Joint Belgian recommendation on screening for DPD-deficiency in patients treated with 5-FU, capecitabine (and tegafur)

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ABSTRACT

Objectives:

Fluoropyrimidines such as 5-Fluorouracil (5-FU), capecitabine and tegafur are drugs that are often used in the treatment of maliginancies. The enzyme dihydropyrimidine dehydrogenase (DPD) is the first and rate limiting enzyme of 5-FU catabolism. Genetic variations within the DPYD gene (encoding for DPD protein) can lead to reduced or absent DPD activity. Treatment of DPD deficient patients with fluoropyrimidines can result in severe and, rarely, fatal toxicity. Screening for DPD deficiency should be implemented in practice

Methods:

The available methods in routine to screen for DPD deficiency were analyzed and discussed in several group meetings involving members of the oncological, genetic and toxicological societies in Belgium: targeted genotyping based on the detection of 4 DPYD variants and phenotyping, through the measurement of uracil and dihydrouracil/uracil ratio in plasma samples.

Results:

The main advantage of targeted genotyping is the existence of prospectively validated genotype-based dosing guidelines. The main limitations of this approach are the relatively low sensitivity to detect total and partial DPD deficiency and the fact that this approach has only been validated in Caucasians so far. Phenotyping has a better sensitivity to detect total and partial DPD deficiency when performed in the correct analytical conditions and is not dependent on the ethnic origin of the patient.

Conclusion:

In Belgium, we recommend phenotype or targeted genotype testing for DPD deficiency before starting 5-FU, capecitabine or tegafur. We strongly suggest a stepwise approach using phenotype testing upfront because of the higher sensitivity and the lower cost to society.

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