ABCB1 (MDR1) GENE VARIANT C3435T

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-008-25
RDM Code: 2159865/R
CND Code: W0106010499
Tests: 25
Reactions: 31
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-GENETIC VARIANTS.**
The FGC-008 kit allows the characterization of the C3435T genetic variant of the ABCB1 gene (rs1045642) 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, 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. This contributes to interindividual variability in pharmacokinetics and, consequently, large differences in treatment response among cancer patients. P-gp is a member of the ABC superfamily of membrane transporters and is involved in the active transport of lipophilic and amphipathic molecules across lipid membranes. 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 first polymorphism c.2677G>T/A (rs2032582) in exon 21 which causes a substitution in the amino acid sequence Ala (G)/Ser (T) or Thr (A), resulting in a possible increase in enzyme function. The second polymorphism is in exon 26 at position c.3435C>T (rs1045642), resulting in more than twofold expression of P-gp. The third polymorphism C1236T (rs1128503) 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

Evaluation of the Association of Polymorphisms With Palbociclib Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3 (ClinicalTrials.gov identifier: NCT01740427 and NCT01942135) paper revealed higher incidence of palbociclib-associated SAEs occurred among homozygous and heterozygous carriers of the c1236C>T variant compared to wild-type, 38% versus 23% (RR=1,65 95%CI 1,19–2,29, p=0,003) and 32% versus 23% (RR=1,37 95%CI 1,03–1.84, p=0,03). An association between the ABCB1 C3435T (rs1045642), ABCB1 G2677T/A (rs2032582) polymorphism and risk of adverse efects of docetaxel was found by meta-analysis. Namely, the TT homozygotes of the ABCB1 C3435T polymorphism may be associated with the risk of hematological toxicity. ABCB1 G2677T T(A)/T(A) genotype may be associated with the fuid retention. Recently it has been demonstrated that 1236TT, 2677TT, and 3435TT carriers (also referred to as “TT-TT-TT” haplotype) need higher methadone doses to avoid withdrawal, probably associated with faster metabolism and consequent lower methadone plasma levels.

§ Clin Transl Sci. 2024 May;17(5):e13781. doi: 10.1111/cts.13781. A systematic review and meta-analysis of the impacts of germline pharmacogenomics on severe toxicity and symptom burden in adult patients with cancer
§ Int J Mol Sci. 2022 Nov 16;23(22):14125. doi: 10.3390/ijms232214125. The Impact of P-Glycoprotein on Opioid Analgesics: What's the Real Meaning in Pain Management and Palliative Care?
§ Cancer Chemother Pharmacol. 2022 Feb;89(2):173-181. doi: 10.1007/s00280-021-04374-3. Epub 2022 Jan 6 Association between gene polymorphism and adverse effects in cancer patients receiving docetaxel treatment: a meta-analysis
§ Oncologist. 2021 Jul;26(7):e1143-e1155. doi: 10.1002/onco.13811. Epub 2021 Jun 7. Evaluation of the Association of Polymorphisms With Palbociclib-Induced Neutropenia: Pharmacogenetic Analysis of PALOMA-2/-3
§ 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.
§ 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 13485:2021

ED.1 REV.0 of 01/10/2024

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-008-25	
Mix oligonucleotides and probes	Mix 10X C3435T ABCB1	1 x 77,5 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	-20°C
Deionized H_20	Deionized H_20	1 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-008-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissue, cells
CONTROLS	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 and 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
LIMIT OF DETECTION (LOD)	≥ 0,016 ng of genomic DNA
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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