 17 randomized subjects, all white males, aged from 22 to 33 years (mean = 26.0 years), with a BMI of 19.9 to 24.6 kg/m^2 (mean = 22.76 kg/m^2) and eGFR values of 86.7 to 124.4 mL/min/1.73m² (mean = 107.81 mL/min/1.73m²) were exposed to at least one dose of IMP, and were included in the safety analysis.

Efficacy

Contrary to the expectation that FMD values decrease after nicotine induced stress, only minor changes in FMD occurred between the 30 min pre-challenge and the repeated post-challenge time points (30, 60, 90, and 120 min) on the first day (start of treatment period) and the last day (end of treatment period) with both IMPs. The effect of nicotine was inconsistent both in intensity or duration, although previous test experiments had shown prolonged effects.

Safety Results

Adverse Events

The table below presents the incidence of TEAEs for imeglimin and placebo during the study by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class and Preferred Term:

System Organ Class	Preferred Term	Number (%) of Subjects / Number of Events	
		Placebo (N=15)	Imeglimin (N=17)
Overall	Total	4 (26.7%) / 10	5 (29.4%) / 10
Gastrointestinal disorders	Total	4 (26.7%) / 8	3 (17.6%) / 6
	Abdominal pain	1 (6.7%) / 1	0 (0.0%) / 0
	Abdominal pain upper	1 (6.7%) / 1	0 (0.0%) / 0
	Diarrhoea	2 (13.3%) / 2	2 (11.8%) / 2
	Gastric disorder	0 (0.0%) / 0	1 (5.9%) / 1
	Nausea	3 (20.0%) / 3	2 (11.8%) / 2
	Vomiting	1 (6.7%) / 1	1 (5.9%) / 1
General disorders and administration site conditions	Total	0 (0.0%) / 0	1 (5.9%) / 1
	Malaise	0 (0.0%) / 0	1 (5.9%) / 1
Infections and infestations	Total	1 (6.7%) / 1	0 (0.0%) / 0
	Tonsillitis	1 (6.7%) / 1	0 (0.0%) / 0
Nervous system disorders	Total	1 (6.7%) / 1	3 (17.6%) / 3
	Headache	1 (6.7%) / 1	2 (11.8%) / 2
	Tension headache	0 (0.0%) / 0	1 (5.9%) / 1

CONCLUSIONS

Efficacy

- Based on descriptive data, 2 mg of orally applied nicotine (buccal application by lozenge) did not induce any relevant changes in FMD in the placebo and imeglimin group. Due to the lack of nicotine induced vascular stress, it was not possible to perform the planned efficacy analyses.

Safety

- Imeglimin at oral doses of 1500 mg b.i.d. was well tolerated in healthy subjects. Safety data were consistent with the known profile from previous studies with imeglimin.

Overall Conclusion

Based on descriptive statistic data from 17 healthy subjects, imeglimin administered orally at a dose of 1500 mg b.i.d. over a period of 8 to 11 days was well tolerated. The limitations of the study (insufficient induction of nicotine induced vascular stress) prevented detection of possible effects of imeglimin.