ABCB1 GENE VARIANT C1236T (MDR1)

For in vitro diagnostic use

CE IVD

ORDERING INFORMATIONS

REF: FGC-003-25
RDM Code: 1875566/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 PCR-PHARMACOGENETICS TEST.**
The FGC-003 kit allows the characterization of the genetic variant C1236T of the ABCB1 gene (rs1128503) 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

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. Numerous polymorphisms described in this gene significantly affect the pharmacokinetics of many anticancer drugs. There are three main polymorphisms affecting P-gp activity: the c.2677G>T/A polymorphism in exon 21 (rs2032582) 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 (rs1045642), resulting in more than twofold expression of P-gp. The third C1236T polymorphism (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 serious adverse event (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 effects 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 fluid 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.

BIOMOL LABORATORIES S.R.L.
Via Arcora 110 (Palazzo Gecos)
80013 Casalnuovo di Napoli, NA
info@biomollaboratories.com
biomollaboratories.it

EN ISO 9001 CERTIFICATE
EN ISO 13485 CERTIFICATE

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DESCRIPTION	LABEL	VOLUME	STORAGE
		FGC-003-25	
Mix oligonucleotides and probes	Mix 10X C1236T ABCB1	1 x 85 µl	-20°C
Mix buffer and Taq-polymerase enzyme	Mix Real-Time PCR 2X	1 x 425 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-003-25	
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 genomic DNA
ANALYTICAL SENSITIVITY: LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%

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