ABCB1 GENE VARIANT G2677T/A (MDR1)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-009-25
RDM Code: 2190182/R
CND Code: W010699
Tests: 25
Reactions: 31 x 2
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**. Detection of genetic variant G2677T; G>T / G2677A; G>A) of the gene ABCB1 (rs2032582) 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 Dx, Biorad Opus Dx and Agilent AriaDx.

SCIENTIFIC BACKGROUND

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. Polymorphisms in genes encoding drug efflux transporters, such as P-glycoprotein, can affect the absorption and excretion of anticancer drugs. It is encoded by the multidrug resistance 1 (MDR1) gene (ABCB1, ATP-binding cassette transporter superfamily B member 1) located on chromosome 7q21. There are three main polymorphisms affecting P-gp activity: the c.2677G>T/A polymorphism in exon 21 which causes a substitution in the amino acid sequence Ala (G)/Ser (T) or Thr (A), with consequent possible increase in enzyme function. The second polymorphism is in exon 26 at position c.3435C>T, resulting in more than twofold expression of P-gp. The third C1236T polymorphism in exon 12 does not directly affect P-gp expression but has an indirect effect as it alters the stability of the mRNA encoding the protein.

CLINICAL SIGNIFICANCE

Docetaxel and paclitaxel are cytotoxic taxanes that inhibit mitosis causing the death of cancer cells. They are mainly used in the treatment of breast, ovarian and lung cancer. For taxanes, the ABCB1 gene is considered one of the best candidates to explain variations in clinical responses and toxicity.

Doxorubicin, an anthracycline widely used as mono- or combination therapy in the treatment of solid tumors including breast cancer, is also the substrate of P-gp. Significantly impaired clearance and decreased plasma concentration of doxorubicin have been observed in patients with one of the three above described polymorphisms of the ABCB1 gene. Irinotecan, a topoisomerase I inhibitor, plays an important role in the treatment of colorectal cancer in monotherapy or in combination with 5-FU. The antitumor activity is mainly due to the SN-38 metabolite which is metabolized to SN-38G, which has 1/100 of the antitumor activity and is practically inactive.

§ Clinical utility of ABCB1 genotyping for preventing toxicity in treatment with irinotecan. Pharmacol Res. 2018 Oct; 136:133-139.doi:10.1016/j.phrs.2018.08.026. Epub 2018 Sep 11.
§ Genotypes Affecting the Pharmacokinetics of Anticancer Drugs. Clin Pharmacokinet. 2017 Apr; 56(4):317-337. doi: 10.1007/ s40262-016-0450-z. Review.
§ Influence of the ABCB1 polymorphisms on the response to Taxane-containing chemotherapy: a systematic review and meta-analysis. Cancer Chemother Pharmacol. 2018, Feb; 81(2):315-323.doi: 10.1007/s00280-017-3496-1. Epub 2017 Dec 5.
§ Irinotecan Pathway Genotype Analysis to Predict Pharmacokinetics. Clin Cancer Res. 2003 Aug 15; 9(9):3246-53.
§ Are pharmacogenomic biomarkers an effective tool to predict taxane toxicity and outcome in breast cancer patients? Literature review. Cancer Chemother Pharmacol. 2015 Oct; 76(4):679-90. doi: 10.1007/s00280-015-2818-4. Epub 2015 Jul 22.

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ISO 9001:2015
ISO 13485:2016

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DESCRIPTION	LABEL	VOLUME FGC-009-25	STORAGE
Mix oligonucleotides and probes	Mix 10X G2677T ABCB1 G>T	1 x 85 µl	-20°C
Mix oligonucleotides and probes	Mix 10X G2677A ABCB1 G>A	1 x 85 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 850 µl	-20°C
Deionized H_20	Deionized H_20	2 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control +1	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control +2	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control +3	1 x 22 µl	-20°C

TECHNICAL CHARACTERISTICS

COD. FGC-009-25

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 at 95 °C (10 min) 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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