DPYD VARIANTS (DIHYDROPYRIMIDINE DEHYDROGENASE) (DPYD *2A, *13, Asp949Val)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-001-25
RDM Code: 1860017/R
CND Code: W0106010499
Tests: 25
Reactions: 31 x 3
Manufacturer: BioMol Laboratories s.r.l.

CONTENTS OF THE KIT

The kit consists of: reagents for Real-Time PCR amplification
**the reagents for the extraction of genomic DNA are not supplied in the kit.*

PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-PHARMACOGENETICS TEST.** Determination of genetic variants *2A (rs3918290, 1905 +1G>A, IVS14 +1 G>A), *13 (rs5588606, 1679 T>G), and Asp949Val, (rs67376798, 2846 A>T) of the DPYD gene by amplification with oligonucleotides and specific probes (allele-specific genotyping) and subsequent detection with qPCR-Real-time. Kit optimized for Real-Time PCR instrumentation Biorad CFX96, Biorad Opus Dx, Agilent AriaDx.

SCIENTIFIC BACKGROUND

The treatment of neoplastic pathologies has increasingly become personalized in relation to the large inter-individual differences that exist in the effect of the therapy and its toxicity. Polymorphisms in genes encoding proteins responsible for drug metabolism can significantly influence the absorption, metabolism and elimination of anticancer drugs. As a result, the different pharmacokinetics can greatly influence the efficacy and toxicity of drugs.

Pharmacogenetic screening and/or drug-specific phenotyping of cancer patients eligible for treatment with chemotherapy drugs can identify patients likely to be reactive or resistant to proposed drugs. Similarly, identification of patients with an increased risk of developing toxicity allows for dose adaptation or application of other targeted therapies.

§ Eur J Cancer. 2018 Oct; 102:31-39. doi: 10.1016/j.ejca.2018.07.009. Epub 2018 Aug 13. Pharmacogenetic analyses of 2183 patients with advanced colorectal cancer; potential role for common dihydropyrimidine dehydrogenase variants in toxicity to chemotherapy.

§ Curr Ther Res Clin Exp. 2018 Oct 31;90:1-7. doi: 10.1016/j.curtheres.2018.10.001. eCollection 2019. Evolution of Dihydropyrimidine Dehydrogenase Diagnostic Testing in a Single Center during an 8-Year Period of Time.

§ Genotypes Affecting the Pharmacokinetics of Anticancer Drugs. Clin Pharmacokinet. 2017, Apr;56(4):317-337. doi: 10.1007/ s40262-016-0450-z. Review.

§ Int J Cancer. 2015 Dec 15;137(12):2971-80. doi: 10.1002/ijc.29654. Epub 2015 Jul 14. Clinical validity of a DPYD-based pharmacogenetic test to predict severe toxicity to fluoropyrimidines.

§ JGH Open. 2019 Feb 8;3(5):361-369. doi: 10.1002/jgh3.12153. eCollection 2019 Oct. Review.

§ Br J Cancer. 2019 Apr; 120(8):834-839. doi: 10.1038/s41416-019-0423-8. Epub 2019 Mar 12. The Clinical Relevance of Multiple DPYD Polymorphisms on Patients Candidate for Fluoropyrimidine Based-Chemotherapy. An Italian Case-Control Study

§ EMA recommendations on DPD testing prior to treatment with fluorouracil, capecitabine, tegafur and flucytosine. 30 April 2020

CLINICAL SIGNIFICANCE

The main chemotherapeutic agents used in many types of cancer are fluoropyrimidines, namely 5-fluorouracil (5-FU), capecitabine and various derivatives. Treatment with these agents is not well tolerated in a subset of patients as moderate to severe (fatal) toxicity occurs in 20% to 40% of cases, manifesting as nausea and vomiting, diarrhoea, mucositis/stomatitis, myelosuppression, and hand-foot syndrom. The main route of degradation of fluoropyrimidines is the enzyme dihydropyrimidine dehydrogenase (DPYD). The reduced functionality of this enzyme causes an increased exposure to the active metabolites, which can lead to different degrees of toxicity. The DPYD gene is on chromosome 1p22 and has 23 exons. More than 100 variants have been reported. Among these, three were associated with toxicity and decreased enzyme activity: DPYD *2A (c.1905 + 1G> A; rs3918290), DPYD *13 (c .1679 T>G p. [Ile560Ser], rs55886062), and c .2846A>T p. (Asp949Val), rs67376798.

As reported in the 2018 guidelines of the CPIC (Clinical Pharmacogenetics Implementation Consortium (CPIC®) and in the 2019 recommendations of the AIOM (Italian Association of Medical Oncology), SIF (Italian Society of Pharmacology) and EMA (European Medicines Agency), the DPYP pharmacogenetic analysis is recommended to optimize the therapeutic dose and possibly define a reduction in the drug dose (25-50%) for Intermediate Metabolizers patients and the evaluation of an alternative therapy for Poor Metabolizers.

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ISO 9001:2015
ISO 13485:2016

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-001-25	
Mix oligonucleotides and probes	Mix 10X DPYD *2A	1 x 85 µl	-20°C
Mix oligonucleotides and probes	Mix 10X DPYD *13	1 x 85 µl	-20°C
Mix oligonucleotides and probes	Mix 10X DPYD Asp949Val	1 x 85 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 1230 µl	-20°C
Deionized H_20	Deionized H_20	2 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control +1	1 x 40 µl	-20°C
Genomic DNA or recombinant DNA	Control +2	1 x 40 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-001-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissue, cells
POSITIVE CONTROL	Recombinant DNA for at least 3 analytical sessions
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx e Agilent AriaDx
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle (10 min) at 95 °C; 45 cycles at 95 °C (15 sec) + 60 °C 60 sec
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
ANALYTICAL SENSITIVITY : LIMIT OF DETECTION (LOD)	≥ 0,016 ng of DNA
ANALYTICAL SENSITIVITY : LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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