

**Routine *CYP2C19* Genotyping to Adjust Thienopyridine Treatment after primary PCI for ST-elevation Myocardial Infarction: Results of the GIANT study**

Running title: Routine *CYP2C19* genotyping to adjust antiplatelet therapy

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**Supplemental data :**

**Supplemental methods**

**Supplemental Table 1**

**Annex**

## Supplemental methods

### Trial design and patients

The GIANT study was a prospective, multi-center, observation study performed at 57 sites in France (supplemental data, annex 1). The protocol was approved by ethics committee and national authorities and all enrolled patients provided informed and signed consents to participate the study and to genetic analyses. The population consisted of all patients presenting with STEMI of less than 24-hour onset and admitted for primary percutaneous coronary intervention irrespective of whether bare metal stents or drug-eluting stents were used. Patients were prescribed a course of dual antiplatelet therapy with aspirin and clopidogrel or prasugrel as standard of care treatment according to local practice at that time. Following the primary angioplasty and stent implantation procedure, a complete *CYP2C19* genetic profiling was performed in the study patients. The genotyping results were communicated to the study investigators for potential adjustment and optimization of thienopyridine treatment according to running recommendations at the time of the recruitment period.

### Objectives

The primary objective was to demonstrate that the rate of ischemic events observed in *CYP2C19* LOF carriers detected by a routine genotype and receiving an adjusted higher intensity thienopyridine treatment is similar to the one observed in patients with *CYP2C19* wild-type genotype or gain-of-function allele and receiving a standard thienopyridine treatment. The primary endpoint was difference in 12-month outcomes (including death, myocardial infarction and stent thrombosis) between patients with normal and rapid *CYP2C19* metabolic status (Class 1) and patients with reduced *CYP2C19* metabolic activity who received high intensity

thienopyridine treatment (Class 2). The secondary endpoint involved the difference in 12-month MACCE between and the major bleeding complications (based on the criteria used in the STEEPLE clinical trial(25)) at 12 months between groups. Sub-groups were predefined according to gender or AMI localization.

### **Statistical analysis**

Continuous variables are presented as mean and standard deviation (SD) when appropriate.

Categorical data are presented as numbers and percentages.

We performed survival curves using the Kaplan-Meier method, and compared group curves using Log-rank. Time was measured from the day of procedure. The first occurrence of any significant event between day 1 and 12 months was analyzed. Patients were censored at twelve months or on the final follow-up day (or date of death) if the event occurred before twelve months.

Proportions were compared using the Fisher's exact test or chi-square test and continuous variables using Wilcoxon test or Student test when appropriate.

Statistical Analysis System software (version 9.3) was used for all analyses.

**Supplemental Table 1. Demographic data in non-adjusted patients with slow/very slow metabolism status**

	<b>N</b>	<b>Class 3</b>
Male gender	46	34 (73.9)
Age (years) mean and SD	46	68.1 (15.1)
<u>CV History :</u>		
Myocardial infarction	46	4 (8.7)
PCI	46	3 (6.5)
CABG	46	0
Stroke	46	1 (2.2)
<u>Risk factors :</u>		
Family History	46	7 (15.2)
Smoking :		
<i>Past or current</i>	45	25 (55.5)
Treated diabetes	45	7 (15.6)
Dyslipidemia	45	17 (37.8)
Hypertension	45	22 (48.9)
Single vessel disease	46	22 (47.8)
2-vessel disease	46	19 (41.3)
3-vessel disease	46	9 (19.6)
Ejection fraction >50%	35	18 (51.4)
Genotype :		
Slow		
*2 *1		43 (93.4)
*4 *1		1 (2.2)
Very slow		
*2 *2		3 (6.5)

## Annex 1.

### Steering Committee Members:

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