Document title	**ABBREVIATED CLINICAL STUDY REPORT SYNOPSIS**
Study title	**Patient pREference and satisFaction for pErindopril oRodispersible vs convENtional tablets in daily Clinical practicE** ***PREFERENCE*** **Interventional clinical open study, conducted at general practitioner consultation**
Test drug code	**Perindopril arginine (S90652)**
Indication	**Arterial hypertension**
Development phase	**Phase IV**
Protocol code	**DM4-90652-001**
Study initiation date	**07 February 2013**
Study completion date	**28 April 2014**
Main coordinator	[redacted]
Sponsor	**Les Laboratoires Servier (LLS)** **50 rue Carnot,** **92284 Suresnes Cedex - France**
Responsible medical officer	[redacted]
GCP	**This study was performed in accordance with the principles of Good Clinical Practice.**
Date of the report	**10 January 2017**
Version of the report	**Final Version**

~~**CONFIDENTIAL**~~

2. SYNOPSIS

Name of Sponsor: LLS, 50 rue Carnot - 92284 Suresnes Cedex - France		*(For National Authority Use only)*
Test drug **Name of Finished Product:** Coversyl® orodispersible **Name of Active Ingredient:** Perindopril arginine (S 90652)		
Individual Study Table Referring to Part of the Dossier	**Volume:**	**Page:**
Title of study: Patient pREference and satisFaction for pErindopril oRodispersible vs convENtional tablets in daily Clinical practicE Study acronym PREFERENCE Protocol No.: DM4-90652-001 EudraCT No.: 2011-003328-11		
Coordinator: [redacted] **Investigators:** [redacted]		
Study centres: 2 centres located in France included 12 patients.		
Publication (reference): Not applicable.		
Studied period: Initiation date: 07 February 2013 (date of first visit first patient) Completion date: 28 April 2014 (date of last visit last patient)	**Phase of development of the study:** Phase IV	
Objectives: The **main objective** was to study, in hypertensive patients, followed in general practice and whose blood pressure was well controlled by a monotherapy with tablets of perindopril arginine, their preference and acceptability in favour of the orodispersible form of this medicinal product one month after changing the dosage form. The **secondary objectives** were: To describe the general profile of patients who showed a subjective preference for the orodispersible form, and to search for any differences relative to those who did not show such a preference, in an exploratory manner. To study the antihypertensive treatment compliance with the orodispersible tablet, 3 months after changing the dosage form. To verify the maintenance of the blood pressure control under treatment with the orodispersible form. To describe the emergent adverse drug reactions reported.		
Methodology: This was a phase IV, open-label and non-randomised study carried out in general practice consultation. It was performed in strict accordance with Good Clinical Practice including the archiving of essential documents.		
Number of patients: Planned: 100 patients Included: 12 patients. The lower than planned number of patients was due to major difficulties in recruitment of patients leading to the premature discontinuation of the study. Therefore, it was decided to present an abbreviated clinical study report that comprised only the synopsis.		
Diagnosis and main criteria for inclusion: The main inclusion criteria were adult male or female, without upper limit for the age, with body mass index ≤ 30 kg/m², followed by a general practitioner for arterial hypertension and well-controlled (systolic blood pressure (SBP) < 140 mmHg and diastolic blood pressure (DBP) < 90 mmHg) with perindopril arginine as tablet, 5 or 10 mg per day at stable dose for at least 3 months.		
Test drug: Perindopril arginine: orodispersible tablet, administered orally, at 5 to 10 mg once daily. At inclusion, patients switched from their usual perindopril arginine administered orally as tablet at 5 to 10 mg once daily to the perindopril arginine orodispersible tablet.		
Comparator (Reference product and/or placebo): not applicable		
Duration of treatment: maximum of 3 months		

Criteria for evaluation:

Efficacy measurements:

Primary criterion: Score obtained at the preference questionnaire for the orodispersible form to be filled in by the patient at the general practitioner one month visit.
5 questions were asked to the patient:

- Question 1: Preference between orodispersible form versus usual tablet ?
- Question 2: Is orodispersible form the most convenient ?
- Question 3: Is orodispersible form the most appropriate ?
- Question 4: Would you use orodispersible form for a long treatment period ?
- Question 5: Would you use orodispersible form for the further 2 months ?

Secondary criteria

- A questionnaire for the evaluation of the compliance was completed by the patient at baseline, D30 and D90. Following the answer of the patient to the 6 questions of the compliance questionnaire, patients were assessed as having 'good', 'minor problem' or 'bad' compliance.
- Blood pressure at rest: SBP and DBP on sitting (at least 5 minutes of rest) and standing position at D30 and D90 measured with an automatic device (2 measurements, the second measurement was taken as reference).
  Sitting heart rate (auscultation method).

Safety measurements:

Description of adverse events

Statistical methods:

Due to low number of patients included, it had been decided to not carry out statistical analysis on the data collected and only individual data were provided. Therefore, regarding the primary endpoint (preference for orodispersible versus tablet perindopril arginine form), only answers to each question of the preference questionnaire were provided.

SUMMARY - CONCLUSIONS

12 patients were included and all completed the study (*i.e.* D90 visit performed).

BASELINE CHARACTERISTICS

Patients were 6 women and 6 men, aged between 32 and 78 years. The age was missing for one man and was estimated to be probably within range 18-64 years, as this patient had an on-going professional activity and was a senior officer. Body mass index was between 20.8 and 26.7 kg/m^2.

The duration since arterial hypertension (HTA) diagnosis was from 1 to 14 years before inclusion. At entry in the study, the dose of perindopril tablet prescribed was 5 mg once daily for 8 patients and 10 mg once daily for 4 patients, and this dose was stable for at least 3 months for all included patients.

Five patients reported at least one surgical or medical history other than HTA: depression, dyslipidemia, migraine, atrial fibrillation and impotence (1 patient), peritonitis appendiceal and Meniere disease (1 patient).

All patients had both sitting and standing SBP $\leq$ 140 mmHg and DBP $\leq$ 90 mmHg.

Compliance with the perindopril usual tablet assessed as inclusion criterion was evaluated by the investigator as acceptable for all included patients at baseline.

EFFICACY RESULTS

Primary endpoint: Preference for orodispersible versus tablet perindopril arginine

As no statistical analysis was performed for the primary endpoint regarding the score obtained at questionnaire, the answers to each question of the 12 questionnaires are presented hereafter:

- Question 1: 7 patients preferred the orodispersible form versus their usual tablet and 5 patients had no preference,
- Question 2: 7 patients answered that the orodispersible form was the most convenient and 5 patients answered that orodispersible form was as convenient as usual tablet,
- Question 3: 7 patients answered that the orodispersible form was the most appropriate and 5 patients answered that orodispersible form was as appropriate as usual tablet
- Question 4: 6 patients would use the orodispersible form for a long treatment period and 6 patients would use either orodispersible form or usual tablet,
- Question 5: 11 patients would use orodispersible form for the further 2 months and 1 patient would use usual tablet.

EFFICACY RESULTS (Cont'd)

Secondary criteria
The compliance evaluation at D30 was good for 10 patients and 'with minor problem' for 2 patients. The same results were observed at D90.

Blood pressures: both sitting and standing SBPs were ≤ 140 mmHg as well as DBPs ≤ 90 mmHg at D30 and D90.

SAFETY RESULTS

No emergent adverse event including none-serious was reported during the study.

This study was conducted in very few patients, followed by their doctor, for whom the HTA was well controlled with perindopril arginine 5 or 10 mg per day administered as tablet for at least 3 months. In the PREFERENCE study, patients switched from this background therapy to the same drug same dose but with an orodispersible form for a short duration. It is probably why no non-serious adverse event occurred.

CONCLUSION

This was a phase IV, open-label and non-randomised study carried out in general practice consultation in patients with arterial hypertension previously treated with perindopril arginine as tablet, 5 or 10 mg per day, and at stable dose for at least 3 months. Included patients switched from this background therapy to the same drug same dose but with an orodispersible form for a further 3-month period. The primary objective of the study was to assess the preference of patients for the orodispersible form compared to the conventional tablet at one month.

The study was prematurely terminated due to difficulties in recruitment of patients. Only 12 patients out of the 100 planned were included and completed the study. Therefore, no statistical analysis was carried out. After one month of treatment, the answers to the preference questionnaire showed that: 7 out of the 12 patients preferred the perindopril orodispersible form, and answered that the orodispersible form was the most convenient and appropriate. A total of 11 patients would use the orodispersible form for the further 2 months and half of them for a long treatment period. Compliance was satisfactory and blood pressure remained controlled over the whole study duration.

No emergent adverse event was reported during the treatment period.

Date of the report: 10 January 2017

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