



MEETING ABSTRACT

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# OR2-002 – The risk of FMF in *MEFV* heterozygotes

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## Introduction

Familial Mediterranean fever (FMF) is an autosomal recessive autoinflammatory disorder due to *MEFV* mutations and one of the most frequent Mediterranean genetic diseases. The observation of many heterozygous patients in whom a second mutated allele was excluded led to propose that heterozygosity could be causal; however, this might often be coincidental due to the very high rate of mutations in Mediterranean populations.

## Objectives

To better delineate the pathogenicity of heterozygosity in order to help genetic counselling and better manage the disease.

## Methods

Complementary statistical approaches were used: estimation of FMF prevalence at population levels, genotype comparison in siblings from 63 familial forms, and genotype study in 557 patients from four Mediterranean populations.

## Results

At population level, we did not observe any contribution of heterozygosity to the disease prevalence. In affected siblings of patients carrying two *MEFV* mutations, 92% carry two mutated alleles whereas 4% are heterozygous with typical FMF diagnosis. We also demonstrated statistically that patients are more prone to be heterozygous than healthy individuals, as shown by the higher ratio heterozygous carriers/non carriers in patients ( $p < 10^{-7}$  -  $p < 0.003$ ). The risk for heterozygotes to develop FMF was estimated between  $2.1 \times 10^{-3}$  and  $5.8 \times 10^{-3}$  and the relative risk, as

compared to individuals carrying no *MEFV* mutation, between 6.3 and 8.1.

## Conclusion

This is the first statistical demonstration that heterozygosity is not responsible for classical Mendelian FMF, but constitutes a susceptibility factor for clinically-similar complex conditions. We also provide a first estimate of the risk for heterozygotes to develop FMF.

## Disclosure of interest

None declared.

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