XL t(14;20) IGH/MAFB DF

Translocation/Dual Fusion Probe

Order No.:
D-5105-100-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 use. FISH probes generally are used in symptomatic individuals and are not to be used to screen asymptomatic individuals. Genetic aberrations detected by FISH diagnostics are usually rare (prevalence <50) and therefore large-scale cohort testing is difficult. Data gained from routine diagnostic testing accumulated over time allows performance assessment in such cases.

The test population for this product consists of patients with confirmed or suspected multiple myeloma (MM). MM is a mature cell disease of the lymphatic system in more than 90% of cases, which means that the clonal plasma cells usually do not show any proliferation activity (S3 Leitlinie Diagnostik, Therapie und Nachsorge für Patienten mit monoklonaler Gammopathie unklarer Signifikanz (MGUS) oder Multiplem Myelom). Therefore, classical chromosome banding analysis is normally not performed in routine diagnostics and cannot be used as a reference technology to confirm FISH data.

For this reason, the evaluation of this probe follows the Prevalence Comparison approach. The prevalence of positive rearrangements detected by the product in the test population in selected reference laboratories is compared with the prevalence of the corresponding rearrangement in the test population reported in scientific literature. An overlap of the CI 0.95 determined from the validation data with the confidence level interval across all evaluated publications/studies demonstrate conformance of the prevalence data determined with the product with prevalence data from published literature.

Specimens examined were CD138 + cells.

Rearrangement	Total No. of Cases	Prevalence	CI 0.95
IGH::MAFB-rearrangements, t(14;20)(q32.3;q12)	155	5.16 %	2.25 %-9.92 %

The prevalence determined from routine data is 5.16%, the confidence interval is 2.25%-9.92% at a confidence level of 0.95.

Prevalence of positive rearrangements in the test population reported in peer-reviewed scientific literature.

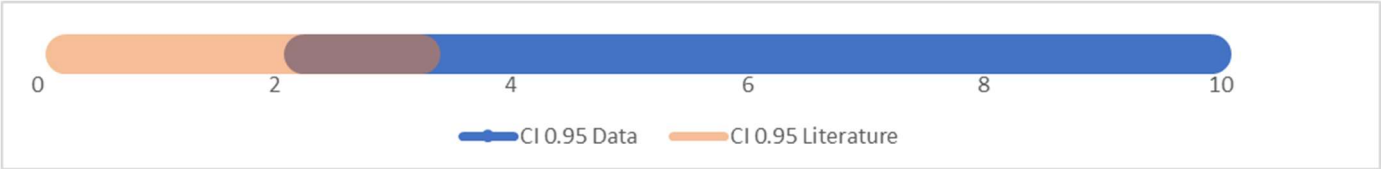
Publication #	Test Population	Sample Size	Positive	Prev. Literature	CI 0.95
1	MM	1830	27	1.5%	0.97%-2.14%
2	MM	268/792*	3/14	1.1%/1.8%	0.23%-3.24% / 0.97%-2.95%
3	MM	463	4	0.9%	0.24%-2.20%
4	MM	1962	20	1.0%	0.62%-1.57%
Cross-publication CI 0.95 Literature #1-4					0.23%-3.24%

* In this study, two cohorts were examined independently.

1. Ross et al (2010) Haematologica:doi:10.3324/haematol.2009.016329
2. Tian et al (2014) Genes Chromosomes Cancer: doi:10.1002/gcc.22165
3. Walker et al (2015) Nat Commun:doi:10.1038/ncomms7997
4. Abdallah et al (2020) Blood Cancer J:doi.org/10.1038/s41408-020-00348-5

The prevalence reported in published literature ranges from 0.9% to 1.8%, the cross-publication confidence interval is 0.23%-3.24% at a confidence level of 0.95.

The CI 0.95 determined from data from routine diagnostic testing overlaps with the cross-publication CI 0.95.



This demonstrates conformance of the prevalence data determined with the product with prevalence data from published literature and supports the clinical performance of the probe.

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 patterns of 400 nuclei from each of 10 karyotypically normal individuals 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)	100 %	0.0 %

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 were performed with 100 nuclei each. Reproducibility is given as the degree of deviation from the mean by the relative standard deviation (%RSD). The acceptance criterion for reproducibility is a relative standard deviation ≤5 %.

Conditions	Reproducibility (%RSD)
Day-to-Day (same lot and same individual at three days)	0.0 %
Lot-to-Lot (same individual and day with three lots)	0.0 %
Sample-to-Sample (same lot and day with three individuals)	0.0 %

The cut-off for a qualitative test is the threshold above which the result is considered positive and below which the result is considered 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	0.8 %

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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