BIOARRAY
Genetic Diagnosis

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CONSENT FORM FOR GENETIC DIAGNOSIS BY LIQUID BIOPSY

PATIENT: _____ date of birth: __/__/___.

Identification number: _____

- Due to my personal and/or clinical history, I present an increased risk of suffering a cancerous process.
- The present diagnosis by liquid biopsy allows obtaining information about the global dynamics of the cancerous process, although the procedure to be followed is exclusively up to the medical personnel in charge of my case. The qualified personnel will decide at all times the treatment to follow, taking into account, in particular, the results obtained during the standard clinical evaluation.
- I understand that liquid biopsy results have not been tested in clinical trials, and, despite of its possible usefulness according to the previous point, should be considered experimentally valid.
- In this regard, I have received information about the procedures and investigations that can be carried out, success rates, limitations and risks, all of which I will find below. This document consists of four pages.

Objective

When a cancer develops, mechanisms that help to maintain integrity of genetic information in your cells (integrity of DNA) no longer work properly. As a result, a high number of DNI molecules with point changes. As a result, a high number of DNA molecules with point changes (variations) and/or rearrangements (modifications to the organization of gene sequences) appear. Because of this, each tumor has a unique genetic profile of rearrangements and variants.

The purpose of this genetic test is to identify the mutations derived from somatic cancer in certain “hotspot” (places with special incidence of mutations) in some of the genes known as cancer carriers and involved, mainly in breast, ovarian, lung and colorectal cancers. The test method used to detect these somatic mutations is known as liquid biopsy. This test is offered as a preventive surveillance for people at high risk of developing cancer, and as an early disease detection tool. Identification of any of the somatic mutations tested (They are also known as biomarkers) may help indicate that a patient may have a malignant tumor, customize disease management by providing tumor profiles, monitor disease progression and tumor progression and help provide treatment options if necessary.

During the present test, around 160 positions (“hotspot”) are analyzed, specific for breast cancer, about 176 mutations related to lung cancer, and 242 mutations related to colon cancer. These mutations affect genes such as, EGFR KRAS, FOXL2 o TP53, as well as the genes BRCA1 y BRCA2, among others. Knowing this information can help the patient and/or health care provider make informed decisions about how to proceed in medical care. Including additional screening tests and medical management based on what is known about the mutations identified and the type of cancer associated with them.

Procedure

Bioarray's liquid biopsy screening test uses a patented method to isolate the tumor's circulating free DNA from the bloodstream (ctDNA). This ctDNA is DNA that has been released into the bloodstream by tumor cells, in limited quantity and quality, but they can be analyzed by means of the newest systems of massive sequencing (NGS).

Using the powerful sequencing tools available today, this ctDNA is analysed to detect certain somatic mutations in those genes commonly mutated in the tumor tissue of patients with specific types of cancer. The identification of a particular mutation may have implications for care management and surveillance or treatment.

A positive result indicates that one or more of the somatic mutations tested in the liquid biopsy test have been identified. The identification of a mutation in the sample will have different implications depending on

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the variant(s) detected. However, this screening test is not designed to diagnose cancer. Additional tests, including imaging studies, may be required as a follow-up to a positive result. Recommendations for follow-up testing will be provided by qualified medical personnel.

A negative result indicates that none of the somatic mutations analyzed were identified in the sample. A negative result does not mean that you are not currently undergoing a tumorous process, or that you are not at risk for it in the future. This result only indicates that no tumor DNA associated with one of the mutations being analyzed was detected. Other tumors or other mutations may not be detected by this test, as it is not within the protocol analysis; in view of this, we can indicate that the number of mutations analyzed with this test is constantly increasing.

Finally, the amount of ctDNA emitted by the tumor may be below the detection capacity of the test. If this happens, the results will be considered indeterminate, and a second sample will be requested for analysis, a positive or negative result will be reported as appropriate.

Risks and limitations

It is important to understand the general risks and limitations of genetic testing, including the following:

- Two blood tubes (10ml each) will be required to perform the liquid biopsy, obtained in special tubes supplied by Bioarray. The risks of having blood drawn are rare, but may include dizziness, fainting, pain, bleeding, bruising, and, rarely, infection.
- Genetic testing should not be used as a sole and/or exclusive substitute for the treatment or diagnosis of the tumor process.
- Not detecting any mutations does not mean that you definitely do not have a tumor today, nor does it mean that you do not have a risk of developing cancer at a later time.
- The screening test offered is only intended to test for mutations associated with some of the most common types of tumors. There may be types of tumors usually associated with these mutations that have not developed the specific mutations being tested. There may also be tumors that are not yet releasing cfDNA into the bloodstream and therefore cannot be detected. Finally, other tumors not associated with the somatic mutations analyzed will not be identified by this test.
- This test may not provide informational results for other reasons, such as:
  (1) Non-genetic factors, (2) individual genetic variation, (3) insufficient scientific information on the relationship between genetic information and health outcomes; (4) laboratory problems and/or other technical reasons, or (5) incomplete gene sequence information.
- This test does not test for hereditary cancer syndromes. The test is designed to detect only somatic mutations in cfDNA, that is, generated during the cancerous process in the tumor mass.
- Other risks that may be experienced as a result of these tests include: unjustified alarm and/or false guarantees that can discourage preventive measures. Related emotional problems, impact on certain life decisions, potential genetic discrimination and loss of confidentiality. Test results and information may be part of the patient's permanent medical record and may be available to individuals and organizations with legal access to such records.

Economic and cost information

The fees for the liquid biopsy test are detailed in the attached estimate. In any case, due to the specific genetic characteristics of each individual and/or family member, modification and/or extension of the genetic study may be mandatory. If necessary, we will inform you promptly.
The amount of ctDNA emitted by the tumor may be below the detection capability of the test. If this happens, the results will be considered indeterminate, and a second specimen will be requested for reanalysis at no additional cost. After re-testing of the second blood sample, a negative or positive result will be reported, as appropriate.

Consent

I understand that this test is voluntary and I give my consent for this test to be performed at Bioarray. My signature below acknowledges that:"

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- I have read and fully understand this consent form. I have had the opportunity to ask all the appropriate questions and these have been answered to my satisfaction. In addition, I agree with all of the above.
- I am of legal age and have the legal authority to provide this consent and for the authorization of genetic testing, under all applicable laws.
- In the chaos of being underage, I have obtained the authorization of my father, mother or legal guardian, who has understood and accepts this consent and expresses it with his signature.
- I understand that Bioarray may use my clinical information obtained in this study in medical research work for subsequent publication, if appropriate. I understand that my name as well as any personal information not related to this technique will not be used or linked in ANY CASE with the results of the studies and/or publications derived from them.
- I understand that I may receive a copy of this consent at any time upon written request to Bioarray SL. I can also revoke my authorization for the use of my personal data and of the material previously given in writing to Bioarray SL. Av. De la Universidad s/n, Edificio Quorum III, 03202 – Elche.

Data protection

In accordance with data protection regulations, we provide you with the following treatment information: Responsible party: BIOARRAY, S.L.

Rights that assist you: access, rectification, portability, deletion, limitation and opposition.

More treatment information: http://bioarray.es/es/

BIOARRAY S.L. is responsible for the processing of personal data of the Interested Party and informs that these data will be treated in accordance with the provisions of Regulation (EU) 2016/679 of April 27 (GDPR) and Organic Law 3/2018 of 5 December (LOPDGDD), so the following treatment information is provided:

Purposes and legitimation of the treatment

For the legitimate interest of the responsible party (GDPR, Article 6.1.f): maintain a professional relationship, send communications, analyze data and publish scientific and informative articles.

By consent of the interested party (GDPR, article 6.1.a): sending communications, analyzing data and publishing scientific and informative articles.

Data retention criteria: will be kept for no longer than necessary to maintain the end of the treatment and when it is no longer necessary for this purpose, they will be eliminated with adequate security measures to guarantee the pseudonymisation of the data or the total destruction thereof.

Communication of the data: the data will not be communicated to third parties, except legal obligation.

I give my consent for the storage and preservation of the samples for possible use in the research on genetic disease and I authorize the transfer of the results of the clinical studies in an anonymous form for the study and pharmacological development, the sending of communications, data analysis and publication of scientific and informative articles:

□ Yes □ No

Informed person (Name and signature):
ID number (if available):
Relationship with the patient:

Physician (Name and signature):

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Diagnóstico Genético

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For BIOARRAY Use Only

TEST REQUISITION FORM

PLEASE, COMPLETE THIS FOR TO THE BEST OF YOUR KNOWLEDGE
IF REQUIRED FIELDS ARE NOT PROVIDED, TESTING MAY BE DELAYED.

PATIENT INFORMATION

First Name _____ Last Name _____ Patient ID _____ DOB *(MM/DD/YYYY)* _____ Sex ☐ F ☐ M

Address _____ City _____ State _____ Postal Code _____ Country _____ Primary Phone _____

CURRENT DIAGNOSIS/PATIENT HISTORY

Diagnosis (Full Description Primary Cancer type) _____ Stage _____

Sample provided: ☐ FFPE Tissue Primary Tumor ☐ FFPE Tissue Metastasis Metastasis location/description: _____
☐ Peripheral Blood

Sample tumor cellularity: _____ Collection date (Obligatory for blood samples): _____

Reason for referral

Summary Clinical History (include Histopathology description or family history if relevant):

Prior/Current Targeted Therapies *(optional)* .....

PLEASE ATTACH:

☐ Extended clinical history of the patient

☐ Test results from all other Molecular Diagnostic Assays by FISH, IHC, orother genetic assays, e.g., *ER, PR, HER2, EGFR, KRAS,* etc.

TREATING PHYSICIAN INFORMATION (Please provide best contact information for case follow-up)

Facility/Hospital

Facility /Hospital address

Treating Physician

Email

Phone

Additional Physician/contact to be copied (optional)

Email

TEST REQUEST (Mark one with an X)

Select	Test requested	Specimens accepted *
	Comprehensive Assay Plus	FFPE Tissue or Fine needle aspiration
	Comprehensive Assay	FFPE Tissue or Fine needle aspiration
	Clarity Test (Hereditary Cancer Risk Evaluation)	Peripheral Blood or Saliva
	BRCA test	FFPE Tissue (or Peripheral Blood for germline assay)
	BRCA extended test	FFPE Tissue (or Peripheral Blood for germline assay)
	Colorectal cancer test	FFPE Tissue (or Peripheral Blood for germline assay)
	MSI test	FFPE affected + normal Tissue
	Pan-cancer Liquid Biopsy	Peripheral Blood
	Breast cancer Liquid Biopsy	Peripheral Blood
	Colorectal cancer Liquid Biopsy	Peripheral Blood
	NSCLC Liquid Biopsy	Peripheral Blood

* Check information about specimen requirements, sample collection and transportation before sending samples.

ADDITIONAL TESTS (Immunohistochemistry markers)

Select	Marker requested
	MLH1
	MSH2
	MSH6
	PMS2
	HER2
	PD-L1

* Check information about specimen requirements, sample collection and transportation before sending

BILLING INFORMATION

Facility/Hospital/Insurance

Address

Contact information

Email

Phone

Authorized representative

Signature

TEST AUTHORIZATION AND PHISICIAN SIGNATURE

My signature constitutes a Certificate of Medical Necessity, certifies that this test information will inform the patient's ongoing treatment plan, and certifies that I am the patient's treating physician. I have explained to the patient the nature and purpose of the testing to be performed and have obtained informed consent, to the extent legally required, to permit Bioarray to 1. perform the testing specified herein, 2. retain the test results for an indefinite period for internal quality assurance/operations purposes, 3. de-identify the test results and use or disclose such de-identified results for future unspecified research or other purposes, and 4. release the test results to the patient's third-party payer as needed for reimbursement purposes.

My signature also authorizes Bioarray to proceed with the test, ensuring that the selected test in this form has been chosen by a medical exert following the patient case study, understanding the information that I may be able to obtain and limitations of the test.

Signature

Date

*FFPE SAMPLES

- For genetic analysis a FFPE block containing the **unstained tissue** must be sent.
- Alternatively, if sending FFPE tissue slides, 2-3 slides of 10µm each are required. Slides are requested to be sent in individual collection tubes or individual microscope slides with no cover.
- Samples of at least 20% tumor cellularity are required.
- Samples should be stored at room temperature and kept away from extreme temperatures.

*BLOOD SAMPLES

- Liquid biopsy testing: 1 tube of peripheral blood must be provided (10mL). Blood will be collected into tubes containing Streck preserving medium (10mL). After blood collection, tube should be gently but properly mixed by inverting (10 times) and kept at room temperature, away from extreme temperatures (do not freeze, do no refrigerate). Samples should be sent as soon as possible after blood extraction. We strongly advise to send the same sample the same day that the extraction is performed.
- Clarity test: 1 tube of peripheral blood must be provided (10mL). Blood will be collected into EDTA tubes (10mL). After blood collection, tubes should be gently but properly mixed by inverting and kept at room temperature, away from extreme temperatures (do not freeze). Samples should be sent as soon as possible after blood extraction.
- Non-liquid biopsy blood samples: 1 tube of peripheral blood must be provided (10mL). Blood will be collected into EDTA tubes. After blood collection, tubes should be gently but properly mixed by inverting and kept at room temperature, away from extreme temperatures (do not freeze). Samples should be sent as soon as possible after blood extraction.

- All samples must be properly identified with patient credentials.
- All samples should be transported at room temperature with appropriate containers that buffer significant temperature changes.
- Blood samples should be sent the day of the collection or the following day so ensure the integrity of the sample.

DO NOT HESITATE TO CONTACT OUR TEAM FOR QUESTIONS RELATED TO SAMPLE COLLECTION, ACCEPTED MATERIAL OR TRANSPORTATION METHODS.