XL BCR/ABL1 plus

Translocation/Dual Fusion Probe

Order No.:
D-5052-100-OG

Clinical performance

Clinical performance means the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user. Relevant clinical performance parameters related to FISH probes are diagnostic sensitivity and diagnostic specificity.

Diagnostic sensitivity is defined as the ability of a device to identify the presence of a target marker. It is calculated as the quotient of true positive tests and the sum of true positive tests plus false negative tests. Diagnostic specificity is defined as the ability of a device to recognize the absence of a target marker. It is calculated as the quotient of true negative tests and the sum of true negative tests plus false positive tests.

The evaluations are based on the confirmation of the presence of the target marker in positive cases and the absence of the target marker in negative cases by FISH in cases confirmed by chromosome banding analysis and whole genome sequencing. Specimens examined were CD138+ cells, bone marrow, and peripheral blood. The test population consisted of patients with confirmed or suspected ALL, AML, CML/MPN, MDS and HES.

Analyte	Total No. of Cases	Diagnostic Sensitivity	Diagnostic Specificity
Rearrangements between ABL1 at 9q34.1 and BCR at 22q11.2region at 13q14.2	14134	99.3 % *	100 %

* 31 out of 14134 cases analyzed showed a negative FISH result but chromosome banding analysis revealed a t(9;22)(q34;11). These cases were classified as false negative for FISH. For 21 of these cases RT-PCR results were available showing that the number of positive cells was below the detection limit for FISH.

The determination of the clinical performance parameters diagnostic sensitivity and diagnostic specificity of XL BCR/ABL1 plus is based on data from a European routine laboratory accredited according to ISO 15189 and ISO/IEC 17025. This evaluation is based exclusively on existing data; no patient samples were taken for this purpose.

PERFORMANCE DATA

MetaSystems Probes

Analytical performance

Analytical performance means the ability of a device to correctly detect or measure a particular analyte. Relevant analytical performance parameters related to FISH probes are analytical specificity, analytical sensitivity, reproducibility, and cut-off.

Analytical specificity is calculated as the percentage of correct targets detected on metaphases out of the total number of targets detected. Lymphocytes of 5 different chromosomally characterized males with no indication of the genetic aberration of interest were included in the analysis. Calculated analytical specificity is 100 % after 20 evaluated metaphases from 5 different chromosomally characterized males. The acceptance criterion for analytical specificity is ≥98 %.

Analytical sensitivity is calculated as the percentage of interphase nuclei that have the expected normal signal pattern out of the total number of interphase nuclei analyzed. The signal pattern of 400 nuclei of 10 karyotypically normal individuals each were analyzed. The degree of deviation from the mean is represented by the relative standard deviation (%RSD). The acceptance criterion for analytical sensitivity is ≥95 %.

Pattern	Sensitivity	%RSD
2G 2O (normal)	95.7 %	1.5 %

Reproducibility is the degree of agreement between the results of analytical sensitivity studies conducted under different conditions (Day, Lot and Sample). For each condition three analyses with 100 nuclei each were performed. Reproducibility is given as degree of deviation from the mean by the relative standard deviation (%RSD). The acceptance criterion for reproducibility is relative standard deviation ≤5 %.

Conditions	Reproducibility (%RSD)
Day-to-Day (same lot and same individual at three days)	0.6 %
Lot-to-Lot (same individual and day with three lots)	1.6 %
Sample-to Sample (same lot and day with three individuals)	2.8 %

The cut-off for a qualitative test is the threshold above which the result is reported as positive and below which the result is reported negative. The cut-off value was calculated based on probe hybridizations on interphase nuclei of 10 karyotypically normal individuals. Cut-off values are based on 400 scored nuclei each.

Pattern	Cut-off
2GO 1G 1O	1.2 %

The cut-off value is informative and depends on several laboratory-related parameters. Therefore, for diagnostic use, cut-off values have to be determined individually by each laboratory.

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