

ABCB1 GENE VARIANT G2677T/A (MDR1)

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.

For in vitro diagnostic use



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

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.

§ 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.

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.

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| DESCRIPTION | LABEL | VOLUME | STORAGE |
|--------------------------------------|---|-------------------|---------|
| | | FGC-009-25 | |
| 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 ₂ O | Deionized H ₂ O | 2 x 1 ml | -20°C |
| Genomic DNA or recombinant DNA | Control +1 Homozygous G2677G ABCB1 | 1 x 35 µl | -20°C |
| Genomic DNA or recombinant DNA | Control +2 Heterozygous G2677T ABCB1 | 1 x 35 µl | -20°C |
| Genomic DNA or recombinant DNA | Control +3 Homozygous T2677T ABCB1 | 1 x 35 µl | -20°C |

TECHNICAL CHARACTERISTICS

COD. FGC-009-25

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| 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% |