Oncofocus
PERSONALISED ONCOLOGY

THE WORLD’S MOST COMPREHENSIVE
PRECISION ONCOLOGY TEST
LINKING ALL SOLID TUMOUR TYPES
TO THE MOST APPROPRIATE TREATMENT

oncologica

1ST PRECISION ONCOLOGY TESTING SERVICE IN EUROPE
“The linking of specific cancer genetic alterations to molecular targeted therapies is driving a new era of personalised medicine.”

Oncologica addresses this new era of precision medicine by exploiting state of the art molecular profiling enabling a patient’s tumour to be matched directly with the most appropriate molecular targeted therapy.

Oncologica’s semiconductor profiling technology reduces the number of tests required for comprehensive tumour analysis, delivers faster results and at a much lower cost.
Our scientists and clinicians utilise state-of-the-art next generation semiconductor sequencing technology (NGS) to rapidly detect actionable mutations in patients’ tumour samples to precisely match these alterations with new generation targeted therapies.

The Oncofocus Assay, a targeted sequencing platform, is designed to detect actionable mutations in cancer genes targeted by on-market oncology drugs or treatments in clinical trials. Intelligent design is driven by Oncologica’s bioinformatics platforms linked to the world’s largest curated compendium of cancer genomic information, including content aligned to approved therapies, current practice guidelines and open clinical trials.

Our targeted next generation sequencing assay enables simultaneous detection of thousands of genetic variants across 52 genes relevant to solid tumours. Targeted actionable hotspots include SNVs, indels, CNVs and gene fusions.

Analysis of the output from the Oncofocus assay is performed using Oncofocus Reporter, an analytical system used to identify and prioritise potential treatment strategies. This analytical platform enables Oncofocus detected variants to be linked to over 270 targeted therapies.

Oncologica carries out DNA sequencing of patients’ tumour samples using semiconductor chip technology directly translating chemically encoded information (A, C, G, T) into digital information.

Semiconductor sequencing has major advantages over other sequencing technologies because it can be used to sequence low DNA/RNA input FFPE biopsy samples with high throughput and at a reduced cost.

- Nucleotides flow sequentially over an Ion semiconductor chip
- One sensor per well per sequencing reaction
- Direct detection of natural DNA extension
- Millions of sequencing reactions per chip
- Fast cycle time, real time detection

Oncologica is the first laboratory in Europe to offer Oncofocus, the world’s most comprehensive precision oncology test.
Delivering New Generation Molecular Profiling for cancer targeted therapies to optimize treatment efficacy

- Comprehensive analysis of major cancer driver genes in one single workflow dramatically reducing the cost of molecular profiling and accelerating reporting times
- Reduced number of tests that cancer patients require
- NGS semiconductor platform uses low DNA/RNA input (10ng) from FFPE samples enabling detection of actionable variants in fine needle biopsies and core needle aspirates
- Generates a comprehensive picture of actionable mutations providing the clinician with a detailed molecular blueprint for optimal therapy choices and improved patient outcomes
- Prevent the unwarranted prescribing of expensive targeted therapies to patients unlikely to benefit from such treatments

- Identification of specific mutations known to be associated with response or resistance to targeted therapies
- Identification of new driver mutations following relapse allowing a switch to additional more appropriate targeted therapies
- Identification of driver mutations and linked therapies in rare tumour types for which treatment protocols are limited
- Molecular profiling conducted on routine diagnostic histological samples (formalin fixed paraffin embedded specimens) and liquid biopsies including circulating tumour DNA and circulating tumour cells (ctDNA and CTCs)
TARGETED NGS FOR ALL SOLID TUMOUR TYPES

The fully integrated Oncofocus Assay and linked Oncofocus Reporter Database provides unparalleled information regarding an individual's tumour that can be exploited to optimise treatment selection using the new generation of molecular targeted agents.

TARGETED TREATMENTS

35 genes and hundreds of variants tested in this tumour type

Over 110 potential treatments in this tumour type
TARGETED NGS FOR ALL SOLID TUMOUR TYPES

TARGETED THERAPIES

The fully integrated Oncofocus Assay and linked Oncofocus Reporter Database provides unparalleled information regarding an individual's tumour that can be exploited to optimise treatment selection using the new generation of molecular targeted agents.

TUMOUR TYPE

GENETIC VARIANTS

TARGETED THERAPIES

Over 90 potential treatments in this tumour type

35 genes and hundreds of variants tested in this tumour type
TARGETED TREATMENTS

The fully integrated Oncofocus Assay and linked Oncofocus Reporter Database provides unparalleled information regarding an individual’s tumour that can be exploited to optimise treatment selection using the new generation of molecular targeted agents.

TARGETED THERAPIES

Over 30 potential treatments in this tumour type

*contraindicate
ONCOFOCUS PATIENT TEST REPORT

TEST RESULTS SUMMARY

<table>
<thead>
<tr>
<th>Gene Variant</th>
<th>EMA</th>
<th>US-FDA</th>
<th>ESMO</th>
<th>US-NCCTN</th>
<th>Global Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAF V600E mutation</td>
<td></td>
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<td></td>
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<tr>
<td>ALK fusion</td>
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<tr>
<td>ERBB2 amplification</td>
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<tr>
<td>EGFR exon 19 deletion</td>
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</table>

RELEVANT THERAPIES SUMMARY

BRAF V600E mutation

- dabrafenib
  - Cancer type: Melanoma
  - Label as of: 2015-06-03
  - Variant class: BRAF V600E mutation
  - Reference:

- trametinib
  - Cancer type: Melanoma
  - Label as of: 2015-02-04
  - Variant class: BRAF V600E mutation
  - Reference:

- vemurafenib
  - Cancer type: Melanoma
  - Label as of: 2015-06-03
  - Variant class: BRAF V600E mutation
  - Reference:

PUBLISHED THERAPIES DETAIL - EMA GUIDELINES

<table>
<thead>
<tr>
<th>Relevant Therapy</th>
<th>EMA</th>
<th>US-FDA</th>
<th>ESMO</th>
<th>US-NCCTN</th>
<th>Global Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>vemurafenib</td>
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<tr>
<td>dabrafenib</td>
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<tr>
<td>trametinib</td>
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<tr>
<td>dabrafenib + trametinib</td>
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<tr>
<td>alpeluzumab</td>
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<td>nimotuzumab</td>
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<tr>
<td>pembrolizumab</td>
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</tbody>
</table>

DISCLAIMER:

a detected variant or the variant is not classified as a genetic driver for cancer.

Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Reporter as a genetic driver of cancer are not listed in the results section of this report. All other genes listed in the Test Description that do not appear in the results section either did not have

BRAF V600E mutation

- dabrafenib + trametinib, trametinib
  
  Cancer type: Melanoma  
  Label as of: 2014-01-08  
  Variant class: BRAF V600E mutation

Indications and usage:
MEKINIST is a kinase inhibitor indicated as a single agent and in combination with dabrafenib for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. The use in combination is based on the demonstration of durable response rate. Improvement in disease-related symptoms or overall survival has not been demonstrated for MEKINIST in combination with dabrafenib.

Limitation of use: MEKINIST as a single agent is not indicated for treatment of patients who have received prior BRAF-inhibitor therapy.

**DISCLAIMER:**

The data presented here is a result of the curation of published data sources as of 2015-09-08, but may not be exhaustive.

**CURRENT US-NCCN INFORMATION**

- **Population segment (Line of therapy):** Cancer type:
- **Melanoma**  
  
  NCT01739764  
  A Phase IV, Post-Marketing, Open-Label, Extension (Roll-over) Study of Vemurafenib in Patients With BRAF V600D/600E Mutations-Positive Metastatic Melanoma Previously Treated in an Antecedent Vemurafenib Protocol

- **Cancer type:** Melanoma  
  
  Variant class: BRAF V600 mutation

Other identifiers: CAVC - 3835, EudraCT Number: 2012-003144-80, Extension (Roll-over) Study: GS038599, NL43324331, TrialPhaseID-177525, UKCRN ID: 18400, USMAVVEM

**Population segments:** Line of therapy: N/A, Stage IV

**Phase:** IV  

**Therapy:** vemurafenib

Countries: Argentina, Brazil, China, Germany, Japan, Korea, Malaysia, Mexico, Spain, United Kingdom, United States

US States: AR, CA, IL, NY, TX

US Contact: Hoffmann-La Roche Contact 1888-462-6728; genentechclinicaltrials@druginfo.com

**REFERENCES:**

- NCCN Guidelines® - Melanoma [Version 3.2015]

**PUBLISHED THERAPIES DETAIL - US-FDA GUIDELINES**

**ALK fusion**

- crizotinib
  
  Cancer type: Non-Small Cell Lung  
  Variant class: ALK fusion

ESMO Recommendation category: I, A

Population segment (Line of therapy):
- Metastatic NSCLC (First or second-line therapy)


**DISCLAIMER:**

Current US-FDA Information is current as of 2015-05-04. For the most up-to-date information search www.fda.gov.

**REFERENCES:**

- NCCN Guidelines® - Melanoma [Version 3.2015]

**PUBLISHED THERAPIES DETAIL - OPEN CLINICAL TRIALS**

**Current Global Clinical Trials Information**

Global Clinical Trials information is current as of 2015-05-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search clinical trial authority website by local identifier listed in ‘Other identifiers’.

**NCT01739764**

- **Other identifiers:** CAVC - 3835, EudraCT Number: 2012-003144-80, Extension (Roll-over) Study: GS038599, NL43324331, TrialPhaseID-177525, UKCRN ID: 18400, USMAVVEM

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- **US Contact:** Hoffmann-La Roche Contact 1888-462-6728; genentechclinicaltrials@druginfo.com

**REFERENCES:**

- NCCN Guidelines® - Melanoma [Version 3.2015]

**NCT01985858**

- **Other identifiers:** ML28711, TrialnovelID-190333

- **Population segments:** First line, Second line or greater/Refractory/Relapsed, Stage IV

- **Phase:** IV

- **Therapy:** vemurafenib

- **Countries:** South Africa

**REFERENCES:**

- NCCN Guidelines® - Melanoma [Version 3.2015]
LONGITUDINAL DYNAMIC MONITORING OF PATIENTS RECEIVING TARGETED THERAPIES

PROFILING FLOW EXAMPLE

1. Primary diagnosis
2. Routine histological samples
3. Initial profiling e.g. EGFR L858R mutation
4. Liquid biopsy e.g. ctDNA, CTCs
5. Relapse
6. Secondary profiling, e.g. EGFR T790M resistance mutation
7. Candidate treatment: erlotinib, gefitinib, afatinib, dacomitinib, neratinib

SERVICE FLOW

TURNAROUND TIME: 10 DAYS

1. Sample receipt FFPE block, curl or liquid biopsy
2. DNA+RNA extraction
3. Construct Library
4. Prepare template
5. Template enrichment
6. Run sequence
7. Data Analysis
8. Report generation
9. Return of hard copy and sample
10. Secure electronic transfer of report

ONCOFOCUS PATIENT TEST REPORT

- ACTIONABLE DIAGNOSIS
- DRUG RESPONSIVENESS ANALYSIS
- CLINICAL TRIALS INFORMATION

Candidate treatment: AZD/9291
Oncofocus was developed as part of the US NCI-MATCH (Molecular Analysis for Therapy Choice) program for precision oncology involving 2400 NCI-affiliated hospitals, >700,000 patients samples, 120 phase 3 and 215 early phase trials.

The Oncofocus test utilises state of the art semiconductor technology to rapidly sequence DNA/RNA extracted from routine FFPE surgical biopsy material. The assay is designed to detect thousands of genetic alterations including SNPs, indels, CNVs and fusions across 52 of the major cancer driver genes linked to solid tumours. The data generated by the Oncofocus test is analysed using Oncologica's bioinformatics platforms linked to the world’s largest curated compendium of cancer genetic information, enabling genetic alterations/variants to be linked to over 280 targeted therapies. Targeted therapies include all classes: 1) FDA approved therapies, 2) NCCN, EMA and ESMO guideline referenced therapies and 3) therapies entered into phase I, II, III and IV clinical trials worldwide, including all EU trials.

ONCOLOGICA TEST MENU FOR PERSONALISED ONCOLOGY

**Oncofocus Test**
Comprehensive NGS targeted panel for precision therapy

Oncofocus was developed as part of the US NCI-MATCH (Molecular Analysis for Therapy Choice) program for precision oncology involving 2400 NCI-affiliated hospitals, >700,000 patients samples, 120 phase 3 and 215 early phase trials.

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**ONCOFOCUS PANEL 52 GENE LIST SUMMARY**

<table>
<thead>
<tr>
<th>HOTSPOT GENES</th>
<th>COPY NUMBER VARIANTS</th>
<th>FUSION DRIVERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKT1</td>
<td>FGFR3</td>
<td>ABL1</td>
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<tr>
<td>ALK</td>
<td>GNA11</td>
<td>AKT3</td>
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<td>GNAQ</td>
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<tr>
<td>CDK4</td>
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<tr>
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<td>MAP2K2</td>
<td>ERG</td>
</tr>
</tbody>
</table>

**Additional tests for targeted therapies available.**
Please visit [www.oncologica.com](http://www.oncologica.com) or contact us for more information.
Professor Gareth Williams and Dr Marco Loddo are Co-founders and Directors of Oncologica and have in-depth knowledge and expertise in diagnostic oncopathology, translational biology, biomarker discovery and drug development.

Kitty Williams is the Senior Commercial Manager and is responsible for providing advice and implementation on commercial and corporate matters.

Philippa Jones is the Senior Operations Manager and directs the tissue based diagnostic services of the company.

Katherine Marquis is the Senior Biomedical Scientist who directs the precision oncology services for targeted therapies.

Keeda-Marie Snelson is the Lead Clinical Scientist with extensive expertise in the analysis of cancer genetic variants of clinical prognostic and predictive significance.

Rebecca Cadman is the Business Development Manager and is responsible for exploring new market opportunities and providing comprehensive support for existing clients.

Read more about our team by visiting www.oncologica.com/about-us/our-team/