PHARMACOGENETIC-GUIDED TREATMENT IN PATIENTS WITH DYHYDROPIRYMIDINE DEHYDROGENASE (DPD) DEFICIENCY

Fernández-Fradejas J1, Morín-Rodriguez M2, Gemeno-López E3, Delgado-Silveira E1, Moreno-Pelayo MÁ2, Álvarez-Díaz AM1

1 Pharmacy Department. Hospital Universitario Ramón y Cajal. Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS)
2 Genetics Department. Hospital Universitario Ramón y Cajal. Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS)

BACKGROUND AND IMPORTANCE

In 2020, the European Medicines Agency recommended that patients should be tested for the deficiency of DPD prior to treatment with fluorouracil, capcitabine or tegafur.

AIM AND OBJECTIVES

- To assess the prevalence of DPYD variants in cancer patients treated with fluoropyrimidines.
- To evaluate the safety of pharmacogenetic guided treatment in patients with DPD deficiency.

MATERIAL AND METHODS

Study design and inclusion criteria
- Prospective, observational study at a third level hospital.
- Cancer patients who underwent genotyping test for DPD deficiency between 1 November 2021 and 15 September 2022 were included.

DNA was obtained from peripheral blood samples. Four DPYD polymorphisms were analyzed:
- rs3918290
- rs55886062
- rs67376798
- rs75017182

DPD deficiency and clinical outcomes assessment
- Patients were classified as normal, intermediate or poor metabolizers according to the result of pharmacogenetic test.
- Grade 3-4 toxicities in intermediate and poor metabolizers were screened during the first two cycles of treatment.

RESULTS

Patients
- N = 345 (52.6% male)
- Age (mean) 68.3 (SD 11.7)

DPD deficiency prevalence
- Fourteen patients were classified as intermediate metabolizers.
- No poor metabolizers were identified.

Clinical outcomes
- Eleven of the intermediate metabolizers received fluoropyrimidine based chemotherapy with an initial 50% dose reduction.
- Patients underwent treatment without suffering any severe adverse event.
- No further dose reduction or treatment delays were required in these patients.

CONCLUSION AND RELEVANCE

- Overall, 4.1% of the patients of our cohort had partial DPD deficiency.
- Treatment individualization based on DPYD genotyping can be useful to avoid severe adverse events in patients treated with fluoropyrimidines.

Graphic 1. Cancer diagnoses

Graphic 2. DPYD polymorphisms

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5PSQ-132 jffradejas@salud.madrid.org @j_ffradejas