Roche Diagnostics Oncology Portfolio
Clinical decision support and research

Companion diagnostics

PCR-based mutation detection

NGS genomic profiling
cobas® EGFR Mutation Test v2
CDx for EGFR TKI

- 42 mutations: Exon 18, 19, 20 & 21 including T790M (87.6% NSCLC EGFR coverage)
- CDx
- Tarceva®, TAGRISSO® and IRESSA® in 1L treatment (Exon 19 deletions and L858R)
- TAGRISSO® (T790M) in 2L treatment
- Tissue and Plasma (2 mL) sample types
- Results available in < 1 day
- CE-IVD and FDA-approved
- SQI reporting tool for monitoring*
# cobas® EGFR Mutation Test v2

Comparison between plasma and tissue

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample (N)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>FASTACT2¹</td>
<td>238</td>
<td>75%</td>
<td>96%</td>
</tr>
<tr>
<td>Aarhus Study²</td>
<td>199</td>
<td>61%</td>
<td>96%</td>
</tr>
<tr>
<td>CO-1686³</td>
<td>108</td>
<td>73%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>64%</td>
<td>98%</td>
</tr>
<tr>
<td>AURA⁴</td>
<td>72</td>
<td>82-87%</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>73%</td>
<td>67%</td>
</tr>
<tr>
<td>ENSURE⁵</td>
<td>441</td>
<td>76.7%</td>
<td>98.2%</td>
</tr>
<tr>
<td>AURA2⁶</td>
<td>341</td>
<td>76-83%</td>
<td>98%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>59%</td>
<td>80%</td>
</tr>
<tr>
<td>FLAURA⁷</td>
<td>584</td>
<td>74%</td>
<td>99%</td>
</tr>
</tbody>
</table>

5. cobas® EGFR Mutation Test v2, US-IVD Package Insert ver 4
7. Roche data on file
## cobas® EGFR Mutation Test v2
*Performance vs NGS or dPCR*

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample (N)</th>
<th>PPA</th>
<th>NPA</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>EURTAC¹ (tissue)</td>
<td>487</td>
<td>94%</td>
<td>97.7%</td>
<td>High concordance to NGS</td>
</tr>
<tr>
<td>AURA Extension and</td>
<td>673</td>
<td>90%</td>
<td>98%</td>
<td>High concordance to NGS</td>
</tr>
<tr>
<td>AURA² (tissue)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AURA Extension and</td>
<td>562</td>
<td>95%</td>
<td>91-97%</td>
<td>High concordance to NGS</td>
</tr>
<tr>
<td>AURA² (plasma)</td>
<td></td>
<td></td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>AURA³</td>
<td>72</td>
<td></td>
<td></td>
<td>High concordance to BEAMing dPCR</td>
</tr>
<tr>
<td>ASPIRATION¹</td>
<td>128</td>
<td>87.5%</td>
<td>96.8%</td>
<td>High concordance to NGS</td>
</tr>
</tbody>
</table>


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# Overall Response Rate (ORR) in plasma and tissue

**ORR (95% CI)** | **AURA extension** | **AURA2** | **Pooled AURA Phase 2 studies (AURA extension and AURA2)**  
--- | --- | --- | ---  
**Plasma T790M+** | 59.1% (50.0–67.7) | 69.7% (60.2–78.2) | 64.0% (57.5–70.1)  
**Tissue T790M+** | 61.3% (54.2–68.1) | 70.9% (64.0–77.1) | 66.1% (61.2–70.7)  

In the AURA Phase 2 pooled analysis, the ORR for the plasma T790M-positive subset was similar to that of the full evaluable set (selected using tissue testing).
cobas® EGFR Mutation Test v2
Clinical response rates to osimertinib are consistent between tissue and plasma EGFR T790M (AURA III)

Mok, et al. NEJM 2016

Intent to treat population

T790M mut+ tissue and plasma
New reporting tool for management of NSCLC patients

**What is SQI?**

A measure that can be used to reflect a change in the amount of mutant cfDNA over time per corresponding target mutation within a patient.

**SQI example:**

<table>
<thead>
<tr>
<th></th>
<th>Result time 1</th>
<th>Result time 2</th>
<th>Result time 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex19Del:</td>
<td>7.24</td>
<td>MND*</td>
<td>7.10</td>
</tr>
<tr>
<td>T790M:</td>
<td>MND</td>
<td>MND</td>
<td>16.47</td>
</tr>
</tbody>
</table>

* MND – mutation not detected

** SQI is not available in the U.S.**

cobas® EGFR Test v2 CE-IVD package insert

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cobas® EGFR Mutation Test v2
Serial monitoring of EGFR mutations in plasma

Ex19Del mutation correlates with initial response and progression with new T790M mutation

*SQI is not available in the U.S. Sorenson, et al. Cancer 2014

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cobas® EGFR Mutation Test v2
Longitudinal detection of response to 1L TKI therapy

SQI correlation to tumour shrinkage*

SQI is not available in the U.S.
Marchetti et al. J Thorac Oncol 2015
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cobas® EGFR Mutation Test v2
Sample-to-result in one shift

< 4 HOURS

PLASMA WORKFLOW
- Draw blood
- Separate plasma from blood
- cobas® cfDNA sample prep

< 8 HOURS

TISSUE WORKFLOW
- Tissue biopsy sample
- Macro dissect tumour content
- cobas® DNA sample prep
- cobas® EGFR Test v2 PCR setup
- Reporting
### BRAF/NRAS and KRASv2 LSR

*Life science research*

- **Highly multiplexed**
- **Allele-specific PCR test**
- **High sensitivity**
- **Total of 64 mutations**

#### Mutations detected

<table>
<thead>
<tr>
<th>BRAF/NRAS Mutation Test (LSR)</th>
<th>KRAS Mutation Test v2 (LSR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 BRAF mutations</td>
<td>28 KRAS mutations (tissue and plasma)</td>
</tr>
<tr>
<td>25 NRAS mutations (tissue and plasma)</td>
<td></td>
</tr>
</tbody>
</table>

#### Mutation coverage

- **BRAF:** 96% melanoma, 98% CRC
- **NRAS:** 96% melanoma, 97% CRC
- ≥99% in CRC, NSCLC, PDAC

#### DNA input

<table>
<thead>
<tr>
<th>BRAF/NRAS Mutation Test (LSR)</th>
<th>KRAS Mutation Test v2 (LSR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>150ng DNA</td>
<td>150ng DNA</td>
</tr>
<tr>
<td>2mL plasma</td>
<td>2mL plasma</td>
</tr>
</tbody>
</table>

#### Sensitivity

- ≥5% mutant FFPE DNA in a background of wild-type DNA
- ≥100 copies/mL for most common mutations
- ≥1% mutant FFPE DNA in a background of wild-type DNA
- ≥100 copies/mL for most common mutations

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For Life Science Research Only (LSR). Not for use in diagnostic procedures

1. BRAF/NRAS Mutation Test (LSR) Package Insert
2. KRAS Mutation Test v2 (LSR) Package Insert
3. COSMIC Database v80

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Results show nearly 99% overall concordance to NGS

**Method comparison: study design**

- 186 plasma samples collected
- cfDNA isolated
- same eluate used for both test methods

**LSR and MiSeq method correlation summary**

<table>
<thead>
<tr>
<th></th>
<th>MiSeq</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>LSR</td>
<td>48</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>136</td>
</tr>
</tbody>
</table>

- Overall agreement: 184/186 (98.9%)
- Negative agreement: 136/136 (100%)
- Positive agreement: 48/50 (96.0%)
BRAF/NRAS and KRASv2 LSR

Comparison of KRAS Mutation Test v2 vs NGS

Results show high concordance to NGS for tissue and plasma¹

Method correlation summary

<table>
<thead>
<tr>
<th></th>
<th>FFPE</th>
<th>MiSeq</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRAS Mutation Test v2</td>
<td>+</td>
<td>122</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

Overall agreement: 298/299 (99.7%)
Negative agreement: 176/176 (100%)
Positive agreement: 122/123 (99.2%)

<table>
<thead>
<tr>
<th></th>
<th>PLASMA</th>
<th>MiSeq</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRAS Mutation Test v2</td>
<td>+</td>
<td>227</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>44</td>
</tr>
</tbody>
</table>

Overall agreement: 583/634 (92.0%)
Negative agreement: 356/363 (98.1%)
Positive agreement: 227/271 (83.8%)

¹. doi: 10.5858/arpa.2017-0471-OA
². Nine tissue specimens with different KRAS mutations, and nine WT
³. Forty plasmids representing 20 KRAS mutations, 25-75 copies/mL
⁴. Precision (repeatability) test was performed over multiple, instruments, operators and replicates, resulting in 100% accuracy for tissue and plasma

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AVENIO family of NGS oncology assays
A uniquely versatile solution for comprehensive tumour profiling, monitoring and concordance analysis

AVENIO Tumour Tissue Analysis Kits
Three NGS tumour tissue assays

AVENIO ctDNA Analysis Kits
Three NGS liquid biopsy assays

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AVENIO family of NGS oncology assays

Three liquid biopsy and three corresponding tumour tissue assays with exactly-matched panels

**Targeted Kits**
- **17 genes**
- **81kb**
  - 17 guideline-aligned and 60 emerging biomarkers for expanded comprehensive genomic profiling of solid tumours

**Expanded Kits**
- **77 genes**
- **192 kb**
  - 17 guideline-aligned biomarkers for comprehensive genomic profiling of solid tumours

**Surveillance Kits**
- **197 genes**
- **198 kb**
  - 17 guideline-aligned plus 180 genes specially optimized for longitudinal monitoring of tumour burden and detection of minimal residual disease in lung and colorectal cancer

Analytical concordance facilitated by:
- exactly-matched tissue and ctDNA panels
- inclusion of the same 17 guideline-aligned biomarkers in all AVENIO panels

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A versatile solution for multiple research applications

Three different panels for two sample types support a variety of research applications

**Example A**

**Targeted Kit**
Identify biomarkers in NCCN Guidelines

**Example B**

**Surveillance Kit**
Monitor tumor burden longitudinally in lung cancer and colorectal cancer

**Example C**

**Surveillance Kit**
Survey post-surgery for minimal residual disease in lung cancer and colorectal cancer

AVENIO Targeted, Expanded and Surveillance panels contain biomarkers relevant to clinical research over the course of disease evolution.

* The Tumor Tissue Surveillance Kit may also be used if a tumor tissue sample is available.

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Four mutation classes, exceptional performance

Detection of all four mutation classes with exceptional sensitivity and specificity from a single DNA workflow

Four mutation classes

- SNV (Single Nucleotide Variant)
- Indel (Insertion or Deletion)
- Fusion
- CNV (Copy Number Variant)

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Streamlined end-to-end workflow
Extraction to analysis and reporting in 5 days

Ready-to-use AVENIO assays, which include reagents, analysis and reporting, empower labs to take control of their oncology tests and samples by bringing high-quality NGS liquid biopsy and tissue testing in-house.