INESSS
LE SAVOIR PREND FORME

CLINICAL TOOL | INFORMATION TO BE PROVIDED TO YOUR PATIENT

DPYD status and risk of severe toxicities with 5-FU or capecitabine-based chemotherapies

This clinical tool is provided for information purposes only and should not replace the clinician's judgement. The report on which it is based is available in the Publications section of INESSS's website inesss.qc.ca.

Here is the information your patient should know before starting his or her therapy:

Risk of severe toxicities	In 10 to 40% of patients, 5-FU or capecitabine-based chemotherapy can cause severe and sometimes fatal (0.5 to 1%) toxicities. One of the causes of these toxicities can be dihydropyrimidine dehydrogenase (DPD) deficiency.
DPD deficiency	DPD deficiency is characterized by a decrease in (or the complete absence of) DPD enzyme activity. In patients whose treatment plan consists of 5-FU or capecitabine-based chemotherapy, DPD deficiency can cause an accumulation of active metabolites and increase the risk of severe toxicities.
***DPYD* genotyping**	*DPYD* genotyping is used to identify 4 genetic variants that can put certain individuals at risk for severe toxicities with a standard dose of 5-FU or capecitabine. Approximately 7% of individuals carry one or more of these genetic variants.
Implications of the *DPYD* genotyping result	**– Negative result** • If none of the genetic variants tested for is detected, the standard dose is prescribed. ⚑ There remains a residual risk of developing a severe toxicity, but this risk is similar for all patients who do not carry the variants in question. **+ Positive result** ⚑ If a genetic variant is detected, the initial dose of 5-FU or capecitabine should be reduced to adjust the treatment to the patient's metabolic capacity and reduce the risk of severe toxicities (see table on overleaf). ⚑ During the subsequent cycles, the dose is readjusted according to the patient's tolerance in order to achieve safe maximum exposure and optimize the treatment's effectiveness.

Québec

Dosage adjustment according to *DPYD* genotype

RESULTS FOR TESTED ALLELES	DOSAGE ADJUSTMENT
− Negative results	**A**
+ Positive results	
1236G > A (1 allele)	**B**
1236G > A (2 alleles)	**D**
1236G > A **and** 2846A > T	**D**
1679T > G (1 allele)	**C**
1679T > G (2 alleles)	**F**
1679T > G **and** 1236G > A	**E**
1679T > G **and** 2846A > T	**E**
DPYD*2A (1 allele)	**C**
DPYD*2A (2 alleles)	**F**
DPYD*2A **and** 1236G > A	**E**
DPYD*2A **and** 1679T > G	**F**
DPYD*2A **and** 2846A > T	**E**
2846A > T (1 allele)	**B**
2846A > T (2 alleles)	**D**

A	**No indication for changing the dose or treatment** A negative genotyping result for specific *DPYD* alleles (even combined) is not a guarantee of no DPD activity impairment or severe toxicities following fluoropyrimidine-based therapy. Vigilance should be maintained during first exposure to fluoropyrimidines.
B	**Reduce† the standard initial dose by 25 to 50%** Each patient's individual circumstances should be taken into consideration to determine if a cautious approach (50% reduction†) or an approach aimed at optimizing effectiveness despite a potentially higher risk of toxicity (25% reduction†) is preferable.
C	**Reduce† the standard initial dose by 50%**
D	**Avoid the use of fluoropyrimidines** If there is no good therapeutic option, the initial dose can be reduced† by 50 to 75% (expert opinion). Each patient's individual circumstances should be taken into consideration to determine if a cautious approach (75% reduction†) or an approach aimed at optimizing effectiveness despite a potentially higher risk of toxicity (50% reduction†) is preferable.
E	**Avoid the use of fluoropyrimidines** If there is no good therapeutic option, the initial dose can be reduced† by at least 75% (expert opinion).
F	**Avoid the use of fluoropyrimidines**

† During the subsequent cycles, the recommended initial dose is readjusted according to the patient's tolerance in order to achieve safe maximum exposure and optimize the treatment's effectiveness. The initial dosage adjustment depends on other factors as well, including the chemotherapy protocol and the patient's characteristics.

1236G>A is used as a proxy for the 1129-5923C>G allele

DPYD*2A refers to the 1905+1G>A allele

Available antidote: Uridine triacetate (Vistogard)
Information: Refer to the Groupe d'Étude en Oncologie du Québec (GÉOC) at www.geoq.info/fr/connexion - Connexion membre / Antidote / Fiches antidotes
If emergency: Contact the Québec Poison Control Centre at 1-800-463-5060

Institut national d'excellence en santé et en services sociaux
Québec