

## CYP2C19 SNP'S INFLUENCE ON CLOPIDOGREL RESPONSE IN PERIPHERAL ARTERY DISEASE PATIENTS

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**Background and Objective:** Clopidogrel is a prodrug, metabolized to its active metabolite especially by the CYP2C19 enzyme. The effect of CYP2C19 polymorphisms on clopidogrel efficacy in coronary disease had been widely researched. Even, the clopidogrel label recommends testing the CYP2C19 loss of function alleles before the start of the treatment and, DPWG and CPIC pharmacogenetic dosing guidelines, recommend switching clopidogrel in case of carrying the CYP2C19\*2 SNP in coronary patients with stent. This remains unstudied in peripheral artery disease (PAD) patients. The aim is to explore the influence of CYP2C19 genetic polymorphisms on clopidogrel response in PAD patients.

**Methods:** Peripheral artery disease (PAD) patients treated with clopidogrel after percutaneous transluminal angioplasty (PTA) were recruited. They were tested for carrying the CYP2C19\*2, \*3 (loss of function, LOF) and \*17 (Gain of function, GOF) allele. The primary endpoint was the occurrence of atherothrombotic ischemic events, diagnosed by ultrasound imaging, during 12 months follow-up. Furthermore, we collected data about clinical parameters (age, sex, ethnicity), co-medication during follow-up, vascular risk factors and surgical parameters. We tested the association between carrying LOF or GOF alleles and the primary endpoint in a univariate analysis, and multivariate analysis including those clinical parameters previously related to clopidogrel response. OR and HR were calculated and p-values <0.05 were considered statistically significant.

	EVENTO PRIMARIO		OR (IC 95%)	p- valor	OR (IC 95%)*	p- valor*	OR (IC 95%)^	p- valor^
	SI (n=25, 34.7%)	NO (n=47, 66.3%)						
CYP2C19 LOF	11 (44%)	7 (15%)	4.49	<b>0.009</b>	4.89	<b>0.018<sup>a</sup></b>	6.16	<b>0.003</b>
CYP2C19 no-LOF	14 (56%)	40 (85%)	(1.45-13.84)		(1.32-12.83) <sup>a</sup>		(1.81-21)	
CYP2C19 GOF	8 (32%)	18 (38%)	0.76	0.596	-	-	0.91	0.868
CYP2C19 no-GOF	17 (68%)	29 (62%)	(0.27-2.11)				(0.30-2.79)	

\*Ajustado por: <sup>a</sup> HTA, IBP, sexo, B-bloqueantes; <sup>b</sup> HTA, IBP, HBPM

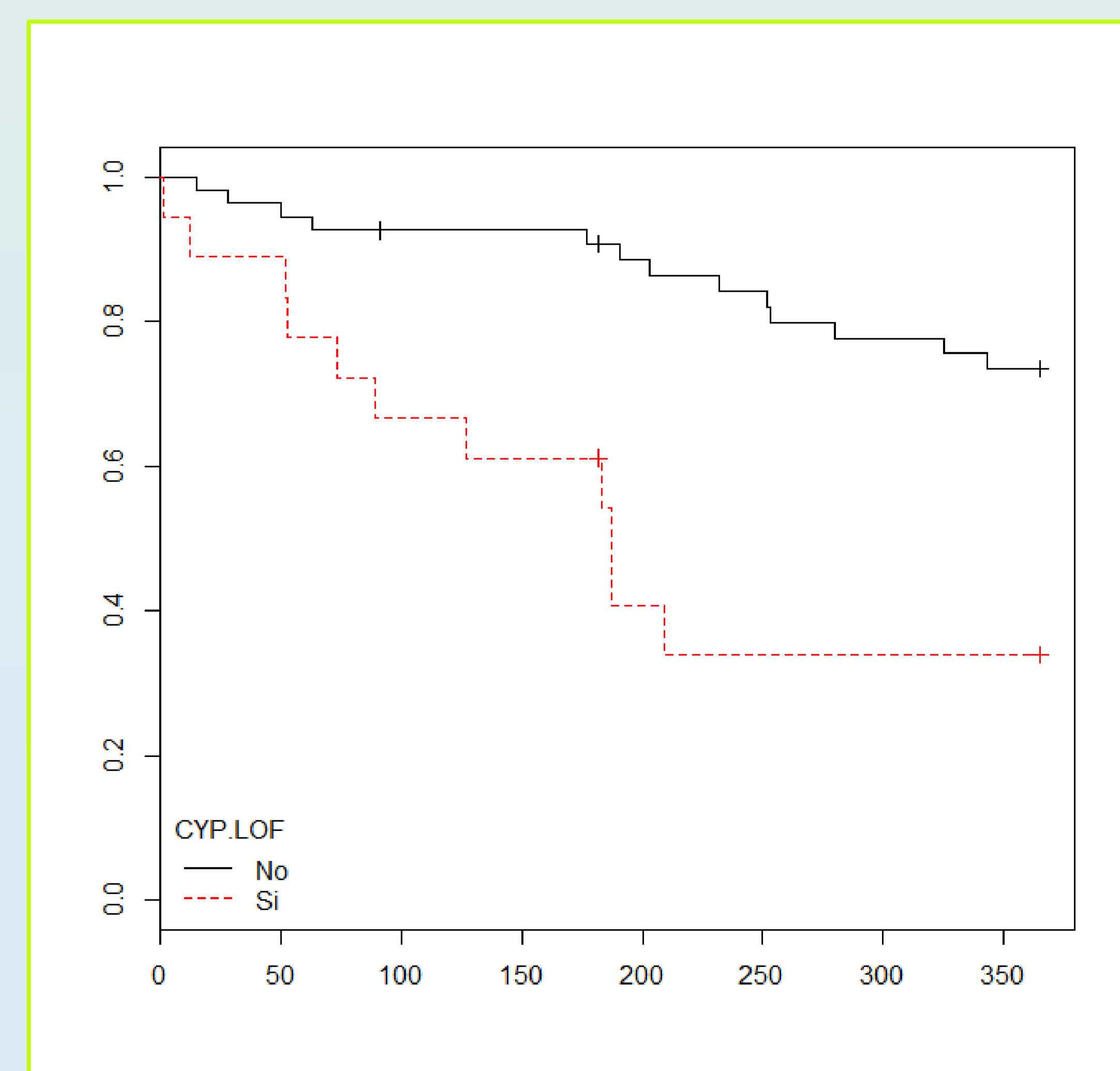
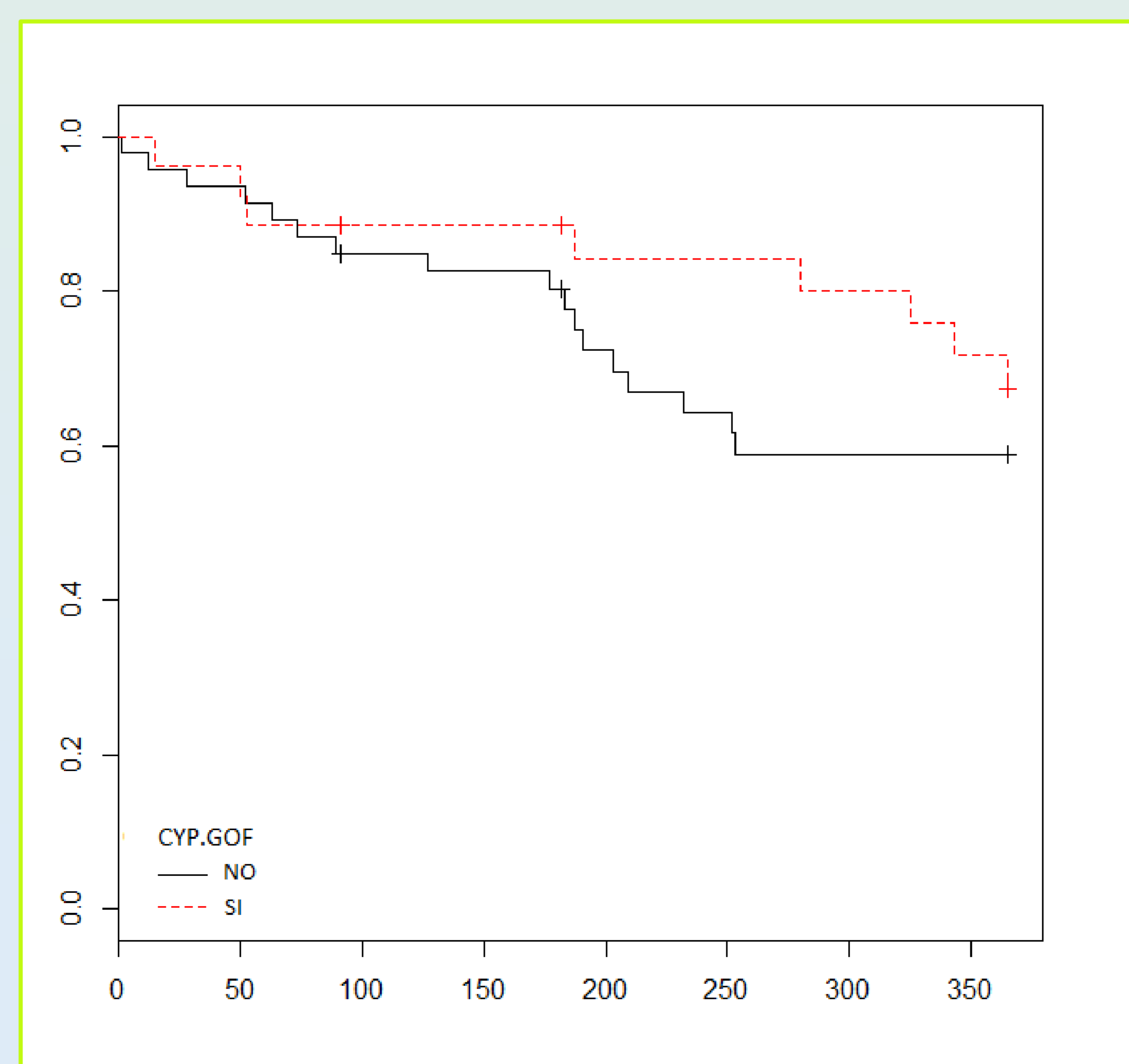
^ Ajustado por el resto de los polimorfismos.

En azul los p-valor<0.05

## RESULTS



<http://www.eahp.eu/24-5PSQ-008>



CYP2C19 LOF		CYP2C19 GOF	
HR (IC 95%)	p-valor	HR (IC 95%)	p-valor
4.07 (1.80 – 9.20)	<b>&lt;0.001</b>	0.69 (0.30-1.61)	0.394

**Discussion:** CYP2C19 LOF polymorphisms show a higher effect on clopidogrel response in PAD patients than that provided in acute coronary syndrome patients. These SNP's may be used as genetic marker of clopidogrel response in PAD patients.

## Conclusions:

As in ACS patients, CYP2C19 genotyping should be considered before clopidogrel treatment in patients with PAD after PTA