# PREVALENCE OF THE CYP2C19 *2 ALLELE IN MALTESE PATIENTS ON CLOPIDOGREL THERAPY

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## BACKGROUND

The CYP2C19 loss-of-function (LoF) *2 allele is associated with reduced CYP2C19 activity which impairs clopidogrel bioactivation and increases the risk of adverse cardiac outcomes after percutaneous coronary intervention (PCI). To-date, prevalence of the CYP2C19 *2 allele in the Maltese population has not been reported.

## AIMS

To genotype Maltese patients undergoing PCI for the CYP2C19 *2 allele and to compare prevalence of the *2 allele in this Maltese population to other populations bordering the Mediterranean Sea.

## METHOD

1. Following ethics approval and informed written consent, 5 mL of peripheral blood was collected from 244 Maltese patients undergoing PCI and who were on dual antiplatelet therapy with aspirin and clopidogrel.
2. Genomic DNA extraction was carried out using the QIAamp® DNA Mini QIAcube kit *(Qiagen)*.
3. CYP2C19 SNP genotyping for the *2 (rs4244285) allele was performed using a TaqMan® drug metabolism assay *(Life Technologies)* on the 7500 real-time PCR system *(Applied Biosystems)*.
4. Patients were genotyped as non-carriers (*1/*1) and carriers (*1/*2 or *2/*2) of the CYP2C19 *2 allele.
5. Prevalence of the CYP2C19 *2 allele and *2/*2 genotype in this population was compared to 12 populations bordering the Mediterranean Sea using the 'difference between two proportions test'. A p-value < 0.05 indicated that the proportions differed significantly, while a p-value > 0.05 indicated that the proportions were comparable.

## RESULTS

- From the 244 patients, 184 (75.4%) were non-carriers (*1/*1) and 60 (24.6%) were carriers of one *2 allele (*1/*2). No patients were genotyped as *2/*2.
- Total frequency of the *2 allele in this Maltese population was 12.3%. Frequency of the *2 allele ranged from 10.9% in Egyptians to 16.9% in Bosnians. Prevalence of the *2 allele in this Maltese population was comparable (p>0.05) to all Mediterranean populations studied (Table 1).
- Prevalence of *2/*2 genotype ranged from zero in Tunisians to 3.1% in Lebanese. Prevalence of *2*/2 genotype in this Maltese population was comparable (p>0.05) to Egyptian, Southern French, Slovenian, Turkish and Tunisian populations (Table 1).

*Table 1: Distribution of CYP2C19 *2 allele and *2/*2 genotype in Maltese vs. other populations bordering the Mediterranean Sea*

| Population[a] (reference) | Number of patients (number of alleles) | CYP2C19 allele frequency % (p-value) | CYP2C19 *2/*2 genotype frequency % (p-value) |
|---|---|---|---|
| *Maltese* (current study) | 244 (488) | 12.3 | 0 |
| Bosnian[(1)] | 77 (154) | 16.9 (0.144) | 2.6 (0.011)* |
| Croatian[(2)] | 200 (400) | 15.0 (0.242) | 3.0 (0.007)* |
| Egyptian[(3)] | 247 (494) | 10.9 (0.490) | 0.8 (0.162) |
| French (Marseille)[(4)] | 213 (426) | 12.0 (0.889) | 1.0 (0.116) |
| Greek[(5)] | 283 (566) | 13.1 (0.697) | 2.1 (0.023)* |
| Israeli Jewish[(6)] | 140 (280) | 15.0 (0.289) | 2.9 (0.008)* |
| Italian (Messina)[(7)] | 360 (720) | 11.1 (0.522) | 1.7 (0.040)* |
| Lebanese[(8)] | 161 (322) | 13.4 (0.646) | 3.1 (0.006)* |
| Slovenian[(9)] | 129 (258) | 15.9 (0.171) | 0.8 (0.162) |
| Spanish (Valencia)[(10)] | 362 (724) | 13.1 (0.772) | 1.9 (0.030)* |
| Turkish[(11)] | 404 (808) | 12.0 (0.873) | 1.0 (0.116) |
| Tunisian[(12)] | 100 (200) | 11.5 (0.772) | 0 (1.000) |

*[a]Populations listed alphabetically; *p<0.05*

## CONCLUSIONS

Twenty-five percent of this Maltese population were carriers of the CYP2C19 LoF *2 allele and the prevalence was comparable to all the Mediterranean populations studied. This finding has important clinical implications for clopidogrel use in Malta since according to CYP2C19 genotype-guided therapeutic recommendations[13], an alternative antiplatelet agent, such as prasugrel, should be considered in carriers of the *2 allele, provided there is no contra-indication.

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