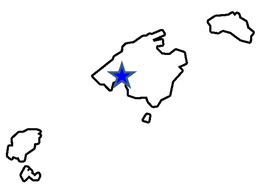
DETERMINATION OF DIHYDROPYRIMIDINE DEHYDROGENASE GENOTYPES TO GUIDE PHYSICIANS IN THE DOSING OF FLUOROPYRIMIDINES

CPS12257



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WHAT WAS DONE?

Design of a protocol for the Implementation of **dihydropyrimidine dehydrogenase (DPD) genotype tests** in our hospital so that the results can be clinically **interpreted by the pharmacists**, and then used to **guide physicians in the dosing of fluoropyrimidines** (5-fluorouracil/capecitabine). The project was done with the collaboration of the Genetic and Genomic Laboratory (GGL) located in the reference hospital of our territory.

WHY WAS IT DONE?

Treatment with fluoropyrimidine produces **severe toxicity in about 30% of the patients**. This toxicity has been **related to a reduction in the activity of DPD**, the rate-limiting enzyme for fluoropyrimidine catabolism. This is due to certain **genetic variants of DPYD,** the gene encoding DPD. For this reason, regulatory agencies such as the European Medicines Agency (EMA) recommend determining DPD deficiency in all patients who are candidates for treatment with fluoropyrimidines.

HOW WAS IT DONE?

The elaboration of the protocol took place as follows, coordinated by the oncology pharmacyst:

Informatics. They created a formulary at the electronic prescription programme (HP-HCIS®) for the inclusion of the patients in the testing protocol.

Oncologysts and nursing service. They were trained in the implementation of this new determination, as well as in the procedure for obtaining and sending samples to the GGL.

GGL. They conducted the DPYD genotype tests and reported the results to the oncology pharmacyst.

Oncology pharmacyst. They did the clinical interpretation of the result based on the following European Society for Medical Oncology (ESMO) recommendations:

DPYD variant	% of standard fluoropyrimidine dose
*DPYD*2A (rs3918290)*	*50*
c.1679T>G (rs55886062)	*50*
c.2846A>T (rs67376798)	*75*
c.1236G>A/HapB3 (rs56038477)	*75*

WHAT HAS BEEN ACHIEVED?

Since the implementation of the protocol, **73 determinations of DPYD** polymorphisms have been performed (November 202 to August 2022). **Three patients (4.1%) were found to be heterozygous DPYD gene variant carriers** (two DPYD*2A and one c.2846A>T).

The average time for obtaining the results was 17.5 days. For this reason, in most cases the treatment was started before the result was obtained.

WHAT IS NEXT?

We are working in the implementation of a new fluorescence technique that will allow us to **shorten the time of obtaining the result** of the determinations.