SOLVO MDQ Kit™

Multi Drug Resistance Protein function measurement in Hematology

Novelty

In acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL), multidrug resistance protein (MDR) function measurement in white blood cells is a prognostic and predictive marker. In AML, MDR protein function is an independent negative prognostic biomarker. Testing of MDR efflux function has therefore multiple benefits for hematology patients: it allows patient risk stratification and can help to choose tailored treatment strategy contributing to better patient outcome and quality of care. SOLVO MDQ Kit™ is the first CE-IVD certified biomarker-based diagnostic kit for the determination of MDR protein function by flow cytometry.

Clinical relevance

- MDR protein function is an independent negative prognostic biomarker in AML
- The incidence of *de novo* AML patients is approximately 40%
- Conventional anticancer drugs (e.g.: doxorubicin, imatinib) are substrates of MDR transporters
- Elevated MDR protein activity can be correlated with prognosis, drug efficiency and disease activity
- MDR protein activity determination is a safe measurement of patients on highly demanding cytotoxic / immunosuppressant drugs

Application in hematology

1. **Forecasting disease prognosis in CN-AML patients**

MDR protein function is an independent prognostic marker in AML for the intermediate prognostic group, especially in cases without cytogenetic abnormalities. Presence of elevated MDR activity is related to any of the three drug efflux transporters, MDR1, MRP1 and BCRP detected alone or simultaneously is seen as a negative prognostic marker.

2. **Predicting the success of fludarabine-based induction therapy in AML patients**

MDR protein function is a predictive marker in cases where fludarabine-based induction therapy is applied

3. **Guiding therapy decisions in certain CLL patients**

For CLL patients who do not fit the criteria for the first line FCR therapeutic regimen, have relapsed, or have a refractory disease, MDR activity may help with further therapeutic considerations especially in the absence of other bad prognostic factors

Features

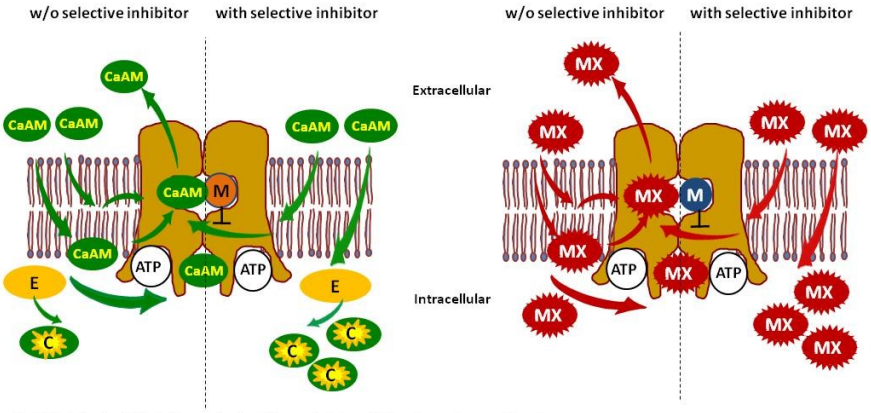
- 10 independent MDR1/MRP1 and BCRP measurements could be carried out in triplicate
- Uses highly selective inhibitors and probe substrates
- Compatible with cell surface markers
- Contains ready-to-use reagents
- Specimen: cell suspension peripheral blood cells, bone marrow
- The first results can be expected within 90 minutes

Principle of the test

For quantitative measurement of MDR1 and MRP1 activities in viable cells, SOLVO MDQ Kit™ applies the proprietary Calcein-assay technology. This assay utilizes the fluorogenic dye calcein-acetoxymethyl ester (calcein-AM) which is a hydrophobic, non-fluorescent compound that readily penetrates the cell membrane. After entering the living cell, calcein-AM rapidly hydrolyzed by endogenous esterases. As a result of cleavage, highly fluorescent free acid derivative of the dye is formed which becomes trapped in the cytoplasm due to its hydrophilic character. Since calcein-AM is an excellent substrate of both MDR1 and MRP1, the activity of these efflux transporters results in a lower cellular accumulation of the fluorescent calcein.

Addition of selective inhibitors of MDR1 and MRP1 in excess blocks the dye extrusion activity of the relevant transporter and increases calcein accumulation in the cells. Activities of MDR1 and MRP1 transporters are reflected by the difference between the amount of calcein accumulated in the presence or absence of the selective inhibitors. The difference is normalized to dye uptake measured in the presence of the inhibitor and the results of the expressed MDR activity factor (MAF) values. Thus the result of test becomes independent from factors influencing the cellular accumulation of calcein other than the activity of multidrug transporters. These variables include the differences in cellular properties (membrane composition, intracellular esterase activity, cell size, cell surface, etc.) and the methodological differences (e.g. use of different equipment, amplification and individual variables). Since the influence of these factors is diminished by the simple normalization approach mentioned above, the intra-and interlaboratory comparison of MAF values is possible.

BCRP activity is measured using a similar principle: intracellular accumulation of the fluorescent BCRP-specific reporter substrate is measured in the presence and absence of selective BCRP inhibitor. However, the BCRP-specific reporter substrate is directly fluorescent and does not require cleavage by intracellular esterases.



CaAM: Calcein-AM; C: free calcein; M: modulator; MX: mitoxantrone; E: esterases

Availability

PRODUCT	SIZE	CAT. NO
SOLVO MDQ Kit™ CE IVD	10 assays	MDQ0101D

Further information

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Biomarker-based Diagnostics

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