ANALYSIS OF THE DPYD GENE MUTATIONS IN CANCER PATIENTS WHO ARE CANDIDATES FOR TREATMENT WITH FLUOROPYRIMIDINES

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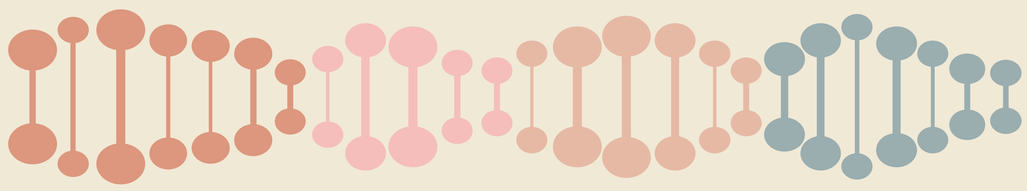
Introduction

Dihydropyrimidine dehydrogenase encoded by the DPYD gene, is the rate-limiting enzyme of fluoropyrimidines catabolism

Among around 450 missense DPYD single-nucleotide polymorphisms, only approximately twenty of them acquire a functional significance

Four of these variants are considered to be of clinical relevance for recognized effects on the protein, their identified higher risk of severe toxicity, and for their population frequency



Objectives

To analyse DPYD gene mutations in all patients who are candidates for receiving a fluoropyrimidine-based regimens and their influence on the individualization of cancer treatment.

Material and methods

Observational, retrospective study

July 2020 to July 2022

genotyping test for DYPD

- Age
- Sex
- Type of cancer

Loss-of-function variants in the DPYD gene:

- c.1905+1G>A (rs3918290) that identifies the DPYD*2A haplotype
- c.1679T>G (rs55886062) that identifies the DPYD*13 haplotype

Reduced function variants in the DPYD gene:

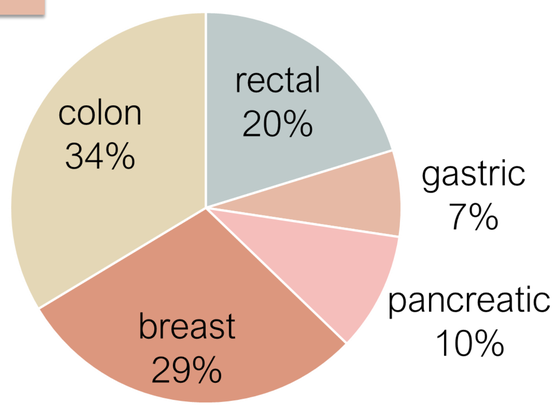
- c.1129-5923C>G (rs56038477) that identifies the HapB3 haplotype
- c.2846A>T (rs67376798)

Results

638 DPYD gene determination

mean age 63 years

53 % men



32 (5,0%) had some mutation in the DPYD gene
4 (0,6%) patient was heterozygous for c.1905 + 1G> A
1 (0,16%) patient was heterozygous for c.1679T>G
4 (0,6%) patients were heterozygous for c.2846A> T
23 (3,6%) patients were heterozygous for c.1129-5923C> G

All intermediate metabolizers
It´s recommended to start treatment with a dose reduced to 50%

The individualization of treatment was:
16 patients started treatment at 50% of the dose
7 patients the chemotherapy regimen were changed
7 patients adjuvant therapy were dismissed
1 patient received radiatiotherapy alone
1 patient was not treated

Conclusion

The determination of DPYD polymorphisms prior to the start of treatment with fluoropyrimidines, allows to identify DPD-deficient patients, and avoid may experience serious side effects when treated with fluoropyrimidines; and thus clinicians' decisions are influenced by the results of DYPD genotyping.

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