

TECHNICAL SHEET IDYLLA™ GENEFUSION PANEL

Intended Use

The Biocartis Idylla™ GeneFusion Panel is a fully automated in vitro diagnostic test intended for the qualitative detection of specific gene fusions of ALK, ROS1, RET as well as MET exon 14 skipping. The Idylla™ GeneFusion Panel is intended for use with formalin-fixed, paraffin-embedded (FFPE) tumor tissue sections from patients with non-small cell lung cancer (NSCLC). The Idylla™ GeneFusion Panel covers the entire process from sample to result, including fully integrated RNA and DNA extraction, reverse transcription of mRNA, real-time PCR amplification and detection, data analysis, and result reporting.

Indications for Use

The Idylla™ GeneFusion Panel is for use by healthcare professionals for identifying the panel gene rearrangements for patients with NSCLC, to predict the most appropriate treatment options. The Idylla™ GeneFusion Panel is not intended to diagnose NSCLC.

FEATURES

| Fusion specific detection | | |
|---------------------------|-----------|----------------------------|
| ALK fusions (17) | EML4-ALK | EML4 exon 2; ALK exon 20 |
| | | EML4 exon 6a; ALK exon 20 |
| | | EML4 exon 6b; ALK exon 20 |
| | | EML4 exon 13; ALK exon 20 |
| | | EML4 exon 15; ALK exon 20 |
| | | EML4 exon 17; ALK exon 20 |
| | | EML4 exon 18; ALK exon 20 |
| | | EML4 exon 20; ALK exon 20 |
| | KIF5B-ALK | KIF5B exon 15; ALK exon 20 |
| | | KIF5B exon 17; ALK exon 20 |
| | | KIF5B exon 24; ALK exon 20 |
| | HIP1-ALK | HIP1 exon 28; ALK exon 20 |
| | | HIP1 exon 30; ALK exon 20 |
| | KLC1-ALK | KLC1 exon 9; ALK exon 20 |
| | TPR-ALK | TPR exon 15; ALK exon 20 |
| | TFG-ALK | TFG exon 4; ALK exon 20 |
| | | TFG exon 6; ALK exon 20 |

| Fusion specific detection - continued | | |
|---------------------------------------|---|-------------------------------|
| ROS1 fusions (13) | CD74-ROS1 | CD74 exon 6; ROS1 exon 32 |
| | | CD74 exon 6; ROS1 exon 34 |
| | SDC4-ROS1 | SDC4 exon 2; ROS1 exon 32 |
| | | SDC4 exon 4; ROS1 exon 32 |
| | SLC34A2-ROS1 | SDC4 exon 4; ROS1 exon 34 |
| | | SLC34A2 exon 4; ROS1 exon 32 |
| | | SLC34A2 exon 13; ROS1 exon 32 |
| | EZR-ROS1 | EZR exon 10; ROS1 exon 34 |
| | TPM3-ROS1 | TPM3 exon 8; ROS1 exon 35 |
| | GOPC-ROS1 | GOPC exon 4; ROS1 exon 36 |
| GOPC exon 8; ROS1 exon 35 | | |
| LRIG3-ROS1 | LRIG3 exon 16; ROS1 exon 35 | |
| RET fusions (7) | KIF5B-RET | KIF5B exon 15; RET exon 11 |
| | | KIF5B exon 15; RET exon 12 |
| | | KIF5B exon 16; RET exon 12 |
| | | KIF5B exon 22; RET exon 12 |
| | | KIF5B exon 23; RET exon 12 |
| | KIF5B exon 24; RET exon 11 | |
| CCDC6-RET | CCDC6 exon 1; RET exon 12 | |
| MET exon 14 skipping | MET exon 14 skipping transcript detection at the exon 13-exon 15 junction | |

Expression imbalance detection

ALK expression imbalance
 ROS1 expression imbalance
 RET expression imbalance

Expression imbalance measures the difference between the 3' gene expression level and the 5' gene expression of the kinase gene. Expression imbalance results are only reported in case the specific fusion is not detected. A 'detected' expression imbalance result is indicative for the presence of a fusion and the result should be used in combination with an alternative gene fusion test method (e.g. IHC, FISH or NGS).

Internal GeneFusion controls

| | |
|-------------------------|---|
| RNA Housekeeping gene 1 | ERCC3 |
| RNA Housekeeping gene 2 | TMUB2 |
| RNA MET Wild Type | Detection of the Wild Type MET isoform mRNA containing the MET exon 14 sequence |
| DNA control | KIF11 |

Minimum specimen requirements

Sample type 1 x 5 µm FFPE tissue section if tissue area $\geq 20 \text{ mm}^2$
3 x 5 µm FFPE tissue sections if tissue area $< 20 \text{ mm}^2$

Neoplastic cells $\geq 10\%$, if less macrodissection is required

Total turnaround time

Time Approx. 180 minutes

Analytical performance

| | Gene rearrangement | LoD in copies / Cartridge |
|------------------------|--------------------|---------------------------|
| Analytical sensitivity | ALK | 3 000 – 10 000 |
| | ROS1 | 3 000 |
| | RET | 5 000 |
| | METex14 skipping | 3 000 |

Between laboratory reproducibility 99% agreement
(648 results at 3 sites with 6 artificial FFPE samples) (645/648)

Between lot reproducibility 98.9% agreement
(96 results on 3 lots with 4 clinical FFPE samples) (95/96)

Clinical performance

The clinical performance evaluation compared the Idylla™ GeneFusion Panel with IHC (VENTANA ALK (D5F3) Assay, Roche Diagnostics GmbH) for ALK. ROS1, RET and METex14 were compared with NGS (OncoPrint™ Focus Assay, Thermo Fisher Scientific). PPA, NPA and OPA for ALK, ROS1 and RET were calculated based on fusion specific results only as well as by combining the fusion specific results with the expression imbalance results.

Concordance of the Idylla™ GeneFusion Panel versus IHC for ALK.

| ALK | Fusion Specific Results Only | | Including Confirmed* Expression Imbalance | |
|-----|------------------------------|---------------|---|---------------|
| | Rate | Agreement (%) | Rate | Agreement (%) |
| PPA | 34/38 | 89.5% | 38/38 | 100.0% |
| NPA | 118/119 | 99.2% | 118/119 | 99.2% |
| OPA | 152/157 | 96.8% | 156/157 | 99.4% |

* Confirmed = samples that are expression imbalance positive using the Idylla™ GeneFusion Panel and that were confirmed with the reference method. Expression imbalance results are indicative for the presence of a fusion and should be confirmed with another technology.

Concordance of the Idylla™ GeneFusion Panel versus NGS for ROS1.

| ROS1 | Fusion Specific Results Only | | Including Confirmed* Expression Imbalance | |
|------|------------------------------|---------------|---|---------------|
| | Rate | Agreement (%) | Rate | Agreement (%) |
| PPA | 12/15** | 80.0% | 12/15 | 80.0% |
| NPA | 187/187 | 100.0% | 187/187 | 100.0% |
| OPA | 199/202 | 98.5% | 199/202 | 98.5% |

* Confirmed = samples that are expression Imbalance positive using the Idylla™ GeneFusion Panel and that were confirmed with the reference method. Expression imbalance results are indicative for the presence of a fusion and should be confirmed with another technology.

** Of the 3 discordant ROS1 positive samples, the Oncomine™ Focus Assay indicated that there was a low read count for 2 of the 3 samples. All 3 discordant samples tested negative for ROS1 with IHC.

Concordance of the Idylla™ GeneFusion Panel versus NGS for RET.

| RET | Fusion Specific Results Only | | Including Confirmed* Expression Imbalance | |
|-----|------------------------------|---------------|---|---------------|
| | Rate | Agreement (%) | Rate | Agreement (%) |
| PPA | 13/14 | 92.9% | 14/14 | 100.0% |
| NPA | 188/188 | 100.0% | 188/188 | 100.0% |
| OPA | 201/202 | 99.5% | 202/202 | 100.0% |

* Confirmed = samples that are expression Imbalance positive using the Idylla™ GeneFusion Panel and that were confirmed with the reference method. Expression imbalance results are indicative for the presence of a fusion and should be confirmed with another technology.

Concordance of the Idylla™ GeneFusion Panel versus NGS for METex14 skipping.

| METex14 | Rate | Agreement (%) |
|---------|---------|---------------|
| PPA | 48/53* | 90.6% |
| NPA | 149/149 | 100.0% |
| OPA | 197/202 | 97.5% |

* Of the 5 discordant METex14 positive samples, the Oncomine™ Focus Assay indicated that there was a low read count for 4 of the 5 samples.

LoD: Limit of Detection – PPA: Positive Percent Agreement – NPA: Negative Percent Agreement – OPA: Overall Percent Agreement

Catalog number

Idylla™ GeneFusion Panel

A0120/6



The Idylla™ GeneFusion Panel contains SuperScript™ III Reverse Transcriptase and is provided subject to a license under patents or patent applications owned by or licensed to Life Technologies Corporation, which license is limited to the human diagnostic field and research field and specifically excludes applications in forensics (including human identity testing). The SuperScript™ III trademark is owned by Life Technologies Corporation. Patents US 7,700,339, 8,168,383, 8,481,279, 8,486,645, 8,232,060, 8,288,102, 8,377,642, 9,988,688, 9,523,130, 9,096,855, 10,526,661, 9,364,477, 9,539,254, 10,551,383 and pending US applications and all their respective foreign equivalents under license from Cell Signaling Technology, Inc. Idylla™ Platform and Idylla™ GeneFusion Panel are available as an IVD in Europe and many other countries outside the US.

Please check availability with a local Biocartis representative. © Biocartis NV, February 2023

OUS.FL051.EN.R1.03/2023