SYNOPSIS ***ANNEX I***

Name of Sponsor/Company: Jacob Eifer Møller, Department of Cardiology, Odense University Hospital	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use only)*
Name of Finished Product: Entresto		
Name of Active Ingredient: Sacubitril/valsartan		
Title of Study: ANGIOTENSIN–NEPRILYSIN INHIBITION IN DIASTOLIC DYSFUNCTION AFTER AMI		
Investigators: Professor Jacob Eifer Møller, MD PhD DmSci and Peter Hartmund Frederiksen, MD		
Study centre(s): Odense University Hospiatal		
Publication (reference): Not yet publised		
Studied period (years): date of first enrolment: 12/04/2018 date of last completed: 07/06/2022	Phase of development:	
Objectives: The main objective of this study is to assess the effect of angiotensin–neprilysin inhibition on central hemodynamics, myocardial structure and myocardial function in patients with a recent AMI and Doppler echocardiographic signs of diastolic dysfunction and preserved systolic function		
Methodology: Efficacy: To assess the effect of 6 months treatment with LCZ696 compared withplacebo on ratio of pulmonary capillary wedge pressure/cardiac index during exercise in patients with a recent AMI and Doppler echocardiographic signs of diastolic dysfunction and preserved systolic function.		
Number of patients (planned and analysed): Planned: 100, analysed: 49		
Diagnosis and main criteria for inclusion: Documented ST segment elevation or non ST- myocardial infarction, left ventricular ejectionfraction > 45% and signs of diastolic dysfunction		
Test product, dose and mode of administration, batch number: oral sacubitril/valsartan 97+103 mg b.i.d.		
Duration of treatment: 6 months		
Reference therapy, dose and mode of administration, batch numbe oral placebo tablets bi.i.d		

***ANNEX 1** cont.*

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Name of Finished Product: Entresto		
Name of Active Ingredient: Sacubitril/valsartan		

Criteria for evaluation:
Ratio of pulmonary capillary wedge pressure to cardiac index at peak exercise after 26 weeks treatment with LCZ696 or placebo.
Safety:
Adverse events related to the test product

Statistical methods:
Analyzed using linear regression and mixed effects models.

SUMMARY - CONCLUSIONS **EFFICACY RESULTS:**

49 patients underwent randomization six patients withdrew consent or were excluded thus the primary analysis consists of 43 patients, 21 assigned to placebo and 22 assigned to sacubitril/valsartan (sac/val). The majority of patients were male (84%) and age were 67 years on average (SD 7.4). The PCWP/CI ratio at peak exercise 3.8 (SD 2.6) mmHg/L/min/m^2 (SD 2.6) in patients treated with sac/val and 3.6 (SD 1.6) mmHg/L/min/m^2 in placebo treated patients. The difference was not statistical significant, p=0.102.

SAFETY RESULTS:
14 serious adverse events were reported during the study period, none were related to the investigational product.

CONCLUSION:
In patients with a recent myocardial infarction and echocardiographic signs of diastolic dysfunction, 6 months of treatment with sac/val did not change the primary outcome of PCWP/CI.

Date of the report: 12/04/2024