ASSOCIATION OF DIHYDROPYRIMIDINE DEHYDROGENASE DEFICIENCY WITH CAPECITABINE TOLERANCE

Peláez Bejarano A, Rodriguez Molins E, Gomez-Sayago L.
RIOTINTO HOSPITAL, PHARMACY, HUELVA, SPAIN.

BACKGROUND
Dihydropyrimidine dehydrogenase (DPD) is the first of the enzymes in the fluoropyrimidine metabolic pathway. Recently, the Spanish Agency of Medicine and Health Products reported an informative note warning that patients with partial or total deficiency in DPD activity cannot adequately degrade fluoropyrimidines, increasing the risk of serious toxicity. DPD genotyping is recommended as standard practice for predicting the occurrence and severity of capecitabine toxicity.

AIM AND OBJECTIVES
To assess the rate of deficiency of the metabolising enzyme DPD in patients treated with capecitabine and to describe the associated toxicity.

MATERIAL AND METHODS

- Observational and retrospective study
- Data collected: Age, gender, Eastern Cooperative Oncology Group (ECOG) and diagnosis
- Pharmacogenomics analysis
  (Polymerase Chain Reaction technique)
  DPD genotyping was performed on 25 patients (69%)
  Mutated allele heterozygote was detected in 3 (8.3%) patients
  rs 56038477 (n=2, 5.5%)
  rs 67376798 (n=1, 2.8%)

RESULTS
36 patients were included. Median age 70.9 (50–88) years. ECOG 0–1 was observed in 94% of cases.

DIAGNOSIS
- Colorectal cancer (n=22, 61%)
- Gastric cancer (n=9, 25%)
- Breast cancer (n=5, 14%)

Most common AE
- Weakness (n=18, 50%)
- Diarrhea (n=17, 47.2%)
- Gastrointestinal (n=10, 27.8%)
- Dactylitis (n=8, 22.2%)
- Mucositis (n=8, 22.2%)
- Paresthesia (n=8, 22.2%)
- Hyperpigmentation (n=6, 16.7%)
- Constipation (n=4, 11.1%)

Without DPD mutation
- Dose reduction was required in 8 (32%) patients

With DPD mutation
- Mutated allele heterozygote was detected in 3 (8.3%) patients
  rs 56038477 (n=2, 5.5%)
  rs 67376798 (n=1, 2.8%)

All patients with DPD mutation and 20 (80%) without DPD mutation presented AE

CONCLUSIONS AND RELEVANCE
It is important to know the DPD polymorphism to correctly adjust the capecitabine dose. A considerable percentage of patients without DPD mutation report AE. Determination of variants of DPD can help avoid serious or fatal EA.

QR Code

4CPS-035
L01 - ANTI NEOPLASTIC AGENTS

Área Sanitario NORTE DE HUELVA

variants of DPD